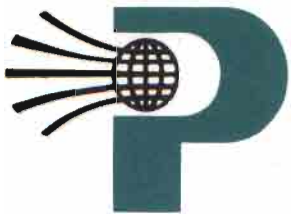

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BISSAU: AN UNPLANNED LONGITUDINAL STUDY

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BISSAU: AN UNPLANNED LONGITUDINAL STUDY

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INTRODUCTION

The title of the paper may be a contradiction in terms. However, the project was initially not planned to last more than a year or two if things went well. Interaction with the first observations forced us to go on collecting more data, which again produced observations which needed to be explained, etc. It is a process which is essential in research but often difficult to get funded in these days where the research process is getting more and more formalized as rigorous testing of specific hypotheses. The range of possible answers to the research question needs to be reasonable clear and well-defined to be considered worthwhile funding. This makes research somewhat trivial, at least to an anthropologist whose concept of research is exploring and making sense of the unknown (18).

The present paper is the history of why and how the project in Bissau became an ungoing inquiry. The development of the project falls naturally in three phases according to the different institutional affiliations it has had. The emphasis in the description is on the relation between interventions, research and how observations were made.

HISTORY OF THE PROJECT

PHASE I: Nutritional study, 1978-1983

1) Background and objectives:

Guinea-Bissau became totally independent in 1974 after a long and violent war of liberation. Survey data on the age distribution of the children conducted in the first two years after independence indicated that under-five mortality in Bissau was likely to be in the order of 500/1.000. Swedish researchers responsible for these surveys assumed that malnutrition played a major role in the excessively high childhood mortality and therefore suggested a study of the nutritional situation in the country (3). At this time there was virtually no people in Bissau with an academic degree, much less anybody with a training in research. The Ministry of Health (MOH) therefore asked SAREC - Swedish Agency for Research Cooperation with Developing Countries - to organize a study which should help the MOH to define the nutritional priorities in preventive health care for the people. Both the experience of the party, PAIGC, during the liberation struggle as well as the "spirit" of the time placed emphasis on popular mobilization and the project was described in the same terms. The project should define the problems in order that the population could be mobilized to change their own nutritional and health related practices such that the situation would improve for the ordinary people. In the

words of the deputy minister of health, it was possibly too late with the current generation of adults but we should suggest what the new generation should be taught in school and cultivate in the school gardens.

2) Staff and organization

The project was explicitly inter-disciplinary with an emphasis on social science. The team funded by SAREC consisted of three full-time members, an anthropologist (project coordinator), a nutritionist and a pediatrician and a short term substitute for the anthropologist (PA). It was not the team members' project, they were employed to carry out a projet which was only defined in very general terms. None of the researchers had extensive experience in health related research. Initially the project was only planned and funded for one year partly due to the lack of experience of the team and partly due to the conditions in Guinea-Bissau (infra-structure, political situation) which made it difficult to know to what extent the work could continue. However, it was understood that it could be prolonged if successful in terms of work carried out.

The team should undertake anthropometric surveys using them for defining the nutritional problem and its associated possible causes. The anthropologists should live in the villages to determine the socio-cultural causes of bottle-necks in production and distribution of foods and problems in child care as well as defining the feasibility of popular mobilization for changing practices. It was imagined that we should carry out experiments in initiating popular mobilization - a "health generating process" as it was described in project documents. This emphasis was important in making us decide to work with total communities rather than the samples the statistical consultant had suggested. Initially, it was not planned to do follow-up studies. The funding as well as the situation in Bissau precluded that. However, the registration in censuses and surveys was sufficiently good to allow the reidentification of all study children when it became possible to carry out reexaminations.

3) Urban studies

The focus of the project was on rural areas and it was also here it was envisioned that experiments in popular mobilization should be carried out. However, when the team members arrived in October 1978 cars would not be available for some months so it was decided to use the mean time to do a study in Bandim 1, an urban districts in the capital where we would have our residence between field visits to the rural areas. In collaboration with the political committee and the youth organisation, all houses in Bandim 1 were mapped. In the subsequent census we got information on names, ages, family relations, current pregnancy, schooling, profession and housing quality for a population of 6.278 persons. In December 1978 after the census, all children under six years of age were called for a general examination where they were checked for obvious signs of nutritional deficiencies, weighed, and measured for height and arm-circumference. The mother or guardian was asked about

nutritional practices and morbidity. 81.3% of the 1462 children under six years of age participated in the examination.

After the general examination, we initiated a more intensive study of a sample of 4% of the children, with interview with the mother and monthly information on food intake and morbidity (never analyzed because the files were accidentally thrown out). As a preparatory activity for the health center that the MOH had planned to establish in Bandim, ante-natal consultations were organized for the women who had been identified as pregnant in the census. After the census and the general examination we also initiated a registration of births and deaths in Bandim 1. Through the first 3-4 months, the mapping, the census and the general examination were carried out by 4 assistants provided by the MOH and voluntaries from the youth organization in Bandim. However, when the routine registration was started, it was decided to employ two of the best (female) volunteers as assistants. It was imagined that this should be carried out in collaboration with the local political committee; whenever there was a birth or deaths the committee representative from the sub-district (8 zones in Bandim 1) should report to one of our two assistants in charge of registration. However, after some months it became clear that this did not work, our assistants had to be responsible for the registration if we wanted reliable data. Thus from mid-1979, we started a monthly registration of pregnancies in all houses which has become the basis for the registration in Bandim 1 (3).

4) Rural surveys

When the work in Bandim had been initiated, team members started in one of the rural areas (Tombali) inhabited by the Balanta ethnic groups. The plan was to do surveys with the major ethnic groups which also corresponded to relative distinct ecological zones in order to find out whether there were major differences in the nutritional status. In the first survey in Tombali, we started the work with a census in the villages selected before examining all the children under six months. Due to poor state of the roads and the fact that many villages required boat transport, accessibility was a major consideration in the selection of villages. We also tended to select villages in the rage of 400-500 which would have 80-100 children under six which was a suitable number to examine in one day in a line of flow (registration, age determination, weighing, measuring of height, information on nutritional practices and morbidity, clinical examination). The work in Tombali clearly showed that it would take too long if we had to carry of a census in all regions before starting the anthropometric surveys. Therefore, we subsequently changed the procedure for the surveys in the other four regions (Biombo, Oio, Bijagos, Cacheu). After discussion with the local political committee which had to call the mothers, we made general examinations of all the children under 6 years of age. At least in some of the regions, this procedure gave a reasonable coverage as judged from the number of children under five in relation to the total number of persons counted in the village by the national census (1979). Later on, when time permitted we carried out household censuses in some of the

villages where a general examination had been done. We managed to register 400-500 children under five (corresponding to an adult population of 2.000-2.500) in each of the five regions (3).

5) Anthropological studies
The anthropologists in the team made short field stays among the different ethnic groups to obtain more detailed socio-cultural background data, as well as information on food production, control over resources, food security, food preparation and distribution, breastfeeding and weaning patterns. Some information was also sought on morbidity and disease perception. Neonatal tetanus was assumed to be a major cause of high mortality rates during the first month of life, and interviews therefore emphasized hygiene in connection with birth practices.

