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A Nonparametric Multivariate Test for a Monotone Trend among k Samples

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Abstract

The nonparametric bivariate two-sample test of Bennett (1967) is extended to the multivariate k sample test. This test has been easily modified for a monotone trend among k samples. Often in applications it is important to consider a set of multivariate response variables simultaneously, rather than individually, and also important to consider testing k samples altogether. Different approaches of estimating the null covariance matrices of the test statistics resulted in the same limiting form. The multivariate k sample test is applied to the non-normal data of a randomized trial conducted for a period of four weeks in mental hospitals. The purpose of the trial is to compare the efficacy of three different interventions for a relief of the frequently occurring problems of constipation, caused as a side effect of antipsychotic drugs during hospitalization. The bowel movement status of patient for a week is summarized into a single severity score, and severity scores of four weeks comprise a four-dimensional multivariate variable. It is desirable with this trial data to consider a multivariate testing among k samples.

Keywords: U statistics, multivariate test, nonparametric test, severity scores.

1. Introduction

A daily habit is not only natural but necessary, and including physicians many persons regard a normal bowel habit as being at least one bowel movement per day (Elliot *et al.*, 1983). However, patients receiving drugs such as neurotoxic chemotherapeutic agents, narcotic analgesics, antidepressants, tranquilizers, and muscle relaxants have often faced with a significant problem of constipation. With no exception, schizophrenic inpatients who receive antipsychotic drugs have difficult or infrequent defecation. A randomized trial is planned for the evaluation of efficacy of nursing interventions of four weeks long for relieving these frequent adverse effects (Yang, 1992): (1) Patients were randomly divided into three groups among which one group is a control group; (2) patients in the first treatment group had fluid and 15 minutes daily exercises and patients in the second treatment group had dietary fiber supplements additionally, and finally control patients had neither muscle exercises nor dietary fiber supplements; (3) each patient's condition is monitored

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daily for four weeks, after the first two weeks of patient selection period. Therefore, in respect of the characteristic of these interventions, the effectiveness of intervention could be tested with an alternative that the two interventions are indeed more efficacious than no intervention at all. The outcome of intervention efficacy can be measured by bowel movements in each day, and the failure of defecation in each day is represented by a run of one, indicating no bowel movements that day. In order to test the improvements of bowel movements during the trial period, scores were computed for each patient based on runs of no bowel movements every week, and thus a multivariate scores of four weeks are obtained for three intervention groups, in which one group is control. These scores appear to be definitely non-normal.

We propose a nonparametric multivariate test for difference among k samples. The multivariate scores of three intervention groups are tested for a general alternative, but can simply be modified to test for a monotone trend. As related works, Dietz and Kileen (1981) proposed a test for a time trend based on Kendall's τ statistic by incorporating changes in each continuous variable over the course of the experiment. However, this multivariate test of Dietz and Kileen (1981) is a case of a single sample. Earlier, Bennett (1967) proposed a nonparametric bivariate two-sample test. Our nonparametric statistic corresponds to an extension of Bennett's (1967) bivariate two-sample test to a multivariate k sample case for a general alternative. Related work is found in Dietz (1989) who proposed multivariate Jonckheere's (1954) trend test, not a multivariate test under a general alternative. Other nonparametric approaches to multivariate tests, that are related to the generalized median of Oja (1983), have been proposed based on multivariate signs and ranks in the sphere (Randles, 2000; Oja and Randles, 2004). In the multivariate test proposed in this paper, the covariance matrix needs to be derived when there are more than two treatment groups under consideration, and the covariance matrix is presented in Theorem 2.1 in Section 2. A monotone trend alternative among k samples can also be conceived and its test statistic is presented in Section 4.

2. Multivariate k-Sample Test

Let $\mathbf{X}_{ij} = (x_{ij1}, x_{ij2}, \ldots, x_{ijp})^T$ be a $p \times 1$ vector of observations on p variables for the i^{th} subject in treatment j, $j = 1, \ldots, k$, $i = 1, \ldots, n_j$. Assume that X_{ij}'s are independent with continuous distribution functions $F(\mathbf{x})$ and the marginal distribution functions, $F_j^{(1)}(x), \ldots, F_j^{(p)}(x)$, $j = 1, \ldots, k$. We consider the null hypothesis

$$H_0 : F_1(\mathbf{x}) = F_2(\mathbf{x}) = \cdots = F_k(\mathbf{x})$$

and the general alternative hypothesis

$$H_a : F_j(\mathbf{x}) \neq F_{j'}(\mathbf{x}), \quad \text{for at least two treatments } j \text{ and } j', \text{ for } \ j, j' = 1, \ldots, k.$$

Nonparametric test statistics mainly depend on the ranks of the data and in the multivariate test $N = \sum_{j=1}^{k} n_j$ observations of the k samples are arranged in an non-decreasing order in each coordinate. In a randomized clinical trial data that will be analyzed in this paper, k equals to 3, indicating the groups of control, experimental 1 and experimental 2, and p equals to 4 indicating four weeks of interventions; k samples are arranged from control, first treatment and second treatment groups. Low values indicate intervention efficacy as opposed to the general case that higher values are considered to indicate good outcomes from interventions, which is reflected in the definition of $\phi(a, b)$ below. For a test of the null hypothesis, we calculate $pk(k-1)/2$ Mann-Whitney U statistic

