How do dataset characteristics affect the performance of propensity score methods and regression for controlling confounding in observational studies?

How do dataset characteristics affect the performance of propensity score methods and regression for controlling confounding in observational studies? A simulation study.

J. Wilkinson[*1], M. A. Mamas[2], E. Kontopantelis[3]

[1] Centre for Biostatistics, Manchester Academic Health Science Centre, Faculty of Biology, Medicine, and Health, University of Manchester, Rm 1.307 Jean McFarlane Building, University Place, Oxford Road, Manchester, M13 9PL, UK. jack.wilkinson@manchester.ac.uk

[2] Keele Cardiovascular Research Group, Centre for Prognosis Research, Keele University, Keele, UK.

[3] Division of Informatics, Imaging & Data Sciences, University of Manchester, Manchester, UK.

Abstract

Background

In observational studies, researchers must select a method to control for confounding. Options include propensity score methods and regression. It remains unclear how dataset characteristics (size, overlap in propensity scores, exposure prevalence) influence the relative performance of the methods, making it difficult to select the best method for a particular dataset. Given the increasing availability of large electronic health resources, performance for the analysis of big data is of particular interest.

Methods

A simulation study to evaluate the role of dataset characteristics on the performance of several propensity score methods (followed by logistic regression), compared to multiple logistic regression, for estimating a marginal odds ratio in the presence of confounding. Outcomes were simulated from logistic and complementary log-log models, and size, overlap in propensity scores, and prevalence of the exposure were varied.

Results

Multiple regression showed poor coverage for small sample sizes (100), but with large sample sizes (10,000 or above) it was more robust to imbalance in propensity scores and low exposure prevalence than were propensity score methods. Propensity score methods frequently displayed suboptimal coverage, particularly as overlap in propensity scores decreased. Problems associated with lack of overlap were exacerbated at larger sample sizes. Power of matching methods was particularly affected by lack of overlap, low prevalence of exposure, and small sample size. Performance of inverse probability of treatment weighting depended heavily on dataset characteristics, with poor coverage and bias with reduced overlap. The advantage of regression for large data size became less clear in the sensitivity analysis with a complementary log-log outcome generation mechanism and with unmeasured confounding, with superior bias and error but lower coverage than nearest neighbour and 1-to1 propensity score matching.

Conclusions

Matching on the propensity score performed better in very small samples, but the performance of multiple regression was comparable in sample sizes of 1,000 and became increasingly superior as sample sizes increased. In contemporary large observation studies, of national registries or primary care electronic health records, multiple regression estimation is predominantly the optimal choice, both in terms of simplicity and performance.

Keywords: confounding, propensity scores, odds ratio, marginal odds ratio, regression standardisation, logistic regression, simulation

Introduction

Observational studies employing large, routinely collected datasets are now commonplace in the health sciences, exploiting new opportunities to study the effects of treatments or exposures in representative cohorts. A key concern in observational studies is how to address confounding, in order to permit the estimation of the effect of the exposure on an outcome. [1, 2] Researchers frequently use regression or propensity scores (PS) for this purpose, with the latter increasing in popularity in the past few decades [3].

The popularity of PS methods for observational health data can be attributed to several attractive features. For example, they offer intuitive checks for balance between groups which are not possible using regression methods [2, 4]. Additionally, they can be formulated without reference to the outcome. This might reduce bias arising from "p-hacking" (when analyses are selected on the basis of the results they produce) [5], because the impact on the estimated treatment effect is not known during development of the PS model [2]. Another advantage is the fact that regression methods implicitly but heavily rely on extrapolation when exposed and unexposed individuals have very different confounder distributions [6, 7]. This is more explicit for PS methods, because it manifests in the form of highly variable inverse probability weights or a lack of good matches. It is also appropriately reflected by reduced certainty in the estimated exposure effect [6, 7]. A final reason may lie in the fact that PS methods, particularly when PS are used for matching, are frequently described as "emulating" a randomised controlled trial. However, it might not be clear to those using this phrase that the success of this emulation depends on all confounders being included in the estimation of the PS.

The variety of available methods for handling confounding in observational studies creates a challenge for the applied health researcher, who must select the best analytic approach for the particular study at hand. For example, PS matching excludes some data from the analysis, and so its performance might depend on factors such as the study size and the proportion of individuals who are exposed. In addition, PS methods were developed in an era preceding the widespread availability of large health datasets, and evaluations of their performance have generally not considered large sample sizes. Evidence is therefore lacking on the relative performance of these methods for the analysis of big data. Previous studies have compared the results obtained by applying different methods [8], or have used simulation without investigating the impact of dataset characteristics on performance [9, 10]. We therefore conducted a comprehensive simulation study to evaluate commonly used approaches for confounding control, and to investigate the factors affecting their performance, with the aim of providing guidance for health researchers. We considered the roles of data size, imbalance in confounding variables, and the relative number of exposed to unexposed individuals.

Methods

Methodological details are provided in the supplementary file.

Propensity score

In a comparison of an exposed with a control group, PS can be estimated using multiple logistic regression where the binary outcome denotes membership of an exposed or a comparator group.

Covariates hypothesised to be associated with the outcome should be included in the multiple logistic regression model. The PS is the predicted probability p of exposure. In practice, the regression coefficients must be estimated and hence there is uncertainty in p that is not usually accounted for in the process (although it is possible to do so, e.g. [7, 11]). Following estimation, the next concern is to verify that these are balanced across the two groups [2]. Finally, PS are incorporated into the analysis using one of several approaches.

Stratification using the PS has been found to perform poorly, and so we decided not to consider it in our simulation study [12, 13]. Regressing the outcome on exposure and PS has been found to be the most commonly used approach in reviews of practice [14, 15]. Inverse probability of treatment weighting (IPTW) is an alternative, often used approach [16]. However, PS matching has gained a reputation as the best PS method for removing baseline imbalance and is widely used[17-19]. The most common version is one-to-one matching without replacement [2], where each "case" in group A is matched to one "control" in group B, if the difference in their PS is below a predefined arbitrary threshold or "caliper" [20]. This approach entails sample size reductions, which can become extreme if there is great imbalance in baseline characteristics (resulting in largely non-overlapping PS distributions in the study groups), or if there is a large imbalance in group sizes. An alternative is one-to-one nearest neighbour matching with replacement, which will generally result in fewer observations being discarded compared to matching on a caliper, at the expense of greater discrepancies in PS distributions between groups.

Simulation study

We conducted a simulation study to evaluate PS methods and covariate adjustment for confounding control in observational studies, and the dataset characteristics affecting their performance.

Data generating model

To investigate the influence of data size, we considered sample sizes of 100, 1000, 10,000, and 100,000, to capture scenarios in which large databases are available for analysis. We also investigated various scenarios for the distribution of the exposed and comparator groups: equal group sizes, imbalanced group sizes, and substantially imbalanced group sizes. A third varying parameter was baseline imbalance for the covariates, which took on five different patterns, ranging from well-overlapping propensity scores to almost completely non-overlapping propensity scores for the two comparison groups. Figure 1 shows the PS distributions when for equal exposed and comparator group sizes.

The simulation was implemented in Stata v15.1 [21]. We used the *drawnorm* command to draw observations from multivariate normal distributions, which were dichotomised for some variables. The generated variables included: binary exposure E, binary covariate X_1, and continuous covariates X_2, X_3,X_4 and X_5. Correlations were set to be low between all variables except for two of the covariates and the exposure. Following that, the outcome Y was generated using a logit model. However, as a sensitivity analysis, we generated Y using a complementary log-log model, to ensure that performance of PS methods and regression was evaluated under more neutral conditions. In additional sensitivity analyses, we included an unmeasured confounder in the outcome generation mechanism (a continuous covariate X_6 which did not feature in the analytical models), for either the logit or complementary log-log model.

Analyses

A total of 5 analytical approaches were evaluated. First, PS were calculated using the PSMATCH2 module.[22] During this step we performed nearest neighbour one-to-one matching on the PS with replacement. Next, the PS were used in four logistic regression models: 1) exposure and the PS as independent variables (*PS covariate*); 2) exposure as the only independent variable, with the number of times each observation appeared in the aforementioned nearest-neighbour-matched dataset as a frequency weight (*nearest neighbour matching*); 3) exposure as the only independent variable, following one-to-one matching without replacement, when absolute difference on the PS was below 10^{-2} (*Caliper matching*); 4) exposure as the only independent variable and the PS used as an inverse probability treatment weight (*IPTW*). Note that in this study, we use standard logistic regression following matching, rather than a version intended for matched data; we return to this point in the discussion. We also performed logistic regression with the exposure and all five covariates included as independent variables (not using the PS), followed by regression standardisation, as a fifth approach [23]. Standardisation is necessary so that regression targets the same quantity as PS approaches (see *Target of inference*). We used the margins command with the post option following logistic regression to achieve this and used the delta method to compute confidence intervals on the log odds scale.

Target of inference

We evaluated the methods against the marginal odds ratio, which is a measure of the exposure effect at the population level. We calculated the marginal odds ratio for each simulated dataset, using the method described by Austin [9]. When there is no heterogeneity in treatment effect, caliper and nearest neighbour matching, IPTW, and multiple logistic regression with standardisation all estimate the marginal odds ratio [9, 23]. PS covariate actually targets a different quantity; the odds ratio conditional on the PS [7, 24, 25]. We include it here due to its popularity, and to compare to other methods.

Performance measures

1,000 datasets were simulated for each scenario. We considered four performance measures: mean error, bias, coverage and power. Mean error is the mean of the absolute difference between the estimate and the true parameter. Bias is the mean difference between the estimate and the true parameter. Coverage is the proportion of 95% confidence intervals for the estimate, based on a normal approximation, that contain the true parameter. Finally, we calculated power by the proportion of iterations where the null was rejected when it was actually false. Although power as a metric can be problematic in the presence of bias, it is essential for a complete comparison. However, in order to obtain a more meaningful metric, power-related statistical significance was calculated one-sided (i.e. statistically greater than zero, rather than statistically different). We also evaluated model convergence. The other metrics were only computed when convergence for a particular method in a simulation setting was 25% or above, otherwise they were set to missing.

Results

Figures 2 to 7 show the results of the main simulation study. Supplementary tables S 1-3 give the numerical results, including standard errors for the performance metrics. Results for the sensitivity

analyses (neutral comparisons, and introduction of an unmeasured confounder) are shown in the Supplementary File. We describe the results for the main analysis below, noting where sensitivity analyses resulted in departures from the main study results.

Convergence

As expected, convergence of all methods was adversely affected by reduced exposure prevalence, decreasing overlap in PS, and reduced sample size (Figure 2). All approaches converged infrequently at smaller sample sizes when there was little overlap in PS; IPTW and multiple logistic regression were most robust. With n=100,000, these two methods generally converged even when the PS distributions were not overlapping (scenario 5) and exposure prevalence was very low (5%), although use of a complementary log-log link for outcome generation adversely affected this behaviour (Supplementary File). Convergence for PS covariate was particularly affected by confounding (lack of PS overlap); convergence was actually reduced when there was little overlap for larger (n = 100,000) compared to smaller (n = 1,000, 10,000) sample sizes. This was also observed when comparing datasets of n=100,000 to n= 10,000 for caliper matching, and nearest neighbour matching when exposure prevalence was low (10%) or very low (5%).

Bias and absolute error

Bias and absolute error were consistently low for multiple logistic regression compared to other methods (Figure 3, 4), although IPTW was less biased for n = 100, when exposure prevalence was very low (5%) and there was overlap in PS distributions. Both measures were affected by sample size, with bias and/or error in the presence of non-overlapping PS distributions actually becoming more pronounced with increasing data size for some methods. IPTW in particular had high bias and error when overlap was low and sample sizes were large. Caliper matching was consistently better than nearest neighbour matching. Despite targeting a different estimand, PS covariate fared relatively well, although performance broke down under challenging circumstances (combinations of low exposure prevalence, small sample size, and little overlap in PS).

Power and coverage

In the main scenario, power was generally as high or higher than other methods for multiple logistic regression, although IPTW had higher power in several scenarios where PS distributions were non-overlapping (Figure 5). Coverage of IPTW was generally poor in these scenarios however (Figure 6), and performance was consistently inferior when both power and coverage were considered (Figure 7). Power of matching methods was greatly affected by lack of overlap in PS distributions. For caliper matching without replacement, when there is substantial imbalance there will tend to be few matches. Consequently, power when there was reduced overlap was sometimes superior for nearest neighbour matching. Additionally, sample size following matching is smaller when exposure prevalence is low, and this also affected power for matching compared to other methods, particularly when sample sizes were small to start off with. Coverage was decreased at n = 100,000 for the matching methods compared to sample sizes of 1,000 and 10,000 when there was imbalance in PS. Power of PS covariate compared to other PS methods was only favourable when there was considerable overlap in PS distributions or 50% exposure prevalence; coverage was frequently but not consistently superior. However, when a complementary log-log link was used, coverage was sometimes inferior for logistic regression compared to 1-to-1 and nearest neighbour propensity score matching, specifically with larger data size and modest or high imbalance in PS. This was exacerbated

when an unmeasured confounder was added to the complementary log-log link scenario. Power tended to be poor for matching methods in these scenarios (both with and without unmeasured confounding). Overall, when considering power and coverage as a composite, 1-to-1 and nearest neighbour matching appeared superior to regression for large data size with a complementary log-log outcome in the presence of unmeasured confounding. However, logistic regression remained superior in both absolute error and mean bias across all these scenarios.

Discussion

We conducted a simulation study to compare several approaches to estimate a marginal odds ratio in the presence of confounding and to investigate how dataset characteristics influenced performance. In the main study, multiple logistic regression followed by standardisation was consistently superior to PS approaches, although coverage still fell short of the advertised level for very small sample sizes (n=100) or for sample sizes of 1,000 when there was limited overlap in PS distributions. It was observed to be quite robust to imbalance in PS for large sample sizes, even when exposure prevalence was very low.

We explored whether simulating from a logistic model conferred an advantage to multiple logistic regression, using an alternative outcome generation approach (complementary log-log link). We also introduced an unmeasured confounder in additional sensitivity analyses. The combination of a complementary log-log outcome generating model and introduction of an unmeasured confounder resulted in somewhat different results for large data sizes. While bias and absolute error remained lower for logistic regression, coverage became very poor at times, even when imbalance in PS was not severe. While matching methods had poor power for the combination of large data size, high imbalance in PS, and presence of unmeasured confounding, 1-to-1 and nearest neighbour matching appeared superior to regression when considering a composite of coverage and power. This was due to regression having a much smaller model standard error compared to matching in the large data scenario, since these two matching approaches discard data. This resulted in the regression confidence interval frequently failing to cover the true value, while the much wider matching confidence intervals would frequently span both the true value (hence, higher, but still suboptimal coverage) and the null (hence, lower power).

However, logistic regression remained the best performer in terms of absolute error and mean bias, across all these scenarios. In addition, the size of the true effect is relevant here, and the effect we modelled was relatively large for samples of 10,000 or 100,000, thus not allowing for discrimination in power in these scenarios (power was 100%). We a-priori decided on the modelled effect to allow for at least some discrimination in the results of the smaller samples, and we did not vary it across scenarios to allow for meaningful comparisons. However, a smaller modelled effect would greatly reduce power for the matching approaches (due to standard errors two to three times those of logistic regression), leading to logistic regression being the best performer in the cumulative of power and coverage, in line with what we observed for samples of 1,000.

Coverage of PS methods was frequently suboptimal, as has been previously observed for a non-null marginal odds ratio [9]. As anticipated, relative performance of PS methods depended on dataset

characteristics. Ahead of the study, it was anticipated that matching using PS might be particularly affected by small sample size, imbalance in the PS distributions, and low exposure prevalence. While power was affected by these factors, overall performance of matching methods withstood these challenges better than IPTW. Matching methods also converged more frequently than did adjusting for the PS as a covariate in the presence of imbalance in PS distributions and large data sizes. Caliper matching was slightly preferred to nearest neighbour matching overall, although nearest neighbour did achieve superior power and coverage in some scenarios.

IPTW displayed poor performance as overlap in PS decreased. This suggests that IPTW is only suitable when there is substantial overlap in PS, highlighting the importance of examining distributions of the estimated PS [2, 26]. Vandersteedt and Daniels similarly found poor performance of IPTW when there was limited overlap in PS, up to a sample size of 1000; our results show that sample sizes considerably larger than this do not alleviate the problems [7]. However, we did not consider the use of stabilised or truncated weights [27], and it is unclear whether these would have led to improved performance. PS covariate does not estimate the marginal odds ratio but instead targets a different, and arguably unusual quantity – the odds ratio conditional on the PS. Performance against the marginal odds ratio was generally unacceptable, frequently falling short of the advertised coverage level when there was not high overlap in PS distributions and when there were small numbers of exposed participants, and for large data sizes balance did not guarantee appropriate coverage. PS covariate did not usually converge for larger data sizes when there was less overlap in PS distribution.

While we have considered the role of dataset characteristics in selecting a method for controlling confounding, there are several outstanding questions. One question is whether a paired or unpaired version of regression should be used after PS matching. There is uncertainty around this point, because people matched on their PS may nonetheless differ in terms of their covariate values. This question has been addressed in relation to continuous outcomes [28], but it remains to settle the issue in relation to binary outcomes. Suboptimal coverage against a non-null marginal odds ratio has been previously observed for several methods for analysing paired data following PS matching [9], and in the present study we also found this to hold when using an unpaired regression method. A direct comparison would be useful for future work.

By design, we did not include covariates in the regression models incorporating the PS (as a covariate, with IPTW, or following matching). Including covariates in the PS covariate approach results in a doubly-robust estimator, which offers valid inference in relation to some summary measures of the exposure effect (other than odds ratios) provided that one of the PS model and outcome model are correctly specified [29, 30]. Aside from this protection against misspecification, Vansteelandt and Davies found some power advantages when additionally adjusting for covariates in the outcome regression model compared to adjusting for the PS alone [7]. Consistent benefits of adjusting for covariates when using IPTW were not observed.

We have not considered the case where there is heterogeneity in the exposure effect across strata defined by the PS. When there is heterogeneity, different PS methods target different quantities, and might produce substantially different answers as a result [31], [32]. For example, matching estimates the exposure effect in the population corresponding to those who were exposed in the study, because the matching process produces a sample with similar PS distributions to the exposed group [32] (or

rather, for caliper matching, similar to the exposed participants *for whom unexposed matches could be found* [31]). These considerations motivate the suggestion that the possibility of an interaction between the PS and exposure should be routinely examined [33].

