83-022
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SECTION I: RESEARCH PROTOCOL

(1)   Title: _Child Mortality: Social and Biological_
Determinants

(2)   Principal Investigator: Anne R. Pebley, Ph.D.
       Co-Investigator(s), if any: A.K.M. Alauddin Chowdhury, Ph.D.
(3)   Starting Date: (for entire project): June 1, 1983
(4)   Completion Date: May 31, 1985
(5)   Total Direct Cost: (ICDDR,B Subcontract): $10,298
(6)   Scientific Programme Head:

       This protocol has been approved by the _C S R W G_
       Working Group.

                         Signature of the Scientific Programme Head
                              Date: 23 May 1983

(7)   Abstract Summary:

This project involves the secondary analysis of data which were
collected for another study (the Determinants of Natural Fertility
Study in Matlab). No new data will be collected. The data contain
no identifying information on individual subjects and, therefore,
there is no risk of violating confidentiality. Use of demographic
data from this population is vital to the study since we are
investigating the relationship between nutritional status, morbidity
and the risk of child mortality in a high mortality population.
Especially since the data already exist, we feel that the benefit
of further analyses to identify the determinants of child mortality
for outweigh any possible risks.

(8)   Reviews:

       (a) Ethical Review Committee:_____
       (b) Research Review Committee:_____
       (c) Director:_____

SECTION II - RESEARCH PLAN

A. SPECIFIC AIMS

The major aim of the proposed research is to describe the complex relationships of malnutrition and morbidity with infant and child mortality. This project will involve secondary analysis of existing prospective data on the health and nutrition of children collected in major projects (two involving public health intervention and one in a a 'natural' or non-intervention setting) in three developing countries. Newly developed methodology that permits far more complex questions to be addressed with small samples than previously possible will be employed. The need for analysis of data of this type using a common framework and more sophisticated methodology that may lead to a better understanding of the determinants of infant and child mortality has been recognized by both demographers and public health workers (Preston, 1978; Gwatkin, et al., 1980). Our specific objectives are:

1. to determine how socioeconomic factors often found to be strongly associated with infant and child survival (such as maternal education) affect the probability of children dying through more proximate causes of death (e.g., disease, nutritional status and injury);
2. to determine the relative magnitude and importance, as determinants of the probability of dying for infants and young children, of:
   a. nutritional status (both acute and chronic)
   b. episodes of gastrointestinal, systemic, and respiratory disease and other types of disease and injury
   c. the interaction of nutritional status and disease
3. to examine the relative contributions of nutritional deprivation and disease during different periods of a child's growth to the probability of dying;
4. to evaluate the relative utility of several measures of nutritional status and of morbidity as predictors of a child's risk of dying.

Over the past 20 years, at least a dozen public health intervention programs have been carried out in rural areas of developing countries with a variety of research and practical aims. Many of these projects involved the introduction (or improvement) of modern medical care; others provided nutritional supplements, nutrition education, and improved water supplies and sanitary facilities to part of their study populations. Some collected detailed information on vital events, nutritional status, and illness. We plan to carry out comparable analyses of data from two of the

* Throughout this proposal we use the term 'intervention' to refer to a field study that introduced improved health care and/or nutritional supplementation programs to a malnourished population, usually in a developing country.

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most carefully designed and executed of these projects, both of which were conducted during the 1970s: the Nutritional Institute of Central America and Panama's (INCAP) study of several Guatemalan villages and towns, and the Narangwal study conducted by the Indian Council of Medical Research and Johns Hopkins University. For comparison, the analysis will also be replicated using data collected by the International Center for Diarrheal Disease Research, Bangladesh (ICDDR,B) in villages in Matlab Thana, Bangladesh, which received no public health intervention except occasional emergency care and diarrheal treatment. These studies are described in detail in section D. Comparisons of results between the INCAP and Narangwal studies, which took very different approaches to public health intervention, and the Matlab data, will permit the disentanglement of results due to the particular characteristics of the interventions, and the cultures in which these studies took place, from results pertaining to more broadly generalizable biological and social relationships.

B. SIGNIFICANCE

Although developing countries have experienced dramatic declines in mortality at all ages since World War II, their mortality rates are still significantly higher than those of industrialized nations. Unfortunately, improvements in survivorship in developing countries seem to have slowed down or leveled off, despite the fact that mortality remains at relatively high levels (Gwatkin, 1980; Chen, 1981). A substantial proportion of these deaths occur among infants and children, and gastrointestinal and respiratory infections are leading causes.

The continuation of sustained mortality decline in developing countries will require a more precise understanding of the associations of these gastrointestinal and respiratory infections, and the intimately related problem of malnutrition, with mortality. While it has been recognized for several years that the synergism between malnutrition and infection increases the risk of mortality over the risk due to either factor alone (Scrimshaw and Gordon, 1968), a consensus on a model of possible mechanisms through which these and other factors affect mortality has only recently begun to be reached. Two versions of this model, which is described in greater detail in section D, have been presented by Mosley (1980) and Chen (1981). In the model, the risk of dying is dependent on four proximate determinants: morbidity (mediated by treatment of the disease after its inception), nutritional status, maternal characteristics, and genetic endowment. Socioeconomic and cultural factors affect these determinants either directly (as in the case of nutritional status), or indirectly (e.g. by influencing exposure to disease by affecting a child's physical environment). Unfortunately, the relationships posited by this model are, as Chen (1981:12) says, 'still inadequately documented, [and] poorly understood.'

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The evidence that is available on determinants of infant and child mortality comes primarily from two types of research, one which concentrates on the socioeconomic correlates and the other on more proximate influences on mortality. The first type includes studies by demographers and social scientists, using information from censuses, vital statistics, and surveys, and often employing multivariate models (see, for example, Behm, et al., 1976 and 1979; Haines, Avery, and Strong, 1981; Haines and Avery, 1982; Schultz, 1979; Caldwell, 1979; Carvahal and Burgess, 1978; Chackiel, 1981; Trussell and Preston, 1981; Trussell and Hammerslough, 1982). A central finding of these studies has been the importance of maternal education in reducing a child's risk of death, even when other social, economic, and environmental factors are held constant. Residence in an urban area, higher income, occupational status, the availability of medical care and modern sanitary facilities, and better housing quality have also been shown to decrease the risk of infant and child mortality. These studies play a vital role in delineating appropriate target groups for mortality reduction programs. Due to the limitations of data used, however, they have been unable to describe adequately the associations of disease and nutritional status with mortality, or to examine thoroughly the relationship between these proximate causes of death and the social, economic, and environmental factors they show to be related to the risk of dying.

The second group consists of studies carried out by epidemiologists, nutritionists, and physicians using information collected in public health interventions in developing countries. Analyses in this group have more

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Evidence available from several other types of research not discussed above provides little information on the effect of morbidity, malnutrition, and socioeconomic factors on the individual risk of dying. Puffer and Serrano's (1973) investigation of causes of death listed on death certificates is an example of numerator analysis that cannot be used to examine the effect of malnutrition on the probability of dying since there is no information on the population at risk. Clinical studies of malnourished patients (see, for example, Viteri and Pineda, 1971), while contributing information on the biological mechanisms of malnutrition and morbidity that was important for the formulation of the model described above, provide no information about the relative importance of these factors for infant and child mortality in the population. There have also been numerous aggregate analyses of the relationship between mortality rates and changes in food supply, national income, or medical techniques, either cross-sectionally or over time (see, for example, Preston, 1976; Stolnitz, 1955 and 1956; McKeown and Record, 1962; Post, 1976; Stein, et al., 1975; Curlin, et al., 1976; Solimano and Vine, 1980). While these studies contribute important information on the reasons for aggregate variations in mortality, their results provide only a very rough indication of the impact of malnutrition, morbidity and socioeconomic factors on the risk of infant and child death.

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directly examined relationships between mortality and its proximate determinants. While the quality and amount of information collected in these interventions varies widely (Gwatkin, et al., 1980), several of these projects kept very accurate records of demographic events, morbidity, and nutritional status. Two types of results have been produced by these studies. The first is estimates of the change in mortality attributable to the intervention itself, and in some cases the monetary cost of producing the change (see Gwatkin, et al., for a summary of several major projects). While these results provide an estimate of the cost of producing a mortality decline by replicating a particular type of intervention, they do not directly address the reasons for the mortality change occurring during the intervention. The second type of analyses generated by these studies are more detailed examinations of the effects on mortality of factors such as maternal supplementation during pregnancy and lactation, birth weight, the incidence of particular disease, and measures of nutritional status (for example, Mata, 1978; Mora, et al., 1978; Baertl, et al., 1970; Lechtig, et al., 1978; Kielmann, et al., 1978; Chen, Chowdhury, and Huffman, 1980; Kielmann and McCord, 1978, among others). Studies in this group have usually been handicapped by an inability to include several variables simultaneously in the analysis due to small sample size. Many also compound the small sample size problem and create sample selection bias by limiting their sample to individuals who have been under observation during the entire study period, or for a substantial portion of the project. In addition, comparison of the published results of these studies is always difficult (and often impossible) because they use a variety of variables and analytic techniques. Summarizing results from studies of this type, Preston (1978:14) said that 'the demographic returns from these studies have been disappointing ... None has provided a rich description of the main factors that seem to differentiate high mortality from low mortality groups and families ... it is appropriate only to say that much of the promise of these studies for demographic research on mortality has yet to be realized.'

The proposed research is intended to extend previous analyses of determinants of mortality significantly by thoroughly examining the relationship of gastrointestinal, systemic, and respiratory disease and malnutrition -- major roadblocks to continued mortality reductions in developing countries -- to the risk of dying. To accomplish this task we will reanalyze data from two major intervention projects and a natural setting using recently developed statistical methods. These three

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* Some of these estimates were based only on the difference in mortality rates before and during the intervention, making it difficult to attribute any change solely to the intervention itself. A few studies included a control group that was monitored during the project, and based their estimates of change on differences between the treatment and control groups. But even this procedure often was fraught with problems (Gwatkin, et al., 1980).

