DEMOGRAPHY AND THE BIOMEDICAL SCIENCES

THE INTEGRATION OF DEMOGRAPHIC AND EPIDEMIOLOGIC APPROACHES TO STUDIES OF HEALTH IN DEVELOPING COUNTRIES

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Demographers and biomedical scientists, particularly epidemiologists, have long had common interests in population-based studies of health problems in developing countries. Demographers have traditionally been concerned, among other issues, in measuring levels of mortality, and differentials in mortality associated with socioeconomic characteristics such as education and income. However, demographic inquiries seldom address problems of the disease processes leading to death. Epidemiologic studies on the other hand have tended to focus on specific diseases or constellations of diseases, and their modes of transmission, prevention or treatment.

These differences in disciplinary focus are reflected in basic study methodology, in explanations of mortality levels, trends and differentials, and in policy prescriptions for future mortality reduction. However, there is a growing consensus on the need for disciplinary integration at both a descriptive and explanatory level. Mosley and Chen (1984) have provided a major step toward disciplinary convergence by the recent development of a framework for analysis of child survival which incorporates both the underlying socioeconomic determinants of mortality commonly addressed by demographers, and the proximate determinants of mortality (risk factors, disease processes, prevention and treatment), commonly addressed by epidemiologists (Figure 1). In this framework, the underlying socioeconomic determinants affect
mortality through the proximate determinants. Also, Mosley and Chen have extended the dependent variable of mortality to include growth faltering as a relevant outcome, since it is clear that in developing countries compromised nutritional status is a strong predictor of death. There is, however, a recognized need to operationalize this conceptual framework by the integration of epidemiologic and demographic methodologies.

The rationale for operationalizing this framework is the need for improved health information in developing countries:

(a) to provide descriptive data measuring the relative magnitude of different health problems so as to establish health priorities,

(b) to identify differentials which might define risk factors or subgroups at highest risk, so as to identify causal relationships and devise interventive strategies, and

(c) to provide baseline and post-intervention data needed for the evaluation of health interventions or related activities.

The object of the present paper is to review approaches to field studies of health in developing countries, and to suggest some practical modifications. The two basic questions are: how can demographic studies provide more information on health (i.e., on the proximate determinants of mortality), and how can epidemiologic methods provide more information on the underlying determinants or other proximate risk factors for disease and death? Much can be learned from available experience and the intention is to suggest a synthesis rather than to develop totally new methodologies.
The following review will consider issues of mortality and morbidity within the Mosley-Chen (1984) framework, and suggest alternative study strategies. The initial discussion will focus on the use of algorithms for the identification of diseases or disease processes which may be used as indicators or markers for the proximate determinants of mortality, and on how such information can be obtained from surveys of morbidity or mortality. Then consideration will be given to the risk factors for disease, which implies measurement of the underlying determinants and factors such as maternal characteristics, environmental conditions, diet, etc., which influence the probability of disease, the severity of illness, and the effects of medical care. I will then address epidemiologic approaches to the study of risk factors which could be integrated with demographic studies.

STUDIES OF MORTALITY

Demographic studies mainly employ estimates of vital rates derived from either registration data, or retrospective information on mortality obtained by interview in censuses or sample surveys. Because deaths are relatively rare events, there is a need to study large populations, and the logistics often require relatively brief death registration forms or interview schedules which limit the amount and quality of information on mortality determinants. The primary emphasis has been on the complete recording of events and basic information on the characteristics of the deceased, or in the case of child mortality on the characteristics of the parents, rather than the underlying diseases leading to or associated with death. With the exception of certain middle-level
developing countries, sample registration systems or research oriented demographic surveillance, routine national vital registration has not yielded reliable information. In many countries demographic estimation is based on robust indirect techniques using retrospective data, particularly maternity histories or, more recently, information on the outcome of last pregnancy (UN, 1983; MacRae, 1979). Epidemiologic studies of mortality in developing countries have been mainly prospective cohort type investigations which estimate mortality rates among individuals with and without certain predisposing conditions (e.g., malnutrition), or trials of preventive and therapeutic measures with specific disease endpoints (e.g., vaccination, oral rehydration).

Registration or surveillance systems generally record 'cause of death,' but these data are frequently defective since the symptoms or mode of death are reported rather than the underlying disease or condition leading to death. Thus, a high proportion of deaths are attributed to ill-defined symptoms such as senility, fever, etc. (WHO, 1980). In many situations registration is performed by lay workers, and WHO has attempted to systematize the lay classification of causes of disease and death (WHO, 1978). However, the personnel responsible for registration are often insufficiently trained, supervised and motivated to permit adequate reporting using the WHO system. Also, the WHO lay reporting system covers a large number of conditions, many of which are difficult to diagnose in the absence of clinical data. The average lay reporter or registrar would find it hard, if not impossible, to learn and use the twenty groups of morbid conditions listed, and to code them appropriately. Even in the Matlab demographic surveillance area, lay
diagnosis based on local terminology of illness provided suboptimal cause-specific mortality data (Chen et al., 1980; Islam et al., 1982).

Very few demographic surveys have attempted to obtain data on 'cause of death,' in part because of the difficulties with retrospective lay diagnosis, and in part because of the limitations on interview time and questionnaire complexity. However, recent developments in infectious disease epidemiology and experience with specialized mortality studies may provide methodology to obtain more data on 'cause of death' in demographic inquiries. Essentially the diagnosis of a given disease is based on a series of questions addressed to surviving relatives regarding symptoms and signs which are reasonably specific to the condition, and which have been directly or indirectly validated by independent means. Clearly not all diseases can be diagnosed in this manner, but many of the major disorders leading to infant or child death can potentially be identified by diagnostic algorithms, and can serve as marker diseases for the proximate determinants suggested by Mosley and Chen (1984).

As a preamble to the discussion of diagnostic algorithms and their application to demographic surveys, it is first necessary to consider the concept of 'cause of death.' Traditionally, classification of the cause of death has been based on the assumption that there is an underlying disease which, through a sequence of morbid conditions, leads to death (WHO, 1980). The WHO International Classification of Diseases (ICD) provides complex coding systems to establish sequences and to decide on the 'underlying' cause. Allowance is made for coding parallel disease processes contributing to death but which are not a part of the underlying disease sequence. The system is complex, and even with
physician diagnoses in industrialized countries, it has been shown that cause of death data are frequently inaccurate due to misdiagnosis, misclassification, coding errors and 'diagnostic habit' (i.e., physician preference for certain diagnoses) (WHO, 1980). Moreover, analysis of data using multiple causes of death has shown that the concept of an 'underlying cause' is untenable in many situations, especially at the extremes of age, where in many cases death is due to multiple causes (WHO, 1980; Goodman et al., 1982).