The point of the more intensive interviews was to discover different production and feeding patterns which could be related to differences in the nutritional status of the children. We thought it most effective to try to find local positive variation and reinforce the connected practices rather than try to introduce new types of food or feeding patterns. At the same time, the anthropological studies sought to indentify possible obstacles in term so cultural beliefs, traditions, productive patterns or division of labour which might hinder efforts to improve the health of children. Although we did study hygiene surrounding birth practices, overall more emphasis was placed on nutritional practices rather than morbidity patterns, and little systematic morbidity data were collected.

6) Nutritional assumptions and the measles epidemic
The first anthropometric examinations in Bandim and Tombali were worrying for the basic assumptions of the project. In spite of the high mortality which was also confirmed by maternity histories, the nutritional status of the children were not really bad, the mean weight-for-age(w/a) being 92% (of the international standard) in Bandim and 88% in Tombali. In Bandim, we had only encountered 2 marasmic children out of 1187 examined and no case of kwashiorkor. This impression was further reinforced during a measles epidemic which started shortly after the anthropometric survey in Bandim. The case fatality rate (CFR) during this epidemic was as high as 22% for children under five years of age, one of the highest CFR ever registered in an African community (25). Since the project was supposed to be a mobilization project, we organized community meetings in each of the 8 sub-districts of Bandim emphasizing the importance of nutrition for severity of measles. During a certain part of the epidemic, measles cases were examined and treated at home by a medical doctor, but mortality was equally high for those children treated at home (only penicillin and cloroquin available). A preliminary analysis of the medically examined children who died of measles also showed that they were not different in nutritional status from other children in the community (5). Though the team registered a certain uneasiness from the fact that mortality was very high in spite of a reasonably good state of nutrition, we took no immediate

consequences in terms of reorganizing data collection. Most critical was the fact that we did not organize a proper registration of all cases and the transmission pattern during the measles epidemic in Bandim 1.

7) Reexamination
After one year, we started reexaminations of all the children in Bandim and three of the regions in order to get data on growth and mortality in the intervening period. Due to the epidemic in Bandim, we asked all guardians whether the child had had measles in order to get a better assessment of the impact of measles. Susceptible children who attended the reexamination in December 1979 were offered a measles vaccine. Prior to this there had been no general measles vaccination campaigns in the country due to fear of poor storage and handling of vaccines. Vaccinations had not been considered when the project started. The measles vaccines given in December 1979 were considered a service to the community and not a research issue; we did not register the vaccination on the examination form but only on the growth card of the child which stayed with the mother.

8) Information campaigns and mobilization for heath
A long series of community meetings were organized in connection with the reexaminations. In these meetings, we emphasized nutrition, treatment of diarrhoea and antenatal care with tetanus vaccination. However, this was more an information campaign than something which could be called mobilization for health. Since we felt uneasy about the correct message, we did not venture into organizing more ambitious community programmes for health. Furthermore, the MOH had in the beginning of 1979 started a primary health care project emphasizing essential drugs, education of village health workers and traditional mid-wives. Hence, it made more sense to provide data for this project than trying to organize a separate mobilization initiative. Finally, in Bandim, where we had much help from the committee in the first period of the project, internal conflicts in the committee made it unrealistic to try any ambitious project of changing peoples beliefs and behaviour.

9) Continued data collection and preventive activities
Instead we came to emphasize the need for more data on determinants of nutritional status and mortality and the need for using data to organize preventive health activities. Before leaving the country in the spring of 1980, we therefore wrote manuals for routine data collecting systems in Bandim and in the villages in the interior. The registration in Bandim was to be carried out by four assistants employed by the project and the registration in the interior was to be handled by the mobile team of four assistants who had been put at the disposal of the project by the MOH. In both instances, the basic idea was that we had to combine registration with preventive activities and to use the obtained results for defining high risk groups and setting priorities. Both systems were based on the registration of pregnancies in order to get adequate data on the very high peri- and neonatal mortality (3). In Bandim, houses were

visisted every months and pregnant women were called to ante-natal care at the health center which had been established in Bandim in 1979. In the villages in the interior, pregnant women were registered at the 6-monthly visits and information meetings were organized for them after the examination of the children. After birth, children were included in the general examinations carried out with an interval of 3 months in Bandim and 6 months in the rural areas. Children were weighed in order to identify the malnourished children at risk. More intensive follow-up of families with high risk children were to be carried out by the nurses in Bandim and by the committee in the villages in the interior. Vaccinations were to be provided at these general vaccinations as well. Initially it was only measles vaccine which was provided, but from 1981 the full set of EPI vaccines became available except when there were interruptions of stock. All children who did not attend the examination should be controlled to determine its whereabouts. In this way, it was hoped that we would get reliable information on mortality and that has indeed been the case. On the basis of the data collected the health center staff in Bandim and the mobil team should put together quarterly or biannual statistics on important health parameters like the nutritional status, breastfeeding length, time of introduction of supplementary feeding, vaccination coverage, proportion malnourished children, proportion of malnourished recuperated since last visit, use of antenatal care, level of mortality and major causes of deaths. This information should be used to define priorities in collaboration with the committees in the villages and with the staff at the health center.

10) Analysis of data

In the later 70s there was no computing facilities in Bissau, so during the first period of the project the results from the examinations and reexamination (but not the censuses) were coded on code pages and sent to Sweden for being entered into a mainframe computer. We did not manage during the stay in Bissau to get a feedback between the data collected and the continued field-work. After 18 months of work in GB, the team returned to Sweden to analyse the data and write the report which had to be presented to the MOH in Bissau in the beginning of 1981.

The data confirmed the initial assumptions about a very high mortality level, under five mortality being 454/1000 in Bandim. But we had no real interpretation of the data which made sense in relation to initial assumptions of the project about the importance of nutrition (3). Preliminary analysis of the nutritional data was frustrating. There was no indication that nutritional practices such as the time of introduction of supplemntary feeding, length of breastfeeding, number of meals, consumption of palm oil, or availability of staple food (rice) had any impact on the growth pattern of the children. Nor was there any correlation between the state of nutrition and the socio-economic background factors. Quality of house, education of father and mother, religion, work situation, type of child care, co-residence with mother or other relative, birth order, age of mother or proportion of dead children of mother did not

have a clear association with nutritional status. It was only when the analysis of all the measles death which had occurred in the community during 1979 showed that there was no relation between state of nutrition and the risk of dying, that we started looking for a different interpretation. What trickered a new line of inquiry was the observation that mortality tended to cluster in houses with several cases of measles. Furthermore, many other deaths clustered in the houses where there had been measles. These observations, however, made it evident that essential data had not been collected. We had only information on measles infection from the children who had participated in the reexamination in December 1979 (3). Thus we missed information on measles infection for children who had been absent, moved, or died (with other diagnoses). Furthermore, in many cases it was not the mother who had provided the information. A reinvestigation to recuperate this data in Bandim was therefore warranted.

