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A SIMULATION MODEL OF CASE FINDING AND TREATMENT IN TUBERCULOSIS CONTROL PROGRAMMES

by

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1. INTRODUCTION

The central role of operations research methods in planning methodology has often been stressed (WHO Fourth Report of the Expert Committee on Public Health Services, 1961; Report of a WHO Study Group on Integration of Mass Campaigns against Specific Diseases into General Health Services, 1965). A plea for the development of models in the field of public health has been made by Andersen (1964). In the field of tuberculosis several documents have referred to this approach.

Regarding the role of models, one may distinguish between decision models and simulation models. While the former are designed to assist the decision process so as to optimize some function under constrained conditions, the latter, less ambitious in scope, merely aim at describing a system or process in a quantifiable way. Such for instance are models of Waaler (1962), Brøgger (1965), that describe the dynamics of the tuberculosis epidemiology.

The present document is an attempt to describe the operation of a service for the diagnosis and treatment of tuberculosis in an unsophisticated mathematical form. This model was implicit in earlier documents issued in this Series, such as WHO/TB/Techn.Information/17. In its present form some factors have been made more explicit. The release of this document by the Tuberculosis Unit of WHO is meant to stimulate more formal rethinking of tuberculosis control in its ecological context, to help formulate more clearly concepts in assessment of health and in particular tuberculosis programmes, to provoke creative criticism from the public health administrator, the medical sociologist, the biometrician, the computer programmer. It is hoped tuberculosis specialists will also contribute theirs.

2. ANALYSIS OF THE SYSTEM: DIAGNOSIS AND TREATMENT OF SELF-REPORTING CASES

Curative services may be considered from the angle of logistics i.e., the series of "operations" leading from the whole population to a selected group, viz, the cured patients. The operational efficiency of the service can then be expressed in terms of the outputs of work, and of the probabilities of coverage achieved by each successive "operation". In other words: an individual may be a "case" of tuberculosis or not. He may - or may not - live in a zone where health services operate effectively. He may - or may not - seek medical advice if urged by chest symptoms. His disease may be efficiencly diagnosed - or not. He may be successfully treated - or not. What are the chances that a case of tuberculosis, in a given situation will proceed right up to the end of the line, where he may be considered to have been successfully treated? This approach involves an analysis of that situation and the formulation of a simplified model to represent it wherein a series of interlocked subsystems are expressed quantatively by a limited number of epidemiological, sociological, administrative, operational and technical parameters. The object of this systems analysis is to determine which of the parameters can be expected to exert the greatest influence over the total efficiency of the system in a given situation, so as to guide the planning and implementation of the services (investment of resources), and to serve as a forecast of efficiency against which the observed performance in the course of implementation will later be measured. See Appendix I.

Each subsystem and its parameters are now introduced in detail.

Caseload:

The basic epidemiological parameters that are relevant to the present systems analysis are the clinical, bacteriological or radiological evidence of tuberculosis in individuals, and the probability with which such evidence would be observed under ideal conditions in an individual at a point of time. A description of the curative services depends therefore essentially on the basic definition of the word "case". From the epidemiological standpoint, persons excreting tubercle bacilli transmit infection. Let these persons be termed "cases of tuberculosis". By what criteria can one identify them?

The analysis of the material collected in WHO-assisted tuberculosis surveys provides an indirect answer to this question. In a study reported by Roelsgaard (1964) various definitions of a "case of tuberculosis" have been assessed in terms of the probability of transmission - as estimated by the prevalence of infection among young household contacts of the "case". It was found that when:

(a) persons excreting tubercle bacilli in a single sputum specimen, and

(b) persons who, in the absence of bacilli in the first sputum specimen, present a positive tuberculin test and one or more cavities on X-ray,

are defined as "cases", and only so, the risk of infection among children contacts is significantly (actually three to five times) higher than among children presumably without any such household contact.

These persons may therefore be considered as genuine cases of tuberculosis for the purpose of this paper and not much would be gained by adopting a more liberal definition. It is therefore proposed to retain the above epidemiological definition as the basis for the following analysis.

If we note α_i for the "state of health", α_1 may denote the presence of bacilli in the first sputum specimen and α_2 the presence of a cavity and of tuberculin positivity, but without bacilli. We can express that the probability of an individual being a "case of tuberculosis" $Pr_{(TB)} = Pr\alpha_1 + Pr\alpha_2$. At any point of time the sum of individuals with one and/or the other findings constitutes the caseload. The rest of the community consisting of individuals without bacilli or cavities are presumed to be non-tuberculous. They are referred to in the following as the "community" or the "public". Let α_3 denote their state of health.

Note:

It is often said that a more advanced epidemiological model is the key to tuberculosis control. This may be true when most operational factors have been controlled, such as in economically advanced countries. In most developing countries, however, neither the detailed age/sex incidence, nor the tuberculin status, nor the geographical distribution of the caseload, if known, would give clues to economically effective substitutes for the coverage of the whole community, especially over long periods of time. However nothing prevents in principle, the inclusion of more epidemiological classes such as "non-bacillary-non-cavitary infiltrates in tuberculin positive subjects" etc. The development of the model would not be basically affected.

