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ETHICAL REVIEW COMMITTEE, ICDDR,B.

Date 27/4/86

Principal Investigator A. Briend

Application No. 86-015

Title of Study Evaluation of the risk of death in the interval between 2 6-monthly home visits...

Trainee Investigator (if any) _____

Supporting Agency (if Non-ICDDR,B) _____

Project status:

( ) New Study

( ) Continuation with change

(X) 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 NA
   - (b) Procedures to be followed including alternatives used — Yes No NA
   - (c) Physical risks — (Yes) No
   - (d) Sensitive questions — Yes No NA
   - (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 NA
   - (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.

(PTO)

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

A. Briend

Principal Investigator

Trainee

86-015
27/4/86

SECTION I : RESEARCH PROTOCOL

1. "EVALUATION OF THE RISK OF DEATH IN THE INTERVAL BETWEEN TWO 6-MONTHLY VITAMIN A CAPSULE DISTRIBUTIONS"

2. a. Principal Investigator(s): Dr. A. Briend, Dr. V. Fauveau

b. Co-Investigators: Dr. M.G.M. Rowland, Dr. B. Wojtyniak

c. Consultants: Dr. M. Cohen, Dr. M. Mitra, Dr. M.M. Rahaman

3. Starting Date: 1st July, 1986

4. Completion Date: 31st Dec.1988 (2-1/2 yrs. from start)

5. Total Incremental Cost: US$9,432/-

6. Scientific Programme Head: Dr. MGM Rowland

This protocol has been approved by the Community Research Working Group and Nutrition Working Group

Signature of the Scientific Programme Heads:

Nutrition Working Group

Date: 23/4/1986

Community Research Working Group

Date: 20.4.86

7. ABSTRACT SUMMARY

This protocol aims at indirectly testing the relation between mild vitamin A deficiency and increased risk of death in under five children by determining whether mortality in this age group increases in the later part of the 6 month interval between two rounds of vitamin A capsules (VAC) distribution. All villages of the Matlab MCH-FP treatment and comparison areas (with a total population of 190 000) will be randomly divided into two groups in which VAC distribution will be out of phase by three months to eliminate the effect of seasonal variations of mortality. The interaction of vitamin A deficiency with breast feeding, morbidity and protein energy malnutrition in relation to child survival will be investigated in the children of the MCH-FP area in which relevant information is already routinely collected.

8. Reviews: (Leave Blank)

(i) Chairman, Ethical Review Committee: _____ Date: _____
(Approved/Not Approved)

(ii) Chairman, Research Review Committee : _____ Date: _____
(Approved/Not Approved)

(iii) Director, ICDDR,B : _____ Date: _____
(Approved/Not Approved)

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## SECTION II : RESEARCH PLAN

### A. INTRODUCTION

#### 1. Objectives

- To determine whether mortality varies in the intervals between two 6-monthly distributions of vitamin A.

#### 2. Background

Regular 6 monthly distribution of high potency vitamin A capsules (VAC, 200 000 International Units) to children below the age of 6 years is a standard recommendation in countries like Bangladesh where there is a high prevalence of eye lesions due to Vitamin A deficiency. Although this cannot be considered as an adequate long term strategy to solve the problem of xerophthalmia, the potential benefit in terms of prevention of severe eye lesions which can be derived from these interventions is no longer in question (1-5).

Vitamin A distribution may however have a more general effect than prevention of ocular lesions (6). Animal experiments show that vitamin A deficiency is associated with a poor response to infection: vitamin A deficient animals have a higher mortality when challenged with infectious agents (7). This seems to be due to a deterioration of various component of the antiinfectious defense (8-10) but the production of secretory IgA which plays a key role in the defense against diarrhoea seems particularly affected (8).

The hypothesis that vitamin A may play a role in humans in the defense against infection and that mild vitamin A deficiency

may be associated with an increased morbidity and mortality received some support from a recent community study (11,12) and results of a yet unpublished community experiment from Indonesia (13). These studies suggest that mild vitamin A deficiency is associated with an increased diarrhoeal morbidity, increased risk of death and that regular vitamin A supplementation may result in a substantial decline in 1 to 5 year child mortality even when given to children with no clinical sign of vitamin A deficiency. A confirmation of these findings would put VAC distribution among the top priorities in strategies currently being developed for improving child survival.