In developing countries the majority of deaths in childhood cannot be attributed to a single disease or 'cause.' Death often results from the cumulative effects of multiple recurrent illness in combination with impaired nutrition (Chen et al., 1980b; Heywood, 1982; Mata, 1978; Martorell and Ho, 1984; Mosley and Chen, 1984; Puffer and Serrano, 1973). We therefore have to consider the constellation of diseases associated with death rather than single conditions. However, even this concept may have limited value since, with some notable exceptions such as neonatal tetanus or other neonatal conditions, the sequence leading to death is often the lifetime burden of morbidity, whereas information collected during a terminal illness or after death may relate only to those conditions present shortly before demise. For example, in a recent Gambian study children with measles had persistently higher mortality than children without measles for nine months after the acute illness (Hull et al., 1983). Nevertheless, the diseases occurring shortly before death can provide important information of relevance to public health priorities.

In summary, it is proposed that retrospective information on a limited number of diseases associated with death be obtained from
relatives of deceased persons interviewed in demographic surveys, and that these conditions can be considered as markers for the proximate determinants of mortality.

Diagnostic Algorithms

Over the past two decades, numerous biomedical studies of specific diseases have provided diagnostic questions (algorithms) that can be used by lay workers in the field to obtain retrospective information from relatives regarding the illnesses preceding death. In particular, maternal interview data have been used to diagnose illness in dead and living children.

Potential diagnostic algorithms, their validation and limitations are described for neonatal deaths, post-neonatal or childhood deaths, and certain adult conditions. The sensitivity and specificity of these algorithms (i.e., the ability to detect true cases and non-cases of disease) and predictive value cannot be precisely quantified. Moreover, the predictive value would vary with prevalence of the disease, and all three measures might vary with the time period between death and interview, and cultural or educational factors affecting respondent recall (Barker and Rose, 1979). The principles of validation are illustrated in Table 1.

Many algorithms appear sufficiently pathognomonic to estimate the frequency of certain illnesses in field studies, and where diseases are recognized by the population, local terminology could be used to supplement these algorithms. The following section gives examples of algorithms, and although this is not exhaustive, the illustrations encompass most childhood diseases of major importance in developing countries.
Table 1. Principles of Validation

<table>
<thead>
<tr>
<th>Algorithm Diagnosis</th>
<th>True Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Positive</td>
<td>a</td>
</tr>
<tr>
<td>Negative</td>
<td>c</td>
</tr>
</tbody>
</table>

Sensitivity = \( \frac{a}{a+c} \) = (True positives detected)

Specificity = \( \frac{d}{b+d} \) = (True negatives detected)

Predictive Value = \( \frac{a}{a+b} \)

(SOURCE: Barker and Rose, 1979)

**Neonatal Deaths**

**Neonatal Tetanus**

Neonatal tetanus was once noted for its 'peculiar quietness,' and although recognized in many cultures, was frequently under-diagnosed and under-reported by health authorities. The disease is caused by contamination of the umbilical cord stump with spores of *Clostridium tetani* due to unhygienic methods for the ligation and dressing of the severed cord. The organism grows in the necrotic tissue and releases a toxin which results in muscle spasm, and protection can be provided by vaccination of the mother. Thus, neonatal tetanus reflects obstetrical care (vaccination), delivery practices, and environmental contamination as sources of tetanus spores (Foster, 1984; Stanfield and Galazka, 1984).

The WHO Expanded Program of Immunization (EPI) has conducted numerous surveys and hospital-based studies, and devised an
algorithm which appears relatively specific for neonatal tetanus (Table 2) (Stanfield and Galazka, 1984; WHO EPI, 1983).

Table 2. Diagnostic Algorithm for Neonatal Tetanus

1. Babies born alive who die between the third and thirtieth day of life.

2. History of normal suckling and crying at birth and for at least two days after birth.

3. Onset of illness between 3 and 28 days of age.

4. History of an inability to suckle followed by stiffness and/or unremitting muscle spasm ('convulsions').

(SOURCE: WHO EPI, 1983)

This lay diagnosis has been validated by the following criteria:

(a) The age distribution of putative tetanus deaths conforms to the expected distribution based on physician diagnosis (mean age of death between 7 and 10 days), and differs from the age distribution of other neonatal conditions which predominantly occur within two days of birth (Figure 2).

(b) Putative tetanus cause-specific mortality is negligible if mothers received two or more tetanus toxoid vaccinations during pregnancy, or if traditional birth attendants (TBAs) are trained in proper aseptic care of the umbilical cord stump (Table 3).

(c) Total neonatal mortality is reduced if mothers have received tetanus toxoid vaccination in populations with prior evidence of a high incidence of neonatal tetanus (Table 4).
Table 3. Influence of Training of Traditional Birth Attendants (TBA) and Administration of Tetanus Toxoid During Pregnancy on Neonatal Mortality Rates by the Cause of Death, Bangladesh, 1980

<table>
<thead>
<tr>
<th>Study Group:</th>
<th>No. of Children Delivered</th>
<th>No. of Deaths</th>
<th>Neonatal Mortality Rates (per 1,000 live births)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery by trained TBA</td>
<td>713</td>
<td>17</td>
<td>24 6 7 6 6 6</td>
</tr>
<tr>
<td>Immunization with tetanus toxoid (2 doses)</td>
<td>771</td>
<td>30</td>
<td>39 1 23 10 4</td>
</tr>
<tr>
<td>Control Group</td>
<td>998</td>
<td>85</td>
<td>85 24 25 17 19</td>
</tr>
</tbody>
</table>

(SOURCE: Stanfield and Galazka, 1984)
Table 4. Neonatal Mortality Rates, by the Immunization Status of the Mothers and by the Age at Death (0-28 days or 4-14 days), Bangladesh, 1979

<table>
<thead>
<tr>
<th>Immunization Status of Mother</th>
<th>Mortality Rates (per 1,000 live births)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Days 0-28</td>
</tr>
<tr>
<td>Two doses of tetanus toxoid</td>
<td>43</td>
</tr>
<tr>
<td>in 1978-79 during the pregnancy</td>
<td></td>
</tr>
<tr>
<td>Primary immunization in 1974, and reimmunization in 1978-79 during the pregnancy</td>
<td>56</td>
</tr>
<tr>
<td>Two doses of tetanus and diphtheria toxoid (Td) in 1974, four to five years before the pregnancy</td>
<td>64</td>
</tr>
<tr>
<td>One dose of tetanus and diphtheria toxoid in 1974, or one dose of tetanus toxoid in the pregnancy</td>
<td>68</td>
</tr>
<tr>
<td>Never immunized against tetanus</td>
<td>78</td>
</tr>
</tbody>
</table>