Health Coverage

The second subsystem expresses the chances that any individual in the community, or any case, will receive preventive and curative health services. These parameters, it is assumed, would in turn determine the proportion of the tuberculosis case-load that an integrated tuberculosis programme might reach (Refer to maps, and definitions, Appendix II).

The role of the health institutions and their contribution to the coverage of the total population may be briefly reviewed in the context of a national tuberculosis programme. While the ultimate aim is to deal with the entire caseload in the "zone of responsibility", it is assumed that the antituberculosis work of these institutions may be limited, at first, and will be most effective thereafter in communities within the "zone of comprehensive services", for the following reasons: the "zone of curative services" demarcates the potential case-finding area of the national tuberculosis programme (the vertically shaded areas of Map b). In that zone, because of the usual flow of patients, information that an antituberculosis service is available is all that is required to attract symptom-motivated patients of tuberculosis. On the other hand, the supply of drugs near the patients' residence and the organization of a domiciliary service to retrieve treatment defaulters constitute the essential other steps required to extend effective tuberculosis services; the capacity of a health institution to do so may often be the limiting factor in integrated tuberculosis control. This is interpreted to mean that the potential treatment area of a tuberculosis service is limited to those communities regularly visited by health workers - in other words, to what has been termed the "zone of preventive services" - (horizontally hatched in Map c). In these terms, the "zone of comprehensive services" is presumably one where a tuberculosis case has the best chance of being diagnosed, and where, once diagnosed, he would also be treated (see Map d).

If we note β_j for health coverage, let β_1 be the probability that an individual lives in the zone of curative services, let β_2 be the probability that he lives in the zone of preventive health services, while β_4 denotes the fact of not being covered by any health service. In these terms, the probability that an individual lives in a zone of comprehensive service is: $Pr(\beta_3)$.

Note

It is assumed in the model that these probabilities are independent, at least initially, from that of being a case of tuberculosis. As services develop, however, then probabilities may become interdependent, with a negative correlation between them, presumably as an influence of the effectiveness of services on the risk of tuberculosis.

Participation of patients in the tuberculosis programme

The third subsystem discusses the current demand ("felt need") of the public in general for adequate diagnostic and curative services for chest complaints, and of the caseload in particular for a tuberculosis programme. Demand may be defined here as the probability that an individual in a community will spontaneously seek medical advice on account of chest symptoms. The actual participation of the public and of patients may be used as convenient estimators of demand. It varies considerably with the type of patient and with the quantity and quality of services available. To analyse participation quantitatively, two sociological parameters are introduced: awareness of symptoms suggestive of chest diseases ("awareness"), and the amount of initiative displayed by persons with such symptoms in having their disease diagnosed and treated medically ("motivation").

Awareness of chest symptoms is a subjective expression of: the amount and variety of chest diseases in a given community; the capacity of these locally prevalent diseases to produce ordinary chest symptoms; the relative importance attached by the given community to these symptoms (and/or to the diseases, if recognized as clinical entities, that produce them); and finally the influence of all these socio-medical factors on the individuals' perception of symptoms that may be induced by any one of these diseases. Depending on whether one considers the community, or the caseload, one may distinguish awareness in the community and awareness in the tuberculosis cases, which presumably only differ in degree. Let $Pr(A/\alpha_i)$ be the probability that an individual in the community is aware of chest symptoms.

Note

Awareness may be influenced by the availability of services, and so one might distinguish different probabilities in different zones. For the purpose of the present paper however one single probability will be taken into account, i.e., independent from the availability of service.

Motivation reflects the critical amount of suffering that is required, against a given cultural background, to produce anxiety in the individuals concerned, a wish to secure relief, and a decision to seek medical advice. One could distinguish between motivation in non-tuberculous persons complaining of chest symptoms and motivation in patients with genuine tuberculosis. Probably more than that, motivation depends on the adequacy of the available services in satisfying the felt need of a group, and the group's confidence in these services (Banerji & Andersen, 1963). The frequency of proper diagnosis and treatment (the criterion of adequacy as seen by the public) is therefore reflected in the motivation of the patients. If motivation is strongly induced by the availability of good services, one may distinguish various levels or probabilities of motivation in the different zones of health coverage. Let this be noted $pr(M/\beta_j)$. In accordance with what was said earlier about the relevance of various services, one may expect that $pr(M/\beta_3) > pr(M/\beta_1) > pr(M/\beta_2) > pr(M/\beta_4)$ the latter being actually = 0.

The probability that an individual in the community will participate in a tuberculosis programme is the product of the probability of his/her being aware of chest symptoms: multiplied by the conditional probability that he/she is motivated by them to seek advice. If we note provisionally P for participation: $pr(P/\gamma_{ij}) = pr(A/\alpha_i)\ pr(M/\beta_j)$.

The expression (α i) pr(P/γ_{1j}) is relevant to estimating the <u>expected workload</u> imposed by the community on the health services on account of various chest disorders (including tuberculosis). On the other hand, the expected participation of a case of tuberculosis in a case-finding programme based on self-reporting is expressed as: (pr(α_1) pr(P/γ_{1j}) + pr(α_2) pr(P/γ_{2j}). This expression is relevant to estimating the <u>potential case yield</u> that could be expected when the health services are geared to deal adequately with self-reporting chest patients.