Conclusion

Researchers analysing observational data often face difficult analytical choices, while propensity score approaches are not easy to implement in large databases of electronic health records. Our results show how key features of a dataset (size, exposure prevalence, imbalance in propensity scores) affect the performance of several approaches aiming to address confounding. This study suggests that multiple logistic regression is relatively robust to low exposure prevalence and imbalance in PS, outside of very small sample sizes. For large sample sizes, multiple logistic regression was clearly the preferred method, especially in the main scenario, while PS methods performed poorly as imbalance in PS distributions increased, and this was not mitigated by large sample size or balanced group sizes. This highlights the importance of examining overlap in PS if these methods are to be used, but also suggests that their performance is worst when the problem they are intended to solve is most severe. Coverage of logistic regression was inferior to 1-to-1 and nearest neighbour propensity score matching methods in some large-data scenarios, however, particularly when a complementary log-log outcome generating model was used and either a) imbalance in PS was moderate or high, or b) an unmeasured confounder was introduced. However, this was driven by much larger standard errors in these two matching approaches, while logistic regression remained the best performer in absolute error and mean bias. In contemporary large observation studies, of national registries or primary care electronic health records, multiple regression estimation appears to be the optimal choice, both in terms of simplicity and performance.

References

[1] Rosenbaum PR, Rubin DB. The Central Role of the Propensity Score in Observational Studies for Causal Effects. Biometrika. 1983;70:41-55.

[2] Austin PC. An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. Multivar Behav Res. 2011;46:399-424.

[3] Sturmer T, Joshi M, Glynn RJ, Avorn J, Rothman KJ, Schneeweiss S. A review of the application of propensity score methods yielded increasing use, advantages in specific settings, but not substantially different estimates compared with conventional multivariable methods. J Clin Epidemiol. 2006;59:437-47.

[4] Rubin DB. Estimating causal effects from large data sets using propensity scores. Ann Intern Med. 1997;127:757-63.

[5] Simmons JP, Nelson LD, Simonsohn U. False-Positive Psychology: Undisclosed Flexibility in Data Collection and Analysis Allows Presenting Anything as Significant. Psychol Sci. 2011;22:1359-66.

[6] Tan Z. Comment: Understanding OR, PS and DR. Statistical Science. 2007;22:560-8.

[7] Vansteelandt S, Daniel RM. On regression adjustment for the propensity score. Stat Med. 2014;33:4053-72.

[8] Elze MC, Gregson J, Baber U, Williamson E, Sartori S, Mehran R, et al. Comparison of Propensity Score Methods and Covariate Adjustment: Evaluation in 4 Cardiovascular Studies. J Am Coll Cardiol. 2017;69:345-57.

[9] Austin PC. The performance of different propensity score methods for estimating marginal odds ratios. Stat Med. 2007;26:3078-94.

[10] Austin PC. The relative ability of different propensity score methods to balance measured covariates between treated and untreated subjects in observational studies. Med Decis Making. 2009;29:661-77.

[11] Williamson EJ, Forbes A, White IR. Variance reduction in randomised trials by inverse probability weighting using the propensity score. Stat Med. 2014;33:721-37.

[12] Lunceford JK, Davidian M. Stratification and weighting via the propensity score in estimation of causal treatment effects: a comparative study. Stat Med. 2004;23:2937-60.

[13] Austin PC, Grootendorst P, Anderson GM. A comparison of the ability of different propensity score models to balance measured variables between treated and untreated subjects: a Monte Carlo study. Stat Med. 2007;26:734-53.

[14] Weitzen S, Lapane KL, Toledano AY, Hume AL, Mor V. Principles for modeling propensity scores in medical research: a systematic literature review. Pharmacoepidemiol Drug Saf. 2004;13:841-53.

[15] Shah BR, Laupacis A, Hux JE, Austin PC. Propensity score methods gave similar results to traditional regression modeling in observational studies: a systematic review. J Clin Epidemiol. 2005;58:550-9.

[16] Rosenbaum PR. Model-Based Direct Adjustment. J Am Stat Assoc. 1987;82:387-94.

[17] Austin PC. A critical appraisal of propensity-score matching in the medical literature between 1996 and 2003. Stat Med. 2008;27:2037-49.

[18] Austin PC. Propensity-score matching in the cardiovascular surgery literature from 2004 to 2006: a systematic review and suggestions for improvement. J Thorac Cardiovasc Surg. 2007;134:1128-35.

[19] Austin PC. Primer on statistical interpretation or methods report card on propensity-score matching in the cardiology literature from 2004 to 2006: a systematic review. Circ Cardiovasc Qual Outcomes. 2008;1:62-7.

[20] Rosenbaum PR, Rubin DB. Constructing a Control-Group Using Multivariate Matched Sampling Methods That Incorporate the Propensity Score. Am Stat. 1985;39:33-8.

[21] StataCorp L. P. Stata Statistical software for Windows. 15.1 ed2015.

[22] Leuven E, Sianesi B. PSMATCH2: Stata module to perform full Mahalanobis and propensity score matching, common support graphing, and covariate imbalance testing. 2017.

[23] Sjolander A. Regression standardization with the R package stdReg. Eur J Epidemiol. 2016;31:563-74.

[24] Wan F, Mitra N. An evaluation of bias in propensity score-adjusted non-linear regression models. Stat Methods Med Res. 2018;27:846-62.
[25] Wan F. An interpretation of the properties of the propensity score in the regression framework. Communications in Statistics - Theory and Methods. 2019;https://doi.org/10.1080/03610926.2019.1659369.
[26] Austin PC, Stuart EA. Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. Stat Med. 2015;34:3661-79.
[27] Cole SR, Hernan MA. Constructing inverse probability weights for marginal structural models. Am J Epidemiol. 2008;168:656-64.
[28] Wan F. Matched or unmatched analyses with propensity-score-matched data? Stat Med. 2019;38:289-300.
[29] Van der Laan M, Robins JM. Unified Methods for Censored Longitudinal Data and Causality: Springer Science and Business Media; 2003.
[30] Tan Z. A Distributional Approach for Causal Inference Using Propensity Scores. J Am Stat Assoc. 2006;101:1619-37.
[31] Lunt M, Solomon D, Rothman K, Glynn R, Hyrich K, Symmons DP, et al. Different methods of balancing covariates leading to different effect estimates in the presence of effect modification. Am J Epidemiol. 2009;169:909-17.
[32] Kurth T, Walker AM, Glynn RJ, Chan KA, Gaziano JM, Berger K, et al. Results of multivariable logistic regression, propensity matching, propensity adjustment, and propensity-based weighting under conditions of nonuniform effect. Am J Epidemiol. 2006;163:262-70.
[33] Glynn RJ, Schneeweiss S, Sturmer T. Indications for propensity scores and review of their use in pharmacoepidemiology. Basic Clin Pharmacol Toxicol. 2006;98:253-9.

Figures

Figure 1: Simulated propensity score scenarios, when Pr(E=1)=0.5

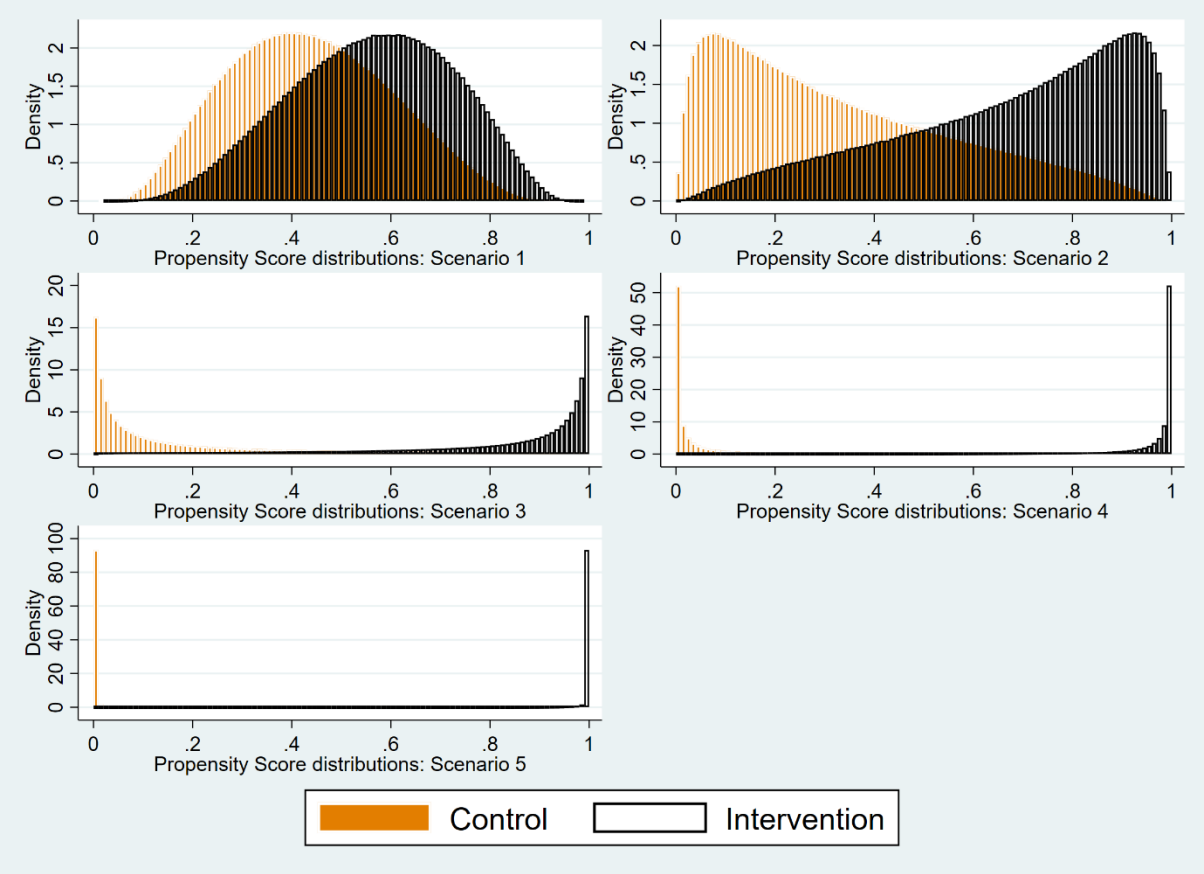


Figure 2: Convergence (%)

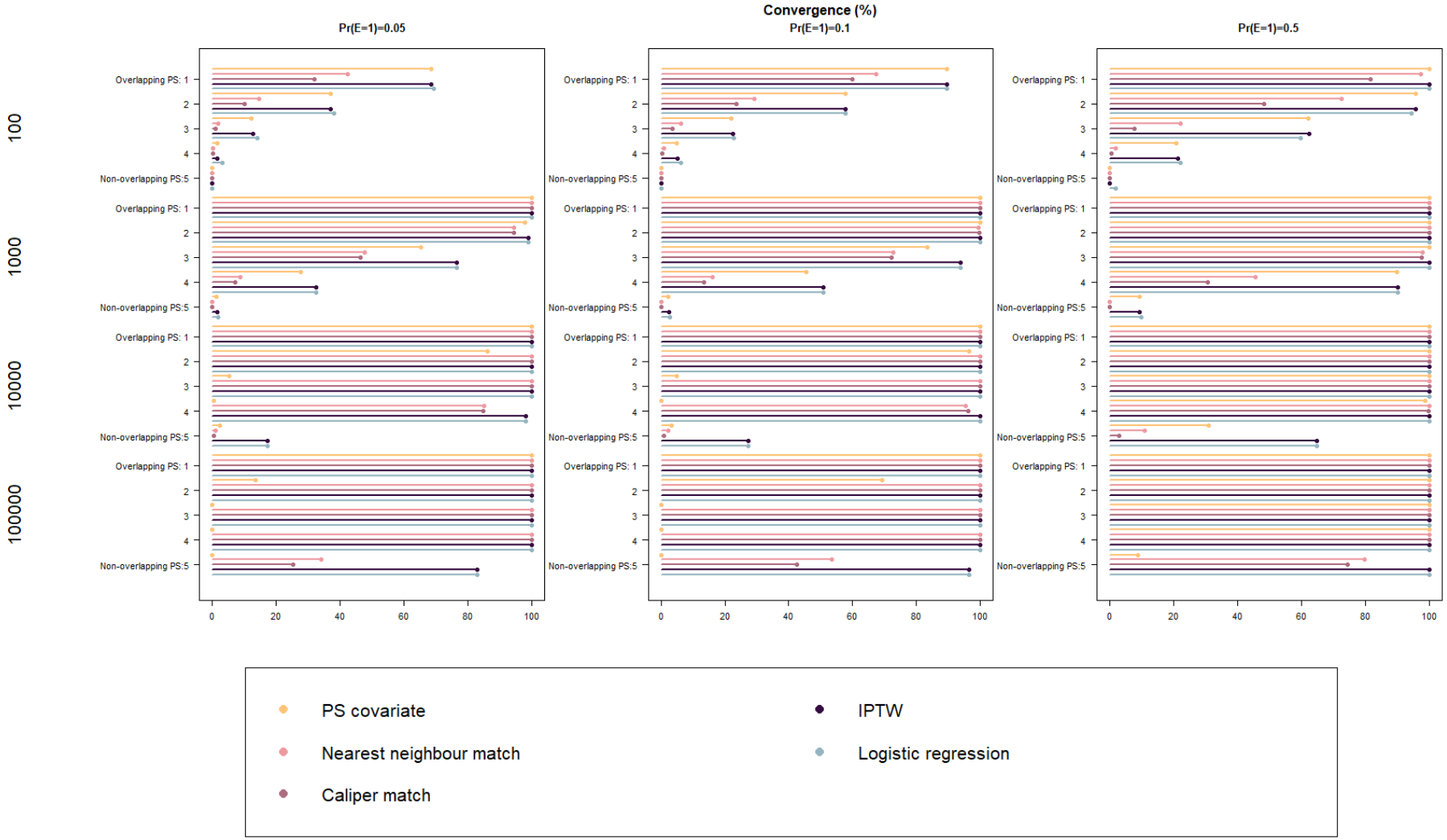


Figure 3: Bias

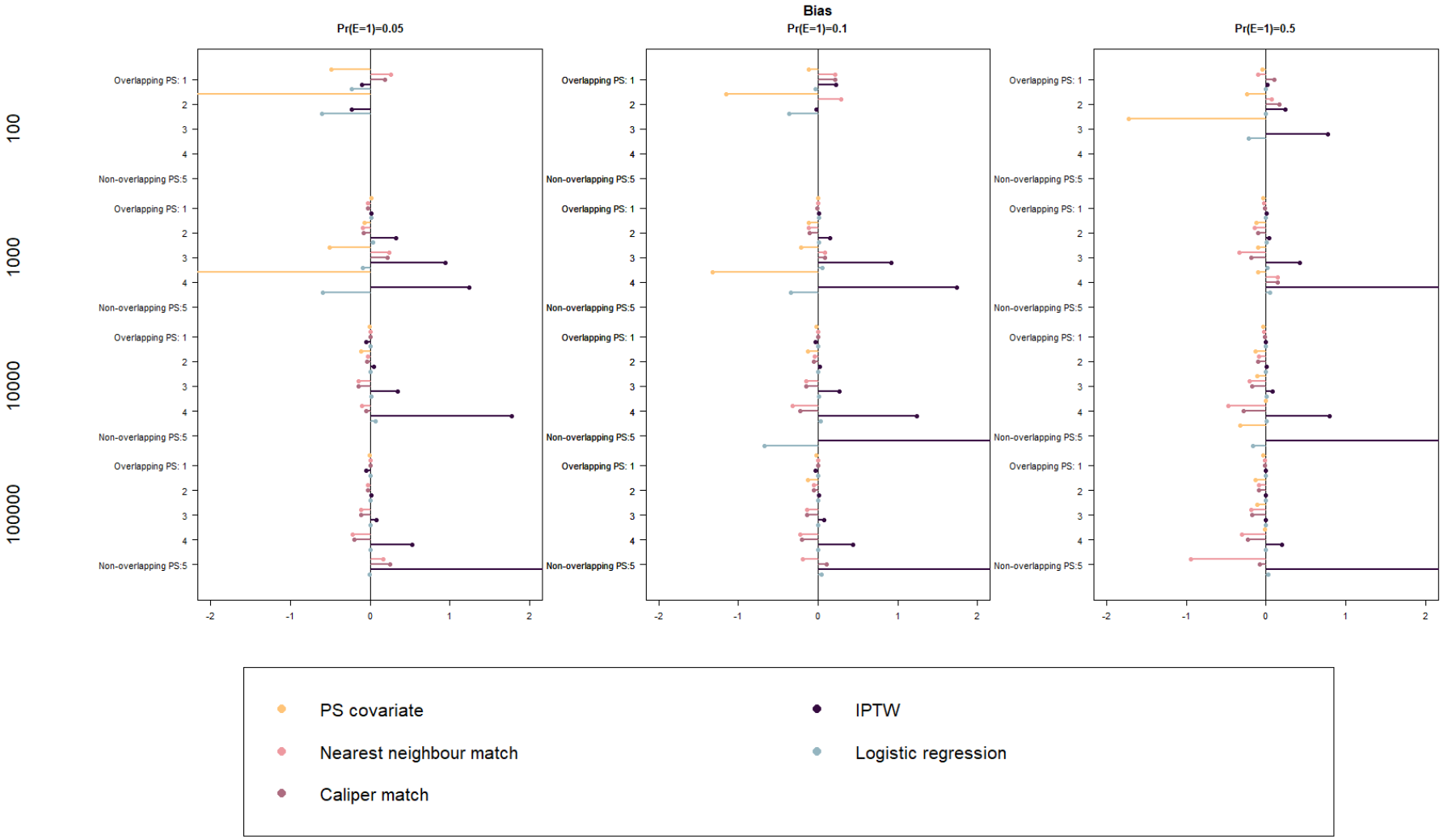


Figure 4: Absolute error

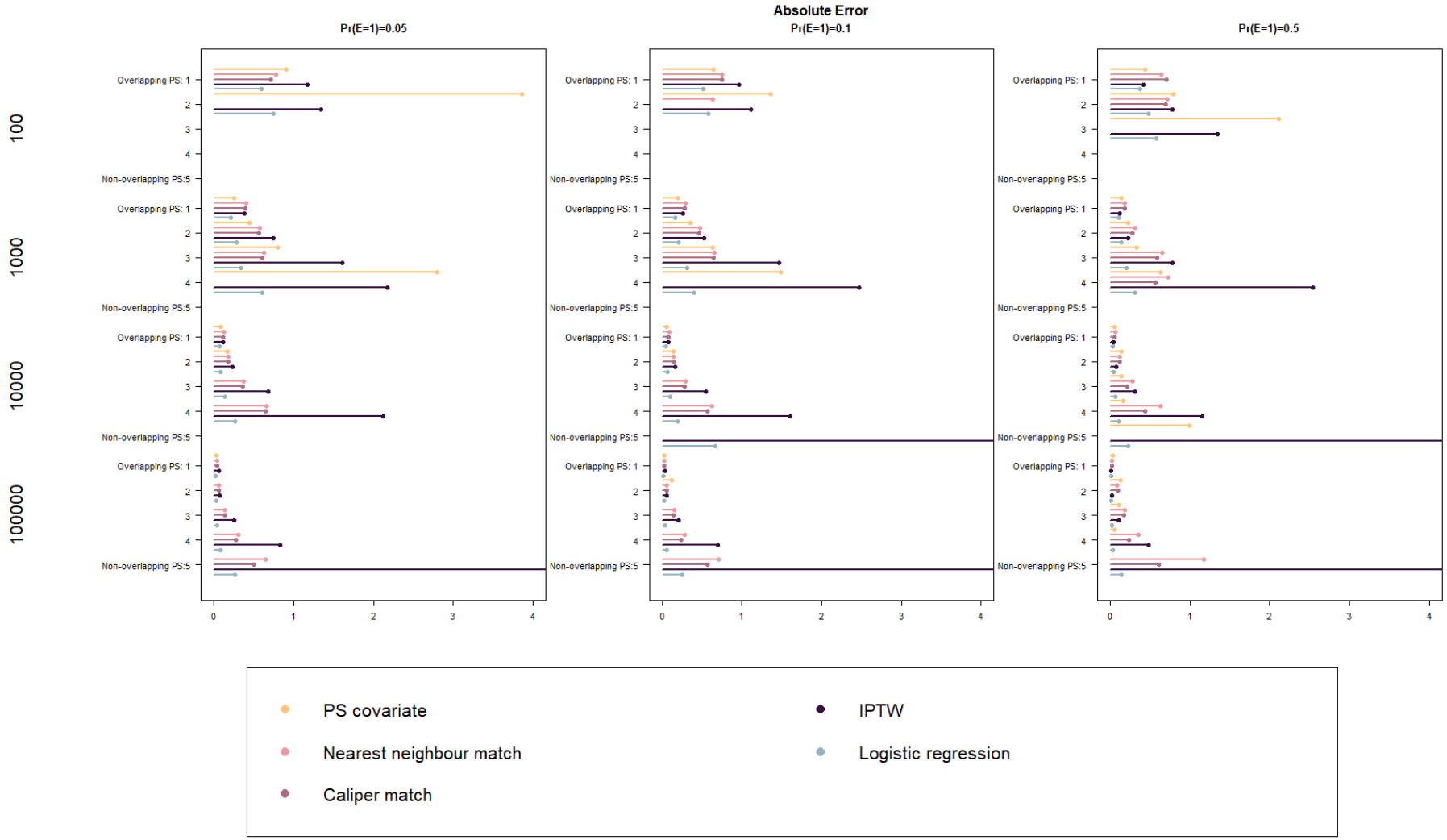


Figure 5: Power (%)

