The Use of Verbal Autopsy Methods
to Determine Selected Causes
of Death in Children

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"The Use of Verbal Autopsy Methods to Determine Selected Causes of Death in Children," by Dr. Ronald H. Gray, Department of Population Dynamics, and Drs. Gordon Smith and Peter Barss, Department of Health Policy and Management, The Johns Hopkins University School of Hygiene and Public Health.

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PREFACE

The Johns Hopkins University Institute for International Programs

The Institute for International Programs, part of The Johns Hopkins University School of Hygiene and Public Health, brings together leading Hopkins experts in biomedical, environmental, social science, and health management fields with the goal of strengthening public health programs in developing countries. These professionals, together with distinguished collaborators from established research centers and major academic institutions throughout the world, provide a comprehensive approach to international development. The Occasional Papers Series of the Johns Hopkins University Institute for International Programs (JHU/IIP) was established to disseminate information on advances in international health.

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This paper presents the results of an international workshop on the verbal autopsy method that was held at The Johns Hopkins University School of Hygiene and Public Health on March 13-15, 1989. The workshop was convened to examine verbal autopsy methods with the goal of achieving a consensus on methodologic approaches. The focus was on deaths during childhood because mortality among children still constitutes a major public health problem in developing countries. Administrative support for the workshop was provided by the Johns Hopkins University Institute for International Programs (JHU/IIP). Funding for the workshop was provided by the Agency for International Development (A.I.D.) through Cooperative Agreement DPE-5951-A-00-5051-00, with additional support from the International Union for the Scientific Study of Population (IUSSP).
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1. INTRODUCTION

Information on levels of mortality and causes of death is critical for determining public health policy, planning health programs, and evaluating intervention results. For example, the distribution of causes of death in a population (proportional mortality ratios) helps to define the major disease problems and thus to establish priorities for health programs. Trends in cause-specific mortality are also important indices for evaluating the impact of specific health interventions. The verbal autopsy method of gathering data on mortality and morbidity has proven useful in many field studies in developing countries and, with refinement, may be applicable to future studies.

Data on the occurrence and causes of death are conventionally obtained from vital registration systems in which a physician completes a death certificate recording the diseases or conditions directly leading to death and assigning an underlying cause of death. Additional information is often obtained on contributory causes of death and on sociodemographic factors or health care relating to the fatal illness. There is a long tradition of vital statistics collection, but, as William Farr, the first Registrar General in Britain said, "the death rate is a fact, anything beyond this is an inference". The inferences we draw about causes of death affect our interpretation of the health status of a population, and even in industrialized countries such inferences can be problematic. Numerous studies have shown that physicians differ in their diagnostic practices and classification of causes of death; that there are significant discrepancies between clinical diagnoses of causes of death and autopsy diagnoses; and that tabulations based solely on underlying causes of death may lead to misclassification of certain conditions, or underestimate the contribution of multiple illnesses to mortality (Kircher et al., 1985; Battle et al., 1987; Anderson et al., 1989). These problems do not invalidate cause of death statistics, but they emphasize the need for caution in interpretation.

The problems of measuring cause-specific mortality in developing countries are more severe. Vital registration systems are often incomplete or nonexistent, and many deaths are omitted. Frequently, patients are not seen by physicians or other health personnel prior to death, so no death certificate is available; and even when a death certificate is
completed, the information is often of uneven quality and diagnoses are frequently couched in non-specific terms. Moreover, the practice of assigning a single underlying cause of death cannot adequately describe the contribution of multiple acute and chronic conditions that frequently lead to deaths during infancy and childhood in developing country settings. Thus, cause of death statistics from many developing countries suffer from serious deficiencies. To overcome these problems, investigators have used information obtained from interviews with relatives of the deceased person to reconstruct the illnesses leading to death (Gray, 1989). These postmortem interviews, often referred to as "verbal autopsies", provide important information, but there has been no critical and systematic review of verbal autopsy methods, nor agreement on common procedures for interview or criteria for interview-based diagnoses (Garenne and Fontaine, 1986; Zimicki, 1986; Gray, 1989).

A workshop was convened to address this deficiency, to draw upon the experience of investigators from around the world, and to strive towards consensus on methodologic approaches. The focus was on deaths during childhood because mortality among children still constitutes a major public health problem in the developing world. The workshop was held at The Johns Hopkins University School of Hygiene and Public Health on March 13-15, 1989, with support from the Johns Hopkins University Institute for International Programs (JHU/IIP) and the International Union for the Scientific Study of Population (IUSSP). A list of participants is given in the appendix of this report.

2. BACKGROUND TO VERBAL AUTOPSY METHODS

The basic premise underlying verbal autopsy is that certain diseases have characteristic symptoms and signs that can be recognized and recalled by a lay observer during an interview, and that these characteristics are sufficiently distinctive to differentiate the diseases of interest from other conditions with which it might be confused. In essence, the postmortem interview attempts to replicate key elements of the conventional medical history used by physicians to establish a differential diagnosis. However, verbal autopsies, in addition to depending on a third-party respondent, lack the supporting information from physical examination or special investigations that is usually needed to establish a definitive diagnosis.
A verbal autopsy is an interview designed to identify specific medical syndromes, using information about the terminal illness elicited from relatives of the deceased person. In clinical terms, a syndrome is defined as "a distinct group of symptoms or signs which, associated together, form a characteristic clinical picture or entity." Thus, the diseases amenable to verbal autopsy diagnoses are those conditions that form relatively discrete syndromes, and which are thought to be important common causes of morbidity and mortality. In neonates, the main focus has been on neonatal tetanus, although there have been efforts to identify prematurity/low birthweight, septicemia, and birth injury. In the postneonatal period or during childhood, the main diseases of interest are measles, diarrhea/dysentery, acute lower respiratory infection (ALRI) and injury, and some efforts have been made to diagnose more difficult conditions such as pertussis, malaria, meningitis, hepatitis, tuberculosis, acquired immune deficiency syndrome (AIDS), and malnutrition. However, it must be noted that verbal autopsies cannot reliably identify all conditions leading to death, and in most studies investigators have focused on specific conditions thought to be important in the local disease ecology. There will, therefore, always remain a proportion of deaths of unknown cause.