(Mann and Whitney, 1947) (called U statistic afterwards), $U_{uv} = (U_{uv}^1, U_{uv}^2, \ldots, U_{uv}^p)$ given by

$$U_{uv}^g = \sum_{i=1}^{n_u}\sum_{i'=1}^{n_v} \phi(x_{iug}, x_{i'vg}), \quad g = 1, \ldots, p, \;\; 1 \le u < v \le k, \tag{2.1}$$

where

$$\phi(a,b) = \begin{cases} 1, & \text{if } a > b, \\ 0, & \text{otherwise.} \end{cases}$$

First we describe the bivariate two-sample testing situation considered in Bennett (1967). For the variable g, U_{uv}^g is the number of times that the observations of treatment u precedes the observations of treatment v. The mean and variance of U_{uv}^g under H_0 are $n_u n_v/2$ and $n_u n_v(n_u + n_v + 1)/12$, respectively (Hollander and Wolfe, 1999). Bennett (1967) calculated the covariance of two correlated U statistics, U_{uv}^1 and U_{uv}^2 of variable 1 and 2 that are observed on the same subject. It is based on conditional probabilities, which is equivalent to the concordance probabilities of Kendall (1962). The covariance is

$$C\left(U_{uv}^1, U_{uv}^2\right) = \frac{1}{2}n_u n_v \pi_1 + \frac{1}{2}n_u n_v(n_u + n_v - 2)\pi_2 - \frac{1}{4}n_u n_v(n_u + n_v - 1), \tag{2.2}$$

where (y_{i1}, y_{i2}), $i = 1, \ldots, n_u + n_v$ is a bivariate random vector when each component represents the combined sequence of $(n_u + n_v)$ observations from two independent variates (x_{iu1}, x_{iv1}) and (x_{iu2}, x_{iv2}), and

$$\pi_1 = \{y_{i2} < y_{i'2} \,|\, y_{i1} < y_{i'1}\}, \tag{2.3}$$

$$\pi_2 = \{y_{i2} < y_{i''2} \,|\, y_{i1} < y_{i'1}\}. \tag{2.4}$$

The correlation coefficient estimate from (2.2) is then defined

$$r = \frac{3t}{(n_u + n_v + 1)} + \frac{6(n_u + n_v - 2)}{(n_u + n_v + 1)}\left(p_2 - \frac{1}{2}\right) \tag{2.5}$$

in terms of the corresponding estimate, t of Kendall's τ-coefficient ($\tau = 2\pi_1 - 1$) and the estimate, p_2 of (2.4).

Now we consider the k sample testing situation. When we take into account of the covariance of U-statistics, specifically between U_{uv}^g and $U_{uv}^{g'}$ for any two variables g and g' among k variables, the concordance probabilities of Kendall (1962) can be applied again, because the calculation of these probabilities is based on the marginal distribution function $F^{(g,g')}(x,y)$, where x and y indicate variables for g and g'-coordinates respectively, and the covariance depends on the common assumed distribution $F.$ under H_0. We define the concordance probabilities of two types from p variables over k treatments as follow: For $1 \le g \ne g' \le p$,

$$\pi_1^{gg'} = \{w_{ig'} < w_{i'g'} \,|w_{ig} < w_{i'g}\}, \tag{2.6}$$

$$\pi_2^{gg'} = \{w_{ig'} < w_{i''g'} \,|w_{ig} < w_{i'g}\}, \tag{2.7}$$

where $(w_{ig}, w_{ig'})$, $i = 1, \ldots, N = (\sum_{j=1}^k n_j)$ represents N observations from the k combined sequence of the variates $(x_{i1g}, \ldots, x_{ikg})$ and $(x_{i1g'}, \ldots, x_{ikg'})$. The covariance between U_{uv}^g and $U_{uv}^{g'}$ is similar to the covariance formula of (2.2) and is given by

$$\text{Cov}\left(U_{uv}^g, U_{uv}^{g'}\right) = \frac{1}{2}n_u n_v \pi_1^{gg'} + \frac{1}{2}n_u n_v(n_u + n_v - 2)\pi_2^{gg'} - \frac{1}{4}n_u n_v(n_u + n_v - 1). \tag{2.8}$$

Theorem 2.1. *Under H_0, the covariances between U^g_{uv} and $U^{g'}_{st}$ for any $1 \le g, g' \le p$ and $u, v, s, t \in \{1, \ldots, k\}$ are*

$$(U^g_{uv}, U^{g'}_{st}) = 0, \qquad \text{for all distinct } u, v, s, t \in \{1, \ldots, k\}, \tag{2.9}$$

$$Cov(U^g_{uv}, U^g_{ut}) = \frac{n_u n_v n_t}{12}, \qquad \text{for } 1 \le u < v, t \le k,\ v \ne t, \tag{2.10}$$

$$Cov(U^g_{uv}, U^g_{su}) = \frac{-n_u n_v n_s}{12}, \qquad \text{for } 1 \le s < u < v \le k, \tag{2.11}$$