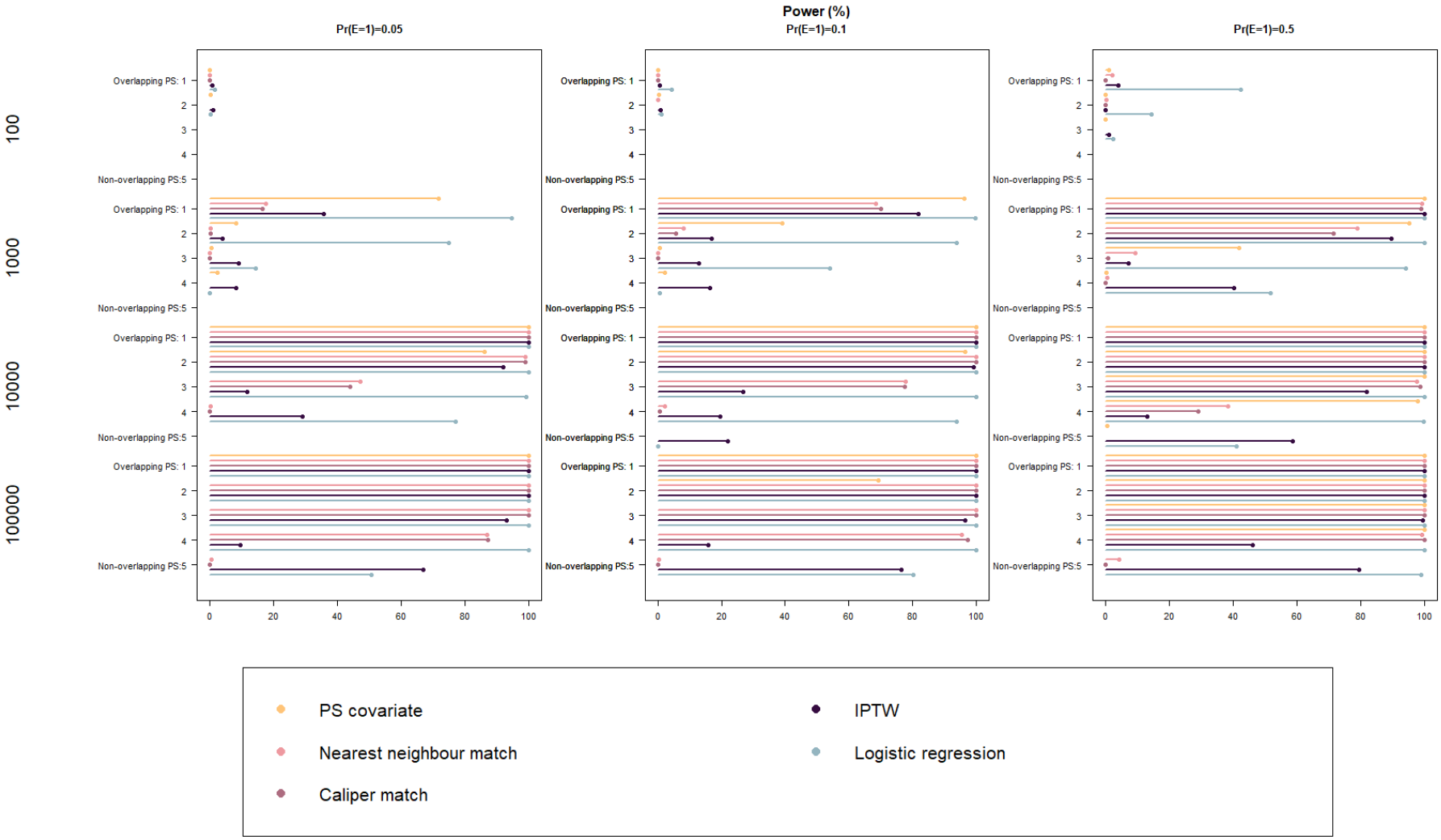


Figure 6: Coverage (%)

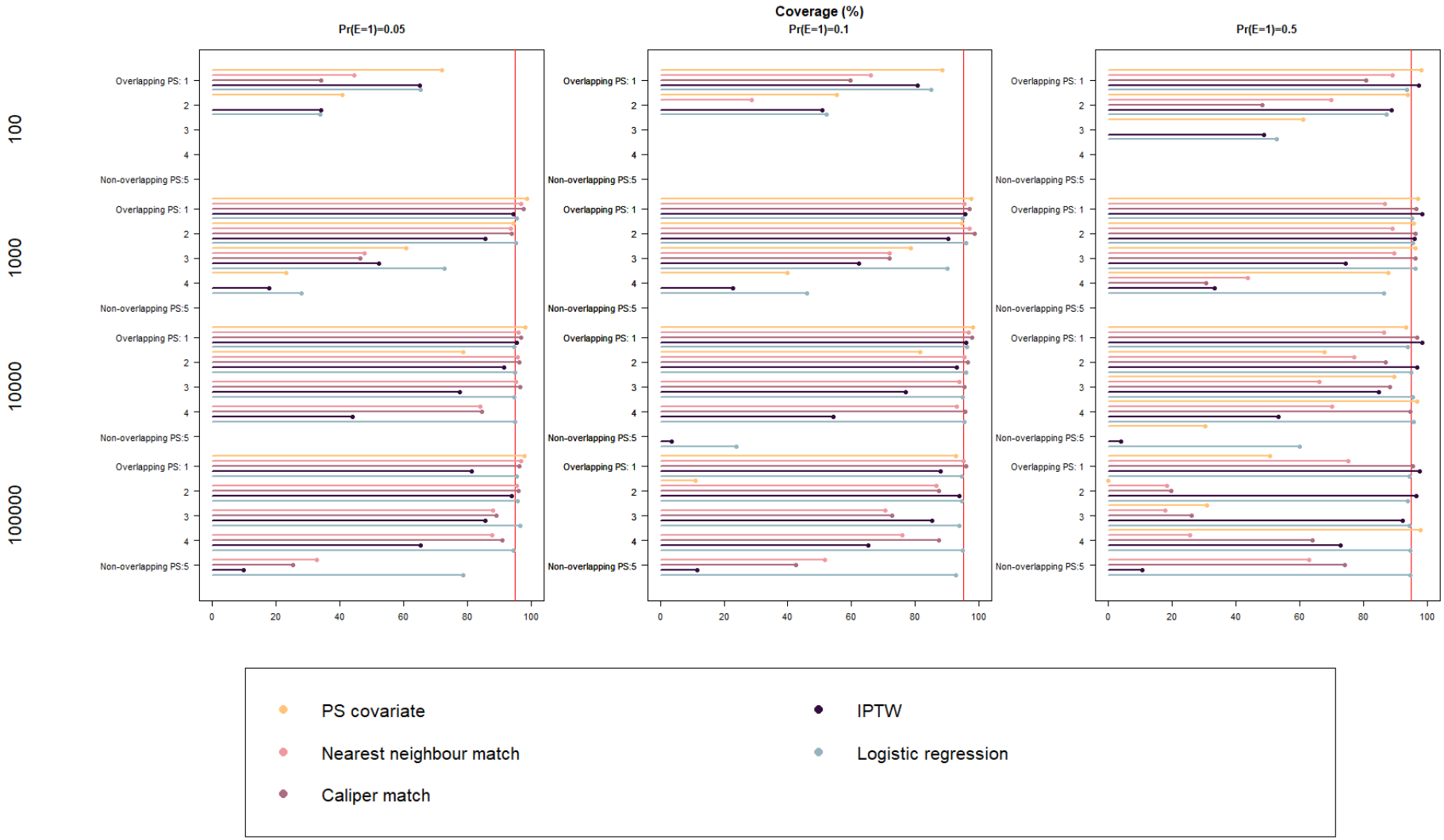
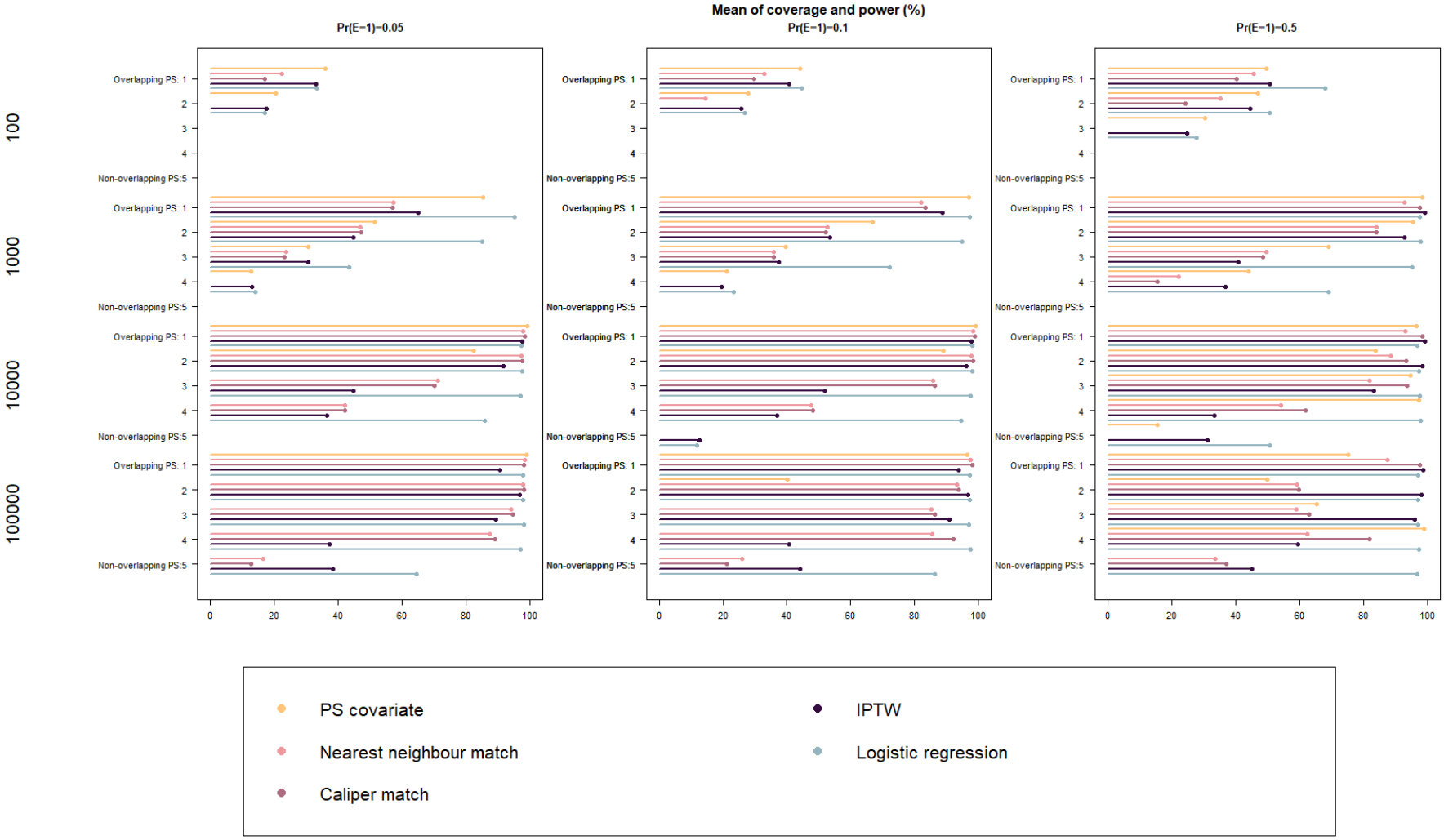


Figure 7: Mean of coverage and power (%)



Supplementary file for "How do dataset characteristics affect the performance of propensity score methods and regression for controlling confounding in observational studies? A simulation study."

Methods

Propensity score

In a comparison of an exposed with a control group, PS can be estimated using multiple logistic regression where the binary response variable *E* denotes membership of an exposed (*E* = 1) or a comparator (*E* = 0) group. We suppress a subscript *j* corresponding to the *j* = 1, …, n participants included in the study. Covariates $x_1, x_2, \ldots, x_k$ hypothesised to be associated with the outcome should be included in the multiple logistic regression model. The PS is the predicted probability p of exposure (E= 1):

$$Log\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 x_1 + \cdots + \beta_k x_k \qquad (1)$$

In practice, coefficients β_i, *i =1,…,k* must be estimated and hence there is uncertainty in p that is not usually accounted for in the process (although it is possible to do so, e.g. [1, 2]). Following estimation, the next concern is to verify that these are balanced across the two groups [3]. Finally, PS are incorporated into the analysis using one of several approaches.

Stratification using the PS has been found to perform poorly, and so we decided not to consider it in our simulation study [4, 5]. Regressing the outcome on exposure and PS has been found to be the most commonly used approach in reviews of practice [6, 7].

Inverse probability of treatment weighting (IPTW) is an alternative approach [8]. Weights corresponding to the inverse of the probability that the participant is included in their group are defined:

$$w = \begin{cases} 1/PS & if\ E = 1 \\ 1/(1-PS) & if\ E = 0 \end{cases} \qquad (2)$$

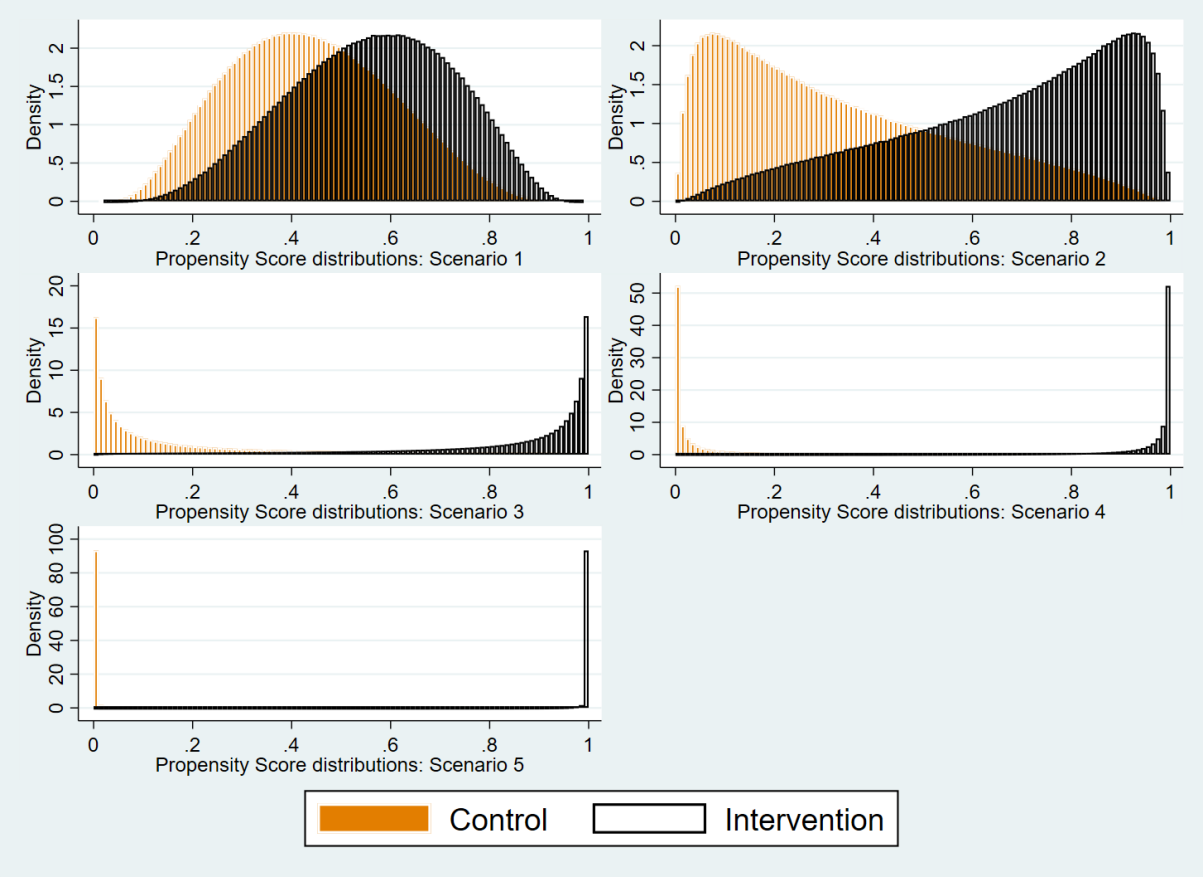
Observations are then weighted accordingly in the analysis. PS matching has gained a reputation as the best PS method for removing baseline imbalance and is widely used[9-11]. The most common version is one-to-one matching without replacement [3], where each "case" in group A is matched to one "control" in group B, if the difference in their PS is below a predefined arbitrary threshold or "caliper" δ, i.e. $|PS_A - PS_B| \leq \delta$ [12]. This approach entails sample size reductions, which can become extreme if there is great imbalance in baseline characteristics (resulting in largely non-overlapping PS distributions in the study groups), or if there is a large imbalance in group sizes. An alternative is one-to-one nearest neighbour matching with replacement, which will generally result in fewer observations being discarded compared to matching on a caliper, at the expense of greater discrepancies in PS distributions between groups.