When the preliminary results were presented at an internal meeting in SAREC, we were told to stop the line of inquiry since such theories did not exist in medicine. This led to a disruption in the research group. What we had believed to be exciting moments of questioning commonly held beliefs and trying to provide alternative interpretations turned out to become "an administrative problem"; we should only write what the whole team could agree upon. However, enforced consensus is not a recipe for analysis. In the end (June 1981), SAREC got two reports and decided that they could not be presented to the MOH in Bissau. SAREC decided to discontinue the funding of the non-medical members of the team and wanted to close the project as soon as possible. However, since a report had not been delivered to the MOH, the assistants in Bissau were financed to continue the data collection. Thus work could continue in spite of the non-funding of expatriates. (SAREC continued funding the field operation to June 1983. A project report was not given to the MOH).

11) Follow-up studies of measles
We had to find alternative funding (DANIDA) for doing a restudy of the measles epidemic (7, 21). A recensus was carried out in the e of 1981 and information on measles infection was collected from all children under 15 years of age. In the beginning of 1982, interviews were conducted in all houses which reported cases of measles during the epidemic. Despite the delay in relation to the epidemic, it was possible to recuperate most of the missing information because we had a census of all the persons registered in the community prior to the epidemic. Out of these interviews grew the tradition of interviewing about the transmission history for all cases of measles in Bandim and the rural areas with measles outbreaks. Similar interviews were later carried out in Niakhar in Senegal (47, 74).

PHASE II: Monitoring preventive health interventions, 1983-1988
1) New objectives
Several observations made it essential to continue data

collection in Bissau. Prospective data on the transmission of measles and the severity of infection were necessary to control the generality of the first information on the role of intensive exposure. It was also considered important to study the long-term impact of measles infection. Furthermore, a preliminary analysis of data from Bissau had indicated that measles vaccine had a major impact on child survival. It was therefore considered important that the project should monitor the impact of improved measles vaccination coverage.

2) New organization
Despite the fact that SAREC had discontinued the project,we established collaboration with the Danish section of IMCC (International Medical Cooperation Committee) and succeeded in obtaining money from DANIDA (Danish International Development Agency) for a project which emphasized monitoring of preventive activities. This formulation opened for the possibility of doing some research on the impact of health interventions, though DANIDA had little interest in research at that time. IMCC was to send two last-year medical students each year to supervise the continued data collection in Bissau and to organize preventive activities.

3) Routine registration
Data collection and routine preventive activities continued much the same way in Bandim 1. New pregnancies were registered once a month. Newborns were registered as soon as possible after birth. Once every third month, all children under three years of age were called for weighing and vaccination. The MCH programme had initially emphasized that all children under five should be weighed every month. We decided however that this would require too many ressources and probably add little in terms of better detection of high risk children. Since most deaths were under three, this age group was emphasized. Whenever we found that someone had died, child or adult, a simple lay death registration form with information on symptoms at death was filled out by the assistant responsible for the subdistrict. Much the same activities went on in the rural areas, though the interval between examinations was 6 months rather than 3 months.

4) Routine registration as a way of organizing primary health care (PHC)
When the students started working in Bissau we initiated two new activities; extending the primary health care work to neighbouring districts in Bissau and trying to improve measles control with early vaccination with Edmonston-Zagreb (EZ) vaccine. Nurses at the health centers were supposed to do extention work in order to mobilize the population for the PHC priorities, ante-natal consultations, growth monitoring, immunizations, diarrhoea and malaria control and health information. However, little was done since routines were not sufficiently defined and supervised. In this situation the experience from Bandim with integrating registration and health

center activities was considered a model and it was suggested by the MOH that we should use the experience from Bandim to create a system for the other districts. The system that the students came to try out built on a simplified version of the Bandim system with registration and preventive activities. However, we did not employ assistants to carry out the registration work. The nurses at the neighbouring health center (Belem) were given responsibility for certain sub-districts were they (during afternoon hours where there was little work at the health center) should find pregnant women and get them to attend ante-natal consultations and get them to give birth at the hospital if necessary, to assure that the infants were immunized in time and grew well and to teach the mothers nutrition, hygiene and diarrhoea treatment. If carried out properly, the system would also give important data on health and service delivery like neonatal and infant mortality and proportion taking prophylaxis during pregnancy, vaccination coverage and prevalence of malnourished children. This system did not work for a number of reasons. The students as students probably had insufficient authority; the nurses had little schooling and lacked motivation. The work done by the students and the nurses undoubtedly increased service delivery in the district, but the data collected were useless and since the nurses increasingly refused, the project was stopped when two of the four nurses went on pregnancy/delivery leave at the same time. Simultaneous with this more ambitious program we had also tried in a different neighbouring district to raise vaccination coverage through collaboration between health center staff and the local political committee who would do home visits to call the mothers for vaccination at certain gathering places in the area once a week. This programme was very effective in raising the vaccination coverage but did not involve the other priorities of PHC in Bissau. When the more ambitious project of combining data collection and preventive activities were abandonned, we opted for trying to extend the vaccination coverage in the other districts of Bissau city. It was part of the motivation for this decision that vaccination was the activity in Bandim 1 which had been clearly most effective in reducing child mortality. Through the years 1985-1988 the students succeeded in extending this vaccination work to most of the districts of Bissau, of course great helped by the initiation of EPI's accelerated immunization campaigns in 1986-87. However, after the project stopped in 1988, it has not been possible to maintain the system and vaccination coverage in Bissau city is declining. During the initial phase of these experiments, registration of pregnancies, births, child deaths, vaccination and infections was also initated in the two nabouring districts to Bandim 1, namely Bandim 2 and Belem. Though the frequency of contact was less than in Bandim 1, data has been good and the system has been maintained even when the other activities was abandonned. Thus at the monent the project in the city of Bissau covers a population of around 30.000 people.

5) EZ measles vaccination

The other major activity in these years was two trials with EZ

measles vaccine. The first studies from Bandim had shown that measles vaccine had an enormous impact on mortality. In the first years children had been vaccinated from 6 months of age but this subsequently had to be stopped following the standization introduced by EPI that children should only be vaccinated from 9 months of age. Nonetheless many children developed measles before 9 months of age. So when the first reports appeared of successful immunization with EZ measles vaccine in the presence of maternal antibodies, it was decided in collaboration with Dr. Whittle at MRC Laboratories in The Gambia to test the clinical efficacy of this vaccine. It was an added motivation that the reduction in mortality following Schwarz measles vaccination had been so large that I hoped we could show that mortality was reduced by this vaccine. Two trials were carried out in Bandim 1; children born August 1, 1984 to September 30, 1985 and those born May 1, 1986 to April 30, 1987 were included in the studies. The EZ vaccine turned out to be protective against clinical measles before the normal age at vaccination even when the children had been vaccinated at 4-5 months of age. Furthermore, it apparently provided better protection against measles than the standard Schwarz measles vaccine. Though this was promissing, subsequent experiences from the second trial has suggested that recipients of EZ vaccine may have higher mortality than children in the control group most of whom were vaccinated with Schwarz standard at 9 months.