Experimental study designs which are most appropriate to confirm these findings require a control group of several thousand children who would not receive vitamin A supplementation. This cannot be done in Bangladesh without interfering with the regular distribution of VAC by the government blindness prevention programme. This would be ethically unacceptable given the high prevalence of blinding malnutrition in the country. Theoretically, a surveillance system could be established for the control group to detect and treat any child who has signs of mild vitamin A deficiency , as a substitute for regular VAC distribution. However, night blindness is difficult to detect in young children and severe corneal lesions, in unsupplemented malnourished children, can develop in a few days of intercurrent illness without being preceded by signs of mild xerophthalmia (4, 14, 15). In rural Bangladesh the high prevalence of malnutrition and dysentery

would make the prevention of blindness for such a control group by this approach rather ineffective.

A recent survey of VAC coverage by the government programme in Matlab area of a 1 in 10 sample of children under 35 months (currently in the ICDDR,B demographic surveillance programme) showed that approximately 47 % of them are reached by this programme (16). This creates a quasi-experimental situation which theoretically could be exploited to examine the relation between VAC receipt and risk of death. However, this would require that VAC coverage should be frozen for at least two years at the present level. This would interfere with the wish to improve Maternal and Child Care and Family Planning (MCH-FP) services in the the area of Matlab under ICDDR,B medical supervision. A retrospective study could be designed to avoid these problems. However, assuming a relative risk of death of 1.2 for children who did not receive vitamin A with a VAC coverage of 50 % in the community, the sample size needed to have a 80 % chance to detect a significant effect requires 1890 cases and as many controls (17). This by far exceeds the number of deaths occurring every year in Matlab in the 1-4 years age group (684 in 1983). Information would have to be collected from several years ago and would be unreliable. An observational study limited to the area where ICDDR,B has no input could be considered. However the population under demographic surveillance is not large enough to give an acceptable chance of finding significant results.

In addition to that, all designs based on the quasi experimental approach have a common weakness which makes them unacceptable. VAC coverage is higher in MCH-FP villages near

Matlab Bazaar with better access to ICDDR,B, government or private treatment facilities. This would make difficult the interpretation of any difference in mortality associated with VAC distribution either in a prospective or a retrospective study. In 1983, the 1-4 year death rate was 21.6 per thousand in MCH-FP villages compared to 35.3 per thousand in other villages (18). The risk ratio between the two zones (1.63) is higher than the risk ratio expected for children who do not receive VAC. Moreover, it is not known to what extent different components of existing services (some of which are outside ICDDR,B supervision) contribute to the reduction of mortality in MCH-FP villages. It seems therefore impossible to adjust this mortality differential by including service related covariates in the analysis.

Although 6 monthly distribution of high potency VAC is known to prevent severe eye lesions, there is biochemical evidence that this is inadequate for keeping children's vitamin A reserves at a high level for more than a few weeks time (2,4). After VAC absorption, in children on a vitamin A deficient diet, serum levels rise in a few hours (19) but decline rapidly to fall below 20 microgrammes per 100 ml in 10-12 weeks (4,20,21). A VAC contains 60 mg of retinol (200 000 IU). Even by optimistic estimates, no more than 50% of this amount is absorbed by the child, far less if he has diarrhoea (4,22). Given every 6 month, a VAC tops up the daily intake by 166 microgrammes whereas WHO estimates for daily requirements for 1-4 years old children varies between 300 and 400 microgrammes (23). For children who are frequently sick and eat a diet grossly deficient in vitamin

A, VAC distribution every 6 months is unlikely to fill the gap between the children's dietary intake and the recommended requirements.

Presumably, for the prevention of eye lesions, this difference between international recommendations of vitamin A intake and the actual quantity given by 6 monthly supplementation has no practical relevance. WHO estimates of daily requirements of vitamin A are based on the quantity needed to maintain serum levels at what is considered to be an 'optimal level'. Other methods estimating the minimal quantity needed to prevent the occurrence of clinical signs of vitamin A deficiency give much lower estimates (24). On the other hand, if mild deficiency in vitamin A is associated with an increased risk of death, then this difference between requirements and the quantity of vitamin A which can be given by 6 monthly distribution of capsules may have important consequences: at the end of the 6 months period, risk of death could be increased even in the absence of eye lesions in supplemented children.

In rural Bangladesh children have a high prevalence of diarrhoea and eat a rice based diet very low in vitamin A content (25-27). The six- monthly distribution of VAC for blindness prevention is likely to keep their vitamin A status to an optimal level only for a few weeks time. This protocol aims at indirectly testing the relation between mild vitamin A deficiency and increased risk of death by determining whether mortality increases in the later part of the 6 month interval between two VAC distributions.