Note

For the purpose of the following, therefore, a tuberculous patient is understood to mean "a person reporting spontaneously to some health agency on the basis of his/her symptoms, and in whom tubercle bacilli are demonstrable by direct microscopy or culture, or in whom, in the absence of tubercle bacilli in the sputum on the first examination, X-rays will demonstrate the presence of one or more cavities". The number of persons fitting this definition is obviously less than the caseload, but all are genuine cases. As services demonstrate their capacity to deal adequately with <u>all</u> such patients, the definition may conceivably be extended to cover non-symptomatic disease as well, if this is epidemiologically required; but if the above basic definition is applied in practice, this will usually absorb the available resources of a developing country. Nothing would prevent one from considering later, at least theoretically, the unaware group, i.e. individuals as eligible for some kind of case-finding and treatment programme in addition to that geared to symptom motivated, self-reporting patients.

Case-finding efficiency

This analysis has now reached the point where an individual presenting chest symptoms, reports to health institutions for diagnosis and treatment. In this fourth subsystem, an analysis will now be made of the case-finding operations undertaken by these institutions, with a view to expressing the quantitative efficiency of the examination policy, and the qualitative efficacy and reliability of the diagnostic techniques involved. This case-finding subsystem consists therefore of three parameters expressing the probability 1) that an individual presenting himself for investigation will be dealt with according to a stated examination policy, 2) that if he has evidence of tuberculosis, it will be diagnosed as such, and 3) that this diagnosis will be confirmed if assessed independently. This analysis may then be summarized in the form of a suitable index.

Examination policy: Different diagnostic techniques (clinical, bacteriological, radiological) may be applied, separately or combined in various sequences, in one or more institutions. This results in a variety of examination policies.

A policy consists of a well-defined sequence of examinations, E_k, each successive examination being defined in terms of the technique k ($k = 1,2,3,\ldots,p$) that is applied; let for instance: examination of all by tuberculin test be (E_1), radiological examination of tuberculin positive be (E_2) sputum culture for all X-ray "positive" be (E_3). This constitutes one policy. Within a policy (all examinations being freely available to all), the probability that any individual in the public avails himself of examination by the kth technique can be expressed as $Pr\ (E_k/\gamma_{ij})$. This probability is not necessarily uniform for all examinations within a policy, even if these are performed independently, all on the same day and in the same place. To completely specify a policy of examination, the statement must therefore include an indication of who is eligible for examination E_k. This may be: all, none, all positive at previous examination, or all negative at previous examination, for example. We introduce a parameter ε_{ijk} which may take any value between 0 and 1 and expresses the probability that an individual in the ith state of health and in the jth zone of health services will be eligible for examination by the kth technique.

Diagnostic efficacy: Within a policy, a genuine case of tuberculosis would have a prior probability of diagnosis by a given technique More generally a person in the ith state of health has a prior probability of being diagnosed as such by the kth examination technique $Pr\ (D_k/\alpha_i)$. The table attached as Appendix III gives an estimate of this probability for various i and ks. The relative efficacy of the diagnostic techniques has been discussed elsewhere (Mahler & Piot 1966) in terms of the probability of positive, negative, false positive and false negative results, given the state of nature. On the epidemiological evidence collected in WHO surveys, where these techniques were used independently, it is possible to estimate the marginal yield in terms of positive findings of any technique associated in a defined sequence and relationship with any other(s).

Diagnostic reliability: The techniques involved in diagnosis may fail in two directions: over- and under-diagnosis. While, for assessment purposes, both are equally significant in the context of the present analysis, over-diagnosis is the only relevant of the two in that any person declared a "case" would be eligible for treatment, while a "false negative" may be retrieved at a later examination. Over-diagnosis occurs by over-reading of a smear or of an X-ray film; independent reading of smears or films achieves an objective assessment, in that no reader is presumed right while another is wrong: it merely states cases in which agreement is reached (and not reached). The reliability of the diagnosis by the kth technique may be expressed as $pr(R_k)$, i.e., the probability that a person thus examined and diagnosed as "positive" will be so classified by an independent assessor also.

If we note δ_{ijk} for reliable diagnosis, i.e. where $pr(\delta_{ijk}) = pr(Ek/\varepsilon_{ij})\ pr(Dik/_{Ek})\ pr(Rik/_{Dik})$, the efficiency of case finding can then be expressed as:

$$pr(\varepsilon_{ijk}/\gamma_{ij})\ pr(\delta_{ijk}/\varepsilon_{ijk})$$

Note I:

It is assumed implicitly that case-finding efficiency is independent from the true frequency of cases among the consulting patients. This assumption may not be entirely correct in that the marginal yield of any examination may be decreasing for a variety of causes. Yet, as estimates would be regularly revised in the light of experience, the error involved in the initial assumption would be corrected in time.

Note II:

Different (and presumably higher) values of pr (Ek) may be expected in the zone of comprehensive services from that observed outside it, i.e. among the more strongly motivated tuberculous patients. Analysis of data from national tuberculosis programmes strongly suggests this fact (O'Rourke 1964). In practice this is taken care of by introducing the parameter γ_{ij} into the conditional probability

Treatment efficiency:

The fifth and last subsystem analyses the efficiency of treatment. Efficiency there, can be defined as the probability that a case starting a prescribed course of treatment will be successfully rendered quiescent at the end of it. This probability may be seen as depending on two parameters: the management of the patient and the efficacy of the regimen.