PHASE III: Research and monitoring of PHC, 1989-1992
1) New organization
The IMCC project ended in 1988. However, there was still an interest in continued work in Bandim and the other areas of Bissau. Among the priorities when the future work was planned were more research into the mechanisms of the long-term consequences of measles, the best vaccination strategy, better control of measles, diarrhoea and neonatal mortality and studies into HIV-2. At this time DANIDA extended its assistance to Guinea-Bissau by financing a PHC project including construction of health centers and technical assistance for the training and supervision of PHC workers in two regions of the country. The project has been administered by a Danish NGO, Danchurchaid. Research had by now become more acceptable and continued work of the Bandim project was funded as a research and monitoring unit, with one physician and a half-time anthropologist (PA).

2) Handling of data and introduction of microcomputers
During the first 1" year of the project, data had been entered at a mainframe computer in Stockholm. When funding stopped there was no money available for routine handling of data in Denmark, nor was it possible to organize handling of data in Bissau. Thus, until 1989 routine data were only handled manually, which natually reduced the accessability of the data. With the appearance of transportable computers more resistant to the extreme conditions of humidity and dust in Bissau, it was decided to introduce microcomputers and a database system (DBaseIV) for the handling of routine data from the registration system. This has partly succeeded though the lack of expertise

locally as well as among the expatriates has delayed the process considerably. A system has been constructed where the routine data on children is entered in separate data bases for census date, birth related information, infection and vaccination information, anthropometric examinations, movements within study area and death information. Data entry in the different databases is organized throught the census-registration in order to assure that information is always linked on the correct identification number. Since much of the information is collected in connection with the three-monthly and 6-monthly examinations where all children in a certain age group are controlled, the system is constructed so that follow-up will be reviewed and updated on the examination day for all children in a specific village or subdistrict. The assistant needs only enter the new weights, armcircumference or information on vaccination and infection.

3) Continued work on measles
Much of the time has been devoted to follow-up on the children in the EZ studies. The fact that the second trial suggested higher mortality for the recipients of EZ than for the controls (mortality ratio (MR) = 1.56 (0.96-2.55), p=0.075) has meant that larger studies of the impact on measles control were not carried out in Bissau. The hospital has been one of the most important places for the transmission of measles in Bandim 1 where the vaccination copverage has been high (>80%) and it had been envisioned that the EZ should have been tested among hospitalized children. Instead we have had a very important epidemic in 1990-1991 with the hospital again acting as one of the most important sources of introduction of measles in the study.
Since children exposed to measles at home have been found to be the high risk group for severe disease, we have tested during the recent epidemic whether vaccination at the time of exposure is protective against disease and/or mortality. (Results not available yet).

4) Other studies
During the period that IMCC was involved in the project, two more specialized longitudinals studies on diarrhoea (50, 52, 64) and HIV-2 infection (44, 53, 57, 61, 75, 79) were initiated. After measles control had improved in the beginning of the project, it was clear that diarrhoea was the major symptom at death. From 1987 a epidemiological study of diarrhoea and different pathogens was therefore initiated. This study has involved the children living in 300 randomly selected houses in Bandim 2. The work has implied un upgrading of the laboratory work at the national public health laboratory where many of the examinations had to be carried out. One of the most important observations from this study is probably that cryptosporidium seem to be an important cause of not only diarrhoea but also both acute and delayed mortality (52). Though there was only full-time medical supervision of the laboratory work during the first year from 1987-88, we decided to continue the weekly registration of morbidity and collection of faeces speciments

from children with diarrhoea on the day of the home visit. At the moment this data is being used as the basis for an experiment to reduce diarrhoea incidence through improved case-management and reduction in the frequency of premature lactation stops.

In the beginning of 1986, the first reports were published of a second AIDS virus, subsequently to be named HIV-2. The virus was initially isolated from patients from Bissau and Capo Verde and the epicenter of this virus seems to be Bissau. In 1987 we started a longitudinal study of a random selection of 100 houses from the three urban districts in Bissau city to get more information on the natural history, clinical development and epidemiology of this disease. The cohort of people in these houses have been followed with bi-annual surveys to get information on the incidence and in alternating years immunological and case-control studies to determine the risk factors for the disease. In connection with studies of the long-term immunological consequences of measles and HIV-2, we succeeded in adapting a method for detection of subsets of T-cell lymphocyte to conditions of field-work in tropical countries (49).

A number of other studies of twins (50), neonatal mortality, malaria and immunology have also been carried out. Most recently, we have at the request of MOH and UNICEF started to follow a national cohort of 10.000 women of fertil age (100 clusters of 100 women) in order to determine the level of peri- and neonatal mortality. The emphasis is on neonatal mortality in view of the goal to eradicate neonatal tetanus by 1995. However, once the cohort is started it will be easy to collect a number of other indices of health and use of health services.

PHASE IV: Continued longitudinal studies, 1993-

1) New objectives and new affiliation

The present project will end in 1992. What will happen with the project is not clear except that a new institutional affiliation will be necessary since the aid agency currently administering the project (Danchurchaid) find "research" too much out of its field competence. Efforts will be made to find new funding because there are many research topics which need to be pursued: In view of the disappointing results with the EZ vaccine, there is a need for a new strategy and two-dose schedule with the standard vaccine or a smaller dose of EZ may well improve measles control. The long-term consequences of measles as well as the effect of cross-sex transmissions should be further studied. Since the measles studies have shown that measles is a disease with both high acute and delayed mortality which are not mere expression of underlying weaknesses in the children who dies, specific interventions against measles are indicated. There are good reasons to examine whether other infections behave the same way or whether their severe forms are results of environmental or host conditions.

OBSERVATIONS

The essence of research is observations. One could therefore imagine that methodology would deal with how to make new observations. However, it seems rather that the increasing professionalization of epidemiology has entailed that method has become the rules for observing something already seen or perceived. No matter whether the objective is hypothesis testing or a descriptive study, reality is "collected" and analyzed in terms of pre-determined categories and relations between these categories. This type of research is highly reproducible, but maybe not very interesting. There seems to be good reasons to explore how new observations are made. One of the advantages of longitudinal studies may be that they have the capacity to both generate new observations and to verify them without too many restrictions on method.

In the this perspective, I review the major observations made in Bissau and what produced them. Though observations have also been made in other areas, the following description is restricted to the research on measles. In this area the most important observations seem to have been:

a) Pre-morbid state of nutrition did not determine outcome of infection (2,3,4,5,7, 11, 24, 27).

b) Clustering was important for the case fatality ratio (CFR) in the sense that mortality increased when several children were since in the same social unit (household, house or compound) (4, 5, 7, 14, 25, 29, 34, 66).

c) Intensive exposure as a secondary case (infected at home) increased the CFR relative to index cases who had contracted measles in contact with someone from a different family (7, 14, 16, 19, 20, 21, 23, 24, 25, 27, 34, 42, 47, 55, 58, 73).

d) Deaths cluster in the same houses over time (3). This has been found to contain at least three mechanisms: previous measles cases have delayed mortality (4, 8, 47); children exposed to measles before six months of age have excess mortality later in life (43, 70); and children of mothers exposed to measles during pregnancy have higher peri- and post-perinatal mortality (32, 40).

e) Measles vaccinations have a much larger impact on mortality than predictable from the number of acute measles deaths (1, 4, 8, 21, 31, 37, 55).

f) Children who have measles after vaccination have milder infection and lower CFR (21, 27, 55).

g) The hospital is one of the major sources for transmitting measles and causing measles deaths in an environment where the vaccinations coverage is good (13).

h) Treatment with immunoglobulin can reduce the CFR in measles (26).

i) There is amplification of severity or mildness in the sense that a severe case generate a more severe case and a mild case generate a mild case (21, 55, 58).

j) Infection from the opposite sex increases severity of infection. (16, 50, 56, 59, 60, 65, 74).

k) The delayed consequences of measles are also connected with intensity of exposure (10, 47, 55).