3. Rationale

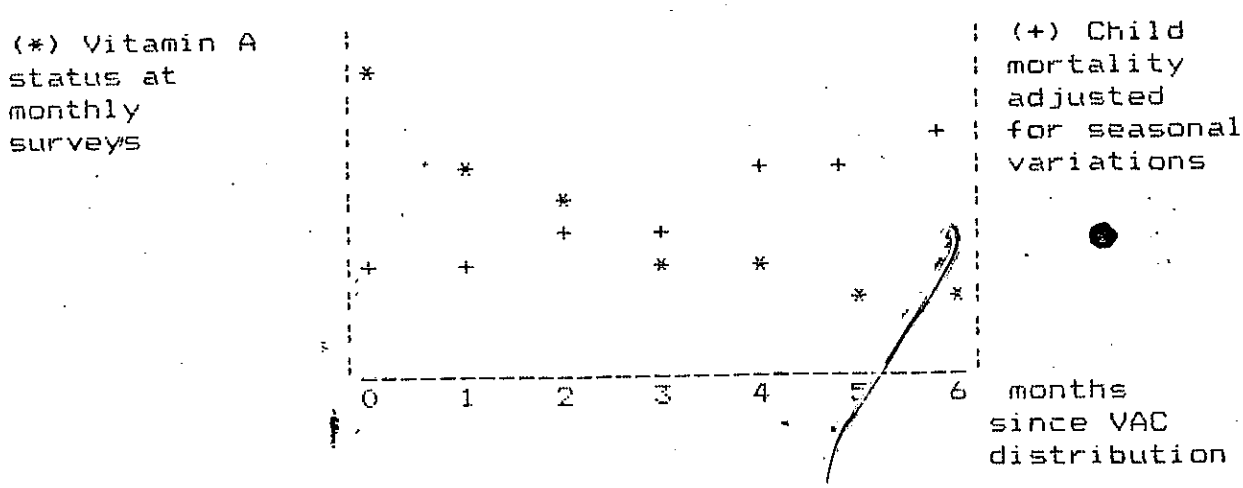
- Direct confirmation of the possibility of reducing 1-5 year child mortality by regular vitamin A supplementation is not possible in the community under ICDDR,B surveillance for both practical and ethical reasons.

- There are theoretical grounds to believe that 6 monthly distribution of VAC cannot maintain vitamin A status to an optimal level for more than 3 or 4 months.

-During regular 6 monthly VAC distribution, vitamin A status of under 5 children is likely to move from suboptimal to optimal levels and vice versa twice a year. This current practice provides the opportunity to test the relation between vitamin A status and mortality.

FIG. 1

PROPOSED THEORETICAL MODEL TO TEST THE RELATION BETWEEN VITAMIN A STATUS AND MORTALITY



B. SPECIFIC AIMS

- To reorganise 6 monthly distribution of VAC to children in Matlab MCH-FP and comparison areas and to aim at maximum coverage.

- To determine whether mortality increases during the interval between two VAC distributions.

C. METHODS OF PROCEDURE

1. Description of the study area.

Since 1963, the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B), formerly the Cholera Research Laboratory, has been conducting a health-oriented research programme in Matlab Upazila, Chandpur District, a rural area of Bangladesh (18). Matlab is located about 45 km from Dhaka, the country's capital. The 149 villages under surveillance have a total population of 191 000. Since October 1977, the data collection has been modified in conjunction with the development of a village-based Maternal and Child Health and Family Planning (MCH-FP) Programme in 70 villages. The remaining villages are referred to as "comparison" villages.

2. Vitamin A capsule distribution.

To reorganise VAC distribution, government services will be approached and ICDDR,B will propose to take over this service. VAC can be given every 6 months by Community Health Workers (CHW)

who visit every household fortnightly for demographic surveillance. CHW's in the MCH-FP area are already provided with a computer printed book with the name of every under five child in which they routinely record information about maternal and child health. These CHW's will personally give the contents of the VAC to the children and record the event in their book. In the comparison area where CHW's do not have such a book, they will be provided with a computer print-out of eligible children before VAC distribution both for identifying children and for recording receipt.

Vitamin A status seems to vary considerably according to seasons in this part of the subcontinent (25, 28, 29). Mortality in Matlab is also affected by seasons (30). A classical 6 monthly VAC distribution which would recur at the same time of the year

TABLE 1

VITAMIN A DISTRIBUTION SCHEME
IN MATLAB MCH-FP AND COMPARISON AREAS

| Months | -3 | 0 | 1 | 2 | 3 | 5 | 5 | 6 | 7 | 8 | 9 | 10 | .... |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Group 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Group 2 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |

Groups 1 and 2 represent half of the children under the age of 5 in Matlab MCH-FP and comparison areas. Randomisation will be made at village level.
Month 0: earliest possible date for the beginning of the study, assuming that this distribution scheme is started at month -3.

could create spurious associations with mortality. For that reason, villages will be randomly divided into 2 groups (after stratification by size) in which VAC distribution will be out of phase by 3 months as shown in Table 1. To ensure that no group remains without VAC coverage at the beginning of the study, a first round of comprehensive VAC distribution will be given as soon as ICDDR,B gets clearance from Government of Bangladesh for this distribution scheme.