Simulation study

We conducted a simulation study to evaluate PS methods and covariate adjustment for confounding control in observational studies, and the dataset characteristics affecting their performance.

Data generating model

To investigate the influence of data size, we considered sample sizes of 100, 1000, 10000, and 100000, to capture scenarios in which large databases are available for analysis. We also investigated the impact of the distribution of E: we considered equal group sizes $Pr(E = 1) = 0.5$, imbalanced group sizes $Pr(E = 1) = 0.1$, and substantially imbalanced group sizes $Pr(E = 1) = 0.05$. A third varying parameter was baseline imbalance for the covariates, which took on five different patterns, ranging from well-overlapping propensity scores to almost completely non-overlapping propensity scores for the two comparison groups. S Figure 1 shows the PS distributions when Pr(E=1)=0.5.



S Figure 1: Simulated propensity score scenarios, when Pr(E=1)=0.5

Generation of covariates

The simulation was implemented in Stata v15.1 [13]. We used the *drawnorm* command to draw observations from multivariate normal distributions, which were dichotomised for some variables. The generated variables included: binary exposure E, binary covariate X_1 (with $Pr(X_1 = 1) = 0.5$), and continuous covariates X_2, X_3,X_4 and X_5 (with $X_i \sim N(0,1)$ for $i = 2,3,4,5$). Correlations were set to be low between all variables (≈0.1 Pearson's correlation) except for two of the covariates and the exposure ($corr_{Tetrachoric}(X_1, E) \approx 0.3$ and $corr_{Pearson}(X_2, E) \approx 0.5$). These associations were necessarily affected to a small extent when baseline differences were incorporated by shifting the

distributions of the covariates for the $E = 1$ group. When PS distributions were simulated to be overlapping (S Figure 1, Scenario 1), all continuous covariates were edited for $E = 1$ so that the mean difference $E(X_i|E = 1) - E(X_i|E = 0) = 0.5$ for $i = 2,3,4,5$, while $Pr(X_1 = 1|E = 1)$ was set to 0.45. For scenarios 2 to 5 (S Figure 1), the mean difference was 1.0, 1.5, 2.0 and 3.0, respectively; and $Pr(X_1 = 1|E = 1)$ was 0.40, 0.35, 0.30 and 0.20, respectively. Note that providing exact distributions for continuous covariates when $E = 1$ is not straightforward due to the modelled correlations (e.g. the distribution for X_2 differs across E regardless of the other simulation parameters).

Outcome generation

In the last step, the outcome Y was generated:

$$logit(\pi) = -2.3 + ln(2)\,E + ln(1.3)\,X_1 + ln(1.5)\,X_2 + ln(6)\,X_3 + ln(3)\,X_4 + ln(1)\,X_5, \quad (3)$$
$$Y \sim \text{Bernoulli}(\pi).$$

X_5 is an instrumental variable; it is associated with exposure, but not with outcome.

Alternative outcome generation approaches

To examine the robustness of results to varying the outcome generation mechanism, we also used a complementary log-log link to generate the outcome Y:

$$log\{-log(1-\pi)\} = -2.3 + ln(2)\,E + ln(1.3)\,X_1 + ln(1.5)\,X_2 + ln(6)\,X_3 + ln(3)\,X_4 + ln(1)\,X_5, \quad (4)$$
$$Y \sim \text{Bernoulli}(\pi).$$

In additional sensitivity analyses we introduced an unmeasured confounder X_6, in each of the two link approaches, which was not included in any of the analytical models:

$$logit(\pi) = -2.3 + ln(2)\,E + ln(1.3)\,X_1 + ln(1.5)\,X_2 + ln(6)\,X_3 + ln(3)\,X_4 + ln(1)\,X_5 + ln(2)\,X_6, \quad (5)$$
$$Y \sim \text{Bernoulli}(\pi).$$

And

$$log\{-log(1-\pi)\} = -2.3 + ln(2)\,E + ln(1.3)\,X_1 + ln(1.5)\,X_2 + ln(6)\,X_3 + ln(3)\,X_4 + ln(1)\,X_5 + ln(2)\,X_6, \quad (6)$$
$$Y \sim \text{Bernoulli}(\pi).$$

Analyses

A total of 5 analytical approaches were evaluated. First, PS were calculated using the PSMATCH2 module.[14] During this step we performed nearest neighbour one-to-one matching on the PS with

replacement. Next, the PS were used in four logistic regression models: 1) exposure and the PS as independent variables (*PS covariate*); 2) exposure as the only independent variable, with the number of times each observation appeared in the aforementioned nearest-neighbour-matched dataset as a frequency weight (*nearest neighbour matching*); 3) exposure as the only independent variable, following one-to-one matching without replacement, when absolute difference on the PS was below 10^{-2} (*Caliper matching*); 4) exposure as the only independent variable and the PS used as an inverse probability treatment weight (*IPTW*). Note that in this study, we use standard logistic regression following matching, rather than a version intended for matched data; we return to this point in the discussion. We also performed logistic regression with the exposure and all five covariates included as independent variables (not using the PS), followed by regression standardisation, as a fifth approach [15]. Standardisation is necessary so that regression targets the same quantity as PS approaches (see *Target of inference*). We used the margins command with the post option following logistic regression to achieve this, and used the delta method to compute confidence intervals on the log odds scale.

Target of inference

We evaluated the methods against the marginal odds ratio, which is a measure of the exposure effect at the population level. We calculated the marginal odds ratio for each simulated dataset, using the method described by Austin [16]. When there is no heterogeneity in treatment effect, caliper and nearest neighbour matching, IPTW, and logistic regression with standardisation all estimate the marginal odds ratio [15, 16]. PS covariate actually targets a different quantity; the odds ratio conditional on the PS [1, 17, 18]. We include it here due to its popularity, and to compare to other methods.

Performance measures

1000 datasets were simulated for each scenario. We considered four performance measures: mean error, bias, coverage and power. Mean error is the mean of the absolute difference between the estimate and the true parameter: $\frac{1}{1000}\sum_{i=1}^{1000}|z-\hat{z}_i|$ where z is the true association and $\hat{z}_i$ is the estimate of the association. Bias is the mean difference between the estimate and the true parameter, or $\frac{1}{1000}\sum_{i=1}^{1000}(z-\hat{z}_i)$. Coverage is the proportion of 95% confidence intervals for the estimate, based on a Normal approximation, that contain the true parameter. Finally, we calculated power by the proportion of iterations where the null was rejected when it was actually false. Although power as a metric can be problematic in the presence of bias, it is essential for a complete comparison. However, in order to obtain a more meaningful metric, power-related statistical significance was calculated one-sided (i.e. statistically greater than zero, rather than statistically different). We also evaluated model convergence. We used default settings for convergence evaluation in Stata 15.1 MP [13]. The other metrics were only computed when convergence for a particular method in a simulation setting was 25% or above, otherwise they were set to missing.

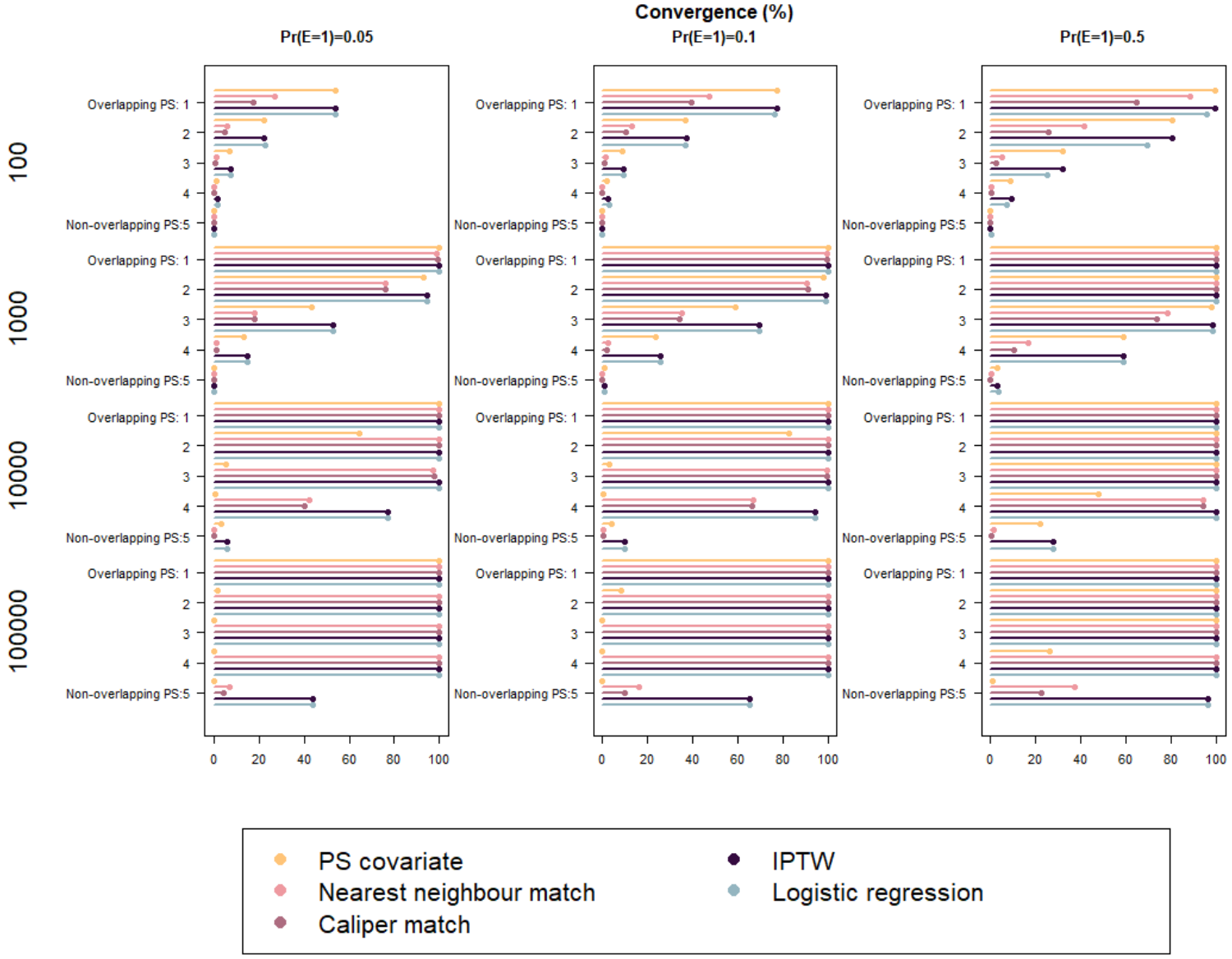
References

[1] Vansteelandt S, Daniel RM. On regression adjustment for the propensity score. Stat Med. 2014;33:4053-72.

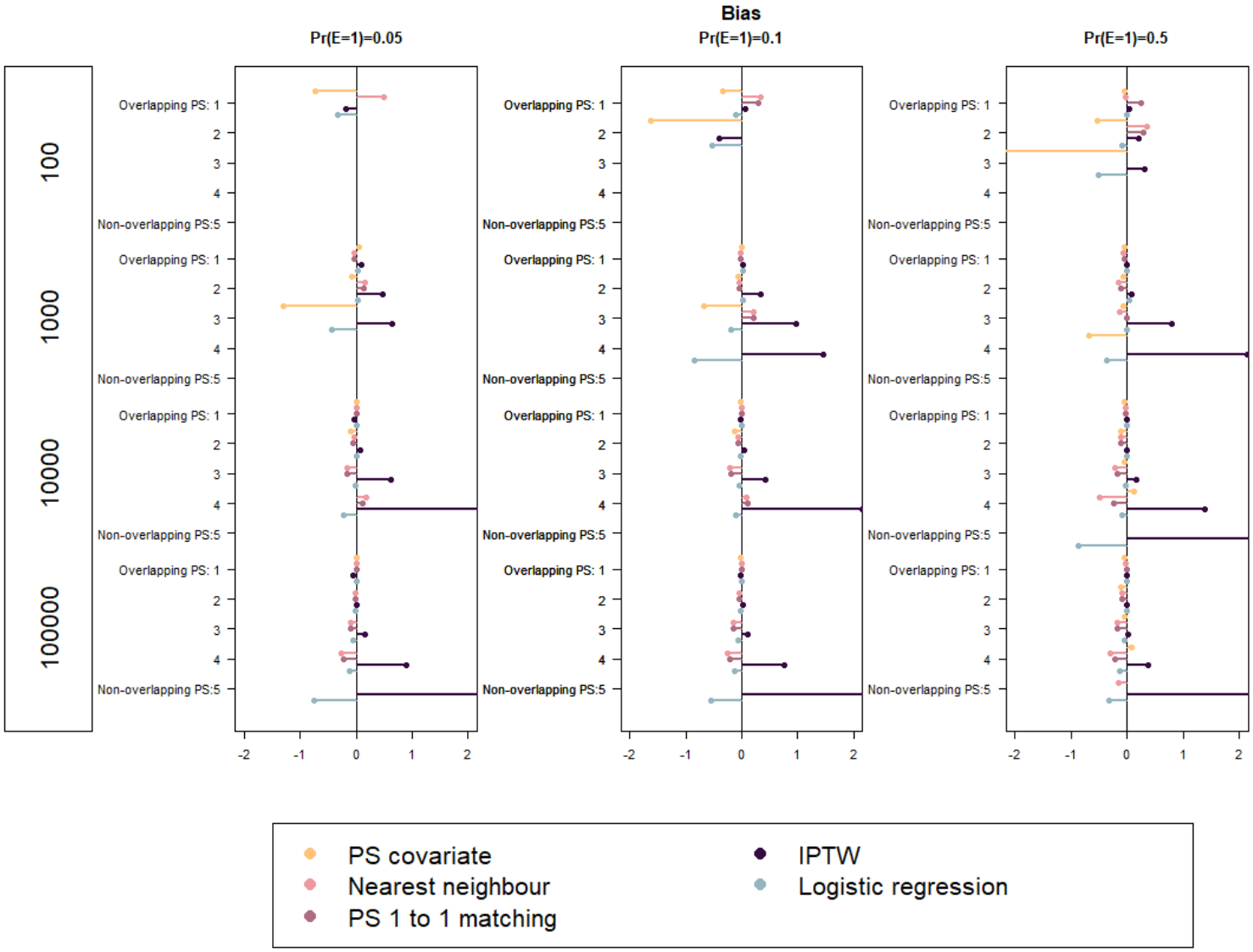
[2] Williamson EJ, Forbes A, White IR. Variance reduction in randomised trials by inverse probability weighting using the propensity score. Stat Med. 2014;33:721-37.

[3] Austin PC. An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. Multivar Behav Res. 2011;46:399-424.
[4] Lunceford JK, Davidian M. Stratification and weighting via the propensity score in estimation of causal treatment effects: a comparative study. Stat Med. 2004;23:2937-60.
[5] Austin PC, Grootendorst P, Anderson GM. A comparison of the ability of different propensity score models to balance measured variables between treated and untreated subjects: a Monte Carlo study. Stat Med. 2007;26:734-53.
[6] Weitzen S, Lapane KL, Toledano AY, Hume AL, Mor V. Principles for modeling propensity scores in medical research: a systematic literature review. Pharmacoepidemiol Drug Saf. 2004;13:841-53.
[7] Shah BR, Laupacis A, Hux JE, Austin PC. Propensity score methods gave similar results to traditional regression modeling in observational studies: a systematic review. J Clin Epidemiol. 2005;58:550-9.
[8] Rosenbaum PR. Model-Based Direct Adjustment. J Am Stat Assoc. 1987;82:387-94.
[9] Austin PC. A critical appraisal of propensity-score matching in the medical literature between 1996 and 2003. Stat Med. 2008;27:2037-49.
[10] Austin PC. Propensity-score matching in the cardiovascular surgery literature from 2004 to 2006: a systematic review and suggestions for improvement. J Thorac Cardiovasc Surg. 2007;134:1128-35.
[11] Austin PC. Primer on statistical interpretation or methods report card on propensity-score matching in the cardiology literature from 2004 to 2006: a systematic review. Circ Cardiovasc Qual Outcomes. 2008;1:62-7.
[12] Rosenbaum PR, Rubin DB. Constructing a Control-Group Using Multivariate Matched Sampling Methods That Incorporate the Propensity Score. Am Stat. 1985;39:33-8.
[13] StataCorp L. P. Stata Statistical software for Windows. 15.1 ed2015.
[14] Leuven E, Sianesi B. PSMATCH2: Stata module to perform full Mahalanobis and propensity score matching, common support graphing, and covariate imbalance testing. 2017.
[15] Sjolander A. Regression standardization with the R package stdReg. Eur J Epidemiol. 2016;31:563-74.
[16] Austin PC. The performance of different propensity score methods for estimating marginal odds ratios. Stat Med. 2007;26:3078-94.
[17] Wan F, Mitra N. An evaluation of bias in propensity score-adjusted non-linear regression models. Stat Methods Med Res. 2018;27:846-62.
[18] Wan F. An interpretation of the properties of the propensity score in the regression framework. Communications in Statistics - Theory and Methods. 2019;https://doi.org/10.1080/03610926.2019.1659369.

