Date 7th July 1975

ETHICAL REVIEW COMMITTEE, ICDDR,B.

Principal Investigator: A. R. I E N D-

Application No. 85-020P

Title of Study: Evaluation of monthly measurement of arm circumference as a simple method for detection

Trainee Investigator (if any)

Supporting Agency (if Non-ICDDR,B)

Project status: Pilot

(X) New Study
( ) Continuation with change
( ) No change (do not fill out rest of form)

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

1. Source of Population:
   (a) Ill subjects — Yes No
   (b) Non-ill subjects — (Yes) No
   (c) Minors or persons under guardianship — (Yes) No
2. 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)
3. 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)
4. 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.

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

Principal Investigator

Trainee

85-020P
14/7/85

SECTION-I : RESEARCH PROTOCOL

Title:

EVALUATION OF MONTHLY ARM CIRCUMFERENCE MEASUREMENT AS A SIMPLE METHOD FOR SELECTION OF MALNOURISHED CHILDREN WITH A HIGH RISK OF DEATH IN THE 6-36 MONTHS AGE GROUP

PILOT PROTOCOL

INCREMENTAL COST : US $ 4975

Principal Investigator: A. Briend

Co-investigators: J. Chakraborty, A.M. Sarder, M. Yunus, B. Wojtyniak

Consultants: M.G.M. Rowland, M. Rahaman, M. Koenig

Starting Date: 15th August 1985

Completion date: 15th February 1986

Incremental cost: US $ 4975

Source of funds: DSS and MCH-FP Projects.

Scientific Programme Head: M.G.M. Rowland

This protocol has been approved by the Community Services Research Working Group.

Signature of the Scientific Programme Head:

Date: 7 July 1985

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Abstract Summary

This protocol will estimate the proportion of deaths associated with malnutrition in the 6-36 months age group which can be predicted by monthly measurement of arm circumference. The relevance of dietary practices and of the recent morbidity history of the child to evaluate the risk of death will also be tested. This information is necessary before implementing any targeted nutritional programme aiming at reducing the number of deaths in under three children. This will also determine the upper limit of the reduction in mortality which can be expected from such an intervention.

Reviews:

Ethical Review Committee:_____

Director:_____

SECTION-II : RESEARCH PLAN

A. INTRODUCTION

1. Objectives

- To evaluate monthly arm circumference measurements as a simple method to detect malnourished children with a high risk of death in the 6-36 months age group.

- To determine whether simple information about dietary and morbidity history of the child is relevant to estimate the risk of death

- To provide a baseline and a simple evaluation technique for future interventions aiming at reducing malnutrition associated mortality.

2. Background

Regular monitoring of nutritional status is widely claimed to be a key element for reducing mortality in under 5 children (1). It is assumed that malnutrition is a leading cause of death in this age group, that growth monitoring will lead to an early detection of malnourished children with a high risk of death and that extra food or medical attention targeted on these 'at risk' children will avert a substantial number of deaths. Unfortunately, none of these assumptions has ever been tested adequately and one may wonder to what extent growth monitoring will be really effective. In any case, more information is needed

before using it on a large scale to prevent deaths.

That malnutrition is a major cause of death among under 5 children is derived mainly from indirect evidence: it has been known for long that highest infant and childhood mortality rates are observed in poorest communities where malnutrition is widespread. Ver few studies however have shown a close association between malnutrition and the risk of death. Puffer and Serrano in 1973 (2) in a review of post-mortem studies of 9 Latin-American countries gave evidence that 57% of children who died before the age of 5 were grossly underweight and interpreted this finding as evidence that malnutrition is a major cause of death in this age group. This conclusion however is not convincing. If all children in these communities are underweight, the children who die are bound to be also underweight, even if the risk associated with a weight deficit is low. Post-mortem studies by themselves do not allow any conclusion. To have an estimation of the risk of death associated with malnutrition, the prevalence of malnutrition in deceased and surviving children must be known.