Vitamin A capsules may induce anorexia, nausea and vomiting in 1 to 3 % of children (4). CHW's will be informed about this side effect and will be asked to mention this possibility to the parents before giving a capsule.

3. Age group

For all children under the age of 6 years and for mothers within a month of delivery, capsules will be given according to

TABLE 2

VITAMIN A PROPHYLAXIS SCHEDULE

| Individual | Oral dose | Timing |
|---|---|---|
| 1-11 months infants | 100 000 IU | every 6 months |
| Children > 12 months | 200 000 IU | every 6 months |
| Mothers | 300 000 IU | within 1 month of giving birth |

WHO guidelines and official recommendation of the Government of Bangladesh (3) (Table 2). Children and infants will receive a dose of vitamin A corresponding to their age every time there is a distribution scheduled in the village. For analysis however only data about VAC intake of children under 5 years of age will be collected. Collection of data for older children would need a redesigning of the MCH-FP recording book with little advantage for the study since mortality in this age group is low compared with younger children.

4. Power of the study

The power of this study can be defined as the probability of finding that the risk of death in the vitamin A deficient intervals will be greater than during the protected intervals. It can be estimated from the size of the sample under study, the expected death rate, and the relative risk of death expected during vitamin A deficient periods (31).

Results from the previous intervention study in Indonesia suggest that the mortality reduction which can be expected by improving vitamin A status is mainly observed in 1-4 years old children (13). For that reason only this age group will be taken into account for the calculation of the power of this study although data of all under five children will be included in the analysis. This study is planned for 2 years, and will take place in the total population of the Matlab area under demographic surveillance with a total 1-4 year population of 23500 children. Assuming a total of 15 % of children not reached by the VAC

distribution, refusing to ingest the capsule or lost during follow up, this will provide for calculation of power a total of 480 000 child month intervals.

The increase of mortality associated with a low vitamin A status in the 1-4 year age group in Indonesia was 35%. To be on the safe side it was assumed for this study that the risk of death in the months with a low vitamin A status would be only 1.2 times higher than during the control periods.

Previous studies in children receiving a low vitamin A diet (2, 20, 21), suggest that vitamin A status may fall below suboptimal levels between 2 and 4 months after a capsule has been

TABLE 3

EFFECT OF DIFFERENT HYPOTHETICAL DURATIONS OF IMPROVEMENT OF VITAMIN A STATUS AFTER INTAKE OF A VAC ON THE POWER OF THE STUDY.

| Hypothesis about vitamin A status | Number of children at risk | months controls | Power of the study |
|---|---|---|---|
| Good for 2 months, Insufficient for 4 months | 300 000 | 160 000 | 78% |
| Good for 3 months, Insufficient for 3 months | 240 000 | 240 000 | 84% |
| Good for 4 months, Insufficient for 2 months | 160 000 | 300 000 | 80% |

The power has been calculated for the detection of a relative risk of 1.2 in low vitamin A periods. Mortality has been assumed to be 0.2% per month in the control intervals.

given. Table 3 gives an estimate of the number of children months falling in the high risk and control categories depending on the hypothesis made about the length of the interval during which a child is fully protected. For the first and the third hypotheses involving a different number of high risk and control children months, it was assumed that 20 000 children intervals will have to be removed from the analysis to give a balanced distribution of control and high risk intervals over time and to avoid the confounding effect of secular trends of mortality (See fig.2 to 4). Table 3 shows that these different hypotheses have little effect on the power of the study which will be around the acceptable level of 80%. All these hypotheses can be tested from the same study design and all of them will be examined when the collection of data is finished.

5. Collection of information on breast feeding, nutritional status and illnesses.

Collection of information about the breast feeding status of every child, and recent diarrhoeal illnesses is now done routinely in Matlab MCH-FP treatment area. Collection of information about nutritional status assessed by arm circumference and prevalence of respiratory diseases is about to be started. Information about measles continues to be collected although the recent immunisation of nearly all eligible children makes this less relevant. All this information will be useful in determining whether the possible relation between vitamin A status and mortality could be explained by an increased prevalence of respiratory diseases and diarrhoea in deficient

children as suggested by a previous Indonesian study (12). It can also determine whether the lack of marked effect of vitamin A supplementation during the first two years of life suggested by the Indonesian study (13) could be due to a high proportion of breast fed children in young age groups. Monthly measurement of arm circumference will help to determine whether there is an interaction between protein energy malnutrition and vitamin A deficiency as also suggested by Indonesian data (11).

