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ADVISORY COMMITTEE ON MEDICAL RESEARCH

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Item 12 of the Agenda

PLANS FOR THE CREATION IN WHO OF
A DIVISION OF RESEARCH IN EPIDEMIOLOGY
AND COMMUNICATIONS SCIENCE

Ref: RES 5/5

2 May 1966

PLANS FOR THE CREATION IN WHO OF
A DIVISION OF RESEARCH IN EPIDEMIOLOGY
AND COMMUNICATION SCIENCE *

Many of you will be aware that for some four years WHO has been seeking ways of extending its activities in biomedical research. Since the adoption of the resolution by the WHA in 1958, authorizing WHO to embark upon a research program, many members of the staff have felt that WHO's essentially passive research activities in the grant support of research and its coordination through the grant mechanism was unsatisfactory. With this opinion I have always agreed. Early in 1962 the Director-General decided that, considering the changing circumstances in health-related matters throughout the world, the existing system would not enable the Organization to fulfill its obligations to member states, and that it would have to enter actively into the conduct of research itself. There was in fact considerable justification for this change of policy. The best research laboratories were interested in what interested them. The importance of a problem from an international public health point of view had little effect on their research program, so that there were important areas of ignorance in which few if any of the best scientists and their laboratories were investigating.

The Director-General therefore initiated a study of how WHO might more effectively fill its role. The director of this study was attached to the Director-General's office and a long series of meetings of experts in various fields was convened. I had the privilege of attending many of these meetings. Out of this came a proposal for the establishment of a World Health Research Centre, staffed by WHO and financed in the regular budget at very considerable

*Prepared for the Fifth Meeting of the PAHO/ACMR by Committee Member
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expense. Many of us felt that this was not the best way of approaching the Director-General's objectives. Nevertheless the proposal was put forward to the Governing bodies of the Organization and was, as anticipated, turned down. However the work that had been put into this proposal was certainly not wasted. The WHA recognized "the need for a planned development of WHO research activities to promote, co-ordinate, support and conduct medical research and research training on major world health problems." (WHA 18.43) Historically this resolution will be looked back upon as the first time that WHO had been given a firm authorization by the Assembly to conduct research, as opposed to promote, coordinate and support it, which had been the previous practice, although the Constitution empowered the Organization to do so.

The Assembly went further and "requested the Director-General to take action necessary to develop WHO research activities and services in epidemiology and the application of communications science" and to submit a detailed program to the Executive Board and eventually the Assembly. This has now been done. The program has been approved by the Executive Board at its meeting in January, but at the time of writing (April) it has not as yet been considered by the Assembly.

The proposed program was presented to the Executive Board in document EB37/11, attached. According to the current practice in WHO it was first considered by the Standing Committee of the Executive Board on Administration and Finance. It was received with some suspicion, largely because of the financial implications, which were considerable, even though only a fraction of those involved in the original proposal referred to above. However it

became clear that much of the opposition was the result of the lack of understanding of the content and implications of the research proposed. The Director-General therefore asked two consultants to present the program before the full Executive Board. I had the privilege to be one of them; Dr. Murray Eden from MIT was the other. The statements are attached. After hearing these, the proposal was adopted by the Board unanimously with one abstention which was on financial and not on technical grounds.

The program consists in essence of the creation of a new Division of Research in Epidemiology and Communications Science staffed by 15 senior scientists with supporting staff--39 posts in all--with a budget of approximately \$500,000. The scientific staff will be drawn from the following disciplines: epidemiology, biology (ecology), sociology, anthropology, demography, biometry, mathematics, operations research, and computer science.

The details of the program have not yet been worked out pending the selection of the staff. They will follow the general lines laid down in document EB37/11.

Major areas will be the epidemiological study of the health consequences of rapidly changing conditions in the context of rural-urban migration; the development of improved surveillance systems for communicable diseases; the development of monitoring systems for the early detection of toxic hazards from drugs and environmental pollutants; the application of operations research techniques in public health research; and the application of mathematical and computer science in health research.

The Division will be developed in such a way as to use to the maximum the existing research competence of WHO staff and cooperating universities and institutions so as to avoid duplication. These will be supplemented as necessary by the recognition of additional regional or national centres where the appropriate expertise can be found. Much of the actual field work will be done by or through these centres. One of the major roles of the Division will be the planning, supervision and coordination of field studies so as to ensure comparability of international studies performed under a wide variety of contrasting conditions.

It is worthy of note that some of the ideas behind this program were stimulated by the discussion on the Environmental Determinants of Community Well-being, held by this Committee two years ago, and the report of those discussions will undoubtedly be of great value in the further development of this program.

On my return to WHO I will have the responsibility of initiating this program, selecting the senior staff, etc. Any advice or suggestions this Committee can give me will be deeply appreciated.

ATTACHMENT 1

WORLD HEALTH
ORGANIZATION

ORGANISATION MONDIALE
DE LA SANTÉ

EXECUTIVE BOARD

EB37/11
3 December 1965

Thirty-seventh Session

ORIGINAL: ENGLISH

Provisional Agenda item 2.11

EXTENSION OF WHO ACTIVITIES IN RESEARCH

Report by the Director-General

INTRODUCTION

The Eighteenth World Health Assembly in its resolution WHA18.43¹ recognized "the need for a planned development of WHO activities to promote, co-ordinate, support and conduct medical research and research training on major world health problems", and considered that "such contributions . . . could best be made by an international research programme involving collaboration with and development of regional and national institutions.". In paragraph 2 of this resolution, the Director-General was requested "to take the action necessary to develop WHO research activities and services in epidemiology and the application of communications science" and in paragraph 3 "to prepare a detailed programme . . . to be submitted to the Thirty-seventh Session of the Executive Board."