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projects were selected because they generated three of the most complete and carefully collected data sets available from developing countries, for the purposes of this project. Our analysis will focus on the mortality of infants and children, for three reasons. First, the risk of mortality is highest at these ages, and therefore the potential impact of programs attempting to reduce mortality is greatest among infants and children. Second, since death, even in high mortality settings, is relatively infrequent for adults, estimates of adult mortality in small populations such as those to be included in this study are subject to major sampling errors. The number of infant and child deaths is comparatively large and less subject to large random fluctuation. Third, much of the anthropometric information to be used in the analysis was collected only for infants and children.

The major product of the proposed research will be numerical estimates of many of the associations proposed in the model described by Mosley (1980) and Chen (1981). In particular, we will attempt to estimate the relative contribution of nutritional status, morbidity, and the interaction of these two factors to the risk of a child dying at a given age, holding constant possibly confounding factors such as maternal age and parity. We should be able to determine, for example, how much acute, moderate malnutrition increases the risk of death of a child with a recent history of measles. Similarly, we can compare the impact of chronic and of acute malnutrition on mortality, holding constant indices of morbidity history, and estimate the size of the interaction effect between malnutrition and episodes of diarrheal disease. We will also examine differences in these associations among age groups, to determine which factors and combinations contribute most heavily to mortality at different stages of a child's development.

Results from this analysis, compared across three very different populations, should produce detailed information about the relationships between the extent and type of improvements in nutritional status and health, and the magnitude of reduction in infant and child mortality. Combined with published data from intervention projects and from health ministries on the approximate costs of improvements in nutritional status and reduction in levels and severity of morbidity, these results should improve our ability to determine the most cost effective means to continue reductions in infant and child mortality in developing countries. More generally, the results are expected to provide a clearer picture of the process leading to mortality, and more specific and, it is hoped, more fruitful direction for future studies of mortality.

The proposed research will also attempt to determine how social and economic factors known to be associated with infant and child mortality operate through nutritional status, morbidity and use of medical services. Why, for example, do the children of more highly educated mothers experience lower mortality? Results from this part of the analysis should help to fill the gap between studies of socioeconomic mortality-determinants and research on factors that actually are the proximate causes of mortality.

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Finally, as a byproduct, the proposed research will evaluate the relative efficacy of different measures of nutritional status and morbidity as predictors of the risk of death. Our methodology will permit us to determine, for example, how much the relative risk of dying is increased for a child who is moderately malnourished by each of several measures (such as weight-for-height, height-for-age, and weight-for-age). These results should be a useful addition to current research by nutritionists and epidemiologists attempting to find appropriate measures of risk to be used in nutrition surveillance programs (for example, Trowbridge and Staehling, 1980).

C. EXPERIENCE AND QUALIFICATIONS

This project will be an interdisciplinary collaborative effort by researchers with complementary skills and experience. Familiarity with the settings and data collection procedures used in the three studies included in this analysis and experience working with the complex data sets they generated is essential to the execution of the proposed research. All of the researchers who will participate in the proposed project have expertise on one of the three projects involved. The principal investigator, Dr. Anne Pebley, is a demographer, with a strong background in research methodology as well as training in nutrition and agricultural economics. Since 1976, she has been associated with INCAP (where she worked during the summers of 1976 and 1977), and has participated in the cleaning and analysis of the INCAP-Rand surveys (see Pebley, Delgado and Brineman, 1979 and 1981; and Pebley, 1981). She also worked on developing estimates of vital rates in the INCAP study villages and towns, employing the longitudinal data to be used in this project.

Her co-investigator, Dr. Sandra Huffman, is a nutritional epidemiologist with training in population. For the past six years, she has worked with ICDDR,B on several projects (see Huffman, Chowdhury and Mosley, 1977; Huffman, Chowdhury and Sykes, 1980; Chen, Chowdhury and Huffman, 1980), including the collection of the Matlab data used in the analysis.

Dr. Alauddin Chowdhury, who has previously collaborated with Dr. Huffman, is a demographer employed as a research scientist at ICDDR,B. He is thoroughly familiar with Matlab Thana, and has participated in several projects in the Matlab villages, including collection and analysis of the Matlab data to be used in this project (see Chowdhury and Becker, 1981, and Chen, Chowdhury and Huffman, 1980).

Dr. Robert Parker, a physician and epidemiologist at Johns Hopkins, was a research associate and project officer on the Narengwal Project in Punjab, India, between 1967 and 1969. Since 1973, Dr. Parker has been involved in the analysis of data collected in this intervention project

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(see Kielman, Taylor and Parker, 1978; Taylor, et al., 1978). He brings to the proposed analysis a broad background in public health and nutrition and an intimate knowledge of the Narangwal villages and the complex intervention project conducted there.

Dr. Mark Wolff is a statistician and research associate in the Department of International Health at Johns Hopkins. He is currently restructuring the Narangwal computer data base in collaboration with members of the Narangwal working group.

Dr. James Trussell, a mathematical demographer at the Office of Population Research, is currently engaged in research on socioeconomic determinants of infant and child mortality using data from the World Fertility Survey. He has previously worked on the development of hazards models for use in demography and has recently completed a variety of demographic applications of these models, one of which is presented in the appendix to this proposal. Dr. Trussell served as a consultant to ICDDR,B in Dacca in 1975 and provided demographic advice on the collection of data in Matlab for the Determinants of Natural Fertility Study.

D. METHODS

THE STUDIES

Despite their differing designs and aims, the three studies included in this analysis all carefully collected prospective information of relatively high quality from predominantly agricultural populations in developing countries, in which chronic malnutrition and infections were common. While several other intervention studies were considered for inclusion, (see Gwatkin, et al., for a summary of some of them) most were not suitable for at least one of three reasons: (1) they did not collect adequate information on nutritional status, morbidity, and mortality, (2) the data collected were not available (or likely to be available at the beginning of the project) on computer tape or cards, or (3) their sample sizes were far too small. The characteristics of the three studies included are discussed below and summarized in Table 1. The availability of data (by type and frequency) relevant to the proposed project is listed in Table 2 for each of the three studies.

The Narangwal Nutrition Study

This project was carried out during 1968 to 1973 near Narangwal, Punjab, India as a collaborative effort between the Indian Council of

	MATLAB	**INCAP**	
Organization Conducting the Fieldwork	International Center for Diarrheal Disease Research, Bangladesh (ICDDR,B) (formerly Cholera Research Laboratory)	Division of Human Development Instituto de Nutrición de Centroamerica y Panama (INCAP)	Indian Council of Medical Research and Johns Hopkins University
Period of Study	October 1975 to April 1978	2 rural villages: 1/69-9/77 2 rural villages: 5/69-9/77 2 urban towns: 1974-1976	October 1968-May 1973 (Services started 1/70)
Original Research Objectives	Impact of Biological and Behavioral Factors on Natural Fertility	Impact of mild to moderate malnutrition on physical growth and mental development.	1. Relative impact of nutrition care and illness care on child growth, morbidity and mortality 2. Demonstrate auxiliary based nutrition and health care program.
Location	Matlab, Thana, Bangladesh	El Progreso (and more briefly, Petapa), Guatemala	Narangval, Punjab, India
Age Group Studied	0-5 year olds	0-7 year olds	0-3 year olds
Sample	Youngest children of all married women of reproductive ages, who were aged 0-5 years old at the beginning of observation, in the 14 study villages	All children 0-7 in villages between 1/69 and 3/73. Selected children in Petapa.	All children in chosen villages
Approx. Sample	2000 children	1623 children observed for at least 1/4 time	2900 children observed end of the project
Experimental Design	No intervention. Monthly measures on mothers and children.	All villages had medical clinic staffed by aux. nurse & visited weekly by doctor. Two villages received high protein-high carb. supplement. Two received low carb-low protein supplement. Same supplementation in Petapa.	Villages divided into 4 groups 1. nutrition care only 2. medical care only 3. combined nutrition and medical care 4. no treatment except for emergencies.
Reported Pre-Study IMR	125 per 1000 births	160 per 1000 births	129 (control group)
Reported Pre-Study CMR	35 per 1000 children (0 to 4 years old)	28 per 1000	19 per 1000 1-3 year olds (Control group)
Reported Post-Study IMR	Not applicable	50 per 1000 births	89/1000 (Nutrition) 70/1000 (Medical) 81/1000 (Both)
Reported Post-Study CMR	Not applicable	6 per 1000	10/1000 (Nutrition) 11/1000 (Medical) 13/1000 (Both)

	MATLAB	INCAP (In Progress)	NARANGWAL
Anthropometry for Children	Weight taken at monthly intervals	Weights, heights and 16 other measures collected at a series of specific ages	Weight and height collected monthly from 0-9 months; every 2 months from 10-21 months; every 3 months from 22-36 months. Other measures less frequently.
Maternal Anthropometry	Weight at the beginning of the study; weight and arm circumference monthly	Several measures taken during each trimester of pregnancy and	Weighed and measured at time pregnancy was detected.
Biochemical/Clinical	Not measured for children. Biochemical tests for mothers in the first year of study	Regular clinical checkups and biochemical tests	Periodic cross-sectional biochemical surveys
Dietary	Recorded duration of breast-feeding and type of weaning food	24-hour recall once every 3 months from 0-36 months; every 6 months until 60 months; yearly until 8 months.	Dietary survey every 2 months
Nutritional Supplementation	None	Supplementation quantity recorded	Supplementation quantities recorded
Morbidity	Not measured for children. Mothers -- monthly recall	Bi-weekly home visits for household with preschool children	Weekly visits for children up to 3 years of age. (Checklist of 44 clinical symptoms checked during illness.)
Mortality	Recorded for all children as part of the Matlab demographic surveillance system.	Collected by morbidity interviewers and through continuous updates of INCAP census	Collected by resident family workers, specially appointed vital statistics investigators, and the traditional village chowdikar.
Social and economic	Regular census. Questionnaire on socio-economic status administered to mothers at the beginning of the study.	Bi-annual census asked questions on education, housing quality, and ownership of durable goods. Battery of cross-sectional socio-economic and demographic surveys between 1974 and 1976.	Cross-sectional socio-economic surveys. Longitudinal fertility survey at 2 month intervals. Frequent census.