1) Early vaccination with high-doses of EZ measles vaccine is connected with higher mortality compared with children who have received the standard schedule of Schwarz measles vaccine at 9 months of age (68, 71, 77).

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a) Pre-morbid state of nutrition did not determine outcome of infection.

This observation had certainly not been planned. It was facilitated by the fact that we did a follow-up study where we tried to reidentify all the children and that we did home-treatment of the children during the epidemic which showed that the enormous mortality did not really fit the reasonably good state of nutrition that we had observed just before the epidemic. The contradiction in the initial survey between the good state of nutrition and the high mortality level reported by the parents would not have been sufficiently convincing in itself. Maybe the most surprising is that the observation resisted being seen for so long. We disregarded several hints before finally realizing that something was fundamentally wrong. The initial anthropometric survey had shown a good state of nutrition in the community. When we made in-depth interviews on maternity history and disease perception just before the outbreak of the epidemic, it became quite evident that measles was the disease that mothers feared the most. The epidemic taught us that they were right: the CFR was as high as 25% for children under three years of age even among those who had received treatment at home. The state of nutrition of the treated children who died was also tested and found to be no different for those who survived. Yet we continued to entertain th possibility that the children examined and treated at home could constitute a particular group. Only minor changes in data collection was introduced in order to get more precise information on the epidemiology of measles, e.g. we asked at the reexamination whether the child had had measles. It was not until 1" year after the epidemic when the team had left for Sweden and we had all the data in the computer that it became definitely clear that state of nutrition could not be the major determinant of the level of measles mortality. Then it became clear that much data was missing.

b) Clustering was important for the case fatality ratio (CFR) in the sense that mortality increased when several children were sick in the same social unit (household, house or compound). In a situation where common assumptions have failed there is a strong inducement to formulate alternative hypotheses. Examining the CFR in relation to different socio-cultural background factors we found no relation with breastfeeding, housing conditions, age, education, work situation of the mother or adoption. The only tendency was a slightly higher CFR in the polygamous families (3). We imagined that an explanation of the hig CFR in Bissau had to be sought in a multitude of different factors, including higher rates of complications and improper treatment of the ill, for example, withholding of water. However, co-incidentially we received a list with follow-up results from our assistants who had done a reexamination in one of the rural areas (Quinhamel) where there had also been an

epidemic of measles. On the list for each village, there was a clustering of deaths in the sense that the deaths from measles had adjacent numbers. Since the children from the same compound had come more or less at the same time for the examination, this suggested that deaths often belonged to the same family or compound. Hence, it suggested that disease somehow became more severe when several children were sick at the same time. It was also an attractive hypothesis because it would explain why children had higher mortality in polygamous families. This was immediately verified with the data from the outbreak of measles in Bandim. This however implied a reorganization of the data at a household/house level to include other children as a determinant factor for the individual children. The "observation" of clustering was very much a visual affair; the clustering on the list of children had the capacity to produce a new categorization which has turned out to be very important since all subsequent studies have confirmed the tendency. However, the immediate implication of the hypothesis was that we missed inportant information because we had no information on measles infection among children older than six years, among those who had moved or not attended the reaxamination in December 1979, among guests who might have been present during the epidemic and among those who had died from other causes than measles. Since this information could imply a reclassification of the isolated cases which had low CFR, we needed to do a reexamination in all house of Bandim. This was feasible because we had done a census of all individuals just prior to the epidemic. Thus, it was likely that we could get information on virtually all children who had been at risk during the epidemic.
c) Intensive exposure as a secondary case (infected at home) increased the CFR relative to index cases who had contracted measles in contact with someone from a different family.
This observation was essentially a deduction from the previous observation. Though children in large families have lower state of nutrition, there was no indication that state of nutriton within the large families with several cases was a determinant factor for outcome. Furthermore, in an African context there may well be a direct rather than an inverse relation between number of children and socio-economic status. The size of family would tend to reflect the power of the head of family. Thus it seem natural to look for something which was different in the "disease" rather than in the environment. It was therefore hypothesized that that secondary cases, i.e. those infected after prolonged contact within the home, were more severe than the index cases who had caught the infection from someone outside the home. During fieldwork in Bissau, we had not collected the data we needed to test this hypothesis. However, for the small number of cases that had been examined clinically during the epidemic, it was possible to examined whether there was any difference in mortality for index and secondary cases. Though not statistically significant, these data supported the hypothesis. The observation made it even more essential that we should carry out a reexamination of the outbreak with interviews of the mothers to get information on exposure in order to recuperate the missing information. This proposition was not

acceptable to the funding organization, SAREC, which thought it methodologically unacceptable since we had not had the hypothesis prior to the study. Since we could not do a new study to verify the hypothesis without vaccinating the children at the same time thus limiting the possibility of observing the phenomenon, we insisted on doing a reexamination of the outbreak in Bandim. Eventually we had to get funding elsewhere to do this study. All subsequent studies have confirmed the tendency (table 1)(55).

d) Deaths cluster in the same houses over time. This has been found to contain at least three mechanisms: previous measles cases have delayed mortality; children exposed to measles before six months of age have excess mortality later in life; and children of mothers exposed to measles during pregnancy have higher peri- and post-perinatal mortality.

In this instance again, the visual aspect was important. In Stockholm, while coding the deaths which had occurred in Bandim during the first year, it became noticable that very often when a measles death had occurred during the epidemic in the beginning of the year there was another death in the same house later on. The association with perinatal mortality was particularly strong. The suggestion that these phenomena could be causally related was considered outrageous since the mothers had not had measles and everybody knew that it was not possible to be reinfected with measles. However, similar observations were done during a later epidemic in Quinhamel.

The observation of clustering of mortality over time turned out to be far more important than initially imagined. It was not only perinatal mortality which was increased after exposure to measles. Previous measles cases also continued to have strong excess mortality during the following years; children who had been exposed to measles during the first six months of life had a 3-4 times higher mortality through childhood than community controls with such exposure; the children of mother exposed during pregnancy also had two times higher mortality in the post-perinatal period to the age of five years. All of these observations had been repeated in subsequent epidemics before they were published.

e) Measles vaccinations have a much larger impact on mortality than predictable from the number of acute measles deaths.