The first study which compared the risk of death of children of different nutritional categories came from Bangladesh. In 1970, Sommer and Lowenstein looked at the relation between the nutritional status of children assessed cross sectionally by the Quac stick (which gives an estimate of arm circumference for height) and subsequent mortality (3). This study followed up 3757 children in theage group 1 to 4 years with 42 deaths in the 6 months following the nutritional assessment. Children were divided in three nutritional categories and those who were

classified as malnourished and who represented 6.7% of the initial sample accounted for 29% of deaths. In other words, children classified in the lower nutritional category had a risk of death 5.6 times higher than the better-off. Although this relative risk of death is quite high, these figures suggest that a nutritional intervention based on this classification of malnutrition would have produced poor results in terms of reduction of mortality: the total number of children classified as malnourished in Matlab area in the 1-5 year-old age group would have been approximately 1500. This means that with existing resources, only minimal support could have been given to every individual child and that a fraction of the 29% of the total number of deaths could have been averted. If we assume that the number of deaths among malnourished children could have been halved by such an intervention, which is a rather optimistic hypothesis, the total reduction of the number of deaths in this age group would have been 14%. This is much less than what is needed in a community where 1 to 4 year mortality is several times higher than in industrialised countries.

Two other studies which investigated the relative risk of death of malnourished children gave similar results: In Punjab, it was shown by Kielmann and McCord (4) that children below 60% weight for age had a risk of death 7 times higher than well nourished children. However, the number of deaths occurring among malnourished children accounted only for 15% of the total. In Bangladesh, another study by Chen et al. (5) showed that the 5% most malnourished children accounted for 25% of the total of

deaths. This means that in these studies the majority of deaths occurred in children classified as moderately malnourished and that a nutritional intervention targeted on most severely malnourished children selected by anthropometry would have failed to reduce infant and childhood mostality to acceptable levels.

In all previous studies, a greater proportion of deaths could have been predicted by using higher cut-off points to select 'at risk' children but this would have lead to the selection of a very large proportion of children for intervention which would be out of reach with the level of resources allocated to child care in developing countries. The low sensitivity at high specificity levels of classical nutritional indices to predict death, or in other words, their poor validity, limits the potential effect which one may expect from a nutritional intervention.

A recent reanalysis of Sommer and Lowenstein data (6) showed that using nutritional indices on short time interval to predict deaths increases dramatically their validity. This suggests that Chen et al. study (5) which attempted to predict deaths from one measurement on a two years period is likely to lead to an underestimate of the effect one may expect from a nutritional intervention. This reanalysis also showed that arm circumference without any correction for age or height seems to be a good predictor of death and might be even better than weight for age used in the Punjab study: in contrast to weight for age, arm circumference is little correlated with height which has been shown to have no predictive value (6).

The present protocol will determine the proportion of deaths

which can be predicted by repeated measurements of arm circumference. This approach seems to be the most promising to obtain a high validity: arm circumference is a simple measure which can be repeated every month and should yield estimations of the risk of death much more specific than found previously. In addition to that, the relevance of basic information about breast feeding, recent morbidity history measles to assess the risk of death will be tested. This information is easy to collect and may be a simple mean to substantially increase the quality of the selection of 'at risk' children.

3. Rationale

- The potential reduction of infant or child mortality which can be expected from a targeted nutritional intervention is limited by the validity of nutritional indicators used to define 'at risk' children.

- Available evidence suggests that the validity of a nutritional index can be dramatically increased by repeating it at short time intervals.

- Arm circumference without correction for age or for height is a good predictor of death. It is a simple measure which can be repeated every month.

- Simple information on dietary history and recent morbidity may improve the assessment of the risk of death.

- Repeated measurements of arm circumference with basic dietary and morbidity histories should increase the upper limit of the reduction in mortality which can be expected from a

targeted nutritional intervention.

B. SPECIFIC AIMS

- To measure every month arm circumference of children in the 6-36 months age group in Matlab comparison area and collect simple information on feeding and morbidity histories.

