TESTA

WORLD HEALTH ORGANIZATION

ORGANISATION MONDIALE DE LA SANTÉ

WHO/Mal/67.625

ENGLISH ONLY
(avec résumé en français)

THE DESIGN OF AN EXPERIMENTAL MALARIA ERADICATION PROJECT FOR KANKIYA, NORTHERN NIGERIA

(Preliminary communication)

by

Cecil V. Foll
World Health Organization Field Research Project
Kankiya, Northern Nigeria
George Macdonald
Director of the Ross Institute of Tropical Hygiene and
Professor of Tropical Hygiene in the University of London, England
and
Caton B. Cuellar
Research Assistant
Ross Institute of Tropical Hygiene, London, England

1. Introduction

An outline of the epidemiology of malaria in Kankiya has been set out in a previous paper (Macdonald et al., 1967). A study of this has led to the preliminary conclusion that it might be appropriate to test the effect of periodic mass treatment as an adjuvant to the use of the insecticides which, though they have been shown to have some effect, have failed to interrupt transmission completely. It has been shown how the malaria situation can be analysed and it has been concluded that under the conditions of partial interruption of transmission by insecticides there remains transmission represented by a reproduction rate of 6.0 for five months of the year and greatly reduced transmission represented by a reproduction rate of 1.0 for the remaining seven months. The associated parameters are, a man-biting habit for the mosquito not exceeding 0.5, and a probability of mosquito survival through one day of 0.8. It has been suggested that the previous

inadequate results might be converted into a successful eradication programme by the additional use of mass treatment and the object of the present exercise was to select a regimen which might be appropriate and to examine its potential capacity.

The problem of selecting an appropriate regimen has two principal facets: the type of result which may be expected from any given combination of efficiency and periodicity in treatment, and the ability of the organizer of a programme to achieve any particular standard of either efficiency or of periodicity in administration. There was already experience of the administrative aspect of frequent coverage of the area and the principal question which the operator had to consider concerned the coverage of the total population which he might achieve by mass medication at intervals of one, two or more months. Though there was no previous experience of mass medication, it was his appreciation that total coverage would in any case be impossible owing to the probability that a substantial proportion of the population might be absent from its home on any given occasion. Some of these might be expected to be absent from the village and neighbourhood and others merely inaccessible in the locality (collecting water, herding cattle or working on the farms) and in consequence it was thought unwise to postulate a total coverage exceeding 80% on any one day, though every effort was intended to better this figure.

Furthermore, the efficiency of coverage was deemed to be probably inversely proportional to the interval between administrations. Both staff efficiency and public relations are involved here and the tendency of both is to make carefully administered administration at a relatively long interval much more effective than frequent and sometimes inevitably inadequately supervised treatments. The problem of designing a programme was to see what regime of mass treatment, if any, would fit into these conditions and support the insecticidal programme to the extent of producing early eradication.

2. Methods of design

On the basis of descriptions already given it was clearly possible to run a large number of computer programmes showing the probable effect of different combinations of efficiency and interval and, after some initial trials, these were limited to efficiencies of 50%, 60%, 70% or 80% and intervals between applications of one, two,

three or four months. The various combinations of each of these were tested for both deterministic and simple stochastic solutions based on a population of 100 people. These combinations amounted to 32 programmes, though with the benefit of experience it might in later series be foreseen that some of them would be unnecessary.

The first question disposed of was the most appropriate time at which to start mass treatment. It had at one time appeared logical to emphasize this during the main transmission season but it soon became obvious that this was not the case. It became clear from the initial computer results that the most effective line of policy was to start mass treatment at the beginning of the off-season and to carry it through with as much intensity as possible throughout that season in the hope that there might be local eradication from a great many foci before the onset of the following rains, and that in those where eradication was not achieved the level might be reduced and thereafter maintained at a very low figure until the next dry season when eradication might be completed. Further programmes were therefore all run on this basis.

It would clearly be in principle desirable to choose the programme of highest efficiency with the shortest possible interval between doses were it not for the practical difficulties of ensuring really efficient coverage at short intervals. The chief question at issue was therefore the greatest interval between application which would be considered tolerable in that it could be expected to reduce most local foci to extinction level within the course of a dry season. Figure 1 illustrates nine of the 32 test runs used to study this question. Treatments in the upper row of Figure 1 have all been given at intervals of one month and efficiencies of 60%, 70% and 80% have been postulated. It will be clear that any one of these three might have achieved the desired results, though operationally a monthly administration seemed to present serious difficulties and it was doubtful what degree of coverage might be achieved, not only in the first, but in successive months. Figures in the second row represent the same efficiencies of treatment given at intervals of two months and here it is obvious that the 60% and 70% treatments fail completely to achieve the objective in that there is still a substantial amount of malaria present at the end of the dry season, allowing a resurgence during the following rainy season and it is only the 80% effective treatment which might be adequate. Figures in the lower row represent similar