Out of the observations about clustering, intensity of exposure and long-term consequences of measles, there grew the idea that severe measles was not merely a reflection of underlying poor social conditions but that the disease had the capacity to cause problem in its own right. If this was true it was not merely the "weak" children who died and they would not simply died from other causes if saved from measles. Thus a strong impact on survival could be expected after measles vaccination. Ethical consideration would have precluded a study of this problem. However, before leaving Bissau we had vaccinated against measles all the susceptible children who attended the reexamination whereas the children who did not come had not been vaccinated. During the first year of the study there was no difference in mortality between children who attended and children who did not attend the general

examination. Before leaving for Stockholm in May 1980, we took with us a copy of the registration forms for the children who had died in Bandim during the first 4-5 months of 1980. With these forms it was possible to examine whether vaccination against measles had a protective effect against mortality. There had been little measles in Bandim during these months so a major effect was not to be expected. However, the effect turn out to be edxtremely large. Excluding the children who had had measles in 1979 and therefore could suffer from the long-term consequences of measles, those who had been offered measles vaccination at the reexamination had 6-8 times lower mortality than the children who had not attended and therefore would not have been vaccinated against measles. There had been no other intervention specific for the children attending reexamination than measles vaccination. Though selection bias could play some role, it had not done so the first year and the effect was too large to be reasonably ascribed to socio-economic or cultural selection. At this time, Lancet published a study from Zaire which had in fact attempted to examine whether the "Darwinistic" model was correct in the sense that those saved from measles would be more likely to die of other causes and therefore the net impact of vaccination would be minimal. The paper concluded that in the long-run there tended to be no difference in survival between vaccinated and unvaccinated children and that measles vaccination was not a priority. Fortunately for my observation from Bissau, there was no connection between data and conclusion in the Zaire study. In the age range between 7 months and three years where the children in Zaire had been followed, the unvaccinated groups had twice the mortality of measles vaccinated children. This clearly indicated that the reduction in overall mortality after measles vaccination was more than the share of acute measles deaths. All subsequent studies of this phenomenon has confirmed the tendency (table 2).

f) Children who have measles after vaccination have milder infection and lower CFR.

During the restudy of the 1979 epidemic as well as the cases which had occurred in 1980 and 1981 in Bandim in the beginning of 1982, mothers of all cases were asked who was the first case in the house and how the child had contracted measles. It turned out that quite a number of the children who had been vaccinated by the project in 1979 and later had contracted measles. Though we had vaccinated down to 5-6 months of age, this was clearly not the major explanation for the many cases. The mothers repeatedly indicated that they thought the vaccinated children had milder measles than they were accustomed to. This was potentially an interesting observation since the immunization progran the notion that vaccine induced immunity is permanent and that vaccine failure is due to improper handling or neutralization by maternal antibodies. The study of the outbreak showed that the mothers were correct. Vaccinated children had much lower CFR. Furthermore, infection among vaccinated children was related to intensity of exposure since there were more secondary cases among the vaccinated children and severity of infection was important since the attack rate among vaccinated children was higher in houses where someone had died of measles.

This observation in fact questioned the basis for the stategy of one dose of Schwarz standard measles vaccine at 9 months. Studies in Kenya had calculated that vaccination at 8 and 9 month would prevent the same number of cases assuming that the children who had seroconverted would not subsequently get measles and that the children who had not seroconverted would in fact get measles later on. The reason for choosing 9 rather than 8 months was that vaccination at 8 month would produce more vaccine failures and that this was assumed to lead to lack of confidence in the immunization programme. No such tendency of lack of confidence was found in Bissau and to the extend that mothers are right that vaccinated children have milder measles infection it may in fact be much better to have measles after vaccination at 8 month than to have unprotected infection before 9 months of age. It seems likely that a large comparative study of the impact on survival of vaccination after 7, 8 or 9 months of age would have shown 7 or 8 month to be a better strategy than 9 months. It was quite clear that such a study should have been carried out. There are too many possible interactions in the disease environments such that public health policies of major importance can not just be based on desk deductions (based on unproven assumptions).

g) The hospital is one of the major sources for transmitting measles and causing measles deaths in an environment where the vaccinations coverage is good.

The interviews with the mothers also provided the imformation that many of the children had contracted measles during a hospitalization for diarrhoea or fever or while staying with a sibling at the hospital. As much as 30% of the acute measles deaths subsequent to the introduction of measles vaccination in Bandim could be traced back to contact at the hospital; these children had either contracted measles themselves at the hospital or they had been infected by someone who brought it home from the hospital. The implication of this seems rather clear. All children hospitalized ought to get vaccinated against measles at least during outbreaks of the disease. This is still not routine practice in many places in Africa.

h) Treatment with immunoglobulin can reduce the CFR in measles.

From the observation of the importance of intensity of exposure grew the hypothesis that severity of measles was related to the dose of infection which had not previously been assumed to be important in droplet infections (15). A logical implication of this was that maybe severe measles could be treated by providing "immune capacity" to the infected individual. The only way this was imaginable around 1980 was in the form of immunoglobulin. However, this contradicted the notion that measles is exclusively dependent on cell-mediated immunity, a notion coined by Burnet who said that measles antibodies were an epi-phenomenon. We were told by SAREC not to mention the possibility of treatment with immunoglobulin in the report to the Ministry of Health. Not being a physician there was no way of getting a possibility of testing this. However, a review of the literature from the 40s and the 50s showed that several studies had in fact provided date which supported this tendency though none of them had shown conclusively that hospital mortality from measles was

reduced. Furthermore, all reports of fatal cases of measles suggested that fatal cases had low levels or no measles antibodies at a time when cases of measles normally have antibodies. Subsequently a study from Maputo has shown that the CFR in measles was reduced from 25% to 14% at the hospital. Since vitamin A supplementation has recently been shown to reduce measles mortality, it is important to note that the effect was on top of vitamin A since all children received vitamin A. For practical reason it was not a randomized study, but the treated and untreated children were the children hospitalized during two subsequent months in the middle of the same epidemic. The result was consistent in the sense that effect was strongest among the smallest children since all received the same dose and the effect was higher the earlier treatement had been instituted.

i) There is amplification of severity or mildness in the sense that a severe case generate a more severe case and a mild case generate a mild case.

It followed from the studies of measles among vaccinated children that the severity of a case was important for the attack rate and it seemed likely that it would also have an impact on severity of the infected person. The fact that children infected at the hospital had higher CFR also supported this line of reasoning. This was subsequently tested with data from 1915-1925 from the infectious disease hospital in Copenhagen showing that the CFR was 4 times higher for a secondary case when the index case had pneumonia than when the index case did not have pneumonia. Data from Niakhar also showed that in compounds with several generation of cases there was a dramatic increase in severity for the later generation of cases. The tendency towards amplification is likely to be the cause of the enormously high CFRs observed in institutional or virgin-soil outbreaks of measles.

j) Infection from the opposite sex increases severity of infection.