6. Prevention of blindness of children under study.

On the basis of previous studies, it is expected that VAC distribution will reduce the incidence of potentially blinding corneal lesions by at least 80% (1-5). Nevertheless, CHW's will be trained to recognise these lesions and will be asked to refer children with corneal lesions urgently to Matlab hospital at the project's expense where a physician could confirm the diagnosis and give adequate treatment. Records will be kept of all children having corneal lesions in the course of the study and will be linked afterwards with vitamin A distribution records. This will help to determine the origin of corneal lesions occurring in areas where VAC distribution programmes are in progress. It is still not known whether these cases are true failure of VAC to prevent corneal lesions or whether they occur only in children who are not reached by these programmes (4).

To further prevent blindness in children under study, physicians in Matlab hospital will be instructed to give routinely VAC to severely malnourished children ( defined by arm

circumference below 110 mm) and to those suffering from chronic dysentery (defined as the emission of bloody or mucoid stools for more than 8 days) even in the absence of any sign of vitamin A deficiency. Records will be kept of all patients given a VAC in the hospital for exclusion from the analysis in the relevant intervals. Prescription of additional vitamin A for children who received a VAC in the preceding 6 months will be discouraged for other conditions. Families will be asked not to buy the low dosage vitamin A capsules now available in the village shops.

7. Statistical analysis.

Initially, data on mortality for all high risk child intervals and for control periods will be arranged in 2x2 tables and the significance of any difference will be assessed by chi-2 tests. First, the data on the first two months of the interval between two VAC distributions will be compared with the last four months, then the first three months versus the last three months and finally the first four months versus the last two months (Table 4).

In a second step analysis will be restricted to children of the MCH-FP area for which additional information is available. Similar 2x2 tables will be made for breast fed and non breast fed infants, for children falling in different categories of arm circumference and for children who had or had not diarrhoea or other illnesses during the intervals. A Mantel-Haenszel Chi-2 test (32) on these set of tables would determine whether any possible association between time elapsed since last VAC

TABLE 4

DUMMY TABLE

SURVIVAL OF CHILDREN IN HIGH RISK AND CONTROL MONTHS
(all child intervals pooled together)

| | 2 Months following VAC distribution | Next 4 months |
|---|---|---|
| Died | | |
| Survived the interval | | |

Risk ratio = Chi-2 =

| | 3 Months following VAC distribution | Next 3 months |
|---|---|---|
| Died | | |
| Survived the interval | | |

Risk ratio = Chi-2 =

| | 4 Months following VAC distribution | Next 2 months |
|---|---|---|
| Died | | |
| Survived the interval | | |

Risk ratio = Chi-2 =

distribution and mortality could be due to a confounding variable, although the VAC distribution scheme on two groups of randomised villages makes such a bias unlikely. These different sets of 2x2 tables will also indicate whether there is an interaction between vitamin A status and other variables by comparing the relative risks of different categories of arm circumference, breast feeding, morbidity pattern etc...

Following this first analysis, all child months will be pooled together and the number of months elapsed since vitamin A distribution will be included in a logistic regression model to test whether it is significantly related to the risk of death. This technique is the most suitable to determine which factors are related to a dichotomous dependent variable such as survival and death (32) and may show a relation between Vitamin A status and survival which could have remained non significant by other techniques. Moreover, for the MCH-FP area for which additional information is available, the logistic regression model will allow us to test formally the significance of interaction which might have been found at the early stage of the analysis. In practical terms, the confirmation of a synergism between protein energy malnutrition or breast feeding or various illnesses and vitamin A deficiency would suggest that different supplementation schemes are needed for these different clinical conditions.

D. SIGNIFICANCE

Although this study will not test directly the hypothesis that 6 monthly VAC distribution reduces child mortality, it can be reasonably expected that it will give new insight into the

relation between vitamin A status and the risk of death in Bangladesh. In any case, it will determine whether the 6 month interval now recommended for VAC distribution in blindness prevention programmes should be shortened to improve child survival.

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# ABSTRACT SUMMARY FOR ETHICAL REVIEW

1. This protocol aims at indirectly testing the hypothesis that mild vitamin A deficiency may result in a higher risk of death, even in the absence of clinical signs of vitamin A deficiency. For that purpose, vitamin A distribution will be reorganised in Matlab MCH-FP and Comparison areas: villages will be randomly allocated to two groups in which vitamin A distribution will be out of phase by three months. This will give the opportunity to test whether mortality increases at the end of the interval between two vitamin A capsules (VAC) distributions when vitamin A status is supposed to become suboptimal, without the confounding effect of seasonality.

