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## INQUIRY BY QUESTIONARY

It is the results rather than the methods of Professor Bradford Hill's inquiries into the doctor's work and pay that have commanded the interest of the medical profession. But in giving his inaugural address<sup>1</sup> (briefly reported at page 1218) on November 22 as president of the Royal Statistical Society he dwelt rather on the techniques he had used, for he had had to elicit facts by questionnaire from people whom he had not met, whose accuracy might be questioned by the Government, and whose reticence or eagerness to co-operate might have resulted in the subjects rather than the investigator deciding what was or was not relevant. That both Spens Committees and the Government accepted Professor Hill's tables as an accurate plan by which to dispose many millions of pounds of public money is a tribute to his methods. The fact that negotiations are still proceeding with those original maps on the table is not from any doubt of their accuracy but due rather to argument about how far they refer to the changed country we know to-day. Professor Hill was addressing an audience of statisticians, but concluded his address in the hope that his inquiries would "offer something of *general* interest, and especially in the statistical field of survey work—indeed in its most dangerous and treacherous form, the inquiry by *questionnaire*." Interest in the methods should in fact be more general than he suggested. Many doctors doing clinical research but not claiming to be statisticians carry out investigations that require a sceptical care in appraising the evidence: no technical skill can bring sharp definition to a photograph that was taken out of focus, though some hand-some retouching is occasionally attempted both in photography and in research. Commonly enough a doctor treats a series of cases and then follows them up, perhaps a year later, by means of a postal questionnaire. He is lucky if all his patients can be traced, or if traced reply, or if replying write objectively; luckier still if they can be found and will reply five years later. Some of the methods Hill used are applicable in such an investigation and are worth studying in detail when his address is printed in full.

<sup>1</sup> To be published in the *Journal of the Royal Statistical Society*.

In the first inquiry he was asked by the B.M.A. to find out how many services of various kinds insurance practitioners gave to their N.H.I. patients. They included attendances, visits, operations, injections, certificates, and reports. Because of seasonal fluctuations in illness the inquiry had to cover a year. The "universe" of N.H.I. practitioners was known; a randomly selected sample was chosen so large (over one-third of the total body) that the doctors taking part did not need to keep records for the whole year or of all the services on which information was sought. Sub-samples were then allotted to each month of the year, and the doctors in each sub-sample kept records for one month only. Having thus reduced the task for each doctor to one month's duration, Hill then lightened the burden further by splitting the sub-samples into groups, and asking doctors in each group to supply special information on those topics that were of subsidiary interest. All the doctors in each sub-sample therefore kept records of attendances and visits, while doctors in each group within the sub-sample kept records special to that group—of operations, or injections, or certificates, and so on. Thus the number of doctors who neglected to make a return was very small, as Hill pointed out, "by virtue of the experimental design." Given the opportunity of designing a questionnaire the investigator is apt to forget that data are easier to assimilate than to produce. He may avoid frightening his subjects into silence by spreading the work among them in some such way as this. The results were carefully checked for consistency by the usual methods, and their uniformity suggested that the samples were good and the records efficiently kept.

Professor Bradford Hill's second inquiry was into the professional income and expenditure of general practitioners in 1936–8. It was carried out in 1945 for the B.M.A. so that accurate evidence could be presented to the Spens Committee on remuneration of general practitioners. Here again there was a ready-made "universe," obtainable through the Central Medical War Committee; but it had a serious defect, for the sample drawn from it could contain, of the doctors practising in 1938, only those still alive in 1945. The incomes of doctors who had died between those years could not be included; their omission affected the figures for the older doctors, and gave incorrect weightings to the older age groups if all ages were combined. The response was disappointing and only two-thirds of the required sample was obtained. Failure by doctors to answer requests to take part in the inquiry was not related to age, but refusal to co-operate was, being more prevalent among the older. Though the circumstances of this inquiry militated against a wholly successful result, for the information required was nearly 10 years old and at least 1,000 of the doctors approached were in the

armed Forces, the Spens Committee accepted the figures as sufficiently accurate. No doubt it did so mainly because every care had been taken to choose the sample by random methods. Though they could not be wholly successful, any departure from them would have vitiated the results. No juggling with a sample will make it random once it has been drawn, but probable departures can be discovered, as they were here, and some allowance made for them.