The postmortem diagnosis of a syndrome can often be achieved by use of an algorithm based on the presence of certain symptoms or signs, the age of the decedent, and the timing of onset and duration of symptoms/signs during the terminal illness. In many cultures there is local terminology for common and well-recognized diseases that can assist diagnosis. The general description provided by the relative or caretaker who observed the terminal illness can also be of value, and a knowledge of general disease ecology (e.g., the occurrence of an epidemic) can provide important clues. Thus, verbal autopsies frequently include specific questions that can be incorporated into a diagnostic algorithm, as well as open-ended information that can be used for clinical judgment.

The validity of a verbal autopsy diagnosis is difficult to assess, in part because it depends on the degree to which an index condition is associated with a distinct syndrome, as well as the frequency of other diseases that may be confused with the index condition. The issue here is one of sensitivity (i.e., the ability of the verbal autopsy to identify
all or a high proportion of true cases of the index disease) and specificity (the ability to correctly identify all or a high proportion of individuals without the disease) (Swets, 1988). In order to measure the sensitivity and specificity of a verbal autopsy, it is necessary to have an unequivocal diagnosis based on conventional clinical criteria that can be used as a reference standard. However, there have been few rigorous epidemiologic studies to establish the validity of verbal autopsy diagnoses, because many patients are not seen by physicians before death, and because physicians' diagnoses are themselves subject to error or are poorly documented. An alternative approach is to validate diagnostic algorithms in living patients, using either a physician's diagnosis or confirmatory laboratory tests as a reference standard. This has been done for diseases such as ALRI, measles, diarrhea, and AIDS (Campbell et al., 1989; Cherian et al., 1988; Leeuwnburg et al., 1984; Greenwood et al., 1987; Kalter et al., 1989; Mann et al., 1986; Widy-Wirski et al., 1988).

Epidemiologic field studies allow indirect evaluation of verbal autopsy as a diagnostic method. For example, if the descriptive epidemiology of a disease based on verbal autopsy diagnosis is similar to the epidemiology based on physician's diagnosis, it is plausible to argue that the verbal autopsy reflects the true incidence and distribution of the disease. Thus, validity may be indirectly inferred from the consistency and plausibility of epidemiologic observations.

It is also possible to undertake intervention trials whereby preventive or therapeutic measures such as immunization or oral rehydration therapy (ORT) are introduced, and cause-specific death rates, as estimated from verbal autopsies, are monitored to evaluate impact. If cause-specific death rates decline in response to the intervention, it can be inferred that the intervention was efficacious and that the verbal autopsy actually measured the disease of interest. Diagnostic algorithms for diseases such as neonatal tetanus, measles and diarrhea have been indirectly evaluated in this manner (Galazka and Stroh, 1986; Fauveau et al., 1989; National Control of Diarrhea Project, 1988). This before-and-after approach can be useful, but it is vulnerable to interviewer bias because field workers, who know the expected outcome of the intervention, may be prone to ascribe death to another cause rather than the target disease (transfer of diagnosis). A further difficulty in the interpretation of such before-and-after studies is that declines in mortality
from a specific disease (e.g., measles) may also be reflected in mortality declines from other associated conditions (e.g., postmeasles pneumonia), or there may continue to be mortality due to the presence of unrelated diseases (often termed replacement or compensatory mortality). Alternatively, diagnostic habits may persist even after a disease has been controlled, and spurious cases continue to be reported despite true declines in incidence (Gray, 1986). This is particularly a problem with diseases such as malaria, which often do not present a clear-cut clinical syndrome, and for which diagnosis is unreliable in the absence of a confirmatory blood smear.

In summary, experience suggests that verbal autopsies can be used to ascertain causes of death for diseases that present with relatively distinct syndromes, and that verbal autopsy diagnosis has been of value in providing descriptive epidemiologic data needed to determine program priorities and to evaluate program impact. The following sections of the report review experience with different approaches to verbal autopsy that have been applied in diverse field settings in developing countries.

3. REVIEW OF INDIVIDUAL STUDIES

Information on completed or ongoing studies was obtained by review of the literature and by a questionnaire sent to investigators known to be working with or to have used verbal autopsies. A summary of these studies is presented in Table 1, and discussion of the projects in Sections 4 and 5.

4. DATA COLLECTION: DEATH REPORTING, INTERVIEWING, AND QUESTIONNAIRE DESIGN

a) Reporting of deaths: Most studies using verbal autopsies are population-based and have a reporting system to ensure that all deaths in the study area are detected. Some longitudinal projects have used local reporters to regularly (often every two weeks) survey households near their residence and report vital events to a central project office. Others have relied on annual demographic surveys by mobile teams. Projects in more developed countries may rely on the usual vital statistics system to record the death, but collect more detailed information by verbal autopsy. Where local reporters

1 Comments from workshop participants are indicated in italics.
are used, the tendency has been to use either all males or all females, depending somewhat upon the cultural circumstances. Most studies have found that reporters with at least a few years of schooling are necessary to carry out the work satisfactorily. The usual system involves the reporting of deaths to a central office; an interviewer then goes out to conduct the mortality interviews. In periodic demographic studies, deaths are detected at the time of survey, and a verbal autopsy is usually completed at the time of the initial interview.

b) Interviewer: The person who conducts the mortality interviews has varied. Some studies have relied upon medically-trained staff such as physicians, nurses, or social workers to do specialized parts of long interviews. Medical interviewers are costly and do not appear to be necessary; however, lay interviewers do need to be carefully trained and regularly supervised by professional staff. Interviewers are usually chosen from the same ethnic group as the population to be studied. Some studies have found that persons with several years of secondary education are most satisfactory. It is felt that the use of interviewers with a large amount of medical training may potentially bias the data, since the interviewer may try to interpret the responses. The sex of the interviewer needs to be determined by the particular cultural circumstances.

