PRINCIPLES OF MEDICAL STATISTICS

XIV—FURTHER FALLACIES AND DIFFICULTIES

The Crude Death-rate

In using death-rates, or fatality-rates, in comparison with one another, or as a measure of the success attending some procedure, it must be remembered that such rates are usually affected considerably by the age and sex constitution of the population concerned. The fact that the death-rate of Bournemouth in 1935 was 13·3 per 1000, while the rate in Bethnal Green was only 10·3, is no evidence of the salubrity of the latter area. The greater proportion of old persons living in Bournemouth compared with Bethnal Green *must* lead to a higher death-rate in the former, since old persons, however well-housed and fed, die at a faster rate than young persons. The 1931 census shows that there were at that time 2½ times as many persons in Bournemouth as in Bethnal Green at ages over 75 years, 70 per cent. more at ages 50–74, and 10 per cent. less at ages 10–40. Any population containing many persons round about the ages of 5 to 20, where the death-rate is at its minimum, must have a lower *total* death-rate than that of a population containing many infants or old people, at which points of life the death-rate is relatively high, even though comparisons at every age show an advantage to the latter. For example, the following fictitious figures may be taken.

Age-group (years).	District A. Population.		District A. Deaths.	District A. Death-rate per 1000.	District B. Population.		District B. Deaths.	District B. Death-rate per 1000.
0–	500	74 %	2	4	400	28 %	1	2·5
15–	2000		8	4	300		1	3·3
30–	2000		12	6	1000		5	5
45–	1000	26 %	10	10	2000	72 %	18	9
60–	500		20	40	2000		70	35
75+	100		15	150	400		50	125
All ages	6100		67	11·0	6100		145	23·8

Comparison of the two districts shows that B has *in every age-group* a lower death-rate than A. Yet its death-rate at all ages, the *crude* death-rate, is more than double the rate of A. The fallacy of the crude rates lies in the fact that like is not being compared with like: 72 per cent. of B's population is over age 45 and only 26 per cent. of A's population; in spite of B's relatively low death-rates at these ages over 45, the *number* of deaths registered must be higher than in A's smaller population and therefore its total death-rate must be high.

Comparison of the rates at ages is the most satisfactory procedure for then like is being placed against like, at least in respect of age (so long as the age-groups are not too wide; in the above example they were made unduly wide for the sake of compression and clarity).

The Standardised Rate

At the same time a legitimate desire is often felt for a single mortality-rate, summing up the rates at ages and yet enabling satisfactory comparisons to be made between one rate and another. For this purpose the standardised death-rate is required. For its calculation (by what is known as the *direct* method) the mortality-rates at ages in the different districts are applied to some common standard population, to discover what would be the total death-rate in that standard population if it were exposed first to A's rates and then to B's rates at each age. These total rates are clearly fictitious for they show what *would* be the mortality in A and B if they had populations which were equivalent in their age-distributions instead of their actual differing populations. But these fictitious rates are comparable with one another, and show whether B's rates at ages would lead to a better or worse total rate than A's rates if they had populations of the same age type.

For example, if the standard population taken for A and B consisted of 500 persons in each of the age-groups 0–15 and 75 and over, 2500 in each of the age-groups 15–30 and 60–75, and 3000 in each of the age-groups 30–45 and 45–60, then in this standard population A's death-rates would lead to a total of 235 deaths and B's rates to 201 deaths, giving standardised rates at all ages of 19·6 and 16·8 per 1000. Taking a population of the same age-distribution thus shows the more favourable mortality experience of B, and the fallacy of the crude rate is avoided. (The deaths that would occur at each age in the standard population, at the death-rates at ages in each district, are found by simple proportion; they are summed and divided by the total population in the standard to give the standardised rate.)

Clearly these fictitious but comparable rates will be affected by the choice of the standard population. It must be observed, however, that their *absolute* level is not of interest; it is the *relative* position that matters and, within limits, this relative level is not likely to be materially altered by the use of different standards.