Management of the patient: Extensive clinical data, (Fox 1964)have shown that, in the average patient completing one year of regular treatment with a suitable standard chemotherapy regimen, there is high probability of lasting quiescence. This one-year rule has thus become a standard in the management of the patient in the chemotherapy of tuberculosis. If this rule is the policy, the degree of compliance with it may be estimated and expressed in terms of the probability that one patient will complete one year's treatment with the required number of drug collections. Let $pr_{(T)}$ be such a probability. This probability depends on all administrative measures, educational guidance, statistical intelligence, etc., available to ensure continuity of drug intake among the patients under one's care. In ambulatory chemotherapy, two such measures may be to control the regularity of drug collections by means of an appointment system, and to retrieve defaulters by home visits. Others include domiciliary supervision of drug administration, pill counts, urine testing, and the organization of follow-up examinations for the sake of public relations. The probability of one patient taking the correct amount of drugs is affected, in other words, by his place of residence in relation to health services, i.e. by β_j. On the other hand the probability may also be construed as affected by the patient's own assessment of his condition, i.e. in terms of α_i. If one considers in addition that the choice of a suitable regimen would depend upon the type of lesion diagnosed by technique k and on the availability of services to deliver it (nurses for inspection, house visitors etc) one may conviently define T in terms of jk (jk = 11,..,..,., mn). Pr (Tjk/δ_{ijk}) is the notation for the probability that a person in the ith state of health diagnosed by the kth technique and residing in the jth zone of health services completes one full year's course of treatment with regimen jk.

Examples of regimens jk and of the way in which pr(Tjk) can be estimated are given in Appendix

Efficacy of the regimen: The intrinsic value of a chemotherapeutic regimen is conveniently defined as the probability that a correctly treated case will achieve, under experimental conditions, quiescence at the end of one year's treatment. In WHO programmes, the results from the Madras Chemotherapy Centre are taken as standard of the quality of a regimen. Let $pr(Qijk/_{Tjk})$ be the probability that a patient treated with a full course of regimen jk will achieve quiescence at one year. Since it is assumed in this model that unconfirmed cavity cases are epidemiologically equivalent to bacteriologically confirmed cases, the same probabilities might apply to both.

The efficiency of treatment for each category of patient is then expressed $pr(\varphi ijk) = pr(Tjk/\gamma_{ijk})\ (Qijk/_{Tjk})$.

Summary of notation

Symbol		Examples	
αi	state of health	$i = 1$	α_1 = bacilli to be found in first sputum specimen by direct miscroscopy
		$i = 2$	α_2 = no bacilli, but a cavity on first chest X-ray film, and a positive tuberculin test
		$i = 3$	α_3 = non tuberculous
A	awareness of chest symptoms		
βj	health coverage	$j = 1$	β_1 = living in zone of curative services
		$j = 2$	β_2 = living in zone of preventive services
		$j = 3$	β_3 = living in zone of comprehensive services
		$j = 4$	β_4 = living in zone not covered by any health service
M	motivation to consult health services		
γij	parameter relevant to participation in case finding : P		

$$pr(\gamma ij) = pr(A/\alpha_i)\ pr(M/\beta_j)$$

Symbol		Examples
E_k	examination by the kth technique of diagnosis	
		k = 1 E_1 = direct microscopy of one sputum specimen
		k = 2 E_2 = X-ray examination
		k = 3 E_3 = tuberculin test
$\mathcal{E}_{ik}$	eligibility for examination by the kth technique	
		k = 1 $pr(\mathcal{E}_1) = 1$ examination to all
		k = 2 $pr(\mathcal{E}_2) = [1 - pr(\delta_{i1})]$ examination to negative on E_1
		k = 3 $pr(\mathcal{E}_3) = [pr(\delta_{i2})]$ examination of positive on E_2
Dik	"positive" diagnosis on examination by the kth technique	
Rk	agreement with independent assessor on "positive" diagnosis by kth technique	
δ_{ik}	examination, positive diagnosis, agreement	

$$pr(\delta_{ik}) = pr(E_k/\mathcal{E}_{ik})\; pr(D_{ik}/E_k)\; pr(R_k/D_{ik})$$

Tjk	one full course of treatment with regimen jk	
		jk = 11 T_{11} = one year's course of INH-SM twice weekly schedule (ambulatory)
		jk = 21 T_{21} = one year's course of INH-PAS daily (ambulatory)
		jk = 31 T_{31} = initial INH-SM twice weekly schedule followed by INH-PAS for rest of year (ambulatory)
		jk = 41 T_{41} = institutional INH-SM daily
		jk = 12, 22, 32, 42 T_{12}, T_{22}, T_{32}, T_{42} = one year's course of INH-TSC daily (ambulatory)
Qijk	state of quiescence at one year after regimen jk given for ith state of health, under clinical trial conditions.	
φ_{ijk}	state of quiescence at one year conditional on one year's course of treatment	

