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Bonferroni and Holm approximations for Šidák and Holland–Copenhaver q -values

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Abstract. I describe the use of the Bonferroni and Holm formulas as approximations for Šidák and Holland–Copenhaver formulas when issues of precision are encountered, especially with q -values corresponding to very small p -values.

Keywords: st0300, parmest, qqvalue, smileplot, multproc, multiple-test procedure, familywise error rate, Bonferroni, Šidák, Holm, Holland, Copenhaver

1 Introduction

Frequentist q -values for a range of multiple-test procedures are implemented in Stata by using the package `qqvalue` (Newson 2010), downloadable from the Statistical Software Components (SSC) archive. The Šidák q -value for a p -value p is given by $q_{\text{sid}} = 1 - (1 - p)^m$, where m is the number of multiple comparisons (Šidák 1967). It is a less conservative alternative to the Bonferroni q -value, given by $q_{\text{bon}} = \min(1, mp)$. However, the Šidák formula may be incorrectly evaluated by a computer to 0 when the input p -value is too small to give a result lower than 1 when subtracted from 1, which is the case for p -values of 10^{-17} or less, even in double precision. q -values of 0 are logically possible as a consequence of p -values of 0, but in this case, they may be overliberal. This liberalism may possibly be a problem in the future, given the current technology-driven trend of exponentially increasing multiple comparisons and the human-driven problem of ingenious data dredging. I present a remedy for this problem and discuss its use in computing q -values and discovery sets.

2 Methods for q -values

The remedy used by the SSC packages `qqvalue` and `parmest` (Newson 2003) is to substitute the Bonferroni formula for the Šidák formula for such small p -values. This works because the Bonferroni and Šidák q -values converge in ratio as p tends to 0. To prove this, I show that for $0 \leq p < 1$,

$$dq_{\text{bon}}/dp = m \quad \text{and} \quad dq_{\text{sid}}/dp = m(1 - p)^{m-1}$$

and that the Šidák/Bonferroni ratio of these derivatives is $(1 - p)^{m-1}$, which is 1 if $p = 0$. By L'Hôpital's rule, it follows that the ratio $q_{\text{sid}}/q_{\text{bon}}$ also tends to 1 as p tends to 0.

A similar argument shows that the same problem exists with the q -values output by the Holland–Copenhaver procedure (Holland and Copenhaver 1987). If the m input p -values, sorted in ascending order, are denoted p_i for i from 1 to m , then the Holland–Copenhaver procedure is defined by the formula

$$s_i = 1 - (1 - p_i)^{m-i+1}$$

where s_i is the i th s -value. (In the terminology of Newson [2010], s -values are truncated at 1 to give r -values, which are in turn input into a step-down procedure to give the eventual q -values.) The remedy used by `qqvalue` here is to substitute the s -value formula for the procedure of Holm (1979), which is

$$s_i = (m - i + 1)p_i$$

whenever $1 - p_i$ is evaluated as 1. This also works because the two s -value formulas converge in ratio as p_i tends to 0. Note that the Holm procedure is derived from the Bonferroni procedure by using the same step-down method as is used to derive the Holland–Copenhaver procedure from the Šidák procedure.

3 Methods for discovery sets

The SSC package `smileplot` (Newson and the ALSPAC Study Team 2003) also implements a range of multiple-test procedures by using two commands, `multproc` and `smileplot`. However, instead of outputting q -values, `smileplot` outputs a corrected critical p -value threshold and a corresponding discovery set, defined as the subset of input p -values at or below the corrected critical p -value. The Šidák-corrected critical p -value corresponding to an uncorrected critical p -value p_{unc} is given by $c_{\text{sid}} = 1 - (1 - p_{\text{unc}})^{1/m}$ and may be overconservative if wrongly evaluated to 0. In this case, the quantity that might be wrongly computed as 1 is $(1 - p_{\text{unc}})^{1/m}$. When this happens, `smileplot` substitutes the Bonferroni-corrected critical p -value $c_{\text{bon}} = p_{\text{unc}}/m$. However, this is a slightly less elegant remedy in this case because the quantity $(1 - p_{\text{unc}})^{1/m}$ is usually evaluated to 1 because m is large and not because p_{unc} is small.

To study the behavior of the Bonferroni approximation for large m , we define $\lambda = 1/m$ and note that

$$dc_{\text{bon}}/d\lambda = p_{\text{unc}} \quad \text{and} \quad dc_{\text{sid}}/d\lambda = -\ln(1 - p_{\text{unc}})(1 - p_{\text{unc}})^\lambda$$

implying (by L'Hôpital's rule) that in the limit, as λ tends to 0, the Šidák/Bonferroni ratio of the two derivatives (and therefore of the two corrected thresholds) tends to $-\ln(1 - p_{\text{unc}})/p_{\text{unc}}$. This quantity is not as low as 1 but is 1.150728, 1.053605, 1.025866, and 1.005034 if p_{unc} is 0.25, 0.10, 0.05, and 0.01, respectively. Therefore, the Bonferroni approximation in this case is still slightly conservative for a very large number of multiple comparisons over a range of commonly used uncorrected critical p -values, but is less conservative than the value of 0, which would otherwise be computed.

This argument is easily generalized to the Holland–Copenhaver procedure. In this case, `smileplot` initially calculates a vector of m candidate critical p -value thresholds by using the formula

$$c_i = 1 - (1 - p_{\text{unc}})^{1/(m-i+1)}$$

for i from 1 to m and selects the corrected critical p -value corresponding to a given uncorrected critical p -value from these candidates by using a step-down procedure. If the quantity $(1 - p_{\text{unc}})^{1/(m-i+1)}$ is evaluated as 1, then `smileplot` substitutes the corresponding Holm critical p -value threshold

$$c_i = p_{\text{unc}}/(m - i + 1)$$

which again is conservative as $m - i + 1$ becomes large (corresponding to the smallest p -values from a large number of multiple comparisons), but is less conservative than the value of 0, which would otherwise be computed.

Newson (2010) argues that q -values are an improvement on discovery sets because, given the q -values, different members of the audience can apply different input critical p -values and derive their own discovery sets. The technical issue of precision presented here may be one more minor reason for preferring q -values to discovery sets.

4 Acknowledgment

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About the author

Roger B. Newson is a lecturer in medical statistics at Imperial College London, UK, working principally in asthma research. He wrote the `parnest`, `qqvalue`, and `smileplot` Stata packages.