ETHICAL REVIEW COMMITTEE, ICDDR,B

Date May 16, 1984

29

ncipal Investigator John D. Clemens

lication No. 84-020(P)

le of Study Further Definition of Post-
spital Discharge Mortality Risk Factors
ng Children Attending Matlab Hospital

Trainee Investigator (if any)

Supporting Agency (if Non-ICDDR,B)

Project status:
( ) New Study
( ) Continuation with change
( ) No change (do not fill out rest of form)

cle the appropriate answer to each of the following (If Not Applicable write NA).

Source of Population:
(a) Ill subjects — Yes / No
(b) Non-ill subjects — Yes / No
(c) Minors or persons under guardianship — Yes / No

Does the study involve:
(a) Physical risks to the subjects — Yes / No
(b) Social Risks — Yes / No
(c) Psychological risks to subjects — Yes / No
(d) Discomfort to subjects — Yes / No
(e) Invasion of privacy — Yes / No
(f) Disclosure of information damaging to subject or others — Yes / No

Does the study involve:
(a) Use of records, (hospital, medical, death, birth or other) — Yes / No
(b) Use of fetal tissue or abortus — Yes / No
(c) Use of organs or body fluids — Yes / No

Are subjects clearly informed about:
(a) Nature and purposes of study — Yes / No
(b) Procedures to be followed including alternatives used — Yes / No
(c) Physical risks — Yes / No
(d) Sensitive questions — Yes / No
(e) Benefits to be derived — Yes / No
(f) Right to refuse to participate or to withdraw from study — Yes / No
(g) Confidential handling of data — Yes / No
(h) Compensation &/or treatment where there are risks or privacy is involved in any particular procedure — Yes / No

5. Will signed consent form be required:
(a) From subjects — Yes / No
(b) From parent or guardian (if subjects are minors) — Yes / No

6. Will precautions be taken to protect anonymity of subjects — Yes / No

7. Check documents being submitted herewith to Committee:
___ Umbrella proposal - Initially submit an overview (all other requirements will be submitted with individual studies).
___ Protocol (Required)
___ Abstract Summary (Required)
___ Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw (Required)
___ Informed consent form for subjects
___ Informed consent form for parent or guardian
___ Procedure for maintaining confidentiality
___ Questionnaire or interview schedule *

* If the final instrument is not completed prior to review, the following information should be included in the abstract summary:
1. A description of the areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy.
2. Examples of the type of specific questions to be asked in the sensitive areas.
3. An indication as to when the questionnaire will be presented to the Cttee. for review.

Retrospective study

ree to obtain approval of the Ethical Review Committee for any changes ving the rights and welfare of subjects before making such change.

17 MAY 1984

Principal Investigator

Trainee

SECTION I - RESEARCH PROTOCOL (PILOT)

1. Title: Further Definition of Post Hospital Discharge Mortality Risk Factors Among Children Attending Matlab Hospital.

2. Principal Investigator: John D. Clemens

   Co-Investigators: J. Chakraborty, Alauddin Chowdhury, K. Sheikh Bonita Stanton, Bogdan Wojtynyk.

3. Starting Date: July 1, 1984

4. Completion Date: December 31, 1984

5. Total Direct Cost: $2,994.80

6. Scientific Program Head:

This Protocol has been approved by the W.B. Community Services Research Working Group.

Signature of Scientific Program Head: W.B.

Date: 06.05.84

7. Abstract Summary:

Recent work indicates that certain subgroups of children who attend Matlab Hospital for care of diarrhoea may have a substantially increased risk of dying after discharge from the hospital. In particular, children who are severely malnourished and aged 24-36 months appear at high-risk. In this study, using a larger sample of post-discharge deaths and studying all children 0-60 months of age, we will assess other factors, evident during hospitalization, that predict mortality. The study is designed as a case-control analysis. Cases will be defined as deaths occurring within 6 months after discharge of children who are aged

0-60 months at the time of hospital admission. Cases will be drawn from patietns attending Matlab Hospital during the interval 1979-82, and will be identified by linking DSS death records with hospital admission logs. Controls will be defined as patients who survive at least 6 months after discharge; for each case three controls will be selected randomly from among patients admitted the same day as each corresponding case. For each patient we will obtain demographic characteristics of the patient and the patient's family (from census data) as well as clinical data (from clinical records) describing the character, severity, and duration of diarrhoea, isolated etiologic pathogens. coexisting illnesses, treatments required, duration of hospitalization and weight at discharge. The odds ratio relating death to each of these features closely approximates the relative risk of death in patients having the feature vs. those lacking the feature. When combined in a multiple logistic regression, moreover, the ln (coefficient) for each factor correspond to the odds ratio, controlling for all other factors in the equation. In this way, the strongest independent predictors of mortality can be discerned and a "decision rule" demarcating groups at highest risk on the basis of conjoint consideration of several risk factors can be developed for use in future interventions.