(SOURCE: Stanfield and Galazka, 1984)

(d) Putative neonatal tetanus deaths are higher in rural than urban areas where contamination of the cord stump with animal excreta containing tetanus spores is more frequent. The disease is also more common in societies which use animal excreta to dress the cord stump or as material for housing construction. (Table 5).
Table 5. Number of Neonatal Deaths and Neonatal Tetanus Deaths and Their Respective Mortality Rates per 1,000 Live Births in Three Ecological Areas, Based on a National Tetanus Mortality Survey in Pakistan, 1981

<table>
<thead>
<tr>
<th>Ecological Area</th>
<th>No. of Live Births</th>
<th>Neonatal Mortality</th>
<th>Neonatal Tetanus Mortality</th>
<th>Proportion of All Neonatal Deaths Due to Tetanus (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No. of Deaths</td>
<td>Rate per 1,000 Live Births</td>
<td>No. of Deaths</td>
</tr>
<tr>
<td>Urban: slums</td>
<td>4,237</td>
<td>172</td>
<td>41</td>
<td>78</td>
</tr>
<tr>
<td>Rural: agriculture</td>
<td>6,347</td>
<td>362</td>
<td>57</td>
<td>216</td>
</tr>
<tr>
<td>Rural: Cattle/ horse raising</td>
<td>3,274</td>
<td>189</td>
<td>58</td>
<td>138</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13,858</td>
<td>724</td>
<td>52</td>
<td>432</td>
</tr>
</tbody>
</table>

(SOURCE: Stanfield and Galazka, 1984)
Low Birthweight, Birth trauma, and Asphyxia

Low birthweight due to intrauterine growth retardation is prevalent in many developing countries as a result of poor maternal nutrition, short birth spacing, or infections during pregnancy, particularly with malaria (Villar and Belizan, 1982; McGregor et al., 1983). Birth trauma and asphyxia usually are due to complications of delivery associated with poor obstetric care. These three conditions generally lead to death during the early perinatal period. Although diagnostic algorithms have not been carefully devised and tested, these conditions can be potentially diagnosed by the algorithm in Table 6.

Table 6. Birth Trauma, Asphyxia, and/or Low Birthweight

1. Stillborn infant or infant dying within the first week of life.
2. Failure to suckle or cry normally after birth and at any time prior to death.
3. Very small infant (suggestive of low birthweight due to intrauterine growth retardation or prematurity).
4. History of prolonged or complicated labor.
5. Signs of trauma, particularly bruising or indentation of the skull.

(SOURCE: Adapted from WHO, 1978)

There is a need for simplified measures to identify low birthweight infants, since most births occur in the home where scales are not available for weight measurement. One possibility is the measurement of upper arm circumference, and research should be done to determine whether this permits the correct identification of low birthweight.
1.3 Congenital Abnormalities

Even in industrialized countries congenital abnormalities are frequently underdiagnosed at birth (Christianson et al., 1981). However, major external deformities such as anencephaly, spina bifida or limb reduction defects are easily recognized by the mother, and death frequently occurs in the early neonatal period.

In summary, if a death is reported during the first month of life it should be possible to discriminate between neonatal tetanus, birth trauma/asphyxia and low birthweight, or external congenital abnormalities.

2. Post-neonatal and Childhood Deaths

2.1 Diarrhea/Dysentery

Numerous studies have shown that diarrhea is associated with infant and child deaths, particularly among non-breastfed infants or during supplementation and weaning. The age-specific incidence of diarrhea or diarrheal deaths varies with feeding practices in different societies, and the rates show marked seasonal variation. Investigation of the bacterial, viral or parasitic etiology show a common transmission mechanism of fecal contamination of food or water through poor personal hygiene, inadequate sanitation and water supplies, and unhygienic food preparation or storage. Also, poor nutrition is associated with a longer duration of diarrhea, and conversely diarrhea may impair nutrition both during the acute phase of the illness and cumulatively over the longer term. Rehydration using oral rehydration therapy can markedly reduce the
case fatality from diarrhea (Black et al., 1982; Black et al., 1983; Mata, 1983). Thus diarrhea mortality reflects environmental conditions, nutritional status and medical care.

In most studies an episode of diarrhea can be defined as a history of three to four or more liquid stools per day, and an episode of dysentery as the passage of frequent liquid stools containing blood and mucus. In addition, acute diarrheal deaths are generally associated with dehydration which can be identified by maternal interview. The suggested algorithm is given in Table 7.

Table 7. Diarrhea, Dysentery and Dehydration

1. History of 3-4 or more liquid stools per day (diarrhea).
2. Passage of blood and mucus (dysentery).
3. Dry mouth, dry wrinkled skin, sunken eyes, lack of urine, and in young infants depressed fontanelle (dehydration).
4. The above conditions should have occurred at time of death.

(SOURCE: Adapted from Black et al., 1982)

In a Bangladesh study, this definition was validated by obtaining a history from the mother and examining a single stool specimen. Agreement was obtained in 80% of cases. Also, the mothers' subjective reports of diarrhea were compared with reports based on the above definition, and agreement was obtained in 97% of cases (Black et al., 1982). However, a less stringent definition of diarrhea used in the Machakos project led to an overestimation of diarrheal incidence based on maternal recall (Leeuwenburg et al., 1984b). Validation has also been derived from studies of prevention or treatment.
Measles

Measles is a significant cause of infant and child mortality in developing countries. Case-fatality is higher in younger children, children with severely impaired nutrition, and in cases of more severe illness with associated complications such as diarrhea or pneumonia (Foster, 1984; Hull et al., 1983; Koster et al., 1981; Morley, 1963). Medical care can reduce mortality by the treatment of complications (Jacob et al., 1980). Recent studies have also shown higher measles mortality associated with overcrowding (Loening and Coovadia, 1983) or with the occurrence of several cases within a single family (Aaby et al., 1981), suggesting that severity of infection may be related to the infective dose. Vaccination can reduce short-term mortality (Hull et al., 1983), although longer-term survival may not be improved due to the competing risk of other diseases (Kasongo Project Team, 1981). Thus, measles mortality is reflective of the epidemiology of the disease (epidemics and age of infection), preventive and curative measures, nutritional status, and environmental/socioeconomic conditions (e.g., crowding).

The WHO EPI (1983) algorithm for the diagnosis of measles is given in Table 8. Lay diagnoses have been used successfully in numerous field studies of vaccine efficacy (Aaby et al., 1981; Hull et al., 1983; Leeuwenburg et al., 1984a; Kasongo Project Team, 1981). Also, the disease is commonly recognized by the community.
Table 8. **Measles Algorithm**

1. History of a blotchy rash lasting 3 or more days, followed by peeling of the skin.
2. History of fever.
3. History of cough, runny nose, and red eyes.
4. The above conditions should have occurred within 3 months of death.

