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THE UNIVERSITY OF OKLAHOMA

GRADUATE COLLEGE

AN APPLICATION OF MULTIVARIATE HOMOGENEITY OF VARIANCE TESTS TO THE ELECTROCARDIOGRAM IN MYOCARDIAL INFARCTION

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AN APPLICATION OF MULTIVARIATE HOMOGENEITY OF VARIANCE TESTS

TO THE ELECTROCARDIOGRAM IN MYOCARDIAL INFARCTION

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AN APPLICATION OF MULTIVARIATE HOMOGENEITY OF VARIANCE TESTS TO THE ELECTROCARDIOGRAM IN MYOCARDIAL INFARCTION

CHAPTER I

STATEMENT OF THE PROBLEM

Wishart (1928) published the distribution known by his name in 1928, and this publication may be regarded as the beginning of multivariate sampling distribution theory. This was followed by the work of Wilks (1932) who pointed out that the variance-covariance matrix of a multivariate population was the logical multivariate extension of the variance of a univariate population. Because of the univariate theory in which statistical test criteria are based on variance ratios, it seemed only natural to investigate the ratios of variance-covariance matrices.

In the same publication, Wilks (1932) developed the theory necessary for the multivariate extension of various univariate test criteria. However, at the end of that publication, he stated, "The practical application of the criteria developed in this paper must be left for further discussion". Since that time, Pearson and Wilks (1933) have solved the problem for the case of k bivariate populations, and Wilks (1946) has done the same for one p-variate population. Kendall (1961) says, "Methods of a parallel kind could be followed for the testing of k samples of p-variate populations, although I am not aware that the general case has

been worked out explicitly". That is the purpose of this investigation.

In other words, we are interested in the derivation of statistical test criteria for the testing of the three null hypotheses given below in k p-variate normal populations.

H_1: The k populations have equal mean vectors and equal variance-covariance matrices.

H_2: The k populations have equal variance-covariance matrices irrespective of their mean vectors.

H_3: The k populations have equal mean vectors given that the variance-covariance matrices are equal.

In addition to the development of the test criteria, it shall be necessary to investigate their distributions in order that an appropriate test of the three hypotheses can be made. This shall be done in subsequent chapters.

Following the derivation of the test criteria and their distributions, a practical example of the use of these test procedures shall be given. This example was obtained from clinical medicine, and is an attempt to test the three hypotheses given above in 4 populations of patients experiencing an acute myocardial infarction. The variables to be used are measurements obtained from electrocardiograms.

Although much of this theory was first developed by Wilks (1932), it shall be re-developed using matrix notation, and shall be applied so as to arrive at a practical test procedure for the three null hypotheses in k p-variate populations. In so doing, we shall make use of methodology first reported by Tukey and Wilks (1946) and Box (1949).

Of the hypotheses, H_3 is the multivariate analog of the

univariate analysis of variance, and as we shall see, its test criterion has a simpler distribution function than either H_1 or H_2.

With this background, let us now turn to the development of the test criteria. This shall be done in CHAPTER II. CHAPTER III will be devoted to the derivation of the moments of the distributions of the three test criteria. The nature of the exact distribution of the test criteria will be investigated in CHAPTER IV, and approximations to these exact distributions will be obtained in CHAPTER V. Finally, CHAPTER VI will contain the application of this theory to clinical electrocardiographic parameters.

CHAPTER II

DERIVATION OF THE TEST CRITERIA

In this chapter, we shall be concerned with the derivation of the test criteria for testing the three hypotheses discussed in CHAPTER I. These results were first obtained by Wilks (1932) using the method of maximum likelihood developed by Neyman and Pearson (1928). This derivation will differ from Wilks' in that matrix notation and methods will be used.

We shall adopt the following notation for our k p-variate normal populations. Let $\mu^{(t)}$ represent the vector of means for the $t^{\underline{th}}$ population, $V^{(t)}$ the matrix of variances and covariances for the $t^{\underline{th}}$ population, $R^{(t)}$ the inverse of $V^{(t)}$, $n^{(t)}$ the sample size from the $t^{\underline{th}}$ population, $X_i^{(t)}$ the vector of observations obtained from the $t^{\underline{th}}$ population, and $|V|$ the determinant of the matrix V. The range of t will be from 1 to k and the range of i will be from 1 to $n^{(t)}$ for the $t^{\underline{th}}$ population. We shall use $\hat{V}$ to represent an estimate of V. $n = \sum_t n^{(t)}$.

With this notation the distribution for the $t^{\underline{th}}$ population will be:

$$f(X) = \frac{\left| R^{(t)} \right|^{\frac{1}{2}}}{(2\pi)^{\frac{1}{2}p}} \exp\left[-\tfrac{1}{2} (X^{(t)} - \mu^{(t)})' R^{(t)} (X^{(t)} - \mu^{(t)}) \right].$$

Now if a sample of size $n^{(t)}$ is drawn from this population, the likelihood

function for the sample can be written as:

$$L^{(t)} = \frac{\left| R^{(t)} \right|^{\frac{1}{2}n^{(t)}}}{(2\pi)^{\frac{1}{2}pn^{(t)}}} \exp\left[-\tfrac{1}{2} \sum_i (X_i^{(t)} - \mu^{(t)})' R^{(t)} (X_i^{(t)} - \mu^{(t)}) \right].$$

Therefore, the joint likelihood for samples obtained from all of the populations is:

$$L = \prod_{t=1}^{k} \frac{\left| R^{(t)} \right|^{\frac{1}{2}n^{(t)}}}{(2\pi)^{\frac{1}{2}pn^{(t)}}} \exp\left[-\tfrac{1}{2} \sum_t \sum_i (X_i^{(t)} - \mu^{(t)})' R^{(t)} (X_i^{(t)} - \mu^{(t)}) \right]$$

Taking the logarithm, we get:

$$\ln L = \tfrac{1}{2} \sum_t n^{(t)} \ln \left| R^{(t)} \right| - \tfrac{1}{2} p \sum_t n^{(t)} \ln 2\pi$$

$$-\tfrac{1}{2} \sum_t \sum_i (X_i^{(t)} - \mu^{(t)})' R^{(t)} (X_i^{(t)} - \mu^{(t)}) .$$

We shall first maximize this likelihood function in the unrestricted parameter space, that is, without restricting the values of the means, variances, or covariances of the k populations. To do so, we need the partial derivatives of ln L with respect to the $\mu^{(t)}$ and $v^{(t)}$.

$$\frac{\partial \ln L}{\partial \mu^{(t)}} = \tfrac{1}{2} \sum_i 2 R^{(t)} (X_i^{(t)} - \mu^{(t)})$$

Setting this equal to zero and solving, we get:

$$\hat{\mu}^{(t)} = (n^{(t)})^{-1} \sum_t X_i^{(t)} = \bar{X}^{(t)} . \qquad (1)$$

Similarly:

$$\frac{\partial \ln L}{\partial R^{(t)}} = \frac{n^{(t)}}{2} \frac{\left|R^{(t)}\right| \left[R^{(t)}\right]^{-1}}{\left|R^{(t)}\right|} - \frac{1}{2} \sum_i 2(X_i^{(t)} - \mu^{(t)})(X_i^{(t)} - \mu^{(t)})'.$$

Again, equating this expression to zero we get:

$$\hat{V}^{(t)} = (\hat{R}^{(t)})^{-1} = (n^{(t)})^{-1} \sum_i (X_i^{(t)} - \bar{X}^{(t)})(X_i^{(t)} - \bar{X}^{(t)})' . \qquad (2)$$

Substituting these expressions into L, the maximum of L can be written as:

$$L(\Omega) = \prod_{t=1}^{k} \left| \hat{V}^{(t)} \right|^{-\frac{1}{2}n^{(t)}} (2\pi)^{-\frac{1}{2}pn^{(t)}} \exp(-\tfrac{1}{2}n) . \qquad (3)$$

Let us now consider H_1: $\mu^{(1)} = \mu^{(2)} = \ldots = \mu^{(k)} = \mu$, and $V^{(1)} = V^{(2)} = \ldots = V^{(k)} = V$. With these restrictions, ln L becomes:

$$\ln L = -\tfrac{1}{2}np \ln 2\pi + \tfrac{1}{2}n \ln |R| - \tfrac{1}{2} \sum_t \sum_i (X_i^{(t)} - \mu)' R (X_i^{(t)} - \mu) .$$