$$Cov(U^g_{uv}, U^g_{vt}) = \frac{-n_u n_v n_t}{12}, \qquad \text{for } 1 \le u < v < t \le k, \tag{2.12}$$

$$Cov(U^g_{uv}, U^g_{sv}) = \frac{n_u n_v n_s}{12}, \qquad \text{for } 1 \le u, s < v \le k,\ u \ne s, \tag{2.13}$$

$$Cov(U^g_{uv}, U^{g'}_{ut}) = \frac{n_u n_v n_t}{4}\left(2\pi_2^{gg'} - 1\right), \qquad \text{for } 1 \le u < v, t \le k,\ v \ne t,\ g \ne g', \tag{2.14}$$

$$Cov(U^g_{uv}, U^{g'}_{su}) = \frac{-n_u n_v n_s}{4}\left(2\pi_2^{gg'} - 1\right), \qquad \text{for } 1 \le s < u < v \le k,\ g \ne g', \tag{2.15}$$

$$Cov(U^g_{uv}, U^{g'}_{vt}) = \frac{-n_u n_v n_t}{4}\left(2\pi_2^{gg'} - 1\right), \qquad \text{for } 1 \le u < v < t \le k,\ g \ne g', \tag{2.16}$$

$$Cov(U^g_{uv}, U^{g'}_{sv}) = \frac{n_u n_v n_s}{4}\left(2\pi_2^{gg'} - 1\right), \qquad \text{for } 1 \le u, s < v \le k,\ u \ne s,\ g \ne g', \tag{2.17}$$

where $\pi_2^{gg'}$ is from (2.7).

Theorem 2.1 is proved in the Appendix.

To estimate the concordance probabilities, $\pi_1^{gg'}$ and $\pi_2^{gg'}$, arrange $\{(w_{ig}, w_{ig'}), i = 1, \ldots, N\}$ in ascending order, first for g coordinate and secondly for g' coordinate. Then the unbiased estimates of $\pi_1^{gg'}$ and $\pi_2^{gg'}$ are

$$p_1^{gg'} = \frac{2}{N(N-1)} \sum_{i=1}^{N-1} \sum_{i'=i+1}^{N} \phi(w_{ig}, w_{i'g})\, \phi(w_{ig'}, w_{i'g'}), \tag{2.18}$$

$$p_2^{gg'} = \frac{3}{N(N-1)(N-2)} \sum_{i=1}^{N-2} \sum_{i'=i+1}^{N} \sum_{\substack{i'' \ne i' \\ i'' > i}}^{N} \phi(w_{ig}, w_{i'g})\, \phi(w_{ig'}, w_{i''g'}). \tag{2.19}$$

From Theorem 2.1 and the concordance probability estimates, (2.18) and (2.19), an estimate of correlation coefficient between U^g_{uv} and $U^{g'}_{ut}$ is

$$r^{gg'}_{uv,ut} = \frac{3 n_v n_t \left(2p_2^{gg'} - 1\right)}{\sqrt{n_v n_t (n_u + n_v + 1)(n_u + n_t + 1)}}.$$

Let $\mathbf{U} = (U^1_{12}, \ldots, U^p_{12}, \ldots, U^1_{(k-1)k}, \ldots, U^p_{(k-1)k})^T$, $pk(k-1)/2 \times 1$ vector and $\mathbf{u}$ be the standardized $\mathbf{U}$, whose element is given by $(U^g_{uv} - 1/2 n_u n_v)/\{1/12 n_u n_v (n_u + n_v + 1)\}^{1/2}$.

The covariance matrix Σ of $\mathbf{u}$ is defined by

$$\begin{pmatrix} 1 & r^{12}_{12,12} & \cdots & r^{1p}_{12,(k-1)k} \\ r^{21}_{12,12} & 1 & \cdots & r^{2p}_{12,(k-1)k} \\ \vdots & \vdots & \ddots & \vdots \\ r^{p1}_{(k-1)k,12} & r^{p2}_{(k-1)k,12} & \cdots & 1 \end{pmatrix}$$

By Theorem 7.1 of Hoeffding (1948), the joint distribution of the standardized $\mathbf{U}$ statistic, $\mathbf{u}$, is asymptotically mutilvariate normal distribution, as n_j for all j increase to indefinity. Under H_0, $\mathbf{u}^T\Sigma^{-1}\mathbf{u}$ is asymptotically $\chi^2(pk(k-1)/2)$, if Σ is of full rank. If Σ is of rank $q < pk(k-1)/2$, then $\mathbf{u}^T\Sigma^{-}\mathbf{u}$, where Σ^{-} is any generalized inverse of Σ, is asymptotically $\chi^2(q)$.