*(SOURCE: WHO EPI, 1983; Leeuwenburg et al., 1984a)*

The Machakos project in Kenya examined the discriminating value of different signs of measles (see Figure 7). It was shown that the rash and subsequent peeling skin (desquamation), cough and conjunctival inflammation provided maximum discrimination between cases with confirmed measles and control children with other illnesses (Leeuwenburg et al., 1984a). Table 9 shows the sensitivity, specificity and predictive value of measles diagnosis based on an algorithm of clinical signs, compared to laboratory diagnoses based on virus isolation or antibody titres. The sensitivity and predictive value of the algorithm exceed 90 percent.

Table 9. **Validation of Measles Diagnosis**

<table>
<thead>
<tr>
<th>FINAI. LABORATORY DIAGNOSIS</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLINICAL DIAGNOSIS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>441</td>
<td>44</td>
</tr>
<tr>
<td>Negative</td>
<td>18</td>
<td>53</td>
</tr>
<tr>
<td>459</td>
<td>97</td>
<td>556</td>
</tr>
</tbody>
</table>

Sensitivity = 441/459 = 96%
Specificity = 53/97 = 54%
Predictive Value = 441/485 = 91%

*(SOURCE: Leeuwenburg et al., 1984a)*
Whooping Cough

Studies suggest that whooping cough (pertussis) is a significant cause of death in Africa (Morley et al., 1966; Voorhoeve, 1978; Muller et al., 1984), and like measles, mortality is higher in younger children and in cases with associated complications. Whooping cough adversely affects child nutrition and can lead to persistent respiratory symptoms (Morley et al., 1966; Mata, 1978). The disease can be prevented by vaccination (Voorhoeve et al., 1978; Muller et al., 1984). Thus, whooping cough mortality reflects the disease epidemiology, and preventive or curative care. The WHO EPI algorithm is given in Table 10.

Table 10. Whooping Cough

1. History of severe cough persisting for 2 or more weeks.
2. Recurrent bouts of coughing with characteristic "whoop".
3. Cough followed by vomiting.

(SOURCE: Adapted from WHO EPI, 1983; Voorhoeve et al., 1978)

In a Kenyan study using similar diagnostic criteria based on lay interviews, the diagnosis of whooping cough could be confirmed by more objective clinical investigations in 40 percent of cases. Also, when mothers of children with confirmed whooping cough were reinterviewed after an interval of 6-12 months, 96 percent gave a concordant or affirmative history of previous whooping cough, suggesting reliability of recall for positive cases in which a clinical diagnosis had been made (Voorhoeve et al., 1978). A number of vaccine trials have shown declines in whooping cough cases diagnosed by similar algorithms (Cook, 1978; Muller et al., 1984).
Acute Lower Respiratory Tract Infections

Acute lower respiratory tract infections (ALRTI) such as pneumonia and bronchiolitis of bacterial and viral origin have been identified as major causes of child mortality, particularly in highland populations of Papua New Guinea (Riley et al., 1981a), but also may be important in the Sub-continent (Bulla and Hitze, 1978; Chen et al., 1980a). The case-fatality rate is higher among infants, undernourished children, and in overcrowded conditions, and antibiotic treatment can reduce mortality substantially (Foster, 1984; McCord and Kielmann, 1978; Riley et al., 1981b). Thus like measles and pertussis, ALRTI reflect disease epidemiology (geographic area, age, season), nutrition, living conditions and medical care.

An algorithm for ALRTI is given in Table 11. Although not adequately validated, vaccine trial data suggest these disorders can be diagnosed by history (Riley et al., 1981a).

Table 11. Acute Lower Respiratory Tract Infection

1. Cough and fever
2. Difficulty in breathing or rapid respiration due to shortness of breath or chest pain.
3. Duration less than two weeks.

(SOURCE: Riley et al., 1981a; Essex, 1978)

Tuberculosis

Tuberculosis in childhood is difficult to recognize due to its numerous manifestations and chronic symptomatology. Table 12 gives a possible algorithm based on WHO suggestions which have not been evaluated (WHO, 1978; WHO FPT, 1983).
Table 12. Tuberculosis

1. Chronic cough for 3 months or more (unresponsive to antibiotic treatment).
2. Weight loss.
5. Abdominal swelling.
6. Painless swellings (lymphnodes) in neck, under the arms or in the groin.
7. Swelling of the joints of slow onset.

(SOURCE: Adapted from WHO, 1978; WHO EPI, 1983)

Malnutrition

Protein-calorie malnutrition is well recognized as a serious health problem. Undernourished children have a higher probability of death, and of more severe or protracted illness from diseases such as diarrhea, ALRTI, measles and whooping cough, due to impaired immune response or impairment of other body defenses (e.g., integrity of the mucus membrane of the gut or respiratory tract) (Black et al., 1983; Mata, 1983; Martorell and Ho, 1984). Diagnosis of malnutrition or under-nutrition is usually based on clinical signs or anthropometric measures and may be difficult to identify from history alone. Puffer and Serrano (1973) conducted a Latin American study of childhood mortality in which a series of questions were asked about the nutritional status of dead children. They found that they could identify clinical malnutrition from retrospective data even though the death certificates often specified other underlying causes. The algorithm is given in Table 13.
Recent studies in Indonesia suggest that vitamin A deficiency, which is a known cause of blindness, may also be associated with increased risk of child mortality, and a higher incidence of morbidity from diarrheal or respiratory disease (Sommer et al., 1983 and 1984). Night blindness is a characteristic defect with vitamin A deficiency and may provide a simple field test for this condition. Studies by Sommer et al. (1980) show that 97% of children with night blindness have objective evidence of impaired vision on ophthalmic examination, and mean serum levels of vitamin A in children with night blindness (13.4 μg/dl ± SE 0.35) were significantly lower than for normal children (18.3 μg/dl ± SE 1.00). Moreover, a history of night blindness correctly identified 84% of children with clinical evidence vitamin A deficiency (xerophthalmia). Thus, night blindness appears to be a useful marker for vitamin A deficiency, which in turn is related to nutritional practices and to risks of morbidity and mortality.

The algorithm for night blindness is given in Table 13. The condition is recognized by mothers in Indonesia as "buta ayam" (chicken blindness).