After the general practitioners came the consultants with their Spens Committee. An initial problem was that no defined "universe" existed from which a sample could be drawn. With the help of the Central Bureau of Hospital Information and medical officers of health, Hill succeeded in identifying about 6,000 possible subjects for the inquiry. Replies were received from 4,793 doctors, but about half of these were not relevant to the inquiry because they were not engaged predominantly in consultant or specialist practice in 1938-9. In the general-practitioner inquiry it was thought that some doctors had refused to co-operate because they were asked to sign their returns. This objection was now overcome by asking the consultant to give the required information, unsigned, on one form, and to state on another form, over his signature, that he had filled in the first. The two forms were sent to separate addresses and thus could not be linked.

Requiring a small sample, which could be followed up if necessary, to use as a check against the large mass of returns, Hill had to adopt a special, and indeed ingenious, device to enable him to separate the forms in this sample from the bulk of them when they were returned to him unsigned. At the bottom of 90% of the forms the instruction "[P.T.O.]" was set; in 10% of them, which were to constitute the special sample, the bracket was omitted. The names in the sample, as in the main group, were known to the secretaries of the committee collecting evidence, but they saw no income returns; only these, and whether or not they were in the special sample, were known to Professor Hill. If a doctor in the sample did not respond, that would be known to the committee, and he could be asked again; Hill knew only how many of the sample doctors had failed to reply, not which ones. By using both halves of the information secrecy was maintained and defections were followed up. Cross-checks between sample and main group on such features of the investigation as failure to reply, distribution of specialists by specialty, and mean net income indicated that the special sample had been a useful device and that the figures of the main inquiry could be accepted "without serious qualms."

Such in brief were some of the methods used. They depend for their efficacy not on abstruse mathematical procedures but on the realization that a sample from

which generalizations are made must be unbiased. Neither the investigator nor the subjects he is investigating must allow their preconceptions, albeit unconscious, to influence the composition of the sample. Such perfection is rarely possible in inquiry by questionnaire; checks must therefore be introduced to test departure from it. The methods require clear thought, not elaborate technique, and they are such as any medical man can apply when carrying out an investigation, however slight.

## TERRAMYCIN

If "aureomycin" and "chloromycetin" (chloramphenicol) may be described as the newer antibiotics, then the newest is "terramycin," at least among those with any assured therapeutic future. The clue to American success in producing this series of valuable antibiotics is to be found in their names. Each of these from streptomycin onwards is derived from a soil actinomycete, and several American firms have for some time been engaged in examining samples of soil from all parts of the world in the hope of discovering new organisms of this type forming hitherto unknown antibiotics. Laboratories so engaged have examined many thousands of such samples and screened immense numbers of cultures from them. The more promising are submitted to closer investigation, including, in particular, tests of toxicity of the antibiotics formed by them. It has been said that several hundred thousand cultures may be examined in order to find one or two worthy of going forward to the pilot-plant stage—that is, production on a scale adequate for thorough experimental and possibly clinical trial. Such work involves a large and continuous outlay, which may or may not reap a gigantic reward. To those manufacturers whose efforts have been fortunate must now be added the name of Pfizer and Co.—familiar to many as the makers of much of the penicillin used in the Army and elsewhere during the latter part of the war—for terramycin is their product. Its existence was announced in the early part of this year,<sup>1</sup> and since then it has undergone extensive therapeutic trial. The main source of information on this product is the report<sup>2</sup> of a conference devoted to it which was held by the Section of Biology of the New York Academy of Sciences in June last. The authors of the 32 papers include many of those who have done pioneer work in the clinical study of other antibiotics from penicillin onwards, and their combined contributions give a good general picture of what terramycin may be expected to do.

<sup>1</sup> See annotation in the *British Medical Journal*, 1950, 1, 1309.

<sup>2</sup> *Ann. N.Y. Acad. Sci.*, 1950, 53, 221-460.

<sup>3</sup> *Ibid.*, p. 253.

<sup>4</sup> *Ibid.*, p. 309.

<sup>5</sup> *Ibid.*, p. 266.

<sup>6</sup> *Ibid.*, p. 297.

<sup>7</sup> *Ibid.*, p. 448.