Response to AE's Report

We would like to thank the AE for the constructive suggestions and comments. In light of your comments, we have thoroughly revised the paper, which we believe has significantly improved its quality and presentation. Below, we outline the major changes and then provide a point-by-point response.

Major Changes

- 1. We have followed the AE's suggestions to polish the Section "Usage of the Package" significantly. Particularly,
 - In the revised Table 2, we have provided comprehensive explanations for all functions in our package, detailing their inference objectives and functionalities.
 - For each main function, we have now provided detailed explanations on how to determine the values for each argument, including the default values when not specified. Each argument is presented in a paragraph-by-paragraph format, with cross-references to theoretical formulas mentioned earlier in the article.
 - We have polished the presentation of code examples by adding detailed explanations of the simulated setup and interpretations of the obtained results.
- 2. We have followed the AE's suggestion and added a comparison between SIHR and the plug-in Lasso estimator, demonstrating the bias correction's effectiveness. The comparison is now presented in the section "Comparative Analysis of SIHR and Other Methods"; see Figure 1
- 3. Enhanced Real Applications Section: We have added a detailed overview of the data and presented the data structure. Additionally, we have polished the data section presentation and comprehensively discussed the obtained results.
- 4. **Coding:** Following the AE's suggestion, we have polished the code in our package on CRAN. The updates include but are not limited to consistent coding styles and splitting long functions into several smaller ones.
- 5. **Webpage:** We have also created a package website using pkgdown at SIHR Package, along with several detailed vignettes to enhance the accessibility and usability of our documentation.

1 Response to comments on the paper

1. The article describes the derivation of statistical tests and examples of how to use their implementation to examine effects in high-dimensional scenarios. The implementation relates to methods previously introduced by the authors in other (cited) articles. The package described in this article contains five key functions LF(), QF(), CATE(), InnProd(), Dist() implementing different scenarios for testing. Testing in high-dimensional scenarios (p >> n) is a real-life problem, and the article may be useful for those working with such data. But the description of the implementation's workarounds is poor and needs to be significantly expanded for a wider group of people to use this package responsibly. Currently, the paper is quite rich in theoretical introduction, but poor in the description of the package and how to use it. In the following review, I suggest elements that are worth expanding in this paper.

Response: Thank you very much for your appreciation of our work and for the constructive comments and suggestions. We have followed your suggestions to polish the paper and provide the point-to-point response in the following.

2. The paper is about the SIHR package, in that case the most important part of the paper is where the functionalities of this package are presented. Here it is the table 2 from page 7. But this table is very poor and doesn't say much. The description of the LF() function is 'Generate an LF object.' If this is the central table presenting the functionality of the package then it should definitely be better described.

Response: Thank you for pointing this out. We have followed your suggestions and fully revised Table 2. The updated Table 2, now on page 8, includes comprehensive explanations for all functions in our package, detailing their inference objectives and functionalities.

3. The code in this article should be formatted in a readable way. For example, at the beginning of page 8 is an example call to the LF() function without any spaces, line breaks, etc. This is a very unreadable way of showing the LF() function.

Response: Thank you for highlighting this issue. We have revised the example to follow your suggestion, ensuring proper formatting with adequate spacing and line breaks. Additionally, we have reviewed and improved the formatting of all other code examples throughout the manuscript. We have also included explanations and comments before each code snippet to enhance clarity and readability.

- 4. Descriptions of function arguments should be understandable to the average/lay user. For example, now the description starts with the argument 'loading.mat' to which one sentence is devoted. The description of each relevant argument should be more detailed with a discussion of how to determine the parameter. It is best to discuss the arguments paragraph by paragraph.
 - **Response:** Thank you for the suggestion. We have revised the descriptions to provide detailed explanations on how to determine the values for each argument, including the default values when not specified. Each argument is now presented in a paragraph-by-paragraph format. Additionally, we have implemented the same revisions for all other functions in the package to ensure clarity and comprehensiveness.
- 5. Table 3 provides a very brief recap of the various arguments. It is worth referring to the previously presented formulas in it. E.g. There is a rescale argument in the LF() function, how does it relate so the formulas presented in the first part of the paper?

Response: Thank you for your suggestion. We have revised the explanations of the function arguments to reference the theoretical formulas mentioned earlier in the article wherever applicable. For instance, the argument rescale now refers to Remark 1.

6. In the code snippets on page 8, the comments should not be in the code but in the main text. The text itself should describe with more detail what is happening in the snippet and why.

Response: Thank you for pointing out this matter. We have added comprehensive discussions between code segments to explain the simulation setup and interpret the obtained results. Additionally, we have implemented these changes across all examples featured in the article, ensuring that the main text provides detailed explanations for each code snippet.

7. When 'loading.mat' is introduced in the code on page 8 it would be useful to have a description of why this matrix is structured this way.

Response: Thank you for highlighting this point. The LF() function performs inference for $x_{\text{new}}^{\intercal}\beta$, where x_{new} denotes the future observation/loading, and β is the regression coefficient. The structure of the loading.mat is designed so that each column corresponds to a future observation x_{new} . This matrix structure optimizes computational efficiency by allowing the debiasing algorithm to process multiple linear functionals simultaneously; that is, when loading.mat contains multiple columns, the LF() function only requires computing the initial estimator once. Specifically, when loading.mat is set as the identity matrix of dimension p, where p represents the number of covariates, the LF() function conducts inference for all p individual regression coefficients concurrently. We have added this explanation in Remark 2 on page 8 when we explain the loading.mat argument.

