Research Master's programme: Methodology and Statistics for the Behavioural, Biomedical and Social Sciences
Utrecht University

Master's Thesis Anaïs Fopma (6199356)
Title: A blended distance to define "people-like-me"
Date: 09-05-2022

Supervisors: Prof. Dr. Stef van Buuren, Dr. Gerko Vink & Mingyang Cai

Preferred journal of publication: Statistics in Medicine
Word count: —-

A blended distance to define "people-like-me"

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Summary

Curve matching is a powerful tool to predict the development of a child (the target) with the data of other children (donors). The technique relies on predictive mean matching, which matches donors that are most similar to the target based on the predictive distance. Even though this approach ensures high prediction accuracy, there are two disadvantages. Firstly, it requires users of curve matching to select a particular future time point to base the matches on. In some cases, it may be difficult to choose this time point. Secondly, the predictive distance may make matches look unconvincing, as the profiles of the matched donors can substantially differ from the profile of the target, even if they are close on the predicted time point. To counterbalance these disadvantages, similarity between the curves of the donors and the target can be taken into account when selecting donors. The objective of the current study is to do so by combining the predictive distance with the Mahalanobis distance, thus creating a 'blended distance' measure.

KEYWORDS:
Curve matching, predictive mean matching, donor selection, multiple imputation, distance measures, metrics

1 | INTRODUCTION

The first three years of childhood form a crucial stage in determining children's subsequent development and health outcomes.[1] For this reason, growth monitoring is considered to be an integral part of paediatrics. It can aid in the identification of problems in development such as growth stunting, and ensure timely treatment or intervention to improve the child's health.[2] However, growth monitoring solely provides insights in the past and current developmental stages of the child. Growth curve modeling, on the other hand, can be used to predict future development. It could therefore provide more specific answers to questions health professionals, parents, and insurance companies may have, such as: 'Given what I know of the child, how will it develop in the future?' and 'Does this child get the most effective treatment available?'[3]

1.1 | Curve matching

An approach currently used for growth curve modeling is curve matching. Curve matching[3] is a nearest neighbour technique for individual prediction that constructs a prediction by aggregating the histories of "people-like-me". Its aim is to predict the growth of a target child by using the data of other children that are most similar to the target child.

In order to select these donors, some form of similarity needs to be defined to match the donors to the target child. Therefore, the key question is: How are good matches obtained? The current approach uses predictive mean matching (PMM). PMM is a multiple imputation technique that makes use of an existing donor database, containing the growth data of children who are

older than the target child, and of which information at a later age is available. The first step is to fit a linear regression model on the donor database. Then, this model is used to predict the values for all donors and for the target at a certain point in the future, for example at 14 months. Finally, the distance between the predicted value of each of the donors and the predicted value of the target is calculated, which is referred to as the predictive distance. A number of donors – usually five - with the smallest predictive distance are selected as the best matches. Their growth curves are then plotted and point estimates can be calculated by averaging the measurements. The growth patterns of the matched children thus suggest how the target child might develop in the future.

1.2 | Alternative approach

PMM has proven to be promising in growth curve matching and the advantage of this techniques is its high prediction accuracy.[3][3] However, there are two reasons to move beyond the predictive distance used in PMM and investigate an alternative metric. Firstly, PMM requires users of curve matching to select a particular future time point to base the matches on (e.g. 14 months of age). In some cases, it may be difficult to choose this time point, especially when the 'future' is more vaguely defined as a time interval.[4] Secondly, the predictive distance may make the matches look unconvincing. The trajectories of the selected donors may all be close to the prediction for the target child at 14 months, but this does not imply that the histories are identical. After all, different profiles may lead to the same predicted value. Consequently, the curves of some of the matches may be quite far from the curve of the target child. Some users of curve matching feel that such discrepancies are undesirable, as these matches do not appear to be *people-like-me*.[4] It is useful to investigate these shortcomings not only for the purpose of improving growth prediction, but other applications of multiple imputation as well, such as patient recovery after an operation, prediction of longevity, and decision-making when multiple treatments are available.[3]

For the aforementioned reasons, the practical implementation and use of curve matching can in theory be improved by combining the predictive distance with another distance measure, thus creating a "blended distance" measure. Such a blended metric would take into account historical similarity between the donors and the target. For example, when blending the predictive distance with the Mahalanobis distance, more weight is given to similarities between units in the full predictor space. This would theoretically lead to selection of donors with profiles more similar to the target, and therefore to selection of true people-like-me. The objective of this study is to implement such a blended distance measure and to investigate its properties, blend ratio, and the validity of its resulting inferences.

2 | METHODS

2.1 | Blended metric

The blended distance measure to be evaluated is a weighted version of the predictive distance and the Mahalanobis distance. The predictive distance is the distance between the predicted value of a donor and the predicted value of the target at a particular future time point. The Mahalanobis distance is defined as the distance between two N dimensional points scaled by the variation in each component of the point. For example, if $\vec{x}$ and $\vec{y}$ are two points from the same distribution which has covariance matrix $\mathbf{C}$, then the Mahalanobis distance is given by

$$((\vec{x} - \vec{y})'\mathbf{C}^{-1}(\vec{x} - \vec{y}))^{\frac{1}{2}}. \tag{1}$$

Two potential versions of the blended metric will be compared: one that uses ranking and one that uses scaling. In theory, these two versions of the blended distance should yield similar results. However, the scaled version would be computationally more efficient. Both versions are included in this study to confirm that they produce similar results. I do think it might be useful to mention this here, because it is the main reason we used both versions right? I think I might otherwise get questions about the reason for using two different versions With the ranked blended metric, the predictive distance and the Mahalanobis distance are first calculated for each donor. Then, the k donors with a low value for both the predictive distance and the Mahalanobis distance are selected. In order to do so, the rank is calculated for the predictive distance PD and the Mahalanobis distance MD, where ties are randomly broken. The ranked blended distance RBD is given by:

$$RBD = p \cdot \text{rank}_{PD} + (1 - p) \cdot \text{rank}_{MD}, \tag{2}$$
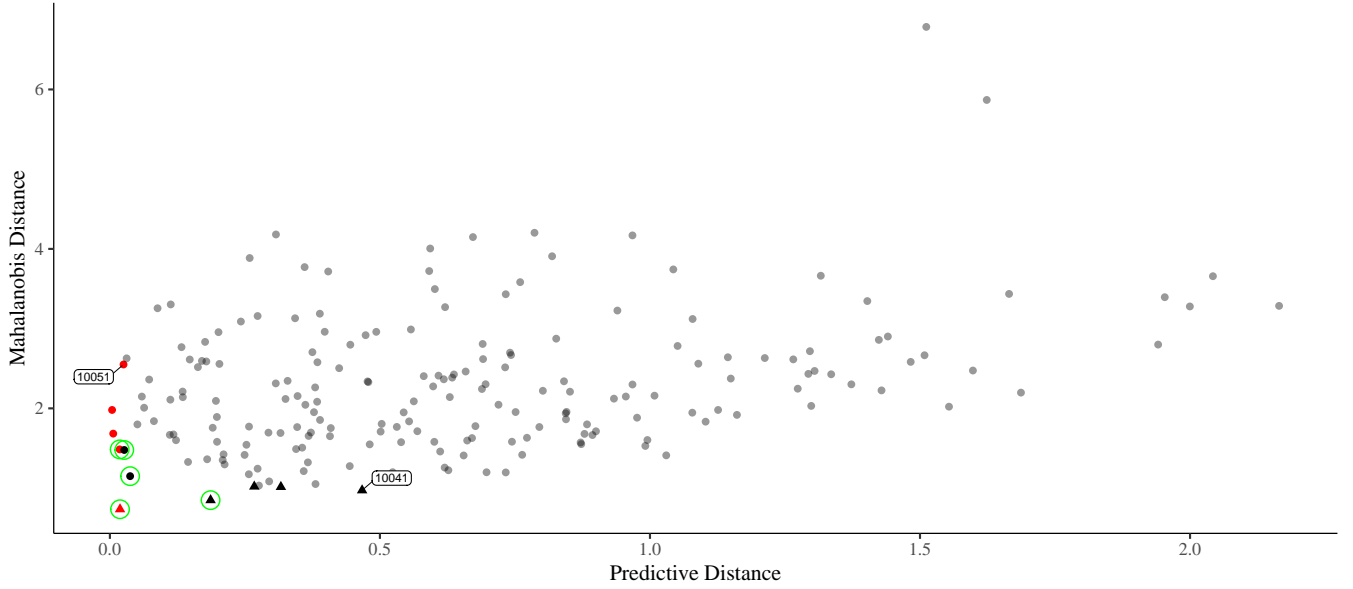
FIGURE 1 Mahalanobis distance plotted against predictive distance for each of the 199 donors. The donors in red are the five matches with the smallest predictive distance, the triangular donors those with the smallest Mahalanobis distance, and the donors circled in green those with the smallest blended distance.