8. Reviewers:

(a) Research Involving Human Subjects: _____

(b) Research Review Committee: _____

(c) Director: _____

SECTION II - RESEARCH PLAN

A. INTRODUCTION:

1. Objective:

To evaluate factors which predict post-discharge mortality in children treated at Matlab Hospital and to develop a "decision-rule" by which high-risk children can be identified for intensive follow-up and future interventions.

2. Background:

Little is known about the ultimate fate of children given acceptable care for diarrhoea in treatment centers in developing countries. In an important study, S.K. Roy and colleagues provided initial information about a cohort of 551 children aged 0-4 years seen at Matlab Hospital during 1979 (1). During the 12 months following presentation, 23 (4%) of the children died, as opposed to the 19 deaths expected on the basis of age-specific general population mortality rates. Although this did not represent a statistically significant excess of deaths, it was impressive that 70% of deaths occurred within 3 months of discharge and that a statistically significant excess of deaths was evident for children aged 24-35 months. In this age group, the excess mortality was attributable largely to mortality among children with severe(≤55% NCHS standard, weight for age) malnutrition.

In this study, however, deaths among children 24-36 months with ≤55% of the NCHS weight for age accounted for only 8 of the 23 deaths observed in the study. Accordingly, although age and nutritional

status are important determinants of prognosis, other factors of prognostic importance clearly exist. In this study, we propose to expand the observations of Roy et al to identify additional prognostic factors. We also propose to develop a "decision rule" formed on the basis of conjoint consideration of several important prognostic factors for demarcating subjects at high and low risk of post-discharge mortality.

METHODS

General

The research strategy for this study will be a case-control study. Cases will be children <5 years who die within 6 months of discharge from Matlab Hospital. Controls will be patients admitted the same day as the cases, but surviving at least 6 months after discharge. Three controls will be randomly selected for each case. For each case and control, we will collect demographic characteristics, as well as clinical information about the admission and nutritional status at discharge. Demographic, nutritional, and clinical variables will then be tested for their ability to predict death, and multivariate techniques will be used to develop a decision rule to demarcate patients at particularly high risk of death.

Overall Eligibility and Sampling Frame

Patients will be potentially eligible for the study if: a) they attended Matlab Hospital for care of diarrhoea between January 1, 1979 and January 1, 1983; b) they were aged ≤60 months at the time of admission; and c) they

were residents of villages included in the Demographic Surveillance System at the time of admission. No constraints will be placed upon gender, or severity or duration of diarrhoea. Moreover, "diarrhoea" will be defined as a complaint of diarrheoa motivating a patient to seek care at the treatment centre.

Case Definition

For the purpose of this study, a "case" will be defined as a subject who fulfilled the above eligibility requirements and who died within 6 months of discharge from the hospital.

Case Selection

To select cases, we will generate lists of all children 0-60 months of age seen at Matlab Hospital between 1.1.79-1.1.83. We will then match these lists with computer files of all deaths occurring in children 0-67 months between 1.1.79-8.8.83. Matching will make use of DSS registration numbers. This will ensure that children who are hospitalized as long as one month will still have follow-up for fatal events for 6 months after discharge. Those fatalities occurring within 6 months of discharge will comprise the "cases".

Control Definition

Controls will be defined as DSS residents ≤60 months of age admitted to Matlab Hospital between January 1, 1979-January 1, 1983, who were discharged alive and who survived at least 6 months after discharge.

Control Selection

For each case, 3 controls, (chosen from 6-month survivors who were admitted immediately prior to or after the case) will be selected. After compiling the list of the controls, it will be ascertained by matching with DSS migration files that the control did not migrate out of the DSS area within 6 months of discharge.

Prognostic Features: Data Acquisition

Prognostic features to be examined will be of two major types: demographic and clinical. Demographic features, obtained from relevant census information, will include age, gender, maternal education, family size, antecendent childhood deaths in the family, and socio-economic indicators such as land and animal ownership, and construction of dwelling. Clinical information will be obtained from the clinical record. Admission data will include type of diarrhoea (watery vs. non-watery; dysentery), duration of diarrhoea, severity of dehydration, height of temperature, as well as associated illnesses that were noted. Post-admission data will include types of rehydration (IV vs. oral) and non-rehydration therapies received (e.g. antibiotics), duration of hospitalization, complications, and weight at discharge (to ascertain pecentile weight for age). Any etiologic pathogens isolated will also be noted. All information will be entered onto pre-specified data forms specially prepared for this study.

