

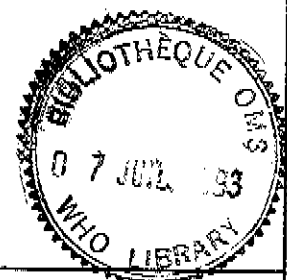
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PROGRAMME  
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Series: "Measles Control in the 1990s"

Generic protocol for determining  
measles case fatality rates  
in a community, either during  
an epidemic or in a highly endemic area

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**GENERIC PROTOCOL FOR DETERMINING MEASLES CASE FATALITY RATES  
IN A COMMUNITY, EITHER DURING AN EPIDEMIC OR IN A HIGHLY  
ENDEMIC AREA**

**1. Scope**

This generic protocol is intended to address the practical issues involved in determining the acute case fatality rate (CFR) in relation to an outbreak of measles. Although it covers key issues in the subject, there may be parts which need amending or augmenting to meet local needs within a country.

"Outbreak" in this context is taken to mean cases of measles occurring in a population which is defined at the outset of the investigation in terms of time and space. It may therefore either refer to a particular "window of time" during an on-going endemic situation, or may relate to a particular epidemic.

"Community" in this context is used to indicate all cases within the specified population, whether they were located at home, in hospital, or in any other situation. Case fatality rates may vary considerably between community and hospital admissions; many times hospital admissions are already seriously ill and represent a biased sample who are more likely to experience a high case fatality rate. Low case fatality rates in hospital studies may identify good case management, but may not truly reflect the severity of measles out in the community.

"Acute" CFR in this context refers to deaths which occur within one month of the onset of illness due to measles, regardless of the apparent cause of death.

A "case of measles" is defined as:

- *generalized maculo-papular rash of 3 or more days duration*
- AND
- *history of fever of 38°C or more*  
*(or "hot to touch" if not measured)*
- AND
- *at least one of: cough, cold or upper respiratory tract infection or conjunctivitis.*

A principle investigator may choose to modify this definition to include cases occurring during an epidemic which are felt to have been be measles but who may not fully fit the above case definition.

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Cases included in an investigation under this protocol will therefore:

- have had measles as defined above,
- have developed measles within the time limits defined for the outbreak under investigation,
- either be normally resident within the geographical limits defined for the outbreak under investigation, or be found to have resided there temporarily for a minimum of 10 days before the onset of disease,
- be established to be either dead or alive (i.e. not moved away, etc.) one month after the onset of disease.

## **2. Sources of Cases**

Within the above definitions, cases may have contact with health services in a wide variety of ways. It is important to remember that, in measuring a community CFR, all cases of measles should be included, whether or not they have sought health care. Some examples of case types follow, though this is not intended as an exhaustive list:

- admissions to hospital with measles as the primary complaint (but note residence requirement above)
- nosocomial infections (i.e. measles caught in hospital during an admission for another reason) in hospital patients and contacts, particularly during a severe epidemic
- out-patients at health centres and clinics, with measles as the primary complaint
- other clinic contacts where measles is discovered (may be particularly important in malnutrition clinics, etc.)
- schools, day nurseries, etc.
- cases at home, known to members of the community
- cases detected during house-to-house enquiries

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### 3. Factors known to influence measles mortality

In order to investigate CFRs in measles outbreaks, it is important to understand, and quantify, factors which have been shown to influence mortality in measles cases. Previous research has shown that measles mortality may depend on:

- age
- sex
- acquiring disease from contacts in the same household
- intensity of exposure
- nutrition (general status, and Vitamin A deficiency)
- receiving treatment with Vitamin A
- measles immunization status
- availability of health care services
- HIV status of mother

The effects of some of these factors appear to be quite complex, and may not be well understood. Nevertheless, in investigating the CFR associated with a particular outbreak, it is important to record details relating to these factors, so that subsequent comparisons of CFRs from different outbreaks can be meaningfully made. In addition, in a sufficiently large investigation, recording these details may allow comparisons between CFRs in different sub-groups within the outbreak.

### 4. Procedures for finding and recording cases

To determine a CFR for a community, it is very important to investigate the situation that already exists in the community. From an epidemiological point of view, there is a danger that carrying out a survey such as this will result in an altered outcome for cases identified and sent for treatment. Case fatality rates could be expected to be lower than if the survey had not been carried out. It is therefore not acceptable to include current cases of measles in the investigation, since the health personnel undertaking the investigation would be ethically obliged either to offer treatment or arrange for the referral of such cases. Therefore for the CFR investigation, the cases of interest are those who (a) have had measles, and (b) have survived for the following one-month period, rather than current cases of measles.

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Children seen by investigators who are currently suffering from measles should therefore not be included in the study but should certainly be referred to a health care facility for appropriate support or treatment.

