Peng, Cheng

From:	em.pone.0.8682d2.c63bd78e@editorialmanager.com on behalf of PLOS ONE <em@editorialmanager.com>
Sent:	Friday, October 6, 2023 3:24 AM
To:	Peng, Cheng
Subject:	Invitation to re-review a revised paper - PLOS ONE PONE-D-23-22450R1 - [EMID:5705fbc64565e695]

Dear Dr. Peng,

Thank you for your previous review for *PLOS ONE* submission "Confidence interval comparison: Precision of maximum likelihood estimates in LLOQ affected data" (PONE-D-23-22450R1). Your comments were shared with the authors, who have now submitted a revised version of their manuscript. I would be grateful if you could review this revised submission and evaluate whether the authors have addressed your concerns and made the manuscript acceptable for publication. At the end of the submission PDF, you will find a response to previous reviewer comments from the authors, as well as a version of the revised manuscript with tracked changes, if available.

Manuscript #: PONE-D-23-22450R1
Title: Confidence interval comparison: Precision of maximum likelihood estimates in LLOQ affected data
Authors: Tanja Bülow; Ralf-Dieter Hilgers; Nicole Heussen
Article type: Research Article

The abstract is appended below, along with more detailed information about *PLOS ONE* and its publication criteria.
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With kind regards,
Dr. Harald Heinzl
Academic Editor

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Title: Confidence interval comparison: Precision of maximum likelihood estimates in LLOQ affected data
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Authors: Tanja Bülow; Ralf-Dieter Hilgers; Nicole Heussen

Abstract:
When data is derived under a single or multiple lower limits of quantification (LLOQ), estimation of distribution parameters as well as precision of these estimates appear to be challenging, as the way to account for unquantifiable observations due to LLOQs needs particular attention. The aim of this investigation is to characterize the precision of censored sample maximum likelihood estimates of the mean for normal, exponential and Poisson distribution affected by one or two LLOQs using confidence intervals (CI).
In a simulation study, asymptotic and bias-corrected accelerated bootstrap CIs for the location parameter mean are compared with respect to coverage proportion and interval width. To enable this examination, we derived analytical expressions of the maximum likelihood location parameter estimate for the assumption of exponentially and Poisson distributed data, where the censored sample method and simple imputation method are used to account for LLOQs. Additionally, we vary the proportion of observations below the LLOQs.
When based on the censored sample estimate, the bootstrap CI led to higher coverage proportions and narrower interval width than the asymptotic CI. The results differed by underlying distribution. Under the assumption of normality, the CI's coverage proportion and width suffered most from high proportions of unquantifiable observations. For exponentially and Poisson distributed data, both CI approaches delivered similar results. To derive the CIs, the point estimates from the censored sample method are preferable, because the point estimate of the simple imputation method leads to higher bias for all investigated distributions. This biased simple imputation estimate impairs the coverage proportion of the respective CI.
The bootstrap CI surpassed the asymptotic CIs with respect to coverage proportion for the investigated choice of distributional assumptions. The variety of distributions for which the methods are suitable gives the applicant a widely usable tool to handle LLOQ affected data with appropriate approaches.