- To compare these data for children who die during follow up and those who survive.

- To estimate the upper limit of the proportion of deaths which could be averted if these criteria of predictions were used to select 'at risk' children for intervention.

C. METHODS OF PROCEDURE

1. Age group.

Children under the age of 3 years have a high mortality. The study will be done on this age group only. Although traditionally measurement of arm circumference is recommended after the age of one year, in this study, measures will be started earlier, at 6 months. A yet unpublished study on the relation between anthropometry and mortality in ICDDR,B hospital showed that this indicator can be used to estimate the risk of death with good results before the age of one year. No measurement will be taken before 6 months since a nutritional intervention aiming at reducing mortality before this age seems out of reach in the present situation. Children in the age group 3 to 5 years will not be included in the sample. Demograhic data from Matlab

show a decline of mortality at this age and it is preferred to concentrate efforts on younger children.

2. Frequency of measurements.

Reanalysis of Sommer and Lowenstein's data (6) showed that specificity - sensitivity curves improved constantly when the follow-up after measurement was reduced from 6 to 1 month. Available data did not allow to examine what happened with shorter intervals. It seems however that more frequent measurements would have little advantage: the number of deaths in such a short time interval is too small to yield substantial information for statistical analysis.

3. Duration of the study

For logistic reasons, this study will have to be started in Matlab comparison area only: the record keeping system used in MCH-FP area is such that collection of additional information can be included in the routine work of CHW's at the begining of the year only, when new books for data collection are printed. ICDDR,B has little possibility of intervention in the comparison area and the problem of treatment and referral of children who will be found to be 'at risk' will be beyond the reach of the investigators. For this reason, it is proposed to stop the study as soon as enough information is collected to design an other protocol with an attached targeted nutritional intervention to be implemented in MCH-FP area. In any case, the duration of the study will not exceed six months, since it is felt that long term

observation of malnutrition associated deaths in this area where we have little possibility of intervention could create frustration among the families.

4. Sample size.

In the Matlab comparison area, there are some 8400 children in the age group 6-36 months. It can be expected from previous years data that approximately 30 deaths will occur in this age group every month. This should be enough to give rapidly an answer to the questions raised by this protocol, even after the initial sample is broken down by age and sex in different categories.

5. Technique of measurement of arm circumference.

Arm circumference will be measured on the left middle upper arm as described by Jelliffe (9). The precision of the measurement will be increased by using insertion type tape measures which should also reduce reading mistakes (10). Measurements will be made monthly by Community Health Workers during one of their fortnight visits. They will also be asked to check for the presence of leg oedema by pressure during half a minute on pretibial region.

6. Collection of dietary and morbidity histories.

Every months mothers will be asked whether their child is fully breast fed, partially breast fed or totally weaned. Basic information on recent attacks of diarrhoea, respiratory

infections and on measles will also be collected. The attached questionnaire will be used by Community Health Workers for that purpose.

7. Attitude towards severely malnourished and critically ill children

Before the beginning of the study, the CHW will receive some training in nutrition which will allow them to give sound advice whenever they find a severely malnourished child. It is most likely however that every month, some CHW's will come across severely malnourished children whose bad condition and risk of imminent death will be obvious and for which nutritional advice will be clearly not enough. Unfortunately, possibilities of intervention from ICDDR,B in the comparison area are limited and it will be difficult to offer them adequate support. In this case, CHW's will be briefed to refer the child with ICDDR,B transport either to ICDDR,B Matlab station, or to Matlab government hospital or to a nearby physician , the choice between these options being left to the families.