Dr. Garenne noted that good interviewers report exactly what people say, and do not interpret what is said. In his experience, nurses often want to interpret and need extra training to overcome this; he has not had this problem with physicians. Dr. Fauveau reported that for the investigation of maternal deaths, male interviewers are unable to pick up sensitive information regarding abortion, complications of pregnancy, etc., and he now uses only females for this work in Matlab. Dr. Lehmann noted that the Tari (Papua New Guinea) project has found it necessary to employ two male interviewers, so that at least one of them is able to safely enter tribal areas that would be hostile and dangerous for the other. When the interviewer returns from the field, an epidemiologist reviews the completed interview form with him; the interviewer may be sent back to obtain more information if it is needed to code the death. Dr. Lehmann said that Dr. Ian Riley had compared the results of interviews done by local secondary school graduates trained
on the job with interviews done by himself (a physician), and had not found much difference.

c) Interval from death to interview: In some projects, interviews are done as soon as possible, often within a few weeks after a death. Others have found it preferable to wait three months, by which time grief has been somewhat resolved and the family can more easily discuss the circumstances surrounding the death. Most projects have preferred to do interviews no later than 9-12 months after death, although one early survey of neonatal tetanus deaths did interviews for deaths dating back up to fourteen years. Some projects make special home visits for interviews, others schedule them during routine supervisory visits to check on reporters' work, for example at two monthly intervals. Special trips may be most practical in areas of low population density with many scattered hamlets, while regular interviewing rounds may be more feasible where populations are clustered in large villages.

Dr. Garenne commented that it is best not to do interviews too soon after death when the family members are still involved in the death and grieving process, and that he has found the optimal interval to be from two to four months. He felt that little information is lost during the period from six months to one year after a death, but after one year more information is lost and more undetermined causes result. Dr. Fauveau said that in Matlab, interviews are done an average of 16 weeks after the death. Dr. Lehmann noted that in Asaro 41% of interviews are completed within one month of death, and 71% within three months.

d) Respondent: For child deaths, the investigators in some studies have relied upon interviewing any close family member; others have used the mother as the person of first choice, with father or foster parents, or even neighbors, as a second choice. Occasionally health workers such as nurses or doctors, who may have cared for the patient, have also been interviewed.

Dr. Garenne noted that one has to be careful that certain categories of deaths are not missed entirely. For example, for maternal deaths, other women generally give the most accurate responses, often better than a woman's own husband. Dr. Omondi-Odhiambo pointed out that in investigating child deaths, that the age of the mother can be
important, since young mothers are sometimes confused or unsure about what actually happened. Dr. Fauveau noted that in Matlab they have used the entire family as well as groups of other adult females as respondents in order to obtain a more accurate information about maternal deaths.

e) Questionnaire: Most projects used a structured interview with lists of symptoms and signs to be checked off, or branching symptom/sign trees to be followed, depending on the response to "filter" screening questions. However, the MATLAB project used an unstructured interview with a list of different possible illnesses, injuries, or symptoms leading to death, selected on the basis of the description obtained during the open-ended interview. Not all studies obtained the timing of symptoms and signs, although all investigators agreed that this was critical. The use of a calendar of events could be helpful in this regard.

Some projects have used the same questionnaire for all ages and sexes (Tari, Matlab), whereas others used separate, specialized questionnaires for neonates (0-7 days), children (28 days-14 years; 0-5 years; 0-7 years), and male and female adults aged over 15 years (ORSTOM). However, in order to reduce costs, they now use a single questionnaire for all age groups, with specialized questions for different age groups. The multi-country PAHO project used one questionnaire for all children from 0-5 years of age. Projects with a special interest in neonatal or maternal deaths have tended to develop specialized questionnaires for these subgroups. Questionnaire length varied from one to twelve or more pages.

The content of the questionnaires included some, but not all of the following information, and in varying order:

- Identifiers and demographics (age, sex, race, etc.)
- Education
- Occupation
- Interviewer's identity
- Respondent's identity
- Relationship of respondent to deceased
- Open-ended questions on symptoms and their duration in the final illness
- Lists of symptoms, followed by questions to be asked if the symptom is present. Some questionnaires give a choice of several different questions for each symptom.
- Treatments with location and type (if any)
Type of health worker consulted (if any)

Health card number and information (if any)

Hospital record identifier and information (if hospital was used)

Place of death

Cause of death according to family

History of the diseases and conditions leading to death, i.e., an open-ended history of the events surrounding the death. In some questionnaires, this was placed first as an introduction to let the family express their own views of the death, before structured questioning began; in others, it was placed after the structured questions.

Check list for ordering the causes of death (usually one underlying and variable numbers of associated causes of death, or immediate, underlying, and associated causes).

Project-assigned underlying and associated causes of death (usually one underlying and variable numbers of associated causes of death permitted; others use immediate, underlying, and associated causes).

Basis for diagnosis: interview only, death certificate only, autopsy, hospital, clinical definite/indefinite.

Dr. Garenne commented that the ORSTOM questionnaires use major and minor symptoms, so that if there is a reply of "yes" to a major symptom the interviewer then proceeds to ask about related minor symptoms. The Senegal study uses one questionnaire for all age groups, with separate sections for specific age groups, especially for inquiry about neonatal deaths.

Dr. Pison pointed out that some local terms and names for diseases are very sensitive, in that they cover a broad range of diseases, but because of this breadth they are not very specific. In Senegal, the local terms for measles and diarrhea are fairly well understood, but the term for pneumonia is not, since febrile pneumonia is often confused with malaria. As vaccine programs began to eliminate most deaths from pertussis and measles, he found that the proportion of indeterminate deaths increased. He suggested that as circumstances change, comprehensive questionnaires may need to be modified to focus on a certain cause(s) of death. Dr. Lehmann noted that when disease patterns change, as with the recent typhoid epidemic in the highlands of Papua New Guinea, the usual questionnaire may no longer be adequate.
With respect to specialized questionnaires, Dr. Fauveau reported that IATLAB now uses a special questionnaire for neonates from 4-21 days of age for the diagnosis of neonatal tetanus. They also use a special questionnaire for adult females from 15-44 years of age. He noted that they analyze their data using four age groups; namely, children of less than one month, 1-5 months, 6-35 months, and females 15-44 years.