The example taken above is, of course, a very exaggerated one and such gross differences in population are unlikely to occur in practice. On the other hand the differences that do occur in practice are quite large enough to make the use of crude rates seriously misleading.

For instance, the crude death-rate, in England and Wales, of women from cancer was 103 per 100,000 in 1901–10 and 139 in 1921–30, a very appreciable rise being shown. The corresponding standardised rates were 94 and 99; clearly the larger number of women living in the older age-groups (where cancer is more frequent) in 1921–30 compared with the number in 1901–10 is largely responsible for the increase in the crude rates, and no more subtle factor need be looked for.

With the present increasing proportion of persons living at later ages (owing to the fall in birth- and death-rates) it is certain that the *crude* death-rate from all causes in England and Wales will in time begin to rise, in spite of the fact that the death-rates at each age may continue to decline.

Comparison of death-rates may also be affected by the sex proportions of the populations considered, for at most ages and from most causes females suffer a lower mortality-rate than males. Standardisation, therefore, is sometimes made both for sex and age. (The methods and the alternative method of indirect standardisation are fully described and illustrated in Woods and Russell's "Introduction to Medical Statistics.")

The principles of standardisation are often applicable in experimental work. For instance, some form of treatment is applied to certain persons and others are kept as controls. If the two groups are not equal in their age-distribution a comparison of the total result may be misleading. A comparison in each separate age-group must be made, or to reach a total figure the two sets of rates at ages can be applied to

some selected standard population. A useful method is to use the treated group as the standard and calculate how many deaths would have taken place in it if it had suffered the same fatality-rates at ages as the controls. This expected figure can then be compared with the observed figure.

In considering published crude rates—death, fatality, incidence, &c.—one must always put the questions: do the populations on which these rates are based differ in their age- or sex-distribution, and would such differences materially influence the comparability of the crude rates? Crude rates themselves should never be accepted without careful consideration on those lines.

Statistics of Causes of Death

In making comparisons between death-rates from different causes of death at different times or between one country and another, it must be realised that one is dealing with material which is, in Raymond Pearl's words, "fundamentally of a dubious character." The recorded incidence of a particular cause is influenced by such factors as international differences in nomenclature, differences in tabulation, medical fashions in nomenclature, and the frequency with which the diagnosis of cause of death is made by medically qualified persons. One or two simple examples of the risks of comparison may be taken.

MORTALITY FROM CANCER

The crude death-rate from cancer in the Irish Free State is well below that registered in England and Wales. Part of this difference may be due to a more favourable age-distribution of the population in the Free State—i.e., standardised rates should be used in the comparison—but it is likely that it also arises from differences in the certification of death.

In the Irish Free State considerably more deaths are ascribed to senility than in England and Wales—15 per cent. in the former in 1932 against about 4 per cent. in the latter. Such a difference cannot inspire confidence in the death-rate from such a disease as cancer, in which the majority of deaths fall at advanced ages. In general, in comparing the cancer death-rates of different countries or of the different areas of the same country—e.g., rural and urban—it is not sufficient to pay attention to the cancer rubric; other headings such as "uncertified," "senility," and "ill-defined causes" must be taken into consideration, and an attempt made to determine whether transferences between these rubrics are likely to play a part.

The kind of indirect correlation that one may observe is this. It is stated that the cancer death-rate is associated with the consumption of sugar, and the level of the former is compared with some measure of the latter in different countries. It is found that the countries with a low consumption of sugar have relatively low cancer death-rates. But it is at least possible that those countries which have a high standard of living have a relatively higher sugar consumption, and also a higher standard of vital statistics, and therefore more accurate cancer death-rates, than countries with a low standard of living and less accurate vital statistics. Other "causes" of death—e.g., ill-defined and old age—would need study as well as those attributed directly to cancer.