This is probably the most unexpected of the observations from Bissau. A problem of translation made this observation compelling. In a previous paper an appendix had described the situation of contamination of the children who died of measles, saying something like F.G., female, two years old, had been infected at home by a sibling. This report had to be translated to Portuguese for use in Guinea-Bissau. In Portuguese, there is no word for sibling so the translation was always that the dead child had been infected by an irmao (=brother). Since this was obviously not true, I had to review the records of all the children and it then suddenly became clear that in most instances when a girl had died a boy had infected her and vice-versa when a boy had died. This observation was made on a small subset of the data from the 1979 epidemic namely the children who had been examined by a physician. It would probably have been difficult, not to say impossible to get funding for a study examining this hypothesis. However, the data was already available from the outbreaks of measles in Bandim and Quinhamel and the tendency was clear in both data set. Furthermore, case reports from the medical literature on measles supported the same tendency.

Subsequent studies from Senegal, Gambia, Copenhagen and Greenland have confirmed the tendency. It seems likely that it may also apply to chickenpox and polio, whereas my data from whooping cough does not indicate any similar tendency. Thus it may be a viral phenomenon. Studies of twins showing higher post-neonatal mortality for MF twins than for MM or FF twins also suggest that it is a more general phenomenon.

k) The delayed consequences of measles are also connected with intensity of exposure.

Given the emphasis on exposure and the fact that the children exposed before six months of age who had all been exposed intensively a "at home" had much higher mortality than other children, it seemed logical to hypothesize that intensive exposure was also a major determinant of detrimental long-term consequences of measles. Studies of the epidemiology of subacute sclerosing panencephalitis (SSPE) indicated that this hypothesis did in fact resolve a number of the contradictions in the understanding of this delayed complication of measles. Subsequent studies from Copenhagen and Niakhar have also indicated that delayed mortality is much higher for secondary cases. Thus it seems likely that the dose of infection may also determine the long term consequences of the disease.

l) Early vaccination with high-dose EZ measles vaccine is connected with higher mortality compared with children who have received the standard schedule of Schwarz measles vaccine at 9 months of age.

The previous experiences with early measles, the long-term consequences of measles and the impact on survival of measles vaccination made it imperative to try to control measles before also before 9 months of age. Had EZ vaccine not become available we would have tried a two dose strategy with the first vaccination with Schwarz standard before 9 months of age. However, in 1983 there appeared the first reports of successful immunization with EZ vaccination in the presence of maternal antibodies. The eventual decision in 1989 to recommend the use of high-titre EZ was based on the demonstration of a satisfactory antibody response. However, the experience with Schwarz standard suggested that it would be desirable also to study the impact on morbidity and possibly mortality. Studies were therefore initiated in 1985 in both Bissau and The Gambia. There was no way we could plan a study sufficiently large to show an impact on mortality. However, it was hoped with the previous experience of Schwarz vaccine that EZ would have an equally pronounced effect such that we would be able to show an impact due to improved protection between 4 and 9 months of age as well as to the higher coverage that we would obtain in the EZ group. In Bandim two trials were organized with children born August 1984 to September 1985 and May 1986 to April 1987. While the first assessment of the first trial was positive in the sense that EZ was protective against measles and that EZ children had lower mortality (6.3%) to the age of 2 years than the control children (9.5%), subsequent follow-up of both cohorts have shown excess mortality. As of 1990 when the children were 5-6 and 3-4 years in the two cohorts, mortality was 1.31 times higher in the combined analysis of both trials for the EZ children compared

with the controls. This tendency was particularly pronounced after two years of age where the mortality ratio was 1.76 (). Similar trends have been observed in data from Niakhar, Senegal. Thus, it seems that high-titre measles vaccine may give some of the same long-term consequences that measles infection may induce. Though this was not an illogical observation considering the previous experience with exposure to measles before six months of age and the emphasis on dose as a determinant of outcome. However, it was clearly not an observation that had been planned. It was an observation which had to be made in a longitudinal study area. Few researcher would have thought of the need for following the population for 3-5 years to get a proper assessment of the impact and no research council is likely to have funded a proposal which argued for the need to do so. The data from Bissau and Niakhar were presented at a consultancy meeting at the EPI in Geneva in February 1991. Though the experts found the data insufficiently convincing to change the official policy, they recommended three years follow-up of mortality in other studies. Thus, the experience from West Africa may have demonstrated the need to actually try out whether interventions have the assumed effect on mortality and the need to do long-term follow-up.

There are several other observations on measles which could warrant further discussion (the association between severity and length of incubation period, the number of index cases as a determinant of outcome, that age at infection in the community is not a determinant of the CFR in the society, that children under 6 months of age are not protected against measles, that males do not have a higher CFR in measles, and that measles may occur even in individuals who had antbodies). However, the observations discussed above are probably the most important.

CONCLUSION

There are obviously many problems in a 13-years longitudinal studies carrying out both research and health interventions which would be interesting to discuss; for example, how to relate to the populations studied and explain the research in a way which makes sense to them, the best way to train and organize field-workers, how to undertake interdisciplinary studies, the best balance between analyzing existing data and going on to collect more routine data, how to prevent data death, the mininal set of information which needs to be collected routinely, how to collect data which contradict your assumptions, what should have been done differently, the cost of the operation and how to minimize cost by combining several studies, how could interventions have become more effective and how to improve collaboration with the MOH and its local underpayed staff.

However, the present description has emphasized how observations are made. Research methodology in epidemiology and public health is getting increasing standardized. The emphasis is more and more on testing specific hypothesis. No one is going to get funding for a project which merely state the intention to

find out everything possible about measles or diarhoea. As an anthropologist I would like to fund such projects. Since creativity is hard to evaluate before it occurs, the tendency will be to evaluate research proposals in terms of methodological stricture in verifying the obvious. However, what makes research important to society and exciting to scientist are the new observations. If methodological strictures had been adhered to, none of the observations from Bissau would have been made. It would seem worthwhile to pay more emphasis to how one allows for new observations in research organization. Longitudinal studies may have a particular role in this respect.

Since certain aspects of the general situation including data on survival, morbidity and social conditions are followed within a longitudinal,
reality is allowed to contradict assumptions that had not been questioned. This happened several times in Bissau. Another important aspect of the longitudinal studies are that they make it much easier and cheaper to verify hypotheses which had not been planned in the beginning. There is a possibility of going back and complement data if missing information is essential to a certain hypothesis or interpretation. It is quite likely that the cost of setting up a new study would often be prohibitive for testing a new and "unlikely" hypothesis. Ethical considerations may also preclude testing a hypothesis because the mortality problem studied can be prevented. In this situation retrospective data may be the best that one can hope for. In Bissau, there were several instances where data to test unplanned observations were already available or could be complemented with little extra cost and with better validity than it would been possible if a purely retrospective study had had to be carried out. In the case of the measles studies this process was taken even further because other longitudinal studies were asked if they had data which could be used for verifying the observations from Bissau. Thus collaboration about the verification of clustering, exposure and cross-sex infection has been carried out with Keneba (Lamb 1988, 60), Bandafassi (Pison et al 1988, 65), Niakhar (47, 73, 77), Machakos (42, 59) and Matlab (Koster 1988).