Maximizing this expression with respect to μ and R, one obtains:

$$\hat{\mu} = n^{-1} \sum_t n^{(t)} \bar{X}^{(t)} = \bar{X}_o , \qquad (4)$$

and:

$$\hat{V} = n^{-1} \sum_t n^{(t)} V^{(t)} + n^{-1} \sum_t n^{(t)} (\bar{X}^{(t)} - \bar{X}_o)(\bar{X}^{(t)} - \bar{X}_o)' \qquad (5)$$

$$= \hat{V}_o .$$

Using these estimates, the maximum of L in this restricted parameter space can be written as:

$$\left| \hat{V}_o \right|^{-\frac{1}{2}n} (2\pi)^{-\frac{1}{2}np} \exp(-\tfrac{1}{2}kn).$$

Therefore, the test criterion for hypothesis H_1 is:

$$\lambda_1 = \frac{L(w)}{L(\Omega)} = \left| \hat{V}_o \right|^{-\frac{1}{2}n} \prod_{t=1}^{k} \left| \hat{V}(t) \right|^{\frac{1}{2}n(t)}$$

$$= \prod_{t=1}^{k} \left| \hat{V}_o \right|^{-\frac{1}{2}n(t)} \left| \hat{V}(t) \right|^{\frac{1}{2}n(t)} \tag{6}$$

Let us now consider H_2: $V^{(1)} = V^{(2)} = \ldots = V^{(t)} = V$ irrespective of the value of the means. Under this hypothesis, $L(\Omega)$ remains the same as (3).

In the restricted parameter space:

$$\ln L = \tfrac{1}{2} n \ln |R| - \tfrac{1}{2} np \ln 2\pi - \tfrac{1}{2} \sum_t \sum_i (X_i^{(t)} - \mu^{(t)})' R (X_i^{(t)} - \mu^{(t)}).$$

Differentiating ln L, equating the derivatives to zero, and solving, we obtain:

$$\hat{\mu}^{(t)} = \bar{X}^{(t)} \tag{7}$$

and:

$$\hat{V} = n^{-1} \sum_t n^{(t)} \hat{V}(t) = \hat{V}_a . \tag{8}$$

Using these estimates we find:

$$L(w) = (2\pi)^{-\frac{1}{2}pn} \left| \hat{V}_a \right|^{-\frac{1}{2}n} \exp(-\tfrac{1}{2}kn) \tag{9}$$

and so:

$$\lambda_2 = \frac{L(w)}{L(\Omega)} = \left| \hat{V}_a \right|^{-\frac{1}{2}n} \prod_{t=1}^{k} \left| \hat{V}(t) \right|^{\frac{1}{2}n(t)}$$

$$= \prod_{t=1}^{k} \left| \hat{V}_a \right|^{-\frac{1}{2}n(t)} \left| \hat{V}(t) \right|^{\frac{1}{2}n(t)} . \tag{10}$$

Finally, we shall obtain the test criterion for H_3: $\mu^{(1)} = \mu^{(2)} = \ldots = \mu^{(t)} = \mu$ given that the variance-covariance matrices are all equal.

Now under the unrestricted hypothesis:

$$\ln L = \tfrac{1}{2}n \ln \left| R \right| - \tfrac{1}{2}pn \ln 2\pi - \tfrac{1}{2} \sum_t \sum_i (X_i^{(t)} - \mu^{(t)})' R (X_i^{(t)} - \mu^{(t)}).$$

From this, one can obtain:

$$\hat{\mu}(t) = \bar{X}(t) , \tag{11}$$

and:

$$\hat{V} = n^{-1} \sum_t n^{(t)} \hat{V}(t) = \hat{V}_a , \tag{12}$$

and so:

$$L (\Omega) = (2\pi)^{-\frac{1}{2}pn} \left| \hat{V}_a \right|^{-\frac{1}{2}n} \exp (-\tfrac{1}{2}kn) \tag{13}$$

With the restriction imposed by the hypothesis of equality of means:

$$\ln L = \tfrac{1}{2}n \ln \left| R \right| - \tfrac{1}{2}np \ln 2\pi - \frac{1}{2} \sum_t \sum_i (X_i^{(t)} - \mu)' R (X_i^{(t)} - \mu) .$$

Maximizing this expression, we obtain:

$$\hat{\mu} = \bar{X}_o , \tag{14}$$

and:

$$\hat{V} = \hat{V}_o , \tag{15}$$

and so:

$$L (w) = (2\pi)^{-\frac{1}{2}pn} \left| \hat{V}_o \right|^{-\frac{1}{2}n} \exp (-\tfrac{1}{2}kn) .$$

Using this, we find:

$$\lambda_3 = \frac{L (w)}{L (\Omega)} = \left| \hat{V}_a \right|^{\frac{1}{2}n} \left| \hat{V}_o \right|^{-\frac{1}{2}n} . \tag{16}$$

The next chapter will be devoted to investigating the moments of the distributions of these three criteria so that they can be used for the testing of the three null hypotheses.

CHAPTER III

MOMENTS OF THE DISTRIBUTIONS OF THE TEST CRITERIA

We are now ready to investigate the distributions of the three test criteria developed in the last section, but first we should review a fundamental multivariate distribution.

Let $\hat{V}$ represent the variance-covariance matrix computed from a sample of n items from a p-variate normal population, that is:

$$n\,\hat{V} = \sum_{i} (X_i - \bar{X})\,(X_i - \bar{X})'$$

where the X_i are independent and normally distributed with mean μ and variance-covariance matrix V. The distribution of $n\hat{V}$ was first derived by Wishart (1928), and now bears his name. It is given by:

$$\frac{\left|\hat{V}\right|^{\frac{1}{2}(n-p-2)} \exp\left[-\tfrac{1}{2}\,\mathrm{Tr}(V^{-1}\hat{V})\right]}{2^{\frac{1}{2}p(n-1)}\,\pi^{\frac{1}{4}p(p-1)}\,|V|^{\frac{1}{2}(n-1)}\prod_{i=1}^{p}\Gamma\left[\tfrac{1}{2}(n-i)\right]}\,d\hat{V} \qquad (17)$$

where $\mathrm{Tr}(V^{-1}\hat{V})$ represents the trace of the matrix $(V^{-1}\hat{V})$.

From (17), we have:

$$\int \left|\hat{V}\right|^{\frac{1}{2}(n-p-2)} \exp\left[-\tfrac{1}{2}\,\mathrm{Tr}(V^{-1}\hat{V})\right]\,d\hat{V}$$

$$= |V|^{\frac{1}{2}(n-1)} \; 2^{\frac{1}{2}(n-1)p} \; \pi^{\frac{1}{4}p(p-1)} \prod_{i=1}^{p} \Gamma\left[\tfrac{1}{2}(n-i)\right] \qquad (18)$$

$$= W.$$

Then the kth moment of this distribution can be obtained as:

$$M_k(\hat{V}) = \frac{1}{W}\int |\hat{V}|^{\frac{1}{2}(n-p-2+2k)} \exp\left[-\tfrac{1}{2}\,\mathrm{Tr}(V^{-1}\hat{V})\right] d\hat{V}$$

$$= \frac{1}{W} \; |V|^{\frac{1}{2}(n+2k-1)} \; 2^{\frac{1}{2}p(n+2k-1)} \; \pi^{\frac{1}{4}p(p-1)} \prod_{i=1}^{p} \Gamma\left[\tfrac{1}{2}(n+2k-i)\right]$$

$$= \frac{|V|^{k} \prod_{i=1}^{p} \Gamma\left[\frac{n-i}{2}+k\right]}{2^{-kp} \prod_{i=1}^{p} \Gamma\left[\frac{n-i}{2}\right]}. \qquad (19)$$

With these results, we are now ready to find an expression for the hth moment of the first criterion given by (6). Now, $\hat{V}_o$ can be written as $\hat{V}_o' + \hat{V}_o''$ where:

$$\hat{V}_o' = n^{-1} \sum_t n^{(t)} \hat{V}^{(t)}, \text{ and}$$

$$\hat{V}_o'' = n^{-1} \sum_t n^{(t)} (\bar{X}^{(t)} - \bar{X}_o)(\bar{X}^{(t)} - \bar{X}_o)'.$$

Since the $n^{(t)} \hat{V}^{(t)}$ are independently distributed according to the Wishart distribution (17), and since the sum of two Wishart variates is also a Wishart variate, then under H_1, the distribution of $\hat{V}_o'$ is given by:

$$\frac{\left|\hat{V}_o'\right|^{\frac{1}{2}(n-k-p-1)} \exp\left[-\tfrac{1}{2}\,\mathrm{Tr}(V^{-1}\hat{V}_o')\right]}{2^{\frac{1}{2}p(n-k)}\,\pi^{\frac{1}{4}p(p-1)}\prod_{i=1}^{p}\Gamma\left[\tfrac{1}{2}(n-k+1-i)\right]}. \qquad (20)$$

Also, the means of samples of size $n^{(t)}$ from p-variate normal populations are independently distributed as Gaussian variates. Furthermore, the distribution of these means is independent of that of the variance-covariance matrices. Since $\hat{V}_o''$ represents the sample variance-covariance matrix of $\bar{X}^{(t)}$, $\hat{V}_o''$ also is distributed as a Wishart variate.