3. Ties

Ties were not considered in Section 2 of the multivariate k-sample test, and here we consider the test statistic with ties. It is related to the work of Dietz (1989), who derived the coordinate-wise Jonckheere test statistic, which is equivalent to a sum of U statistics. If there are ties among x_{ijg}'s, the ϕ function in the U statistic of (2.1) is replaced with ϕ^* function defined by

$$\phi^*(a,b) = \begin{cases} 1, & \text{if } a > b, \\ \frac{1}{2}, & \text{if } a = b, \\ 0, & \text{otherwise.} \end{cases}$$

Under H_0, although ties in the x_{ijg}'s do not affect the mean of U^g_{uv}, its variance is reduced to

$$\begin{aligned} \text{Var}^*(U^g_{uv}) = \Bigg[& \frac{n_u n_v(n+1)}{12} - \frac{1}{72}\left\{\sum_{i=1}^{h} t_i^g(t_i^g-1)(2t_i^g+5)\right\} \\ & + \frac{n_u(n_u-1)(n_u-2)+n_v(n_v-1)(n_v-2)}{36n(n-1)(n-2)}\left\{\sum_{i=1}^{h} t_i^g(t_i^g-1)(t_i^g-2)\right\} \\ & + \frac{n_u(n_u-1)+n_v(n_v-1)}{8n(n-1)}\left\{\sum_{i=1}^{h} t_i^g(t_i^g-1)\right\}\Bigg], \end{aligned} \tag{3.1}$$

where $n = n_u + n_v$, h denotes the number of tied groups, and t_i^g is the size of the i^{th} tied group for coordinate g (Hollander and Wolfe, 1999).

For the covariances, we begin by defining the centered version of the statistic U^g_{uv} for $g = 1, \dots, p$, $1 \le u < v \le k$

$$\begin{aligned} T^g_{uv} &= U^g_{uv} - \frac{n_u n_v}{2} \\ &= \sum_{i=1}^{n_u}\sum_{i'=1}^{n_v} \phi^*(x_{iug}, x_{i'vg}) - \frac{n_u n_v}{2} \\ &= \sum_{i=1}^{n_u}\sum_{i'=1}^{n_v} \frac{\text{sign}(x_{iug} - x_{i'vg})}{2}, \end{aligned}$$

where

$$\text{sign}(a) = \begin{cases} 1, & \text{if } a > 0, \\ 0, & \text{if } a = 0, \\ -1, & \text{if } a < 0. \end{cases}$$

Regarding the covariance between T^g_{uv} and $T^{g'}_{st}$ for any $1 \le u, v, s, t \le k$ and $1 \le g \ne g' \le p$, we can extract them from the conditional covariance of coordinate-wise Jonckheere statistics proposed by Dietz (1989) as follow:

$$\text{Cov}(T^g_{uv}, T^{g'}_{uv}) = \frac{n_u n_v}{4(N-2)}\left[\{N - (n_u+n_v)\}\hat{\tau}_{gg'} + \frac{(n_u+n_v-2)(N+1)}{3} r_{gg'}\right],$$

$$\begin{aligned}
\mathrm{Cov}(T^g_{uv}, T^{g'}_{ut}) &= \frac{n_u n_v n_t}{4(N-2)}\left(\frac{N+1}{3}r_{gg'} - \hat{\tau}_{gg'}\right), && \text{for } 1 \le u < v,\ t \le k,\ v \ne t,\\
\mathrm{Cov}(T^g_{uv}, T^{g'}_{su}) &= \frac{-n_u n_v n_s}{4(N-2)}\left(\frac{N+1}{3}r_{gg'} - \hat{\tau}_{gg'}\right), && \text{for } 1 \le s < u < v \le k,\\
\mathrm{Cov}(T^g_{uv}, T^{g'}_{vt}) &= \frac{-n_u n_v n_t}{4(N-2)}\left(\frac{N+1}{3}r_{gg'} - \hat{\tau}_{gg'}\right), && \text{for } 1 \le u < v < t \le k,\\
\mathrm{Cov}(T^g_{uv}, T^{g'}_{sv}) &= \frac{n_u n_v n_s}{4(N-2)}\left(\frac{N+1}{3}r_{gg'} - \hat{\tau}_{gg'}\right), && \text{for } 1 \le u,\ s < v \le k,\ u \ne s, \qquad (3.2)
\end{aligned}$$

where $\hat{\tau}_{gg'} = 2\sum_{i<i'}^{N} \mathrm{sign}\left[(w_{i'g} - w_{ig})(w_{i'g'} - w_{ig'})\right]/N(N-1)$ is a point estimate of Kendall's τ and $r_{gg'} = 3\sum_{i,i',i''}^{N} \mathrm{sign}\left[(w_{i'g} - w_{ig})(w_{i'g'} - w_{i''g'})\right]/(N^3 - N)$ is an estimate of Spearman's rho, $\rho_{gg'}$ and $\{(w_{ig}, w_{ig'})\}$ is the arranged vectors used in Section 2. The covariances in (3.2) do not change even when there are ties because $\phi^*(a) = 0$ for $a = 0$. However, the covariances in the same coordinate are already derived in (2.10)$\sim$(2.13), that are not provided by Dietz (1989).