It is also very important to make sure that the cases included in the investigation are representative of measles cases in the community under investigation. Cases with different treatment-seeking histories (section 2 above) are likely to have different risk factors for mortality (section 3 above). At one extreme, taking mortality data only from hospital records, and assuming that such hospital cases were representative of the community, would be likely to give a biased result.

As stated in section 1, one requirement of this protocol is being able to establish whether or not the case survived the month following the acute attack. Even if a case has been admitted to hospital in the acute phase, it is possible that an investigator would be unable to determine from the hospital records alone whether the child was alive after discharge one month later. Thus for each case of measles in the investigation, it will be necessary to interview either the case or his/her parent or guardian, and record the relevant details on a form designed for the purpose. A suitable form is appended, although local modifications may be required. This form has been designed with a view to computer processing, although it could also be used with a hand-tally system.

## **5. Size of the investigation**

As with any quantitative assessment, it is important to consider the number of cases that need to be investigated in order to obtain a reliable answer. Previous work suggests that measles CFRs in developing countries are likely to be in the region of 5 to 15%. If the actual CFR in a community is 5% or 15%, then the 95% confidence intervals (CI) within which the CFR can be estimated in an outbreak investigation vary with the total number of cases investigated (Figure 1). It should be noted that the reliability of the estimate will increase the narrower the CI. Although it is desirable to have larger sample sizes (number of cases investigated) and narrow CI, investigators faced with small outbreaks may have to settle for a small sample size and wide CI.

Figure 1 shows that at least 500 cases of measles need to be assessed to define the CFR within reasonable limits. It would be even better to undertake an investigation of 1,000 cases, giving closer confidence intervals. However, investigating 1,000 cases will make a considerable difference in the resources required, without having a large effect on the confidence interval. A choice will therefore need to be made at a local level as to how many cases are to be investigated.

Figure 1. Number of cases which need to be investigated for given CFRs and confidence intervals.

CFR	no. of cases investigated	95% CI of CFR
5%	100	1.6% to 11.3%
5%	200	2.4% to 9.0%
5%	300	2.8% to 8.1%
5%	500	3.3% to 7.3%
5%	1000	3.7% to 6.5%
15%	100	7.8% to 22.4%
15%	200	10.3% to 20.8%
15%	300	11.1% to 19.6%
15%	500	11.9% to 18.5%
15%	1000	12.8% to 17.4%

## 6. Plan of action

In order to undertake an investigation of measles CFR in the community, the following parameters have to be decided:

- number of cases of measles to be investigated
- time period
  - date of onset of measles rash in the earliest case to be included
  - date of onset of measles rash in the latest case to be included (which must be at least 1 month before the start of the investigation)
- geographical limits of the area to be included

check: are you reasonably likely to get the number of cases you need within these limits of date and area?

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It may be convenient to take special days (e.g. local festivals) as the dates for earliest and latest cases. This will make it easier to ask about possible cases (e.g. "Did any of your children have measles between Independence Day and Tobaski?"). The choice of time period is also important in terms of realistic expectations of mothers' recall. Whilst it may be possible to remember reasonable details about cases of measles occurring during the previous six months, it is unlikely that an investigation which sought to record all cases of measles during the past five years would be very successful.

Next, in the light of local knowledge, divide the defined area into convenient units. In a rural area these may be villages; in an urban area they may be administrative sub-districts, etc. If health facilities have sufficiently detailed records to be useful (which must include determining one-month survival for the majority of their cases) they can be included as separate units. Make a list of the units within your defined area, and give each one a code letter (e.g. first one A, next B, etc.) that can be used to identify the location of cases when forms are filled in. Make copies of the list for all the investigators.

It is obviously difficult to know in advance exactly how many cases will be found in such an investigation. Depending on the severity of the epidemic, or the level of endemicity, it is likely that a total population base of between 10,000 and 50,000 - perhaps 1,000 to 5,000 households - will need to be investigated, to find 500 cases. Once the limits of dates and area have been defined, as described above, the possible strategies are either (a) to investigate all possible cases within these limits, or (b) to seek cases until the required number have been found. The former strategy is preferable, but, if cases are found more quickly than envisaged, it may be necessary, for reasons of resources, to curtail the investigation once the necessary number has been found. However, potential causes of case selection bias should be borne in mind and avoided. For example, in investigating a village, it would be wrong to concentrate only on a small sector of the community where most measles was thought to have occurred; cases in this area could consequently have experienced higher exposure. The whole village should be covered.