Now, since $\hat{V}_o$ is the sum of two Wishart variates, it also has a Wishart distribution. Consequently from (17) and (19), the mth moment of $\left|\hat{V}_o\right|^{\frac{1}{2}n^{(t)}}$ can be written as:

$$\left|V\right|^{\frac{1}{2}nm} 2^{\frac{1}{2}nmp} \prod_{i=1}^{p}\left[\frac{\Gamma\left[\frac{n(1+m)-1}{2}\right]}{\Gamma\left[\frac{n-i}{2}\right]}\right]. \qquad (21)$$

But $\hat{V}_o$ is a function of $\hat{V}^{(t)}$ and $\bar{X}^{(t)}$, and so, the mth moment of $\left|\hat{V}_o\right|^{\frac{1}{2}n^{(t)}}$ can also be written as:

$$\exp\left[-\sum_t \mathrm{Tr}\; V(\hat{V}_o' + \hat{V}_o'')\right] \prod_{t=1}^{k}\left|\hat{V}^{(t)}\right|^{\frac{1}{2}(n^{(t)}-p-2)} \left|\hat{V}_o\right|^{\frac{1}{2}nm} \prod_t d\hat{V}^{(t)}\, d\bar{X}^{(t)}. \qquad (22)$$

Since (22) represents the product of (k+1) independent integrals of the form of (18), we find, using (19), that the integral given by (22) is

equal to:

$$|V|^{-\frac{1}{2}nm} \prod_{t=1}^{k} \left| \frac{n}{n^{(t)}} V \right|^{-\frac{1}{2}n^{(t)}} \pi^{\frac{1}{4}kp(p-1)+\frac{1}{2}kp} 2^{\frac{1}{2}k} \prod_{i=1}^{p} \left[\frac{\prod_{t=1}^{k} \Gamma\left[\frac{n^{(t)}-i}{2}\right] \Gamma\left[\frac{n(1+m)-i}{2}\right]}{\Gamma\left[\frac{n-i}{2}\right]} \right] . \quad (23)$$

Following the argument given by Wilks (1932), in (22) we replace $n^{(t)}$ by $n^{(t)}(1+h)$, n by n(1+h), and m by -h/(1+h), and then multiply by:

$$\prod_{t=1}^{k} \left[\frac{\left| \frac{n^{(t)}}{n} V \right|^{\frac{1}{2}n^{(t)}} 2^{-\frac{1}{2}k}}{\pi^{\frac{1}{4}p(p-1)+\frac{1}{2}p} \prod_{i=1}^{p} \Gamma\left[\frac{1}{2}(n^{(t)}-i)\right]} \right] .$$

Now the integral given by (22) represents the hth moment of λ_1. Therefore, performing the same operations on (23) gives the solution to (22), and so we get for $M_h(\lambda_1)$:

$$\prod_{t=1}^{k} \left[\left[\frac{n}{n^{(t)}} \right]^{\frac{1}{2}phn^{(t)}} \prod_{i=1}^{p} \left[\frac{\Gamma\left[\frac{n^{(t)}(1+h)-i}{2}\right]}{\Gamma\left[\frac{n^{(t)}-i}{2}\right]} \right] \prod_{i=1}^{p} \left[\frac{\Gamma\left[\frac{n-i}{2}\right]}{\Gamma\left[\frac{n(1+h)-i}{2}\right]} \right] \right] \quad (24)$$

Using this same approach, let us now investigate the moments of the distribution of λ_2 given by (10).

Now, $\hat{V}_a = \frac{1}{n} \sum_t n^{(t)} \hat{V}^{(t)}$, and this is the same expression as that for $\hat{V}_o'$. Therefore, the distribution of $n\hat{V}_a$ is the Wishart

distribution given by (20). With this information, we can use equation (19) to find the general moment for $\left| \hat{V}_a \right|^{\frac{1}{2}n^{(t)}}$, and then following the argument outlined in steps (21 through (24), we find that $M_h(\lambda_2)$ can be written as:

$$\prod_{t=1}^{k} \left[\frac{n}{n^{(t)}} \right]^{\frac{phn^{(t)}}{2}} \prod_{i=1}^{p} \left[\frac{\Gamma\left[\frac{n^{(t)}(1+h)-i}{2}\right]}{\Gamma\left[\frac{n^{(t)}-i}{2}\right]} \right] \prod_{i=1}^{p} \left[\frac{\Gamma\left[\frac{n-k+1-i}{2}\right]}{\Gamma\left[\frac{n(1+h)-k+1-i}{2}\right]} \right] \quad (25)$$

Finally, let us find the moments of the distribution of λ_3 given by (16). Now, let:

$$L_3 = (\lambda_3)^{2/n} = \left| \hat{V}_a \right| \left| \hat{V}_o \right|^{-1} \quad (26)$$

From the above discussion, we know that $n\hat{V}_a$ and $n\hat{V}_o$ are both distributed as Wishart variates, and so L_3 is distributed as the ratio of two Wishart variables. Again following the argument outlined in the derivation of $M_h(\lambda_1)$, we have that:

$$M_h(L_3) = \prod_{i=1}^{p} \left[\frac{\Gamma\left[\frac{n-i}{2}\right] \Gamma\left[\frac{n+1-k-i}{2}+h\right]}{\Gamma\left[\frac{n-i}{2}+h\right] \Gamma\left[\frac{n+1-k-i}{2}\right]} \right] . \quad (27)$$

We now have general expressions for the moments of the distributions of the three test criteria. In the next chapter, we shall investigate the distributions of these criteria.

CHAPTER IV

DISTRIBUTIONS OF THE TEST CRITERIA

To investigate the distributions of the statistical test criteria developed in CHAPTER II, we shall make use of a theorem concerning Beta distributions due to John W. Tukey and S. S. Wilks (1946).

We sahll adopt Tukey's notation. Let:

$$(y)_h = y\,(y+1)\,(y+2)\,\ldots\,(y+h-1), \tag{28}$$

and then:

$$\Gamma(y+h) = (y)_h\ \Gamma(y), \tag{29}$$

and if r is a positive integer:

$$\Gamma(y+rh) = (y)_{rh}\ \Gamma(y) = r^{rh} \prod_{i=1}^{r} \left[\frac{y+i-1}{r}\right]_h \Gamma(y)\ . \tag{30}$$

With this notation, Tukey and Wilks showed that if the moments of the distribution of a statistical test criterion can be written in the form:

$$M_h = \frac{\prod_{i=1}^{r} \left[1/a - G_i + 1\right]_h}{\prod_{i=1}^{r} \left[1/a - D_i + 1\right]_h} \tag{31}$$

where a = 2/n or 2/(n-1), and G_i and D_i are real numbers, then the test criterion is distributed as the product of r independent beta variates.

We shall now show that the $h^{\underline{th}}$ moment of the distribution of a power of a beta variate can be written in a form which is a special case of (31).