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Medical Research and Johns Hopkins University. The study was intended to
test hypotheses about the relationships between malnutrition and
infection, to quantify the impact of nutritional care and medical care on
growth, morbidity and mortality, and to develop and demonstrate the
effectiveness of a paramedic-based population-wide nutrition and pre-
school health care program (Kielmann, Taylor, and Parker, 1978).

The Narangwal intervention consisted of the introduction of medical
care (immunization, health education, and early diagnosis and treatment of
illness) and nutritional care (anthropometric surveillance, food
supplements, and nutrition education) into ten rural villages according to
an experimental design. Three villages received nutrition care only, two
received medical care only, three others received both nutritional and
medical care, and two received no services except for minimal symptomatic
treatment and emergency care. The average mid-year population of children
0 to 3 years old in each village (the age group studied in each of the
experimental groups) was about 200, except for the combined care villages
where the average was approximately 320. By the end of the project, more
than 2900 children had been observed for at least part of the study
period. The project began in October 1968, although services were
initially introduced in only six villages. Between January 1970 and the
termination of the study in May 1973, the experimental design was
operative in all villages.

In the services villages, both nutritional and medical components
relied heavily on surveillence of young children by family health workers
and prompt treatment. Food supplementation was provided twice daily in a
feeding center in the nutrition care villages and taken ad libitum.
Attendance was voluntary. Calorie-enriched milk was distributed in the
morning and a porridge-like gruel in the afternoon. Standard servings of
the daily supplement if consumed both in the morning and afternoon
provided approximately 400 calories and 11 grams of protein. All pregnant
women in the service villages received pre-natal care. In the nutrition
care villages, pregnant women received folic acid and iron throughout
pregnancy and food supplements when necessary. In the medical care
villages, three tetanus toxoid injections were given one month apart
during the third trimester. Morbidity, diet, and anthropometry data were
collected for children between birth and age three. The frequency and

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* Not to be confused with the Narangwal Population Study, which was
  conducted simultaneously and focused on integrated family planning and
  health care.
* Carrying out the experimental design was complicated by the fact that
  one of the control villages was included in the intensive health
  service program of the nearby Government Primary Health Center one year
  after it was included in the Narangwal Study. This and other reasons
  rendered the village no longer comparable, and it was dropped from the
  study in 1972, although mortality observations were continued through
  1973.

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types of data collected are outlined in Table 2. The Narangwal Study is described in greater detail by Taylor et al. (1978).

The INCAP STUDY

The INCAP study was carried out by INCAP's Division of Human Development in four rural villages in the eastern Guatemalan department of El Progreso. Unlike the Narangwal study, which was intended to study malnutrition, morbidity and mortality, the INCAP study was designed to investigate the impact of mild to moderate malnutrition on mental development and physical growth during childhood (Klein, et al., 1975).

The INCAP intervention consisted of the introduction of curative medical care (treatment in a central clinic staffed by two physicians and participation in national vaccination campaigns) into all study villages, and random allocation of villages to one of two nutritional treatment groups. Two villages received atole, a fortified gruel containing 163 calories and 11 grams of protein per cup. The other two received fresco, a 'Kool-aid' type of beverage, containing 59 calories per cup and no protein, as a placebo. As in the Narangwal project, the supplements were available ad libitum to all family members in central feeding centers in each village. Pregnant women received pre-natal medical care, and voluntarily participated in the supplementation programs.

The study was conducted between 1969 and 1977, and a total of 1623 children were observed for at least a quarter of the study. The types and frequency of data collected for children aged 0 to 7 in the El Progreso villages are described in Table 2.

Between 1974 and 1976, a series of cross-sectional social, economic and demographic surveys was conducted by INCAP in collaboration with the Rand Corporation in the El Progreso villages. The study was expanded so that two semi-urban towns near Guatemala city in the municipality of Petapa were added as 'controls.' Longitudinal data collection began in 1974 and the cross-sectional surveys were also conducted in these towns. Clinic-based medical care, similar to that available in the rural villages, was introduced into the Petapan towns. Anthropometric measures were collected for children aged 0 to 7, home dietary and morbidity information was gathered from households containing pre-school children, and vital statistics were recorded in the continuous census update by the morbidity interviewers. Unlike data for the El Progreso villages, this information is only available for a portion of the children in the two towns. Although the primary source of data for this analysis will be the information collected in the El Progreso villages, the inclusion of the Petapa data will increase the variation in nutritional status, morbidity, and socioeconomic status in the INCAP sample. The INCAP study and the INCAP-Rand Surveys are described in greater detail in Klein, et al., (1975), and Clark (1980).

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Matlab Study

Since 1963 the ICDDR,B (formerly Cholera Research Laboratory) has operated a field research program in Matlab Thana, Bangladesh. The program includes the provision of diarrheal health services and maintenance of a vital registration system in an area with a population (as of 1974) of 263,000. The data in this analysis were collected as part of the Determinants of Natural Fertility Study (DNFS) between October 1975 and April 1978. Unlike the Narangwal and INCAP interventions, this study was entirely observational in the sense that neither comprehensive medical care nor nutritional care were introduced into the villages under study.

The type and frequency of data collected in the Matlab study are more limited than in the other two projects. The sample, for the data to be used in the proposed analysis, consisted of the youngest children (under age 5 at the beginning of the study) of married women or reproductive ages (15 to 49) living in the 14 Matlab villages included in the DNFS. Ages of the children are known since birth dates are recorded in the ICDDR,B vital registration system. Weight was measured monthly for all children in the sample. No information on morbidity of children is available, but heights of mothers and socioeconomic data were collected at the beginning of the study, and weights of mothers, monthly throughout the study. Further description of this study can be found in Chowdhury and Becker (1981).

Despite the limitations of the data, the Matlab study will provide a relatively accurate representation of a malnourished population with only limited access to medical facilities with which to contrast results from the Narangwal and INCAP interventions. Because of the somewhat intrusive nature of the continuous data collection in the INCAP and Narangwal studies and the introduction of at least some new health services into all the INCAP villages and almost all Narangwal villages, many of the associations to be examined may differ in important ways from the same relationships in the non-intervention settings in which most children in developing countries live. For example, we may find that the relationship between socioeconomic status and mortality is partly attenuated in the INCAP and Narangwal populations since the availability of nutritional supplementation and medical care to children of all social strata reduced the disparities in nutritional status and access to medical care between poorer and more well-off families. This problem will be only partly eliminated by the inclusion of the experimental groups that received neither or only one type of service. Replicating at least part of the analysis on data from a non-intervention setting such as Matlab will provide a baseline against which to evaluate the effect on the associations of interest of the intervention procedures themselves.

As stated above, diarrheal treatment services for children were available at an ICDDR,B clinic.

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PREVIOUS RESEARCH USING THESE DATA

This section reviews the previous research on the determinants of infant and child mortality using data from the Narangwal, INCAP, and Matlab projects and describes the way in which the proposed analysis will add to previous work. A more general review of research from a variety of sources on determinants of infant and child mortality is provided by Chen (1981).

Narangwal

The Narangwal project has produced a greater body of research on the determinants of infant and child mortality than the other two projects, in part because this was one of its original aims. Several approaches were taken.

The first and simplest method of examining the effects of improved nutrition and reduction in morbidity on mortality was to compare mortality rates among the four experimental groups (Kielmann, et al., 1978). The results indicate that the groups receiving nutrition and medical interventions did experience lower perinatal, neonatal, postneonatal, infant, and 1 to 3 year old mortality rates than the control group. Further comparisons of children in the four groups suggest that nutrition supplementation did, in fact, measurably improve nutritional status, and that medical care reduced the frequency of diarrhea, vomiting, and other morbid symptoms. While these results, like those of other intervention studies (see Gwatkin, et al., 1980), imply that improved nutrition and medical care reduce infant and child mortality, comparisons of this kind provide only rough estimates of the magnitude of the relationships and little information about the mechanisms involved and the effects of variations in other characteristics among experimental groups and among children within groups that may also affect mortality risk.

Kielmann et al. (1978) also aggregated data from all experimental groups in the Narangwal study and examined mortality rates at different ages by social and demographic characteristics. They found that while male mortality was higher during the perinatal period (as is universally observed), females experienced consistently higher mortality after the first 7 days of life. There were also important differences in mortality rates by caste and by season. The analysis, then, compared mortality rates in each group by both experimental group and caste. Kielmann et al. found that these rates were reduced by nutritional and medical care for both castes, although differences remain between the castes. Because the sample was broken down by both experimental group and caste, however, the number of cases in each cell was very small.

Another way in which factors affecting mortality were investigated was to look at causes of deaths occurring in the Narangwal villages

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(Kielmann, Uberoi and Bhatia, undated). The majority of perinatal deaths were due to extreme prematurity, intrauterine asphyxia, and birth trauma. Gastroenteritis, diarrhea, and lower respiratory infections were the major causes of death for older infants and children. An examination of causes of death, however, says little about which factors affect the _probability_ _of dying_. For this reason, Kielmann, Uberoi and Bhatia also compared several characteristics of children who had died with the population of children to attempt to determine which were related to mortality. They found that children who died came from families which had a disproportionate number of prior deaths and were disproportionately likely to be of 7th or higher order than other children in the villages. To examine the relationship between nutritional status and death, they compared the distribution of nutritional status at death for children who died with the average distribution of nutritional status in the villages. Not surprisingly, children who died fell substantially below the average nutritional standards. This analysis was hampered by the fact that only one characteristic at a time could be compared because of small sample size.

