*development of new mortality-targeted scales

ETHICAL REVIEW COMMITTEE, ICDDR,B. Date: 20th June 1984

Principal Investigator Dr. André Briend

Application No. 84-027(P)

Title of Study Analytical investigations into the mortality implications of anthropometric scales and into the *

Trainee Investigator (if any) ~~Dr~~

Supporting Agency (if Non-ICDDR,B)

Project status:
(✓) 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.

A B d

Principal Investigator — 27 JUN 1984 — Trainee

SECTION I - PILOT PROTOCOL

1. TITLE : Analytical investigations into the mortality implications of anthropometric scales and into the development of new mortality-targeted scales

2. PRINCIPAL INVESTIGATORS : A. Briend, J. Clemens

   CO-INVESTIGATOR : A.K.M.A. Chowdhury

3. STARTING DATE : July 1, 1984

4. COMPLETION DATE : December 31, 1984

5. TOTAL DIRECT COST : US$ 1196.00

6. SCIENTIFIC PROGRAM HEAD :

This protocol has been approved by the Nutrition Working Group

Signature of the Programme Head : 

Date : June 20, 1984

7. ABSTRACT SUMMARY

This research project will re-examine the anthropometry-mortality correlation data of Chen and colleagues with two purposes. First, existing several classical anthropometric indexes will be analysed with modelling and non-modelling techniques to assess the interrelationships of the indexes. We will assess the marginal improvement in the prediction of mortality attributable to each index, and the etiologic fraction of mortality that appears to be "explained" by malnutrition--at least as reflected in those anthropometric indexes which are found to provide statistically meaningful and independent predictive power for subsequent mortality. Second, the raw data

(height, weight, arm-circumference) will be examined with discriminant function analyses to assess whether improved mortality-targetted anthropometric scales can be developed.

8. REVIEWS

a. Ethical Review Committee _____

b. Research Review Committee : _____

c. Director : _____

SECTION II - RESEARCH PLAN

A. INTRODUCTION

Numerous anthropometric indices are available to evaluate nutritional status of an individual in a population. Despite the plethora of such indices, relatively little information is available about the relationship between a child's position on an anthropometric scale and the child's subsequent risk of death. Sommers and Lowenstein (1) in Bangladesh and Kielman and Mac Cord in India (2) described mortality risk differences based on inspection of such indices as the "QUAC stick" and weight-for-age. Chen et al (3) in Bangladesh showed sharp risk thresholds of mortality at well-defined points along several anthropometric scales. More recently, the Kassongo project team (4) failed to find any significant correlation between cut-off points of several indices and subsequent mortality. None of these studies, however, has adequately contemplated the relative contribution of different indices to the prediction of mortality (which can only be addressed with multivariate techniques), nor the possibility that the reexamination of the basic data and the construction of new indices, may be warranted for this purpose.

In this project, we propose to reexamine the data of Chen and colleagues. In this data set, 2016 children, aged 13-23 months, in Matlab were assessed in regard to height, weight and arm circumference during November 1975 - January 1976. Death ensuing over the subsequent 24 calendar months were detected through the

Demographic Surveillance System. Successful linkage of anthropometric data and follow up was achieved for 2019 subjects. Overall, 112 children died during follow up.

With this risk data set, we will address two fundamental sets of questions:

1) Among the several indices available for assessing anthropometric nutritional status (weight for age, weight for height, height for age, arm circumsference for age, arm circumference for height, weight quotient, height quotient),

   a) what are the interecorrelations of the indices in respect of classification?

   b) what is the rank order of the indices in "explaining" (via calculation of the etiological fraction) mortality?

   c) which indices contribute statistically independent (e.g. additional) information in predicting mortality?

   d) when all nutritional indices are simultaneously considered and relevant socio-economic factors are controlled, what fraction of mortality does malnutrition "explain" and hence what is the upper-limit of benefits with respect to mortality that can be expected to occur with nutritional interventions?

2) Can improved indices of nutrition be developed using the same basic data but transforming or demarcating the data in a way that is optimally targetted to the risk of subsequent death?

B. ANALYTICAL METHODS

1. Examination of classical indices

a) Interrelationship of Indices

This part of the evaluation of the indices will not consider the risk of subsequent mortality but will analyze the correlations (Pearson's coefficient of correlation) of the above-mentioned indices. Weight for age, weight for height and height for age will be taken as the percentage of Harvard standard. The weight and height quotients will also use age-weight and age-height relationships that correspond to the Harvard medians. Standard for arm circumference will use those published by Jelliffe (5) and those for the "QUAC stick" will employ the technique described by Arnhold (6). In addition, after partitioning the indices according to accepted ranges of "normal nutrition" and "mild, moderate and severe malnutrition", we will examine the agreement (rather than merely the correlation) between indices using suitable techniques in assessing concordance, such as Kappa statistical analysis. Finally, to determine if the association between the different indices themselves suggests clusters of indices which convey different clinical meaning, we will analyse

the clustering of indices using the factor analysis software available in ICDDR,B.