If y is distributed as a beta variate, that is:

$$dF = \frac{\Gamma(r+s)}{\Gamma(r)\,\Gamma(s)} \; y^{r-1} \; (1-y)^{s-1} \, dy \; ,$$

then its $h^{\underline{th}}$ moment can be written in the form:

$$M_h(y) = \frac{(r)_h}{(r+s)_h} \; . \tag{32}$$

If $z = y^v$, that is, if z is a beta variate raised to a power, than its $u^{\underline{th}}$ moment is obtained from (32) by setting $h = v\,u$. Therefore, we can write:

$$M_u(y^v) = \frac{(r)_{uv}}{(r+s)_{uv}} = \frac{\prod_{j=1}^{u} \left[\frac{r+j-1}{v}\right]_u}{\prod_{j=1}^{u} \left[\frac{r+s+j-1}{v}\right]_u} \; . \tag{33}$$

If we let $1/a = (r+s)/v$, $G_i = 1 + (s-i+1)/v$, and $D_i = 1 - (i-1)/v$, then we see that (33) is a special case of (31).

With this background, we are ready to consider the $h^{\underline{th}}$ moment of λ_1 given by (24). If $\frac{1}{2}\,n^{(t)}$ is an integer for all t, we can then use (28), (29), and (30) to obtain:

$$\Gamma\left[\frac{n(1+h)-i}{2}\right] = \left[\frac{n}{2}\right]^{\frac{1}{2}nh} \prod_{j=1}^{\frac{1}{2}n} \left[\frac{n-i+2j-1}{n}\right]_h \Gamma\left[\frac{n-i}{2}\right] ,$$

and:

$$\left[\left[\frac{n^{(t)}(1+h)-i}{2}\right]\right] = \left[\left[\frac{n^{(t)}}{2}\right]\right]^{\frac{1}{2}n^{(t)}} \prod_{j=1}^{\frac{1}{2}n^{(t)}} \left[\left[\frac{n^{(t)}-i+2j-1}{n^{(t)}}\right]\right]_h \left[\left[\frac{n^{(t)}-i}{2}\right]\right] .$$

Using these two expressions, (24) can now be written as:

$$M_h(\lambda_1) = \prod_{t=1}^{k}\left[\prod_{i=1}^{p}\prod_{j=1}^{\frac{1}{2}n^{(t)}}\left[\left[\frac{n^{(t)}-i+2j-1}{n^{(t)}}\right]\right]_h\right] \prod_{i=1}^{p}\left[\left[\frac{1}{\prod_{j=1}^{\frac{1}{2}n}\left[\left[\frac{n-i+2j-1}{n}\right]\right]_h}\right]\right] \quad (34)$$

For a fixed value of i and t, (34) is in the form of (33) as we wished.

Using the same argument as used with $M_h(\lambda_1)$, we find that $M_h(\lambda_2)$ can be written as:

$$M_h(\lambda_2) = \prod_{t=1}^{k}\left[\prod_{i=1}^{p}\prod_{j=1}^{\frac{1}{2}n^{(t)}}\left[\left[\frac{n^{(t)}-i+2j-1}{n^{(t)}}\right]\right]_h\right] \prod_{i=1}^{p}\left[\left[\frac{1}{\prod_{j=1}^{\frac{1}{2}n}\left[\left[\frac{n-k-i+2j-1}{n}\right]\right]_h}\right]\right] . \quad (35)$$

Again, this expression is in the same form as (33) as desired.

Finally, we shall consider $M_h(L_3)$. Using (29), we find that:

$$\left[\left[\frac{n-i}{2} + h\right]\right] = \left[\left[\frac{n-i}{2}\right]\right]_h \left[\left[\frac{n-i}{2}\right]\right] ,$$

and:

$$\left[\left[\frac{n+1-k-i}{2} + h\right]\right] = \left[\left[\frac{n+1-k-i}{2}\right]\right]_h \left[\left[\frac{n+1-k-i}{2}\right]\right] .$$

Substituting these expressions into (27), we obtain:

$$M_h(L_3) = \prod_{i=1}^{p} \frac{\left[n/2 + (1-k-i)/2\right]_h}{\left[n/2 - i/2\right]_h} \tag{36}$$

For a given value of p, this expression is in the same form as (31).

Now, since $M_h(L_3)$ can be written in the form of (31), L_3 is distributed as the product of p independent beta variates according to the theorem given at the beginning of this chapter. However, since $M_h(\lambda_1)$ and $M_h(\lambda_2)$ are both expressible in the form of (33) if $n^{(t)}$ is an even integer for all t, then λ_1 and λ_2 are each distributed as the product of p independent beta variates each of which is raised to a power. Wilks (1946) and Kendall (1952) both give expressions for the exact distribution of L_3 for k = 2 and k = 3. However, the general problem still defies solution, as does the problem of obtaining the exact distributions for λ_1 and λ_2. If the expression for the distribution of L_3 for k = 3 is any indication, the general solution will not be of practical use since the building of tables from these expressions will be an extremely difficult and time consuming task. This is analogous to certain univariate test criteria such as the one for the testing of the homogeneity of sample variances obtained from univariate normal populations. In that particular case, a Chi Square approximation to the distribution was obtained because of the complexity of the exact distribution.

Therefore, although we know the form of the exact distributions

of our three test criteria, it would seem that their complexity would indicate that for practical use, approximations to these distributions should be sought. The next chapter is devoted to consideration of procedures for obtaining useful approximations.

CHAPTER V

APPROXIMATE DISTRIBUTIONS OF THE TEST CRITERIA

Box (1949) has said, "Although in many cases, the exact distribution (of a test criterion) cannot be obtained in a form which is of practical use, it is usually possible to obtain the moments, and these may be used to obtain approximations". This chapter will be devoted to the finding of useful approximations using the moments derived in CHAPTER III.

Simple Chi Square Approximation

In a paper published in 1938, Wilks proved that if a population is distributed such that "optimum" estimates of the parameters exist, then when the null hypothesis is true, and when the sample size is large, $-2 \ln \lambda$ where λ is a maximum likelihood test criterion, is distributed as a Chi Square variate except for terms of order $n^{-\frac{1}{2}}$ where n is the size of the sample. The degrees of freedom of this distribution are the number of parameters of the population less the number of parameters specified by the hypothesis. Maximum likelihood estimates satisfy the "optimum" conditions required of the estimates, and so this theorem is applicable to our three test criteria.

For λ_1, $-2 \ln \lambda_1$ is approximately distributed as Chi Square. To determine the degrees of freedom, we must remember that there are

p means for each of the k populations or a total of kp means to be estimated. In addition, there are $\frac{1}{2}p(p+1)$ distinct variances and covariances for each population yielding a total of $kp + \frac{1}{2}kp(p+1)$ or $\frac{1}{2}kp(p+3)$ parameters associated with our likelihood function. Of these, $p + \frac{1}{2}p(p+1)$ or $\frac{1}{2}p(p+3)$ are specified by the hypothesis, and so the desired degrees of freedom for our Chi Square approximation are $\frac{1}{2}kp(p+3)$ $\frac{1}{2}p(p+3)$ or $\frac{1}{2}p(p+3)(k-1)$.

Turning now to λ_2, $-2 \ln \lambda_2$ is approximately distributed as Chi Square with $\frac{1}{2}kp(p+1) + kp - kp - \frac{1}{2}p(p+1)$ or $\frac{1}{2}p(p+1)(k-1)$ degrees of freedom.

Finally, $-2 \ln \lambda_3 = -2(\frac{1}{2}n) \ln L_3 = -n \ln L_3$ is approximately distributed as Chi Square with $kp + \frac{1}{2}p(p+1) - p - \frac{1}{2}p(p+1)$ or $p(k-1)$ degrees of freedom.

The validity or closeness of this approximation is difficult to judge, however, we do have one guideline. In using this approximation for the distribution of these same test criteria in the case of one p-variate normal distribution, Wilks (1946) found that when k and p are 2 or 3, the Chi Square approximate probability level differed from the exact probability in the third decimal place for n greater than 60. This was also true for p = 4 or 5 in testing the third hypothesis. Since Wilks' distributions are similar to those in this problem, it would seem reasonable to have some confidence in this approximation for n at least 60 if the number of variables and populations is not too large.

Modified Chi Square Approximation

With a very complex mathematical derivation, Box (1949) demonstrated that modification of the simple Chi Square approximation given in the preceding section produced a closer approximation to the exact distribution of maximum likelihood test criteria. This modification consists of multiplication of the simple approximation $-2 \ln \lambda$, by a factor C^{-1}. Because of the length and complexity of Box's derivation, only the method of finding C will be given here.