Table 13. Severe Protein Calorie Malnutrition and Vitamin A Deficiency

1. History of weight loss (moderate or severe).
2. Did the child's arms, legs, body or face become thinner?
3. Did the child's legs, body or face become swollen (edema)?
4. Could the ribs be seen more prominently through the skin?
5. Did the child's hair fall out, pull out easily, or change color?
6. Does the child have difficulty moving around the house or in locating food or toys after dark, compared to other children of the same age? (Vitamin A)

(SOURCE: Puffer and Serrano, 1973; Sommer et al., 1980)
Malaria

Although recognized as a serious cause of morbidity and mortality, and of low birthweight, malaria is difficult to diagnose without laboratory investigations to demonstrate parasites in a peripheral blood smear (Bradley and Keymer, 1984; McGregor et al., 1983).

WHO (1978) has suggested that intermittent high fever with chills and prostration can be used as a crude diagnostic algorithm, but this has not been evaluated, and hospital studies of clinical diagnosis correlated with blood smears show considerable error (Essex, 1978). However, in areas where malaria is endemic, the severe form of the disease (largely due to P. Falciparum) is often a recognized entity, and has a local name which could help identification. Further studies are needed to establish whether diagnosis based on history is feasible.

Trauma

Deaths from trauma are not infrequent both among children and adults. Usually such deaths are easily identified (Chen et al., 1980a; Fortney et al., 1983), although recall may be affected by legal or cultural factors which make respondents reticent to admit to injuries due to suicide or homicide. The WHO (1978) classification of causes of injury is given in Table 14.
Table 14. External Causes of Injuries

1. Bites or stings of venomous animals
2. Accidental burns
3. Accidental drowning
4. Accidental poisoning (other than food poisoning)
5. Transport (traffic) accidents (involving railway, boats, aircraft, motor vehicles, other vehicles, animals being ridden or drawing vehicle)
6. Other accidents
7. Suicide, self-inflicted injury
8. Homicide, assault
9. Violence, unknown whether accident, self-inflicted or assault


Maternal Mortality

Maternal mortality during pregnancy, labor and the puerperium is poorly reported even in industrialized countries (Smith et al., 1984). Limited studies in developing countries have shown extremely high levels of maternal mortality, particularly among very young or older mothers, and primiparous and high parity women, and maternal deaths may contribute substantially to total adult female mortality (Chen et al., 1974; Rhinehart et al., 1984).

Demographic surveys often obtain estimates of adult mortality from information on orphanhood or widowhood (UN, 1983). If a female death was identified it would be possible to inquire whether death occurred during pregnancy, labor or the puerperium, and to identify certain conditions associated with death (e.g., abortion, convulsions, prolonged labor, hemorrhage, and sepsis).
Several investigations have used routine registration, hospital-based data, health care provider interviews, and physician inquiries into maternal deaths, or linkage of birth and death records to estimate maternal mortality in developing countries. However, only two studies in Egypt and Indonesia have utilized lay workers to interview the relatives of deceased women of reproductive age (Fortney et al., 1983). In Egypt, 1,135 deaths in women of reproductive age were identified from registration data, and relatives were interviewed within two months of death. The interview questionnaires were reviewed by a medical panel to reach a final diagnosis. When a 10% sample of interviews was resubmitted to the panel, there was a high degree of consistency in allocating the death to maternal causes (Fortney et al, 1983).

A possible algorithm for use in surveys of adult mortality is given in Table 15.

Table 15. Maternal Deaths

1. Was the woman pregnant when she died, and if so, how many months had she been pregnant? (In some cultures it might be better to ask whether the woman was menstruating regularly in the month before death.)

2. When did death occur in relation to delivery (e.g., before, during or immediately after)?

3. Did the woman have a pregnancy which terminated within two months prior to death?

4. Was death associated with vaginal hemorrhage, prolonged labor (more than 2 days), high fever and shock (sepsis), convulsions (eclampsia)?

5. What was the outcome of the pregnancy (live birth, still birth, neonatal death)?

6. What medical or traditional health care did the woman receive?

7. History of induced abortion.

(SOURCE: WHO, 1978; Fortney et al., 1983)
Problems and Limitations of Diagnostic Algorithms

Experience has shown that retrospective demographic inquiries encounter problems of omission of events, errors in the timing of events, misstatement of age, etc. It is to be expected that these problems of recall and misstatement will be greater if retrospective techniques are used to obtain information on diseases preceding death. However, experience with specific diseases such as neonatal tetanus is reassuring in this regard, and at least suggest the feasibility of studying certain conditions. There is need for further empirical research to determine which questions or groups of questions have most predictive value, and in some cases scoring systems may be required to give greater weight to questions which have greatest predictive value.

Two further issues that need to be addressed are the duration of the interval between death and interview, and the interval between disease onset and death. It is to be expected that omissions or recall errors will be greater with longer intervals prior to interview. For example, studies of neonatal mortality and neonatal tetanus in the Ivory Coast suggest that omissions are minimal for interviews conducted 1-7 months after birth, and that there is more marked underestimation for intervals longer than one year (Stanfield and Galazka, 1984). Although ascertainment and precision of diagnosis may be increased if only recent events are studied, larger sample sizes will be required to ensure sufficient numbers of events.

The interval between disease onset and death is more problematic. Chronic conditions of long duration which persist up to death do not present major difficulties. However, in the case of acute conditions such as measles, although the disease is of short duration, the
subsequent debility due to the acute illness can increase the risk of death for a considerable period of time following the initial episode (Hull et al., 1983). Clearly the reference period may vary from one disease to another and there is a need to use multiple time intervals.

There is no simple solution to the question of appropriate reference periods, but it probably would be best to restrict inquiries to deaths within the past 2-5 years of interview, and to illnesses occurring within a three-month period preceding death. The latter time period could be subdivided into shorter intervals (e.g., at time of death, < 1 week, < 1 month, etc.).

Another question is the appropriate respondent and the unit of observation to be used. Information on infant or child deaths is usually obtained from the mother, but this excludes women who have died, and children of dead mothers may have a very different mortality risk to children whose mothers survive. Also, if women are the sole respondents it would not be possible to estimate female adult or maternal mortality from orphanhood or widowhood data.

Another issue is the importance of studying health problems in the family. There is much evidence to suggest that some women are prone to repeated child loss and that this may relate to family factors. Also, overcrowding is an important factor in infectious disease risk; disease transmission frequently occurs within families; and disease severity may be related to illness clustering within households. These and other considerations would suggest that the unit of observation should be the household or family as in the Malaysian Family Life Survey, rather than an individual woman as in the WFS surveys (Davanzo, 1984; WFS, 1983).
Numerator data on the distribution of diseases associated with death could be used to establish public health priorities. Also, such numerator data can be related to population exposure data (e.g., socioeconomic characteristics) to estimate rates or proportions of outcomes for different exposure groups. However, this only partly addresses the issues raised in the Mosley-Chen (1984) framework, in that underlying socioeconomic determinants are linked to markers of proximate determinants (in this case terminal illness), but there is limited information on the operation of the proximate determinants per se. To complete the schema, information is required on morbidity among survivors, and on the factors associated with disease risk or utilization of medical care, which influence both morbidity and case-fatality. These issues are considered in subsequent sections.