Kielmann and McCord (1978) looked more directly at the relationship between nutritional status and the risk of dying. In the first part of their analysis, they compared weight-for-age collected cross-sectionally with a child's mortality experience in the subsequent six and twelve months. Their results indicate that in each age group the risk of death within one year is six times higher for children at less than 60 percent of the median weight in the Harvard standards than for children at 80 percent or more. As the authors recognized, this type of analysis is limited in several ways. The first is that the longer the child survives after the cross-sectional weight measurement is taken, the less adequately that cross-sectional measurement describes the child's actual nutritional status. This problem severely restricted the investigators' ability to conclude that deaths, except those occurring shortly after the cross-sectional measurement was taken, were related in any way to that particular measure of nutritional status. Another problem is that this analysis does not take morbidity into account. One result of this exclusion is that the risk of mortality from malnutrition may be falsely inflated because part of the malnutrition measured may result from serious illness.

Kielmann and McCord also looked at the relationship between a longitudinal series of anthropometric measures and mortality. Using a type of life table, the probability of dying was calculated for three age groups and four nutritional status groups by dividing the number of deaths in each cell (i.e., each combination of age and nutritional status category) by the child months of exposure in that cell. A child, therefore, might contribute child months of exposure to several nutritional status categories. This procedure has the advantage of more closely relating a child's probability of dying at any particular period of time to their nutritional status _at that time_. The risk of dying for children less than 60 percent of the Harvard weight median was 10 times

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the risk of children at 80 percent or more of the median at ages 1 to 6 months, 25 times at ages 6 to 12 months, and 7 times at ages 12 to 36 months. While providing the best estimate available of the change in the risk of mortality by nutritional status, this analysis was unable to take into account other factors that affect mortality (and interact with nutritional status), such as morbidity, since the number of cases prohibited further breakdowns of the life table.

One other analysis of the information collected at Narangwal, by DeSweemer (undated), examined factors affecting infant and child mortality. DeSweemer's investigation focused on the effect of child spacing on child mortality, and thus only indirectly on the effects of nutrition and infection on mortality. The analysis indicated that children with long interbirth intervals preceding their births had lower age-specific mortality, irrespective of the length of the subsequent birth interval.

The one relevant analysis that used a multivariate framework was an examination of the determinants of weight and height by Taylor, et al. (1978). In this analysis, weight ard height collected at 13 separate ages were each regressed on the following independent variables: sex, caste, number of siblings, maternal age, experimental group, season of measurement, year of measurement, and several interaction terms. Thirteen seperate regressions were run, one on the sample at each age. The results indicated that sex, caste, number of siblings, and to a lesser degree, maternal age and experimental group, were significantly related to both weight and height. Season was also an important determinant of weight.

INCAP

By contrast, the research produced by the INCAP study has focused mainly on the impact of nutrition on mental development and physical growth (see Klein, et al., 1975, among others) and there is relatively little work on the determinants of infant and child mortality. INCAP estimated that the medical care system in the four villages reduced the infant mortality rate from 160 per thousand births in 1968 to about 85 in 1969 (prior to the introduction of supplementation) and the nutritional supplementation program produced a further decline to 47 per 1000 births (Lechtig, et al., 1978). Although Klein, et al. (1975) demonstrated that substantial improvements in child growth appeared to result from the supplementation program, as with similar results from the Narangwal study, the magnitude of the association of morbidity and nutritional status with the risk of dying cannot be determined from these figures alone.

Lechtig, et al. (1978) examined the association between maternal nutrition, socioeconomic status, birth weight, and infant mortality in the

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rural El Progreso villages. Four independent variables, all dichotomized into high and low categories, were used: maternal height (as an indicator of maternal nutritional history), socioeconomic score (a composite reflecting housing quality, quality of the mother's clothing, and a psychological variable indicating the reported extent of teaching various skills and tasks to preschool children by family members), birth weight of the child, and the number of calories from supplementation (either from atole or fresco) the mother consumed during pregnancy. Statistically significant differences in infant mortality rates were found only by maternal height and birth weight. The authors then compared the infant mortality rates between the two categories of each variable, holding constant the other three variables in a four-way table. Shorter mothers and mothers receiving less supplementation during pregnancy had consistently higher infant mortality rates when other factors were held constant. No consistent relationship was found between the socioeconomic score and birthweight and infant mortality. Because of the small sample and the cross-classification procedure used, however, some of the cells contained as few as three cases. For this reason, the authors did not perform tests of statistical significance. Another major limitation of the study was the variables included. Measurement of the quantity of supplement consumed may be a poor indicator of maternal nutritional status during pregnancy since it assumes the home diets of all women in the sample were the same and that no substitution of supplement for other food consumption occurred. The use of a socioeconomic variable combining a psychological index with measures of financial wellbeing also renders any interpretation of the findings of this analysis, with regard to social, economic, and environmental factors, difficult at best.

Matlab

The data on children collected in Matlab Thana that will be included in this study have not been analyzed. A closely related analysis using data from another survey in Matlab has been performed by Chen, et al. (1980). The major object of the analysis was to assess the efficacy of several measures (height-for-age, weight-for-age, weight-for-height, and arm circumference-for-age) of nutritional status, measured cross-sectionally, in predicting subsequent child mortality (observed over a two-year period after the cross-sectional survey). First child mortality rates were calculated for three nutritional variables. The authors found that severely malnourished children (by any of the measures) were two to four times more likely to die than normal to moderately malnourished children. When children were cross-classified by both weight-for-height (representing current nutritional status) and height-for-age (representing nutritional history), mortality rates increased with the severity of malnutrition for each measure, holding the other constant.

A preliminary version of these results was published by Habicht, et al., 1975.

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Chen, et al. (1980) also examined death rates by cause by nutritional status. Malnourished children had uniformly higher death rates from each cause than better nourished children. Even though ICDDR,B provides diarrheal treatment services to all children in Matlab, the diarrheal death rate was almost four times higher among malnourished children. Finally, the authors investigated the differences in mortality by maternal nutritional status and floor space, a measure of housing quality, holding the child's height-for-age constant. Among malnourished children, those with malnourished mothers were significantly more likely to die. Maternal nutritional status made no difference for normal children, however. Floor space was negatively related to mortality when a child's height-for-age was held constant.

Proposed Analyses

Although previous analyses of the data that will be used in this project have examined several aspects of the relationships between the risk of dying and social, economic, and environmental variables and morbidity and malnutrition, none examines these relationships in a comprehensive manner. In the process of carrying out such a comprehensive study, we will expand on previous analyses in several ways. First, we will investigate the joint and separate effects of both morbidity and nutritional status on the risk of infant and child death, in a multivariate framework, for both the INCAP and Narangwal populations. Rather than examining the association between nutritional status and mortality in isolation (as Kielmann and McCord [1978] and Lechtig, et al., [1978] did), we will, for example, compare the effects of nutritional status on the risk of dying, in the presence and absence of illness.

Second, we will attempt to determine how social, economic, and demographic factors (some of which Kielmann, Uberoi and Bhatia, undated, Lechtig, et al., 1978, and Chen, et al., 1980 showed to be related to mortality) are related to the risk of dying, in one unified analysis. The question yet to be answered is whether these factors affect child mortality only through measurable nutritional status and morbidity or whether there are other mechanisms that need to be explored.

Third, we will examine the impact of changes over time in a child's nutritional status (using all three data sets) and morbidity history (Narangwal and INCAP only) on the risk of dying and thus fully exploit the longitudinal aspect of these data. Kielman and McCord's analysis did exactly this with nutritional status but did not include other pertinent variables (especially morbidity) because of methodological difficulties.

Fourth, we will expand the analysis of the INCAP data to include the risk of mortality for children of all ages included in the study (0 to 7 years) rather than focusing only on infant mortality, as have previous analyses.

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A final but important contribution will be to compare, in standardized framework, analyses using data from these three projects. Detailed comparisons between standardized analyses of data such as these have never before been performed. These comparisons will help to sort out apparently universal biological associations with mortality from results which are intervention and culture specific.
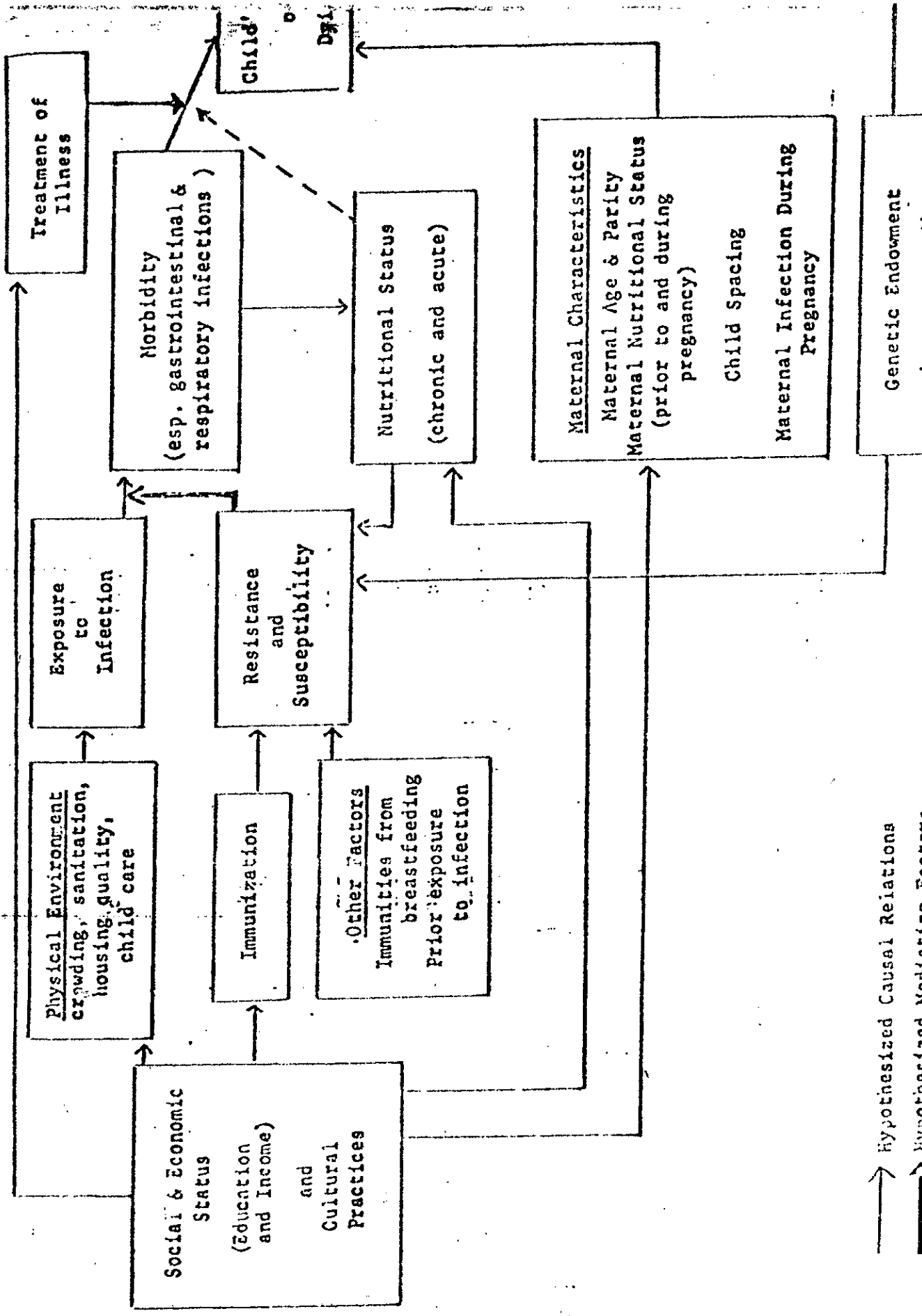
The additional information provided about the child mortality process by further analyses of these data will result partly from a somewhat different analytic perspective (discussed next), but primarily from a newly developed statistical technique (described later in this section) that eliminates several of the methodological problems faced in previous analyses of these data.