treatments at intervals of three months, when it will be seen that the 60% treatment is wholly ineffective. The 70% treatment is here shown as possibly effective: it is however out of step with the two associated runs in that it produces an unexpectedly early termination and further examination shows that it is quite out of step with the associated deterministic run. This is in fact a case where the laws of chance have influenced this particular run in an unusually favourable manner, according to a probability. It has in fact been rejected as an exceptionally favourable result but is here reproduced with the intention of demonstrating the way in which aberrations from normal may occur and how their probability should be suspected. The third run, 80% efficiency, proceeds in this case towards eradication from the focus at the end of the eighth month just after the start of the malaria season and may be regarded as having barely achieved its expected result.

Examination of these runs led to the tentative choice of an objective of at least 80% efficiency of mass treatment to be applied every two months to the entire population of the area, and a run representing this efficiency was therefore further tested to check the fact that it was representative of probable happenings.

One check required was to run the programme again on the basis of a very much larger population involved to see if comparable results might be expected. The outcome is illustrated in Figure 2 which shows a similar run for a population, within the restricted focus, of 1000 people. This is deemed to be much higher than would be expected in nature and it leads to near elimination of the focus before the onset of the rains and, in this example, to total elimination immediately afterwards. The corresponding run on a deterministic basis suggests a reduction to 0.4% of the original value within the seven months of the dry season, subsequently maintained at or below 1% for the wet season leading to early prospects of elimination in the following year however large the foci involved might be.

A further series of tests concerned the effect of miscalculation of the recovery rate on the outcome of an expected result. For this purpose a complete re-analysis was made of the malaria situation using the same input data as on the previous occasion except that in one series the recovery rate was put at 0.01 and another at 0.025, a range which is considered to cover all possible values in nature. This involved the

construction of new patterns or templets against which the known changes in the parasite rate were judged, and for the first of these sets of conditions with a high recovery rate of 0.01 it was concluded that Kankiya conditions could be described by a reproduction rate of 1.5 in the dry season and 3.5 in the wet. For the much lower reproduction rate of 0.0025 values of 0.25 and 12 fitted the known picture in Kankiya. These were therefore incorporated into a new reconstruction which tallied reasonably with the original and the effect of various mass treatments was applied to this.

Figure 3 illustrates three only of these runs, each of them referring an 80% effective treatment applied once every two months. All are run deterministically and the three subsections refer to conditions where the recovery rate is 0.01, 0.005 and 0.0025, the central of these being the standard one already tested. It will be seen from these diagrams that there is some difference from the standard expected result in that the first curve descends somewhat more slowly and there is a certain recrudescence during the rains. It is to be borne in mind that all three of these are deterministic curves and the probability of fade-out during the dry season on all three of them is very considerable. In view of the fact that the range chosen is thought to cover the extreme range of nature it was concluded that possible mis-estimation of the recovery rate would have no great effect on the conclusions which have been drawn.

3. Field operations

With the theoretical design decided upon, it now remained for the operator to set up and start the recommended field activities. A circular area of some 300 square miles (777 km^2) containing approximately 52 000 people was delimited, a comprehensive geographical reconnaissance was completed and a house-to-house census of all occupants undertaken. For operational and epidemiological convenience the area was divided into five sectors, a central and four peripheral, each containing approximately 10 000 people. The central sector was further subdivided into a central indicator zone and centre peripheral zone - each with 5000 people. The intention was to administer a curative dose of a combination of chloroquine and pyrimethamine to the entire population every two months for a total of seven treatments and to spray DDT three times a year at a dosage of technical product 2 g/m^2.

From mid-November to mid-December 1966 the first mass drug administration (MDA) was given with an over-all coverage of 87.2%. The second and third MDA's were completed with coverages of 84.4% and 77.8% respectively. Of those absentees whose actual whereabouts could be determined 34.6% and 18.7% were outside the project area at the two latter MDA's. Visitors found in a village at the time of an MDA were treated. The average total visitors per 100 inhabitants was 1.9, 3.2 and 2.2 each MDA; at the two latter, it was found that 71.6% and 59.1% came from outside the project area.

The first round of DDT spraying started on 10 June 1967 and was completed by mid-July. It had been hoped to spray the first round two months earlier but late arrival of the insecticide precluded this.