Dr. Gray pointed out that questionnaires need to ask "how" the death occurred rather than "why"; if one asks why, often a supernatural explanation will be obtained, whereas if one asks how, it may be possible to obtain a history of the antecedents of death. Dr. Omondi-Odhiambo corroborated this point when he reported that in Kenya motor vehicle accidents were often originally classified as witchcraft, when the people were asked why the person died, rather than how.

Dr. Omondi-Odhiambo also suggested that questionnaires may need to be in the local language; however, he noted that the Machakos (Kenya) project did not use a standardized verbal autopsy questionnaire. The project physicians just took a medical history; this may have resulted in interobserver variation. He felt that while the questionnaire shouldn't be totally open-ended, one does need at least a couple of lead-in questions. Open-ended questions may also provide less biased information in interviews with persons who tend to answer "yes" to all structured questions. Kenyan respondents preferred open-ended questions, because they can emphasize the points they feel are important; a disadvantage is that this information is difficult to analyze.

Whether to start the interview with an open-ended or closed question was discussed. An open-ended question is useful to get the temporal sequence of events, which can be helpful in distinguishing the underlying, immediate, and associated causes. Some investigators felt that structured responses should be obtained first, and then followed with open-ended questions to get the sequence of events.

Dr. Lehmann said that in Tari and Asaro the open-ended question tended to be asked first to facilitate communication with the relatives, but it might be better to ask the
specific questions first and then get clarification of the sequence of events from open-ended questions.

Dr. Zimicki said that if a structured questionnaire is used, the timing and duration of symptoms/signs need to be recorded, i.e., when they started and how long they lasted. A highly sensitive question should be used as a filter, followed by subsidiary questions as "reducers" to increase the specificity, which will be low after a single question of high sensitivity.

Dr. Fauveau noted that the open-ended statement that has been used on the Matlab forms since about 1966 i.e., not a very good filter, and that it has often been difficult to arrive at a cause of death; however, by improving the training of interviewers, they have managed to increase the amount of information recorded from an average of about two lines per form to 14 lines per form. He also felt that the use of structured interviews, as well as diagnostic algorithms for classification, helps to maintain consistency over time.

Dr. Quinley noted from his work in Sumatra, which used both open and closed-ended questions, that as interviewers became more experienced differences between the open and closed responses decreased; new interviewers had more trouble handling the open-ended question. The main utility of the open-ended question was in identifying special cases of those unusual or rare diseases that can be easily diagnosed by parental history.

f) Supplemental information: Where possible, investigators have used supplemental documentary information from medical records. The infant health record card, carried by the mother for most children, was used in the MRC Gambian survey to obtain age, as well as nutritional and immunization status. Information from rural health workers has been used in some cases, but was not particularly helpful due to poor record keeping and symptomatic diagnoses. In the PAHO projects, which included more developed countries, more use was made of hospital, clinic, physician, and autopsy records, as well as newborn records and death certificates. Medicine containers or prescriptions have also provided useful information. However, some projects had no provisions on their questionnaires for the use of supplemental information (ORSTOM, Matlab).
It was noted that information from a vaccination card may be useful, but it is necessary to ensure that one has the card for the correct child. Birth weight and duration of pregnancy are important information that can be obtained from birth or hospital records or a child health card to decide whether prematurity or low birth weight were underlying causes of mortality. Dr. Lehmann noted that in Tari and Asaro information on the hospital death certificate is used when it is available.

5. DIAGNOSIS AND CODING OF CAUSE OF DEATH

The diagnosis and classification of the causes of death is a complex process requiring some medical judgment. Such judgments may be made after the collection of information from open and closed interviews, or the judgment may be a priori, using predefined algorithms of symptoms and signs. The decisions on the underlying, immediate or associated causes of death are usually based on the temporal ordering of illnesses preceding death, and medical knowledge regarding the relationship between diseases (e.g., measles and pneumonia).

a) Classifier-coder: In most projects, the actual coding of the cause of death is done by physicians or epidemiologists, after the field interview has been completed and discussed. In the Tari project, coding was done by a medical epidemiologist with the help of the interviewer, so that supplemental information could be obtained later by the interviewer, if necessary. In the large PAHO project, groups of several different medical specialists had regular conferences where causes of death were assigned; however, final coding was done later at a central office by two principal collaborators and three other medical officers.

In the Matlab project, at least until recently, coding was done mainly by non-medically trained field interviewers at the time of the interview, with some later checking by office workers (coders) and occasional reassignment of causes. However, since 1986 the assignment of the cause of death at Matlab has been done by a group of three physicians; assignment is done independently by each and the majority rules. If all three disagree, then the form is returned to the field for more information. The underlying cause is coded as the primary cause of death. Coding is done by the principal investigator using ICD-9 revised combinations. Large demogra-
phic surveys generally use algorithm-based diagnoses and have relatively little secondary review by physicians.

b) One cause vs. multiples causes: Most, but not all studies have recorded multiple causes of death (only one possible cause of death could be assigned in Matlab.) The cause of death was classified according to a primary and secondary diagnosis (MRC), or by order of appearance (ORSTOM). The Tari project allowed one underlying cause, and other conditions were divided into intervening, direct, or associated causes to be entered as listed in the standard death certificates used in many countries. The study by PAHO allowed one underlying cause and up to three associated causes to be assigned. Demographic studies tend to give multiple causes equal rank, and do not attempt to ascribe an underlying cause.

Problems with coding and classification: The coding of causes of death among infants is particularly difficult.

The study in Senegal (ORSTOM) used specialized questionnaires for the 0-7 day age group and another for the 8-14 year group. They obtained good data for neonates and children below five years, but found that it was difficult to obtain data for older children and adults. In the Matlab study, where coding was until recently done by field workers who used a single non-structured interview, it was found that about 40% of causes were assigned to the nonspecific "other" category. There was also interviewer confusion between local illness classifications and biomedicale disease classifications. There did not appear to be defined rules for recoding by classifiers, so recoding was therefore sometimes done inconsistently, resulting in classifier bias (Zimicki, 1986). In the Tari project, deaths were sometimes deliberately ascribed by respondents to apparently unrelated events that had occurred long before death, particularly wounds from tribal fighting; as a result, considerable evaluation of responses had to be made, based on local conditions and clinical judgment.