VARIABLES

The proposed analysis will be guided by a theoretical model of determinants of infant and child mortality adapted from the versions proposed by Mosley (1980), and Chen (1981). A simplified form of this is presented in Figure 1. The proximate determinants of a child's risk of dying are morbidity, acute (or current) and chronic (or long term) nutritional status, physiological characteristics of a child's mother prior to and during pregnancy, and genetic endowment. The magnitude of the relationship between morbidity and mortality is determined partly by the characteristics of the disease itself (type and severity) and partly by the treatment received by a child who is ill. In this model, nutritional status affects the child's risk of dying from disease, principally by increasing the severity of the illness, although not necessarily increasing susceptibility to infection. Acute malnutrition may result from a bout of infection, while a history of disease may contribute to chronic malnutrition.

Selected physiological characteristics of a child's mother may also alter a child's risk of death through their effect on the reproductive process both during gestation and at the time of birth. There is considerable evidence that the children born to mothers at the extremes of the reproductive ages and both first and greater than fourth parity children are more likely to die (for a review, see Nortman, 1974). Chronic malnutrition stunts a woman's own growth, which may both increase the frequency of birth injuries and decrease the overall efficiency of the reproductive process. Acute maternal malnutrition may increase the risk of dying because fewer nutrients are available to the growing fetus.

Resistance refers to a child's immunological defenses, while susceptibility refers to more general conditions such as malnutrition, repeated illness or extreme fatigue that may increase the risk of developing an infection if the child is exposed to the infectious organism.

A Model of Determinants of Infant and Child Mortality

Child Deaths

Treatment of Illness

Morbidity
(esp. gastrointestinal & respiratory infections)

Nutritional Status
(chronic and acute)

Maternal Characteristics
Maternal Age & Parity
Maternal Nutritional Status
(prior to and during pregnancy)

Child Spacing

Maternal Infection During Pregnancy

Genetic Endowment
(not measured)

Exposure to Infection

Resistance and Susceptibility

Physical Environment
crowding, sanitation, housing, quality, child care

Immunization

Other Factors
Immunities from breastfeeding
Prior exposure to infection

Social & Economic Status
(Education and Income)
and
Cultural Practices

→ Hypothesized Causal Relations

⇒ Hypothesized Mediating Factors

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Similarly, closely spaced children and maternal infection during pregnancy may deplete the resources available to the fetus during gestation.

A child's genetic endowment — which we cannot measure — is also likely to affect his or her risk of death. Much of this effect may operate by increasing a child's susceptibility to disease. Severe genetic errors may to lead to death, more directly.

Although not indicated in Figure 1, the impact of maternal characteristics and genetic errors on the risk of dying is likely to be concentrated in the neonatal period where most deaths result from causes related to the reproductive process. By contrast, the effects of nutritional status and morbidity and the indirect effects of genetic endowment influence a child's risk of dying throughout early childhood.

Social and economic status, by which we refer principally to income and education, and cultural differences are believed to affect the process at several points, which we will describe only briefly.

Both a child's nutritional status and maternal nutritional status during pregnancy are likely to be affected by the ability of a family to produce or purchase food. The quality of food received by mothers and children may depend in part on education, particularly of the mother. The physical environment in which a child lives is also likely to be influenced by his family's financial resources. Maternal education may alter a child's living conditions generally by increasing his mother's ability to control that environment, and in practical ways, such as increasing her knowledge of modern sanitary practices. Access to medical services such as immunization and the treatment of illness may depend both on a family's ability to pay and on their willingness to seek medical help, which may increase with education. Education may alter child spacing, the likelihood that a child is of higher parity, and the age at which a woman has her first and last child, by influencing fertility preferences. Cultural practices may affect both the type of treatment a sick child receives at home (and whether the type of treatment depends on the child's sex) whether or not medical attention is sought, sanitary conditions, house construction, and child care practices, a child's nutritional status (particularly through breastfeeding and weaning customs), and maternal characteristics, such as child spacing and parity.

Despite the richness of the data sets to be employed in this analysis, we obviously can measure only a portion of the variables and examine only some of the associations in the theoretical model. The main focus of the analysis as described in the next section will be to examine the direct effects and interactions of morbidity and nutritional status on the risk of child death, controlling for potentially confounding maternal characteristics when necessary. The impact of socioeconomic status on these proximate determinants will then be explored. By comparing results across the three data sets we may be able to sort out part of the effects of cultural practices on the proximate determinants as well.

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Nutritional status will generally be measured with anthropometry rather than dietary surveys and supplementation quantities because the latter were taken much less frequently and are subject to substantial measurement error. Following Waterlow's (1972) suggestion that height-for-age compared with a standard schedule is a better measure of stunting or chronic malnutrition, while weight-for-height measures wasting or acute malnutrition, we will rely initially on these two measures, although others will also be examined. Maternal nutritional status will be measured by height (a measure of nutritional history), available for at least the majority of the sample in all three studies.

Compared with nutritional status there are relatively few standard indices of morbidity useful in the type of analysis proposed. For this reason, early in the study, we plan to develop and test several measures of the frequency and severity of illnesses of different types to be used in the analyses of the INCAP and Narangwal data. Initially, we will work with three disease categories -- 1) gastrointestinal, 2) respiratory and systemic, and 3) all other types (including tetanus neonatorum and other birth injuries). Possible indicators of recent morbidity experience, for example, are: whether or not a child has experienced an episode of greater than three days duration of one of these illnesses in the past month, the number of episodes of a certain minimum duration occurring in the past six months, or the proportion of days spent ill during the past three months. Because of the frequent monitoring of disease in the Narangwal and INCAP studies, information on frequency of each illness ought to be relatively well reported. Assessment of severity, on the other hand, is rather subjective, and may best be measured by duration of the episode of illness. Another approach that avoids the difficulty of classifying an episode of disease is to look at the incidence and frequency of particular symptoms such as diarrhea or high fever, as Kielmann, et al. (1978) did.

Treatment of disease is likely to affect its outcome at least in part by reducing (and sometimes, in the case of traditional purgatives, increasing) its severity. In this sense measures of the severity of the disease partly reflect treatment. However, medically treated cases may actually be more severe than others because a child's parents do not seek treatment unless the case becomes severe. For these reasons, we will examine the association of severity of illness and treatment by medical practitioners in our preliminary analysis. We will then test both morbidity variables incorporating information on treatment (such as number of treated and number of untreated cases of diarrhea in the past six months) and separate morbidity and treatment variables.

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* Other researchers (including Chen, et al., 1980), however, have argued that weight-for-age is a more sensitive and specific indicator of the risk of dying for use in a nutrition surveillance.

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There are few measurement problems with maternal age and parity. Limited information is available concerning infection during pregnancy from any of these studies. Child spacing can be measured in a number of ways for the INCAP and Narangwal samples, for which complete maternity histories are available, including duration since first birth, average birth interval length, and duration of the interval preceding the birth of the child in question. While variables reflecting both maternal and paternal education will be used in the preliminary analysis, our focus will be on the child's mother's education.

Measurement of household income is especially complex in rural areas because a substantial part of income is non-monetary. Although INCAP conducted two extremely detailed surveys of wealth and income in 1974 and 1975 in the El Progreso villages and Petapa, there is no comparable information from the other data sets. While we will explore the construction of household income measures for the INCAP data (preliminary work has been done by Stein and Kasala (1978), at the Rand Corporation), most of the analysis will include only proxy variables such as housing quality (for which a measure is available for each data set), ownership of durable goods, and the availability of sanitary facilities. In fact, these proxy variables are indicators of the physical environment in which the child lives. The effect of not directly measuring income is probably to attenuate the relationship between the variables representing income and nutritional status, while strengthening their relationship with morbidity.

Cultural factors included will vary according to the setting. For example, Kielmann, et al. (1978) found that caste was an important determinant of mortality in Narangwal, India, while D'Souza and Chen (1980) and Chen, et.al. (1981) found that sex was important in Bangladesh, because of the different treatment of sons and daughters.