2. This study on the relation between the time spent since last VAC distribution and mortality does not require blood specimen. If in relation with this protocol it is decided in the future to make a serological survey on a sample of children, this will be mentioned in an addendum to this protocol which will be submitted beforehand to the Ethical Review Committee for consideration.

3. This protocol does not involve any risk to the patients. Vitamin A capsules will be given to eligible children following international guidelines for the prevention of blindness. Some discomfort (nausea, vomiting) may follow VAC receipt in 1 to 3 % of children. Community Health Workers (CHW) will be asked to inform the families of the possibility of this side effect.

4. All records regarding VAC intake will be considered as confidential. Patients will be only referred to by their code number once the data have been entered in the computer and edited.

5. No consent form will be used for that study: the distribution of VAC has a known value for the prevention of blindness and can be considered as the upgrading of an already existing service approved by the Government of Bangladesh. CHW's however will be asked to explain to the families the purpose of VAC distribution and to accept possible refusal for some children.

6. It is expected as a consequence of this study that the coverage of vitamin A distribution in Matlab area ( with a total population of children under 6 years above 25 000 ) will increase from 47 % to more than 90%. ICDDR,B CHW's pay frequent visits to every household and may reach every eligible child much more easily than government workers who have little logistic support. It is likely that nutritional blindness will decrease sharply in the area under surveillance after the beginning of this study.

# BUDGET

Incremental costs per year.

## 1. PERSONNEL AND SERVICES

| Name | Position | % Effort | Project requirements (US $ per year) |
|---|---|---|---|
| Dr. A Briend | MD, Nutritionist | 40 | not incremental |
| Dr. V Fauveau | MCH-FP Physician | 10 | not incremental |
| Dr. M Rowland | Head, CSRWG | 10 | not incremental |
| Dr. B Wojtyniak | Head, DSS | 10 | not incremental |
| Data Entry Technician (1 month) | | | 400 |

## 2. MATERIAL AND SUPPLIES.

| | |
|---|---|
| Computer stationery | 600 |
| Stationery, xeroxing | 200 |

## 3. INTERDEPARTMENTAL SERVICES

| | |
|---|---|
| ICDDR,B transport, Trips to Matlab 20 at 500 Takas each | 400 |
| Patient referral | 400 |
| Computer time for data analysis | 1 600 |
| Total: | 3 600 |
| Overhead (31%) | 1 116 |
| Grand total US$ | 4 716 |

24/9/96.