In order to find C, it is necessary to first introduce the quantity:

$$A_r = \frac{2r\ \alpha_r'}{v^r\ f} \tag{37}$$

where:

r = An integer specifying a particular A_r,

$$\alpha_r = \frac{(-1)^r\ k}{r(r+1)(r+2)} \sum_{s=1}^{r+1} \begin{bmatrix} r+2 \\ s+1 \end{bmatrix} 2^s\ D_s\ \beta^{r+1-s},$$

and: $\beta = v - \rho\ v$,

ρ = An arbitrary constant ≤ 1,

v = Average degrees of freedom, that is $(n-k)/k$,

α_r' is α_r with $\rho = 1$,

$D_s = \Delta_s\ \gamma_s$,

$$\Delta_s \doteq B_{s+1}\left[-\tfrac{1}{2}(B+p)\right] - B_{s+1}\left[-\tfrac{1}{2}B\right],$$

B_{s+1} is a Bernoulli polynomial and B is a Bernoulli number,

$$\gamma_s = k^{-1} \sum_{t=1}^{k} \left[\frac{v}{v^{(t)}} \right]^{s-1} - k^{-s}$$

f = degrees of freedom of the simple Chi Square approximation,

n, $n^{(t)}$, and k are as previously defined,

and:

$$v^{(t)} = n^{(t)} - 1.$$

Box further gives the first 3 values of Δ_s which are:

s	Δ_s
0	$-\frac{1}{2}p$,
1	$\frac{1}{4}p(p+1)$,
2	$-p(2p^2 + 3p - 1)/16$,

and the first 2 values of α_r which are:

r	α_s
1	$-k(3D_1\beta + 2D_2)/3$,
2	$-k(3D_1\beta^2 + 4D_2\beta + 2D_3)/6$.

In the computation of A_r, we need α_r' which is the corresponding value of α_r with $\rho = 1$ and therefore $\beta = 0$.

In his derivation, Box further showed that if $A_2 = 0$, setting $C = 1 + A_1$ would give the first cumulant of $-(2 \ln \lambda)/C$ to agree with that of the exact distribution to order v^{-2}. Further, if $A_2 = A_1^2$, setting $C = (1-A_1)^{-1}$ would give the same order of approximation. As a matter of fact, for large v, if $A_2 - A_1^2 \geq 0$, the first cumulant of the Pearson type VI curve (F distribution) agrees with that of the exact distribution to order v^{-2}, if $A_2 - A_1^2 = 0$, the agreement is with the

Pearson type III curve (Chi Square distribution), and finally, if $A_2 - A_1^2 \leq 0$, the agreement is with the Pearson type I curve. Therefore, if $A_2 - A_1^2 \geq 0$, then $C = (1-A_1)^{-1}$ would give a chi square approximation sufficient to produce agreement of their first cumulants to order of approximately v^{-2}.

Let us now derive this scale factor C for each of our test criteria. We shall first examine λ_2. The degrees of freedom associated with $-2 \ln \lambda_2$ are $f = \frac{1}{2}p(p+1)(k-1)$, and so substituting into equation (37), we get:

$$A_1 = \frac{(2p^2 + 3p - 1)}{6\,(p+1)(k-1)} \left[\sum_{t=1}^{k} \frac{1}{n^{(t)}-1} - \frac{1}{n-k} \right]$$

and:

$$A_2 = \frac{(p-1)(p+2)}{6\,(k-1)} \left[\sum_{t=1}^{k} \left[\frac{1}{n^{(t)}-1} \right]^2 - \left[\frac{1}{n-k} \right]^2 \right]$$

Therefore, $A_2 - A_1^2$ can be written as:

$$\left[\frac{k}{k+1} \right]^2 \left[\frac{\gamma_2^{\,2}}{36\,(p+1)^2 v^2} \right] \left[6\,(p-1)(p+1)^2(p+2) \left[\frac{\gamma_3}{\gamma_2^{\,2}} \right] \left[\frac{k-1}{k} \right] - (2p^2 + 3p - 1) \right]$$

where the γ_i were defined earlier. As can be seen, $A_2 = 0$ when $p = 1$, and so will not be zero in multivariate situations. A_2 is positive for $p \geq 1$ except when $p = k = 2$ and the $n^{(t)}$ are equal for all t. In that case, $A_2 - A_1^2$ is almost exactly zero. In all other cases, $A_2 - A_1^2$ is positive, and so by the argument given earlier, we choose $C = (1-A_1)^{-1}$, that is:

$$C^{-1} = (1 - A_1) = 1 - \frac{(2p^2 + 3p-1)}{6\,(p+1)(k-1)}\left[\sum_{t=1}^{k} \frac{1}{n^{(t)}-1} - \frac{1}{n-k}\right], \qquad (38)$$

and so the quantity:

$$\left[\frac{(2p^2 + 3p-1)}{3(p+1)(k-1)}\left[\sum_{t} \frac{1}{n^{(t)}-1} - \frac{1}{n-k}\right] - 2\right] \ln \lambda_2$$

is distributed approximately as chi square with $\frac{1}{2}p(p+1)(k-1)$ degrees of freedom.

For λ_1, we have $f = \frac{1}{2}p(p+3)(k-1)$, and so:

$$A_1 = \frac{(2p^2 + 3p-1)}{6(p+3)(k-1)}\left[\sum_{t} \frac{1}{n^{(t)}-1} - \frac{1}{n-k}\right],$$

and:

$$A_2 = \frac{(p-1)(p+2)}{6(k-1)}\left[\sum_{t} \left[\frac{1}{n^{(t)}-1}\right]^2 - \left[\frac{1}{n-k}\right]^2\right]$$

Again, $A_2 = 0$ when $p = 1$ and is otherwise positive. By the same argument as used with λ_2, $A_2 - A_1^2 \geq 0$, and so we choose $C = (1-A_1)^{-1}$. Therefore, the quantity:

$$\left[\frac{(2p^2 + 3p-1)}{3(p+3)(k-1)}\left[\sum_{t} \frac{1}{n^{(t)}-1} - \frac{1}{n-k}\right] - 2\right] \ln \lambda_1 \qquad (39)$$

is distributed approximately as chi square with $\frac{1}{2}p(p+3)(k-1)$ degrees of freedom.

Finally, considering λ_3, we find that:

$$A_1 = \frac{(2p^2 + 3p-1)}{6k(p-1)}\left[\sum_{t} \frac{1}{n^{(t)}-1} - \frac{1}{n-k}\right]$$

and:

$$A_2 = \frac{p(p+1)(p+2)}{6k}\left[\sum_t \left[\frac{1}{n^{(t)}-1}\right]^2 - \left[\frac{1}{n-k}\right]^2\right].$$

By the same argument utilized earlier, we choose $C = (1 - A_1)^{-1}$ and so the quantity:

$$\left[\frac{n\,(2p^2 + 3p-1)}{6k\,(p-1)}\left[\sum_t \frac{1}{n^{(t)}-1} - \frac{1}{n-k}\right] - n\right] \ln L_3 \qquad (40)$$

is distributed approximately as chi square with $p(k-1)$ degrees of freedom.

F Approximation

In the same paper referred to earlier, Box (1949) also showed that if $A_2 - A_1^2$ is positive, and if:

$$f_1 = \frac{f + 2}{A_2 - A_1^2}\,, \qquad (41)$$

and if:

$$b = \frac{f}{1-A_1 - f/f_1} \qquad (42)$$

then $-(2 \ln \lambda)/b$ is distributed approximately as F with f and f_1 degrees of freedom. Because of the complexity of the expressions for $-(2 \ln \lambda)/b$ for our three test criteria, we shall not write them out in their general form, but shall illustrate their use with an example later in this paper.