MATERNAL MORTALITY

It is well recognised that the maternal death-rates of different countries are affected by the varying rules of tabulation in vogue. A sample of deaths associated with pregnancy and childbirth that took place in the U.S.A. was assigned by different statistical offices of the world to puerperal and non-puerperal groups according to the rules of those offices (Children's Bureau Publication No. 229). The variability was considerable. In the U.S.A. 93 per cent. were tabulated to puerperal causes, in England and Wales 79 per cent., in Denmark 99 per cent. Such differences make international comparisons precarious.

MORTALITY FROM RESPIRATORY CAUSES

In England and Wales bronchitis and pneumonia show pronounced differences in their incidence in different parts of the country at certain ages. It appears that the "bronchitis" of one area may include deaths which would be attributed to pneumonia in another. For instance, the Registrar-General concludes that "at both extremes of life London appears to call pneumonia many cases which are elsewhere regarded as bronchitis" (Registrar-General's Annual Report, Text, p. 85, 1932). Such "internal" differences are always closely considered by the Registrar-General and his reports are invaluable to all who are concerned with the changes in the causes of death.

The Average Age at Death

The average age at death is not often a particularly useful measure. Between one occupational group and another it may be grossly misleading. For instance, as Farr pointed out three-quarters of a century ago, the average age at death of bishops is much higher than the corresponding average of curates. But making all the curates bishops will not necessarily save them from an early death. The average age at death in an occupation must, of course, depend in part upon the age of entry to that occupation and the age of exit from it—if exit takes place for other reasons than death. Bishops have a higher age at death than curates because few men become bishops before they have passed middle life, while curates may die at any age from their twenties upwards.

The following misuse of this average is taken from a report on hospital patients.

It is stated that in 31 cases of renal hypertension which came to autopsy the average age of death was 45. "Thus the common fate of the renal hypertensive is to die in the fifth decade of life." This may be a true statement of fact, but it clearly cannot be deduced from the average age; the average might be 45 years without a single individual dying in the fifth decade. The report continues: In 86 cases of essential hypertension which came to autopsy the average age at death was found to be 60, while in 20 cases seen in private practice the average age at death was nearly 70.

"Thus, the fate of the non-renal hypertensive is very different from that of the renal. The subject of uncomplicated essential hypertension may reasonably expect to live into the seventh or even the eighth decade."

The first deduction is probably valid, though obviously information regarding the *variability* round those averages is required. The frequency distributions of the age at death for the two groups should be given. The "reasonable expectation" has no real foundation in the figures given. If the subjects of uncomplicated essential hypertension mainly live into the seventh or eighth decade one might reasonably adopt that as an expectation. But if the average age is derived from individual ages at death varying between say, 40 and 90, one has no justification for using that average as an expectation.

The author regards statistics as "dull things" and therefore refers to them as "briefly as possible"—so briefly that in his hands they are of very little use.

A difference in the average ages at death from, say, silicosis in two occupations may imply that in one

occupation the exposure to risk is more intense than in the other and thus leads to earlier death; but this interpretation can only hold, as is pointed out above, so long as the employed enter the two occupations at the same ages and give up their work at the same ages and to the same extent. It is usually very difficult to secure satisfactory evidence on these points, and the average ages at death must be regarded with some caution.