In the PAHO study, final selection of the single underlying cause often differed from the original locally-assigned cause, due to local lack of knowledge of international coding rules. For almost one-third of the total deaths, after full investigation, the underlying cause on the death certificate was considered to be an associated cause.
The misclassification problem was most severe for neonatal deaths. It was felt that on death certificates, infectious and perinatal causes were most often over-reported as underlying causes, and nutritional causes were most often underreported.

Dr. Garenne commented that in ORSTOM, the coding of the cause of death is based upon the judgment of two physicians, using algorithms to guide their decisions. They use established rules in deciding how to apply the codes. For example, if death occurs within six weeks of measles, then measles is listed as the underlying or main cause of death. With pertussis, if death occurs during a coughing spell within three months after the onset of illness, then pertussis is coded as the underlying cause of death, but if it occurs 3-6 months after the onset, then pertussis is coded as an associated or intermediate cause. For malnutrition, if there are signs of marasmus or kwashiorkor, then malnutrition is coded as the underlying cause of death, and any associated diarrhea or pneumonia is coded as an associated cause. However, he also pointed out that the fairly distinctive symptoms make kwashiorkor relatively easy to diagnose by interview, but that it is much more difficult to diagnose marasmus unless the child was seen in clinic and additional information is available to supplement the interview. Reports of malaria are often difficult to interpret, although there is a close statistical correlation between fever and malaria in endemic areas. He noted that it is important to document the absence of symptoms as well as the presence of symptoms, since high fever and chills of short duration (<3 days), with no other symptoms can often reasonably be interpreted to be malaria, particularly in an endemic area during the rainy season. It is important in assigning the underlying cause that it is primary in the temporal sequence. The analysis is simplified if only one underlying cause is assigned, but if all associated causes are used, then the analysis becomes complex.

A classification problem similar to that which occurs with combinations of malnutrition and infectious diseases in children can arise when premature or low birth weight (LBW) infants die of pneumonia or other infectious disease. Some participants felt that if pneumonia occurs in the presence of LBW or prematurity, that one of the latter should be coded as the underlying cause, and pneumonia as the immediate cause. However, it can be difficult to decide whether an infant was
either low birth weight or premature, since this information may not be available from the interview. In such cases, records should be used whenever available. One project developed a categorization of normal, small, and very small infants. The "very small" infants were designated as LBW.

6. USE OF VERBAL AUTOPSY FOR SPECIFIC DISEASES IN CHILDHOOD

The discussion of disease-specific diagnoses focused on four principal diseases: neonatal tetanus, measles, acute lower respiratory infection (ALRI), and diarrhea; however, injuries and the problems of diagnosing malaria, pertussis, AIDS and meningitis were also discussed. The four principal diseases were selected because there is extensive experience with the use of verbal autopsy diagnosis for these conditions, which present as relatively distinct syndromes because they are common conditions that are thought to be major causes of death in childhood, and because all four are amenable to preventive or therapeutic intervention. Injuries are unique in that a type of "verbal autopsy" is used even in developed countries to determine the cause of death (E or external cause codes).

   a) Neonatal Tetanus: There has been extensive use of verbal autopsy in defining the epidemiology and public health importance of neonatal tetanus (Galazka and Stroh, 1986; Stanfield and Galazka, 1984). The criterion for diagnosis is the following symptom complex: (i) death among liveborn children between the 3rd and 30th day of life; (ii) initially normal early crying and suckling, followed by inability to suckle or difficulty feeding starting between the 3rd to 15th day of life; (iii) generalized stiffness or "convulsions" with unremitting muscle spasms that increase in intensity, and (iv) trismus or risus sardonicus (Galazka and Stroh, 1986; Gray, 1989).

   Although this syndrome appears to be pathognomonic of tetanus, and algorithm-based diagnoses are highly sensitive, there are no studies that have adequately evaluated the specificity of verbal autopsy diagnoses for neonatal tetanus. Particular concern arises from possible confusion with neonatal convulsions due to congenital anomalies or cerebral hemorrhage following birth trauma, postnatal septicemia or meningitis, or metabolic disorders. Disease onset after the third postpartum day excludes most congenital or intrapartum conditions, and in general the nontetanus convulsions are
focal rapid jerking movements while trismus is absent. Meningitis is associated with a bulging fontanelle, whereas this is not a feature of tetanus. However, studies are still needed on the specificity of various symptom complexes for the diagnosis of tetanus.

b) Diarrhea: The diagnosis of diarrhea associated with death is based on the presence of diarrhea shortly before death; diarrhea is defined as frequent stools (> 3 per day) of loose or watery consistency. There are often local terms for diarrhea that are useful in phrasing questions. Diarrhea can be categorized as acute (< 2 weeks duration), chronic (> 2 weeks duration), or dysenteric (with blood in the stool, of any duration) (Black, 1984; Gray, 1989). The diagnosis of dehydration is more difficult, in part because mothers may not recognize or recall signs of dehydration, and also because there are multiple signs of fluid loss. Single signs of dehydration such as sunken eyes or depressed fontanelle tend be sensitive but non-specific, whereas multiple signs of dehydration (> 4) probably give the optimal level of sensitivity and specificity. Such signs include thirst, dry mouth, sunken eyes, depressed fontanelle, decreased skin elasticity, reduced urine output, and deep breathing and drowsiness (Kalter et al., 1989).

c) Measles: The WHO Expanded Programme of Immunization (EPI) and other programs have used verbal autopsy methods extensively for measles diagnosis. Diagnostic algorithms have been validated against clinical and serologic diagnoses (Foster, 1984; Kalter et al., 1989; Leeuwenburg et al., 1984), and were found to have high sensitivity and specificity. The diagnostic criteria for measles deaths were a history of a generalized blotchy rash accompanied by fever, lasting for more than three days in a child older than five months. Information on the progression of the rash may be of some value, but the classical signs of fading of the rash and desquamation may not be present prior to death, if a death occurs early in acute measles. Cough, runny nose and red eyes may be useful ancillary signs. Most cultures have local terminology for measles that may be useful in interviews; however, the specificity of local terms varies, and in some cases they include all rashes during childhood. The presence of a measles epidemic at the time of death is also helpful in establishing a diagnosis, while a proven history of measles vaccination makes the diagnosis suspect.
The major difficulty defining measles as a cause of death is that a fatal acute episode is usually associated with complications such as ALRI or diarrhea, while other children may die some time after the acute episode of measles due to postmeasles complications such as pneumonia. It is generally accepted that measles within three months of death should be considered as part of the causal chain, but the classification of a resolved measles episode as an underlying or associated cause of death varies (Foster, 1984).