A team of investigators will need to be identified who are going to carry out the interviews. Enquiring about children who have died can naturally be a difficult and sensitive undertaking, and so it will probably be necessary to use investigators who have some experience of this kind of work. In addition, local cultural sensitivities in respect of investigators visiting households must be considered - for example, would female investigators be more acceptable? At this stage it will be appropriate to brief all investigators about the investigation in general, about the limits of dates and area within which cases are to be sought, about the sources of cases, and about the procedures for investigating each case, including filling in the form that is

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to be used, as detailed in section 7. Training concerning the retrospective identification of measles will also need to be given. This will vary according to local understanding of the disease - for example, does "measles" have a specific term in local vernaculars? The logistics of the investigation also need to be planned with the team of investigators - for example, should the whole team go together, dealing with each unit consecutively? What transport, food, lodging, etc. will be required?

When an outbreak has occurred and investigation is underway, treatment of cases is essential if deaths from complications are to be avoided. One component of the investigation of CFRs should always be to ensure that services are provided to treat those children who develop complications of measles. As part of this, if a vitamin A supplementation programme is in operation locally, it may be appropriate for investigators to give supplements to any children due for a dose, both as a public health and a public relations exercise. If this is to be done, it will obviously require forward planning with the local vitamin A programme.

If sufficient cases are not found within the defined limits after careful investigation, it may be necessary to extend the investigation either in an adjacent time period or in an adjacent area to obtain sufficient cases. As measles becomes less common, outbreaks may become smaller and less frequent. Thus investigations may be more likely to need extending in time or space in order to find sufficient cases.

## **7. Interviewing**

House-to-house enquiry methods need to be clearly defined, as this will be the most important and the most time-consuming part of the investigation. A large number of households may have to be visited, the majority of which will not have had cases unless an epidemic is particularly severe. The initial enquiry at each household therefore needs to be carefully formulated and standardized between investigators, both to ensure a reliable response and to take the least time possible. A simple question, depending on local terminology, should be used to find out whether there were any cases of measles in the household between the specified dates.

If a negative response is received, then only a single line on the Household Tally Sheet (attached) needs to be completed, showing zero cases, and the number of children normally living in the household. No Measles Case Form should be filled in, and the investigator should proceed to the next household.

A positive response, after filling in the number of cases and the number of children on a line in the Household Tally Sheet, obviously requires further

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investigation, and the completion of a Measles Case Form for each case within the household.

Each Household Tally Sheet should only be used for households visited by one investigator on one day in one location.

When completing Measles Case Forms, it is important to include identifying information for the case. In most situations, this information will consist of name, address and date of discovering the case. In some investigations, it may be possible to include locally available identifiers which are less ambiguous, such as health card numbers, as part of the address. Positive identification of cases may be necessary in order to later resolve the details of individuals who may have been recorded twice (e.g. once from hospital records and once from a home visit).

The location of the case should be filled in with a single letter code from the previously established list. Each investigator should also have two initials previously agreed upon to identify their forms. These should normally be their own initials unless there are 2 or more interviewers in the team with the same initials.

Age (at the time of the illness) where possible should be determined from records such as health cards, identity cards, etc. However, experienced interviewers should be able to assess age within the defined groups with reasonable accuracy in the absence of firm data.

The questions on rash, fever and cough at the time of illness are intended to confirm the clinical details of measles in a particular case. The vast majority of cases should have a "YES" response to all three questions. However, there may be a few cases, for example where a small child dies on the second day of the rash, where there is a "NO" answer, but nevertheless there is no reasonable doubt that the child did indeed have measles. Special circumstances like this should be noted at the bottom of the form.

It is also very important to establish that the case of measles occurred within the time limits defined for the investigation and that the child was in the defined area for at least 10 days before the illness. Similarly, determining whether or not the child survived for one month after the illness is crucially important.

After completing the above questions, the investigator is asked to make an overall assessment as to whether or not the case is eligible for inclusion in the investigation. In most cases eligibility will follow automatically from a series of "YES" answers to the case details and eligibility questions, and a "YES" or "NO" answer to the survival question. However, there may be a few cases with some elements of uncertainty where the investigator will need to

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make a judgement as to the eligibility of the case. If necessary, he/she may decide to discuss the case with the supervising investigator at a later stage.

In the final section questions relate to potential risk factors for measles mortality. Investigators should always try to see health cards where possible; in reality there may be a large number of children without health cards, in which case the best possible answers have to be elicited from mothers by careful questioning. The last question, about the health card, allows subsequent analyses to separate earlier responses verified by health cards from those obtained only by interview, if required.

## **8. Data analysis**

Once all the necessary records have been collected, it is possible to determine the CFR for an outbreak using a hand-tally system. In this case the CFR is simply determined as  $(100 \times \text{the number of cases known to have died within one month of illness})$ , divided by  $(\text{the total number of cases known to be either dead or alive at one month})$ . Only cases which have been assessed as being eligible should be included in this calculation. In addition, the crude attack rate can be calculated from the Household Tally Sheets as  $(100 \times \text{the total number of cases})$  divided by  $(\text{the total number of children})$ .