4. Results

A pretreatment blood film survey was carried out - clusters of approximately 200 people were chosen by random sampling techniques that determined the sector, village and houses from whose occupants the blood films were to be taken. An over-all parasite rate of 24.2% was obtained from the examination of 2066 people in the trial area. (A similarly conducted survey in the comparison area gave a parasite rate of 28.8%.) After the first MDA the over-all parasite rate was 3.1% among 773 randomly selected people in Sector V (the central sector) and after the second MDA it had fallen to 1.8% among 3896 inhabitants of the central indicator zone. Blood films were taken at the time of the fourth MDA from some 9000 inhabitants and visitors in Sector V and these will reflect the effects of three treatments - their examination is not completed but results obtained to date indicate a parasite rate of less than 1.0%.

It is proposed to prepare a further report of the project after the fifth MDA; this will enable an assessment to be made of the results of the four treatments given in the dry season and will include a full account of the methodology that has been developed by experience.

SUMMARY

A description is given of the way in which a design for a malaria eradication project in Kankiya district was prepared. Mass drug administration at two-monthly intervals was to be combined with residual insecticide spraying.

Preliminary results indicate that the proposed coverage of 80% can be achieved in the field and that the fall in the over-all parasite rate after three treatments corresponds to the theoretical expectation.

REFERENCE

Macdonald, G., Cuellar, C. B. & Foll, C. V. (1967) The use of computer models in the analysis of a malaria situation (Document WHO/Mal/67.623)

RESUME

Cette étude décrit comment a été conçu un projet d'éradication du paludisme adapté à une situation épidémiologique déterminée existant au Kankiya, Nigéria. Plusieurs programmes codifiés ont été passés à l'ordinateur afin de déterminer l'effet probable de différentes associations d'efficacité et de périodicité lorsqu'on recourt simultanément à un traitement médicamenteux systématique et à des pulvérisations insecticides rémanentes.

Le plan théorique ainsi déterminé a été mis en application dans une zone de 52 000 habitants par :

a) administration systématique d'une association de chloroquine et de pyriméthamine à toute la population, tous les deux mois, sept fois de suite, et

b) pulvérisations rémanentes de DDT technique à raison de 2 g/m^2 trois fois par an.

D'après les résultats préliminaires, la couverture projetée (80 %) est réalisable sur le terrain et la chute de l'indice parasitaire global après trois traitements correspond aux prévisions théoriques.