where rank$_{PD}$ is the rank for the predictive distance PD, rank$_{MD}$ is the rank for the Mahalanobis distance MD, p is the blending factor (or weight) assigned to rank$_{PD}$, and $0 \leq p \leq 1$. The k donors with the lowest values on RBD are selected as the best matches.

The scaled blended metric is created similarly, but the predictive distance PD and the Mahalanobis distance MD are scaled before combining them. The scaled blended distance SBD is given by:

$$SBD = p \cdot \frac{PD - \bar{x}_{PD}}{\sigma_{PD}} + (1 - p) \cdot \frac{MD - \bar{x}_{MD}}{\sigma_{MD}}, \tag{3}$$

where $\bar{x}_{PD}$ is the mean of the predictive distances, σ_{PD} their standard deviation, $\bar{x}_{MD}$ is the mean of the Mahalanobis distances, and σ_{MD} their standard deviation.

As an example, the blended distance is illustrated in Figure 1. Here, the data of 200 children from the *Sociaal Medisch Onderzoek Consultatiebureau Kinderen* (SMOCK) study are used.[5] The first subject is taken as the target, the 199 other subjects as the donors. For all donors, the Mahalanobis distance for the measurements during the first six months of growth is calculated. In addition, the predictive distance between each donor and the target is calculated. In the figure, the Mahalanobis distance and predictive distance are plotted against each other. The red donors are the five matches with the smallest predictive distance, where especially subject 10051 has a large Mahalanobis distance. The triangular donors are the five matches with the smallest Mahalanobis distance, where especially subject 10041 has a large predictive distance. A weighted blended distance measure would balance the distance measures, such that the donors with a low value for both distance measures are chosen. These are circled in green.

2.2 | Simulations

Two simulations studies will be conducted. Each study is described in accordance with the ADEMP-structure for reporting simulation research.[6] The aims of each study, the different versions of the blended metric (i.e. the methods), the data-generating mechanisms, and the estimand and performance measures are discussed.

2.3 | Software

R version 4.1.2 (2021-11-01)[7] will be used to simulate the data and perform the analyses. The `mice.impute.pmm` function in the `mice`[8] package will be used to perform PMM and an adaptation of this function will be used to calculate the blended distance. Instructions and scripts to reproduce the simulation results are available in the research archive of this project.

3 | SIMULATION STUDY I

3.1 | Aims

The main objective of this simulation study is to investigate what the properties of the blended metric are. More specifically, I want to answer the following questions:

1. Does performance differ when donors are selected from a ranked as opposed to a scaled blended metric?

2. Does a blending factor of 1 yield results identical to those obtained by PMM (i.e. based on the predictive distance only)?

3. How is the performance of the blended metric related to the missingness mechanism, the proportion of missingness in the data, and the distribution of the data?

4. Do the conclusions under 3. differ for varying levels of correlation in the predictor space?

5. Is there a penalty from blending in terms of reduced predictability?

I expect that the ranked and scaled versions of the blended metric yield similar results, as donors with a high ranking will likely have a small value on the scaled corresponding distance, and vice versa. Furthermore, I expect that blending with a factor of 1 does indeed give the same results as PMM does, as this entails that full weight is given to the predictive distance. As pointed out before, PMM has been shown to result in high prediction accuracy. Therefore, I expect that the predictability of the blended distance will decrease as the blending factor favours the Mahalanobis distance. When the correlation in the data is low, the prediction model will fit poorly and I expect the blended metric to perform worse when more weight is given to the predictive distance. When the correlation in the data is high, the prediction model will fit better, and the prediction model will explain more variance in the outcome. In this case, I expect the blended metric to perform better when more weight is given to the predictive distance. Finally, I expect that the blended metric will perform worse in skewed data when more weight is given to the Mahalanobis distance.

3.2 | Metrics

For the blended metric, blending factors of respectively 1, 0.5, and 0 will be evaluated. A blending factor of 1 implies that the blended distance is equal to the predictive distance, whereas a weight of 0 implies that it is equal to the Mahalanobis distance. Therefore, a blending factor of 0.5 gives equal weight to both distance measures. PMM will be used as a reference in order to evaluate whether it does indeed obtain the same results as the blended metric with a blending factor of 1. Using PMM, both the ranking and scaling methods with three different blending factors each, this results in seven different versions of the blended metric to be evaluated.

3.3 | Data-generating mechanisms

In order to answer the previous questions, the blended distance measures are evaluated in simulated data that meet different conditions. All data are generated from one of 24 data-generating mechanisms, with equal means, but with varying missingness proportions, missingness mechanisms, distributions, and variance-covariance matrices. I explain the process of obtaining these data generating mechanisms below.

Three continuous predictor variables $\mathbf{X_1}$, $\mathbf{X_2}$, and $\mathbf{X_3}$ are defined and one continuous outcome $\mathbf{Y}$ is defined. The distribution of the data is varied over two conditions. For the first conditions, the data generating mechanism of the predictor space is a multivariate normal distribution, $\mathbf{X} = \mathcal{N}(\boldsymbol{\mu}, \Sigma)$, with mean vector $\boldsymbol{\mu} = [10, 10, 10]$. For the second condition, it is a strongly skewed multivariate distribution, which is obtained by transforming the predictors:[9] $\mathbf{X} = \mathbf{X^{12}}/\mathbf{max}\{\mathbf{X^{11}}\}$.

The correlation in the data is varied over three conditions. The covariance matrix Σ for the populations with two predictors is given by:

$$\Sigma = \begin{bmatrix} 1 & \sigma^2\rho & \sigma^2\rho \\ & 1 & \sigma^2\rho \\ & & 1 \end{bmatrix},$$

where the off-diagonal elements are 0 for the first simulation condition, 0.1 for the second condition, and 0.7 for the third condition.

The proportion of missingess in the outcome variable is varied over two conditions. The first condition simulates a setting with 25% missingness, the second a setting with 50% missingness.

