Superiority inferences on individual endpoints following non-inferiority testing in clinical trials

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We consider the problem of drawing superiority inferences on individual endpoints following non-inferiority testing. Röhmel, Gerlinger, Benda and Läuter (2006) pointed out this as an important problem which had not been addressed by the previous procedures that only tested for global superiority. Röhmel et al. objected to incorporating the non-inferiority tests in the assessment of the global superiority test by exploiting the relationship between the two, since the results of the latter test then depend on the non-inferiority margins specified for the former test. We argue that this is justified, besides the fact that it enhances the power of the global superiority test. We provide a closed testing formulation which generalizes the three-step procedure proposed by Röhmel et al. for two endpoints. For the global superiority test, Röhmel et al. suggest using the Läuter (1996) test which is modified to make it monotone. The resulting test not only is complicated to use, but the modification does not readily extend to more than two endpoints, and it is less powerful in general than several of its competitors. This is verified in a simulation study. Instead, we suggest applying the one-sided likelihood ratio test used by Perlman and Wu (2004) or the union-intersection $t_{\max}$ test used by Tamhane and Logan (2004).

References

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