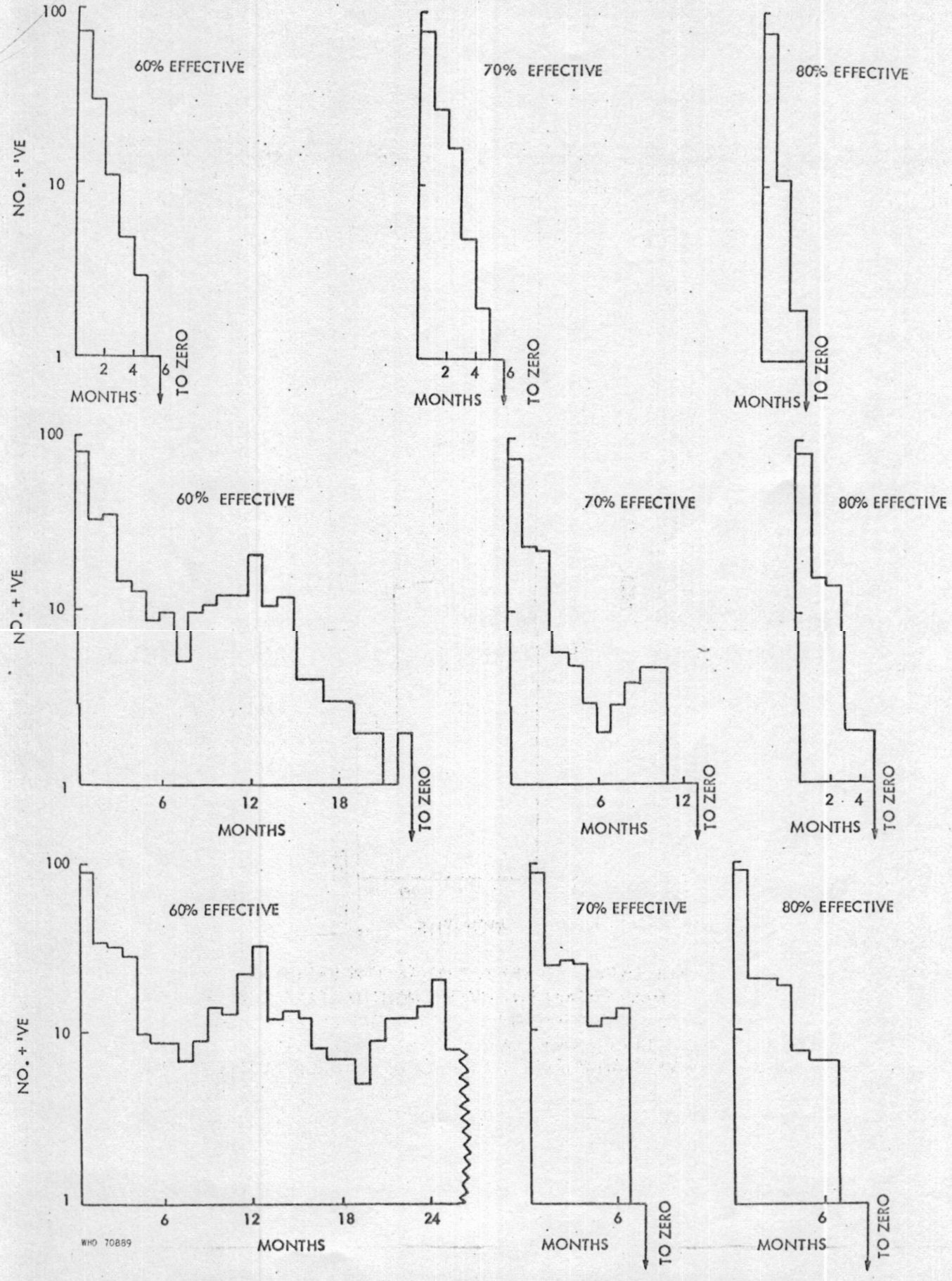

FIG. 1 THE EXPECTED EFFECT OF 60 %, 70 % AND 80 % EFFECTIVE MASS TREATMENT GIVEN ONCE A MONTH (TOP LINE), ONCE EVERY 2 MONTHS (MIDDLE LINE) AND ONCE EVERY 3 MONTHS (BOTTOM LINE): KANKIYA CONDITIONS: STOCHASTIC VERSION.

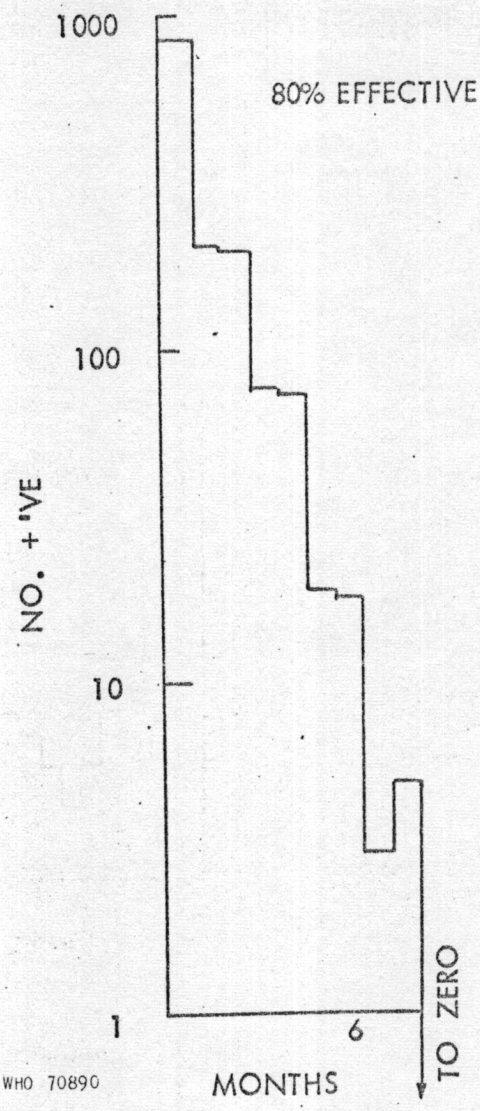

FIG. 2 THE EXPECTED EFFECT OF AN 80 % EFFECTIVE MASS TREATMENT OVER 2 MONTHS STARTING AT THE BEGINNING OF THE DRY SEASON UNDER KANKIYA CONDITIONS: STOCHASTIC VERSION WORKED FOR A POPULATION OF 1,000.