Studies of Morbidity

Demographic studies seldom measure morbidity and this leaves a gap in the information on the causal chain linking underlying socioeconomic characteristics with mortality. For example, in the association between maternal education and child survival, it is important to know whether children of poorly educated mothers have higher mortality because they suffer more frequent or multiple illness as a consequence of exposure or lack of preventive care, because these illnesses are more severe perhaps as a consequence of under-nutrition, or because they have less access to therapeutic care. This information is needed both to understand how education affects health, and to devise appropriate interventions.

To provide these missing links, it is necessary to undertake morbidity surveys in conjunction with mortality surveys, and since
morbidity is a more frequent event than mortality, smaller study samples are required. Ideally, morbidity surveys could be conducted on random subsamples of populations surveyed for mortality, although if specific subgroups are of interest, purposeful selection could be made (e.g., for more educated women in populations with a low prevalence of higher education). Also, cluster sampling may provide a cost-effective approach in certain situations (Henderson and Sundaresan, 1983).

The methodology for morbidity measurement is well established in the epidemiologic literature and could be incorporated into demographic surveys. The disease algorithms previously described can be easily used for this purpose and questions asked about current status as well as illness over variable periods preceding interview.

In addition to a history of illness, it is possible to examine subjects for current illnesses, especially nasopharyngeal and skin infections, and to take anthropometric measurements for evaluation of nutritional status (Martorell and Ho, 1984). Simple observation can also detect disabilities such as blindness or paralysis, and an algorithm for polio is given as an example in Table 16. In an Indonesian study of 50 clinically confirmed cases of polio, 84 percent were diagnosed by the lay interviewers using a similar algorithm (Ulfah et al., 1981).

Table 16. Previous Poliomyelitis

1. Flaccid paralysis of the leg(s), arm(s), and/or trunk with wasting of the affected muscles.

2. History of an acute illness with abrupt onset of paralysis developing fully within 3 days among children under 6 years.

3. History that paralysis was not present at birth or associated with serious injury and mental retardation.

(SOURCE: Adapted from WHO EPI, 1983; Ulfah et al., 1981).
Finally, additional information can be obtained on other relevant factors such as sources of exposure, nutrition and breastfeeding, medical care seeking behavior, and preventive measures (vaccination, contraception, personal hygiene). These will be discussed further in the next section.

The appropriate recall reference period (e.g., illness in the last 3 months, 2 weeks, or currently) would vary with the frequency of the disease and its duration. With acute illnesses of short duration, incidence measures (i.e., new episodes in a given period) are of value, whereas for diseases of long duration, point prevalence measures (i.e., current status) are more appropriate. However, for illnesses of short duration but high incidence, such as diarrhea, prevalence measures are also useful (Black et al.1982; Black, 1984). The relationship between incidence and prevalence depends on the duration of illness; \[ P = I \times D \] (where \( P \) = prevalence, \( I \) = incidence, and \( D \) = duration).

The appropriate reference period will also depend on the recall ability of the respondent. With a disease such as measles which occurs only once in an individual's lifetime and has distinctive characteristics, longer recall periods can be used; whereas for common, recurrent, and less distinctive illnesses (e.g., diarrhea), a shorter recall interval such as two weeks is more appropriate to avoid either omission of episodes or the aggregation of repeated episodes.

Morbidity surveys can be applied to other demographic problems such as infertility. The proportions childless at a given age (e.g., 35 or above) are a reasonable measure of the prevalence of primary infertility and this information is routinely obtained from census or survey data. There is strong evidence to suggest that where primary infertility is a
major problem (e.g., proportions childless over 10 percent), the etiology is likely to be sexually transmitted diseases (STDs) mainly due to gonorrhea or chlamydia, and possibly post-partum or post-abortion infection. The common mechanism underlying infertility is pelvic inflammatory disease (PID) leading to obstruction or damage of the fallopian tubes (Muir and Belsey, 1980).

It is possible to obtain a history of PID in relation to prior STD or obstetric/abortion infection, so as to better assess the causes of infertility. A possible algorithm is given in Table 17.

Table 17. PID and STD

1. History of lower abdominal pain and fever, with or without vaginal discharge (PID).
2. Timing of symptoms in relation to delivery or abortion or known episode of STD.
3. Urethral discharge in males (STD).

(SOURCE: WHO, 1984; Arya et al., 1980)

Information using comparable algorithms has been shown to be of predictive value. Arya et al. (1980) conducted aggregate level studies in low and high fertility areas of Uganda, and found that a history of lower abdominal pain suggestive of PID or a history of urethral discharge in males, to be markedly more prevalent in the population which had a high proportion of primary infertility. In a WHO (1984) case-control study of acute PID in developing countries, a similar algorithm suggestive of prior infection was shown to be associated with an increased risk of a recurrent infection (the relative risks were 5.5 for one prior episode, 12 for 2-3 episodes, and 18 for 4 or more) (Gray,
1985). Other data show that repeated PID episodes increase the risk of infertility (Westrom, 1980). Also, in a study of ectopic pregnancy, women who had a prior history of PID were found to have evidence of past infection at time of surgery in 69 percent of cases (Gray and Campbell, 1984). This experience with aggregate and individual level data suggests that a putative diagnosis of PID or STD is associated with infertility, that a past history of PID is predictive of recurrent episodes and increases the risk of infertility, and that information obtained by interview can be validated by objective clinical evidence.

In summary, given that it is possible to identify diseases associated with morbidity as well as death, it is now necessary to turn to measurements of the risk factors affecting these markers of the proximate determinants.

Measurement of Risk Factors

A risk factor may be defined as an attribute or exposure that increases the probability of occurrence of disease or other outcome. Risk factors are measures of those antecedents of disease such as socioeconomic status, environmental conditions, therapy, etc., which influence the probability of illness, and the outcome in terms of mortality or growth faltering. The chain of events can be investigated in terms of morbidity and mortality since both have shared antecedents.

The range of possible risk factors has been described elsewhere (Mosley and Chen, 1984; Ware, 1984), and need not be exhaustively covered in the present paper. In brief, these factors comprise:
(a) Maternal risk factors such as age, parity, birth interval and child care arrangements.

(b) Environmental risk factors or sources of exposure such as water supplies and sanitation; food preparation/storage, breastfeeding, supplementation and weaning; housing conditions (including overcrowding and construction materials); personal hygiene (use of soap, etc.).