8. Data collection, statistical analysis.

Every Community Health Worker will be supplied with a print out of 3-36 months children in her area. For two weeks every month, this print out will be used to record arm circumferences during one round of the CHW. During the two other weeks, this print out will be sent to Dhaka (or even kept in Matlab if this

station is provided with a micro-computer) for data entry in the computer. This procedure will avoid the time consuming process of data coding: the format of this printout will be designed for this purpose and simple, user friendly software will be developed to facilitate data entry. Once entered in the mainframe, the data will be selected to create a file suitable for case control analysis: records of all dead children and of ten randomly selected controls for every case will be extracted from the main data set and transferred to a personnal computer. This will decrease dramatically computer costs and will avoid delays in the statistical analysis of the results.

The statistical analysis of this subset of data will be done in several sueps. First, sensitivity-specificity curves of arm circumference as an indicator of risk of death will be derived from cumulative frequency tables of this indicator for children who survived and those who died during follow-up. This will allow a comparison with the prediction obtained in previous studies with other indicators. Analysis of risk of death for different arm circumference categories will give an estimate of the proportion of deaths associated to malnutrition in this age group. This analysis will be repeated for males and females children in different age groups and different groups of villages to determine in which circumstances the number of deaths associated with malnutrition is affected.

In a second stage, it will be determined whether the prediction of death obtained from arm circumference measurement can be improved by using a model comprising additional available

information. The usefulness of past measurements of arm circumference to improve the estimation of the risk of death will first be tested. It is usually taken for granted that for any level of a nutritional status indicator, the risk is higher if the child recently deteriorated. This is the rationale for encouraging the health workers to keep records of past measurements and to try to estimate their variations over different periods of time. This hypothesis however has never been tested and one may wonder if such an approach, which is more time consuming, yields substantially better results than the result of the measurement itself. This will be done by incorporating various arm circumference indicators such as the difference of the last measurement with the previous one, or the slope of its curve against time in different logistic models and determining which one is the best to estimate the risk of death. This approach is the most appropriate to test the influence of several related variables on a single dichotomous dependent variable such as survival. The same method will be used to test the relevance of oedema, morbidity and feeding history variables and of other variables routinely collected in Matlab.

D. SIGNIFICANCE

This study will suggest the upper limit of the reduction in mortality which can be expected from a targeted nutritional intervention. Previous studies on the relation between nutritional status and mortality suggests bleak results for such interventions. It is hoped that longitudinal measurements of arm circumference will be a more specific indicator of risk of death

than those used in previous studies and will provide the prospect of more effective interventions.

ABSTRACT SUMMARY FOR ETHICAL REVIEW COMMITTEE.

1. Description of the study

This study aims at evaluating how effectively malnourished children with a high risk of death can be selected by monthly measurement of arm circumference. It will take place in Matlab comparison area for the age group 6-36 months. Arm circumference of children will be measured every month by Community Health Workers who already visit every household. In a first stage, this study will be mainly descriptive. Health workers will be asked to inform mothers if they find that a child is malnourished and will be trained to give sound nutrition education to the families. If the condition of a child is severe, the CHW will be asked to refer the child to a paramedic or to an hospital. A more specific intervention is not included in this protocol for several reasons. First, without solid relevant information at hand, it is impossible to design a nutritional intervention satisfactorily since mass screening of malnutrition has never been started in Matlab: we have little idea of the number of children who will require an intervention and the logistic implications of such an intervention are unknown. Secondly, available evidence suggests that with traditional screening techniques, the prospects of success of such an intervention are very limited. A more optimistic outlook from data collected in this study is necessary before starting any intervention. Finally, the nature

of the intervention to start is still an open question. The relative proportion of children that will have to be treated at home or in a central Nutrition Rehabilitation Unit will depend on the results of this first observational study and of the results of another protocol on the effectiveness of ICDDR,B Dhaka hospital Nutritional Rehabilitation Unit (by the same principal investigator).

The investigators will use the first results of this protocol to propose an intervention project in a separate protocol as soon as possible.

2. No risk, physical or psychological will result from this protocol.

3. NA

4. Children examined during this protocol will be identified by a code number and anonymity will be protected during the analysis.

5-6. NA.

7. Individual subjects examined during this protocol will benefit from additional attention from Health Workers and, if their condition is serious will be sent for referral.