d) ALRI: It was agreed that ALRI may be difficult to diagnose by verbal autopsy, because the presentation varies by the age of the child and by the etiologic agent [e.g., viral bronchopneumonia, pneumococcal lobar pneumonia, and bronchiolitis due to respiratory syncytial virus (RSV)]. Even clinical diagnosis, in the absence of an X-ray or autopsy can also be very difficult. Most work on ALRI has focused on simplified clinical diagnosis and case management (WHO/RSDF 1986), but signs such as a high respiration rate cannot be ascertained by verbal autopsy. There are few studies that have validated algorithm-based diagnoses of ALRI deaths, and studies of ALRI in surviving children show considerable interobserver variation in the detection of clinical signs by physicians, confusion between signs of ALRI and upper respiratory tract infection (URTI), and particular difficulty in neonatal diagnosis due to confusion with other infections (Mulrow et al., 1986; Riley, 1981 and 1985).

The main criteria for postmortem diagnosis of ALRI include prolonged cough for more than four days together with dyspnea (difficult and rapid breathing) for more than one day. It is important to differentiate between agonal respiratory failure at the time of death and ALRI-induced dyspnea in the days before death. Signs of respiratory distress such as nasal flaring, intercostal retraction, cyanosis, and wheezing or grunting can increase the specificity of the diagnosis. Fever is not a particularly useful sign, because many terminally-ill infants cannot mount an adequate febrile response. No combination of signs gives both high sensitivity and high specificity; thus, there is a need for sensitive filter questions (such as the presence or absence of prolonged cough or dyspnea), followed by detailed questions to increase specificity (such as the presence or absence of respiratory distress).
e) **Injuries:** Injuries are an important, but often overlooked cause of death, especially outside the neonatal period. Unlike other causes of death, injury deaths can be easily classified by relatively unskilled workers and do not require accurate medical diagnoses to establish the cause. Even in developed countries, descriptive information on how the death occurred (e.g. a person fell out of a window), is used to describe the external cause of death for injuries. Injuries have two classification systems, an external cause (E code) and the nature of the injury (N code) (WHO, 1977). The nature of injury coding requires accurate anatomical diagnoses but is only used in multiple cause of death classifications and for coding morbidity, while the coding of the primary or underlying cause of death for injuries is essentially a "verbal autopsy" that is subject to little interpretation. As a result, injury deaths are more likely to be accurately diagnosed than other causes. In some countries, however, poisoning, suicide, homicide, or some other conditions may be over or under-reported due to cultural interpretations or beliefs as to "cause of death"; the desire to cover up violent deaths, or to obtain confirmation may also affect how they are reported.

f) **Other diseases:** Malaria is a particularly difficult disease to diagnose accurately by verbal autopsy due to the protean and often non-specific nature of its manifestations. In known malarious areas, high fever, sweats and chills within three days of death, in a child who has not received anti-malarials, provides sufficient evidence for a presumptive diagnosis. However, even in areas such as the MRC study area in the Gambia, where blood slides are frequently taken, a positive slide only indicates that a person died with malaria, but not necessarily of it. In addition, deaths from *Plasmodium falciparum* may be so rapid that testing is not possible. Death due to acute pertussis can be diagnosed in outbreak situations by severe cough persisting for two or more weeks, with recurrent bouts of coughing and the characteristic whoop, often associated with vomiting. However, deaths some time after an episode of pertussis, or during a non-epidemic period, are more difficult to code. Malnutrition is difficult to diagnose in the absence of anthropometric measurements. Some investigators feel that mothers can recognize signs of frank kwashiorkor (edema, change of hair color or loss of hair), but it is more problematic to identify marasmus (Gray, 1989). AIDS in children has been diagnosed clinically on the basis of major signs such as weight loss and slow growth,
chronic diarrhea, and fever accompanied by signs of infection, lymphadenopathy or dermatitis; however, it can be confused with tuberculosis and malnutrition (Mann et al., 1986; Widy-Wirski et al., 1988). No satisfactory validation of verbal autopsy diagnosis of these conditions has yet been done.

7. VALIDATION OF VERBAL AUTOPSY METHODOLOGY

Most projects have not made a systematic effort to externally validate verbal autopsies by comparisons with physician examinations and other information such as laboratory or X-ray findings. However, the MRC project staff in theamba did a validation study, where mothers of 87 children with potentially fatal illnesses were interviewed in hospital, after which the diagnosis obtained by interview was compared with the clinical diagnosis made by hospital staff; the agreement was 76% (Greenwood et al., 1987; Alonso et al., 1987). A second group of mothers was interviewed one month after their child left the hospital; there was 88% agreement between the diagnoses made from the home interview and the clinical diagnoses. The MRC study also found 96% agreement in the assigned causes of death among three physicians who independently coded the deaths after reviewing the questionnaire information. Although the Tari unit did not formally validate their mortality questionnaire, a validation was done of several respiratory symptoms for the diagnosis of pneumonia or of chronic lung disease in living patients. It was found that a combination of breathlessness, chest pain and fever, together with pain on percussion of the chest and the character of the sputum, was 77% accurate when compared with chest X-rays.