A proposal for research by WHO is justifiable only if the research is of such a nature that it cannot properly or adequately be conducted by national research institutes or universities. In fact, many research topics in epidemiology are particularly appropriate to WHO: some are essentially international in concept, some are feasible only when supported by the objectivity and international acceptability of WHO, and some are essential as bases for future WHO health activities. Furthermore, mathematical and statistical theory and computer science are necessary to progress in epidemiological and allied research, and their potentialities will increase with intensive study of their applications in medicine.

¹ Handbook of Resolutions and Decisions, 8th ed., p. 121.

1. Epidemiological research

1.1 Cogent reasons for developing a more extensive programme in this field are:

- (1) knowledge of the variation in the incidence and prevalence of disease throughout the world is still far from complete;
- (2) more detailed knowledge of this variation is essential to the control of many diseases of known etiology;
- (3) combined with study of the characteristics of the local populations and their environments, study of differences in disease incidence and prevalence may provide new clues to the cause of other diseases, the etiology of which is still unknown;
- (4) new hazards are being introduced by rapid socio-economic reorganization and industrial and technological advances and their effects may persist for many years after the hazards are eliminated, it is, therefore important that they should be identified at the earliest possible opportunity;
- (5) extensive changes are taking place in the socio-economic structure of large populations throughout the world, if these studies are not made soon, vital information about diseases that are becoming more common, which could be revealed by differences in existing conditions, will be irretrievably lost;
- (6) man is being increasingly exposed to a wide range of new chemical compounds introduced for medical and other purposes (drugs, pesticides, food additives, cosmetics, etc.) which may have unsuspected effects in addition to the benefits intended. These also must be identified as early as possible in order that assessments can be made of risk relative to benefits;
- (7) in some diseases important variations in incidence and prevalence can be recognized most readily on an international scale, where the contrasts are greatest;
- (8) investigation of the factors relating to these differences frequently requires collaboration across national frontiers in the same or in different regions of the world;

(9) countries with the greatest contrasts may not always have the resources to investigate them in the most fruitful way.

1.2 It is evident, therefore, that WHO has an important role to play in epidemiological research. It cannot limit its activities to any one aspect of the subject, but must be prepared to undertake studies on a broad front. This conclusion is, moreover, reinforced by the knowledge that diseases may not occur independently but the distribution of one may be a decisive factor in the causation of another. It is, however, also clear that WHO cannot undertake the intensive investigation of all diseases at the same time, but that the extent of its work will necessarily be limited by practical considerations of money and manpower. Research in epidemiology should, therefore, be concentrated in fields where there is an acute need for further information, either because of the seriousness or prevalence of the disease or because it is possible to formulate a new hypothesis that can be tested directly and may lead to a productive result of direct value to health administrations. It follows also that the programme should be flexible and permit WHO to apply its resources to new problems as they arise, and, at the same time, take advantage of new developments, new methods and new hypotheses.

2. Research in communications science applied to health problems

The essential activities requiring special research and development under this heading can be classified as follows:

2.1 Applied mathematics

Unsolved biological and epidemiological problems, including surveillance and monitoring procedures, all require the use of specialized mathematical techniques. In particular, the development of appropriate mathematical models is needed to facilitate more precise quantitative evaluation and investigation.

2.2 Statistics, biometry and probability

All biological and clinical material involves large amounts of inherent variation. Probabilistic formulations are essential to describe this variation. The investigation of real data, the planning of surveys, as well as the testing of scientific hypotheses, all therefore entail the use of sophisticated mathematical statistical methods.

2.3 Operational research

In order to make best use of theoretical research and of accumulated knowledge to improve the management both of public health programmes and of its own activities, it would be essential of WHO to develop and apply a full range of operational research techniques.

2.4 Computer science

The mathematical models envisaged above must be fairly elaborate with many variables if they are to achieve an adequate degree of realism. Advanced techniques in numerical analysis will be required for all kinds of mathematical and statistical investigation. In many cases simulation methods will be needed to supplement purely mathematical enquiries. Further, the utilization of operational research methods necessitates a great deal of numerical computation.

2.5 Information analysis

The efficient use of very large quantities of numerical data and other recorded information including reports in natural language require a variety of special techniques for filing, sorting and searching. Aside from the obvious requirement of high-grade computing facilities the extractions of relevant information will depend upon the development of suitable mechanical interrogation languages, and on the techniques of literature analysis, e.g. content analysis of written documents.

In order that all forms of data and records can be utilized with maximum efficiency specific emphasis must be placed on the investigation and building of nomenclatures, on the standardizations required both for case reporting and for computer processing.

3. Action required and objectives

3.1 Such a programme demands the creation of a unified group of highly qualified epidemiologists and communications scientists within the Organization with the following objectives:

3.1.1 To study WHO's current activities in epidemiology in relation to world needs with a view to identifying those fields in which opportunities and technical possibilities promise important progress, especially through development of methodologies for determining contrasting areas of high and low incidence of diseases and for investigating the reasons for these differences.

3.1.2 To investigate the potentially great contributions that techniques of operational research could make to improve the economy and effectiveness of public health programmes.

3.1.3 To develop a research programme designed to identify and study the major factors which affect the health patterns of different populations exposed to rapidly changing living conditions. For this purpose new methods of categorizing and quantifying the health consequences of population dynamics and ecological changes will need to be developed.

3.1.4 To develop mechanisms whereby changing health patterns can be kept under constant review. This would require the development of efficient surveillance systems for different groups of diseases.

This programme would serve the ultimate task of WHO, of devising methods whereby what appear at present to be inevitable sequences can be interrupted and the undesirable effects on health of socio-economic development avoided.

3.2 Some of these objectives will inevitably require a long time to be achieved. However, techniques are now in existence, and can be developed further, especially in their application to health problems, which could greatly accelerate progress.

3.3 Apart from the study of WHO's current and planned activities in epidemiology in order to identify those fields where opportunities exist for rapid progress, priority will be given to developing research programmes concerned with surveillance or monitoring of communicable diseases and drug effects. A programme will be developed for the study of the health effects of ecological change with special emphasis on population dynamics in the context of rural-urban migration. Finally, attention will be given to the application of the techniques of operational research to health problems.