Finally, the missingness mechanism is varied over two conditions. The first concerns a missing completely at random (MCAR) mechanism, where missingness does not depend on the values of the data, missing or observed.[10] The second concerns a missing at random (MAR) right mechanism. This means that missingness does depend on the data, but only through observed components of the data.[10] The MAR right mechanism deletes more high values, so the distribution of the observed data shifts to the left.[11] The MAR right mechanism is considered to be one of the more extreme missingness mechanisms, as it is asymmetrical and causes common statistics such as the mean to be biased.[11] It is unlikely to see such a mechanism in practice, but it is helpful in simulation studies to test the limits of a method: if it performs well under this mechanism, it will also do so in less extreme situations that are more likely to be encountered in practice.[11]

I consider a full-factorial simulation study design, where each of the possible combinations of weighting and data-generating mechanisms are evaluated. As there are seven different methods to be evaluated and 24 different data-generating mechanisms, the simulation will yield 168 results. From each data-generating mechanism, a single complete sample of size 500 is drawn. A 1000 simulated incomplete versions of these data (with missingess proportion of 25% or 50%) are then imputed. The finite population pooling rules by Vink & Van Buuren[12] are used to obtain inferences over the simulated results.

Is it absolutely necessary to explain that the simulation is seed-dependent, and to add the same simulation with a different seed to the research archive? Or is it sufficient to reference the pooling rules as is done now?

3.4 | Estimand and performance measures

The estimands of interest in this study are the predicted (i.e. imputed) values. I assess the statistical validity of each metric under each combination of conditions by means of the bias, 95% confidence interval width, coverage, and explained variance.

3.5 | Results

Table A1 through Table A7 in Appendix A display the simulation results for each of the seven methods. Each table specifies the data-generating mechanisms in the left columns by indicating the missingness mechanism, missingness proportion, skewness of the distribution, and correlation in the data. Figure 2 visualises the results for the coverage, Figure 3 those for the bias, and Figure 4 those for the explained variance. I discuss the results below on the basis of the research questions.

3.5.1 | Comparison of ranked and scaled blended metric

The ranked and scaled versions of the metrics yield similar simulation results. When comparing the results for blending factor = 1 (full predictive distance) in Table A2 and Table A5, they show that the scaled method yields slightly higher coverages but larger biases overall. When comparing the results for blending factor = 0.5 in Table A3 and Table A6, they show that the scaled method outperforms the ranked method. The results for blending factor = 0 (full Mahalanobis distance) in Table A4 and Table A7 show that the ranked method outperforms the scaled method. Overall, the ranked method performs slightly better, except when the blending factor is set to 0.5. As most of the results are similar, however, the scaled version of the blended metric might be preferable, as it is computationally more efficient to use.

3.5.2 | Comparison of PMM and blending factor = 1

In both blended metrics, a blending factor of 1 indicates that full weight is given to the predictive distance. Therefore, using a blending factor of 1 should yield results identical to those obtained by PMM. Even though the results in Table A1, Table A2

FIGURE 2 Coverage results per condition, where each individual plot shows the results for the seven methods. A reference line is given at coverage = 0.95. Above the plots, the condition combinations of missingness mechanism (MCAR, MAR right) and missingness proportion (25%, 50%) are given. On the right, the condition combinations of distribution (normal, skewed) and correlation ($\rho = 0$, $\rho = 0.1$, $\rho = 0.7$) are given.

and Table A5 are similar, they are not identical. This is likely due to the fact that a matching function written in C is used in the original `mice.impute.pmm` function but not in the `mice.impute.blended` function. Therefore any differences are likely due to the different underlying code. In some cases, particularly in the MCAR conditions, the both the ranked and scaled versions of the blended metric with a blending factor of 1 perform slightly better than the predictive metric.

3.5.3 | Effect of data generation conditions on performance

In the data generating models, the missingness mechanisms, proportions, skewness of the data, and correlation in the data were varied, resulting in 24 different simulation conditions. The plots displayed in Figure 2, 3 and 4 illustrate the impact of each of these conditions on the performance of the metrics in terms of coverage, bias, and explained variance. The MCAR conditions show higher performance when compared to the MAR right conditions, and a higher proportion of missingness in the data leads to lower performance, as would be expected. The skewness of the data does not always impact the performance negatively. Under the MCAR conditions, a skewed distribution of the data results in higher coverage rates for some cases when compared to a normal distribution. Under the MAR right conditions, however, the opposite is true. As MAR right creates more missingness in the right tail of the data, and the data are positively skewed, the distribution of the data that are left disproportionately shifts to the left. This causes lower coverage rates and thus less valid inference. Is this the right explanation? The proportion of explained variance (R squared) is quite stable under the normal conditions but shows more variation under the skewed conditions. Finally, a higher correlation in the data under MCAR conditions does not lead to decreased performance, and in some cases to increased performance. It does lead to lower performance under the MAR right conditions. R squared increases with the correlation in the data, and is the largest under the MCAR condition with 25% missingness, skewed distribution and correlation of 0.7.

FIGURE 3 Bias results per condition, where each individual plot shows the results for the seven methods. A reference line is given at bias = 0. Above the plots, the condition combinations of missingness mechanism (MCAR, MAR right) and missingness proportion (25%, 50%) are given. On the right, the condition combinations of distribution (normal, skewed) and correlation ($\rho = 0$, $\rho = 0.1$, $\rho = 0.7$) are given.

3.5.4 | Effect of blending on performance

For the ranked version of the blended metric, the coverage is almost always higher, the bias is often smaller, and the explained variance is almost always larger when the blended metric is weighted more towards the predictive distance. For the scaled version, the results are similar: in most cases, a higher blending factor leads to better performance. There are a few exceptions where a blended metric with a blending factor of 0.5 or 0 outperforms either the predictive metric, the blended metric with a blending factor of 1, or both. This is mostly the case under the MCAR conditions. It is important to note, however, that these differences are small and likely due to chance. The overall trend shows that blending towards the Mahalanobis distance leads to worse performance, especially under the more extreme conditions such as MAR, a large proportion of missingness, and a skewed distribution.

Figure 2 shows that the trend for the coverage is similar across all conditions: the coverage rates become lower when the blended metrics are weighted more towards the Mahalanobis distance. Under the conditions with MCAR, however, the results are similar for blending factors of 1 and 0.5, where a factor 0.5 sometimes outperforms a factor of 1. The Mahalanobis distance always leads to lower coverage rates. The downwards trend is especially pronounced under the conditions with a MAR right missingness mechanism, with coverage rates near only 40% in the worst performing scenarios.

The bias results in Figure 3 show that under the conditions of MCAR, 50% missingness and a normal distribution, the scaled blended metric with factor 0 and ranked blended metric with factors 0.5 and 0 slightly overestimate the predictions, whereas the the predictive metric and the blended metrics with higher blending factors slightly underestimate the predictions. In general, but especially in the more extreme simulation conditions, the predictions are underestimated by all metrics.

Finally, the results for R squared in Figure 4 show that the proportion of explained variance is relatively stable across the different metrics. Performance in terms of the explained variance is more dependent on the correlation in the data than on the

FIGURE 4 R squared results per condition, where each individual plot shows the results for the seven methods. A reference line is given at 0. Above the plots, the condition combinations of missingness mechanism (MCAR, MAR right) and missingness proportion (25%, 50%) are given. On the right, the condition combinations of distribution (normal, skewed) and correlation ($\rho = 0, \rho = 0.1, \rho = 0.7$) are given.

metric used, as would be expected. Overall, however, it decreases as the blending factor decreases. Again, this trend is more strongly pronounced in the more extreme conditions.

