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My dear Gaddum,

I have looked through your paper and am glad to see that you are interesting yourself in these problems, but I should not advise submitting it for publication in either of the journals you mention. The points you consider are some of them so general that they have been discussed in all sorts of connections for nearly 200 years, and even the special problem of fitting a series of frequency ratios with the corresponding ratios of a normal distribution has been treated, with results I think identical with yours, quite fully by Godfrey Thomson (Biometrika, XII, 216) using psycho-physical material.

On the general topic you state your problem as though what was required was an inverse probability distribution for mortality rate, but I doubt if any modern statistician in this country, except, perhaps, Greenwood, has the least faith in inverse probability, which is not in any case necessary for drawing any useful kind of inferences from the data. For my own part

I take the view that inferences about populations (hypotheses) based on a knowledge of samples (observations) are of a different kind from the reverse type of inference and, save in special cases are not, like them, expressible in terms of probability. The relevant mathematical quantity for measuring the degree of rational belief in these cases seems to be not probability but likelihood, and I was glad to see that at one point you used the method of maximum likelihood, though I think inadvertently, and without recognising its independence from all arguments of the inverse probability type.

I gather that the chief point on which you differ from others who dealt statistically with the mortality of experimental animals is in assuming not that equal ranges of mortality are a priori equally probable but that this is true of equal ranges of resistance, as measured by the dose of drug necessary to cause death or by its logarithm. This, as you suggest at one point, is merely a change of convention, and cannot make the difference between a solution exact for small samples, and one which is only correct in the limit when the sample is made infinitely great. The thing is to recognise the fact that we have no knowledge prior to experiment, of the distribution of resistance to any particular drug, and that nearly all assumptions about this distribution any one of which may be inserted in the inverse probability argument, will tend, as the sample is increased indefinitely, to lead to the same result. The particular assumption which you

do introduce is quite attractive mathematically, though, since the range of D is infinite, it does imply that the probability that the 50 per cent. death point shall lie within any assigned range of concentrations is zero; ^{but} that it is not now regarded as necessary to base one's numerical conclusions on any such assumed prior knowledge, beyond the limits of actual or even possible experimental data.

I have jotted down my reaction to a number of special points in the margin. In particular the use of χ^2 with a four-fold table does not involve the assumption that either of the marginal frequency ratios is not affected by errors of random sampling, and in view of the discrepancy you note as to ~~defect~~ ~~of~~ significance it would be as well to make sure that you have not ascribed three degrees of freedom instead of one to it, as was formerly done by Pearson and his pupils, such as Greenwood and Yule in their statistics of Typhoid inoculation, and, as is still assumed in several of Pearson's "Tables for Statisticians". The use of three degrees of freedom which, I believe, is not now defended, naturally greatly underestimates the significance. When correctly used, however, the direct χ^2 test, based on the frequencies alone, without subsidiary hypotheses, must necessarily agree with every other test of significance such as the significance of a correlation coefficient inferred from the same data, ^{if the other test is accurately carried out} for the hypothesis of independence tested by χ^2 is in fact a

general expression of all such special hypotheses as zero correlation.

I hope you will not be unduly discouraged by my criticisms for there is absolutely no reason to be. It is not everyone who, without knowing the literature, can arrive at results which, historically, took a considerable time to win their way to acceptance, especially as you have run, unawares, into the central problem of inductive logic which has certainly not been cleared up until within the last few years.

Yours sincerely,