While many of the observations were derived as deduction from other hypotheses, there were several important ones which were "seen" or "heared" accidentally. The process in these cases are difficult to describe but depends partly on having a problem and therefore being willing to "see". It was also characteristic that several were derived out of context while doing routine work like interviewing, coding or translating. Such routine activities undertaken for other purposes may force you too see patterns you had no intention of finding. While we mostly see reality through already existing cultural/scientific categories, the context may present a new pattern which fundamentally break those categories. This is probably more likely to occur in longitudinal studies because there is simply more context than in a specific short-term study. The other condition is of course that you bring yourself into situation where your categories may be contradicted by "reality". One reason that focus groups have become so popular in social science research is probably that

they open the possibility that people will speak between themselves around a subject in which you are interested and in the process are likely to come to contradict your assumptions. The varied experiences in a longitudinal study may similarly come to contradict your assumptions thus producing new insights.

In this connection it is important to underline that it is dangerous if researchers become too specialized only analyzing the information collected by others according to the researcher's categories about reality. In such situation there is little risk that new patterns will be observed. If they do present themselves they are likely to be interpreted as "noise" due to poor preformance of the field assistants.

Another important aspect of the process of observing is the resistance towards seeing something new. We are apparently likely not to interprete all the contradictions we "know" are there and to assume that they are accidental: in a larger "sample" things would be as we assume them to be. The first rule for seeing something may in fact be to pursue all contradictions between reality and your assumptions. The tendency is often to try explain an unexpected observation as the result of something else that we already know about; in other words "it could be due to something else". While one should obviously disprove the most simple forms of confounding, trying to disprove that a phenomenon is not due to something else is a limitless process which provide no new insight. Trying to verify deductions from an observation/hypothesis is much more likely to produce assurance that the pattern is real than the attempt to disprove "that it could be something else". In this context, the longitudinal study is important because it facilitates the testing of new deductions.

Thus to sum up, the longitudinal study if utilized properly is more likely to produce new observations since it allows for reality to present results which were not imagined and which will not be visible in a short-term highly focused study. Furthermore, the longitudinal study may provide both spatial and temporal contexts on the research issue in a way which facilitate the experience of contradiction, of something new. Finally, it is far easier within a longitudinal study to test deductions from a new hypothesis. This latter benefit may not be limited to the individual project, collaboration between different longitudinal studies may greatly increase the possibility for using already existing data.

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TABLE 1
SEVERITY OF MEASLES INFECTION ACCORDING TO TYPE OF EXPOSURE IN DIFFERENT COMMUNITY STUDIES

Country (reference)	Age (years)	CFR% (deaths/number ill) Index	Secondary	Relative risk(95%CI)
Urban studies				
Guinea-Bissau (Aaby 1989)	0-4	8%(10/128)	30%(48/162)	3.8(2.1-6.7)
Guinea-Bissau (Aaby et al 1988a)	0-4	3%(1/37)	38%(10/26)	14.2(3.4-59.5)
Guinea-Bissau (Aaby et al 1988a)	0-4	5%(3/66)	17%(14/81)	3.8(1.3-11.4)
England (Aaby et al 1986a)	0-2	8%(4/48)	22%(8/36)	2.7(0.9-7.8)
Copenhagen (Aaby 1988a)	0-2	11%(28/252)	27%(49/183)	2.4(1.6-3.6)
Rural studies				
Guinea-Bissau (Aaby 1989)	0-4	7%(1/15)	38%(33/86)	5.8(1.4-24.5)
Senegal (Garenne and Aaby 1990)	0-4	4%(8/198)	14%(37/226)	3.4(1.7-6.7)
Kenya (Aaby and Leeuwenburg 1990)	0-4	3%(11/381)	7%(21/287)	2.5(1.3-4.9)
Bangladesh (Koster 1988)	0-2	1%(1/134)	18%(4/22)	24.4(5.6-106.1)
Bangladesh (Bhuiya et al 1987)	0-4	15%(38/2551)	3%(17/630)	1.8(1.0-3.1)
Germany (Pfeilsticker 1863)	0-14	2%(2/93)	11%(10/95)	3.7(1.1-12.1)
Ratio of severe cases				
Gambia (Lamb 1988)	0-23	7%(3/41)	31%(4/13)	4.2(1.2-15.3)

TABLE 2
EFFICACY OF MEASLES VACCINE AGAINST DEATH. DIFFERENT STUDIES

Country; period (no)	Age at vaccination	Period of follow up	Mortality(%) for unvaccinated(UV), placebo(P) and vaccinated(V) (no. in study)		Vaccine efficacy against death (95% CI)
Nigeria(1)		18 mo	P=12%(25)	V=0%(23)	100%
Zaire(2)	7-9 mo	30 mo	UV=7.0-9.5%	V=3.8%	46-60%
Guinea-Bissau (3)	6-35 mo	12 mo	UV=14.3%(70)	V=1.9%(361)	87%(70-94)
Guinea-Bissau (4)	7-24	24 mo	P=13.2%(53)	V=4.8%(124)	63%(2-86)
Guinea-Bissau (5)	9-23	24 mo			66%(32-83)
Senegal(6)	6-35 mo	30 mo	UV=33.6%	V=23.2%	31%
Haiti(7)	6-13	9-39 mo	UV=6.6%	V=1.3%	85%(36-96)
Bangladesh 9		9-60 mo			36%(21-48)
Bangladesh		9-60 mo	UV(8135)	V(8135)	46%(35-54)

Notes: 1 (Hartfield and Morley 1963) A small placebo study carried out in the beginning of the 1960s.
2. (The Kasongo project Team 1981) The study in Zaire was carried out in the mid-1970s. Vaccination was introduced in one area and mortality compared with a neighbouring comparable area and with data from the same two areas prior to the introduction of measles vaccination.
3. (Aaby et al 1984c) The study was carried out in 1980 in the capital of Guinea-Bissau. Mortality has been compared for children who attended a child examination and were vaccinated against measles and children did not attend mostly because they were temporarily absent. In the year prior to the introduction of vaccination there had been no difference in mortality between children who attended and those who did not.
4. (Aaby et al 1989) The study carried out in 1984-1986 represents a "a natural experiment". When blod samples taken in connection with vaccination were analysed after two years, it turned out that during a short period none of the children had seroconverted. They can be considered to have received a "placebo".
5. (Aaby et al 1990c) The study carried out between 1984 and 1987 compared mortality for children who received vaccination and those who did not in two districts in the capital of Guinea-Bissau.
6. (Garenne and Cantrelle 1986) Two systematic measles vaccination campaigns were carried out in one rural area in Senegal in 1965 and 1967. Mortality was compared with an area where vaccination was not available.
7 (Holt et al 1990). The study compares mortality for children who had participa-ted in a serological study in 1982. The estimate of VE against death takes account of background factors with a significant impact on mortality (socio-economic status, literacy, knowledge and use of oral rehydration and birth interval).
8. (Clemens et al 1988) The study from the Matlab area in 1982-1984 compares vaccination status for 536 children who died and 1072 controls.

9. (Koenig et al 1991) This study of 8135 vaccinated children and controls from the Matlab area covers 1982-1985. The study is partly overlapping with the previous study.

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