Using Theorem 3.6.9 of Randles and Wolfe (1979), the joint limiting distribution of this statistic, $\Omega^g_{uv} = \sqrt{N}T^g_{uv}/n_u n_v$ is $pk(k-1)/2$ variate normal with mean $\mathbf{0}$ and covariance matrix induced from (3.2) and (2.10)$\sim$(2.13). Under H_0, Ω^g_{uv} has limiting variance $1/(12\lambda_u) + 1/(12\lambda_v)$, where $\lambda_j = \lim_{N\to\infty}(N/n_j)$, $0 < \lambda < 1$, $j = 1, \ldots, k$ (Dietz, 1989). The limiting null covariance between Ω^g_{uv} and $\Omega^{g'}_{u'v'}$, for $1 \le g,\ g' \le k$ is given by

$$\begin{aligned}
\mathrm{Cov}(\Omega^g_{uv}, \Omega^{g'}_{u'v'}) &= 0, && \text{if } u, u', v, v' \text{ are different},\\
&= \frac{1}{12\lambda_u}, && \text{if } u = u',\ v \ne v' \text{ and } g = g',\\
&= -\frac{1}{12\lambda_u}, && \text{if } u = v',\ v \ne u' \text{ and } g = g',\\
&= -\frac{1}{12\lambda_v}, && \text{if } v = u',\ u \ne v' \text{ and } g = g',\\
&= \frac{1}{12\lambda_v}, && \text{if } v = v',\ u \ne u' \text{ and } g = g',\\
&= \rho_{gg'}\left(\frac{1}{12}\lambda_u + \frac{1}{12}\lambda_v\right), && \text{if } u = u',\ v = v' \text{ and } g \ne g',\\
&= \frac{\rho_{gg'}}{12\lambda_u}, && \text{if } u = u',\ v \ne v' \text{ and } g \ne g',\\
&= -\frac{\rho_{gg'}}{12\lambda_u}, && \text{if } u = v',\ v \ne u' \text{ and } g \ne g',\\
&= -\frac{\rho_{gg'}}{12\lambda_v}, && \text{if } v = u',\ u \ne v' \text{ and } g \ne g',\\
&= \frac{\rho_{gg'}}{12\lambda_v}, && \text{if } v = v',\ u \ne u' \text{ and } g \ne g', \qquad (3.3)
\end{aligned}$$

where $\rho_{gg'}$ is Spearman's rho. The limiting null covariance of $\sqrt{N}U^g_{uv}/n_u n_v$, derived based on the covariance given in Theorem 2.1, has exactly the same form to the one given here.

4. Trend Test with Coordinate-wise Jonckheere Statistics

In the multivariate k-sample test of Section 2, we can generate the trend statistic using the coordinate-wise Jonckheere (1954) statistic as in Dietz (1954). In other words, the Jonckheere (1954) trend statistics based on the geometric severity scores of three groups are computed in each week and are summarized into a single statistic. The decreasing trend alternative hypothesis among g groups is

$$H_a : F_1^g(x) \geq F_2^g(x) \geq \cdots \geq F_k^g(x), \quad \text{for all } x \text{ and } g = 1, \ldots, p, \tag{4.1}$$

with at least one strict inequality for at least one g. A test against increasing trend alternative can be considered by reversing the directions of inequalities in (4.1), that is, $H_a : F_1^g(x) \leq F_2^g(x) \leq \cdots \leq F_k^g(x)$.

For coordinate-wise Jonckheere (1954) statistics, we define

$$J_g = \sum_{u<v} U_{uv}^g, \quad g = 1, \ldots, p, \quad \text{where } U_{uv}^g \text{ is from (2.1).}$$

Under H_0, J_g has mean $\sum_{u<v} n_u n_v/2$ and variance $V(J_g) = [N^2(2N+3) - \sum_{j=1}^k n_j^2(2n_j+3)]/72$. The covariance between J_g and $J_{g'}$ is

$$C(J_g, J_{g'}) = \sum_{u<v} \left(\frac{n_u n_v \hat{\tau}_{gg'}}{4} + \frac{n_u n_v}{4}(n_u + n_v - 2)\left(2p_2^{gg'} - 1\right) + \sum_{u<t<v} \frac{n_u n_v n_t}{2}\left(2p_2^{gg'} - 1\right)\right), \tag{4.2}$$

where $\hat{\tau}_{gg'}$ is the estimate of Kendall's tau $(= 2p_2^{gg'} - 1)$ and $p_2^{gg'}$ is from (2.19).

Standardized $p \times 1$ vector statistics of $\{J_g\}$, $\mathbf{J}$ has covariance matrix Σ_J, where Σ_J has diagonal and off-diagonal elements one and $C(J_g, J_{g'})/\sqrt{V(J_g)V(J_{g'})}$, respectively. By a large-sample approximation, under H_0, $\mathbf{J}^T \Sigma_J \mathbf{J}$ has $\chi^2(p)$ distribution, as $\min(n_1, \ldots, n_k)$ tends to infinity.

5. Application

5.1. Geometric severity scores derived from runs

In order to depict the degree of seriousness of daily defecation difficulty, we devised geometric scores based on daily recordings of no bowel movements. Adverse effects of psychotic drugs among schizophrenic inpatients are getting serious as hospitalized days are increasing and naturally the number and lengths of runs of no bowel movement days are increasing without any interventions. In order to quantify the large number of runs and longer lengths of runs, the following scoring method is proposed. First of all, score 0 is assigned if more than one bowel movement occurs each day. One assigns a score 1 from the point of no bowel movement for two consecutive days, and a higher score of 2^{l-2} is assigned, if there was no bowel movements for consecutive l days. We call this a geometric severity score, which increases geometrically, in a much faster rate than an arithmetic one.