PROPORTIONAL HAZARDS

The principal statistical tool to be used in the proposed research will be proportional hazards models, also known as covariate life tables. The proportional hazards model was first proposed by Cox (1972) and has been further developed by Breslow (1974), Holford (1976), and Kalbfleisch and Prentice (1980), and used in demographic applications by Menken et al. (1981), Trussell and Preston (1981), and Schirm et al. (1981), among others.

As in a standard life table, the assumption on which the proportional hazards model is based is that there is a certain risk (or hazard) of dying (or more generally, of the outcome of interest occurring) at each duration. In a proportional hazards model, unlike a life table, this risk is assumed to depend on a set of independent variables. The hazard function, μ, at a given duration d, for individual i is

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$$\mu_i(d) = e^{\lambda(d)} e^{\beta'z_i} .$$

where $\lambda(d)$ is the underlying risk of dying at duration d, z_i is a vector of independent variable values for individual i, and β is a vector of estimated parameters. Thus, in this model, the risk of dying for an individual consists of two parts, $e^{\lambda(d)}$, the underlying hazard rate which is dependent only on duration d; and $\exp(\beta'z_i)$ a proportionality factor which is dependent only on the individual's values of the independent variables. A more thorough description of the proportional hazards model and an example of its use are given in the paper by Trussell and Hammerslough (1982) in Appendix 3 to this proposal.

Although it is not a panacea, the proportional hazards method has several distinct advantages for our analysis. First, like a life table, it permits inclusion of the experience of all individuals regardless of the brevity of the period during which they were in the study population. It thus eliminates the problem of censoring (that is, the inability to observe every individual during the entire period in question) and the problem created by the fact that children who die are likely to be observed for shorter periods of time than others. Movement of individuals in and out of observation is especially frequent in longitudinal studies such as these. Such losses and gains occur for a number of reasons including death, inmigration or outmigration of children from the study area, or the beginning of the study after a child's birth or ending of the study before the child completes the ages under study. If some or all of the children for whom complete records are unavailable were excluded from the analysis, the relatively small sample size would be further reduced and the sample would be biased toward children who are less likely to migrate and more likely to survive.

An alternative approach to this analysis might be to calculate life tables by each category of each independent variable. There are at least two drawbacks to such a procedure. First, the sample size in each independent variable category or at each duration quickly becomes too small to calculate life table rates, particularly if two or more independent variables are examined simultaneously. Second, because of the sample size problem, most analyses of this type would be limited to examining the effect of each independent variable separately, thus eliminating the opportunity to examine the incremental impact of one variable holding others constant, or the interactions between variables.

The first step in using a proportional hazards model is to test the assumption of proportionality by looking for an interaction between time and the hazard function. There is substantial evidence, both from demographic studies of mortality using proportional hazards models and from nutritional studies relating anthropometry to the risk of death, that the proportionality assumption will be appropriate for this analysis.

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By contrast, proportional hazards techniques, which were developed for small samples, can be used to estimate a model including several independent variables simultaneously, permitting interactions to be examined directly. As with other multivariate techniques (such as regression), proportional hazards conserves data by simultaneously estimating the magnitude of the associations of the dependent and independent variables, under a set of assumptions about these relationships.

Another major advantage of the proportional hazards procedure (using categorical independent variables and discrete time units) is that we can estimate models that include independent variables that change over the period of observation. This feature is particularly important in studying the effects of nutritional status and morbidity. For example, during the period of observation, a child's weight-for-height may fluctuate between normal and a level indicating mild malnutrition. In a proportional hazards model, this child would contribute experience in each specified time period to the category in which his recorded weight-for-height fell at that time.

DATA CLEANING AND ORGANIZATION

The first task in the proposed project will be cleaning and organizing the data from each study. All three data sets reside on magnetic tape and portions have received preliminary cleaning and checking. We will check, clean, and evaluate the quality of each data set. Our evaluation will include examination of distributions of nutritional status, morbidity and socioeconomic measures, seasonal and other variability in infant and child mortality, the reliability of reported death and birth dates, the internal consistency in measures of socioeconomic status, nutritional status, and morbidity. A file organized so that there is one record per child containing all pertinent information for that individual will be extracted from each data set. Certain new variables may be added that recode data in comparable form for all three data sets. To facilitate comparisons, the variables in each data set must be standardized to some degree. The standardization, however, will be limited in order to fully employ the richness and diversity of the information collected in each project. While the data cleaning and checking will be performed because they are essential to the rest of the study, the results of this effort -- cleaned and organized computer files for each data set — will also be useful for other researchers working with these data. We will provide INCAP, ICDDR,B, and the Narangwal working group at Johns Hopkins with the new versions of the computer tapes and edited codebooks that we develop for their particular data sets.

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THE ANALYSIS

The first part of the analysis will be descriptive and exploratory in nature, and will closely follow the evaluation of data quality. First, we will compare the variation in nutritional status, the incidence of different categories of disease, infant and child mortality rates, indicators of socioeconomic status, and information on environmental conditions among study populations among treatment groups (in the Narangwal and INCAP studies) and among individual children within each study or treatment group. Next, life tables of the probability of dying from birth to the latest age of observation for children in each study will be calculated for different subgroups of the population. Part of this life table analysis will be a preliminary evaluation of the relationship between different measures of acute and chronic malnutrition and morbidity and the risk of dying. The duration variable in these life tables will usually be the age of the child. In general, single decrement tables — the decrement being death — will be used.

The second type of analysis will involve estimation of multivariate models using the proportional hazards technique. The duration variable will again be the age of the child. At least two types of models will be estimated. The first type will include only measures of nutritional status, morbidity, and maternal factors that are discussed above. The second type will also incorporate measures of socioeconomic status and environmental and cultural variables (also described above). Comparison of the results from the two types of models will indicate whether all of the variation in mortality associated with this additional group of variables operates through nutritional status and morbidity, as we would hypothesize. This portion of the analysis will also permit us to estimate the main and interaction effects of each variable on the risk of dying. Additionally, by including different combinations of nutritional status and morbidity measures (chosen, in part, using results from the life table analysis), we will evaluate the efficacy of each measure and combination of measures in predicting the likelihood of child death.

A third type of analysis will explore the relationship between morbidity and malnutrition in greater detail using hazard models. In this case, the unit of analysis will be switched from the child to episodes of a particular type of disease, such as diarrheal infection. A particular child may, therefore, contribute information to the analysis as many times as he has episodes of disease. The duration variable will be the time since the onset of the episode and the decrement will be death. This approach is analogous to the studies of contraceptive efficacy, in which time segments of use of a particular method are the unit of analysis. The central question to be answered in this section is: how do nutritional status, treatment, and other factors, such as socioeconomic status, affect the probability of dying from a particular type of disease, once a child has the disease.

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To determine how factors affecting the risk of death vary at different stages of a child's life, portions of the second and third types of analysis will be repeated for children in different age groups. For example, separate models may be estimated for neonatal infants (birth to one month) and post-neonatal infants (less than one year but not including the first month of life), one to two years olds, and so forth. The age groups that can be used will vary among studies, because they each recorded information up until different ages. The groups chosen will also depend on the distribution of the sample size at each age and the average age at weaning.

Finally, to the degree permitted by the data, we will explore the relationship between mortality and socioeconomic factors, particularly maternal education, which consistently has been found to be negatively associated with infant and child mortality. The yield from this part of the analysis may be somewhat more limited than that from other sections because of the sources of data. Although other aspects of socioeconomic status — such as housing quality and social class — vary substantially in the study areas, women's education varies considerably less, especially in Matlab Thana in Bangladesh and in Narangwal in India. Nevertheless, given the strength of the relationship between maternal education and infant and child mortality, there is a good chance of producing results from this analysis that will help to clarify this association, particularly using data collected by INCAP in the semi-urban towns in combination with information from the rural villages.

At each step of the analysis, comparisons will be made as much as possible among results for three intervention studies. The working hypothesis will be that if nutritional status, morbidity, and maternal factors are adequately and comparably measured, there will be little difference in the size of their effects on mortality between the study populations since basic biological relationships will be measured. However, in reality, we do expect to find some differences in the results, and accounting for these differences is likely to further increase our understanding of the determinants of mortality. We also expect to find major differences in the associations between morbidity, and nutritional status, and socioeconomic status, because of the major cultural, environmental, and social differences between the three study populations.

It should be noted that most of the analysis will be performed on the entire sample from each study, rather than disaggregating the sample into experimental groups that were part of the INCAP and Narangwal studies. The experimental designs in these two interventions serve in this analysis to increase the variation in nutritional status and morbidity among individual children, but will usually not be explicitly incorporated into the analysis. We recognize, however, that differences in mortality may persist between experimental treatment groups even when nutritional status and morbidity are held constant, and we will test for these remaining differences at several points in the analysis.

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E. COLLABORATIVE ARRANGEMENTS

The division of labor and responsibility for this project are
described in the budget justification. The arrangements for collaboration
between Princeton University, Johns Hopkins University, and ICDDR,B
(detailed in this section, the budget justification, and the budget) are
the result of detailed discussions between the collaborators from these
three institutions. If this research is funded, collaborators and
applicant organizations are prepared to establish in writing the required
inter-institutional agreements.

The INCAP data that were collected under a grant from NIH are now
publically available through NIH. Nevertheless, we requested and have
received approval for this analysis from Drs. Robert Klein and Hernán
Delgado at the Division of Human Development, INCAP. Because Dr.
Chowdhury of ICDDR,B was involved in the collection of the Matlab data and
will participate in our analysis, we have verbal permission to use these
data. As participants in this project, the Narangwal group at Johns
Hopkins University has agreed to the use of data from the Narangwal
Nutrition Project for purposes of this analysis.

PUBLICATIONS

At least two types of publications of the results of this project are
planned. The first is a series of papers describing the research on each
of the data sets, comparing the results between the three studies. We
hope to publish the first type of results both in professional journals in
the countries or regions where the data were collected and in American or
European journals. Because of the broad interest in this topic in several
disciplines, we plan to publish the second type of article in public
health, nutrition, and demographic (or population policy) periodicals.
Both preliminary and final results will also be presented at professional
conferences.