Summary

In this chapter we have demonstrated methods for obtaining chi

square and F approximations to the distributions of our three test criteria using methods originally developed by Wilks (1946) and Box (1949). Although the computations necessary to use these approximations are tedious, they do allow us to make use of these test criteria to test a general range of hypotheses. Unfortunately we do not know how close these approximations are to the exact distribution. From results given by Wilks (1946) and Box (1949) with test criteria having similar distributions, we can gain some confidence in these approximations for $n^{(t)}$ large enough, say greater than 60 and for p and k not large. The real determination as to the validity of these approximations must await solution to the problem of finding a workable expression for their exact distribution. However, an approach possible today would be to perform an empirical study and compute the probability levels given by each of these approximations. This would necessitate sampling from known multivariate normal populations letting the sizes of the sample, the number of variates in each distribution, the distribution parameters, and the number of distributions vary. It should then be possible to evaluate those values of the three quantities (sample size, number of variates, and number of distributions) for which the three approximate distributions yield probability levels which agree and those for which the probability values disagree. One could then try to solve the exact distribution for those quantities producing disagreement among the probability levels yielded by the three approximations, and thereby determine which of these three approximations is closest to the exact distributions. Such a study should follow this one.

We have now developed the theory necessary for the testing of

the three null hypotheses outlined in CHAPTER I. The remainder of this study shall be devoted to an example utilizing the theory outlined in these first 5 chapters.

CHAPTER VI

A STUDY OF ELECTROCARDIOGRAPHIC MEASUREMENTS IN ACUTE MYOCARDIAL INFARCTION

This chapter will be devoted to an illustration of the application of the previously developed test criteria and their approximate distributions. The particular problem to be discussed is one from clinical medicine, and is concerned with electrocardiographic parameters in patients experiencing an acute myocardial infarction. With the advent of high speed computing techniques, several workers have studied the electrocardiogram in various illnesses. For example, Rikli, et al. (1961) and Evans (1962) reported differences in electrocardiographic measurements existing between normal and hypertensive persons; Cady, et al. (1961) reported results of an investigation of left ventricular hypertrophy; Caceres, et al. (1962) and Pipberger (1962) discussed the general problem of estimating electrocardiographic parameters using electronic computers; and Cady, et al. (1962) presented methods for the mass screening of electrocardiograms.

In recent years, there has been much interest in the determination of those factors related to prognosis in patients experiencing an acute myocardial infarction. Several large series of patients have been studied in an attempt to solve this problem, but thus far these studies have limited themselves to clinical parameters and electrocardiographic

diagnoses. It is the purpose of this study to investigate the standard clinical electrocardiographic measurements to determine whether one or more of these might be an important prognostic factor. The results of these other studies are summarized in a recent article by Hughes, et al. (1963).

The data for this study were obtained by reviewing records of all patients with a diagnosis of acute myocardial infarction admitted to the University of Oklahoma Medical Center (including the University, Veterans Administration, and Wesley Hospitals) between January, 1953 and January, 1963. The criteria necessary for inclusion of a patient in this study were characteristic QRST electrocardiographic changes, or autopsy demonstration of an acute infarction. It was also necessary that they have a readable electrocardiogram available. Using these criteria, it was possible to obtain 370 patients for the study.

The electrocardiograms used herein were taken by heart station personnel of the hospitals in the routine manner, and the measurements of interest were obtained from the paper reproductions of these electrocardiograms by manual measurement techniques. In every case, the electrocardiogram obtained at the time of admission was used.

In addition to the electrocardiogram, other information was obtained from each patient's record. These are listed in Table 1. Table 2 contains the particular electrocardiographic measurements obtained.

A complete report of a linear discriminant analysis performed on the "clinical measurements" is given by Hughes, et al. (1963). In this report, it was determined that age was one of the most important determinants of mortality following an acute myocardial infarction since

TABLE 1

CLINICAL MEASUREMENTS

Age

Sex

History of Previous Myocardial Infarction

History of Angina Pectoris

History of Diabetes Mellitus

History of Hypertensive Cardiovascular Disease

Systolic and Diastolic Blood Pressure

Pulse

Temperature

Presence of Pulmonary Infarction

Presence of Congestive Heart Failure

Presence of Shock

White Blood Cell Count

Erythrocyte Sedimentation Rate

Serum Glutamic Oxalacetic Transaminase

TABLE 2

ELECTROCARDIOGRAPHIC VARIABLES

X_1 : Longest PR Interval of Leads I, AVF, V4R, or VI

X_2 : Longest QRS Interval of Leads I, AVF, V4R, or VI

X_3 : Longest QT Interval of Leads I, AVF, V4R, or VI

X_4 : Ventricular Rate

X_5 : Maximum P Duration of Leads I, AVF, V4R, or VI

X_6 : Maximum P Height of Leads I, AVF, V4R, or VI

X_7 : Mean QRS Axis

X_8 : Duration of Q or QS Deflection In Region of Infarction

X_9 : Depth of Q or QS Deflection In Region of Infarction

X_{10}: Maximum Amplitude of R in V4, V5, or V6

X_{11}: Intrinsicoid Deflection in V4 or V5

X_{12}: Maximum ST Segment Displacement In Region of Infarction

the mortality rate increased with increasing age especially over 65 years. Therefore, in this study, all patients were placed into one of the following 4 groups, namely (1) patients under 65 who survived their acute infarction (i.e. lived for six weeks after the onset of their symptoms), (2) patients over 65 who survived, (3) patients under 65 who did not survive, and (4) patients over 65 who did not survive. By use of this classification, it should be possible to determine those electrocardiographic measurements which will differ between surviving and dying patients and at the same time account for differences between those over and under 65 years of age. Therefore, this study is concerned with 4 populations each consisting of the 12 variables listed in Table 2.

Preliminary Sample Information

The sample sizes obtained are given by the following: (a) for population 1 (surviving patients under 65), 176; (b) for population 2 (surviving patients over 65), 84; (c) for population 3 (dying patients under 65), 46; and (d) for population 4 (dying patients over 65), 64.

Table 3 contains the means for each of the 12 variables in the 4 samples. It was assumed that the distributions of these variables could be described by multivariate normal distributions.

Tables 4, 5, 6 and 7 give the variance-covariance matrices for each of the 4 samples. In our previous notation, these matrices are $\hat{V}^{(1)}$, $\hat{V}^{(2)}$, $\hat{V}^{(3)}$, and $\hat{V}^{(4)}$ respectively. $\hat{V}_o$ and $\hat{V}_a$ are shown in Tables 8 and 9, respectively.

All of the tables give the values expressed in the original measurement units which are listed in Table 3.

TABLE 3

AVERAGE VALUES FOR ALL SAMPLES

Variable	Sample				
	Living Under 65	Living Over 65	Dead Under 65	Dead Over 65	All Groups Combined
X_1 : Longest PR Interval (sec.)	.15	.15	.13	.13	.147
X_2 : Longest QRS Interval (sec.)	.09	.09	.10	.10	.095
X_3 : Longest QT Interval (sec.)	.37	.37	.34	.35	.360
X_4 : Ventricular Rate (beats)	80.00	79.60	97.50	90.10	83.880
X_5 : Maximum P Duration (sec.)	.07	.06	.06	.05	.060
X_6 : Maximum P Height (mm.)	.89	.97	1.01	.81	.910
X_7 : Mean QRS Axis (degrees)	22.20	1.80	20.40	11.90	15.600
X_8 : Maximum Q Duration (sec.)	.06	.07	.08	.06	.060
X_9 : Maximum Q Depth (mm.)	6.90	7.30	9.60	7.50	7.430
X_{10}: Maximum R Amplitude (mm.)	10.90	11.40	8.50	8.40	10.280
X_{11}: Intrinsicoid Deflection (sec.)	.04	.04	.05	.04	.042
X_{12}: ST Segment Displacement (mm.)	1.23	1.44	2.16	2.08	1.543

Statistical Analysis

The purpose of this study is to determine whether any differences exist among the four populations with respect to the twelve electrocardiographic measurements under consideration. Therefore, we shall first test H_1: the four populations have equal mean vectors and equal variance-covariance matrices. The formula for the test criterion, λ_1, for this hypothesis is given by equation (6). To calculate it, we need the following values:

$$\left|\hat{V}(1)\right| = 3.0810903 \quad (10^{-11}),$$
$$\left|\hat{V}(2)\right| = 5.4584317 \quad (10^{-10}),$$
$$\left|\hat{V}(3)\right| = 1.0459134 \quad (10^{-7}),$$
$$\left|\hat{V}(4)\right| = 1.8851860 \quad (10^{-8}),$$
$$\left|\hat{V}_a\right| = 1.0802156 \quad (10^{-8}),$$

and:

$$\left|\hat{V}_o\right| = 1.3017426 \quad (10^{-8}).$$

Using logarithms, we find that:

$$\Sigma \tfrac{1}{2} n^{(t)} \ln \left|\hat{V}(t)\right| = -3761.93945, \qquad (42)$$
$$\tfrac{1}{2} n \ln \left|\hat{V}_a\right| = -3393.57764, \qquad (43)$$

and:

$$\tfrac{1}{2} n \ln \left|\hat{V}_o\right| = -3359.06892. \qquad (44)$$

Therefore, from (42) and (44):

$$\ln \lambda_1 = -3761.93945 + 3359.06892$$
$$= -402.87053.$$

With the value of $\ln \lambda_1$, we are now ready to make use of the approximate distribution theory developed in CHAPTER V for this test criterion.