3.4 It is proposed that these programmes be carried out by a Division of Research in Epidemiology and Communications Science attached to the Office of the Director-General, for which provision is included in the Proposed Programme and Budget Estimates for 1967.¹ These programmes are considered in more detail below.

¹ Off. Rec. Wld Hlth Org., 146, p. 21.

4. Surveillance and monitoring systems

4.1 Communicable disease surveillance

4.1.1 WHO has since its inception been engaged in a variety of activities pertaining to communicable disease surveillance. However, experience has shown that these are far from adequate in respect of their scope, accuracy and speed. A programme designed to overcome partially these deficiencies has been initiated by the Division of Communicable Diseases and it is clear that a Division of Research in Epidemiology and Communications Science can contribute to it in a number of ways so as to ensure that the information gathered will be of greatest use for the objectives outlined above, as well as for the improvement of the control of communicable diseases per se, by enabling the institution of effective control procedures earlier in the development of disease problems.

4.1.2 It is essential that any surveillance programme should be supported by the development of appropriate theoretical studies. The insights deriving from such studies would provide increased understanding of the phenomena involved, with a consequent improvement in the control of specific outbreaks of epidemic disease or of unusual levels of endemicity.

4.1.3 Two complementary, though related approaches, are identifiable: first, there is the study of population phenomena. This involves, for example, the elucidation of threshold effects, that is to say, the relationship between the chance of a major outbreak of disease and the density of susceptible individuals in the population. One aim would be to calculate the different epidemic curves which would result from different theoretical assumptions about the nature of the epidemic process and to test these against observed epidemics. Much more theoretical knowledge is needed about the behaviour of epidemics in communities that are spatially and socially differentiated.

4.1.4 There is a need for development of sample survey methods which can be initiated rapidly in order to obtain special denominator data needed in the evaluation of surveillance data, or both numerator and denominator data, as in serological surveys. Such methods have been developed in some countries but these cannot readily be adapted to the wide variety of circumstances met with a world-wide application.

4.1.5 In theoretical epidemiology considerable progress has been made in specialized areas, but few data exist for critical tests of generalized epidemic models. Before such theory can become a practical aid to prediction and interruption of epidemics, larger collections of detailed records must be subjected to mathematical analysis. This can be done most readily for the simpler diseases transmitted by person to person contact. In more complex situations, such as the arbovirus diseases in which not only other vertebrates but arthropod vectors also must be taken into account, mathematical formulations have been rudimentary and need extensive development. In the meantime, progress in the control of these infections may be accelerated by mathematical description of segments of the whole situation.

4.1.6 Also, there is the need to discover more detailed biological and clinical features of the disease process such as the time between infection and extrusion of infectious material, the length of the infectious period itself, variations in infectiousness or susceptibility between different individuals, etc.

4.1.7 In general, the use of mathematical models of epidemics may be expected ultimately to provide information of great practical significance to public health authorities, especially when theoretical studies are carried on in close co-operation with the surveillance activities. Decisions about the relative value of immunization programmes, the follow-up of suspects, the institution of quarantine, the restriction of public activities, etc. will be facilitated by a greater understanding of the epidemic processes themselves. Moreover, since such practical measures can be implemented only through executive and administrative action it is vital that the special skills of operational research be called upon to ensure optimal application.

4.1.8 An important part of the surveillance programme is that concerned with studies of the ecology of certain diseases. This requires the accumulation and analysis of considerable bodies of information on disease vectors and reservoirs as well as on the distribution of sub-clinical infection in addition to the data collected on overt disease. Some of these data will be accumulated through the activities of the WHO Serum Bank Programme which can contribute greatly to the study of a wide variety of

fields other than communicable diseases, e.g. human genetics, nutrition and a number of non-communicable diseases. It is evident that the information gathered in this programme is highly relevant to the study of the health effects of ecological change, one of the major objectives of the Division. This programme demands a higher priority than has been accorded to it in the past.

4.1.9 For these reasons the surveillance programme will require full co-operation of a Division of Research in Epidemiology and Communications Science. Further, the biomathematical expertise and automatic computing facilities envisaged are essential for its success. It would seem that only WHO could provide opportunities for research and application in this field on the scale necessary for worthwhile results.

4.2 Drug monitoring

4.2.1 WHO will consider acceptance of responsibility for a pilot research study in drug monitoring, with the assistance of data processing and associated facilities offered for an interim period by the Government of the United States of America. This proposal is discussed in another document¹ concerning the initial research character of the project, and the expectation that eventually WHO would be able to play an effective role in measures for ensuring drug safety are emphasized. If WHO does undertake such a pilot project, a Division of Research in Epidemiology and Communications Science will undoubtedly have a role to play in consultation on epidemiological, statistical, and computer techniques. Irrespective of action taken on the United States offer, however, a Division of Research in Epidemiology and Communications Science should initiate research in this field, both for the sake of developments in monitoring techniques and because of its concern with methodological research.

4.2.2 Monitoring is recognized in principle as an indispensable part of protective measures against dangers from drugs, in addition to the animal studies of drug action and the clinical trials that precede general therapeutic use of a drug. However, considerable research is needed in order to develop adequate monitoring programmes, particularly in respect of the types of records to be collected nationally and internationally, and of the procedures for scanning and analysing extensive files of records.

¹ EB37/12 International Monitoring of Adverse Drug Effects.

4.2.3 WHO can make the special contribution of objective comparison between methods for drug monitoring now rapidly developing in several Member States, establishment of underlying principles common to good monitoring, and identification of the opportunities available in particular countries for accumulation of evidence that the medical structure of other countries is at present unable to provide. The hope that the pilot programme will eventually evolve into a permanent operational system must be kept in mind, but the timing of this (and indeed its ultimate practicability) can be assessed only in the light of intensive research - and research of a kind possible only when records can be studied from many points of view.