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F.   BUDGET JUSTIFICATION

Dr. Anne Pebley will assume primary responsibility for the conduct and coordination of the research. She will supervise the cleaning and the statistical analyses of the data, and will be responsible particularly for the demographic, socioeconomic, and methodological aspects of the analysis. For this reason, we have budgeted half of her time for the duration of the project. Dr. Sandra Huffman will provide the nutritional expertise required to evaluate the quality of the biological data, to specify the models to be tested, and to choose and categorize measures of nutritional status and morbidity to be used in the analysis. Drs. Pebley and Huffman will work in close collaboration on all aspects of the analysis and will be jointly responsible for the interpretation and writing and publishing of the results.

The collaborators will make crucial contributions to the execution of this project. Drs. Robert Parker and Mark Wolff, at Johns Hopkins, will organize the Narangwal data (which must be culled from approximately 200 computer tapes and coherently organized) in year one. In the second year, Dr. Parker will undertake preliminary analyses of these data using crosstabulations and life tables, at Johns Hopkins. He will also participate in the comparison of results from the three studies, and with the principal investigators, write up the Narangwal results. Dr. Alauddin Chowdhury spent the last academic year (9/81 to 5/82) at the Office of Population Research, for the purpose of analyzing birth interval dynamics using data collected in Matlab. This analysis, conducted in collaboration with Drs. Jane Menken, James Trussell, and Dr. Pebley, involves the use of proportional hazards models to look at factors affecting natural fertility. Because of this experience with hazard models during the natural fertility project and his knowledge of the Matlab data, Dr. Chowdhury will contribute substantially to the analysis and interpretation of the results. He will also participate, with the principal investigators, in writing up results from the Matlab study. Preliminary discussion of the analysis began before Dr. Chowdhury returned to Bangladesh. Dr. Chowdhury will subsequently travel to Princeton University at the end of the first year of study to work with Drs. Pebley and Huffman. Funds for this purpose are included in the budget.

Because of his expertise in the use of hazard models, and statistical demography in general, Dr. James Trussell will provide valuable methodological advice throughout the project period. Five percent of his time is included in the budget since he will be consulted at all stages of the analysis.

With the exception of the data extraction and some data cleaning and preliminary analysis that will be performed on the Narangwal data (supervised by Dr. Parker as described above) and initial tabulations on the Matlab data (by Dr. Huffman) at Johns Hopkins, all data cleaning, organization and analysis will be performed at Princeton University on the

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                                              081-38-5143 (SLH)

University computer. A large part of Dr. Wolff's time and computer costs in the Johns Hopkins subcontract will be incurred during the first year, since this is when the data extraction and preliminary cleaning will take place. Similarly, a larger portion of the Princeton computer charges will be incurred during the first year because of data cleaning and organization of three complex data sets. Programmer time at Princeton, however, is not reduced in the second year, because this is the time period in which the proportional hazards models (requiring substantial programming effort) will be estimated, and other types of analysis completed.

Domestic travel included in the budget is of two types. First, there are ten roundtrips (plus per diem) between Princeton and Baltimore to be used by the principal investigators. With a project of this magnitude, frequent trips will be required for consultations and working meetings between Drs. Pebley and Huffman and Parker. Second, there are four trips (travel and per diem) to professional conferences included. Participation in professional meetings will provide the principal investigators a means of discussing the project and preliminary findings in year one with colleagues in demography, nutrition, and public health, and will serve as one of several avenues for dissemination of results in year two.

Funds for a total of five days of consulting are included in the budget. These funds are specifically earmarked for hiring an economic demographer, Dr. Carol Clark, who spend the academic year 1980-81 at the Rand Corporation working with the INCAP longitudinal data. Dr. Clark is intimately acquainted with this data set in its current form, and we anticipate seeking advice from her at several points in the cleaning, organization, and analysis of the INCAP data set. The consulting will be divided into two trips to Princeton by Dr. Clark, a three-day trip in year one and a two-day trip in year two. Funds are included for consultant's fee, per diem, and travel. We have received and attached written confirmation from Dr. Clark that she is willing to serve as a consultant.

REFERENCES

ertl, Juan M., Enrique Morales, Gustavo Verastequi, and George Graham (1970), "Diet Supplements for Entire Communities: Growth and Mortality of Infants and Children". American Journal of Clinical Nutrition 23(6):707-715.

hm, Hugo, et al. (1976, 1979), La Mortalidad en los Primeros Anos de Vida en Paises de la America Latina. Individual Country Volumes. San Jose, Costa Rica: Centr Latinoamericano de Demografia.

reslow, N.E. (1974), "Covariance Analysis of Censored Survival Data". Biometrics 30:89-99.

aldwell, J.C. (1979), "Education as a Factor in Mortality Decline: An Examination o Nigerian Data". Population Studies 33:295-414.

rvahal, Miguel and Paul Burgess (1978), "Socioeconomic Determinants of Fetal and Child Deaths in Latin America: A Comparative Study of Bogota, Caracas, and Rio de Janeiro". Social Science and Medicine 12:89-98.

ackiel, Juan (1981), "Analisis Comparativo de la Mortalidad Infantil en base a la Encuesta Mundial de Fecundedad". Unpublished Manuscript, CELADE.

en, Lincoln (1981), "Child Survival: Levels, Trends and Determinants" in Determinants of Fertility in Developing Countries: A Summary of Knowledge, Panel on Fertility Determinants, Committee on Population and Demography, National Academy of Sciences.

en, Lincoln, A.K.M. Alauddin Chowdhury and Sandra Huffman (1980), "Anthropometric Assessment of Energy-Protein Malnutrition and Subsequent Risk of Mortality Among Preschool Aged Children". American Journal of Clinical Nutrition 33:1836-1845.

en, Lincoln, R.E. Huq, and Sandra L. Huffman (1981), "Nutritional Status and the Ris of Diarrheal Disease Among Children". American Journal of Epidemiology 114(2):284-292.

en, Lincoln, S. D'Souza and R.E. Huq (1981), "Sex Biases in the Family Allocation of Food and Health Care in Rural Bangladesh". Population and Development Review, 7(1).

owdhury, A.K.M. Alauddin and Stan Becker (1981), Determinants of Natural Fertility Study. Volume One: Methods and Descriptive Tables for the Prospective Study 1975-1978. Dacca, Bangladesh: ICDDR,B.

rk, Carol (1980), Overview of the INCAP Longitudinal Study and Its Relation to the INCAP-RAND Survey. The Rand Corporation.

, D.R. (1972), "Regression Models and Life Tables". Journal of the Royal Statistical Society, Series B34:187-220.

rling, C.I., Lincoln C. Chen and Sayed Babur (1976), "Demographic Crisis: The Impact
   of the Bangladesh Independence War". Population Studies. 30:87-105.

Sweemer, Cecile (Undated), "The Influence of Child Spacing on Child Survival".
   Unpublished Manuscript.

Souza, S. and L.C. Chen (1980), "Sex Differentials in Mortality in Rural Bangladesh".
   Population and Development Review 6:257-270.

atkin, Davidson (1980), "Indications of Change in Developing Country Mortality
   Trends: The End of an Era?" Population and Development Review 6:615-644.

atkin, Davidson, Janet R. Wilcox and Joe D. Wray (1980), Can Health and Nutrition
   Interventions Make a Difference? Washington, D.C.: Overseas Development Council
   Monograph No. 13.

bicht, J-P, Aaron Lechtig, Charles Yarbrough, Robert Klein (1975), "Maternal
   Nutrition, Birth Weight, and Infant Mortality" in Size at Birth, CIBA Foundation
   Symposium 27, Amsterdam: Elsevier-Excepta Medica-North Holland.

ines, Michael R. and Roger C. Avery (1982), "Differential Infant and Child Mortality
   in Costa Rica: 1968-1973". Population Studies, forthcoming.

ines, Michael R., Roger C. Avery and Michael A. Strong (1981), "Differentials in
   Infant and Child Mortality and Their Change Over Time: Guatemala, 1959-1973".
   Presented at the annual meetings of the Population Association of America,
   Washington, D.C.

Holford, T.R. (1976), "Life Tables with Concomitant Information". Biometrics
   587-597.

fman, S.L., A.K.M.A. Chowdhury and W.H. Mosley (1978), "Postpartum Amenorrhea: How
   Much is it Influenced by Maternal Nutritional Status?" Science 200: 1155-1157.

fman, S.L., A.K.M.A. Chowdhury and Z.S. Sykes (1980), "Lactation and Fertility in
   Bangladesh". Population Studies 34:337-347.

fleisch, John and Ross Prentice (1980), The Statistical Analysis of Failure
   Time Data. New York: John Wiley.

lmann, A.A., et al. (1978), "The Narangwal Experiment on Interactions of Nutrition
   and Infections: II. Morbidity and Mortality Effects". Indian Journal of Medical
   Research 68:21-41.

mann, A.A. and Colin McCord (1978), "Weight-for-Age as an Index of Risk of Death in
   Children". The Lancet (June 10):1247-1250.

mann, A.A., Carl E. Taylor and Robert L. Parker (1978), "The Narangwal Nutrition
   Study: A Summary Review". American Journal of Clinical Nutrition 31:2040-2052.

Kelmann, A.A., Inder S. Uberoi, and Susham Bhatia (Undated), "Child Mortality in R
Punjab: Level and Causes of Child Deaths". Unpublished Manuscript.

Klein, Robert E., et al. (1975), "Malnutrition and Human Behavior: A Backward Glanc
at an Ongoing Longitudinal Study". Presented at the Conference on Malnutrition
and Behavior, Cornell University, November 6-8.

Lechtig, Aaron, et al. (1978), "Effect of Maternal Nutrition on Infant Mortality" in
W.H. Mosley (ed.) Nutrition and Human Reproduction. New York: Plenum Press.

Mora, J.O., et al. (1978), "Nutritional Supplementation and the Outcome of Pregnancy
III: Perinatal and Neonatal Mortality". Nutrition Reports International 18:
167-175.