To use the simple chi square approximation we need:

$$- 2 \ln \lambda_1 = 805.74106.$$

The degrees of freedom associated with this value are $\frac{1}{2} p(p+3)(k-1) = \frac{1}{2}(6)(15)(3) = 270$. Making use of the equation:

$$\text{Chi Square} = \tfrac{1}{2}(X + \sqrt{2d-1})^2 \qquad (45)$$

where X is the standard normal deviate for the appropriate probability level and d is the degrees of freedom, we find that the tabulated value of the chi square variate for 270 degrees of freedom at the .05 probability level is 309.13163, and at the .01 probability level, it is 326.30672. Since the computed value exceeds this, we reject the hypothesis of no difference among the four populations of the mean vectors and variance-covariance matrices.

Now, to obtain the modified chi square approximation, we make use of equation (39). Substituting into the equation, we get as our statistic:

$$\left[(323/135)(.05311) - 2\right] \ln \lambda_1 = (-1.87824) \ln \lambda_1$$
$$= 756.68754.$$

Again, this value exceeds the tabulated chi square value for 270 degrees of freedom at the .01 probability level, and so, our conclusion to reject the null hypothesis remains unaltered.

To obtain the statistic approximately distributed as an "F" variable, we must first compute f_1 and b given by equations (40) and (41). Substituting, we find that:

$$f_1 = 272/.00383 = 71018.277,$$

and:

$$b = \frac{270}{.93647 - (270/71018.277)} = 289.4915.$$

Therefore, the test statistic $-(2 \ln \lambda_1)/b$ is equal to 2.78329. The tabulated "F" values for 270 and ∞ degrees of freedom are 1.17 and 1.25 for the .05 and .01 probability levels respectively. Since 2.78 is greater than 1.25, we again conclude that the null hypothesis is to be rejected, so all three of the approximations, simple chi square, modified chi square and F, yield the same conclusion.

Rejection of H_1 does not yield information as to whether the existing difference is among the mean vectors, the variance-covariance matrices, or both. It is, therefore, imperative to attempt to obtain such information if possible. The next logical step would be to test H_2: the four populations have equal variance-covariance matrices irrespective of the means. If this hypothesis is not rejected, we then know that any differences must involve only the means; however, if it is rejected, then we will know only that the variance-covariance matrices are not equal but we will have no information about the means. To my knowledge, there is no good solution to the multivariate problem of testing for differences among mean vectors given that the variance-covariance matrices are unequal.

Therefore, let us use the approximations derived in CHAPTER 5 to test H_2. The test criterion, λ_2, is given by equation (10), and using the calculations given in (42) and (43), we obtain:

$$\ln \lambda_2 = - 3761.93945 + 3393.57764$$

$$= - 368.36181.$$

Turning now to the approximate distributions, $-2 \ln \lambda_2 = 736.72362$ is

distributed approximately as chi square with $\frac{1}{2}p\ (p+1)(k-1) = 234$ degrees of freedom under H_2. Again making use of equation (45), we find the tabulated chi square values for 234 degrees of freedom and probability levels of .05 and .01 to be 270.99680 and 286.47802 respectively.

To obtain the modified chi square statistic, it is necessary to use equation (38) to obtain:

$$\left[(323/117)(.05311) - 2\right] \ln \lambda_2 = -1.85338 \ln \lambda_2$$
$$= 682.71441.$$

Finally for the "F" approximation, we need:

$$f_1 = 236/.06544 = 3606.357,$$

and:

$$b = \frac{234}{.92667 - (234/3606.357)} = 271.52156.$$

Therefore:

$$(-2 \ln \lambda_2)/b = 2.71331.$$

The tabulated "F" values for 234 and ∞ degrees of freedom at the .05 and .01 probability levels are 1.17 and 1.25 respectively.

As with H_1, the conclusions yielded by use of the three approximations are the same, namely, to reject the hypothesis of equality of the four population variance-covariance matrices.

As was pointed out earlier, it is not possible to adequately test for equality of the four mean vectors; however, if we visually compare the sample values given in Table 3, we see that the only sizeable differences occur in the variables X_4 (ventricular rate), X_7 (mean QRS axis), X_9 (maximum depth of Q), X_{10} (maximum amplitude of R), and X_{12} (maximum ST segment displacement). Considering X_4, it seems that

the two samples from dying patients had faster ventricular rates than the two living groups. There does not seem to be a relationship with age. This difference is probably a reflection of shock since no patients in our group who developed shock survived. All of these people had rapid pulses (i.e. over 100), and so would tend to increase the average. The difference in mean QRS axis seems to represent an age related rather than a mortality related phenomenon. This tendency towards a leftward shift of the QRS axis with increasing age has been reported by Hiss (1960), and is probably of no significance in mortality prediction. The depth of the Q wave is a very gross measure of the size of the infarcted area of the myocardium. In this study, there is an apparent tendency for the dying patients to have a deeper Q wave than those who survived. Whether differences of this magnitude are of clinical importance is debatable since the depth of the Q wave is influenced by many factors including electrode placement, and spatial orientation of the heart in the chest. These same comments are also applicable to the ST segment displacement since it is also a gross measure of the size of the infarcted area. It appears that there is a smaller R amplitude in the dying group as compared to the survivors. This also may be due to the influence of the patients in shock.

Let us now consider the variances of the twelve variables in the four samples. Here, we see large differences occurring between the dying and living groups in all variables except possibly the QT interval. This is also apparently true of the covariances as well. In every case except for the R wave amplitude, the dying groups are more variable than the living. This finding is compatible with an increased incidence of

other cardiac defects (as for example, conduction and rhythm abnormalities) in the dying group. One would of course, anticipate that the incidence of death would increase with the presence of other cardiac abnormalities. However, this finding is also compatible with the possibility that many of the patients who died had measurements near the extremes of the "normal ranges" and that a combination of several "borderline" measurements might indicate a poor prognosis. Also, these findings could merely represent sampling errors in that the dying samples might not truly represent the populations from which they were obtained and therefore, these variance estimates are too high. Finally, it may be that patients who do not survive may be more electrocardiographically variable than those who do survive, and therefore, this higher inter-patient variation may be a reflection of a higher intra-patient variability. A second larger study aimed specifically at answering these questions should be performed before a final decision is made.

In summary, application of the statistical theory for the testing of three null hypotheses concerning the mean vectors and variance-covariance matrices of four multivariate populations of electrocardiographic measurements resulted in rejection of the hypotheses of equality of both the mean vectors and variance-covariance matrices and of equality of the variance-covariance matrices irrespective of the means. Examination of these matrices revealed that, in general, the dying groups were more variable in all of the measurements except the QT interval. Possible explanations for this were discussed, but the most likely explanation is that these differences reflect an increased incidence of cardiac complications such as arrythmias and conduction abnormalities

in the dying patients. However, further studies involving more patients will be necessary before a definite answer can be given.