However, if computing facilities are locally available, it will probably be worthwhile to make use of them, both in order to make the analysis easier, and to consider breaking down cases into sub-groups using some of the other parameters collected.

Customized software, within the Epi-Info 5 system, is freely available to enable users of this protocol to handle their data, on application to WHO/EPI, Geneva. It is based on the use of the appended form for data collection, and enables data entry and analysis of CFRs to be done without specialist skills being locally available. Users of this protocol who wish to obtain a copy of this software should apply to EPI/WHO Geneva, stating whether the software should be supplied on 5.25" or 3.5" diskettes. This software is suitable for any IBM-compatible PC running under the MS-DOS operating system.

*Permission to use this protocol.* No permission is required. However, if a study is undertaken using this protocol, it would be appreciated if acknowledgements could be given in the write-up to WHO/EPI. And it would also be appreciated if the WHO Regional Office and EPI/Geneva could be informed of the results. Thank you.

*Acknowledgements.* WHO/EPI wishes to acknowledge the cooperation of the Ministry of Health of Niger in assisting to field test this protocol. Acknowledgements are also given to the United States Agency for International Development for their support of the research.

HOUSEHOLD TALLY SHEET

Investigator: \_\_\_\_\_ Date: \_\_\_ / \_\_\_ / \_\_\_ Location: \_\_\_\_\_

	number of cases	number of children
Household 1:	.....	.....
Household 2:	.....	.....
Household 3:	.....	.....
Household 4:	.....	.....
Household 5:	.....	.....
Household 6:	.....	.....
Household 7:	.....	.....
Household 8:	.....	.....
Household 9:	.....	.....
Household 10:	.....	.....
Household 11:	.....	.....
Household 12:	.....	.....
Household 13:	.....	.....
Household 14:	.....	.....
Household 15:	.....	.....
Household 16:	.....	.....
Household 17:	.....	.....
Household 18:	.....	.....
Household 19:	.....	.....
Household 20:	.....	.....

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TOTALS: (for this sheet)

HOUSEHOLDS:

CASES:

CHILDREN:

\_\_\_\_\_

MEASLES CASE FORM

form serial number:

CASE IDENTIFICATION

name: \_\_\_\_\_

address: .....

.....

.....

location of case (use code from local list): .....

date of filling in form: (dd/mm/yy) ...../...../.....

investigator's initials: .....

CASE DETAILS

age group at the time of illness:

TICK ONE ONLY	under 9 months	GROUP 1 ...
	9 to 11 months	GROUP 2 ...
	1 year old	GROUP 3 ...
	2 years old	GROUP 4 ...
	3 years old	GROUP 5 ...
	4 years old	GROUP 6 ...
	5 to 9 years	GROUP 7 ...
	10 to 14 years	GROUP 8 ...
	15 years & over	GROUP 9 ...

sex: MALE / FEMALE

At the time of illness, was there:

a rash for 3 days or more? YES / NO / UNK

a fever of 38°C or "hot to touch"? YES / NO / UNK

any cough, cold/URTI or conjunctivitis? YES / NO / UNK

Eligibility:

did the case have measles within the defined time limits? YES / NO / UNK

did the case live in the defined area for at least 10 days before the illness? YES / NO / UNK

Survival:

was case alive 1 month after illness? YES / NO / UNK

Special notes: (if any) .....

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OVERALL ASSESSMENT BY THE INVESTIGATOR:

This child is an eligible case of measles IF:

- (1) you are satisfied the disease was actually measles  
AND (2) the measles took place within the defined time period  
AND (3) the child was in the area at least 10 days beforehand  
AND (4) you know whether the child survived for one month

Indicate whether or not this child is an eligible case:

ELIGIBLE MEASLES CASE / NOT ELIGIBLE

Additional details:

was the case admitted to hospital?	YES / NO / UNK
had there been another case of measles in the same household in the month before this case?	YES / NO / UNK
was the case malnourished* before he/she became ill?	YES / NO / UNK
was vitamin A supplement** given before the case became ill?	YES / NO / UNK
was vitamin A given after diagnosis?	YES / NO / UNK
had the case received measles vaccine before he/she became ill?	YES / NO / UNK
were these details confirmed from the child's health card?	YES / NO

\* Malnourished may need to be defined eg: <80% height for weight and <70% weight for height.

\*\* Vitamin A supplementation should be defined as a dose of at least 100,000 IU for infants less than a year of age and at least 200,000 IU for children over a year of age.