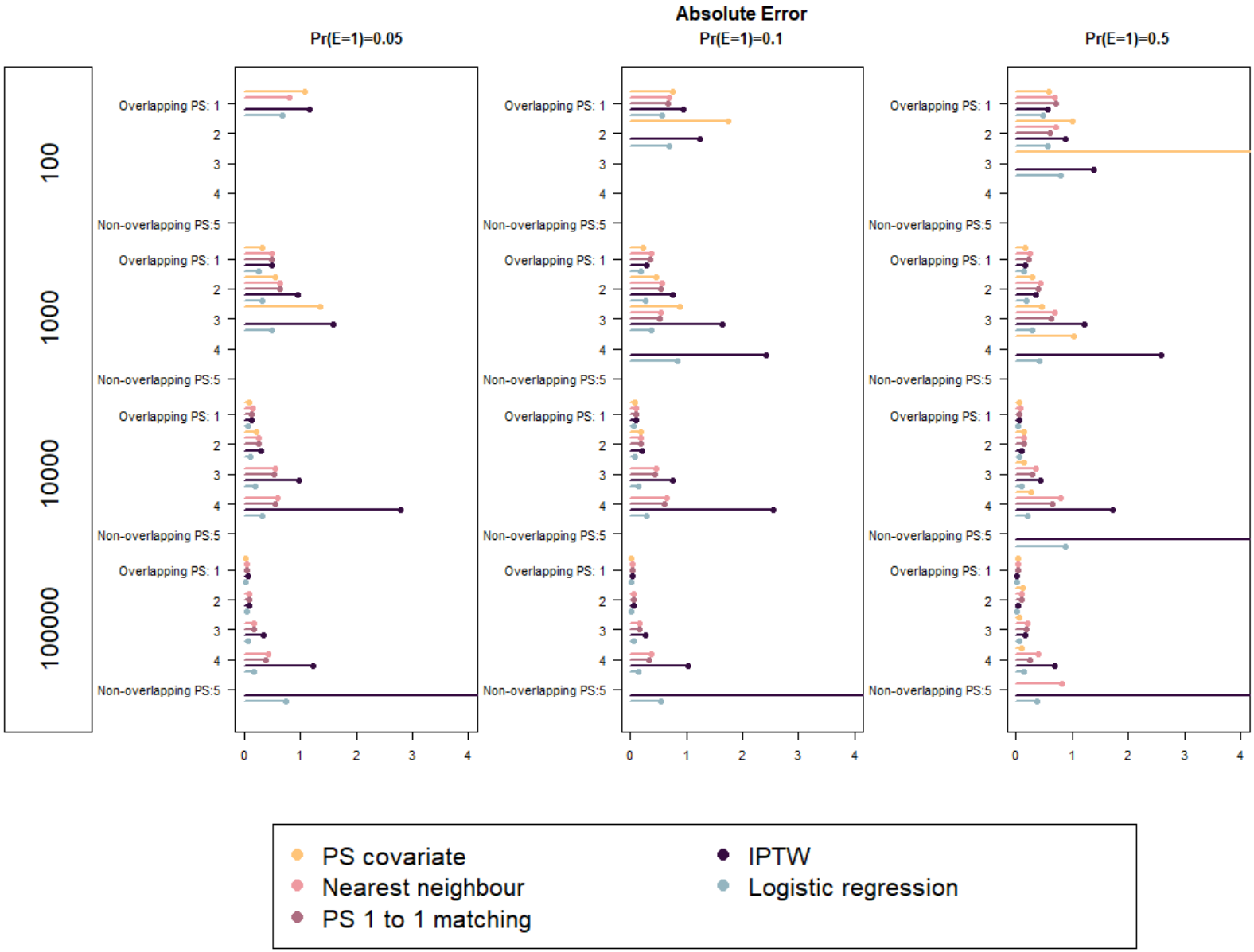
Sensitivity 1: complementary log-log link outcome generation



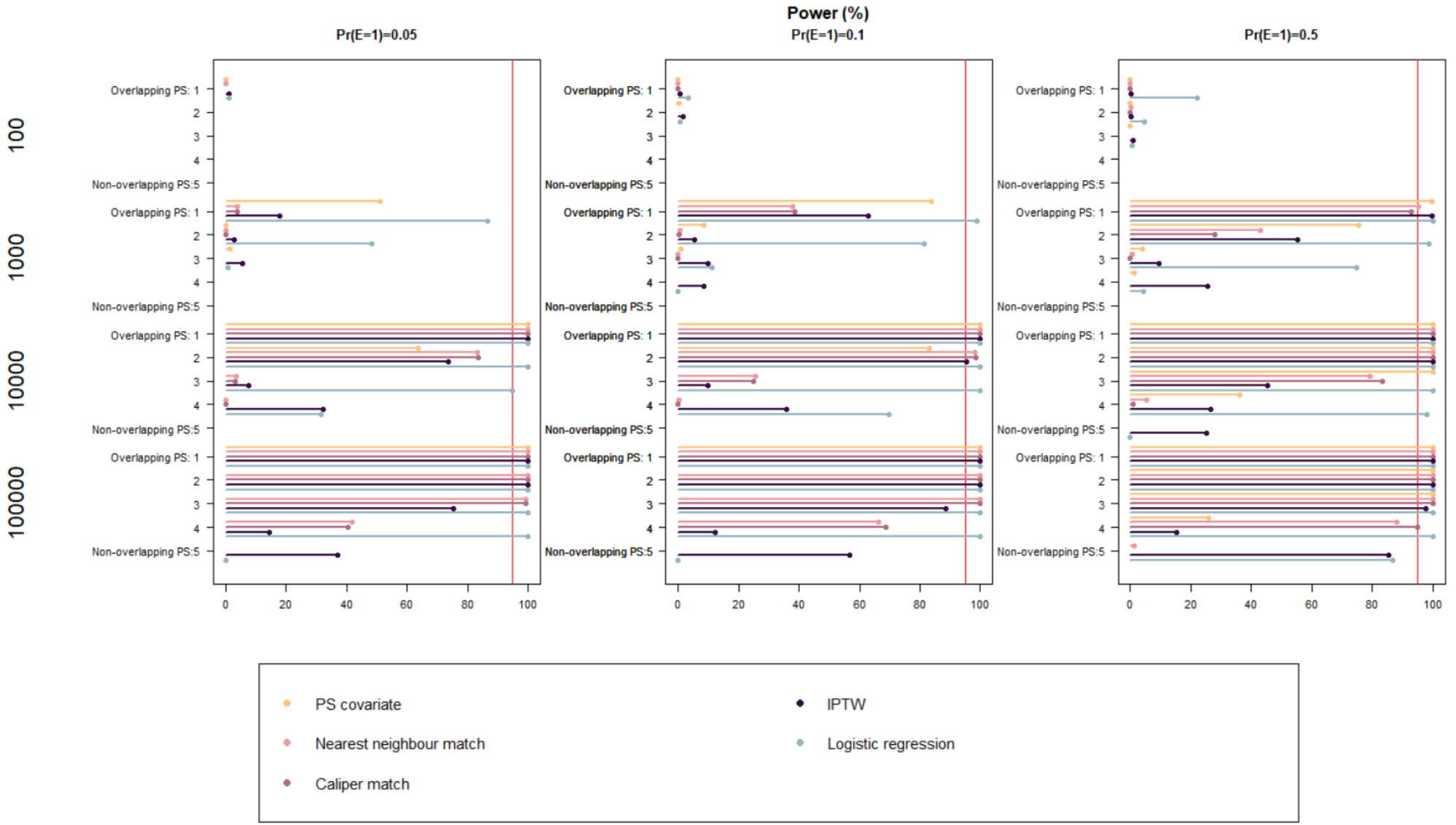
S Figure 1: Convergence (%)



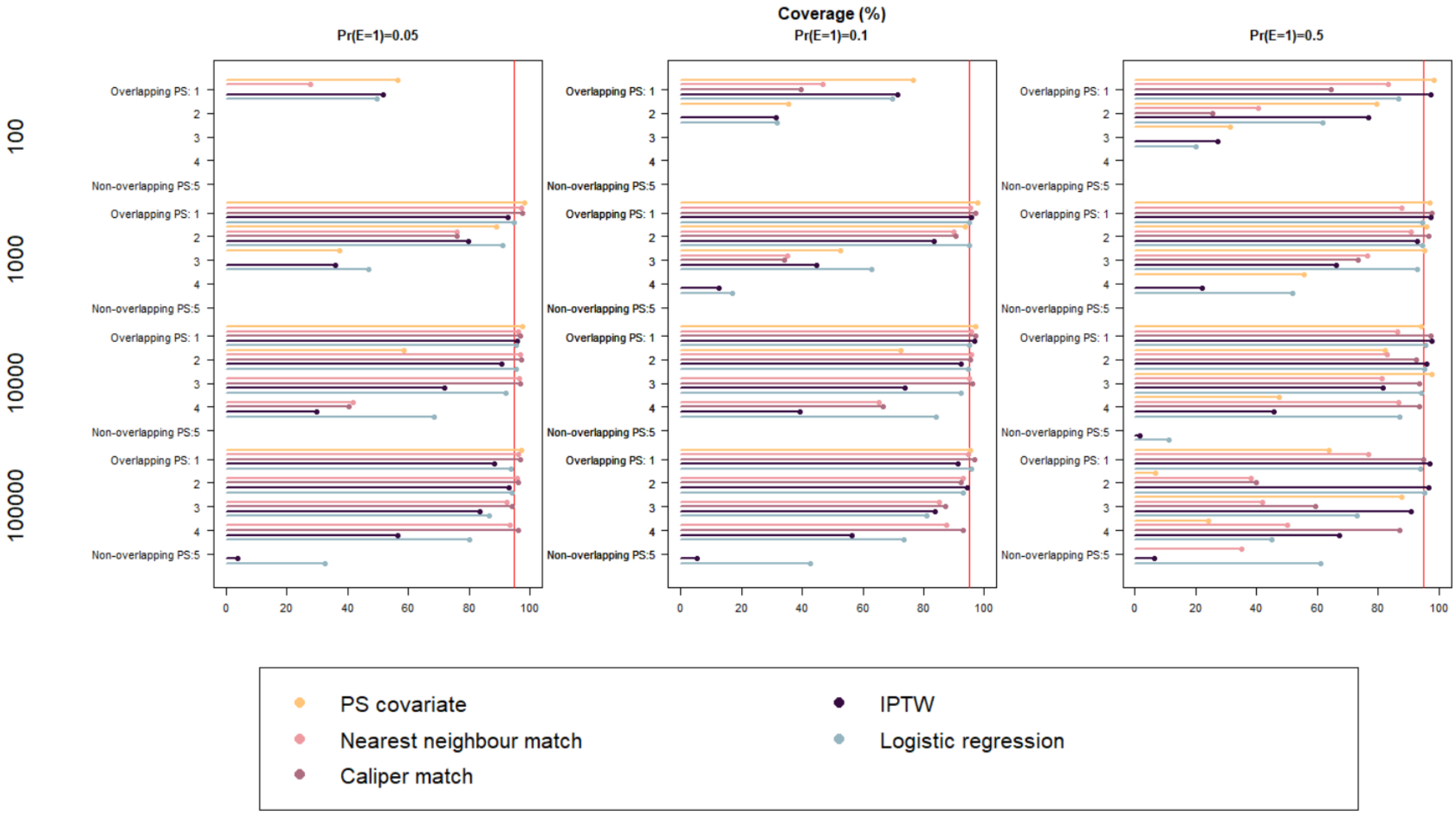
S Figure 2: Bias



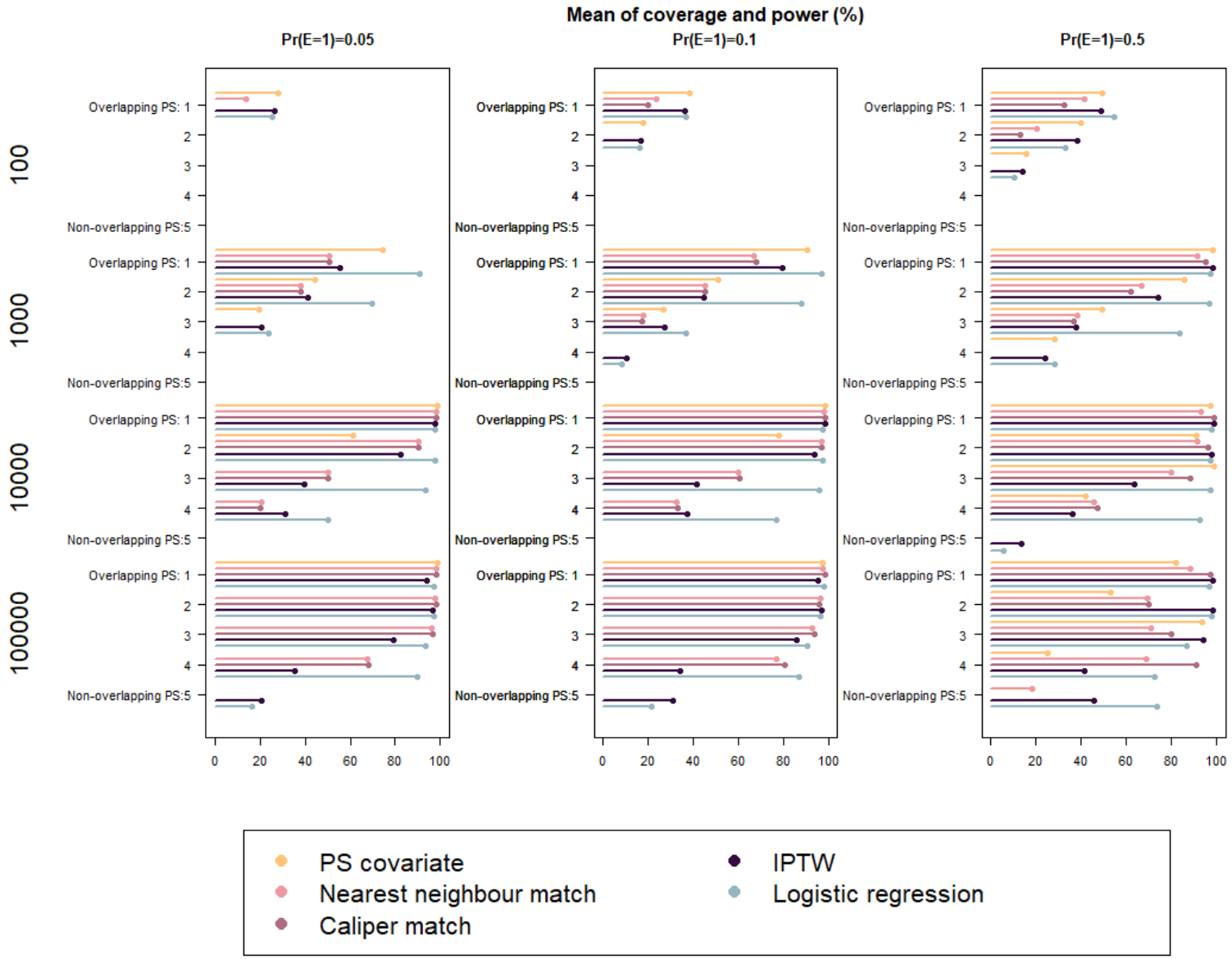
S Figure 3: Absolute error



S Figure 4: Power (%)

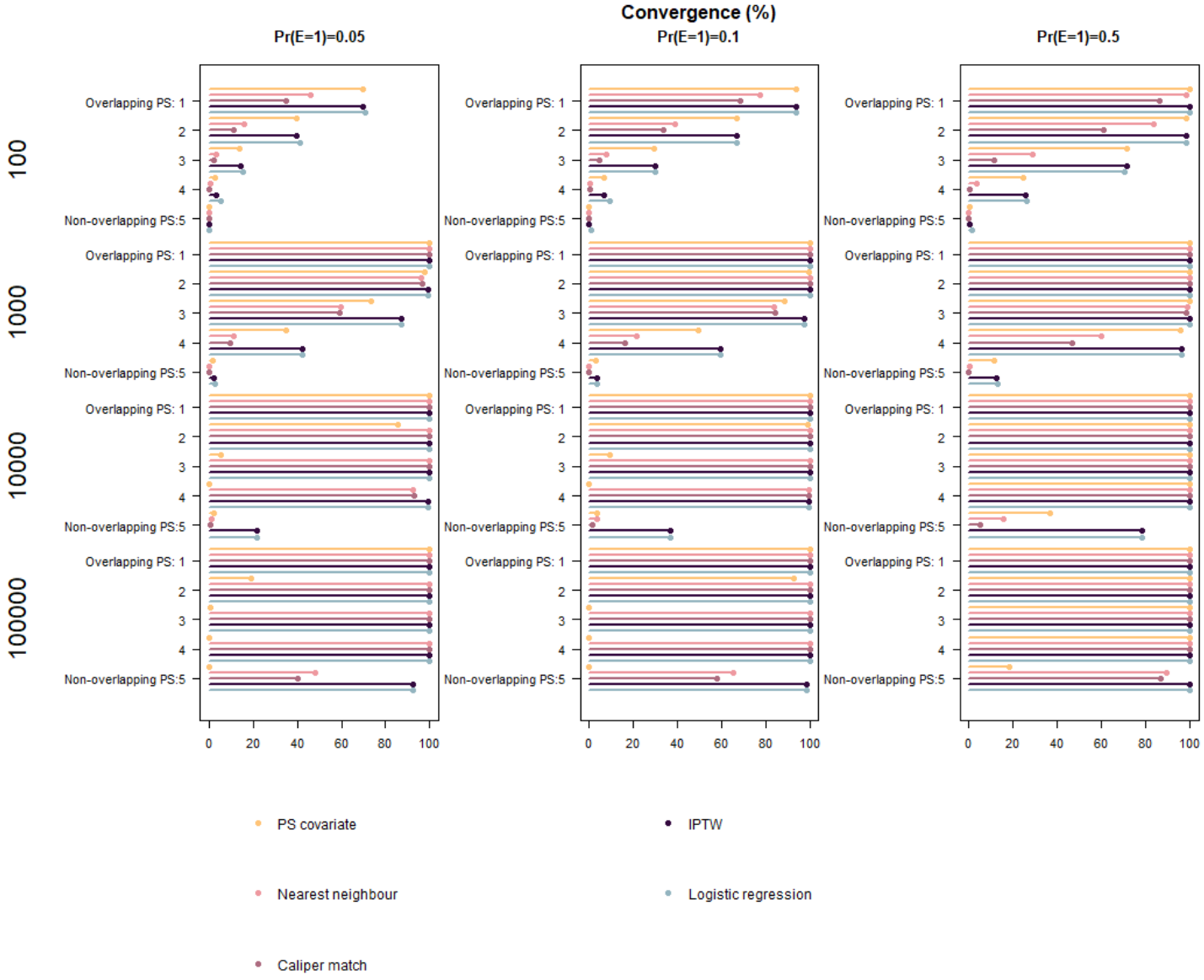


S Figure 5: Coverage (%)

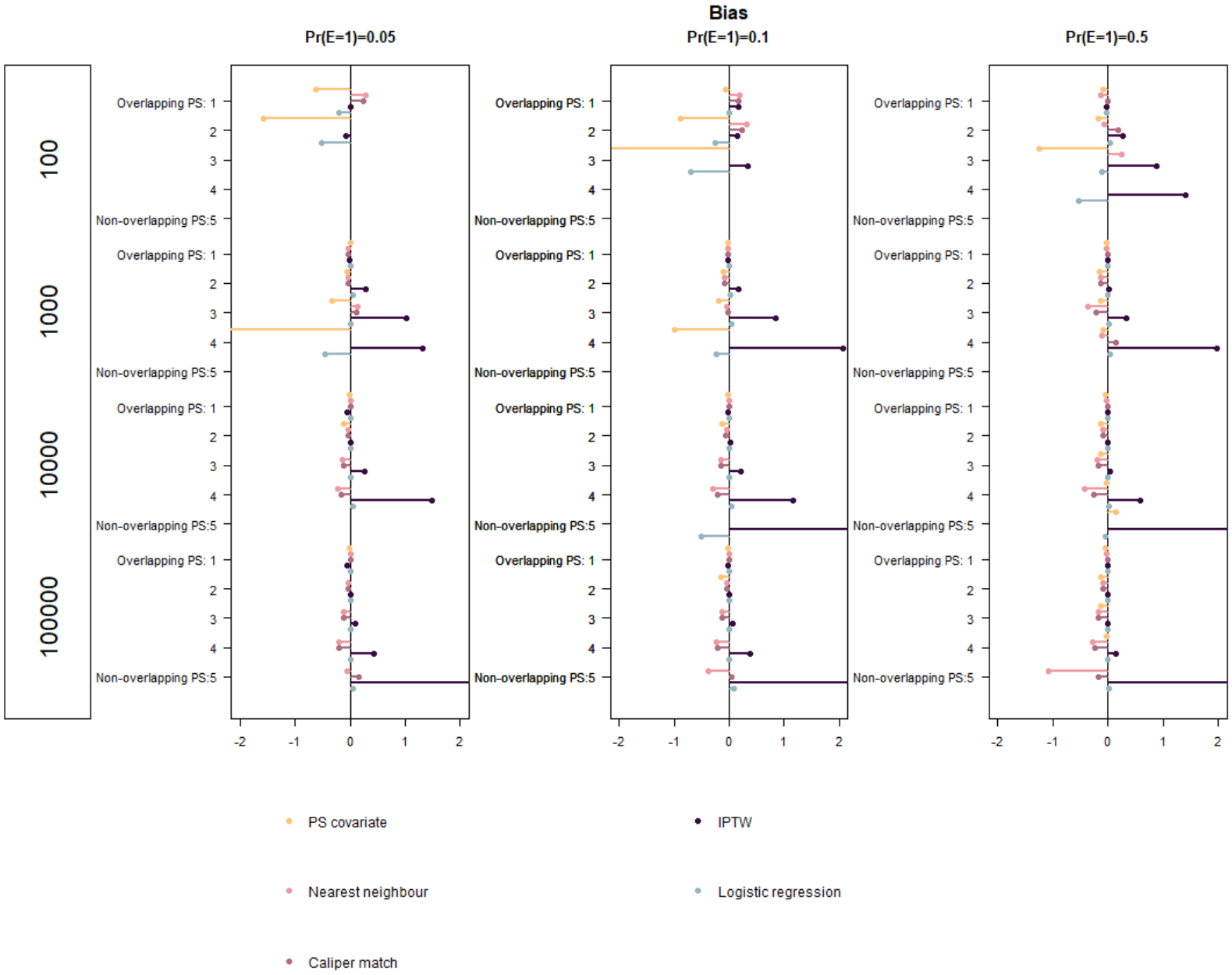


S Figure 6: Mean of coverage and power (%)