$$pr(\varphi_{ijk}) = pr(T_{jk}/\delta_{ik})\; pr(Q_{ijk}/T_{jk})$$

3. THE MODEL

Seen from the angle of the public, the model depicts the probabilities that an individual in the ith state of health and living in the jth zone in terms of health coverage will seek medical advice on account of symptoms and motivated by the reputation of the services; if so, the probabilities that he will be examined by the kth diagnostic technique and reliably diagnosed; if so, the probabilities that he will pursue the prescribed treatment and that he will be quiescent thereafter. Seen from the angle of the public health administrator the model describes the operation of tuberculosis control programme, in the social context, calculates the expected frequency of consultation on account of chest symptoms, the expected frequencies of various examinations, of positive findings, and ultimately the expected frequency of success. Expected frequencies in the latter approach are of course only summations of the probabilities in the former. To avoid repetitions, only expected frequencies will be reproduced below:

1. Expected frequency of consultations for chest symptoms

$$\sum_{i}^{m} \sum_{j}^{n} pr(\alpha i)\ pr(\beta j)\ pr(\gamma ij)$$

2. Expected frequency of examination by the technique k = k

$$\sum_{i}^{m} \sum_{j}^{n} pr(\alpha i)\ pr(\beta j)\ pr(\gamma ij)\ pr(\varepsilon ik)$$

3. Expected frequency of positive diagnosis by technique k = k

$$\sum_{i}^{m} \sum_{j}^{n} pr(\alpha i)(pr\,\beta j)\ pr(\gamma ij)\ pr(\varepsilon ik)\ pr(\delta ik)$$

4. Expected cumulation frequency of successful treatment

$$\sum_{k=1}^{p} \sum_{i}^{m} \sum_{j}^{n} pr(\alpha i)(pr\,\beta j)(pr\,\gamma ij)(pr\,\varepsilon ik)(pr\,\delta ik)pr(\varphi ijk)$$

Note:

A model, one often hears, is as good as the data that are fed into it. And, it is argued, the parameter estimates for a model such as the one suggested here may not always be available and reliable. So, some conclude, models are just "academic", however "elegant". Another document in this Series has introduced an approach to data collection that is closely relevant to estimating the parameter values of the present model. It is for the responsible health administrators to say whether such data ought to, or need not, be collected. But, as a matter of fact, once a simulation model has been formulated, all possible values of all parameters may be imagined (with,necessarily, the true values among them) and the outcome computed. The object of the simulation, however, is not academic, for two very essential things are made explicit in the process - which experience can only apprehend intuitively - namely the sensitivity of the system to various changes, moderate or large, simultaneous or phased, in one or more parameters, and the elasticities of the relationships between parameters. In public health practice, where one cannot experiment with controls, simulation may help, and models of the type presented here find their justification.

So simple a model, however, can only at present be considered a tool to sort out problems. To make the model more realistic one of the first developments that will probably be required is to further disaggregate the diagnosis and treatment by introducing a fourth dimension, namely the health institutions themselves. In this way the role of the distance for instance may be made explicit, which in the present model is aggregated with many other factors in (βj) and (Ek). An illustration of the application of the model is given in Appendix III.

RESUME

L'auteur présente un modèle du dépistage et du traitement de la tuberculose. Ce modèle met en jeu cinq sous-systèmes dont les paramètres principaux sont: l'état de santé de l'individu α i; le type des services sanitaires desservant la localité où il rèside βj; la présence de symptomes pulmonaires, et la confiance qu'inspirent les services de santé déterminent un paramètre γ ij dont dépend la participation de l'individu au programme de dépistage; étant donné les techniques Ek de diagnostic mises en oeuvre par les services de santé, l'individu est justiciable de divers examens selon un schèma préétabli ε ik; les résultats d'examens ("positivité" à l'un ou plusieurs des examens successifs) peut entraîner comme conséquence soit le traitement, soit des examens ultérieurs, selon qu'une évaluation indépendante confirme ou non le diagnostic (δ ijk). Le traitement φ ijk consiste en l'application de régimes chimiothérapeutiques normalisés, d'efficacité reconnue, qui sont prescrits pour une durée fixe, compte tenu du diagnostic (ik) et des possibilités dont disposent les services sanitaires locaux (j) pour assurer une prise régulière des médicaments.

Le modèle est exprimé en termes de la probabilité qu'un individu a de présenter les diverses caractéristiques épidemiologiques et sociologiques ci-dessus, et celle qu'il a de franchir les diverses étapes qui le conduiront, le cas échéant, vers la guérison. Sommées pour l'ensemble de la population, ces probabilités représentent une mesure de l'efficacité des services engagés dans la lutte antituberculeuse, dans des conditions épidémiologiques et de développement précises; à ce titre le modèle présente un intérêt pour l'administrateur de la santé. L'objet de l'étude rapportée plus haut est la simulation sur l'ordinateur des diverses stratégies de lutte antituberculeuse, afin de mettre en évidence les variables dont l'influence apparaît prépondérante à divers degrés de développement de l'infrastructure sanitaire. Il est suggéré à ce titre que le modèle gagnerait en réalisme s'il incorporait explicitement les institutions sanitaires (hôpitaux, dispensaires, centres de santé etc) plutôt que les types de services qu'elles offrent au public. Le modèle est proposé aux administrateurs, aux sociologues, au biostatisticiens et aux spécialistes en matière de tuberculose comme une base commune de discussion.

