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The authors have declared that no competing interests exist. Conceived and designed the experiments: Received Sep 3; Accepted Oct Abstract We propose a new nonparametric test for ordered alternative problem based on the rank difference between two observations from different groups. These groups are assumed to be independent from each other. The exact mean and variance of the test statistic under the null distribution are derived, and its asymptotic distribution is proven to be normal. Furthermore, an extensive power comparison between the new test and other commonly used tests shows that the new test is generally more powerful than others under various conditions, including the same type of distribution, and mixed distributions. A real example from an anti-hypertensive drug trial is provided to illustrate the application of the tests. The new test is therefore recommended for use in practice due to easy calculation and substantial power gain. Introduction The problem of statistically testing the equality of three or more populations has been studied for decades, and many efficient nonparametric tests have been proposed. Kruskal and Wallis [1] introduced a nonparametric test for a general alternative where at least two independent populations differ in median under the alternative. This test does not identify the pairwise group differences or the number of these differences. Specific ordered alternatives, such as the trend among groups, may be more interesting to practitioners and researchers. Many tests have been proposed for different types of ordering alternatives, for example, the test proposed by Mack and Wolfe [2] for an umbrella alternative, the one proposed by Fligner and Wolfe [3] for a tree alternative, the Cochran-Armitage test [4] , [5] for a monotonic alternative with binary endpoints, and the Jonckheere-Terpstra JT test [6] , [7] for a monotonic alternative with continuous endpoints. The monotonic ordering problem with continuous endpoints occurs frequently in a wide range of statistical and medical applications [8] , [9]. This problem has received considerable attention in the literature. After Jonckheere [6] and Terpstra [7] developed the nonparametric test for the nondecreasing ordered alternative based on the Mann Whitney MW testing procedure, many nonparametric tests have been developed for this problem based on the MW test or other tests. Recently, Neuhauser et al. But the power gain would vanish as the sample size increases. The Wilcoxon rank sum test was extended to the k-sample ordered problem by Cuzick [11] referred to as the CU test based on the the Wilcoxon rank sum test. The CU test is a special case of the linear rank test, and is a locally most powerful test for location shifts under the logistic distribution [12]. Later, Le [13] proposed a test for monotonic ordering alternatives analogous to the Kruskal Wallis test, which was shown to be equivalent to the CU test when the sample sizes were equal across groups. The numerical comparison among the JT test, the CU test, and the Le test was performed by Mahrer and Magel [14] , and they found that all three tests were comparable in terms of power. Most aforementioned tests are constructed on pairwise comparisons. More recently, Terpstra and Magel [15] proposed a nonparametric test based on simultaneous comparisons with one observation from each group. In addition, interested readers are referred to Kossler [16] , and Alonzo et al. In this article, we propose a new nonparametric test for the monotonic ordering problem based on the rank difference between two observations from different independent groups. The commonly used JT test statistic is calculated as the total number of pairs whose observation in the second group is greater than that in the first group. In addition to the sign of difference between two observations, the actual difference is also important to detect the ordered alternative. The actual difference can be measured by the rank difference in the nonparametric setting. The new nonparametric test captures not only the sign of the difference between observations, but also the value of the difference. We are the first to propose this new idea for detecting a monotonic ordering, and it can be readily extended to other important statistical problems. The remainder of this article is organized as follows. In Section 2, we introduce the proposed new nonparametric rank test, derive the exact mean and variance of the test statistic under the null hypothesis, and prove the asymptotic null distribution. In Section 3, we compare the performance of the proposed test and other commonly used

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nonparametric tests with regard to power under a wide range of conditions. A real example from an anti-hypertensive drug trial is given to illustrate the application of the nonparametric tests in Section 4. Section 5 is given to discussion and future work. Nonparametric tests The underlying distribution functions of independent populations are assumed to be absolutely continuous and of the form , where is the location parameter for the th group,. The total number of subjects in the study is , with th group, and. There is no difference among the populations under the null hypothesis, and the distributions under the monotone ordering alternative differ by their location parameters. Specifically, the hypotheses are.

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