

Correction

STATISTICS, GENETICS

Correction for “The harmonic mean p -value for combining dependent tests,” by Daniel J. Wilson, which was first published January 4, 2019; 10.1073/pnas.1814092116 (*Proc. Natl. Acad. Sci. U.S.A.* **116**, 1195–1200).

The author wishes to note the following, with apologies: “The paper erroneously states that the asymptotically exact test $\hat{p}_{\mathcal{R}} \leq \alpha_{|\mathcal{R}|} w_{\mathcal{R}}$ controls the strong-sense familywise error rate (ssFWER) at level α , when it should read $\hat{p}_{\mathcal{R}} \leq \alpha_L w_{\mathcal{R}}$.

“Additionally, the paper incorrectly stated that one can produce adjusted p -values that are asymptotically exact, as intended in the original Fig. 1, by transforming the harmonic mean p -value (HMP) with Eq. 4 before adjusting by a factor $w_{\mathcal{R}}^{-1}$. In fact, the HMP must be multiplied by $w_{\mathcal{R}}^{-1}$ before transforming with Eq. 4.

“In the above, $\mathcal{R}$ represents any subset of those p -values; $\hat{p}_{\mathcal{R}} = \left(\sum_{i \in \mathcal{R}} w_i \right) / \left(\sum_{i \in \mathcal{R}} w_i / p_i \right)$ is the HMP for subset $\mathcal{R}$; $|\mathcal{R}|$ gives the number of p -values in subset $\mathcal{R}$; L is the total number of individual p -values; w_i is the weight for the i th p -value, such that the weights sum to one, $\sum_{i=1}^L w_i = 1$; $w_{\mathcal{R}} = \sum_{i \in \mathcal{R}} w_i$ is the sum of weights for subset $\mathcal{R}$; and $\alpha_{|\mathcal{R}|}$ and α_L are significance thresholds provided by the inverse Landau distribution (Table 1).

“The first error originated on page 11 of the Supporting Information, which gave a general version of the closed testing procedure that controls the ssFWER (Eq. 37), but went on to erroneously state that ‘one can apply weighted Bonferroni correction to make a simple adjustment to Eq. 6 by substituting $\alpha_{|\mathcal{R}|}$ for α .’ This reasoning would only be valid if the subsets of p -values to be combined were preselected and did not overlap. However, this would no longer constitute a flexible multilevel test in which every combination of p -values can be tested while

controlling the ssFWER. The examples in Figs. 1 and 2 pursued flexible multilevel testing, in which the same p -values were assessed multiple times in subsets of different sizes, and in partially overlapping subsets of equal sizes. For the multilevel test, a formal shortcut to Eq. 37, which makes it computationally practicable to control the ssFWER, is required. The simplest such shortcut procedure is the corrected test above. One can show this is a valid multilevel test because

$$\begin{aligned} \text{If } \hat{p}_{\mathcal{R}} &\leq \alpha_L w_{\mathcal{R}} \\ \text{Then } \hat{p} &= (w_{\mathcal{R}} \hat{p}_{\mathcal{R}}^{-1} + w_{\mathcal{R}'} \hat{p}_{\mathcal{R}'}^{-1})^{-1} \\ &\leq w_{\mathcal{R}}^{-1} \hat{p}_{\mathcal{R}} \leq \alpha_L, \end{aligned}$$

an argument that mirrors the logic of Eq. 7 for direct interpretation of the HMP, which is not affected by this correction. The second error, which was similarly caused by my carelessness, occurred in the main text in the statement ‘Equivalently, one can compare the exact p -values from Eq. 4 with $\alpha w_{\mathcal{R}}$.’”

The article has been updated to correct the errors. Limited alterations to the text have been made where results are affected quantitatively. Fig. 1 is amended to show the $-\log_{10}$ adjusted harmonic mean p -value for sliding windows of sizes 10kb–50Mb, which in the corrected procedure are directly compared to the HMP significance threshold (gray dashed line). Fig. 2 is amended to show $-\log_{10}$ harmonic mean p -values and the multiple testing-corrected significance thresholds for the HMP (gray dashed lines). Table 1 is amended to update the title and heading of column 1. The *SI Appendix* text has been updated online. An updated version of the harmonicmeanp R package, version 3.0, has been released to address these errors, available at <https://cran.r-project.org/package=harmonicmeanp>.

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