Present day practice

Laboratory precision and diagnostic errors

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In a previous theoretical study (Acland and Lipton, 1967), we showed how the chance of making an incorrect clinical diagnosis on the basis of a quantitative laboratory test could be predicted if both the size of the random error inherent in the method and the true analytical value of the sample were known. It was assumed that the normal limits for the analysis in a healthy population could be defined.

A further prediction is of clinical interest. If the test were performed on all members of a normal healthy population for whom the true analytical values lay within the normal clinical limits, what proportion of the actual observations would lie outside the normal limits as a result of method error?

A solution to this problem is presented in Table I. Two assumptions of a statistical nature were made in calculating this table: (1) that the distribution of true analytical values for the basic population is

Gaussian with mean μ_2 and standard deviation σ_2 , and (2) that the distribution of method errors for a subject (formally defined as the conditional distribution of the test observation on a particular person whose true analytical value is known) is also Gaussian with mean μ_1 equal to the true value of the subject and with standard deviation σ_1 .

In order to use Table I two quantities denoted by N and r must be known or calculated as they provide information on the particular normal range involved and the precision of the method used, respectively. The value of N depends on the percentage limits used to define the normal clinical range, which is represented as $\mu_2 \pm N\sigma_2$. In the present study, as in that of Acland and Lipton (1967), the limits which include 80%, 90%, 95%, and 98% of all normal subjects, were selected. The values of N corresponding to these limits are, respectively, 1.28, 1.64, 1.96, and 2.33.

$r = \sigma_1/\sigma_2$ and the values of r in the Table are 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.8, 1.0. Usually the value of σ_2 used in calculating r will be obtained from the normal limits by subtracting the smaller endpoint from the larger and dividing the result by $2N$.

Table I presents the overall probabilities, expressed as percentages, that a determination on a normal subject, for whom the true value lay within the normal clinical limits, should yield an abnormal result because of error in method. This probability can be taken as a measure of the diagnostic efficiency of a test.

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N	Values of r							
	0.1	0.2	0.3	0.4	0.5	0.6	0.8	1.0
1.28	2	4	7	9	12	16	22	29
1.64	1	2	4	5	7	10	15	20
1.96	1	1	2	3	5	6	10	14
2.33	0	1	1	2	2	3	6	9

Table I Overall probabilities, expressed as percentages, that a 'normal' sample should yield an 'abnormal' result because of method error

A 'normal' sample is defined here as a sample which is taken from a healthy population and whose true analytical value lies within the normal clinical range. 'Abnormal' means outside the normal clinical range.

$N = 1.28$ —Normal clinical range defined by 80% limits

$N = 1.64$ —Normal clinical range defined by 90% limits

$N = 1.96$ —Normal clinical range defined by 95% limits

$N = 2.33$ —Normal clinical range defined by 98% limits

$r = \sigma_1/\sigma_2$, where σ_1 is the standard deviation of the method and σ_2 is the standard deviation of accurate values for healthy individuals.

Normal clinical ranges are denoted by $\mu_2 \pm N\sigma_2$, where μ_2 is the mean accurate value for healthy individuals.

Example

Compare the diagnostic efficiencies of two methods of determining serum calcium levels one of which has a standard deviation of 0.2 mg/100 ml and the other a standard deviation of 0.8 mg/100 ml. The 95% normal limits for the laboratory are 8.0-11.0 mg/100 ml.

Solution

$\sigma_2 = (11-8)/3.92 = 0.77$ (as the 95% normal range is used, $N = 1.96$).

For the first method, $r = 0.2/0.77 \simeq 0.3$ (to the nearest tabular r value), hence entering Table I with $r = 0.3$ and $N = 1.96$ the required probability is 2%.

For the second method, $r = 0.8/0.77 \simeq 1$ (to the nearest tabular r value), hence entering the table with this value of r , and $N = 1.96$ the required probability is 14%.

Thus with the first method 2% of the normal clinical population would be classified as having abnormal serum calcium levels whereas with the second method 14% would be so classified.

A detailed account of the statistical theory involved in this paper is not appropriate here. Under the two assumptions listed earlier, the probabilities in Table I involve essentially a bivariate Gaussian distribution (for a discussion on the relevant basic theory see Hogg and Craig (1965) parts of chapters 2 and 3).

Tables of the bivariate Gaussian distribution (National Bureau of Standards, 1959) were used in compiling Table I. It is believed that the table is correct to the number of figures shown. A considerable number of decimals were held throughout the computation and the final entries rounded off to the number of figures given. The work was considerably facilitated by the use, at many stages of the work, of an Olivetti Programma 101 computer.

References

- Acland, J. D., and Lipton, S. (1967). Precision in a clinical chemistry laboratory. *J. clin. Path.*, 20, 780-785.
- Hogg, R. V., and Craig, A. T. (1965). *Introduction to Mathematical Statistics*, 2nd Ed. Macmillan, New York and London.
- National Bureau of Standards (1959). *Tables of the Bi-variate Normal Distribution and Related Functions*. AMS50 U.S. Government Printing Office, Washington, D.C.