b) Evaluation of the indices in relation to subsequent mortality

In this analysis, we will first consider each index according to the "etiological fraction" of mortality explained for the nutritionally deficient individuals detected by the index. The etiological fraction (EF) can readily be calculated from this data, as:

$$EF = \frac{\sum_{i=0}^{k} p_i (IDR_i - 1)}{\sum_{i=0}^{k} p_i (IDR_i - 1) + 1}$$

where IDR is the incidence density ratio of death for the i^{th} category of the scale relative to a reference category (e.g. normal nutrition) and Pi is the fraction of individuals whose nutritional status is in the i^{th} category. Using a logistic model, in which important socio-economic covariables will be introduced, we will then examine the extent to which the etiological fraction of each index is affected by the control for fixed socio-economic variables. We will then determine which indexes independently predict mortality, again using logistic regression. The first variable (index) in the model will be that variable with the most statistically significant (lowest p value) relationship with mortality assessed with simple bivariate analysis. The next variable to be entered in the model will be that

variable which carries the largest increment in the model Chi-square while retaining significance (p less than 0.05) for its regression coefficient. This process will be interatively repeated until no further indices add significant predictive to the model. The final model will be evaluated with respect to the etiologic fraction (using the natural logarithm of the beta coefficients to calculate incidence density ratios) of the final ensemble of indices, both before and after adding pertinent socio-economic variables. In this way, we will obtain an estimate of the upper limit to which mortality can be altered simply by nutritional intervention. Clearly, this sort of estimate and the development of a methodoloty for obtaining the estimate is of considerable importance in public health planning.

2. Development of new indices

Bivariate indices are easy to use in practice, even by a primary health worker since they may be rapidly evaluated by a graphical method. Our proposal is to find out which are the best bivariate indices which may be derived from the data of Chen and colleagues.

For every child who was followed up, age, weight, height and arm circumference are available. By systematic combination of all these variables, a bivariate index can be derived from the following associations:

weight and age
height and age
arm circumference and age
weight and height
weight and arm circumference
arm circumference and height

The best approach to find the optimal combination of two variables is to introduce them seperately in a discriminant analysis before and after log transformation.

For each couple of variables (x) and (y), a score Z can be calculated by one of the following equations:

$$Z = A(x) + B(y) + C$$

OR

$$Z' = A' \log x + B' \log Y + C'$$

The constant A, B and C and A', B' and C' are calculated to give the best predictive value to the Z score to assess the risk of mortality.

The log equation is equivalent to -

$$Z = k . x^{a} . y^{b}$$

OR

$$Z = k . \frac{x^{a}}{y^{b}}$$

and may give a better prediction if the association between anthropometry and the risk of death is not linear.

After completing these 12 bivariate discriminant analyses, some indices may be proved to be irrelevant and give no more information that the best predicting variable used alone.

For bivariate indices which are found to be relevant, we suggest a comparison with the previously described anthropometric indices. This can be done by two methods. For some indices, such as weight for height, which are equivalent to a simple mathematical function (weight for height can be shown to give the same information as $\frac{\text{weight}}{\text{height}^{2.2}}$ by a log regression from the standards of weight for height), one can simply compare the equations from which the classical and the new indices derive.

When such a comparison is not possible, a comparison of the new and the classical indices by the method of etiological fractions described above will be used.

This approach, with no reference to any nutritional standard and no assumption on the nature of the relation between anthropometry and mortality, is the only way to know whether the use of classical nutritional indices are relevant in the Matlab population.

C. SIGNIFICANCE

These analyses may yield information of considerable practical significance regarding the interrelationships between existing

anthropometric indices and the extent to which they predict subsequent mortality, as well as regarding the development of new indices which can be used in future studies.

SECTION III - BUDGET

PERSONNEL SERVICES	PROJECT REQUIREMENT Taka
Data Coding and Entry (100 hours) @ 30 T/hr	3,000
Programmer's Time (200 hours) @ 30 T/hr	6,000
Computer Time (100 hours + 10% Programmer's time) @ 200 T/hr	20,600
TOTAL	29,600

($ equivalent = $ 1,196)

B. BUDGET SUMMARY

	CATEGORY	TAKA
1.	Personnel	9,000
2.	Supplies	-
3.	Equipment	-
4.	Hospitalisation	-
5.	Outpatient	-
6.	ICDDR,B Transport	-
7.	Travel of Persons	
8.	Transportation of things	-
9.	Rent/Communication (Computer's time)	20,000
		-
10.	Printing	-
11.	Contractual Services	-
12.	Construction	-
	Total	29,000

(US$ 1,196)