Analysis: Evaluation of Prognostic Factors

In a case-control study, the degree of risk conferred by exposure to a particular risk factor is expressed as an odds ratio, relating the

exposure to the outcome. Since the outcome to be studied (death) is rare, this odds ratio closely approximates the relative risk of death among those exposed vs. those not exposed to each prognostic factor. The significance of each association will be evaluated with the chi-square test, and 95% confidence intervals for the odds ratios will be calculated according to the method of Miettinen (2).

Analysis: Development of a Decision Rule

To ascertain the relative independent importance of the prognostic features described above, we will enter all statistically significant ($P<.05$) factors into a logistic regression equation, using the existing software package at ICDDR,B (3). Those variables whose coefficients retain statistical significance in the regression will then be considered in sequential bivariate fashion, in order of the magnitude of their associated regression coefficients. The goal of these sequential bivariate analyses will be to demarcate clusters of variables that predict as high a fraction of deaths as possible, while retaining considerable efficiency (odds ratio ≥ 5) in the prediciton. Assuming the attainment of a variable cluster with $\geq 95\%$ sensitivity in identifying deaths, this will be equivalent to ensuring roughly 80% specificity. By way of comparison, the factors delineated by Roy and colleagues predict post-discharge mortality with 97% specificity, but only 33% sensitivity, with the result that many patients at risk for death are missed at the price of needlessly high specificity.

Preservation of Confidentiality

All records will be kept in a locked file cabinet in the Principal Investigator's Office. No subject will be mentioned by name in any report, and all analysis will be performed using only study numbers of patients rather than names of patients.

Abstract Summary

1. Patients will be eligible if they were aged 0-60 months at the time of presentation to Matlab Hospital between 1979-82, and if they were residents of the OSS area. The study will be retrospective in nature.

2. No risks will be involved, as they study as retrospective and patients' identities will be kept confidential.

3. Risks are non-existent.

4. Records will be kept in a locked filing cabinet. Analysis will be done using patients' study numbers rather than their identities. No reference to patients' names will be made in reports of the research.

5. No consent will be requied.

6. No interview will take place.

7. Benefits include increased understanding of risk factor for post hospital discharge mortality. Risks are non-existent.

8. Medical records will be used.

REFERENCES

1. Roy SK, Chowdhury AKMA, Rahaman MM. Excess mortality among children discharged from hospital after treatment for diarrhoea in rural Bangladesh. British Medical Journal, 1983. 287:1097-1099.

2. Miettinen OS. Estimability and estimation in case-referent studies. Am J Epidemiology, 1976. 103:226-235.

3. Breslow NE, Day NE. Statistical methods in career research. IARC Scientific Publications. Number 32. Lyon: 1980.

SECTION III - BUDGET

A. DETAILED BUDGET

1. PERSONNEL SERVICES:

		% of Effort	Annual Salary	Project Requirements Taka	Dollar
John D. Clemens	P.Investigator	20%	-	-	-
B. Stanton	Co-Invest.	10%	-	-	-
B. Wojtynyak	Co-Invest.	10%	-	-	-
A. Chowdhury	Co-Invest.	10%	-	-	-
K. Sheikh	Co-Invest.	10%	-	-	-
J. Chakrabarty	Co-Invest.	10%	-	-	-
To be named	Coding Asst.(2)	Each 8 months	2,171	34,736	-
		Subtotal:		34,736	

2. SUPPLIES

Office supplies and Xeroxing — 200.00

3. EQUIPMENT None

4. HOSPITALIZATION None

5. OUTPATIENT CARE None

6. ICDDR,B TRANSPORT

Dhaka-Matlab-Dhaka(5) at 1200T/trip — 6000

7-8 TRANSPORT OF PERSONS AND THINGS None

9. RENT None

10. PRINTING OF DATA FORMS — 100.00

11. OTHER CONTRACTUAL SERVICES

Data entry and editing	3,634	
Programming	15,000	
Computer time (40 hours Tk.200/hr)	8,000	
Subtotal:	26,634	300.00

Total: 67,370 Taka — US$300

At 25T/US$: $2994.80

BUDGET SUMMARY

		Dollars	Taka
1.	Personnel		34,736
2.	Supplies	200.00	
3.	Equipment	-	-
4.	Hospitalization	-	-
5.	Outpatient Care	-	-
6.	ICDDR,B Transport		6,000
7-8.	Transport of Persons and Things	-	-
9.	Rent	-	-
10.	Printing of Data Forms	100.00	
11.	Other Contractual Services		26,634
	Total:	300.00	67,370

Dollar equivalent (@25T/US$) = US$2994.80