4 | SIMULATION STUDY II

In order to be able to explain the results from the first simulation study in more detail, I conduct a second simulation. In this simulation study, I evaluate the version of the blended metric that performed best overall in Simulation study I, which is the ranked version.

4.1 | Aims

The objective of the second simulation study is to provide a more detailed explanation of the results found in Simulation study I. In order to do so, I evaluate the version of the blended metric that performed best overall in Simulation study I, which is the ranked version. I simulate a setting where a single value is imputed, and evaluate the blended metric with blending factors ranging from 0 to 1, with intervals of 0.1.

4.2 | Data-generating mechanisms

I expect that the distinction between the performance of the different blending factors will become more apparent under a more extreme data-generating mechanism. Therefore, the data are simulated from a single data-generating mechanism with the conditions under which the blended metric performed the worst in Simulation study I. The same variables are defined as in the

first simulation study, where the data is skewed and the off-diagonal elements in the covariance are set to 0.7. A sample of size 500 is drawn. To simulate the prediction of the height measurement at 14 months for a single target child, a random case in the data will be made incomplete for the outcome.

4.3 | Estimand and performance measures

The number of simulations is set to 10000. In every simulation, 1 case is made missing and imputed 50 times. To assess the statistical properties of the predictive metric and the ranked blended metric with different blending factors, I evaluate their accuracy, validity, and precision. Accuracy is evaluated by means of the (absolute) bias, by evaluating the average of the imputations against the true value, and by the root mean square error (RMSE). Validity is evaluated by the coverage rate. Precision is evaluated in terms of the variance of the imputations.

4.4 | Results

The simulation results in Table 1 show that as the blending factor decreases (which implies weighting in the direction of the Mahalanobis distance), the bias increases. The RMSE also shows a decreasing trend, however, there is a small increase in the RMSE from a blending factor of 0.1 to 0. However, there is no clear trend in the absolute bias. Figure 5 shows that a larger blending factor leads to a larger standard error and higher coverage. The performance measures show that a property of blending is the bias-variance tradeoff. That is, weighting towards the Mahalanobis distance results in more precise, but less accurate estimates. The predictive distance results in less precise, but more accurate estimates. Figure 6 further illustrates this, which shows the distributions of the estimates obtained by the ranked metric with a blending factor of 0 and 1 are shown. The Mahalanobis distance causes the predictions to move more towards the mean.

The distribution of the true data is actually quite normal. I don't understand this, if the predictors are skewed and the outcome is the sum of the predictors, should the outcome not be skewed as well?

TABLE 1 Performance results for Simulation study II.

method	estimate	true	bias	absbias	ssd	se	lwr	upr	cov	rmse
PMM	4.10	4.29	-0.18	8.13	5133.00	7.12	-10.21	18.42	0.94	9.68
Blending factor = 1	4.10	4.29	-0.19	8.12	5126.81	7.12	-10.22	18.41	0.95	9.67
Blending factor = 0.9	3.98	4.29	-0.31	8.15	5182.68	7.15	-10.38	18.34	0.94	9.70
Blending factor = 0.8	3.95	4.29	-0.33	8.13	5153.59	7.06	-10.24	18.15	0.94	9.65
Blending factor = 0.7	3.99	4.29	-0.30	8.10	5116.94	6.97	-10.01	17.99	0.94	9.60
Blending factor = 0.6	4.00	4.29	-0.29	8.08	5107.43	6.90	-9.87	17.87	0.93	9.57
Blending factor = 0.5	3.99	4.29	-0.30	8.10	5118.92	6.85	-9.77	17.75	0.93	9.57
Blending factor = 0.4	3.96	4.29	-0.32	8.05	5082.51	6.77	-9.64	17.57	0.92	9.51
Blending factor = 0.3	3.94	4.29	-0.35	8.00	5025.93	6.66	-9.43	17.32	0.91	9.43
Blending factor = 0.2	3.86	4.29	-0.42	7.99	5014.08	6.52	-9.24	16.97	0.90	9.38
Blending factor = 0.1	3.74	4.29	-0.55	7.93	4948.25	6.29	-8.91	16.38	0.87	9.25
Blending factor = 0	3.74	4.29	-0.54	8.09	5121.67	6.04	-8.40	15.89	0.82	9.32

5 | DISCUSSION

This study investigated the properties of a blended distance measure through two simulation studies. The purpose of Simulation study I was to evaluate the performance of the blended metric under different data generating conditions. This simulation demonstrated that the blended metric performs worse when weighted more towards the Mahalanobis distance, especially under extreme conditions like MAR right. The purpose of Simulation study II was to provide a further explanation of this result. The ranked version of the blended metric was evaluated under the condition of a skewed distribution and correlation of 0.7. The
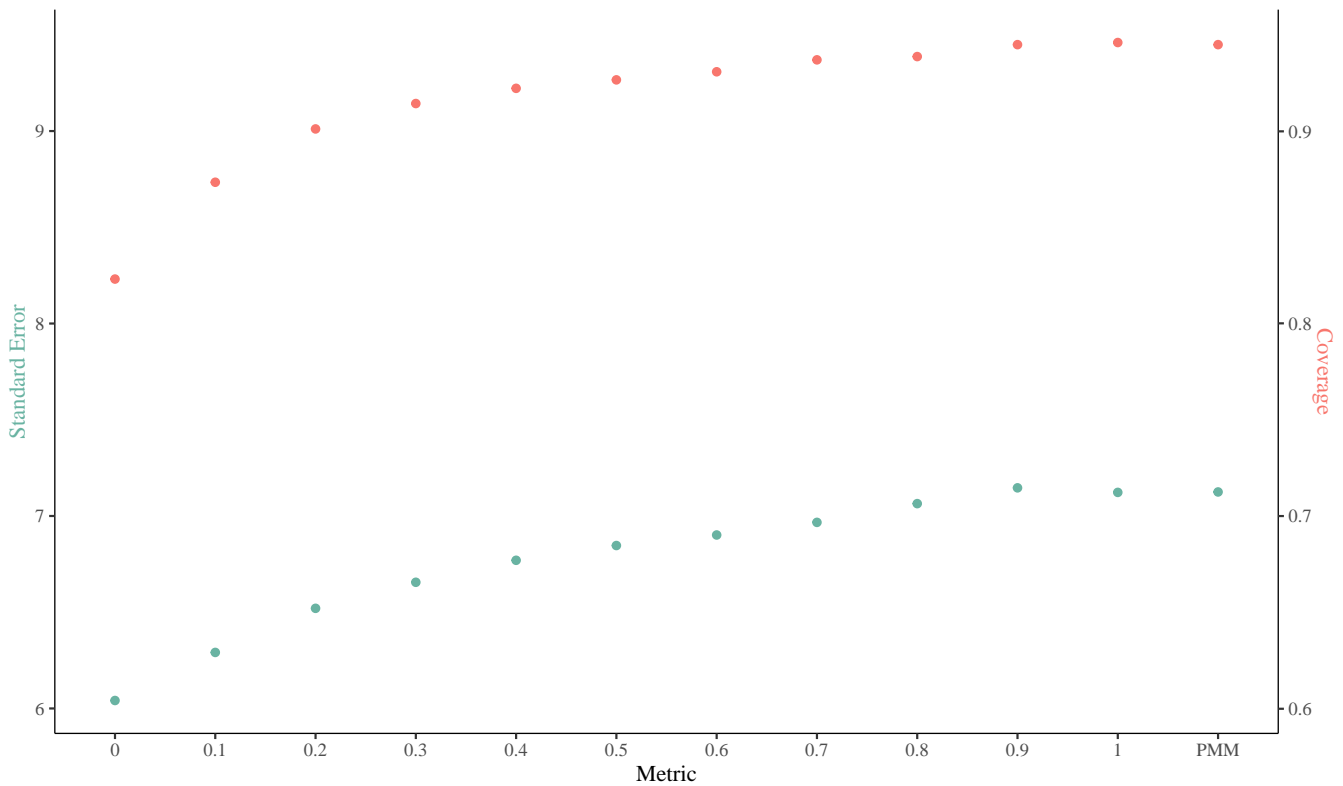
FIGURE 5 Mean of the SE and coverage results for Simulation study II. The values on the x-axis indicate the blending factor used for the ranked blended metric.