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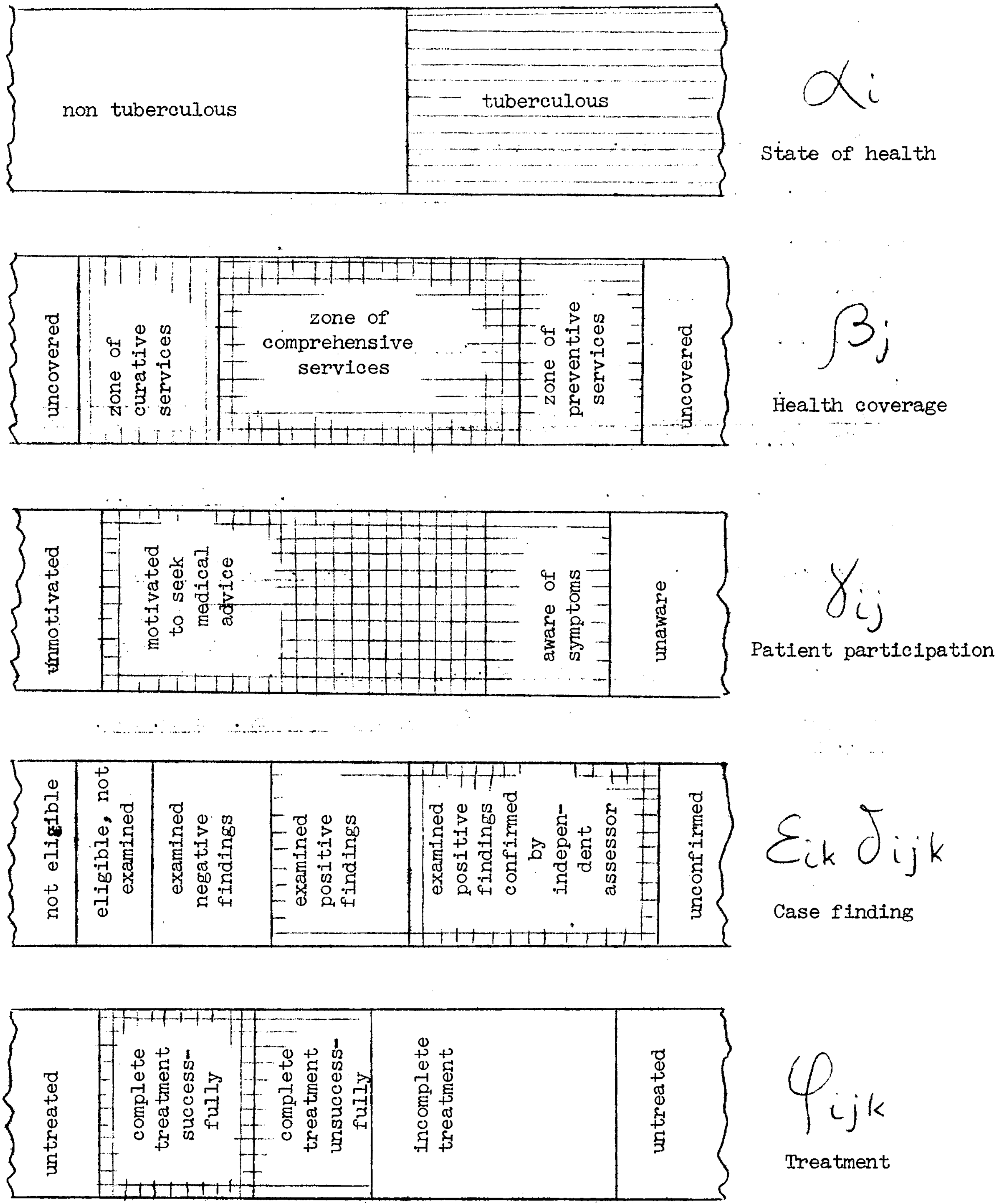
APPENDIX I


non tuberculous
tuberculous
αi
State of health
uncovered
zone of curative services
zone of comprehensive services
zone of preventive services
uncovered
βj
Health coverage
unmotivated
motivated to seek medical advice
aware of symptoms
unaware
γij
Patient participation
not eligible
eligible, not examined
examined negative findings
examined positive findings
examined positive findings confirmed by indepen-dent assessor
unconfirmed
εik δijk
Case finding
untreated
complete treatment success-fully
complete treatment unsuccess-fully
incomplete treatment
untreated
φijk
Treatment