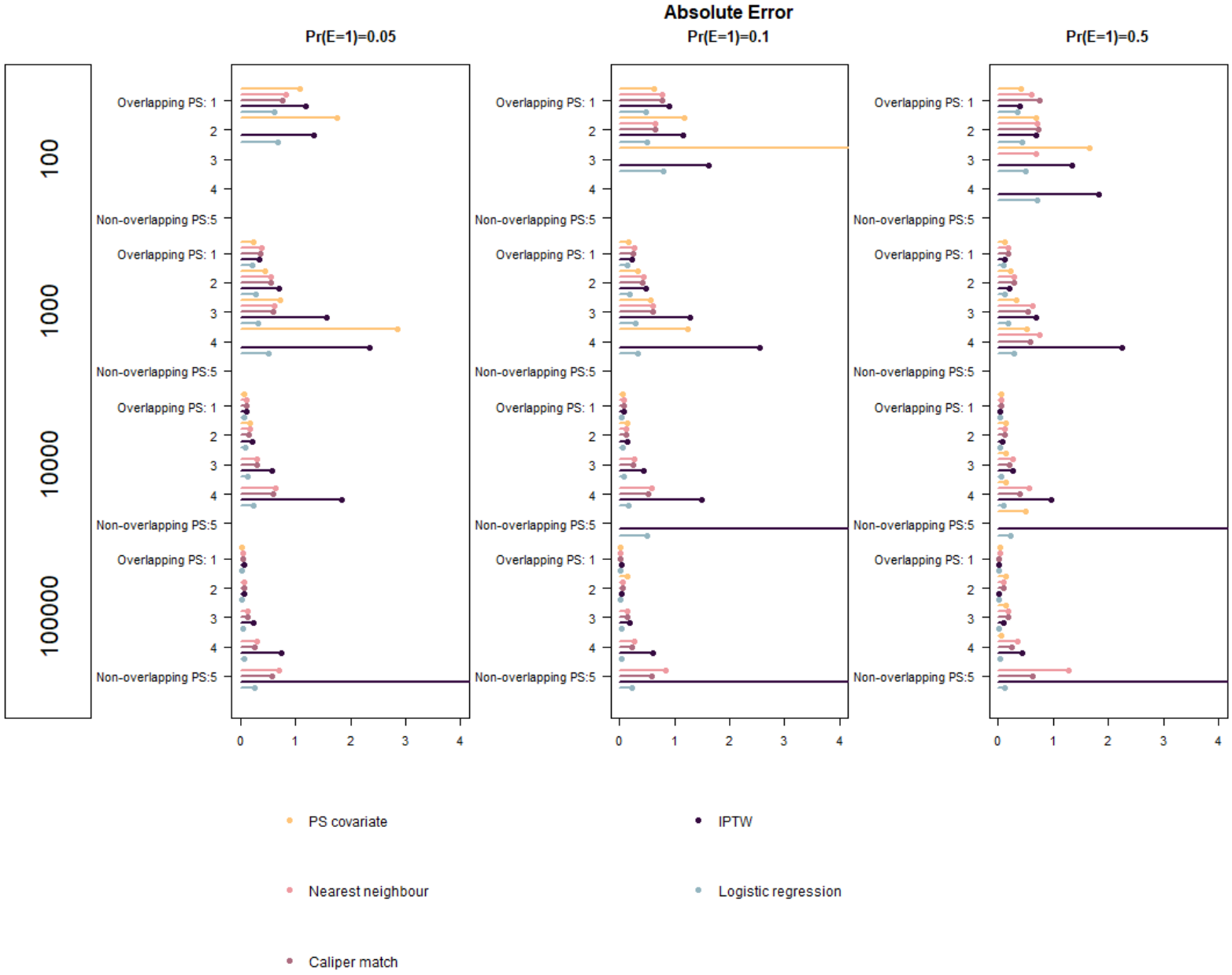
Sensitivity 2: logit link outcome generation & unmeasured confounder



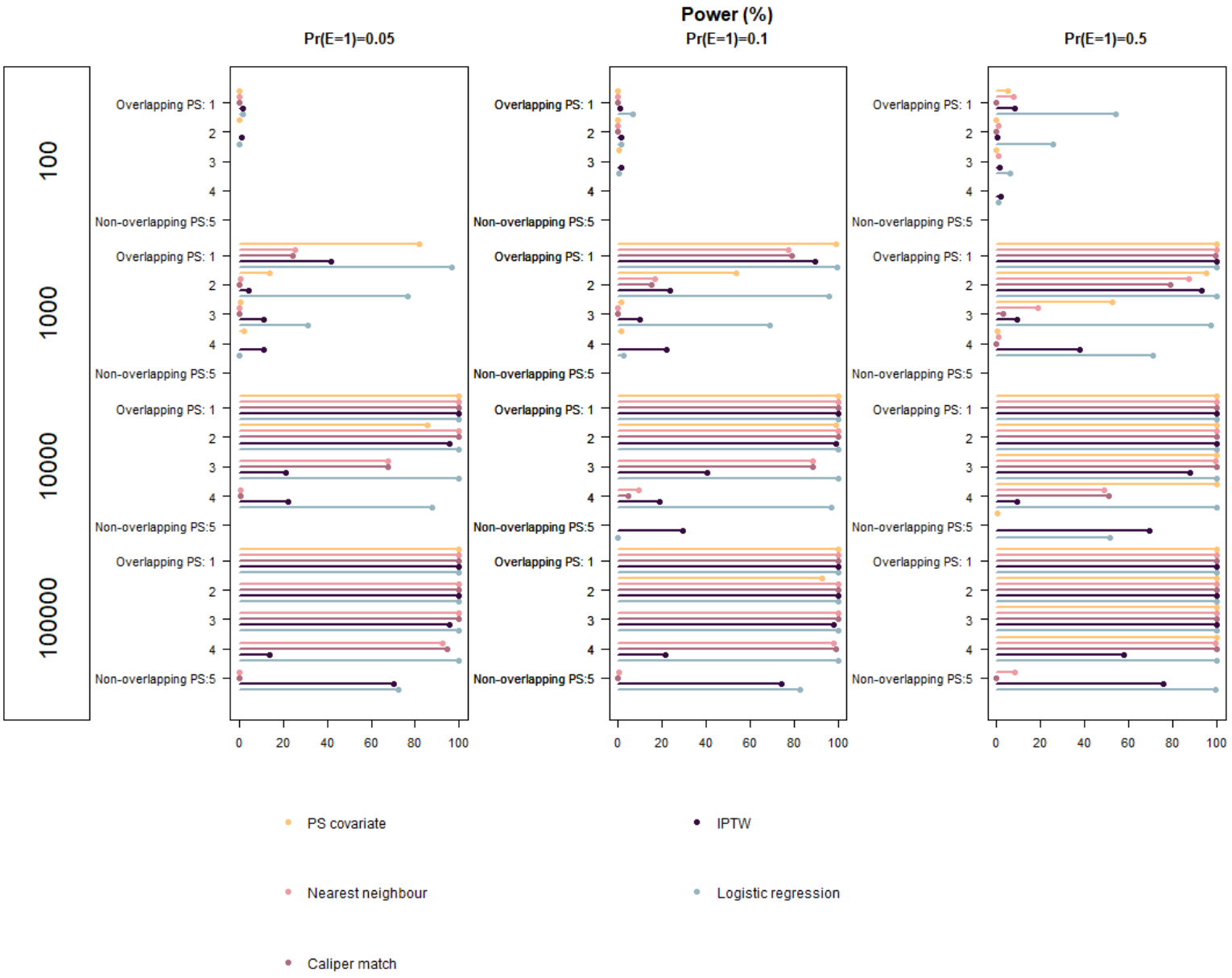
S Figure 7: Convergence (%)



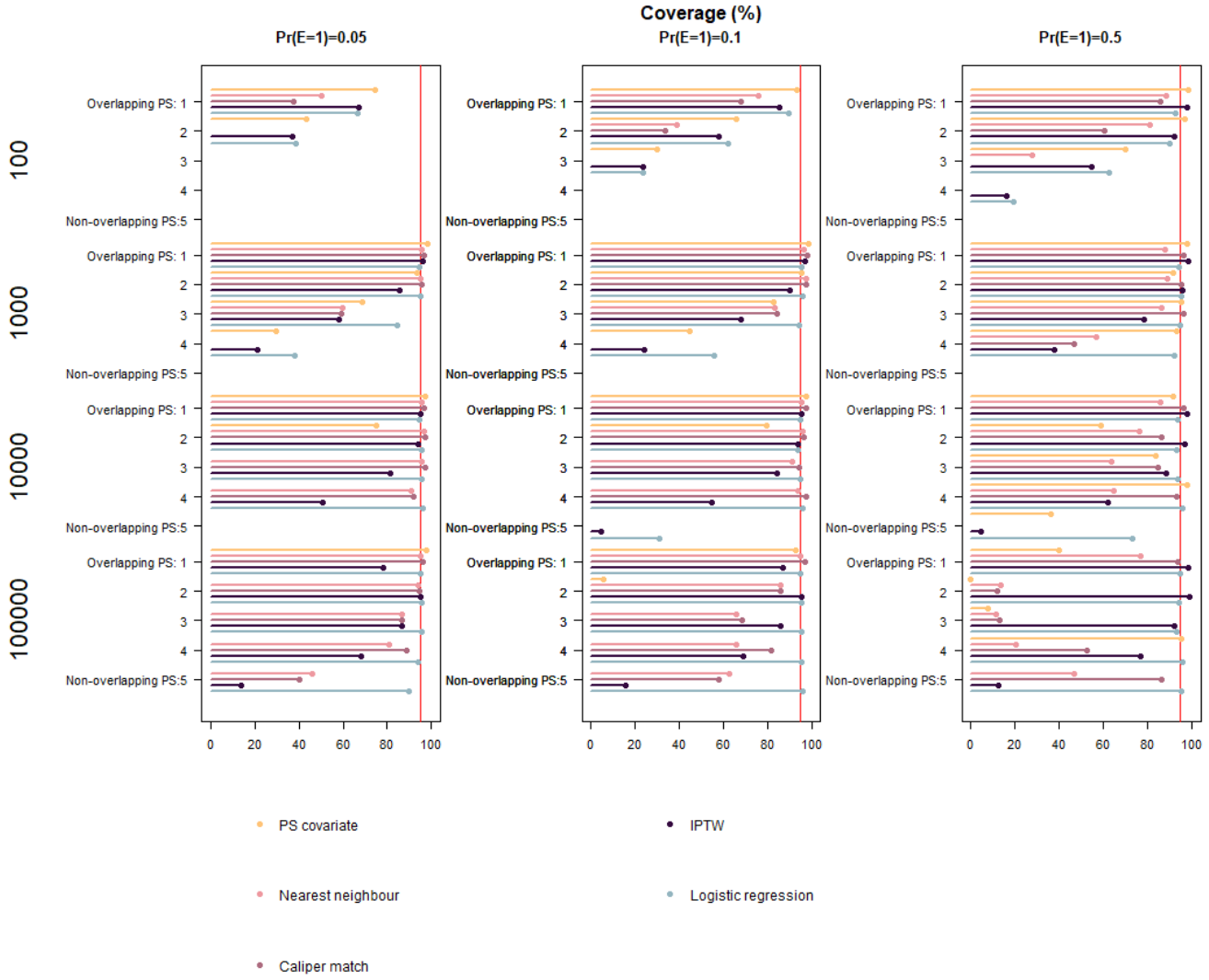
S Figure 8: Bias



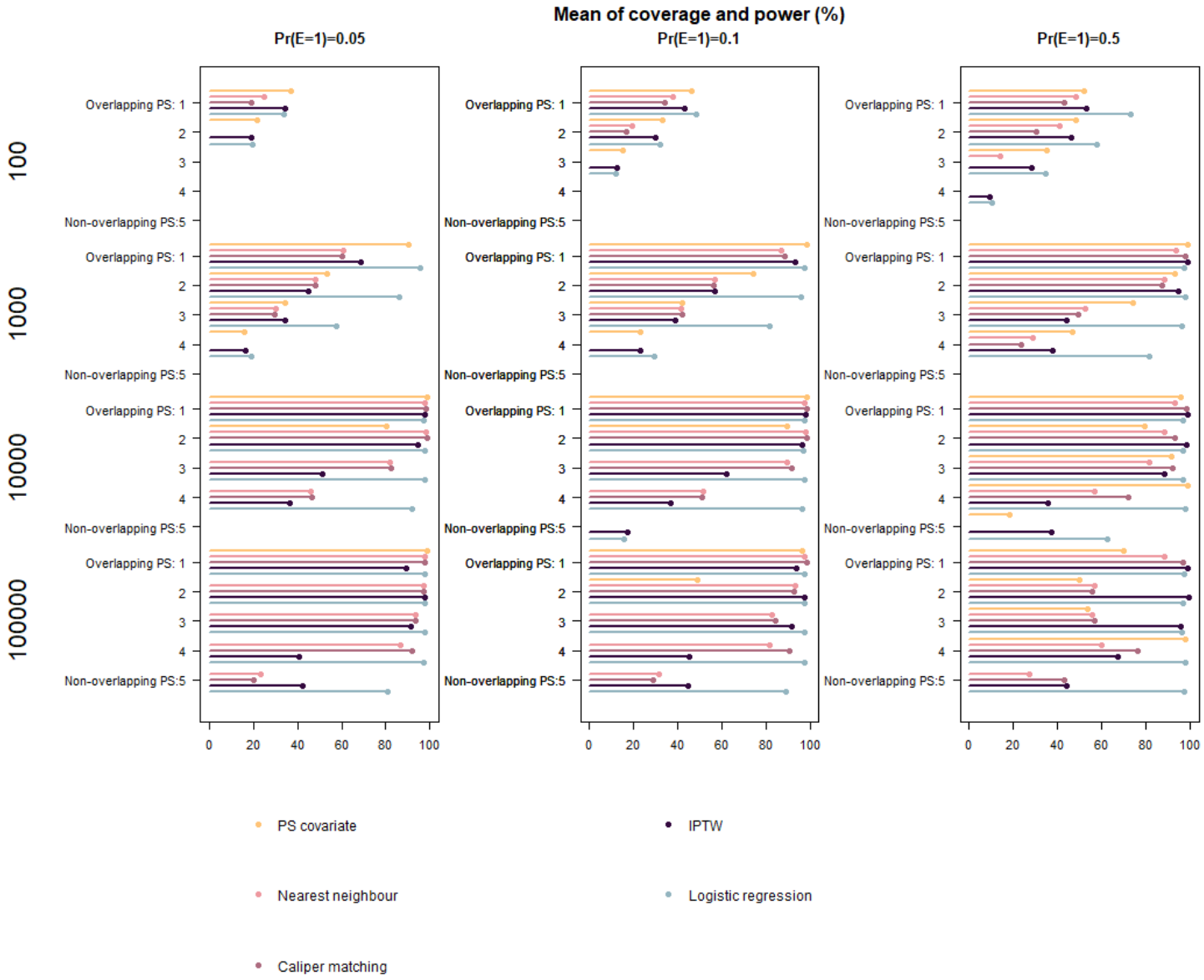
S Figure 9: Absolute error



S Figure 10: Power (%)

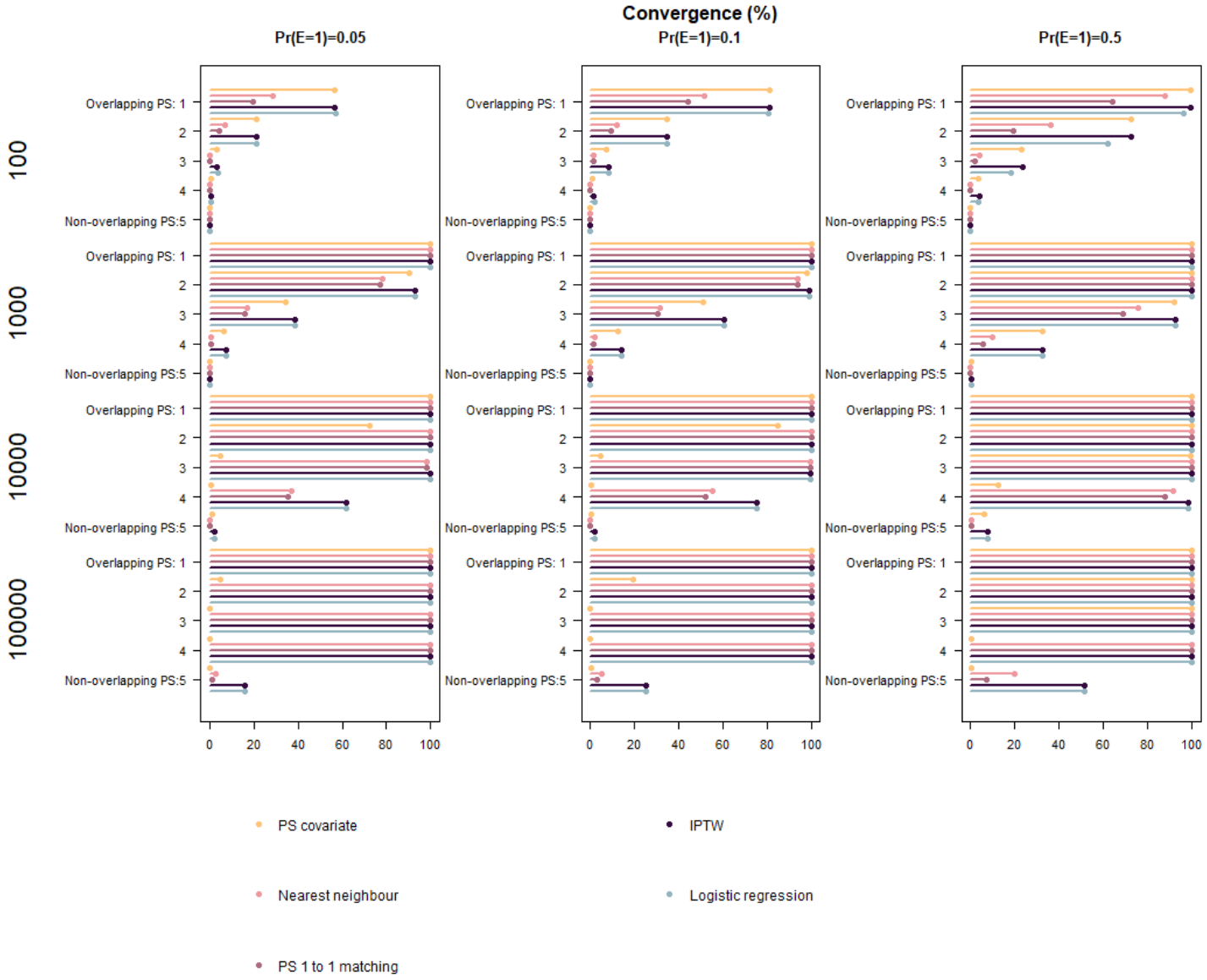


S Figure 11: Coverage (%)