4.2.4 The pilot project would consist of collaborative research between National Centres in the few Member States in which drug monitoring already is or soon will be undertaken (perhaps with the addition of Special Centres elsewhere). A Division of Research in Epidemiology and Communications Science will be able to make specific contributions under such heads as:

- (1) types of record to be collected, and the degree of validation of reports on individual cases required before national records can usefully be passed to an international centre;
- (2) problems of translation and coding inherent in storage of data in the internal language and format of a computer;
- (3) scientific and administrative problems of access to and search of stored data;
- (4) interaction of clinician, biometrician, and computer scientist in the devising of computer programmes for scanning data files that permit the clinical expertise and intuition applicable to small series of case records to be the basis of systematic examination of much larger series;
- (5) epidemiological and statistical study of the nature of inferences that can be drawn from different categories of records, with a view to developing principles of operation in respect of early warnings, calls for additional data or more intensive search for records, research leads in drug therapy, and other types of action that an international monitor might from time to time engender;

- (6) consideration, from epidemiological and statistical viewpoints, of the desirability of any regular systematic reporting from a future WHO international monitoring centre to national health authorities, and of the nature of any such reporting;
- (7) development of very flexible computer programmes for the special interrogation of data files on any topic of immediate interest;
- (8) investigations of manners in which computer facilities can aid the search of literature for relevant information;
- (9) in the light of developing ideas on all these points, continuing constructive criticism of all existing national monitoring systems, with a view to their growth into what is best suited to the needs of each country as well as what serves the international project;
- (10) operational research on comparative utility of alternative report forms, on hospital versus practitioner reporting, on follow-up procedures, etc.;
- (11) investigation of use of figures for drug manufacture, distribution, sale, etc. as an aid to estimating numbers exposed to risk;
- (12) continuing evaluation of the pilot study as a whole and investigation of its deficiencies.

4.2.5 In addition, topics less immediately forming an integral part of routine monitoring should be studied as opportunity offers. For example:

- (1) comparison of reporting of a few drugs used in several countries;
- (2) geographical differences in the occurrence of adverse reactions;
- (3) research on the use of reporting terminology;
- (4) extensions of the early warning system;
- (5) interrelation of adverse effects and chemical composition of drugs;
- (6) studies of patterns of reporting and coherence of data.

4.2.6 As is stated elsewhere,¹ the work of a future WHO international centre on monitoring adverse drug reactions and of the proposed Division of Research in Epidemiology and Communications Science in research on monitoring would supplement, not replace, what should be done at the national level; it would in no way affect the responsibilities of national authorities for interpretation of their own data or for decisions on action to be taken.

4.2.7 The contributions from a Division of Research in Epidemiology and Communications Science outlined above are not only essential to the research on monitoring that must be conducted if WHO acts further on the basis of resolutions WHA17.39² and WHA18.42.³ They are of intrinsic interest to the programme of a Division of Research in Epidemiology and Communications Science in methodological research. Moreover, experience with them and possibly even specific findings in respect of them will be of further value when, as is almost inevitable, WHO is required to advise on or to participate in other monitoring enterprises (e.g. adverse effects of pesticides or other environmental pollutants).

5. Population dynamics and rural-urban migration

5.1 One of the most rapid and dramatic ecological changes occurring in the world today affecting the patterns of life of millions of people is the phenomenon of rapid rural-urban migration. This is bringing in its train a wide variety of health problems and alterations in disease patterns. However, relatively little is known as to which of the changes, involving the biological, physical and chemical, and social environments are most important in causing modifications in health and disease patterns, nor are the mechanisms through which they act understood. If the important factors could be identified, it might become possible to alter them in such a way as to avoid or reduce the undesirable effects on health.

¹ EB37/12 International Monitoring of Adverse Drug Effects.

² Handbook of Resolutions and Decisions, 8th ed., p. 20.

³ Handbook of Resolutions and Decisions, 8th ed., p. 21.

5.2 The speed with which these changes are taking place and the fact that they are occurring in contrasting situations provides an opportunity for comparative studies which might lead to useful results sooner than has been possible in the past. Similarly it provides a unique opportunity for the study of a special form of one of the major problems facing the world today, that of population dynamics.

5.3 Population dynamics involves not only the over-all growth of populations, but also "local" growth resulting from movement of populations, especially that towards cities. This may be regarded as an acute form of population growth which is happening far more rapidly than the over-all growth, and it provides an opportunity for the study of the influence of a variety of factors on population growth, e.g. the influence of crowding, and other social and environmental changes on fertility and fecundity. The Advisory Committee on Medical Research has emphasized that these studies might lead to ways of evaluating and predicting population trends with special reference to the urban situation where knowledge is most urgently needed. These studies will have to be multi-disciplinary, involving epidemiologists, sociologists and anthropologists, and a variety of other disciplines.

5.4 The focus of this part of the research programme of a Division of Research in Epidemiology and Communications Science will initially be on this aspect of population dynamics. However changes in disease patterns influence population growth in a variety of ways. It will therefore be necessary to accumulate information regarding these changes and on the changing environmental pressures to which the population is subjected. Thus a start would be made in the accumulation of information which might lead to the formulation of hypotheses regarding the mechanisms whereby the health changes are brought about. These might form the basis of specifically designed research programmes in the future.

5.5 In order to develop this programme, a Division of Research in Epidemiology and Communications Science will need to include a small number of scientists drawn from the fields of medical epidemiology, sociology, anthropology and perhaps other branches of the health and behavioural sciences. It must be able to draw on the competence in mathematics, statistics, demography, and computer science envisaged for the work in communications science.

5.6 Initially the scientists will need to concentrate on methodology mutually adapting the methods of the different disciplines involved. The parameters which it is desired to measure, and which it is possible to measure, will have to be identified on the basis of the hypotheses to be tested. Standard protocols for field studies will then have to be developed and this should be done in collaboration with those who will be responsible for the field work. It is planned that this should be done through a system of Regional or National Epidemiological Centres, carefully selected on the basis of interest, scientific competence, on the opportunities for developing such studies in the area, and influenced by the nature and quality of the relevant information already available. Initially the studies would be limited to two or three contrasting areas in developing countries and perhaps one or two in more highly developed countries so as to provide a spectrum of contrast which might more readily reveal differences of potential significance.