8. NA.

References:

1. UNICEF's State of the World's Children Report, 1984.

2. Puffer RR, Serrano CV. Patterns of mortality in childhood. Scientific Publication No 262, Pan American Health Organisation. Washington. 1973.

3. Sommer A. and Lowenstein MS. Nutritional status and mortality: a prospective validation of the Quac stick Am. J. Clin. Nutr. 1975, 28: 287-92.

4. Kielman AA and McCord C. Weight for age as an index of risk of death in children. Lancet, 1978: 1: 1247-50.

5. Chen LC, Chowdhury AKMA and Huffman SL. Anthropometric assessment of protein energy malnutrition and subsequent risk of mortality among preschool aged children. Am. J. Clin. Nutr. 1980; 33: 1836-45.

6. Briend A, Zimicki S. Validation of arm circumference as a predictor of death in 1 to 4 year-old children. In preparation.

7. Shafiqul Islam M, Abbas Bhuyia, Yunus MD. Socio-economic differentials of diarrhoea morbidity and mortality in selected villages in Bangladesh. J Diar Dis Res 1984; 2: 232-7.

8. Shaikh K, Mostafa G, Sarder AM, Wojtyniak B. Demographic surveillance system- Matlab. ICDDR,B. 1982.

9. Jelliffe DB. The assessment of the nutritional status of the community. WHO Monograph Series No 53. Geneva: World Health Organisation, 1966.

10. Zerfas AJ. The insertion tape: a new circumference tape for use in nutritonal assessment. Am. J. Clin. Nutr. 1975; xx: 782-7.

QUESTIONNAIRE FOR DIETARY AND MORBIDITY HISTORIES:

1st Question: IS THE CHILD BREAST FED? !__!

-If the child is fully breast fed or if he receives water only as supplement. write 1

-If he receives any kind of food in addition to breast milk write 2

-If the child is no longer breast fed write 3

2nd Question: HAS THE CHILD DIARRHOEA TODAY? !__!

-If the child had less than three loose stools in the last 24 hours write 0.

-If the child has watery diarrhoea without any blood in the stools write 1

-If the child has 'simple' diarrhoea without blood write 2

-If the child has bloody diarrhoea write 3

3rd Question: IF HE/SHE HAS DIARRHOEA, FOR HOW MANY DAYS ? !__!

-If less than 7 days write 0
-If more than 7 days write 1

4th Question: HAS HE/SHE RUNNING NOSE, COUGH, TODAY ? !__!

If no: write 0
If yes: write 1

6th Question: HAS HE/SHE HIGH FEVER, COUGH, RAPID BREATHING AND FLAPPING OF ALAE NASI ?

If yes: REFER THE CHILD write 1
If no: write 0

7th Question: HAD HE/SHE A SKIN RASH WHICH HAS BEEN PRECEDED BY HIGH FEVER, COUGH, RUNNING NOSE AND RED EYES SINCE LAST MONTH ?

If yes: write 1
If no: write 0

BUDGET:

Incremental costs,	US $
1. PERSONNEL AND SERVICES:	
1 Physician Nutritionist (30% time)	Salary not incremental
Head, Matlab Station Officer	Salary not incremental
Manager Health Services, Matlab	Salary not incremental
Manager DSS, Matlab	Salary not incremental
1 Demographer	Salary not incremental
1 Programmer (one month)	275
1 Data Management Officer (50% of time)	800
1 Data Entry Technician Cost: 1 Taka for 80 columns 200 000 bytes/month	600
2. MATERIAL AND SUPPLIES:	
Insertion tapes measure (500, 20 takas each)	400
Computer stationery:	600
Stationery, xeroxing:	200
3. INTERDEPARTMENTAL SERVICES	
ICDDR,B Transport Trips to Matlab 10 at 500 Takas each	200
Speed boat time (100 hours) for patient referral: (Tks 350 per hour)	1500
Computer time	400
Total:	4975 US $