results show that a property of blending is the bias-variance tradeoff: weighting towards the predictive distance results in less precise, but more accurate estimates. Furthermore, the coverage rates drop as the blended metric is weighted more towards the Mahalanobis distance, which entails a decrease in statistical validity.

It is more likely to select donors who are not people-like-me when using the predictive distance. This can be counteracted by the Mahalanobis distance, which causes there to be less variance among the selected donors, and thus selects people-like-me. However, this results in lower coverages, and therefore in less valid estimates. In practice, there is no need for concern about whether or not we select people-like-me, as the uncertainty is necessary for making valid inferences.

The overall conclusion is that the blended metric can be implemented in situations where the missingness proportion is small and is MCAR. This is generally the case in the context of height prediction, as only a single value is to be imputed. It may be attractive for users of growth curve matching to use the blended metric when they have difficulty selecting a particular future time point to base matches on, or when they have more interest in the similarity between donors and the target in the predictor space. However, it is important to keep in mind the severe underperformance of the blended metric under more extreme conditions, and the reliable performance of the predictive distance under any conditions. PMM should therefore always be the preferred method, and the results of this study may minimize doubts about discrepancies between the trajectories of the matched donors. After all, our past does not always define our future, and selecting matches may not so much be a matter of finding "people-like-me" in terms of historic growth, as it is one of future similarity.

The current study investigated the influence of missingness proportion, missingness mechanisms, skewness of the data, and correlation in the data for the use of the blended metric. A limitation is that the blended metric might perform better in practice, and therefore it would be useful to evaluate the metric in empirical data as well. Additionally, alternative combinations of similarity measures and the predictive distance could lead to different results, and these combinations were not studies. Examples of other similarity measures would be the Frechet distance,[13] and the locally supervised metric learning (LSML) measure.[14] Finally, further research could investigate the impact of more variations in simulation conditions such as the sample size and the number of k matched donors, and could determine what the optimal blending factor is to predict outcomes.
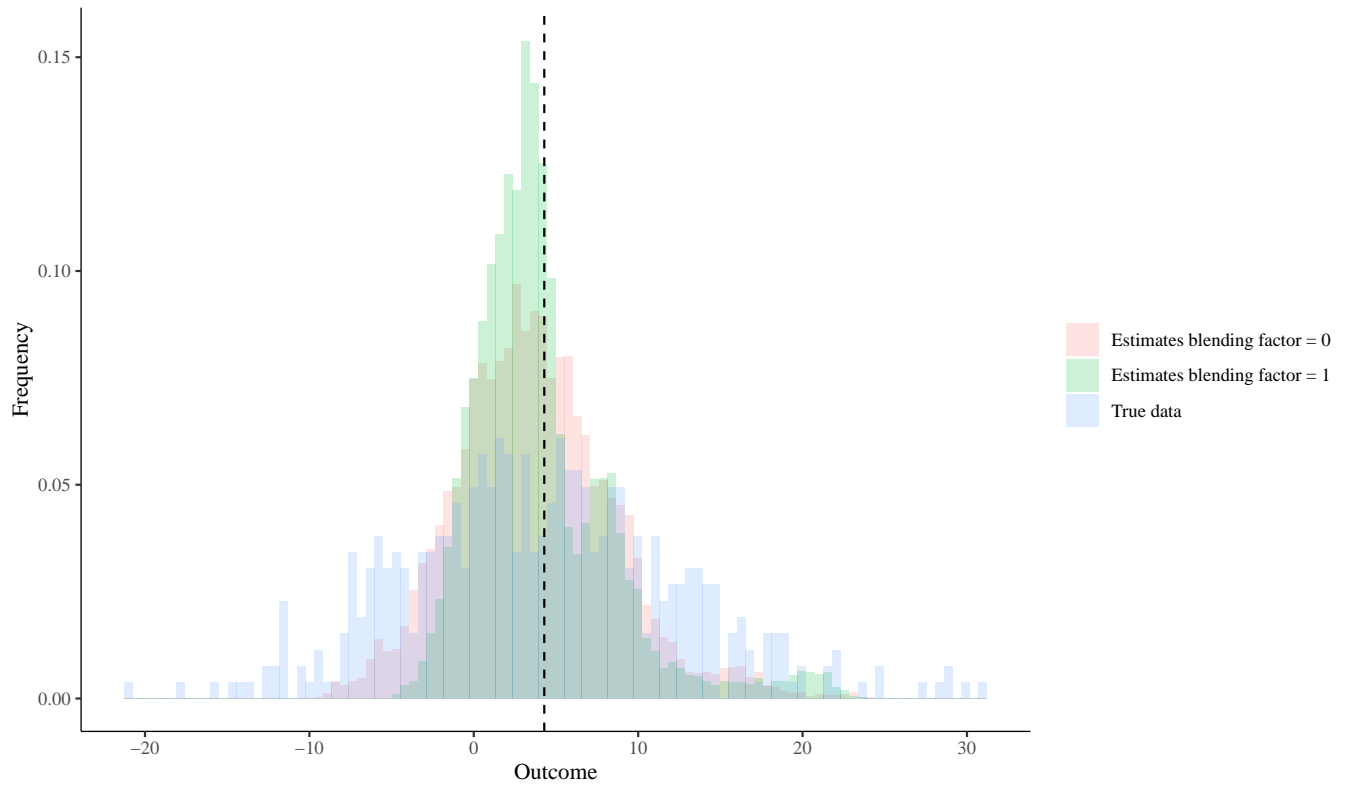
FIGURE 6 Distribution of the estimates obtained with the ranked version of the blended metric, with a blending factor of 0 (Mahalanobis distance) and 1 (predictive distance), respectively. The true value is marked by the dashed line.

ACKNOWLEDGMENTS

SUPPORTING INFORMATION

The scripts used for the simulation study are available in the research archive of this study. The study was approved by the Ethical Review Board of the Faculty of Social and Behavioural Sciences of Utrecht University. The approval is based on the documents sent by the researchers as requested in the form of the Ethics committee and filed under number 21-1906.