Mata, Leonardo (1978), The Children of Santa Maria Cauque. Cambridge: MIT Press.

McKeown, T. and R.G. Record (1962), "Reasons for the Decline in Mortality in England
and Wales during the 19th Century". Population Studies 16:94-122.

Menken, Jane, James Trussell, Debra Stempel and Ozer Babakol (1981), "Proportional
Hazards Life Table Models: An Illustrative Analysis of Socio-Demographic
Differences on Marriage Dissolution in the U.S.". Demography 18:181-200.

Mosley, W.H. (1980), "Social Determinants of Infant and Child Mortality: Some
Considerations for an Analytical Framework". Discussion Paper for a conference
Health and Mortality in Infancy and Early Childhood, Cairo, May 18-20,
The Population Council.

Nortman, Dorothy (1974), "Parental Age as a Factor in Pregnancy Outcome and Child
Development". Reports on Population/Family Planning, The Population Council.

Pebley, A.R., Hernan Delgado and Elena Brineman (1979), "Fertility Desires and Child
Mortality Experience Among Guatemalan Women". Studies in Family Planning 10:
129-136.

Pebley, A.R., Hernan Delgado and Elena Brineman (1980), "Family Sex Composition
Preferences Among Guatemalan Men and Women". Journal of Marriage and the Family
May: 437-447.

Pebley, A.R. (1981), "The Age at First Birth and Timing of Subsequent Fertility in
Guatemala and Costa Rica". Population Studies, forthcoming.

Post, J.D. (1976), "Famine, Mortality and Epidemic Disease in the Process of
Modernization". Economic History Review XXIX:14-37.

Preston, Samuel H. (1976), Mortality Patterns in National Populations, New York,
Academic Press, Chapter 4.

Preston, Samuel H. (1978), "Research Developments Needed for Improvements in Policy
Formulation on Mortality". Presented at the First IRG Workshop on Research
Priorities for Population Policy, Colombo, Sri Lanka, April 26-28.

Washington, D.C., PAHO Scientific Publication No. 262.

hirm, Allen, Jane Menken, James Trussell and William Grady (1981), "Socioeconomic a
Demographic Covariates of Contraceptive Failure". Family Planning Perspectives,
forthcoming.

hultz, T. Paul (1979), "Interpretation of Relations Among Mortality, Economics of th
Household and the Health Environment". Proceedings of the Meeting on
Socioeconomic Determinants and Consequences of Mortality, United Nations and
World Health Organization, El Colegio de Mexico, Mexico City, June 19-25, 1979.

rimshaw, N.S., C.E. Taylor and J.E. Gordan (1968), Interations of Nutrition and
Infection, WHO Monograph Series No. 57.

imano, G.R. and Martin Vine (1980), "Undernutrition, Infection and Infant
Mortality". Presented at the Meeting of the IUSSP Committee on Factors Affecting
Mortality and the Length of Life, Fiuggi, Italy.

in, John and Kathy Kasala (1978), "Income, Wealth and Agricultural Production in
1974: A Guide for Researchers to the Use of Questionnaire R-10 From the Rand-
Rockefeller Guatemala Project". Unpublished Manuscript, Rand Corporation.

in, Zena, Mervyn Susser, Gerhart Saenger, Francis Marolla (1975), Famine and Human
Development. New York: Oxford University Press.

nitz, George (1955), "A Century of International Mortality Trends: I".
Population Studies 9:24-55.

nitz, George (1956), "A Century of International Mortality Trends: II".
Population Studies 10:17-42.

or, C.E., et al. (1978), "The Narangwal Experiment on Interaction of Nutrition and
Infections: I. Project Design and Effects Upon Growth". Indian Journal of
Medical Research 68 (Supplement):1-20.

bridge, F.L. and N. Staehling (1980), "Sensitivity and Specificity of Arm
Circumference Indicators in Identifying Malnourished Children". American Journal
of Clinical Nutrition 33:687.

sell, James and Charles Hammerslough (1981), "An Illustrative Analysis of the
Covariates of Infant and Child Mortality in Sri Lanka". Unpublished Manuscript.

ell, James and Samuel Preston (1981), "Estimating the Covariates of Childhood
Mortality from Retrospective Reports of Mothers". Health Policy and Education,
forthcoming.

i, F.E. and O. Pineda (1971), "Effects on Body Composition and Body Function:
Psychological Effects" in Gunner Blix, Yngve Hofvander and Bo Vahlquist (eds.),
Famine: Nutrition in Relief Operations in Times of Disaster, Uppsala: Almquist
and Wiksells.

low, J.C. (1972), "Classification and Definition of Protein-Calorie Malnutrition".
British Medical Journal 3:566-569.

ABSTRACT SUMMARY - PARTICULAR ITEMS

None of the questions for the Ethical Review Committee apply because this study involves only old data sets, and will not involve contact with any patient or population surveyed.

SECTION III – DETAILED BUDGET

SUBCONTRACT BUDGET
(UNDER R01-HD-17709)
INTERNATIONAL CENTER FOR DIARRHOEAL DISEASE RESEARCH, BANDLADESH
### June 1, 1983 – May 31, 1985

	YEAR 1	YEAR 2
Personnel		
A. Chowdhury (10% effort)	$3,300	$3,498
Other Expenses		
Telephone and Office Supplies	250	250
Travel		
1 round-trip Bangladesh/Princeton	3,000	0
TOTAL COSTS	$6,550	$3,748

Child Mortality: Social and Biological Determinants

Principal Investigators: Anne R. Pebley, Ph.D.
                            Sandra L. Huffman, Sc.D.

Collaborators: Robert Parker, M.D., M.P.H.
                  A.K.M. Alauddin Chowdhury, Sc.D.
                  James Trussell, Ph.D.
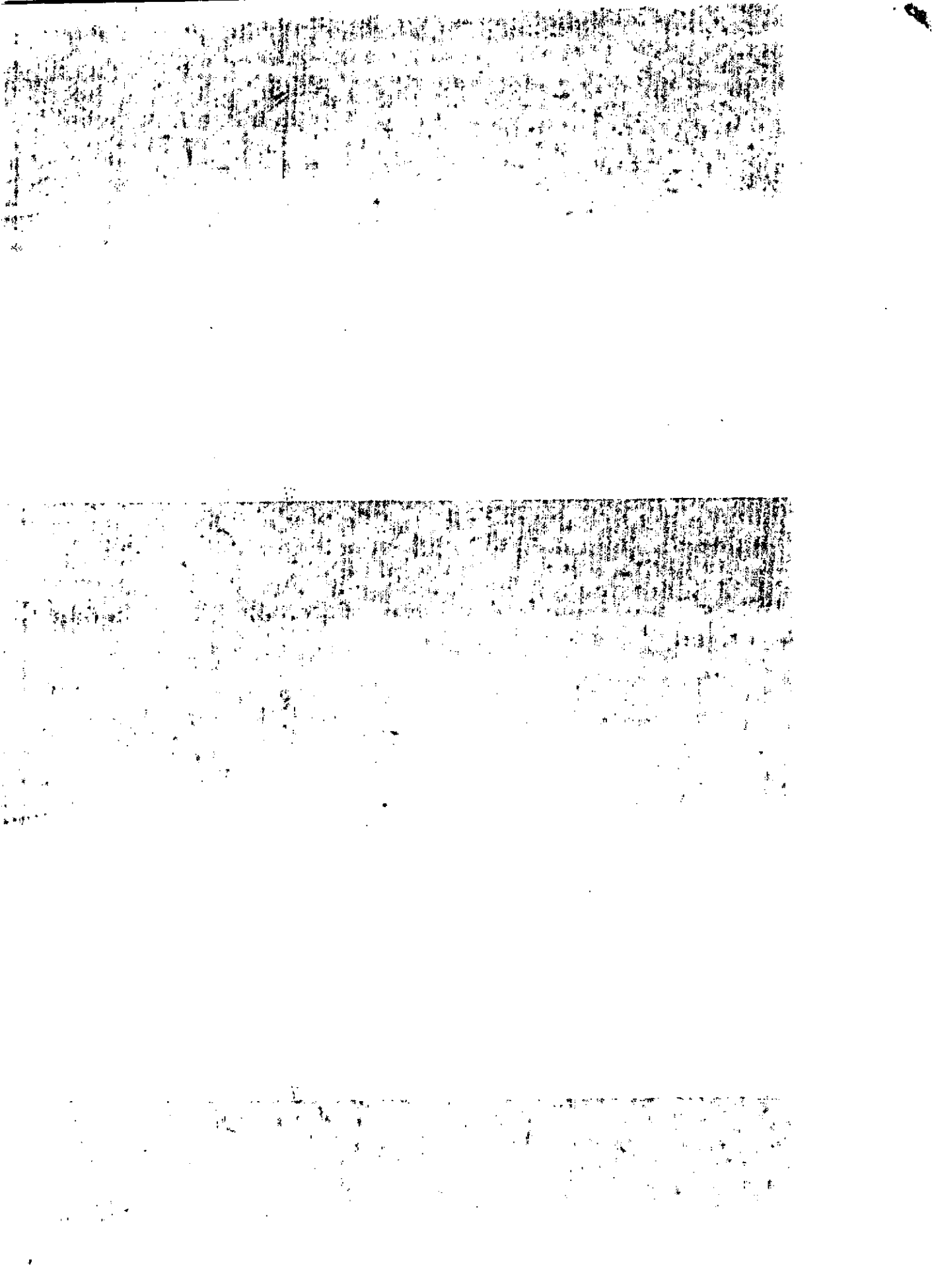
Director

Alauddin Chowdhury   25 May, 1983

Subcontract with Princeton University

I shall take the responsibility for the work subcontracted
in the project "Child Mortality: Social and Biological
Determinants."

I will also make sure that proper internal review and clearance
by ERC and RRC is made.

cc: Chairman, ERC/RRC
     Dr. Anne Pebley