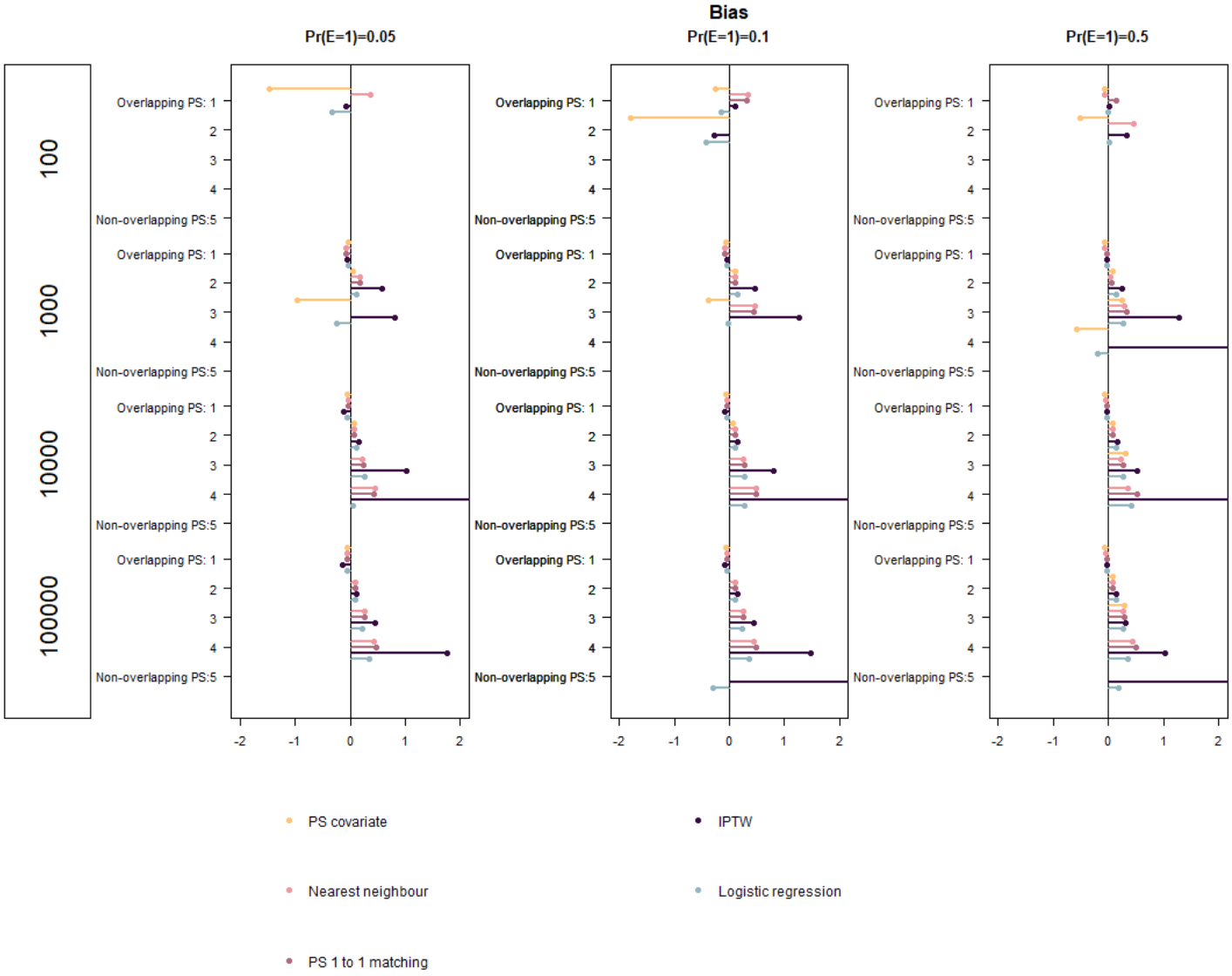


S Figure 12: Mean of coverage and power (%)

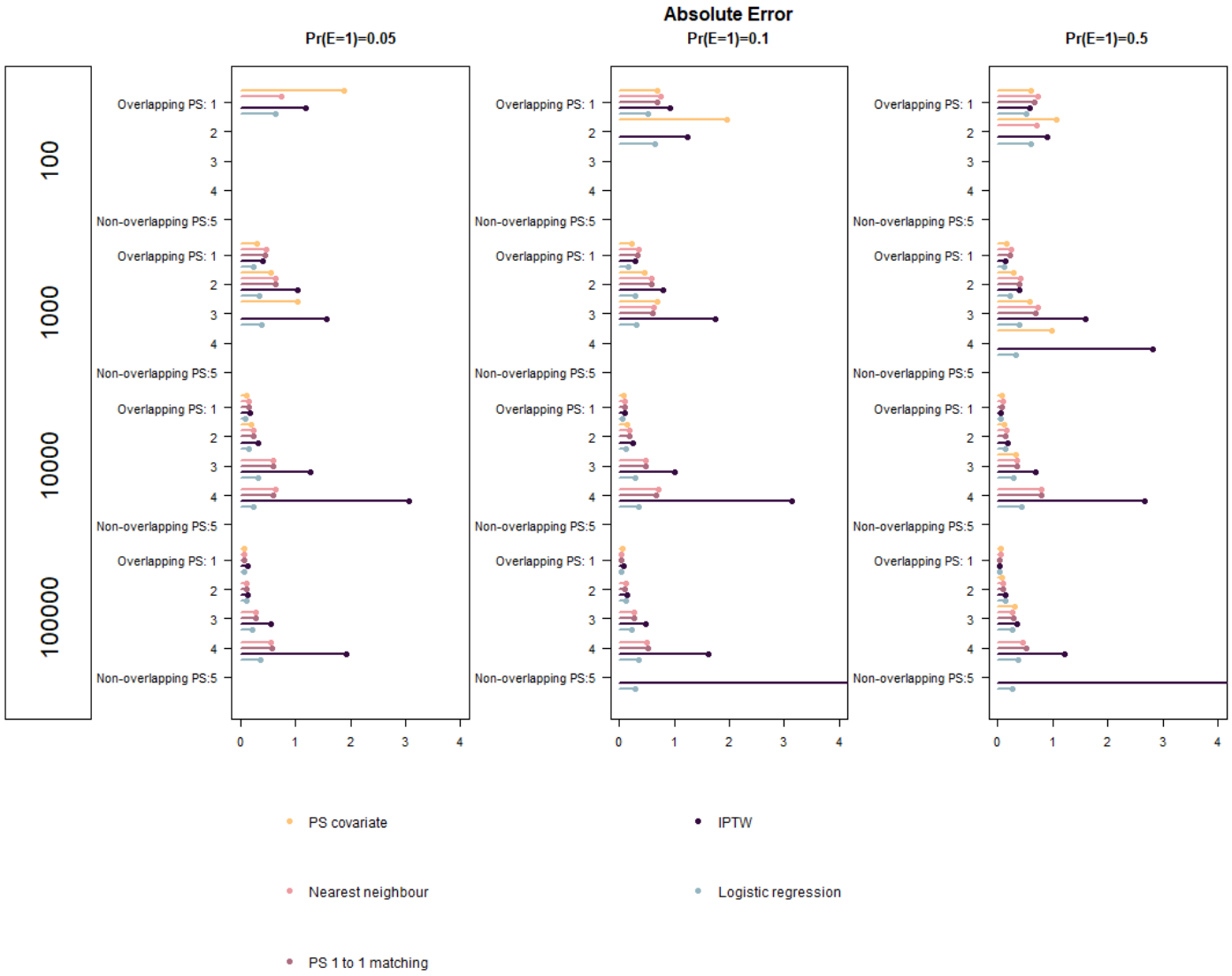
Sensitivity 3: complementary log-log link outcome generation & unmeasured confounder



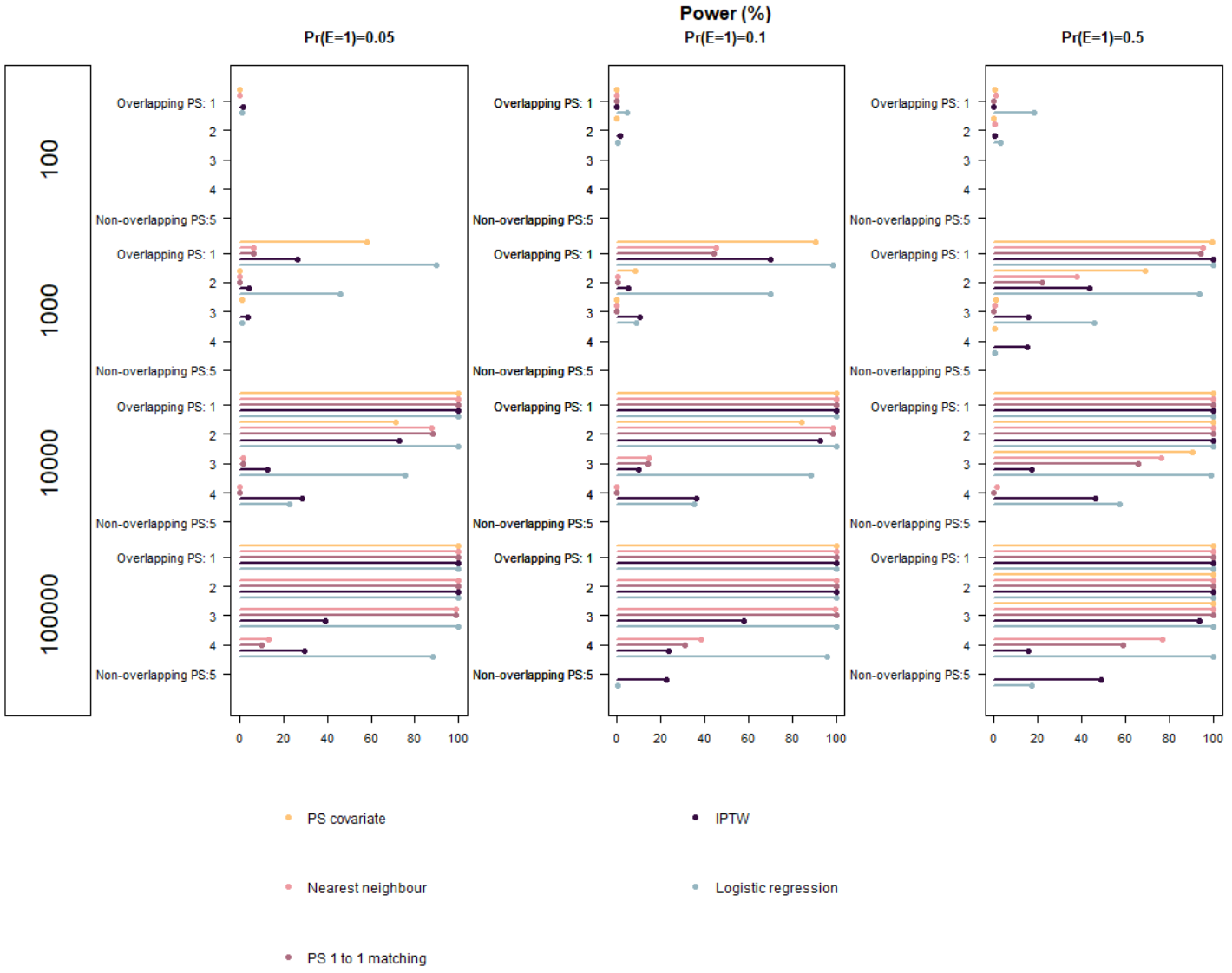
S Figure 13: Convergence (%)



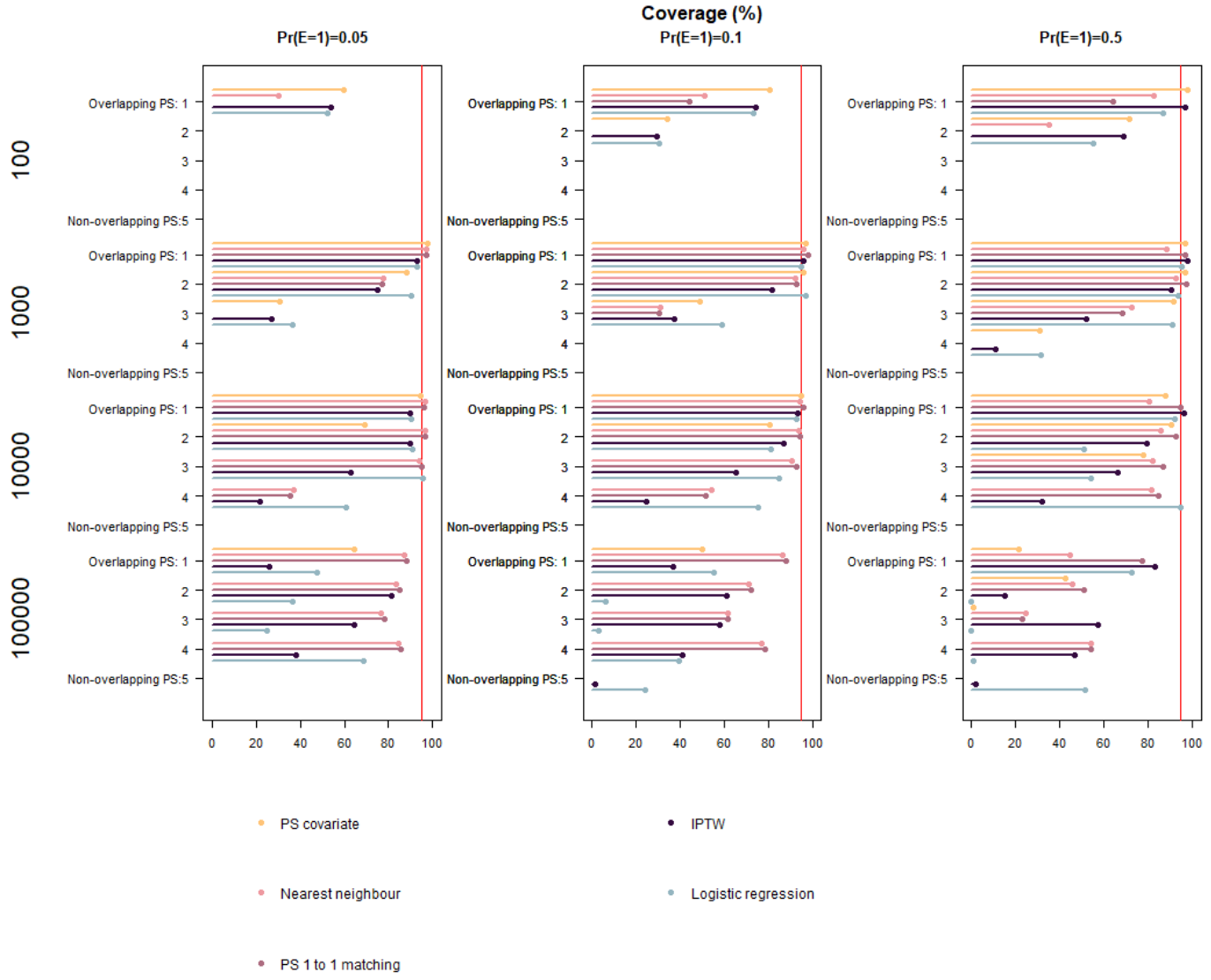
S Figure 14: Bias



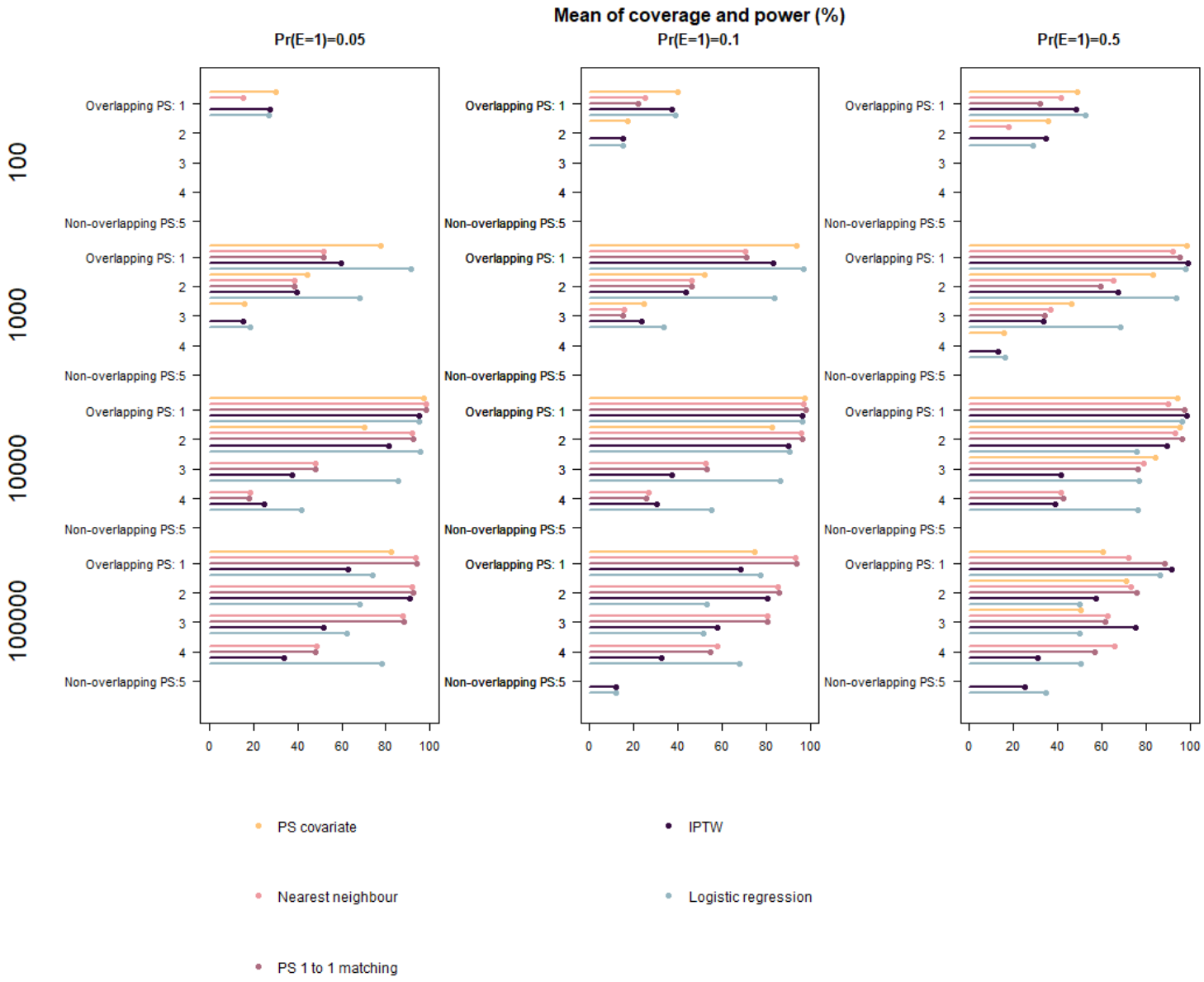
S Figure 15: Absolute error



S Figure 16: Power (%)