5.7 In developing this programme close attention will be devoted to research programmes under way or projected in several countries concerned with urban development, including sociological aspects. However, it seems that in most of these attention to the health aspects is minimal or lacking altogether. The proposed research might serve to introduce the important health component into these programmes, thus greatly increasing their value.

6. Operational research

6.1 As medical care needs increase and as medical and public health programmes are extended to meet them, it is fortunate that a body of knowledge and techniques known as operational research is being developed to aid the public health administrator in the making of sound decisions. There are two kinds of major decisions which frequently face the public health administrator and they are as follows:

- (1) How does one assess the relative needs for and the values of alternative programmes which must draw upon limited resources in funds, material and trained manpower?
- (2) How shall available resources be best allocated and applied once a decision on priorities has been made?

Both problems have been intensively studied. Operational research has contributed generally acceptable solutions in such fields as economic planning, business management, industrial development and military logistics.

6.2 Although these questions constantly recur in public health administration, there have been a relatively small number of applications of operational research to public health. These include the automation of day-to-day hospital management and accounting, those public health matters which are almost exclusively economic, the optimal location of medical facilities and a few specific projects as in the planning of one of the large-scale WHO tuberculosis control programmes. This lag in the application of operational research to public health is understandable, because this administrative device has only come into general use during the past two decades. It was first applied in military logistics then, by extension, to related industrial problems, later to general economic planning and business management, and now to public health. Its evolution was favoured by the concurrent development of the electronic computer.

6.3 In essence, operational research aids the administrator in decision making by providing, on the basis of those criteria of choice which can be specifically measured, an accurate analysis of the consequences and costs of alternative procedures. The responsible administrator eventually makes his final decision in the light of the operational research report, other expert opinion and the relevant imponderables.

6.4 The assistance which the existing body of knowledge of operational research could contribute to the public health administrator is illustrated by the following examples:

Transportation flow theory can be used to calculate optimal distribution, location and itineraries of field teams assigned to mass health surveys or disease control.

The mathematical solution of the "inventory problem" can be used to calculate the minimum investment in an inventory of drugs or medical supplies needed for normal or foreseeable emergency use.

The techniques of "optimum time scheduling" (frequently referred to as PERT) could assist the administrator in his planning of the orderly and efficient expansion of public health services and its logistic support.

Feed-back information from existing public health programmes analysed by the "control theory of Pontryagin" and in accordance with the "dynamic programming theory" of Bellman could provide estimates of the effect of the programme on the public health need, and aid in keeping the programme commensurate with the needs.

6.5 In addition to the direct application of existing operational research knowledge and techniques, new theory will have to be developed to satisfy the special requirements of biomedical and public health problems. For example, the application of inventory theory to blood banks will require taking into account the perishable nature and limited life of human red blood cells.

6.6 As sound decisions emerge from the use of operational research in limited areas of public health administration, there will result an increasing recognition of the usefulness of this approach in contributing to major policy decisions. Finally the increasing demand for public health services and their ever-mounting costs must eventually favour the adoption of a more systematic approach to decision making over that of ad hoc intuition or the influence of external competing factors.

6.7 A Division of Research in Epidemiology and Communications Science would concentrate on developing the applications of operational research to problems in public health with a view towards providing the public health administrator with quantitative bases for informed decisions between alternative plans.

ATTACHMENT 2

EXECUTIVE BOARD

EB37/WP/2
20 January 1966

Thirty-seventh Session

ORIGINAL: ENGLISH

Agenda item 2.11:

Extension of WHO Activities in Research

STATEMENT ON EPIDEMIOLOGY

by

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The programme in epidemiology outlined in document EB37/11 is a summary of the views of a number of leading epidemiologists regarding the reasons for developing epidemiological research on an international scale and lists some of the areas in which this is most urgent and likely to be most profitable.

This kind of modern epidemiological research is highly sophisticated because it requires the adaptation of research techniques from a variety of disciplines, biological, social, and mathematical sciences and computer technology, into a harmoniously functioning whole. These skills are not adequately represented within the Organization at present.

It may be helpful to touch very briefly on some recent epidemiological concepts which greatly influence modern epidemiological research and from which derives the need for a multi-disciplinary approach.

Epidemiology may be defined as the study of the health of man (groups or populations) in relation to the total environment. Thus it is essentially the study of human ecology, a system of great complexity in which extensive and often obscure interactions take place.

Recognition of these interactions has led to a radical change in the concept of the etiology of disease. The older concept of the specific etiology of disease has proved inadequate to account for the observed behaviour of the great majority of diseases, even communicable diseases, and it is now clear that multiple factors are involved in the causation of all diseases. Understandably the medical profession has in the past tended to be preoccupied with biological

factors, to the neglect of environmental and social factors which may be of over-riding importance. This is true for communicable diseases, but it was the rising tide of chronic, non-communicable diseases which, above all, forced attention to this change in concept.

As a development of the concept of multifactorial etiology of disease, there has been another important conceptual advance. Disease processes may be divided into causation, mechanisms and effects. According to this concept, causation is defined as the sum of all factors, external and internal, which combine to initiate internal biological mechanisms which in turn lead to effects (physiological or pathological) which may be recognized as disease. It should be noted in parenthesis that recognition of an effect as disease depends on a social and not on a scientific decision, and the criteria employed differ between cultures and in the same culture from time to time.