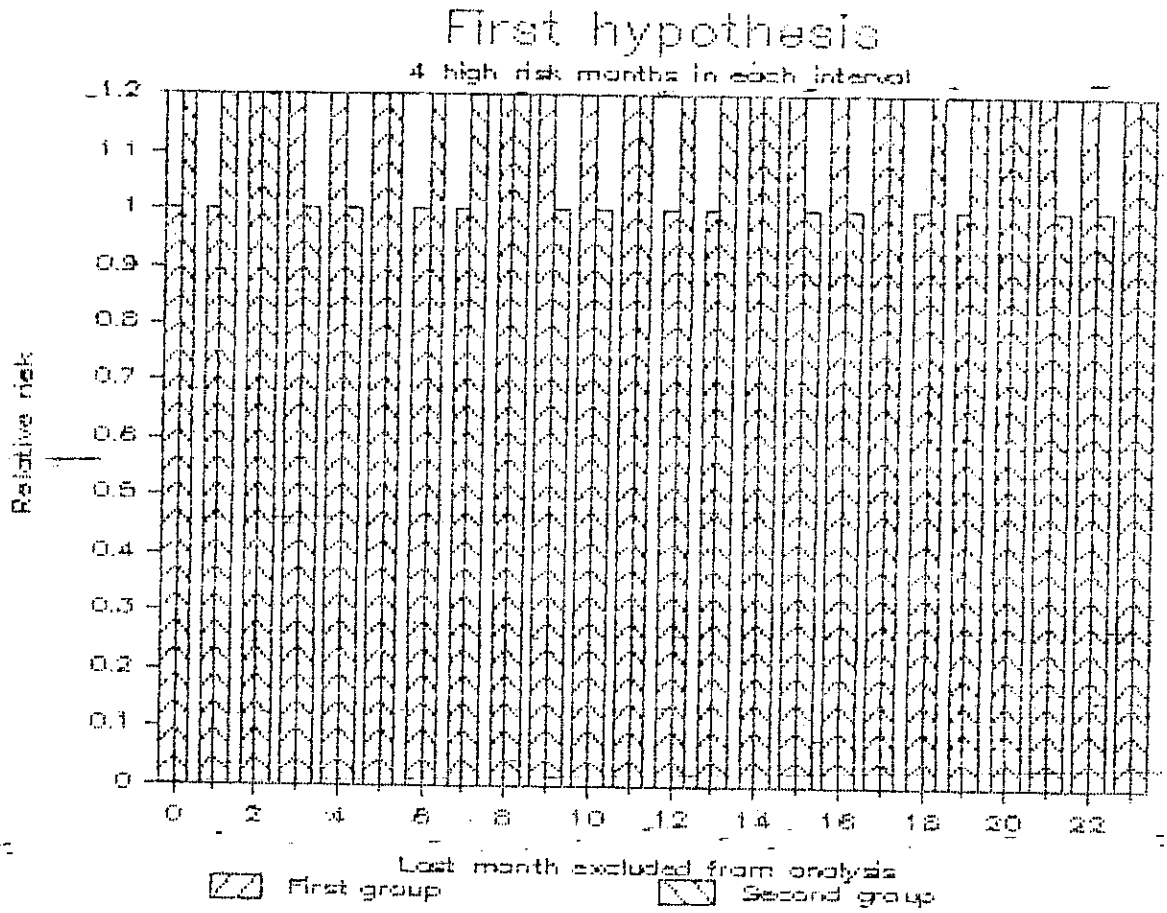
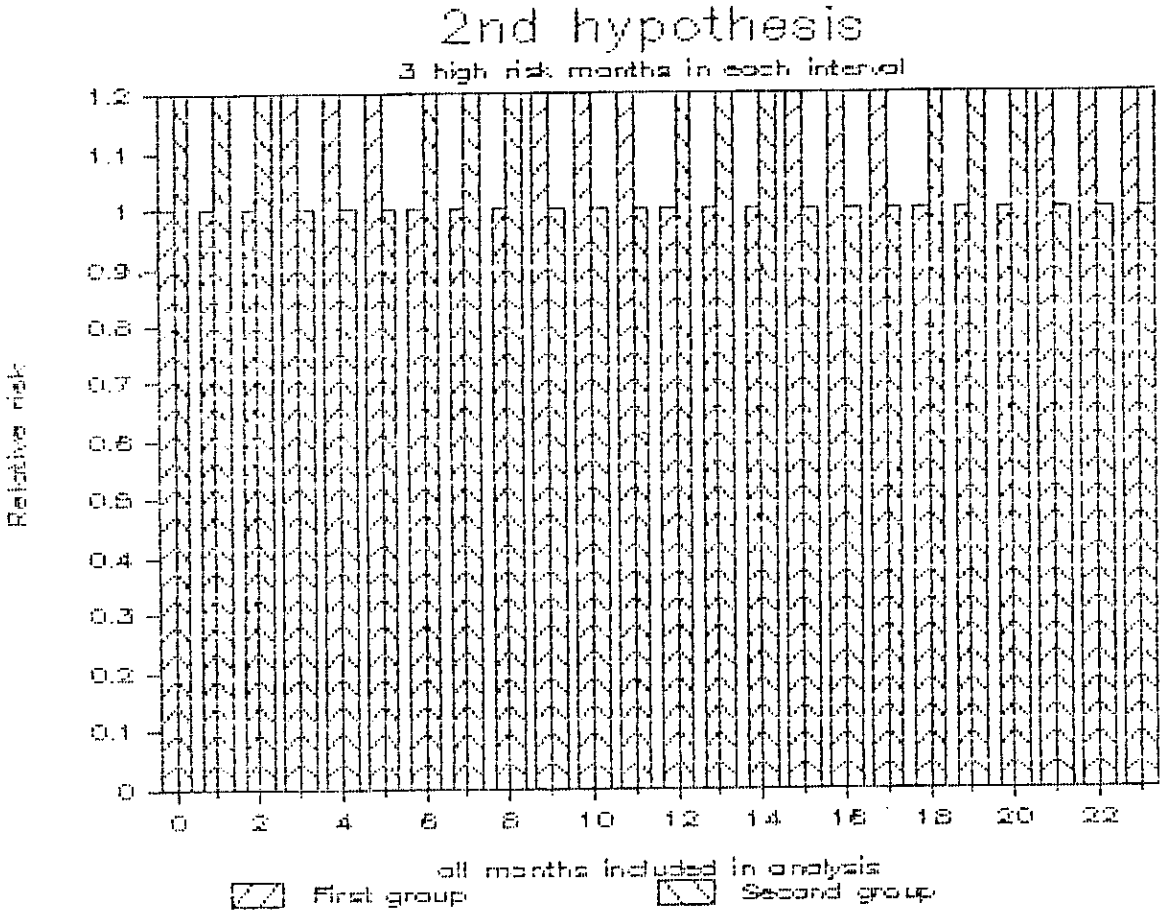

First hypothesis
4 high risk months in each interval
Relative risk
1.2
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0 2 4 6 8 10 12 14 16 18 20 22
Last month excluded from analysis
First group
Second group

Fig 2.