The only formal validation of the actual verbal autopsy itself was conducted in Cebu in the Philippines (Kalter et al., 1989). Different combinations of symptoms and signs obtained from mothers by using structured interviews were compared with physician diagnoses of selected illnesses, for 164 deaths among hospitalized children. The 164 deceased children had 256 physician diagnoses, including acute lower respiratory infection (100), diarrhea (92), measles (48), and neonatal tetanus (16). Forty-three percent of children had multiple illnesses. An algorithm for tetanus (age at death \( \leq 30 \) days, with convulsions or spasms) was 100% sensitive, but specificity could not be estimated due to the small number of neonatal deaths available for comparison. An algorithm for measles (age \( \geq 120 \) days, with rash and fever \( \geq 3 \) days) had 98%
sensitivity and 90% specificity. The diagnosis of ALRI was more difficult, with cough or dyspnea alone yielding 86% sensitivity but low specificity, whereas prolonged cough and dyspnea provided 93% specificity but low sensitivity (41%). Diarrhea diagnoses based on frequent loose or liquid stools had high sensitivity (78-84%) and specificity (79%), irrespective of whether the child died with diarrhea alone or in combination with other illnesses. However, maternal reports of moderate/severe dehydration had low specificity. It was concluded that, in this setting, verbal autopsies can diagnose major illnesses contributing to death in children with acceptable sensitivity and specificity.

Drs. Garenne and Darkaoui reported on a comparison between hospital diagnoses and field interviews for 46 deaths. They found agreement in 45/46 deaths. The fairly high degree of agreement between the verbal autopsies and the hospital diagnoses was reassuring; however, only about 10% of all deaths occurred in hospital in their study area.

Dr. Becker mentioned that in Liberia, the reliability of field interviews was tested by reinterview. They noted a discrepancy between 11% and 35% on the reporting of symptoms by the mother of the deceased child in the two interviews. As expected, reliability was greater for the deaths that had occurred within three years before the interview, than for the deaths that occurred 3-6 years before the survey.

Dr. Lehmann stated that at Tari an informal reliability study had been done, where two physicians (one trained by the other) coded deaths separately; there was greater than 90% agreement. She mentioned several possible ways to measure reliability and validity, including comparisons of hospital data versus interviews of relatives, interobserver and intraobserver (over time) variation, interview of two close relatives, the use of panels of coders, comparisons of the cause of death assigned by a relative versus the coder(s), and the clinical signs of severe disease in hospitalized patients in relation to outcome and to the relatives' assessment.

8. APPLICATIONS TO FIELD STUDIES

There are a variety of potential applications of the verbal autopsy method, including its use to determine impor-
tant causes of death, and to prioritize them for interventions, and also to evaluate interventions. However, a number of constraints need to be considered, including the format and complexity of the questionnaire to be used, and the way in which special questions can be added to large-scale surveys done for other purposes. The careful use of filter questions, modules and skip questions will be necessary to facilitate the use of verbal autopsy in large surveys. Other key issues that must be considered are the sample size of the study, and the use of multiple versus single causes or underlying versus associated causes of death.

Dr. Rutstein presented an overview of the potential use of the verbal autopsy in the Demographic and Health Surveys (DHS). Two surveys that included all births in the last five years have been done by DHS using verbal autopsies (one in Ecuador and the other in Senegal). One concern was the amount of time needed to train interviewers, and the length of the questions necessary for verbal autopsy. It may be better to identify households that have a death, and then to return to these households with a new specialized interviewer. If this is not done, there may be bias because interviewers who may not want to do the extra work necessary to complete a verbal autopsy may undercount deaths. Other concerns were the need for rapid availability of data and how the verbal autopsies will be coded. A number of issues were raised by Dr. Rutstein related to the implementation phase:

1. How culture-bound are the surveys and how applicable are they in different regions?

2. Are people likely to exclude deaths in the distant past and only remember recent deaths? Are neonatal deaths likely to be excluded?

3. Should verbal autopsies be a part of the main survey, or be done as a separate operation with a resultant increase in cost?

4. To be most useful the data need to be broken down into subregions, and there may be insufficient deaths to provide statistically reliable estimates at this level.
Dr. Gray remarked that verbal autopsies should be conducted separately by skilled interviewers; they would do better interviews, and this would also eliminate the extra work imposed upon the usual interviewers. Ms. Osinski was concerned that supervisors should not have to function as verbal autopsy interviewers. Most participants expressed a preference for the use of trained special interviewers to do verbal autopsies, and would prefer to see the routine interviews used simply as an initial screen to obtain notification of deaths.

9. RECOMMENDATIONS FOR RESEARCH AND FUTURE USE

a) Validation/Reliability studies: Most users of verbal autopsy have relied on empirical approaches, with little or no validation of the methods used. There is a need for more validation studies in a variety of settings. Hospitalized children are a potential source of cases with reasonably valid diagnoses, and could be used for comparison with maternal interviews after the patients have returned home. Studies such as those done in Cebu could provide useful information about the reliability of the mother's recall of symptoms. It would also be useful to compare the results of interviews with two different respondents about the death or hospitalization of the same child. An interview with a mother could be followed by an interview with another close family member.

There is also a need for more clinical studies that compare the physical signs observed in clinics with those described by relatives. For example, the capability of parents to describe rapid breathing, specific signs of dehydration, and signs of malnutrition needs to be assessed. The sensitivity and specificity of verbal autopsy for estimating the gestational age and birthweight of premature and low birthweight infants also needs to be evaluated. It will also be important to determine whether data from morbidity studies can be used to predict responses from mortality studies, since morbidity studies may be easier to conduct.

Another issue that was discussed was interobserver variation; it was felt that various interviewers might obtain different histories from the same person. This concern has been corroborated by repeat interviews that have been conducted by Matlab; the information about maternal deaths that was obtained from regular interviews done by males, differed from special follow-up interviews done by female interviewers.
It was felt that it is important to measure interobserver variation. One possible way to reduce interobserver variation is the use of tape-recorded interviews or even videotapes of interviews for training purposes. The optimal duration and type of training for interviewers needs further study.

b) **Diagnosis and classification:** Many participants felt that there are advantages to using well-defined algorithms, rather than relying on clinical judgment, as is presently done in many studies. The differences in results from the two methods need to be compared. Another area of interest is the use of a computer diagnosis, with standard algorithms, which will become very important when the verbal autopsy method moves from being a research tool to widespread use in large surveys.

Efforts should be made to determine the temporal sequence of events, since this can influence the final diagnostic classification. Research is needed to determine how far back in time one should go to define antecedents of death, and to develop better methods for collecting information about the time sequence of the events during the course of the disease.