Coronary heart disease provides an illustration of this. The cause of coronary heart disease is not the thrombus which blocks the artery, nor is it the atheromatous condition of the arterial wall, nor the changed coagulability of the blood, nor raised blood lipids and blood pressure. These are all part of the mechanisms. Causation lies further back in the process, in behavioural and environmental factors such as diet, exercise, occupation, stress, smoking, etc. Such causative factors are a primary interest of modern epidemiology, because it is through their elucidation that true prevention may become possible. It is probable, even certain, that the relative importance of the different factors differs between cultures. On the American scene over-consumption of saturated fats and lack of exercise seem likely to prove the most important in the causation of coronary heart disease though there are still many unanswered questions. On the other hand the deeply tragic death last week would I believe prove to be the result of great and prolonged stress if only we knew better how to measure it. Certainly over-consumption was not a causative factor. There can hardly be a stronger argument for the importance for all countries of research in this field. Coronary heart disease is on the increase in all countries for which reasonably good information is available and it seems to involve first the cream of the country

who have to carry the anxieties and burdens of development. In the light of present knowledge acceleration of this trend seems to be inevitable unless we can discover more about the factors involved and how to modify them.

There is another aspect of the concept of multifactorial etiology which is relevant to the proposed programme. In the last analysis it is the ecology of an area which determines what diseases might become serious problems as conditions are changed in the process of development, or should any of a variety of agents be introduced. Knowledge of it therefore has a predictive value enabling one to foresee future dangers so that preventive action can be taken in good time. For instance, for nearly a decade the dangerous situation with respect to Aedes aegypti in the Carribean islands had been stressed, particularly with respect to dengue fever, especially the haemorrhagic type now spreading in Asia, and not so much yellow fever, because after all we have a highly effective vaccine against the latter. The validity of this was dramatically confirmed three years ago by the extensive dengue epidemic, fortunately not of the haemorrhagic type, which involved up to 70 per cent. of the population in many islands. The epidemic was predicted because the ecological situation was known, but nothing was done and the penalty was paid, although happily it was not as grave as it might have been.

These changed concepts and increased complexities require the development of new theoretical and analytical approaches. We can no longer be content with the solution of simple situations such as one agent of known infectivity, incubation period, etc., in a population of known density and immune status. Mathematical models, which involve the translation of real world problems into symbols and numbers, already exist which enable us to predict, within reasonable limits, the outcome of the introduction of an agent into such a situation.

The new concepts demand the formulation of models many times more complex and require both highly sophisticated mathematical treatment and advanced computer technology. Complex data of this kind cannot be handled in any other way, and formulation of new models demands the aid of mathematicians and computer scientists. The epidemiologist has to provide the factual data on which these models can be based, derived from a wide variety of contrasting situations. It is an axiom

that what you get out of a computer depends on what you put into it, and it is the epidemiologist's job to ensure that what goes in is valid. This is very difficult, especially when cross-cultural studies are needed. The social and behavioural factors, which are now known to be qualitatively so important in the causation of many diseases, are exceedingly difficult to quantify. Furthermore, quantification may require different weighting factors according to race and culture. This will be a major concern of the proposed Division.

By way of illustration, I would like to turn now to just two of the broad areas of research proposed.

The first, and I believe by far the most important area, is an attempt to learn how the social and environmental changes involved in socio-economic development affect health. The objective is to identify specifically those factors which seem to be of greatest importance, and eventually to introduce experimentally modifications of these in order to determine whether we can influence favourably what appear at present to be inevitable sequences. This has to be studied in a specific context.

One of the greatest, if not the greatest, problem facing the world today is the population explosion. WHO's activities in this field have until recently been restricted for reasons of which you are all aware. However, there is an aspect of this problem which seems entirely within WHO's responsibility and which - as a model - may contribute important information towards a better understanding of the over-all problem. It has therefore been selected as the most appropriate context for the studies proposed. I refer to the acute, local form of population explosion resulting from the phenomenon of rural-urban migration which is occurring in most developing countries and even in many developed countries. Well-designed comparative epidemiological studies of this acute phenomenon in different cultural situations would provide information on the influence of crowding, diet, housing, education, "stress", etc., on fertility and fecundity and on the changing disease patterns, including diseases such as coronary heart disease, in the migrants in comparison with those in the areas from which they came, and in the cities to which they come. Because the phenomenon is occurring so rapidly, results could be expected far more quickly than by studying the long-term effects of over-all population growth.

Comparative international studies in different cultural situations are necessary because the relative influence of different factors will surely vary from culture to culture and between different socio-economic groups within cultures, as in the example of coronary heart disease cited above.

A few studies of this kind are already in progress. However, as was emphasized at the meeting of the International Epidemiological Association last year, comparability between studies in different countries has not yet been achieved. Without it they are just isolated studies which cannot validly be compared with others, nor can the results be extrapolated to other circumstances, which is essential if progress is to be made in the understanding of these phenomena.

The second area of research which I would mention, involves the long-term development of ecological maps of the world, including the distribution of infectious agents, vectors, reservoirs and ecological conditions. I would emphasize that this is a long-term objective, but one which would lead to major advances in predictive epidemiology and communicable disease surveillance. The research functions of the Division would be primarily concerned with methodology and technology. As practical measures were devised these would be transferred to the appropriate division of WHO, the central analysis and dissemination of data being undertaken by the communications unit.

There are, of course, many other ways in which the proposed Division would contribute to the effectiveness of both the research and service activities of many existing sections of the Organization. Also, many of their current programmes will have to be brought into the programme of the Research Division, especially those involving reference centres. I can speak personally on this point since two such centres are located in my department at Yale - the International Arbovirus Reference Centre, formerly the Central Virus Laboratory of the Rockefeller Foundation and now renamed the Yale Arbovirus Research Unit, and the WHO Serum Reference Bank for the Americas. These and other centres must play a major role in the Research Division's field activities, and speaking for my Department, we are anxious to do so.

As mentioned in the middle of paragraph 5.6 (page 13) of document EB37/11, the field studies will require a new system of Regional Epidemiological Centres. There are a few institutes or universities which either meet or can soon be developed to meet the requirements for excellence that this research programme demands.

A substantial part of the budget for consultants will be devoted to bringing together directors of these and other laboratories for the detailed design of the research programmes to which they can contribute so much, but which they could not undertake effectively without central co-ordination, support and facilities for analysis. They will be equal partners in this enterprise.