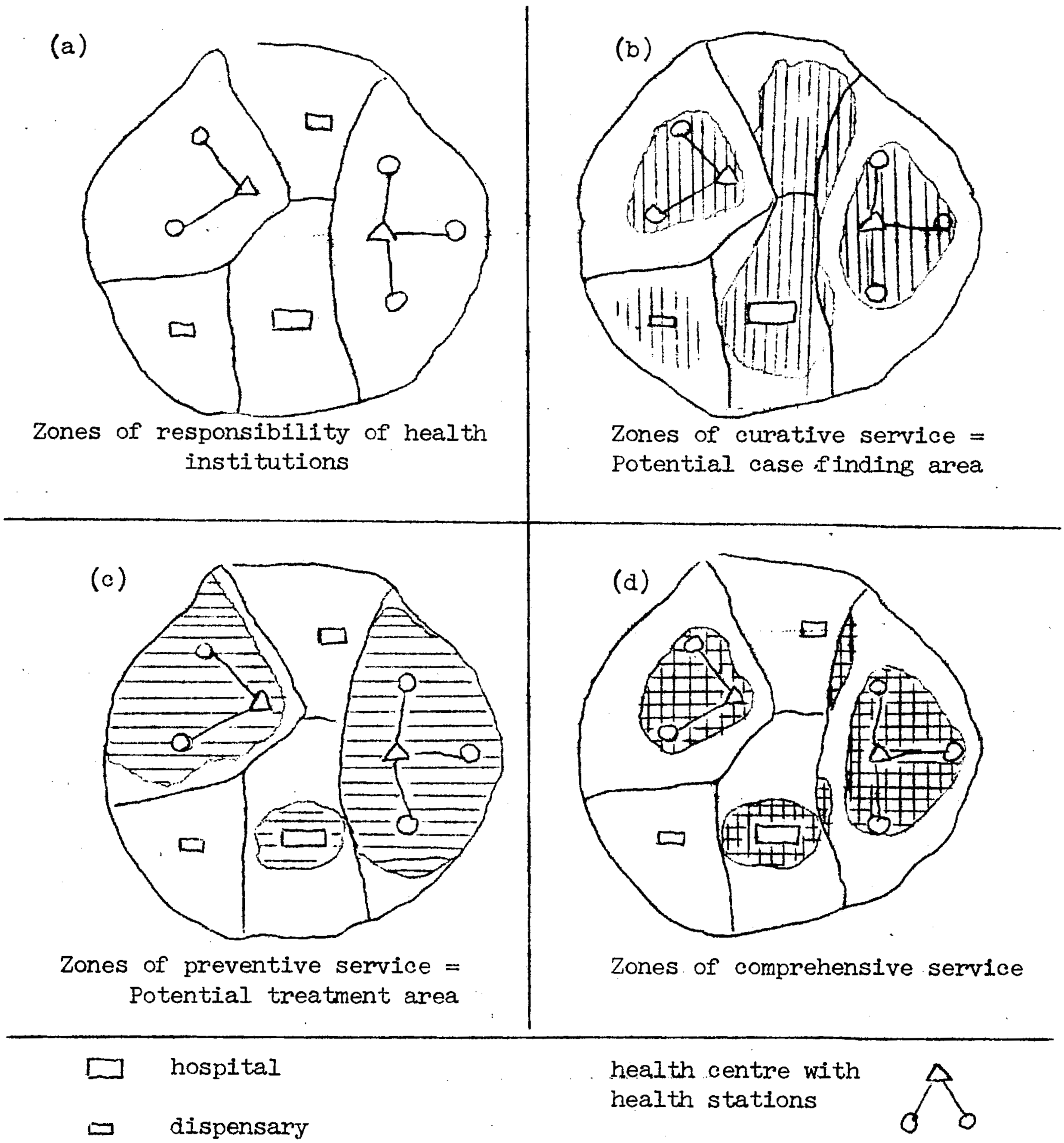
APPFNDIX II

At this juncture it is appropriate to give definitions for some terms that have been adopted in connexion with the activities of health institutions, and, for additional clarity, four diagrams (Appendix II page 2 a,b,c and d) have been drawn to depict the zones in which the various services are provided.

Each health institution is normally responsible for serving a zone which, for convenience, has been called the "zone of responsibility" (a). Most of the patients cared for in this zone live within a relatively short distance of the institution, although a few will certainly be prepared to travel from much farther afield in order to obtain the sort of treatment it provides. Let the "zone of curative service" of the institution be the zone including the towns and villages from which most, say, 80 per cent., of the consulting patients come (b). This zone may be determined with considerable precision if registers of patients are kept. The villages visited at least once a month by one or more members of the field staff of the institution together constitute the "zone of preventive service" (sometimes known as "visiting area") (c). The number of visits paid by the field staff of a health institution to the villages in its zone of responsibility is normally known from the records maintained by the institution.

We have now defined the "zone of responsibility", the "zone of curative service" and the "zone of preventive service" of a health institution. These three zones have been shown in Appendix II page 2 a,b and c by means of different kinds of shading. If the three zones are superimposed on each other, a fourth zone will appear (d) which embraces all the villages visited at least once a month, and from which most of the institution's patients normally come. This has been called the "zone of comprehensive service" of the institution, since the population of this zone may be said to be getting comprehensive health coverage.