5.2. Multivariate analysis

As an example, when a bowel movement for 10 days is recorded as SFFSFFFFSF(S: success and F: failure) for a patient, there are three runs of failure (*i.e.*, no bowel movement) are recorded with the corresponding scores 1, 4 and 0. Thus, the total score is $5(= 1+4+0)$. For another example of two sets of recordings of SFSSFFSFFF and SSSSFFFFFF, which demonstrate the same total number of six days of failure, the geometric severity scores differ however, with 3 and 16, respectively. In the latter set, the longer lengths of runs resulted in a higher severity score in spite of the same total number of runs in the two sets of recordings. A frequent relief of bowel movements in-between in the first set resulted in a low severity score. Therefore, this geometric score properly reflects the severity of patient's discomfort due to no defecation for several days. One can evaluate the efficacy of nursing interventions by analyzing four weeks' severity scores of three groups. The severity scores of four weeks are considered as observations of a four-dimensional variable.

Fifty six schizophrenic inpatients who demonstrated antipsychotic drug induced constipation during the first two weeks of pre-trial period were randomly assigned to three groups in the study of Yang (1992). Twenty patients were assigned to control group and 18 patients each to two experimental groups. Patients in the experimental group 2 was given additional dietary fiber supplements than those in the experimental group 1. The purpose of the analysis is to test whether the interventions considered in the trial are efficacious and to search for the most efficacious nursing interventions of relieving and preventing constipation induced by antipsychotic drugs. Bowel movement status of all patients were monitored everyday for four weeks after the initiation of intervention. The data of geometric severity scores of four weeks are to be analyzed in this paper. Each week of the bowel movement status of all 56 patients were transformed into geometric severity scores and based on the four-dimensional severity score vector. The multivariate statistics described in Section 2 were computed:

$$\begin{aligned}\mathbf{U} &= (U_{12}^1, \ldots, U_{12}^4, U_{13}^1, \ldots, U_{13}^4, U_{23}^1, \ldots, U_{23}^4)^T \\ &= (165, 193, 212, 258, 180, 202, 240, 301, 120, 81, 130, 125)^T,\end{aligned}$$

where indexes i, j of U_{ij}^g represents the order of control group and experimental group 1 and 2, for i or $j = 1, 2, 3$, respectively, and g represents the coordinate, corresponding to four weeks in our study. The standardized U statistic corresponds to

$$\mathbf{u} = (-0.439, 0.380, 0.936, 2.280, 0, 0.643, 1.754, 3.537, -1.329, -2.568, -1.012, -1.171)^T.$$

From these values, one can roughly guess intervention efficacy in the trial. An improvement at the fourth week is noted for the experimental group 1 compared to the control group with the values (−0.439, 0.380, 0.936, 2.280) of the standardized statistics. The standardized statistics value (0, 0.643, 1.754, 3.53) corresponding control versus experimental group 2 demonstrates a dramatic improvement among patients with the intervention as weeks pass by. But, no definite improvement is observed when the two experimental groups are compared. Now we proceed to an overall testing below.

First, the concordance probabilities of type 1 and 2, estimated from the data, range from 0.266 to 0.347 and from 0.284 to 0.319, respectively. The covariance matrix, Σ of $\mathbf{u}$, is obtained based on (2.8), (2.9)∼(2.17) and the test statistic $\mathbf{u}^T \Sigma^{-1} \mathbf{u}$ is found to be 21.211, and $P(\chi^2(12) > 21.211)$ is 0.047. Hence, there is a significant difference for the outcomes of four weeks among three intervention groups.

By considering ties, the multivariate test statistics, $\boldsymbol{\Omega}$, is given by

$$\begin{aligned}\boldsymbol{\Omega} &= (\Omega_{12}^1, \ldots, \Omega_{12}^4, \Omega_{13}^1, \ldots, \Omega_{13}^4, \Omega_{23}^1, \ldots, \Omega_{23}^4)^T \\ &= (0.780, 1.445, 1.486, 2.131, 1.226, 1.580, 2.276, 3.097, 0.554, 0.023, 1.109, 1.317)^T.\end{aligned}$$

Using the estimates of Kendall's τ and Spearman's ρ between coordinates, which range from 0.098 to 0.203 and from 0.151 to 0.323, respectively, the covariance matrix of $\boldsymbol{\Omega}$, Σ^* is obtained based on the variance of (3.1) and covariance of (3.2), (2.10)∼(2.13). The value of the test statistic, $\boldsymbol{\Omega}^T \Sigma^{*-1} \boldsymbol{\Omega}$, which is approximately $\chi^2(12)$ distribution, is 28.799 and thus $P(\chi^2(12) > 28.799)$ is 0.0042. In our data, there is an extensive tied observations. As the variance of the tied data is smaller than that of no tied case, the test statistic for the tied version, $\boldsymbol{\Omega}^T \Sigma^{*-1} \boldsymbol{\Omega}$ is larger than $\mathbf{u}^T \Sigma^{-1} \mathbf{u}$. Thus, the test result of the tied case is found to be more significant.