Consultants will also be needed in a number of important fields in which full-time advice is not necessary. By way of illustration, I mentioned the taxonomy and classification of animal reservoirs and of flora, and biometeorology - that is, the study of biologically important meteorological factors. The WMO is interested in the latter, and will be invited to assist in the programme. External guidance will also be needed on the very complex problems of the quantification of social and behavioural factors under the leadership of the behavioural scientists proposed for the Division.

In this presentation, I have not minimized the difficulty of the problems to be faced. These are great indeed, but not, I am confident, insurmountable. If we succeed - and there can never be a guarantee of success in any form of research (if there is, it is not research) - the dividends for world health should prove enormous. In my opinion the programme outlined in document EB37/11 represents a most important development for WHO, which will help developed countries in their understanding of changing disease patterns and will eventually enable developing countries to avoid or reduce some of the undesirable health consequences associated with socio-economic development, which at present appear inevitable.

ATTACHMENT 3

by

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The Director-General has already presented to you some of the reasons for including research in the applications of communications science together with epidemiology in a new Division within WHO. A fuller justification may be found in EB37/11 "Extension of WHO Activities in Research" and in the reports of meetings of scientific advisers on work in communications science prepared for the 35th meeting of the Executive Board, EB35/13.

I should also like to call your attention to the proceedings of a conference held by the Medical Research Council of the United Kingdom in association with the Health Departments, in Oxford, July 1964, entitled "Mathematics and Computer Science in Biology and Medicine". This report has a foreword written by Sir Harold Himsworth and by Sir George Godber.

I quote first from Sir Harold:

"At first sight an attempt to promote a rapprochement between mathematicians and computologists on the one hand the medical men and biologists on the other may seem something of an innovation: traditionally they are apt to be thought of as belonging to different, almost incompatible, philosophies. Nothing, in my opinion, could be more mistaken. Throughout their history medicine and biology have operated in the context of number. Both take their start in observation of patterns, and the basis of any pattern is association."

He goes on to say:

"G. K. Chesterton once defined heaven as 'like the present only more so'. There are some who see in a new technique simply the possibility of doing the same as before, 'only more so'. That is a more quantitative advance. But this is a very short-sighted view, not borne out by the history of science. There are techniques which have introduced a new dimension of feasibility into human thought; their significance is far more than quantitative, for they have extended the range of what it is possible to contemplate - and have liberated the mind for new qualities of activity. . .

"Medical biologists, mathematicians, physicists and computologists may have more of their outlook in common than we suspect. But they do speak different dialects and they do have different points

of view. This is no new problem for a multidisciplinary subject like medical research. If it is to be solved and the evident necessity for co-operation realized, one thing is essential: we must learn each other's language and understand each other's point of view. The biologists and medical men have much to learn from the mathematicians and the computer scientists; but equally the latter have much to learn from medical and biological workers. Neither is in a position to presume what is good for the other."

Sir George Godber in his foreword touches on yet another aspect:

"In November 1963 a small group, including a consultant physician from the Department of Clinical Measurement of one of the teaching hospitals and a representative of the Medical Research Council, made a visit to the United States to obtain first-hand knowledge of developments there and to gain some insight into the future potentialities of computer techniques. It is significant that after its return the group specially emphasized the value and importance of the interdisciplinary contacts that were an outstanding feature of those centres which were making real progress. The group noticed that computer science and its applications were very much the province of the young. Many studies and investigations which only a few years ago we could not have contemplated are now a practical proposition, and we must adjust our mental processes as well as we can to take account of this new situation; clearly those of younger years have a certain advantage in this respect."

Thus four points are being made:

- 1) that medicine and biology are concerned with the observation of patterns which can be made precise only with mathematics;
- 2) that computers and computer science can open up an entirely new way of studying health problems;
- 3) that this is primarily a young man's game which breaks away from the traditional philosophies of health research;
- 4) finally, that there is a language barrier between the communications scientists on the one side and the physicians, biologists and health administrators on the other; a barrier which must be breached if these new techniques are to work for the betterment of the health of people.

I feel that I can best serve this meeting by helping to overcome this language barrier insofar as I can.

First of all let me explain what we mean by communications science. Historically, communications science began with the study of the ways in which electrical signals are transmitted from place to place, the telegraph, radio and television, but an electrocardiogram is also an electrical signal. It can be measured by the medical scientist. It, too, carries information from the patient's heart to the measuring instrument. However, the information it carries must be studied by methods of both communications science and cardiovascular physiology.

The senses of organisms send electrical signals to the brain, and electrical signals communicate from the brain to the muscles. Here, too, the methods of communications science are essential but they must be applied in conjunction with neurophysiology and neuroanatomy.

As communications science developed it gradually became clear that the same methods could be applied to phenomena that were not necessarily electrical. Now we know that the transmission of information in whatever physical form it may be, in the form of numbers, in statistical tables, in books, in speech, can be studied by similar methods. However, there is a very serious difficulty; the things we wish to study are very complicated - so that even if the methods were available, human life is too short to apply them. Fortunately, computer technology developed at the same time and it is this development that has made a realistic attack on these problems possible.

Thus it is that the principal ingredients in communications science are applied mathematics and computer methods. I would like to illustrate with some examples of what the Division of Epidemiology and Communications Science would be concerned with.

In paragraph 2.1 of EB37/11, reference is made to "mathematical models". The applied mathematician uses this term to cover his process of thought when he tries to translate some of the properties of real world problems into symbols and numbers. Thus, a model of the relation between insect vector, parasite and human population may be very useful in health planning. In order to make a realistic model one would need to know a great number of biological, medical and sociological facts. What is the life cycle of the parasite, of the mosquito? How many times does a mosquito feed? Which members of the human population are susceptible? If they are infected, what is the likelihood that they will pass the infective agent on to the next mosquito which bites?