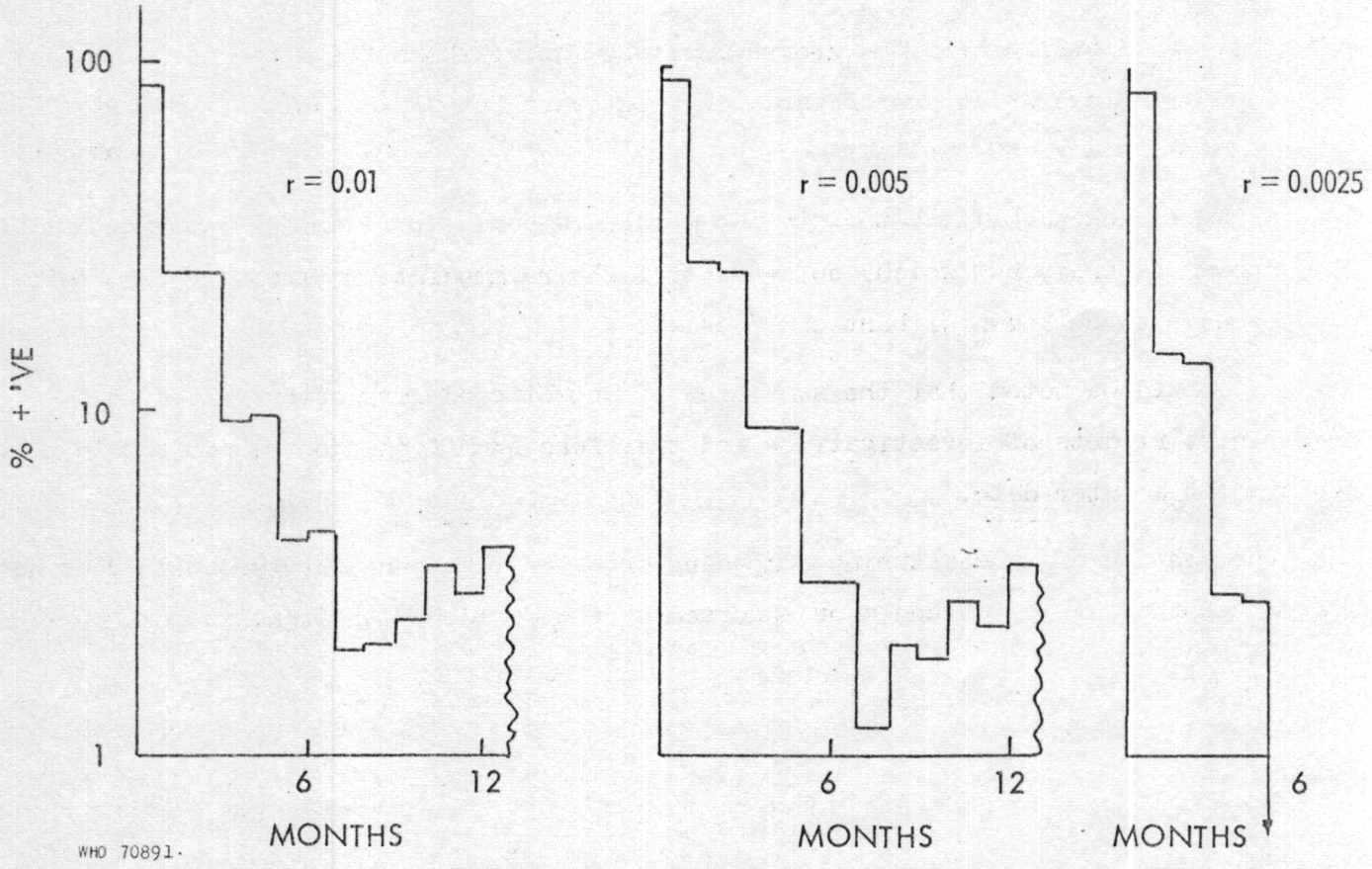

FIG. 3 A CONTRAST IN THE PROBABLE EFFECTS OF MASS TREATMENT AS FORECAST, DEPENDENT ON RECOVERY RATES OF 0.01, 0.005 AND 0.0025.

The purpose of the WHO/Mal series of documents is threefold:

(a) to acquaint WHO staff, national institutes and individual research or public health workers with the changing trends of malaria research and the progress of malaria eradication by means of summaries of some relevant problems;

(b) to distribute to the groups mentioned above those field reports and other communications which are of particular interest but which would not normally be printed in any WHO publications;

(c) to make available to interested readers some papers which will eventually appear in print but which, on account of their immediate interest or importance, deserve to be known without undue delay.

It should be noted that the summaries of unpublished work often represent preliminary reports of investigations and therefore such findings are subject to possible revision at a later date.

The mention of manufacturing companies or of their proprietary products does not imply that they are recommended or endorsed by the World Health Organization.