2nd hypothesis
3 high risk months in each interval
Relative risk
1.2
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
2
4
6
8
10
12
14
16
18
20
22
all months included in analysis
First group
Second group

F.3.3

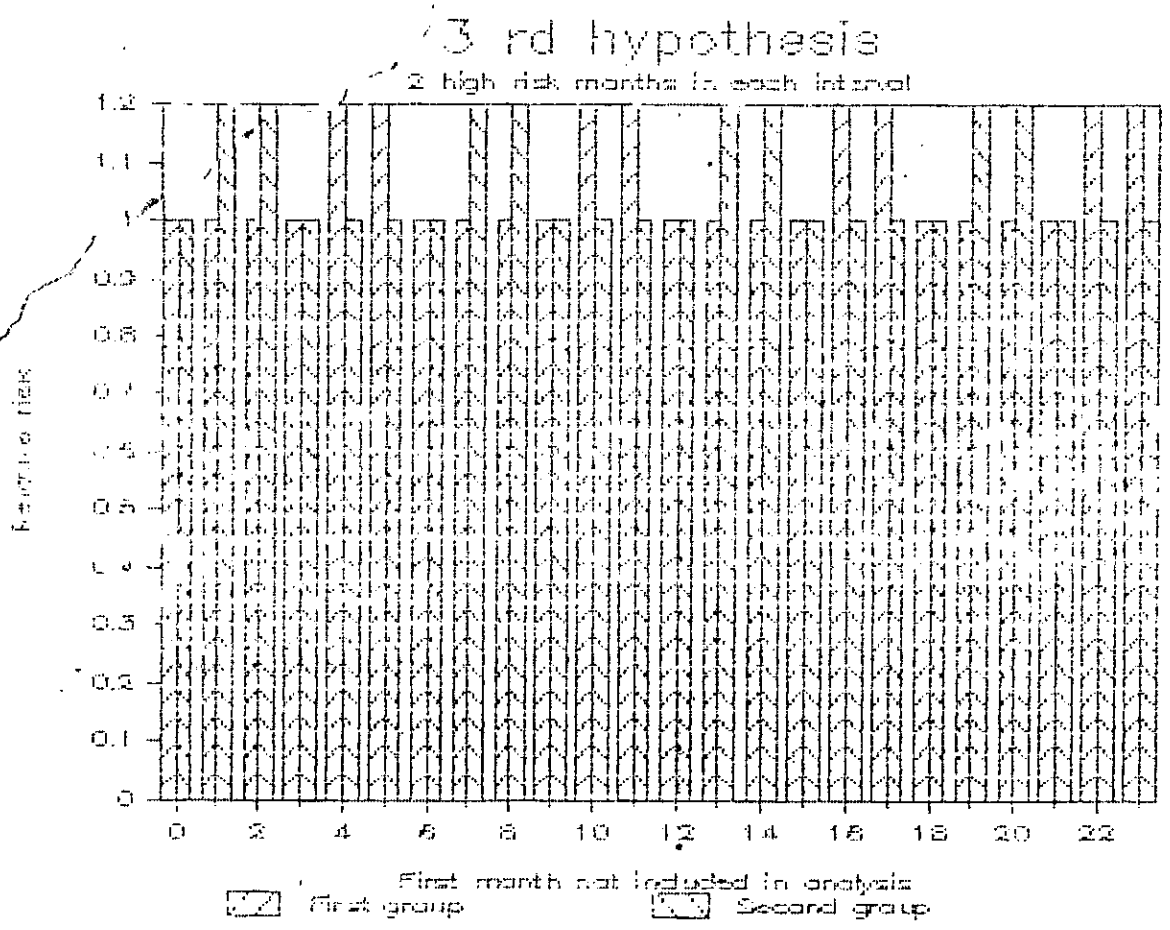

3 rd hypothesis
2 high risk months in each interval
1.2
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
2
4
6
8
10
12
14
16
18
20
22
First month not included in analysis
First group
Second group

Fig 4