6. Discussion

The geometric severity score proposed in this paper for the analysis of data of Yang (1992) summarizes information on both the number and lengths of runs, and being unable to defecate for many consecutive days are more heavily reflected in higher scores than an irregular bowel habit. As it is difficult to know the true distribution function of these geometric severity scores under control and interventions, we relied on nonparametric approaches in testing the effectiveness of the nursing interventions. The purpose of this article was to develop a multivariate test of k samples based on ranks, by making minimal assumptions about the underlying distributions. This nonparametric multivariate test is very simple to compute for any dimension of multivariate vector and number of samples, as the covariances are simple functions of concordance probabilities, Kendall correlation coefficient and sample sizes.

In the analysis of patients' bowel movement data, the sum of severity scores of each week resulted in heavily tied groups. When the variance of the test statistic for a tied version is applied to this data, results were more significant than that of the statistic with the variance of not-considering tied data. One of the possible solutions is that discreteness will disappear or at least will be decreased if one generates the sum by accumulating more than one week's severity scores, and the resulting sum of severity scores will be generally continuous. Above all, the test statistic is easy to compute for a data of non-normal character in any practical dimension.

Appendix: Proof of Theorem

To derive the covariance matrix of the multivariate k sample test, one does not need to calculate the covariance of every combination between U^g_{uv} and $U^{g'}_{st}$ for any $1 \leq g,\ g' \leq p$ and $u, v, s, t \in \{1, \ldots, k\}$, but one simply needs to confine to two or three independent continuous bivariate cumulative distribution functions denoted by $F_j\,(x, y)$, $j = u, v, w$, instead of $F_j\,(\infty, \ldots, x_g, \infty, \ldots, x_{g'}, \infty, \ldots, \infty)$, where x and y indicate variables for g and g'-coordinates respectively and j's are the subscripts of treatment groups compared in the U statistics. The cumulative distribution $F_j(x, y)$, $j = u, v, w$ is defined as

$$F_j\,(x, y) = \int_{-\infty}^{x} \int_{-\infty}^{y} f_j\,(\omega_1, \omega_2)\,\mathrm{d}\omega_1\,\mathrm{d}\omega_2\,, \tag{A.1}$$

where f_j represents the respective density function.

Using the approache of Bennett (1967), we have the mean value of the U statistics of (2.1)

$$E(U^g_{uv}) = \sum_{i=1}^{n_u} \sum_{i'=1}^{n_v} E(\phi(x_{iug}, x_{i'vg})), \tag{A.2}$$

where $E(\phi(x_{iug}, x_{i'vg})) = \int F_v\,(x, \infty)\,\mathrm{d}F_u\,(x, \infty)$. For the g'-coordinate, $E(\phi(x_{iug'}, x_{i'vg'}))$ is calculated from the integration $\int F_v\,(\infty, y)\,\mathrm{d}F_u\,(\infty, y)$.

The covariance between U statistics of the same coordinate g, (2.10) is induced by the following formula, when $1 \leq u < v,\ t \leq k,\ v \neq t$:

$$\begin{aligned} C(U^g_{uv},\, U^g_{ut}) &= \sum_{i}^{n_u} \sum_{i'}^{n_v} \sum_{i''}^{n_t} C(\phi(x_{iug}, x_{i'vg}),\ \phi(x_{iug}, x_{i''tg})) \\ &\quad + \sum_{i \neq i''}^{n_u} \sum_{i'}^{n_v} \sum_{i'''}^{n_t} C(\phi(x_{iug}, x_{i'vg}),\ \phi(x_{i''ug}, x_{i'''tg})), \end{aligned} \tag{A.3}$$

where

$$C\left(\phi(x_{iug},x_{i'vg}),\,\phi(x_{iug},x_{i''tg})\right)=\int F_v\,(x,\infty)F_t\,(x,\infty)\,\mathrm{d}F_u\,(x,\infty)$$
$$-\left[\int F_v\,(x,\infty)\,\mathrm{d}F_u\,(x,\infty)\right]\left[\int F_t\,(x,\infty)\,\mathrm{d}F_u\,(x,\infty)\right],\quad (A.4)$$
$$C(\phi(x_{iug},x_{i'vg}),\,\phi(x_{i''ug},x_{i'''tg}))=0.$$

By using $F = F_u = F_v = F_t$ under H_0, we have $\int F^2(x,\infty)\mathrm{d}F(x,\infty) = 1/3$ and $\int F(x,\infty)\mathrm{d}F(x,\infty) = 1/2$ in the previous integration. Hence, $C(U^g_{uv}, U^g_{ut}) = n_u n_v n_t/12$.

For the coordinate g', the covariance between U statistics in (2.11) is calculated as following: For $1 \le s < u < v \le k$,

$$C\left(U^{g'}_{uv},U^{g'}_{su}\right)=\sum_{i}^{n_u}\sum_{i'}^{n_v}\sum_{i''}^{n_s}C(\phi(x_{iug'},x_{i'vg'}),\,\phi(x_{i''sg'},x_{iug'}))$$
$$+\sum_{i\neq i'''}^{n_u}\sum_{i'}^{n_v}\sum_{i''}^{n_s}C(\phi(x_{iug'},x_{i'vg'}),\,\phi(x_{i''sg'},x_{i'''ug'})),$$

where

$$C\left(\phi(x_{iug'},x_{i'vg'}),\,\phi(x_{i''sg'},x_{iug'})\right)=\int F_v(\infty,y)(1-F_s(\infty,y))\mathrm{d}F_u(\infty,y)$$
$$-\left[\int F_v(\infty,y)\mathrm{d}F_u(\infty,y)\right]\left[\int(1-F_s(\infty,y))\mathrm{d}F_u(\infty,y)\right],$$
$$C(\phi(x_{iug'},x_{i'vg'}),\,\phi(x_{i''sg'},x_{i'''ug'}))=0.$$

Hence, $C(U^{g'}_{uv}, U^{g'}_{su}) = -n_u n_v n_s/12$. Covariances of (2.12) and (2.13) are similarly calculated.