Problems of Inheritance

Literally hundreds of disorders or derangements in mankind have been recorded as showing evidence of hereditary factors. The evidence mainly consists of the appearance of the disease or disability in a more or less orderly fashion among related individuals. In many instances there is no doubt that hereditary factors are important but in others their presence is difficult of proof, in the inevitable absence of controlled breeding experiments and the impossibility sometimes of distinguishing genetic from environmental influences. Cases are reported, for example, of a familial incidence of cancer; a man whose father died of cancer of the stomach died himself of cancer in the same site, while his wife died of cancer of the breast and their six children and one grandchild all died of various forms of cancer. This is a very striking family history but it is not necessarily evidence of an inherited factor. If each of these individuals had been known to have passed through an attack of measles we should not deduce a particular family susceptibility to measles, since we know that measles in the whole population is so widespread that a familial incidence is bound to occur very frequently. Similarly we want to know the probability of observing a series of familial cases of cancer merely by chance. Even if that probability is small it must be remembered that the field of observation amongst medical men is enormously wide and a few isolated instances of multiple cases cannot be adequate evidence. Usually, too, only one part of the field is reported in medical literature, for notice is taken of the remarkable instances and no reference made to the cases in which no inheritance is apparent. The data required in such a problem are reasonably large numbers of family histories, so that, if possible, it may be seen whether the distribution of multiple cases differs from the distribution that might be expected by chance, or whether the incidence in different generations suggests a Mendelian form of inheritance. Even if the distribution of multiple cases differs from that expected on a chance hypothesis, the question of a common family environment cannot be ruled out—e.g., multiple cases of tuberculosis may occur more frequently in families of a low social level not through an inherited diathesis but through undernourishment.

A. B. H.

SPECIAL ARTICLES

PLANT VIRUSES
AND THEIR RELATION TO THOSE AFFECTING MAN AND ANIMAL *

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The first virus disease of any kind to be recognised as such was mosaic in tobacco; it was Mayer of Holland in 1886 who demonstrated both its infectivity by sap inoculations and the absence of any fungi or bacteria in the infective juice. Long before this a protean type of disease producing leaf deformity, dwarfing, and reduction of crop in variable degree had been recognised in the potato, and references to it go back for over 150 years. The disease, which was very widespread in England, was regarded as the result of prolonged vegetative reproduction that had induced an incurable senility. The only remedy for this, it was maintained, was to discard the old and create new varieties from true seed, obtained by the fertilisation of the female portion of the flower with pollen generally of some other variety. There was in fact a widespread if subconscious sympathy with a plant on whom had been enforced a celibacy which was regarded as unnatural and abhorrent by the agriculturist. That the plant reacted by becoming peevish and degenerate was only what might be expected. The cry of "back to nature" came from the heart. This view persisted in many quarters in this country even so late as the last war, indeed I may claim some share in helping to dispel the myth which as late as 1912 was firmly held in certain influential quarters.

* A lecture given before the Southampton Medical Society, Jan. 13th, 1937.

EARLY WORK

In some years this degenerative disease of the potato was so severe and the resultant crop so bad as to threaten the continuance of potato cultivation in this country. In 1778 the Agricultural Society of Manchester invited essays on the cause and possible cure of the trouble. These were printed and some 15 years ago, with Prof. W. Brierley's help, I was fortunate in discovering a copy and making parts of them known once more. Much interest lies in the fact that the chief diseases complained of seem to have been either a chronic form of crinkle—probably a secondary result of infection with the Y virus—or leaf-roll. One competitor felt convinced that the green fly was the cause of all the trouble, thus forestalling by about 140 years the discovery made by Oortwijn Botjes in 1920 that the virus disease leaf-roll was spread in the field by aphids.

Returning to tobacco mosaic, which has ever remained the classic subject for virus research, it was Iwanowsky who in 1892 showed that juice from a diseased plant remained infective after passing through a porcelain filler which would hold back bacteria. He further showed that the infective agent multiplied indefinitely within the plant. The virus, he found, was highly resistant to alcohol and to drying, and he regarded the disease as due to something either held in solution or carried by minute particles in the cell plasma.

Beijerinck (1899), ignorant of Iwanowsky's work, investigated with great thoroughness the disease Mayer had described and reached similar conclusions. He described the infective agent as a "contagium fluidum," and recognised that peach yellows, which Erwin Smith in 1888 had shown was communicable by budding or graft, was but another example of the same trouble. Löffler and Frosch's discovery that the infectious agent of foot-and-mouth disease