Concern was also expressed about the large proportion of undetermined causes of death in most surveys. It was acknowledged that a definite cause cannot be established for all deaths by use of the verbal autopsy. The percentage of undetermined deaths will likely vary with age, as well as with the specific study methods and personnel used. Further work is needed to determine whether symptom complexes can be identified to help reduce the number of deaths attributed to undetermined causes. It may also be useful to include a separate category for deaths where the cause is unclassifiable, but where obvious symptoms are present. Another issue is whether all diagnoses should be considered during the classification, or whether a short list of diagnoses of primary interest should be used. In the latter case, no attempt would be made to identify and separate out other causes of death.

The epidemiologic plausibility of the causes of death that result from any classification should be considered -- for example, social or sex differentials, and seasonal variation. Comparisons should also be made with known outbreaks and with known geographic variation. Before and after comparisons should be made when interventions are
initiated, as well as comparisons between intervention and control areas. More detailed comparisons are needed of differences in causes of deaths that occur in hospital as compared with those that occur at home. This is essential to understand the biases of a sample of deaths obtained from hospital records. Such studies could help to identify reasons why people fail to seek or obtain treatment, and related issues of utilization of health services.

A major area of concern is the current inability to diagnose perinatal and low birthweight deaths; more work is needed to determine what pertinent information can be reliably collected from maternal interviews. Research is also needed to help develop better algorithms for diagnosing ALRI. Even when good clinical histories are available, there is controversy as to the ability of clinicians to distinguish acute lower respiratory tract infections from upper respiratory tract infections. There is believed to be considerable misclassification, particularly in neonates. There is also a need for field testing of algorithms, in conjunction with detailed clinical follow-up.

Long-term longitudinal studies can be affected by shifts in diagnostic classifications over time, and some method of standardization is necessary. It was felt that the use of well-defined algorithms would be helpful, even where the ultimate cause of death is determined by a physician judgement or diagnosis. Drs. Zimicki and Black suggested that a probabilistic method of classification should be developed expressing the degree of certainty of each diagnosis. The specific categories suggested were: likely, probable, possible, and unlikely.

Dr. Gray expressed his concern with the difficulties of deciding upon the underlying cause of death and the specific disease process involved. The issue of single versus multiple illnesses remains still largely unresolved, although it was felt that the use of multivariate analysis, especially discriminant analysis, may provide some useful insights in the analysis of future studies. Dr. Foster discussed the issue of associated and underlying causes and the difficulty of deciding between them, and reemphasized the importance of a temporal sequence in assigning the classification. If we are to make the best use of data obtained by verbal autopsy, it is essential that multiple
causes of death and multiple conditions associated with death should be included in future analyses.

c) Questionnaire structure and study design: The most appropriate way to structure the questionnaire has yet to be fully determined. While closed questions are much easier to code and analyze, open-ended questions are also needed, since many diagnoses still require clinical judgement. Many participants felt that it was probably better to have the open-ended question at the beginning of the interview, but this issue should be studied further.

There is a need to develop better methods to determine the timing of symptoms and the sequence of their development, in order to better establish the condition most directly contributing to the death. Whether this information is best obtained by an open-ended question, by structured questions, or by an events calendar remains to be answered.

It also needs to be determined whether short algorithms of a few questions can be developed to pick up certain diseases with a high degree of sensitivity and specificity. There is a potential conflict between the desire to achieve internationally standardized and comparable data, versus the need to ask questions in a culturally responsive manner. The use of rapid ethnographic assessment methods to determine the most culturally-acceptable ways of asking particular types of questions could be useful.

Another major issue to be researched is how far back in time it is possible to obtain valid information about deaths. Longer recall periods would provide more information with large-scale surveys, such as DHS, which might require longer recall periods of 2 to 5 years. The ideal waiting time between death and interviews has not been determined, but appears to vary between cultures. In the first week or two after the death of an infant, it is believed that many mothers are unable or unwilling to give a coherent history. On the other hand, the accuracy of recall of more distant events is uncertain.

There may be a conflict in maximizing both sensitivity and specificity. For clinical screening, one needs a "filter" question that is very sensitive in order to avoid missing a case, but for assessing the impact of programs, increased
specificity may be desirable. There will generally be some trade-off between sensitivity and specificity.

There is a need to maintain consistency of the quality of data within studies, and concern was expressed about the potential adverse effects of modifying questionnaires in large ongoing studies. These factors may affect measurement of disease trends over time. Where possible, if changes are made, the original questions should be asked first to maintain some consistency.

d) New applications: A major area of potential use of the verbal autopsy lies in the extension of the method to large-scale surveys, such as the Demographic and Health Surveys. Another potential use of verbal autopsies is in routine reporting systems for vital events. These could be established using village-based demographic reporting systems.

While this particular meeting largely dealt with the use of verbal autopsy for child deaths, there is also a need for detailed examination of the uses of the method in other age groups. Where used to study deaths of reproductive age groups, verbal autopsies can provide useful information about causes and rates of maternal mortality. In addition, valuable data on other adult deaths may be obtained, especially on those that occur prior to old age, after which the cause of death often becomes more difficult to ascertain. The cost-effectiveness of the verbal autopsy needs to be compared with that of other methods that are presently used to identify health problems, to establish priorities, and to evaluate health programs.
BIBLIOGRAPHY


### SUMMARY OF VERBAL AUTOPSY STUDIES

<table>
<thead>
<tr>
<th>Country and Investigators</th>
<th>Years of Study</th>
<th>Age Range Considered</th>
<th>Sample Size (Pop. or deaths)</th>
<th>Type of Study</th>
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</tr>
<tr>
<td>13) Yes</td>
<td>Yes</td>
<td>?</td>
<td>?</td>
<td>Panel of MDs</td>
</tr>
<tr>
<td>14) Yes</td>
<td>Yes</td>
<td>20</td>
<td>80</td>
<td>Individual MDs; Lay proj. staff</td>
</tr>
<tr>
<td>15) Yes</td>
<td>Yes</td>
<td>30</td>
<td>93+</td>
<td>Individual MDs; Investigator</td>
</tr>
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</table>
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