APPENDIX II



(a) Zones of responsibility of health institutions

(b) Zones of curative service = Potential case finding area

(c) Zones of preventive service = Potential treatment area

(d) Zones of comprehensive service

hospital

dispensary

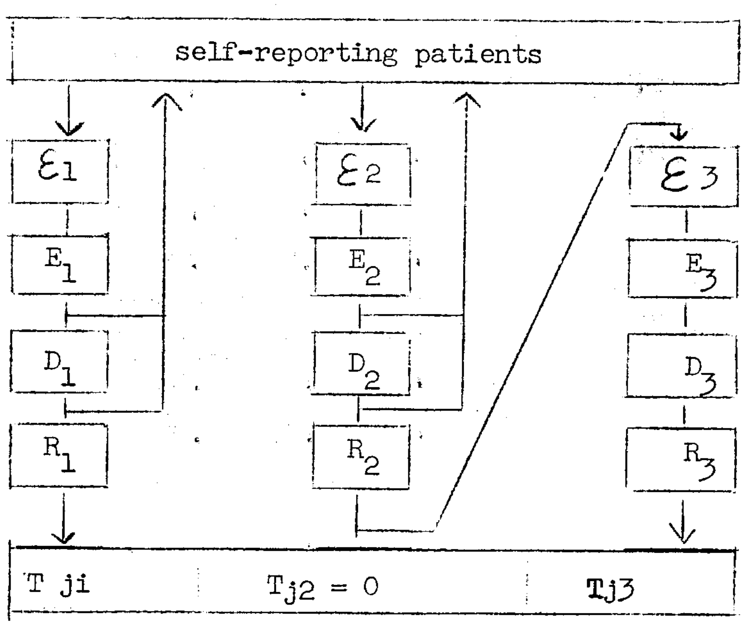
health centre with health stations

APPENDIX III

Example of application

The pattern of case-finding and treatment selected for illustration is as follows:

Case-finding policy: smear to all persons consulting for chest symptoms (k = 1), referral for X-ray of all negative on first smear (k = 2), tuberculin testing of all positive (cavity) on X-ray (k = 3). Treatment policy: bacillary and tuberculous positive cavitary cases are treated ambulatorily if in zones covered by health services, or institutionally, with standard chemotherapeutic regimens (Tij). In the case of ambulatory regimens the choice is guided primarily by the practical possibilities for injections, domiciliary follow-up etc. This may be represented graphically as follows:



The following tables of hypothetical parameter estimates are self explanatory.

APPENDIX III

Hypothetical parameter estimates

i	pr(α i)
i = 1	0.004
i = 2	0.005
i = 3	0.991

A/α i	pr(A/α i)
i = 1	0.9
i = 2	0.7
i = 3	0.056

j	pr(β j)
j = 1	0.19
j = 2	0.20
j = 3	0.34
j = 4	0.27

M/βj	pr(M/βj
j = 1	0.7
j = 2	0.5
j = 3	0.75
j = 4	0.01

pr(γij)=pr(A/αi)pr(M/βj)				
	j=1	2	3	4
i=1	0.63	0.45	0.68	0.009
2	0.49	0.35	0.53	0.007
3	0.039	0.028	0.042	0.0006

	k=	1	2	3
pr(Ek)		1	.7	.85
pr(Dik)	i=1	0.89	0.6	1
	2	0.005	0.85	0.80
	3	0.005	0.03	0.75
pr(Rik)	i=1	0.95	1	1
	2	0.5	0.66	0.98
	3	0.5	0.33	0.98

pr(ε ik)			
	k = 1	2	3
i = 1	1	0	0
2	1	0.94	0.075
3	1	0.94	0.075

pr(δik)=pr(Ek) pr(Dik)pr(Rik)			
	k = 1	2	3
i = 1	0.85	0.60	1.
2	0.0025	0.39	0.67
3	0.0025	0.007	0.63

pr(ε ik) pr(∂ ik)			
	k = 1	2	3
i = 1	.85	0	0
2	0.0025	0.360	0.566
3	0.0025	0.006	0.019

APPENDIX III

Regimen jk

j	= 1	2	3	4
k = 1	INH/TSC daily	INH/SM tw.w	INH/PAS daily	INH/SM/PAS hosp.
2	0	0	0	0
3	INH/TSC daily	INH/SM tw.w	INH/PAS daily	INH/SM/PAS hosp.
p	Nil	Nil	Nil	Nil

Pr(Tjk)

j	= 1	2	3	4
k = 1	.6	.8	.7	.9
2	(.4)	(.7)	(.5)	(.7)
3	.5	.8	.6	.8
p	0	0	0	0

pr Qijk

jk	i = 1	2	3
11 12 13	.80	.90	0
1p	0	0	0
21 22 23	.85	.90	0
2p	0	0	0
31 32 33	.90	.95	0
3p	0	0	0
41 42 43	.95	.95	0
4p	0	0	0

$$pr(\varphi_{ijk}) = pr(Tjk/\delta_{ik})\ pr(Qijk/_{Tjk})$$

jk	= 11	12	13	21	22	23	31	32	33	41	42	43	jp
i = 1	.48	.32	.40	.68	.60	.68	.63	.45	.54	.86	.67	.76	0
2	.54	.36	.45	.72	.63	.72	.67	.48	.57	.86	.67	.76	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0

Example of application: what is the pr(φ131)?

(λ_1)	(β_3)	(γ_{13})	(ε_{11})	(δ_{11})	(φ_{131})	
pr(φ131) = 0.004	x 0.34	x 0.68	x 1.0	x 0.85	x 0.63	= 0.000495

In a population of 1 000 000, 495 bacillary cases would be expected to complete treatment and achieve quiescence in zones of comprehensive coverage of health services.