(c) Nutritional risk factors are food availability, types of foodstuffs and their relative contributions to the diet; food distribution in the family with particular emphasis on inequalities by sex, age, or bodysize. This information is often difficult to obtain by interview because 24-hour dietary histories may be unreliable, especially for children (Brown, 1984). However, since detailed prospective studies are not usually feasible, dietary histories are of necessity the main source of data. Wherever possible, dietary history data should be validated on a subsample using more precise methods. In the Machakos study, semi-quantitative maternal recall data were compared with estimates of nutrient intake based on direct measurements of foods, and reasonable agreement was found for most dietary constituents (Kusin et al., 1984). With infants and young children, breastfeeding, supplementation and weaning are clearly important nutritional risk factors as well as measures of exposure, and in this regard the age of the child at supplementation or weaning is of critical importance (Jason et al., 1984; Seward and Serdula, 1984).

(d) Risk factors for injury are patterns of maternal or surrogate child care, number of children under care, hazards such as cooking
facilities (open fires) or unprotected water (e.g., canals or tanks), motor vehicles, domestic and other animals,

(e) Risk factors measuring personal illness control are preventive measures such as vaccination, contraceptive use, antenatal care, or malaria prophylaxis. Curative measures such as cultural practices in response to illness (e.g., traditional remedies, withholding of food), self-medication using modern technologies (e.g., use of oral rehydration therapy, malaria therapy), and care-seeking behavior (e.g., use of traditional practitioners or modern medical services). With regard to modern service utilization, it is necessary to consider acceptability and availability of services per se, and accessibility in terms of distance or cost (Scrimshaw and Hurtado, 1984).

Finally, again drawing on the Mosley-Chen (1984) framework, underlying socioeconomic determinants may be considered as indirect risk factors (operating through the above proximate risk factors), or as effect modifiers. These underlying determinants are individual-level variables such as parental education, occupation, tradition, attitudes and normative beliefs and practices; household-level variables such as income or wealth; and community variables, e.g., ecology, disease epidemiology, political economy and health system. Some individual- or household-level variables can be easily quantified and are frequently measured (education, occupation, or income), others are more complex subjective states which are difficult to measure, and community-level variables present measurement problems beyond the scope of this paper.

From the foregoing discussion, it is clear that the measurement of risk factors is lengthy, detailed and difficult. The feasibility of
obtaining reliable information varies from item to item, and sources of error or bias abound. Nevertheless, certain key variables have been measured in field settings.

For logistic reasons, information of this detail can only be obtained on limited numbers of subjects, and we next consider how such data may be collected so as to quantify the effects of risk factors on proximate disease indicators or mortality outcomes.

Application of Case-Control Methodology

Case-control studies are epidemiologic investigations in which cases are defined as individuals with a specified disease or outcome (e.g., growth faltering or death), and controls are defined as individuals free of the disease or outcome of interest. Controls should, however, be representative of the population from which cases are drawn. Comparisons are made between cases and controls with respect to risk factors which may be individual characteristics, exposures or behaviors. Case-control studies are retrospective in that information on antecedent risk factors is only obtained after the disease or outcome has occurred in case subjects, and in a strict sense, such studies can only suggest but cannot prove causality. This approach has been extensively applied to epidemiologic problems and there is large literature on the design, conduct, analysis and interpretation of case-control studies of acute or chronic disease, particularly in hospital settings (Schlesselman and Stolley, 1982). However, this study strategy has seldom been applied to problems of child survival in developing countries, in part, due to the difficulty of identifying an unbiased sample of cases and controls. Recently, case-control methods
have been applied to the study of risk factors for fatal and nonfatal outcomes of disease (Ryder et al., 1985), and for the evaluation of vaccine efficacy (Ministry of Health Honduras, 1985; Orenstein et al., 1982).

The advantage of case-control studies is that information need only be obtained on limited numbers of cases or controls, rather than a whole survey sample or population, and simple procedures for estimating sample size are given in Schlesselman and Stolley (1982). This parsimony of sample size makes the collection of detailed information using lengthy interview and record forms more feasible in field settings.

Case-control studies are particularly useful for the investigation of rare diseases or outcomes, but may be applied with more frequent conditions (Gray, 1984). It would, for example, be possible to define a case as a child death identified in the course of a demographic survey, and to define a control as a child which survived. Similarly, cases could be defined as children with growth faltering or with specified diseases identified in morbidity surveys, and controls would be children free of these conditions. In each example, data on risk factors could be obtained from interview with parents. Moreover, if the survey is a random sample of the population, then the cases and controls would constitute an unbiased sample.

The objective is to measure the frequency of occurrence of risk factors among cases and controls to assess the risk associated with a given factor. If exposure is greater in cases than controls it suggests an increased risk, and conversely, if exposure is lower in cases than controls it suggests a reduced risk associated with the factor under study.
The basic tabulation of data is straightforward, as shown in Table 18. The number of exposed and nonexposed cases is denoted by a and c, and the number exposed and nonexposed controls as b and d, respectively.

Table 18.

<table>
<thead>
<tr>
<th>Exposure to Risk Factor</th>
<th>CASES</th>
<th>CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>YES</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td></td>
<td>c</td>
<td>d</td>
</tr>
<tr>
<td>NO</td>
<td>n₁</td>
<td>n₂</td>
</tr>
<tr>
<td></td>
<td>m₁</td>
<td>m₂</td>
</tr>
</tbody>
</table>

The odds of exposure among cases is \( \frac{a}{c} \), and among controls \( \frac{b}{d} \). The risk of disease or outcome in cases associated with exposure to the risk factor is measured by the odds ratio (OR):

\[
OR = \frac{a/c}{b/d} = \frac{a \times d}{c \times b}
\]

An example is given in Table 19.

An odds ratio equal to 1 implies no association, \( OR > 1 \) implies increased risk, and \( OR < 1 \) implies a decreased risk or protective effect of the factor.

A conventional Chi square test on one degree of freedom can be used as a test of statistical significance, and approximate ninety-five percent confidence intervals for the odds ratio can readily be estimated from:

\[
\ln OR \pm 1.96 \quad 1/a + 1/b + 1/c + 1/d
\]
Table 19a. Example of a Case-Control Study of Neonatal Tetanus Deaths in Relation to Birth Attendant

<table>
<thead>
<tr>
<th>CAUSE OF DEATH</th>
<th>Cases (Tetanus Death)</th>
<th>Controls (Nontetanus Death)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Untrained Midwife</td>
<td>102</td>
<td>42</td>
</tr>
<tr>
<td>Relative</td>
<td>24</td>
<td>28</td>
</tr>
</tbody>
</table>

Odds Ratios: Untrained vs. Relative: OR = \(\frac{102 \times 28}{24 \times 42} = 2.83\)

Approximate 95% confidence intervals: 1.5 - 5.4.