The covariance between U statistics of two different coordinates g and g' in (2.14) is, for $1 \le u < v,\, t \le k,\, v \neq t$,

$$C\left(U^{g}_{uv},U^{g'}_{ut}\right)=\sum_{i}^{n_u}\sum_{i'}^{n_v}\sum_{i''}^{n_t}C(\phi(x_{iug},x_{i'vg}),\,\phi(x_{iug'},x_{i''tg'}))$$
$$+\sum_{i\neq i''}^{n_u}\sum_{i'}^{n_v}\sum_{i'''}^{n_t}C(\phi(x_{iug},x_{i'vg}),\,\phi(x_{i''ug'},x_{i'''tg'})),$$

where

$$C\left(\phi(x_{iug},x_{i'vg}),\,\phi(x_{iug'},x_{i''tg'})\right)=\iint F_v\,(x,\infty)F_t\,(\infty,y)\,\mathrm{d}F_u\,(x,y)$$
$$-\left[\int F_v(x,\infty)\mathrm{d}F_u(x,\infty)\right]\left[\int F_t\,(\infty,y)\mathrm{d}F_u(\infty,y)\right],\quad (A.5)$$
$$C(\phi(x_{iug},x_{i'vg}),\,\phi(x_{i''ug'},x_{i'''tg'}))=0.$$

We can use the definition of Kendall's (1962, p.135) concordance probabilities in (A.5) and these probabilities ((2.6) and (2.7)) can be expressed as follows:

$$\pi_1=\iint F(x,y)\,\mathrm{d}F(x,y)\Big/\int F(x,\infty)\mathrm{d}F(x,\infty)$$
$$=2\iint F(x,y)\,\mathrm{d}F(x,y),\quad (A.6)$$

$$\pi_2 = \iint F(x,\infty)F(\infty,y)\,\mathrm{d}F(x,y) \Big/ \int F(x,\infty)\mathrm{d}F(x,\infty)$$
$$= 2\iint F(x,\infty)F(\infty,y)\,\mathrm{d}F(x,y). \tag{A.7}$$

Hence, $C(U_{uv}^g, U_{ut}^{g'}) = n_u n_v n_t(2\pi_2 - 1)/4$. The other covariances of (2.14)~(2.17) are similarly calclulated.

References

Bennett, B. M. (1967). On the bivariate generalization of the Wilcoxon two sample test and its relation to rank correlation theory, *Review of the International Statistical Institute*, **35**, 30–33.

Dietz, E. J. (1989). Multivariate generalizations of Jonckheere's tests

Dietz, E. J. and Kileen, T. J. (1981). A nonparametric multivariate test for monotone trend with pharmaceutical applications, *Journal of the American Statistical Association*, **76**, 169–174. for ordered alternatives, *Communications in Statistics - Theory and Methods*, **18**, 3763–3783.

Elliot, D. L., Watts, W. J. and Girard, D. E. (1983). Constipation: Mechanism and management of a common clinical problem, *Postgraduate Medicine*, **74**, 143–149.

Hoeffding, W. (1948). A class of statistics with asymptotically normal distribution, *Annals of Mathematical Statistics*, **19**, 293–325.

Hollander, M. and Wolfe, D. A. (1999). *Nonparametric Statistical Methods*, John Wiley & Sons, Inc., 2nd edition, 204.

Jonckheere, A. R. (1954). A distribution-free k-sample test against ordered alternatives, *Biometrika,* **41**, 133–145.

Kendall, M. G. (1962). *Rank Correlation Methods*, Griffin & Co., 3rd edition, 135.

Mann, H. B. and Whitney, D. R. (1947). On a test of whether one of two random variables is stochastically larger than the other, *Annals of Mathematical Statistics,* **18**, 50–60.

Oja, H. (1983). Descriptive statistics for multivariate distributions, *Statistics and Probability Letters*, **1**, 327–332.

Oja, H. and Randles, R. H. (2004). Multivariate nonparametric tests, *Statistical Science*, **19**, 598–605.

Randles, R. H. (2000). A simpler, affine-invariant, multivariate, distribution-free sign test, *Journal of the American Statistical Association*, **95**, 1263–1268.

Randles, R. H. and Wolfe, D. A. (1979). *Introduction to the Theory of Nonparametric Statistics*, John Wiley & Sons, Inc.

Yang, S. (1992). Effects of fluid intake, dietary fiber supplement and abdominal muscle exercises on antipsychotic drug-induced constipation in schizophrenics, *Journal of Catholic Medical College,* **45**, 1501–1514.