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APPENDIX

A RESULTS OF SIMULATION STUDY I

TABLE A1 Method PMM.

mech	mis	dist	cor	qbar	se	t	df	b	2.5%	97.5%	true	cov	bias	R2
MCAR	25%	normal	0	30.466	0.191	0.153	97.773	0.035	29.935	30.996	30.47	0.949	-0.004	0.079
			0.1	30.466	0.192	0.155	98.311	0.035	29.933	30.998	30.475	0.96	-0.009	0.09
			0.7	30.502	0.187	0.161	112.474	0.033	29.982	31.022	30.502	0.941	0	0.152
		skewed	0	3.199	0.248	0.187	65.411	0.06	2.511	3.888	3.256	0.969	-0.057	0.106
			0.1	3.238	0.251	0.189	64.18	0.061	2.543	3.934	3.292	0.976	-0.054	0.112
			0.7	4.068	0.259	0.213	67.895	0.064	3.349	4.788	4.109	0.976	-0.041	0.239
	50%	normal	0	30.443	0.339	0.243	30.409	0.109	29.502	31.383	30.47	0.94	-0.027	0.083
			0.1	30.45	0.342	0.248	31.72	0.113	29.499	31.4	30.475	0.953	-0.026	0.093
			0.7	30.495	0.327	0.243	35.429	0.102	29.587	31.403	30.502	0.94	-0.007	0.153
		skewed	0	3.149	0.462	0.373	21.577	0.214	1.867	4.431	3.256	0.977	-0.107	0.106
			0.1	3.167	0.49	0.402	17.865	0.238	1.807	4.526	3.292	0.978	-0.126	0.114
			0.7	4.022	0.516	0.444	18.404	0.257	2.59	5.455	4.109	0.978	-0.087	0.24
MAR	25%	normal	0	30.456	0.185	0.151	105.503	0.033	29.943	30.969	30.47	0.912	-0.014	0.082
			0.1	30.46	0.186	0.153	105.455	0.033	29.943	30.977	30.475	0.897	-0.015	0.093
			0.7	30.483	0.188	0.162	113.281	0.034	29.96	31.005	30.502	0.908	-0.019	0.153
		skewed	0	3.09	0.193	0.154	101.507	0.036	2.556	3.625	3.256	0.878	-0.165	0.077
			0.1	3.143	0.195	0.156	96.792	0.036	2.601	3.685	3.292	0.884	-0.149	0.088
			0.7	3.895	0.194	0.17	107.547	0.036	3.356	4.434	4.109	0.842	-0.214	0.176
	50%	normal	0	30.437	0.303	0.218	41.511	0.089	29.596	31.277	30.47	0.863	-0.033	0.086
			0.1	30.446	0.305	0.221	37.774	0.09	29.599	31.292	30.475	0.868	-0.03	0.097
			0.7	30.451	0.305	0.228	43.159	0.09	29.605	31.296	30.502	0.857	-0.051	0.153
		skewed	0	2.975	0.372	0.271	26.075	0.133	1.942	4.008	3.256	0.911	-0.281	0.081
			0.1	3.021	0.365	0.267	26.939	0.129	2.007	4.035	3.292	0.905	-0.272	0.089
			0.7	3.674	0.37	0.28	28.378	0.132	2.646	4.702	4.109	0.858	-0.436	0.141

TABLE A2 Method ranked, blend = 1.

mech	mis	dist	cor	qbar	se	t	df	b	2.5%	97.5%	true	cov	bias	R2
MCAR	25%	normal	0	30.462	0.192	0.154	97.885	0.035	29.929	30.995	30.47	0.95	-0.008	0.079
			0.1	30.467	0.195	0.156	95.776	0.036	29.927	31.008	30.475	0.961	-0.008	0.091
			0.7	30.504	0.185	0.16	111.671	0.033	29.989	31.019	30.502	0.952	0.003	0.152
		skewed	0	3.211	0.242	0.183	66.725	0.056	2.539	3.883	3.256	0.975	-0.045	0.107
			0.1	3.234	0.254	0.191	60.949	0.062	2.529	3.939	3.292	0.975	-0.058	0.112
			0.7	4.074	0.253	0.21	71.264	0.062	3.37	4.778	4.109	0.968	-0.035	0.24
	50%	normal	0	30.44	0.34	0.244	30.283	0.11	29.496	31.384	30.47	0.949	-0.03	0.083
			0.1	30.454	0.329	0.238	35.708	0.104	29.541	31.366	30.475	0.93	-0.022	0.094
			0.7	30.492	0.328	0.244	35.911	0.103	29.58	31.404	30.502	0.939	-0.009	0.153
		skewed	0	3.147	0.461	0.375	21.325	0.217	1.866	4.428	3.256	0.965	-0.109	0.106
			0.1	3.155	0.487	0.403	19.639	0.238	1.803	4.507	3.292	0.972	-0.137	0.115
			0.7	4.014	0.513	0.442	17.427	0.256	2.589	5.438	4.109	0.982	-0.096	0.24
MAR	25%	normal	0	30.46	0.185	0.151	105.089	0.032	29.946	30.973	30.47	0.898	-0.01	0.082
			0.1	30.458	0.188	0.153	103.006	0.033	29.937	30.979	30.475	0.898	-0.017	0.094
			0.7	30.481	0.188	0.162	110.033	0.034	29.958	31.004	30.502	0.902	-0.021	0.153
		skewed	0	3.088	0.191	0.153	100.427	0.035	2.558	3.619	3.256	0.866	-0.167	0.077
			0.1	3.145	0.193	0.155	98.57	0.035	2.611	3.68	3.292	0.884	-0.147	0.088
			0.7	3.892	0.192	0.169	107.928	0.035	3.358	4.426	4.109	0.825	-0.218	0.175
	50%	normal	0	30.444	0.301	0.218	41.213	0.088	29.607	31.281	30.47	0.852	-0.025	0.086
			0.1	30.442	0.304	0.22	41.027	0.089	29.598	31.286	30.475	0.883	-0.033	0.097
			0.7	30.459	0.301	0.226	45.189	0.087	29.623	31.295	30.502	0.865	-0.043	0.153
		skewed	0	2.983	0.381	0.279	24.606	0.14	1.923	4.042	3.256	0.918	-0.273	0.08
			0.1	3.025	0.372	0.273	27.808	0.134	1.994	4.057	3.292	0.901	-0.267	0.089
			0.7	3.665	0.367	0.276	27.827	0.129	2.646	4.684	4.109	0.836	-0.444	0.142

TABLE A3 Method ranked, blend = 0.5.