(SOURCE: Smucker et al., 1980; estimates by present author from data in Table 2)

Table 19b. Example of a Case-Control Study of Fatal and Nonfatal Diarrhea in Relation to Nutritional Status

<table>
<thead>
<tr>
<th>NUTRITIONAL STATUS</th>
<th>Cases (diarrheal deaths)</th>
<th>Controls (nonfatal diarrhea)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 90th Percentile</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>&gt; 90th Percentile</td>
<td>4</td>
<td>23</td>
</tr>
</tbody>
</table>

OR = 23.0

95% confidence intervals: 2.0 - 262.

(SOURCE: Ryder et al., 1985)

Analysis is not restricted to binary variables, and continuous variables can be categorized to examine "dose response relationships" or consistency of effect (e.g., maternal education can be divided into several subcategories and the risk estimated relative to women in the highest educational group). An example using household "wealth" is given in Table 20.
Table 20. Association Between Household Wealth and Child Death

<table>
<thead>
<tr>
<th>Household Wealth Class</th>
<th>Deaths (cases)</th>
<th>Survivors (controls)</th>
<th>Odds Ratios</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Low)</td>
<td>114</td>
<td>167</td>
<td>2.4</td>
</tr>
<tr>
<td>2</td>
<td>70</td>
<td>136</td>
<td>1.8</td>
</tr>
<tr>
<td>3</td>
<td>74</td>
<td>161</td>
<td>1.6</td>
</tr>
<tr>
<td>4 (High)</td>
<td>44</td>
<td>155</td>
<td>1.0</td>
</tr>
</tbody>
</table>

* Household wealth based on a scoring system and divided into quantities.

(SOURCE: Gemert et al., 1984)

The data may also be stratified or partitioned to examine associations in subgroups or combinations of variables, and logistic regression procedures allow the estimation of odds ratios for multiple risk factors and the assessment of interaction between factors (Schlesselman and Stolley, 1982).

As with all nonexperimental investigations, case-control studies are vulnerable to bias (Sacket, 1979). Selection bias may arise if cases or controls are unrepresentative of the true populations at risk (e.g., if highly educated women utilize medical care facilities more than the poorly educated, then a hospital based case-control study could be biased with respect to education), thus limiting the generalization of results. Also, selection bias may arise differentially between cases and controls if the latter are not identified from a comparable representative population (e.g., cases identified in hospitals, and controls from nonhospitalized populations). Misclassification bias can occur if case diagnosis is incorrect (e.g., true cases of disease are missed and classified as controls, or false cases of disease are
incorrectly included). Such misclassification will dilute the true association between disease and risk factors.

Recall bias can occur if information obtained from case and control subjects differs systematically in completeness or accuracy. To avoid recall bias, it is necessary to use standardized questionnaires and interview procedures and, as far as possible, to keep the interviewers "blind" with respect to the case or control status of the respondent. However, there are subjective factors which may influence recall, for example, the mother of a dead child may be motivated to provide more accurate data than the mother of a surviving child, or a highly educated mother may provide a better history than a poorly educated woman. To evaluate such recall bias one can compare case and control responses to variables suspected to be risk factors, which should be more frequent among cases, and neutral variables which should be equally distributed between cases and controls.

Another major problem with observational studies is confounding, which implies that an apparent association between a risk factor and outcome is antifactual due to the operation of a third variable. For example, if younger women are more educated, and age is related to the risk of disease, then a spurious association may be observed between education and disease. Adjustment can control for confounding (e.g., by examining the association between age and outcome after stratification on education).

Case-control designs have the advantage of parsimony if the outcome such as death is rare, but the approach is equally applicable to situations in which the risk factor of interest is rare. If tertiary education is infrequent in a population, it may not be possible to study
the rates of disease or death among the highly educated because the numbers in this category are too few. However, one can do a case-control study in which individuals are selected by exposure and nonexposure to the risk factor rather than the outcome. In Table 18, the odds of disease among the exposed is $a/b$ and among the nonexposed $c/d$. Thus, the odds ratio of disease among the exposed versus nonexposed is $a/b \div c/d = (a \times d)/(b \times c)$. In other words, the odds of disease associated with a factor are the same as the odds of the factor associated with disease. This allows considerable flexibility of application to field studies. (See example in Table 21.)

Table 21. Example of a Case-Control Study of Birth Attendant in Relation to Tetanus or Nontetanus Death

<table>
<thead>
<tr>
<th>CAUSE OF DEATH</th>
<th>Tetanus</th>
<th>Nontetanus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>102</td>
<td>42</td>
</tr>
<tr>
<td>Controls</td>
<td>24</td>
<td>28</td>
</tr>
</tbody>
</table>

OR tetanus vs. nontetanus = 2.83
95% confidence intervals: 1.5 - 5.4.

(SOURCE: Smucker et al., 1980; adapted from Table 2)

Summary and Conclusions

Demographic and epidemiologic studies of child survival have in the past yielded important information on determinants of mortality. However, if we are to expand our understanding of health problems in developing countries it is necessary to integrate these two disciplinary approaches. This paper has largely dwelt upon the application of
epidemiologic methods to demographic surveys, but equally, epidemiologists have much to learn from demographers. For example, cross-sectional and retrospective surveys could be used instead of logistically complex prospective surveillance studies of morbidity and mortality. This would result in great economies of cost and time, and in principle could yield similar information of relevance to health assessment.

In summary, it is proposed that both epidemiologic and demographic surveys be integrated to explore the use of algorithms for disease diagnosis based on retrospective interview data and direct current status observation; that surveys of mortality be accompanied by parallel surveys of morbidity in random subsamples; that interview information be obtained on risk factors; and that research designs such as case-control studies be more widely employed. Unless new and more cost-effective strategies are adopted, our knowledge of the determinants of mortality and our ability to evaluate the impact of health interventions will be constrained by incomplete information, surveillance of limited and possibly unrepresentative populations, and by the costs of field research. There is a need to further develop these interdisciplinary methodologies and to critically evaluate their feasibility in field settings.
Figure 1. Operation of the Five Groups of Proximate Determinants on the Health Dynamics of a Population*

* Proximate determinants are number 1-5.

(SOURCE: Mosley and Chen, 1984)
Figure 2. Number of Neonatal Tetanus Cases and Deaths, By Day of Death, and Number of Non-Tetanus Neonatal Deaths, By Day of Death, in Colombia (1961-66), Indonesia (Jakarta, 1981-82) and Sudan (1981)

(SOURCE: Stanfield and Galazka, 1984)
Figure 3. Relation between stage of disease and presence of

Number of children in each stage

and control children (broken line) in percent of
3 major and 3 minor criteria for measles (solid line)

(Source: Levenhburg et al., 1984)
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