TABLE 4

VARIANCE-COVARIANCE MATRIX

Sample 1: Living, Under 65						
	X_1	X_2	X_3	X_4	X_5	X_6
X_1	.000961	.000045	.000044	-.107475	.000155	.001392
X_2		.000257	.000027	.030610	.000035	.000283
X_3			.003040	-.382277	.000040	-.000413
X_4				300.9182	-.033675	.938600
X_5					.000296	.000192
X_6						.248200
X_7						
X_8						
X_9						
X_{10}						
X_{11}						
X_{12}						

TABLE 4 - Continued

Sample 1: Living, Under 65						
	X_7	X_8	X_9	X_{10}	X_{11}	X_{12}
X_1	-.091680	.000129	-.000272	-.007733	.000005	.000987
X_2	-.028150	-.000092	-.013890	.007464	.000045	.003779
X_3	.383380	-.000125	-.039141	.036841	.000001	-.000376
X_4	25.1290	.040866	20.7817	-20.0596	-.024205	2.1992
X_5	.082490	.000189	.003498	.009294	-.000001	.002873
X_6	2.2822	-.000761	.193900	-.136000	-.000498	.002100
X_7	2738.5408	.345475	83.9833	-27.7436	-.059946	8.3549
X_8		.002621	.288145	-.060189	.000004	.017224
X_9			101.3470	-18.1576	-.001102	6.5151
X_{10}				48.8965	.030839	-1.0585
X_{11}					.000163	.000071
X_{12}						1.7654

TABLE 5

VARIANCE-COVARIANCE MATRIX

Sample 2: *Living, Over 65*						
	X_1	X_2	X_3	X_4	X_5	X_6
X_1	.003306	.000072	-.000044	-.307585	.000809	.014882
X_2		.000233	.000068	-.031621	-.000025	-.000157
X_3			.003937	-.692452	.000110	-.005589
X_4				467.7136	-.107015	.104200
X_5					.000596	.006187
X_6						.389800
X_7						
X_8						
X_9						
X_{10}						
X_{11}						
X_{12}						

TABLE 5 - Continued

Sample 2: Living, Over 65						
	X_7	X_8	X_9	X_{10}	X_{11}	X_{12}
X_1	-.467537	.000248	.018341	-.076727	.000026	-.015148
X_2	-.046335	.000049	-.021176	.001885	.000041	.000786
X_3	-.407826	-.000145	-.008299	-.015270	-.000005	-.009014
X_4	174.0580	.090983	33.4909	-13.5888	-.014082	3.9545
X_5	-.036560	-.000235	-.059544	-.020555	-.000021	-.002177
X_6	-.102100	.002111	-.024600	-1.0376	.000793	-.094100
X_7	2798.4590	.247023	-27.6965	55.5556	.074211	-1.4005
X_8		.003323	.299576	-.072913	.001614	.017525
X_9			111.8856	-18.6237	.005306	4.1510
X_{10}				61.2180	.034249	-.890300
X_{11}					.000130	.000711
X_{12}						2.2890

TABLE 6

VARIANCE-COVARIANCE MATRIX

Sample 3: Dying, Under 65						
	X_1	X_2	X_3	X_4	X_5	X_6
X_1	.004020	-.000341	-.000334	.184816	.000512	.011722
X_2		.000645	-.000060	-.046376	-.000036	-.003935
X_3			.003026	-1.0468	.000126	-.000017
X_4				725.8982	-.123531	.383800
X_5					.000478	.005373
X_6						.367800
X_7						
X_8						
X_9						
X_{10}						
X_{11}						
X_{12}						

TABLE 6 - Continued

Sample 3: Dying, Under 65						
	X_7	X_8	X_9	X_{10}	X_{11}	X_{12}
X_1	1.5315	-.000450	.132541	-.065130	-.000035	.031520
X_2	-.307101	.000242	.008724	-.026367	.000189	.001472
X_3	-.271110	-.000088	-.086000	.026666	-.000589	-.022177
X_4	-270.2414	.193444	69.3950	-2.1990	.461196	4.4928
X_5	.555797	-.000179	.030338	-.030956	-.000013	.014856
X_6	20.9830	-.002933	1.0985	-.670800	.009587	.303400
X_7	4904.2513	-.856666	64.8406	-92.7681	.156961	52.9396
X_8		.004150	.525777	-.165777	-.001566	.004222
X_9			135.5768	-29.5198	-.190409	2.4754
X_{10}				40.1217	.048268	-2.7430
X_{11}					.007366	.015396
X_{12}						4.9437

TABLE 7

VARIANCE-COVARIANCE MATRIX

Sample 4: Dying, Over 65						
	X_1	X_2	X_3	X_4	X_5	X_6
X_1	.004851	.000026	.000243	-.000679	.001178	.020338
X_2		.000631	-.000098	-.012532	.000056	-.000706
X_3			.003865	-.556054	.000420	.003019
X_4				597.3712	-.008757	1.0824
X_5					.001045	.009874
X_6						.430800
X_7						
X_8						
X_9						
X_{10}						
X_{11}						
X_{12}						

TABLE 7 - Continued

Sample 4: Dying, Over 65						
	X_7	X_8	X_9	X_{10}	X_{11}	X_{12}
X_1	-.511357	-.000034	-.073101	-.027543	.000065	-.002001
X_2	-.129026	-.000088	-.042439	-.018891	-.000010	.001213
X_3	-.606670	.000002	-.003461	.013800	-.000088	.019717
X_4	-1.4355	.000987	.419399	-.070519	-.000600	-.040264
X_5	-.103485	.000309	.063149	-.006112	.000068	.003876
X_6	-7.1832	-.001328	.553300	-.430100	.001113	.076200
X_7	3495.8534	-.331610	-95.3485	62.0913	.317337	-11.3221
X_8		.002320	.258305	-.047362	-.000093	.006454
X_9			73.0024	-7.5769	-.027379	.770400
X_{10}				41.3615	.039981	-5.2319
X_{11}					.000041	-.009993
X_{12}						5.4393

TABLE 8

VARIANCE-COVARIANCE MATRIX

All Samples Pooled And Adjusted For Grand Mean ($\hat{V}_o$)						
	X_1	X_2	X_3	X_4	X_5	X_6
X_1	.002675	-.000090	.000167	-.201762	.000595	.009100
X_2		.000421	-.000083	.062103	-.000031	-.000467
X_3			.003523	-.673325	.000195	-.000979
X_4				521.4965	-.096556	.798000
X_5					.000566	.004035
X_6						.331400
X_7						
X_8						
X_9						
X_{10}						
X_{11}						
X_{12}						

TABLE 8 - Continued

All Samples Pooled And Adjusted For Grand Mean ($\hat{V}_o$)						
	X_7	X_8	X_9	X_{10}	X_{11}	X_{12}
X_1	.039097	.000003	.022135	-.012272	.000009	-.058530
X_2	-.983600	.000021	-.010332	-.014261	.000061	.006419
X_3	-.072389	-.000156	-.043544	.042088	-.000102	-.007964
X_4	3.6862	.129085	42.9710	-28.8832	.051436	6.3838
X_5	.125432	.000049	-.000194	.004396	.000016	.000065
X_6	2.1600	-.000069	.374000	-.415700	.001704	.030800
X_7	3262.3470	.035169	25.0516	-3.9598	.070287	6.8841
X_8		.002937	.320178	-.079566	-.000174	.016457
X_9			103.6011	-19.1231	-.022540	4.9710
X_{10}				51.9087	.034225	-2.8191
X_{11}					.001101	.000957
X_{12}						3.1839

TABLE 9

VARIANCE-COVARIANCE MATRIX

All Samples Pooled ($\hat{V}_a$)						
	X_1	X_2	X_3	X_4	X_5	X_6
X_1	.002599	-.000047	.000090	.149405	.000558	.009012
X_2		.000391	-.000043	.032704	-.000007	-.000508
X_3			.003439	-.616379	.000164	-.001048
X_4				480.1972	-.076472	.750500
X_5					.000539	.003935
X_6						.327700
X_7						
X_8						
X_9						
X_{10}						
X_{11}						
X_{12}						

TABLE 9 - Continued

All Samples Pooled ($\hat{V}_a$)						
	X_7	X_8	X_9	X_{10}	X_{11}	X_{12}
X_1	-.044194	.000029	.027404	.022845	.000012	-.002681
X_2	-.090986	.000001	-.013895	-.008868	.000056	.004433
X_3	-.059762	.000129	-.037528	.030914	-.000095	-.004720
X_4	-1.7757	.104734	38.0102	-21.4602	.041351	4.0807
X_5	.103160	.000059	.001441	-.000292	.000011	.001712
X_6	2.2662	-.000274	.345300	-.433600	.001503	.030500
X_7	3193.7945	.046063	25.0485	-2.6477	.066270	7.5130
X_8		.002914	.316168	-.073679	-.000188	.015079
X_9			102.8632	-18.3944	-.024923	4.7097
X_{10}				50.3845	.034640	-2.3809
X_{11}					.108781	.000647
X_{12}						3.0382

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