mech	mis	dist	cor	qbar	se	t	df	b	2.5%	97.5%	true	cov	bias	R2
MCAR	25%	normal	0	30.477	0.181	0.149	107.792	0.031	29.974	30.98	30.47	0.957	0.007	0.076
			0.1	30.492	0.183	0.151	106.919	0.031	29.985	30.999	30.475	0.943	0.016	0.088
			0.7	30.51	0.18	0.158	119.4	0.031	30.01	31.009	30.502	0.938	0.008	0.148
		skewed	0	3.227	0.204	0.161	90.943	0.04	2.662	3.792	3.256	0.944	-0.029	0.094
			0.1	3.264	0.214	0.167	84.099	0.044	2.67	3.857	3.292	0.951	-0.029	0.102
			0.7	4.05	0.224	0.191	85.852	0.048	3.426	4.673	4.109	0.95	-0.06	0.226
	50%	normal	0	30.486	0.303	0.216	38.173	0.087	29.646	31.326	30.47	0.917	0.017	0.074
			0.1	30.494	0.296	0.212	39.051	0.083	29.673	31.315	30.475	0.928	0.019	0.085
			0.7	30.516	0.293	0.219	47.093	0.082	29.704	31.328	30.502	0.914	0.015	0.142
		skewed	0	3.178	0.351	0.256	31.295	0.12	2.202	4.154	3.256	0.946	-0.078	0.087
			0.1	3.218	0.37	0.271	26.642	0.131	2.191	4.245	3.292	0.946	-0.074	0.094
			0.7	3.941	0.409	0.325	26.368	0.161	2.805	5.076	4.109	0.951	-0.169	0.206
MAR	25%	normal	0	30.421	0.178	0.148	111.804	0.03	29.927	30.915	30.47	0.898	-0.049	0.076
			0.1	30.421	0.177	0.149	116.968	0.03	29.93	30.912	30.475	0.898	-0.054	0.088
			0.7	30.434	0.18	0.158	117.612	0.031	29.934	30.934	30.502	0.898	-0.068	0.145
		skewed	0	3.081	0.177	0.146	114.292	0.03	2.589	3.573	3.256	0.864	-0.175	0.07
			0.1	3.109	0.175	0.146	118.274	0.029	2.624	3.594	3.292	0.847	-0.183	0.078
			0.7	3.76	0.17	0.155	133.762	0.028	3.287	4.233	4.109	0.678	-0.35	0.141
	50%	normal	0	30.406	0.262	0.191	52.803	0.066	29.678	31.133	30.47	0.809	-0.064	0.082
			0.1	30.402	0.273	0.199	48.497	0.071	29.643	31.161	30.475	0.84	-0.073	0.092
			0.7	30.396	0.264	0.202	58.445	0.068	29.662	31.13	30.502	0.802	-0.105	0.145
		skewed	0	2.907	0.301	0.213	37.629	0.087	2.071	3.744	3.256	0.822	-0.348	0.059
			0.1	2.932	0.293	0.207	41.762	0.081	2.12	3.744	3.292	0.801	-0.361	0.065
			0.7	3.547	0.29	0.214	46.431	0.081	2.741	4.353	4.109	0.687	-0.563	0.109

TABLE A4 Method ranked, blend = 0.

mech	mis	dist	cor	qbar	se	t	df	b	2.5%	97.5%	true	cov	bias	R2
MCAR	25%	normal	0	30.462	0.145	0.134	156.897	0.02	30.059	30.866	30.47	0.888	-0.007	0.074
			0.1	30.468	0.146	0.136	159.425	0.02	30.062	30.874	30.475	0.893	-0.007	0.086
			0.7	30.499	0.148	0.145	166.98	0.021	30.088	30.91	30.502	0.882	-0.003	0.144
		skewed	0	3.192	0.147	0.138	158.72	0.021	2.782	3.601	3.256	0.893	-0.064	0.097
			0.1	3.223	0.147	0.139	162.631	0.02	2.816	3.63	3.292	0.889	-0.069	0.103
			0.7	4.003	0.146	0.157	186.987	0.02	3.599	4.407	4.109	0.863	-0.106	0.223
	50%	normal	0	30.494	0.211	0.159	77.005	0.042	29.909	31.079	30.47	0.839	0.024	0.069
			0.1	30.504	0.211	0.161	77.508	0.042	29.918	31.091	30.475	0.851	0.029	0.079
			0.7	30.531	0.212	0.169	87.214	0.043	29.944	31.118	30.502	0.843	0.029	0.132
		skewed	0	3.128	0.209	0.16	79.65	0.041	2.548	3.707	3.256	0.826	-0.128	0.091
			0.1	3.146	0.207	0.161	82.816	0.04	2.571	3.721	3.292	0.835	-0.146	0.097
			0.7	3.846	0.213	0.181	92.397	0.043	3.255	4.438	4.109	0.772	-0.263	0.2
MAR	25%	normal	0	30.408	0.15	0.136	148.803	0.021	29.99	30.825	30.47	0.863	-0.062	0.078
			0.1	30.401	0.151	0.138	152.097	0.021	29.983	30.819	30.475	0.87	-0.074	0.088
			0.7	30.402	0.149	0.145	160.168	0.021	29.987	30.817	30.502	0.84	-0.1	0.144
		skewed	0	3.054	0.145	0.134	158.032	0.02	2.651	3.457	3.256	0.753	-0.202	0.07
			0.1	3.088	0.147	0.135	156.613	0.02	2.681	3.496	3.292	0.758	-0.204	0.074
			0.7	3.681	0.143	0.143	174.906	0.019	3.284	4.077	4.109	0.453	-0.429	0.13
	50%	normal	0	30.357	0.214	0.163	77.74	0.044	29.762	30.952	30.47	0.761	-0.113	0.08
			0.1	30.349	0.215	0.164	74.64	0.044	29.751	30.947	30.475	0.761	-0.126	0.089
			0.7	30.318	0.214	0.171	82.206	0.043	29.724	30.911	30.502	0.736	-0.184	0.141
		skewed	0	2.86	0.205	0.154	78.597	0.04	2.29	3.43	3.256	0.651	-0.396	0.059
			0.1	2.895	0.201	0.154	84.367	0.038	2.336	3.455	3.292	0.638	-0.397	0.065
			0.7	3.44	0.208	0.165	84.385	0.041	2.863	4.018	4.109	0.403	-0.669	0.1

TABLE A5 Method scaled, blend = 1.

mech	mis	dist	cor	qbar	se	t	df	b	2.5%	97.5%	true	cov	bias	R2
MCAR	25%	normal	0	30.461	0.197	0.156	93.518	0.037	29.914	31.009	30.47	0.958	-0.008	0.079
			0.1	30.473	0.189	0.154	103.355	0.034	29.947	30.999	30.475	0.942	-0.002	0.09
			0.7	30.507	0.194	0.164	100.127	0.035	29.968	31.046	30.502	0.964	0.005	0.152
		skewed	0	3.205	0.25	0.188	60.828	0.06	2.51	3.901	3.256	0.968	-0.05	0.107
			0.1	3.236	0.248	0.188	62.727	0.059	2.548	3.924	3.292	0.969	-0.056	0.112
			0.7	4.073	0.255	0.211	72.87	0.063	3.365	4.782	4.109	0.966	-0.036	0.24
	50%	normal	0	30.439	0.338	0.243	31.954	0.11	29.501	31.376	30.47	0.939	-0.031	0.084
			0.1	30.45	0.33	0.24	35.211	0.106	29.534	31.367	30.475	0.936	-0.025	0.093
			0.7	30.488	0.33	0.245	35.929	0.103	29.572	31.405	30.502	0.948	-0.013	0.153
		skewed	0	3.152	0.458	0.371	22.021	0.213	1.882	4.423	3.256	0.969	-0.103	0.107
			0.1	3.171	0.484	0.398	18.633	0.234	1.826	4.515	3.292	0.978	-0.122	0.113
			0.7	4.013	0.518	0.447	17.036	0.259	2.575	5.451	4.109	0.987	-0.096	0.241
MAR	25%	normal	0	30.461	0.185	0.151	104.176	0.032	29.947	30.975	30.47	0.906	-0.009	0.082
			0.1	30.46	0.189	0.154	102.232	0.034	29.935	30.984	30.475	0.916	-0.016	0.093
			0.7	30.489	0.188	0.162	109.703	0.033	29.968	31.011	30.502	0.908	-0.012	0.154
		skewed	0	3.094	0.191	0.153	104.554	0.036	2.563	3.626	3.256	0.868	-0.162	0.077
			0.1	3.14	0.193	0.155	96.462	0.036	2.603	3.677	3.292	0.867	-0.152	0.088
			0.7	3.889	0.193	0.17	111.041	0.035	3.354	4.424	4.109	0.825	-0.221	0.175
	50%	normal	0	30.439	0.299	0.217	44.292	0.088	29.608	31.27	30.47	0.859	-0.031	0.086
			0.1	30.441	0.301	0.218	39.103	0.088	29.604	31.278	30.475	0.866	-0.034	0.097
			0.7	30.457	0.296	0.222	46.435	0.085	29.635	31.278	30.502	0.857	-0.045	0.153
		skewed	0	2.994	0.378	0.279	27.141	0.14	1.944	4.044	3.256	0.904	-0.262	0.08
			0.1	3.029	0.374	0.275	25.454	0.136	1.99	4.068	3.292	0.906	-0.263	0.089
			0.7	3.661	0.371	0.278	27.739	0.131	2.632	4.69	4.109	0.851	-0.448	0.141

