Author's response to reviews

Title: Simulation-based Estimation of Mean and Standard Deviation for Meta-analysis via Approximate Bayesian Computation (ABC)

Authors:

Deukwoo Kwon (DKwon@med.miami.edu)
Isildinha M Reis (ireis@med.miami.edu)

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Author's response to reviews: see over
**Title:** Simulation-based Estimation of Mean and Standard Deviation for Meta-analysis via Approximate Bayesian Computation (ABC)

**Response for Dr. Wan’s comments:**

(1) My major concern is about the simulation settings and model selections. There are too many parameters which are required to be pre-specified, which limits the applicability of the proposed method. For example, the acceptance percentage and the number of repeats are set as 0.01% and 20,000 in the simulation experiments. But the authors suggest using a smaller value of acceptance percentage and 50,000 or more iterations. What's the effect of different choices? Is there any evidence to justify the claim?

We thank your comment since it gives us an opportunity to further clarify how our method can be implemented.

Our simulation-based method needs the following specifications: (a) underlying data distribution, (b) prior uniform distributions for parameters of underlying distribution, and (c) acceptance percentage and number of iterations. We have added this information along with an example to Table 1. Also, with respect to (a) and (b) see answers to (2) and (4).

With respect to (c), our general guideline is set acceptance percentage 0.1% and number of repeats 50,000 or more, so that reliable estimates of mean and standard deviation will be based on top ≥50 simulation results with smaller Euclidean distance or any other distance measure. We corrected typo on page 17 where acceptance percentage should be 0.1% not 0.01%.

The reason we used 20,000 iterations in the simulation study is to get the results of the simulation study in a reasonable time frame. In our study we generated 200 datasets for each of 50 setting, defined by combination of 5 distributions and 10 sample sizes. In real data analysis, we recommend set acceptance percentage 0.1% and number of repeats 50,000 or more.

We have conduct sensitivity analysis for examining impact of value of acceptance percentage and the number of iterations on AREs. We report this on manuscript page 16-17 (also in Additional file 1). We used normal distribution with mean 50 and standard deviation 17 in S1, S2, and S3. We considered two acceptance percentages (0.1% and 0.01%) and three numbers of iterations (20,000, 50,000, and 100,000). All combinations showed comparable performance in estimating standard deviation and mean with ARE approaching zero as sample size increases. (See figure next page). In the standard deviation estimation, all combinations shows comparable performance except in S2. In S2, 0.01% acceptance percentage has lower AREs compared to those of 0.1% acceptance percentage.
Moreover, how does the proposed method perform for different settings of prior parameters? For each assumed distribution, the prior is required with some pre-specified parameters.

In order to implement our method, first we need to choose an underlying distribution. Given a set of summary statistics and the nature of the outcome variable, an educated decision about the underlying distribution can be made. The number of parameters to be estimated is determined by the chosen underlying distribution. For example, if exponential distribution is chosen, there is only one parameter (scale parameter $\lambda$); with normal or lognormal distribution, there are two parameters (location parameter $\mu$, and scale parameter $\sigma$).
The prior distribution for each parameter is always set to uniform distribution. Thus, we need to specify the minimum and maximum values for each prior uniform distribution, and these values can be derived from expected range of values for the outcome. Please see answer to (4) below on how to set minimum and maximum values for prior uniform distribution. Also, see example in revised Table 1.

(3) Since the underlying distribution is unknown, the model selection could be critical issue. The authors presented a solution based on Bayes factor. However, its description is separated into two parts (one in method section and the other in discussion section) for no reason and I did not quite understand it. Can the authors provide a toy example to show how to use summary statistics, say the minimum, the median, the maximum and the sample size, to select models.

In order to make it more clear, we move description on how to select underlying distribution from Method section to Discussion section just prior to the paragraph reporting simulation related to selection of underlying distribution. We also provided example.

(4) I suggest the authors provide a table listing all parameters which should be specified by users and provide a guidance about how to set those parameters. Is there a default setting with which the proposed method could perform well for most cases?

We added to revised Table 1 required settings for simulation-based estimation. There is no single default setting for every situation. However, once we have an educated decision about the underlying distribution, the setting of parameters is straightforward. For example, under normal and log-normal distributions, the minimum and maximum values for uniform distribution for location parameter μ, are easily specified as the available summary statistics (X_{min} and X_{max} in S1; X_{Q1} and X_{Q3} in S2 and S3). Under exponential, beta or Weibull, the prior distribution for scale and shape parameters is uniform distribution U(0, L), where L denotes some large number beyond X_{max} in S1 or X_{Q3} in S2 and S3. See example in revised Table 1.

In order to examine impact of prior distribution setting on AREs we also conducted sensitivity analysis and reported results in Discussion and in the next page. We used normal distribution with mean 50 and standard deviation 17 under S3, and considered three prior distributions, U(0,20), U(0,50), and U(0,100), for σ. Similar to the previous sensitivity analysis we used three numbers of iterations, 20,000, 50,000, and 100,000. We also reported AREs in estimating mean using these settings. In estimating SD, prior U(0,20) for σ gives negative AREs when sample size is <200 while other prior distributions (U(0,50) and U(0,100)) gives positive AREs, regardless of the number of iterations. The opposite direction of AREs between U(0,20) and other prior distributions is related to distance between σ and upper bound of uniform distribution. Since true σ 17 is close to upper bound 20, most accepted values for estimated SDs are lower than 17 and AREs are negative. For U(0,50) and U(0,100), majority of accepted values for
estimated SDs are larger than 17 and AREs are positive. However, as sample size increases, AREs of all three prior distributions converge to zero (See Additional file 2). Note that estimation of means is not affected by prior distribution for $\sigma$.

(5) I did not see the authors mention the availability of their solution. Can they make it available for testing?

Example R code for our method is provided in Additional file 3.
Response for Dr. Blum’s comments:

1. There are many multi-panel figures showing how errors decrease as a function of sample size for the various methods. It would be really nice to have an additional and synthetic figure that would provide the main message of the paper.

   We know that most figures are very busy with too many lines and symbols since we compared several methods. The main message of the paper is that simulation-based method is simple and provide very reliable estimates of mean and standard deviation.

2. In the abstract, I find that the description of the main results is unclear. Please clearly explain when ABC is beneficial compared to other approaches.

   We revised the abstract per suggestion.

3. Instead of selection the best-supported model, averaging over models might be an alternative option, easy to implement with ABC. Authors can discuss this option or even try it in their future research.

   We thank your comment about model averaging. We added in Discussion that we plan to conduct more thorough simulation study for evaluating performance of our simulation-based method in model selection and model averaging in the subsequent paper.

4. When describing the existing methods, please be more explicit about their assumptions.

   Both Hozo et al. and Bland methods have no distributional assumption. Want et al. method is based on normal distribution assumption. We revised our descriptions on pages 5-6.

5. Page 17, the citations to Marjoram et al. and Toni et al. do not follow the standard bracket style.

   We corrected citations.