8. At the beginning of page 9 are the results for the first example, but it would be necessary to compare them with some other method. Maybe with the "usual" LASSO method?

Response: Thank you for your suggestion. We have followed your suggestion and added a new section titled "Comparative Analysis of SIHR and Other Methods" starting on page 13. This section initially compares our approach to traditional plug-in Lasso methods to demonstrate the effectiveness of bias correction, as shown in the following Figure 1 (corresponding to Figure 1 on page 14 in the main article). Additionally, we compare our methods against other inference techniques implemented in other software packages. The results, presented in Table 3 on page 15, illustrate that our method ensures a unified guarantee of coverage across a wider range of settings while significantly enhancing computational efficiency.

9. Example 2 is mostly R code without comments, it is not very readable, the whole example should definitely be more described.

Response: Thank you very much for your suggestions. In the revised manuscript, we have added comprehensive discussions and comments between code snippets to explain the code setup and interpret the obtained results. Additionally, we have decided to remove the original Example 2 to maintain simplicity, keeping only one example for each main function.

10. At the end of page 9 is a comment on plugin estimators, it would be worth comparing these results with another approach, such as the LASSO method.

Response: Thank you for the recommendation. Please refer to the section titled "Comparative Analysis of SIHR" on page 13 of the main article, where we have incorporated simulation studies to compare our proposed estimator against the plug-in LASSO estimator, implemented by the package **glmnet**. Figure 1 (corresponding to Figure 1 in the main article) demonstrates

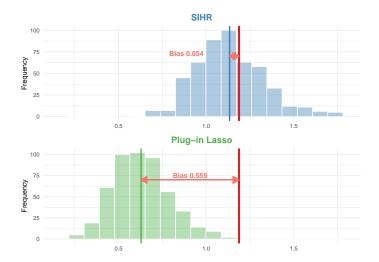


Figure 1: Comparison of the debiased estimates output by **SIHR** and plug-in Lasso estimates for $x_{\text{new}}^{\mathsf{T}}\beta$ in the logistic model with n=400. The upper panel shows the bias-corrected point estimates derived using our package **SIHR**, while the lower panel features the plug-in point estimates from the **glmnet** package. Red vertical lines indicate the target value $x_{\text{new}}^{\mathsf{T}}\beta=1.1875$. Biases between this target and the empirical means of the estimates are highlighted for each method.

that the plug-in LASSO estimators exhibit significant bias. In contrast, our bias-corrected SIHR estimators effectively correct the bias.

- 11. Table 4 lists the arguments of the QF() function, but it is worth describing them in more detail.

 Response: Thank you for your feedback. In the revised paper, we have followed your suggestions and provided clearer, more detailed explanations for each argument of the QF() function on page 10. We have also implemented similar improvements for all other functions.
- 12. The example on page 13 on 'Motif Regression' would benefit if the data itself is presented and discussed first.

Response: Thank you for your valuable input. We have revised this real data example to include a detailed overview of the data, followed by a comprehensive discussion to enhance the reader's understanding. In response to your suggestions, we have displayed several observations of the response variable along with a few covariates, providing a concise glimpse of the dataset. Additionally, we have extended this analysis and discussion to include the "Fasting Glucose Level Data" on page 16.

13. For Figure 1, it is worth having the code that generates it.

Response: Thank you for your suggestion. To maintain the main manuscript's simplicity and readability, we have included the relevant code for generating Figure 1 in the script files provided in the submission folder, along with other simulation code.

14. In the conclusion there is a comment "progress in debiasing inference methods", it is worth showing this bias empirically/simulatively.

Response: Thank you for noting this. In the section titled "Comparative Analysis of SIHR and Other Methods" on page 13, we have integrated simulation studies to contrast our estimator

with current state-of-the-art inference techniques implemented in other software packages. As shown in Table 3, our method ensures a unified guarantee of coverage across a wider range of settings while significantly enhancing computational efficiency.

15. The paper would benefit from being read by a native speaker in terms of the vocabulary used. For example, in the abstract it says "numerical examples" but it probably means "simulated examples."

Response: Thank you for your feedback. We have changed "numerical examples" to "simulated examples" in the abstract. Additionally, we have thoroughly polished the paper to improve its presentation and clarity.

16. On the editing side, it is worth ensuring that each sentence ends with a period, even if the sentence ends with a formula (see page 3 after formula 7 or on page 5).

Response: Thank you for your attention to this. We have made the necessary corrections throughout the paper to ensure that each sentence ends with a period, even when the sentence concludes with a formula.

17. The authors' description is missing the authors' addresses.

Response : Thank you for your observation. We have added the authors' addresses to the manuscript.

2 Response to the code comments

1. Currently, the code for key functions (such as LF()) is single long functions with lots of if's. It is worth trying to split this code into smaller functions that are easier to read and analyze.

Response: Thank you for your observation. We have revised our code, splitting the long functions into several smaller helper functions to improve readability and maintainability. The updated package is now available on CRAN.

2. The package is not very popular yet (judging by the number of downloads or stars on github), but perhaps this is due to sparse documentation. Better examples, more descriptions and vignettes should help.

Response: Thank you for your suggestion. We have built a comprehensive package website at SIHR Package, which includes several detailed vignettes designed to help users effectively utilize our tools.

3. Generating a page using pkgdown should help make the documentation more accessible. More vignettes will also help.

Response: Thank you for your suggestion. We have created a package website using pkgdown at SIHR Package, along with several detailed vignettes to enhance accessibility and usability of our documentation.