These and many other such questions can be written in the mathematics of probability theory. They are interconnected in the mathematical model and the model will have certain consequences. First of all it will point out what new facts must be collected in order to improve prediction: perhaps information on population density, prevailing winds, or the likely number of parasites to be found in an infected mosquito. If the model is a good one it may be able to predict the consequences of certain health actions: for example, what effect will follow from certain strategies of insect eradication.

A realistic model for such an epidemiological problem is very intricate but the power of such models may be illustrated by a simpler example. Some years ago it was discovered that the males of certain insects can be attracted by a tone and captured. Then, of course, they can be killed. However, it was observed that they could be sterilized by radiation without killing them. A model was made including such features as the efficiency of capture, the density of the female insect population, the distance such an insect

would travel in order to mate, etc. Of course, the key fact was that a dead male is out of the picture but a live, sterile one will compete with the uncaptured fertile males for the favours of the female. She doesn't know the difference and the result is a smaller number of fertilized eggs for the next generation. The model showed quantitatively that the sterilization treatment is vastly more efficient than killing the males, so much so, that it pays to raise large populations of the insect in the laboratory so as to increase the sterile male populations even more.

Another topic of study for the Division would be operations research. Operations research, in the fifteen to twenty years of its existence as a mathematical technique, has caused major changes in the military and industrial planning of the developed countries. Yet it may be equally valuable for the developing countries because its goal is to find the most beneficial way to apply limited resources of men and money. It begins with the notion that resources are limited, there is so much money available, there is a certain number of specialists and workers of various kinds, only a certain number of new personnel can be recruited and training them takes some specific length of time. Further, there is only a fixed amount of equipment and raw materials. Secondly, operations research requires that the relative loss of different procedures be estimated. For example, an untreated case of malnutrition may represent a greater loss to a country than an untreated case of malaria. Or to put it more constructively, treating disease A will carry more benefits than treating disease B. A crucial part of the analysis will be to calculate the relative economic cost for the same amount of health benefit when there are alternative plans to be considered. A specific example might be the following. In some locality it may be important to

the health administration to carry on a campaign against tuberculosis. The alternatives may be to immunize wholesale with BCG or to find, isolate and treat tuberculosis carriers. The operations research specialist would include in his analysis such questions as the cost per inoculation, the cost of finding the carriers (it will cost very much more to find, let us say, 90% of the carriers as opposed to 75%; the last few percentage points may involve astronomical costs); he will use estimates of the needed manpower and the training required, the length of time teams would need to cover the district, etc. Depending on the specific facts which exist in a particular district or country, the operations research analysis would predict the costs and time schedules of the alternatives and their likely health effects.

I should make clear that obviously in any health problem there are factors which are not easy or even possible to put into such a mathematical picture, and the health administrator will need to weigh these factors. Still, operations research may provide a firm base of quantitative analysis for many aspects of the ultimate plan of attack.

Another activity of the Division is concerned with analyzing the very large volumes of data which are needed for health research. Here a computer is an essential tool, but the existence of the computer is by no means enough. If the results are to be useful, a good deal of effort and thought must first be made by people. To illustrate from my own experience. I have been collaborating with scientists in preventive medicine at the Harvard Medical School on a study of the quality of medical care in cases of pelvic surgery. The data are 10 000 hospital records of surgery. The computer needs only a fraction of a second per case to provide us with the analysis, but prior to its use, a number of gynaecologists, epidemiologists, two

programmers and myself spent about three years in preparing the study - in standardizing nomenclature and criteria, in settling on the logical structure of the correct diagnosis, in deciding on the factors which would tell us something about the quality of the surgeon's performance, and in programming the computer in an efficient way. (I might comment that our first programmer is now a Professor of Electrical Engineering in the University of California at Berkeley. He is now about 27. So you see Sir Harold was right when he referred to the youth of the computer scientists.)

One further word should be said about computers. We can distinguish two kinds of uses: the numerical on the one hand, and the symbolic or logical on the other. Communications science has demonstrated its value to biology and medicine most strikingly in the first use.

Statistical studies are a typical numerical use of computers and of course they play a very important role in health science and planning. Another example can be found in biochemistry. In recent years the molecular biologists have been able to describe in detail the structure of certain proteins, particularly myoglobin. They used for this work what are called the scatter distributions of X-ray crystallography. For the interpretation of these diagrams they needed the help of specialists in a branch of mathematics called Fourier analysis to develop new methods. Nevertheless, even with the mathematical methods all worked out, the task of computing the structure would have been utterly hopeless if they had not used the largest and fastest computing machines they could find.

While the computer's ability to manipulate numbers is clearly important, it is its other capability which has captured the imagination of health scientists who are trying to deal with non-numerical information.

I would like to quote once more from the remarks of Sir Harold Himsworth. He states:

"The systematic study of medicine and biology are built on the validation of probability in associations. The ability to identify associations - whether in patterns or as cause and effect - depends on the ability to recall experience, one's own or that of others. And it is here that we are entering a new era of feasibility."

The process of medical diagnosis is a logical one and the computer is ideally suited to follow out logical operations even when they are of great complexity. The study of the quality of medical care which I mentioned earlier depends mainly on this capability of computers.

Looking for some information in a library is another logical process which some scientists do quite well but at great expense of time. In EB37/11 we have referred to this process as "content analysis of written documents". The techniques are quite complicated but the basic idea is fairly simple. Every scientist or administrator continually needs to look for certain information, certain facts that are to be found in written documents. The information specialist tries to organize and arrange the material in such a way that the relevant facts can be found efficiently and rapidly. A computer can look words up in indexes, can find entries in tables, can ask, for example: "Is there a paper dealing with the relation of diabetes to level of nutrition? If so, has it been referred to in recent studies of diabetes screening programmes?"

Much work is being done on this subject in developed countries, principally the United States and the Soviet Union. Some results can be applied to WHO's problem but much more research is required to adapt these techniques to global health information.

To sum up, the communications science specialist has skills which until now have not been represented in WHO. He can be useful to world health problems when he develops or adapts his tools to the needs of the health problems.