TABLE A6 Method scaled, blend = 0.5.

mech	mis	dist	cor	qbar	se	t	df	b	2.5%	97.5%	true	cov	bias	R2
MCAR	25%	normal	0	30.467	0.188	0.152	102.834	0.034	29.946	30.988	30.47	0.953	-0.003	0.077
			0.1	30.478	0.18	0.15	112.559	0.031	29.979	30.978	30.475	0.94	0.003	0.088
			0.7	30.496	0.178	0.158	125.64	0.03	30.002	30.99	30.502	0.939	-0.006	0.149
		skewed	0	3.184	0.246	0.186	68.218	0.059	2.502	3.866	3.256	0.96	-0.072	0.098
			0.1	3.228	0.251	0.189	61.883	0.061	2.531	3.925	3.292	0.962	-0.064	0.106
			0.7	4.03	0.256	0.21	69.202	0.063	3.319	4.74	4.109	0.972	-0.08	0.231
	50%	normal	0	30.452	0.31	0.221	35.27	0.09	29.591	31.312	30.47	0.949	-0.018	0.077
			0.1	30.462	0.307	0.221	38.968	0.09	29.61	31.314	30.475	0.923	-0.013	0.087
			0.7	30.487	0.301	0.224	42.769	0.086	29.65	31.323	30.502	0.926	-0.015	0.146
		skewed	0	3.119	0.454	0.365	20.317	0.208	1.858	4.381	3.256	0.963	-0.136	0.091
			0.1	3.151	0.475	0.388	19.111	0.227	1.833	4.469	3.292	0.977	-0.142	0.1
			0.7	3.919	0.509	0.435	17.998	0.252	2.505	5.333	4.109	0.97	-0.19	0.219
MAR	25%	normal	0	30.425	0.184	0.151	105.503	0.032	29.915	30.935	30.47	0.906	-0.045	0.078
			0.1	30.429	0.18	0.151	114.155	0.031	29.93	30.927	30.475	0.9	-0.047	0.089
			0.7	30.444	0.181	0.159	118.405	0.031	29.94	30.948	30.502	0.896	-0.057	0.148
		skewed	0	3.066	0.184	0.149	103.034	0.032	2.554	3.577	3.256	0.856	-0.19	0.072
			0.1	3.091	0.18	0.149	108.706	0.031	2.59	3.592	3.292	0.843	-0.202	0.078
			0.7	3.77	0.183	0.162	119.094	0.032	3.261	4.278	4.109	0.708	-0.34	0.149
	50%	normal	0	30.403	0.284	0.207	47.457	0.079	29.615	31.191	30.47	0.851	-0.067	0.083
			0.1	30.402	0.281	0.205	46.188	0.076	29.621	31.182	30.475	0.838	-0.073	0.093
			0.7	30.407	0.279	0.211	48.836	0.074	29.633	31.182	30.502	0.82	-0.094	0.148
		skewed	0	2.904	0.327	0.234	34.697	0.103	1.996	3.811	3.256	0.866	-0.352	0.064
			0.1	2.936	0.332	0.237	33.535	0.106	2.013	3.859	3.292	0.867	-0.356	0.07
			0.7	3.53	0.34	0.253	33.878	0.112	2.586	4.474	4.109	0.734	-0.579	0.114

TABLE A7 Method scaled, blend = 0.

mech	mis	dist	cor	qbar	se	t	df	b	2.5%	97.5%	true	cov	bias	R2
MCAR	25%	normal	0	30.457	0.143	0.134	163.429	0.019	30.059	30.855	30.47	0.893	-0.012	0.074
			0.1	30.462	0.146	0.136	157.712	0.02	30.058	30.867	30.475	0.895	-0.013	0.085
			0.7	30.496	0.146	0.144	167.413	0.02	30.091	30.901	30.502	0.887	-0.006	0.144
		skewed	0	3.188	0.145	0.137	165.544	0.02	2.785	3.59	3.256	0.89	-0.068	0.096
			0.1	3.223	0.147	0.139	159.723	0.021	2.814	3.633	3.292	0.891	-0.069	0.103
			0.7	4.011	0.147	0.157	183.983	0.021	3.603	4.419	4.109	0.86	-0.098	0.223
	50%	normal	0	30.497	0.202	0.156	86.643	0.039	29.936	31.059	30.47	0.824	0.028	0.069
			0.1	30.505	0.208	0.16	83.654	0.041	29.928	31.082	30.475	0.842	0.03	0.079
			0.7	30.532	0.209	0.167	85.635	0.041	29.953	31.111	30.502	0.843	0.03	0.132
		skewed	0	3.122	0.206	0.159	84.192	0.04	2.55	3.694	3.256	0.832	-0.134	0.09
			0.1	3.15	0.207	0.161	83.346	0.04	2.574	3.725	3.292	0.806	-0.143	0.097
			0.7	3.847	0.209	0.18	97.013	0.042	3.266	4.428	4.109	0.774	-0.263	0.2
MAR	25%	normal	0	30.402	0.15	0.136	153.443	0.021	29.987	30.817	30.47	0.856	-0.068	0.077
			0.1	30.403	0.15	0.138	151.516	0.021	29.985	30.82	30.475	0.859	-0.072	0.088
			0.7	30.406	0.154	0.146	153.178	0.022	29.979	30.833	30.502	0.848	-0.096	0.145
		skewed	0	3.054	0.143	0.133	162.082	0.019	2.657	3.451	3.256	0.742	-0.202	0.069
			0.1	3.084	0.145	0.135	158.785	0.02	2.681	3.486	3.292	0.755	-0.209	0.074
			0.7	3.681	0.144	0.144	175.877	0.02	3.28	4.081	4.109	0.465	-0.429	0.13
	50%	normal	0	30.354	0.214	0.163	77.214	0.044	29.759	30.949	30.47	0.758	-0.116	0.08
			0.1	30.348	0.211	0.162	82.081	0.042	29.763	30.933	30.475	0.752	-0.127	0.09
			0.7	30.318	0.214	0.171	85.563	0.043	29.725	30.911	30.502	0.739	-0.184	0.141
		skewed	0	2.86	0.201	0.154	89.028	0.039	2.301	3.419	3.256	0.638	-0.396	0.058
			0.1	2.891	0.211	0.158	76.828	0.042	2.306	3.477	3.292	0.653	-0.401	0.065
			0.7	3.438	0.204	0.163	86.894	0.039	2.871	4.005	4.109	0.395	-0.672	0.1