S Figure 17: Coverage (%)



S Figure 19: Mean of coverage and power (%)

n	Exposure probability	PS overlap scenario	Method	Convergence (%)	Bias	SE bias	Absolute error	SE absolute error	Power (%)	SE Power	Coverage (%)	SE coverage
1.00E+05	0.05	1	PS covariate	100	-0.006	2.98E-05	0.024288	1.82E-05	100	0	97.8	0
1.00E+05	0.05	2	PS covariate	13.6	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.05	3	PS covariate	0	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.05	4	PS covariate	0	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.05	5	PS covariate	0	NA	NA	NA	NA	NA	NA	NA	NA
10000	0.05	1	PS covariate	100	-0.00561	9.74E-05	0.07874	5.75E-05	100	0	98.2	0
10000	0.05	2	PS covariate	86.2	-0.11707	0.000201	0.170456	0.00014	86.2	1.09067	78.7	1.09067
10000	0.05	3	PS covariate	5.3	NA	NA	NA	NA	NA	NA	NA	NA
10000	0.05	4	PS covariate	0.4	NA	NA	NA	NA	NA	NA	NA	NA
10000	0.05	5	PS covariate	2.4	NA	NA	NA	NA	NA	NA	NA	NA
1000	0.05	1	PS covariate	100	0.013638	0.000323	0.258058	0.000195	71.8	1.422941	98.8	1.422941
1000	0.05	2	PS covariate	98	-0.06677	0.000586	0.44939	0.000372	8.3	0.872416	94.3	0.872416
1000	0.05	3	PS covariate	65.2	-0.50877	0.001441	0.799317	0.001086	0.4	0.1996	60.9	0.1996
1000	0.05	4	PS covariate	27.6	-2.71731	0.017789	2.792996	0.017634	2.3	0.474036	23.2	0.474036
1000	0.05	5	PS covariate	1.3	NA	NA	NA	NA	NA	NA	NA	NA
100	0.05	1	PS covariate	68.4	-0.48205	0.002096	0.900096	0.001777	0	0	71.94474	0
100	0.05	2	PS covariate	37.1	-3.72365	0.076944	3.856661	0.076896	0.111607	0.111545	40.625	0.111545
100	0.05	3	PS covariate	12.3	NA	NA	NA	NA	NA	NA	NA	NA
100	0.05	4	PS covariate	1.4	NA	NA	NA	NA	NA	NA	NA	NA
100	0.05	5	PS covariate	0	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.05	1	Nearest neighbour match	100	0.005783	4.87E-05	0.039887	2.85E-05	100	0	96.7	0
1.00E+05	0.05	2	Nearest neighbour match	100	-0.03161	6.89E-05	0.060404	4.57E-05	100	0	95.6	0
1.00E+05	0.05	3	Nearest neighbour match	100	-0.11476	0.000128	0.140501	9.96E-05	100	0	88.1	0
1.00E+05	0.05	4	Nearest neighbour match	100	-0.2207	0.0003	0.301781	0.000218	87	1.063485	87.7	1.063485
1.00E+05	0.05	5	Nearest neighbour match	34	0.15977	0.002549	0.649535	0.001749	0.4	0.1996	32.7	0.1996

Supp Table 1a: Simulation results for exposure probability of 0.05 (continues in 1b)

n	Exposure probability	PS overlap scenario	Method	Convergence (%)	Bias	SE bias	Absolute error	SE absolute error	Power (%)	SE Power	Coverage (%)	SE coverage
10000	0.05	1	Nearest neighbour match	100	-0.00038	0.000157	0.125769	9.33E-05	100	0	96	0
10000	0.05	2	Nearest neighbour match	100	-0.03023	0.000229	0.182409	0.000142	98.9	0.329833	95.8	0.329833
10000	0.05	3	Nearest neighbour match	100	-0.14593	0.000464	0.365964	0.000321	47.2	1.578658	95.2	1.578658
10000	0.05	4	Nearest neighbour match	85	-0.10145	0.000936	0.657924	0.00054	0.1	0.09995	83.9	0.09995
10000	0.05	5	Nearest neighbour match	0.9	NA	NA	NA	NA	NA	NA	NA	NA
1000	0.05	1	Nearest neighbour match	100	-0.02621	0.000517	0.401647	0.000326	17.6	1.204259	96.9	1.204259
1000	0.05	2	Nearest neighbour match	94.3	-0.09181	0.000758	0.573102	0.000463	0.3	0.172945	93.7	0.172945
1000	0.05	3	Nearest neighbour match	47.7	0.2392	0.001499	0.621684	0.000893	0	0	47.6	0
1000	0.05	4	Nearest neighbour match	8.8	NA	NA	NA	NA	NA	NA	NA	NA
1000	0.05	5	Nearest neighbour match	0	NA	NA	NA	NA	NA	NA	NA	NA
100	0.05	1	Nearest neighbour match	42.4	0.26166	0.002187	0.771822	0.001358	0	0	44.5271	0
100	0.05	2	Nearest neighbour match	14.7	NA	NA	NA	NA	NA	NA	NA	NA
100	0.05	3	Nearest neighbour match	1.9	NA	NA	NA	NA	NA	NA	NA	NA
100	0.05	4	Nearest neighbour match	0.3	NA	NA	NA	NA	NA	NA	NA	NA
100	0.05	5	Nearest neighbour match	0	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.05	1	Caliper match	100	0.005765	4.77E-05	0.038881	2.82E-05	100	0	96.4	0
1.00E+05	0.05	2	Caliper match	100	-0.03257	6.64E-05	0.058612	4.51E-05	100	0	96.1	0
1.00E+05	0.05	3	Caliper match	100	-0.11779	0.000123	0.13966	9.69E-05	100	0	89.1	0
1.00E+05	0.05	4	Caliper match	100	-0.20387	0.000282	0.277968	0.000209	87.2	1.056485	91	1.056485
1.00E+05	0.05	5	Caliper match	25.2	0.245413	0.0021	0.501002	0.001181	0	0	25.2	0
10000	0.05	1	Caliper match	100	0.000123	0.00015	0.119543	9.04E-05	100	0	96.8	0
10000	0.05	2	Caliper match	100	-0.03578	0.000224	0.178132	0.00014	99	0.314643	96.3	0.314643
10000	0.05	3	Caliper match	100	-0.14247	0.000448	0.358378	0.000304	43.9	1.569328	96.5	1.569328
10000	0.05	4	Caliper match	84.7	-0.04771	0.000925	0.650842	0.000518	0	0	84.4	0
10000	0.05	5	Caliper match	0.4	NA	NA	NA	NA	NA	NA	NA	NA

Supp Table 1b: Simulation results for exposure probability of 0.05 (continued from 1a, continues in 1c)

n	Exposure probability	PS overlap scenario	Method	Convergence (%)	Bias	SE bias	Absolute error	SE absolute error	Power (%)	SE Power	Coverage (%)	SE coverage
1000	0.05	1	Caliper match	100	-0.02414	0.000503	0.394209	0.000314	16.5	1.173776	97.6	1.173776
1000	0.05	2	Caliper match	94.4	-0.07907	0.000751	0.56141	0.000465	0.2	0.14128	93.9	0.14128
1000	0.05	3	Caliper match	46.4	0.221823	0.001501	0.602537	0.00089	0	0	46.3	0
1000	0.05	4	Caliper match	7.1	NA	NA	NA	NA	NA	NA	NA	NA
1000	0.05	5	Caliper match	0	NA	NA	NA	NA	NA	NA	NA	NA
100	0.05	1	Caliper match	32	0.181802	0.002686	0.710504	0.00161	0	0	34.00637	0
100	0.05	2	Caliper match	10	NA	NA	NA	NA	NA	NA	NA	NA
100	0.05	3	Caliper match	1	NA	NA	NA	NA	NA	NA	NA	NA
100	0.05	4	Caliper match	0.1	NA	NA	NA	NA	NA	NA	NA	NA
100	0.05	5	Caliper match	0	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.05	1	IPTW	100	-0.05477	4.15E-05	0.05839	3.62E-05	100	0	81.3	0
1.00E+05	0.05	2	IPTW	100	0.009911	9.22E-05	0.074407	5.54E-05	100	0	93.8	0
1.00E+05	0.05	3	IPTW	100	0.082119	0.000305	0.249743	0.000193	93	0.806846	85.7	0.806846
1.00E+05	0.05	4	IPTW	100	0.529221	0.000869	0.834237	0.000582	9.4	0.922843	65.3	0.922843
1.00E+05	0.05	5	IPTW	82.9	5.602679	0.003796	5.815961	0.003296	66.8	1.489215	9.8	1.489215
10000	0.05	1	IPTW	100	-0.04564	0.000137	0.114606	8.82E-05	100	0	95.4	0
10000	0.05	2	IPTW	100	0.043459	0.000287	0.229254	0.000177	92.1	0.852989	91.6	0.852989
10000	0.05	3	IPTW	100	0.342119	0.000798	0.684793	0.000534	11.7	1.01642	77.7	1.01642
10000	0.05	4	IPTW	98.2	1.779791	0.001975	2.121554	0.001586	29	1.434922	44	1.434922
10000	0.05	5	IPTW	17.2	NA	NA	NA	NA	NA	NA	NA	NA
1000	0.05	1	IPTW	100	0.009664	0.000488	0.382063	0.000303	35.8	1.516034	94.3	1.516034
1000	0.05	2	IPTW	99	0.326597	0.000953	0.740059	0.000676	4	0.619677	85.5	0.619677
1000	0.05	3	IPTW	76.6	0.944739	0.002334	1.606316	0.001603	9.1	0.9095	52.1	0.9095
1000	0.05	4	IPTW	32.5	1.239097	0.007387	2.17999	0.0049	8.3	0.872416	17.8	0.872416
1000	0.05	5	IPTW	1.5	NA	NA	NA	NA	NA	NA	NA	NA

Supp Table 1c: Simulation results for exposure probability of 0.05 (continued from 1b, continues in 1d)

n	Exposure probability	PS overlap scenario	Method	Convergence (%)	Bias	SE bias	Absolute error	SE absolute error	Power (%)	SE Power	Coverage (%)	SE coverage
100	0.05	1	IPTW	68.5	-0.09842	0.002126	1.16657	0.001279	0.850159	0.299296	64.93092	0.299296
100	0.05	2	IPTW	37.1	-0.23603	0.00454	1.347151	0.002792	1.004464	0.333136	34.15179	0.333136
100	0.05	3	IPTW	12.7	NA	NA	NA	NA	NA	NA	NA	NA
100	0.05	4	IPTW	1.5	NA	NA	NA	NA	NA	NA	NA	NA
100	0.05	5	IPTW	0	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.05	1	Logistic regression	100	0.000259	2.58E-05	0.02022	1.61E-05	100	0	95.6	0
1.00E+05	0.05	2	Logistic regression	100	0.000473	3.35E-05	0.02669	2.03E-05	100	0	95.7	0
1.00E+05	0.05	3	Logistic regression	100	0.000378	5.11E-05	0.040484	3.11E-05	100	0	96.5	0
1.00E+05	0.05	4	Logistic regression	100	0.007157	0.0001	0.07995	6.08E-05	100	0	94.3	0
1.00E+05	0.05	5	Logistic regression	82.9	-0.01003	0.000372	0.26434	0.000192	50.6	1.581025	78.6	1.581025
10000	0.05	1	Logistic regression	100	0.002097	8.49E-05	0.068273	5.04E-05	100	0	94.7	0
10000	0.05	2	Logistic regression	100	0.003162	0.000108	0.084887	6.65E-05	100	0	95	0
10000	0.05	3	Logistic regression	100	0.018052	0.000179	0.136215	0.000117	99.2	0.281709	94.8	0.281709
10000	0.05	4	Logistic regression	98.2	0.071266	0.000343	0.26686	0.000222	77	1.330789	94.9	1.330789
10000	0.05	5	Logistic regression	17.2	NA	NA	NA	NA	NA	NA	NA	NA
1000	0.05	1	Logistic regression	100	0.012748	0.000271	0.215192	0.000166	94.8	0.702111	95.5	0.702111
1000	0.05	2	Logistic regression	99	0.038222	0.00037	0.282818	0.000239	74.9	1.371127	95.2	1.371127
1000	0.05	3	Logistic regression	76.6	-0.08687	0.000537	0.337659	0.000326	14.4	1.110243	72.7	1.110243
1000	0.05	4	Logistic regression	32.5	-0.59497	0.001088	0.608218	0.001016	0	0	27.9	0
1000	0.05	5	Logistic regression	1.7	NA	NA	NA	NA	NA	NA	NA	NA
100	0.05	1	Logistic regression	69.2	-0.22644	0.00103	0.596547	0.00065	1.6	0.396787	65.2	0.396787
100	0.05	2	Logistic regression	38.1	-0.602	0.001945	0.747228	0.001559	0.1	0.09995	33.7	0.09995
100	0.05	3	Logistic regression	14.1	NA	NA	NA	NA	NA	NA	NA	NA
100	0.05	4	Logistic regression	3	NA	NA	NA	NA	NA	NA	NA	NA
100	0.05	5	Logistic regression	0	NA	NA	NA	NA	NA	NA	NA	NA

Supp Table 1d: Simulation results for exposure probability of 0.05 (continued from 1c)

n	Exposure probability	PS overlap scenario	Method	Convergence (%)	Bias	SE bias	Absolute error	SE absolute error	Power (%)	SE Power	Coverage (%)	SE coverage
1.00E+05	0.1	1	PS covariate	100	-0.01704	2.39E-05	0.023464	1.76E-05	100	0	92.7	0
1.00E+05	0.1	2	PS covariate	69.2	-0.12569	6.13E-05	0.125731	6.11E-05	69.2	1.459918	11	1.459918
1.00E+05	0.1	3	PS covariate	0	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.1	4	PS covariate	0	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.1	5	PS covariate	0	NA	NA	NA	NA	NA	NA	NA	NA
10000	0.1	1	PS covariate	100	-0.02084	7.10E-05	0.059675	4.37E-05	100	0	98.1	0
10000	0.1	2	PS covariate	96.4	-0.12237	0.000136	0.147492	0.000106	96.4	0.589101	81.5	0.589101
10000	0.1	3	PS covariate	5	NA	NA	NA	NA	NA	NA	NA	NA
10000	0.1	4	PS covariate	0.1	NA	NA	NA	NA	NA	NA	NA	NA
10000	0.1	5	PS covariate	3.4	NA	NA	NA	NA	NA	NA	NA	NA
1000	0.1	1	PS covariate	100	0.002621	0.000247	0.19397	0.000153	96.2	0.604616	97.6	0.604616
1000	0.1	2	PS covariate	99.8	-0.11358	0.000436	0.359156	0.000271	39	1.542401	94.5	1.542401
1000	0.1	3	PS covariate	83.3	-0.21604	0.000931	0.63722	0.00059	0.6	0.244213	78.5	0.244213
1000	0.1	4	PS covariate	45.4	-1.31846	0.004582	1.489077	0.004321	2.3	0.474036	39.9	0.474036
1000	0.1	5	PS covariate	2.2	NA	NA	NA	NA	NA	NA	NA	NA
100	0.1	1	PS covariate	89.4	-0.11205	0.000941	0.648192	0.000612	0	0	88.4	0
100	0.1	2	PS covariate	57.8	-1.15622	0.004382	1.362167	0.004201	0.501505	0.223717	55.4664	0.223717
100	0.1	3	PS covariate	21.9	NA	NA	NA	NA	NA	NA	NA	NA
100	0.1	4	PS covariate	4.8	NA	NA	NA	NA	NA	NA	NA	NA
100	0.1	5	PS covariate	0	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.1	1	Nearest neighbour match	100	0.002547	3.70E-05	0.029486	2.25E-05	100	0	95.1	0
1.00E+05	0.1	2	Nearest neighbour match	100	-0.04933	5.48E-05	0.06059	4.20E-05	100	0	86.7	0
1.00E+05	0.1	3	Nearest neighbour match	100	-0.13985	0.000105	0.149107	9.17E-05	100	0	70.5	0
1.00E+05	0.1	4	Nearest neighbour match	100	-0.2244	0.000258	0.281358	0.000194	95.3	0.669261	75.8	0.669261
1.00E+05	0.1	5	Nearest neighbour match	53.4	-0.18803	0.001595	0.707596	0.000954	0.3	0.172945	51.6	0.172945

Supp table 2a: Simulation results for exposure probability of 0.1 (continues in 2b)

n	Exposure probability	PS overlap scenario	Method	Convergence (%)	Bias	SE bias	Absolute error	SE absolute error	Power (%)	SE Power	Coverage (%)	SE coverage
10000	0.1	1	Nearest neighbour match	100	-0.001	0.000106	0.085809	6.30E-05	100	0	96.8	0
10000	0.1	2	Nearest neighbour match	100	-0.04348	0.000175	0.142922	0.000109	99.9	0.09995	95.5	0.09995
10000	0.1	3	Nearest neighbour match	100	-0.15187	0.000339	0.292323	0.000229	77.8	1.314215	93.9	1.314215
10000	0.1	4	Nearest neighbour match	95.4	-0.32307	0.000758	0.625226	0.000509	2.2	0.463853	92.9	0.463853
10000	0.1	5	Nearest neighbour match	2.3	NA	NA	NA	NA	NA	NA	NA	NA
1000	0.1	1	Nearest neighbour match	100	-0.00278	0.000374	0.295212	0.00023	68.4	1.470184	95.5	1.470184
1000	0.1	2	Nearest neighbour match	99.4	-0.11419	0.000613	0.472871	0.000403	8.2	0.867617	97.1	0.867617
1000	0.1	3	Nearest neighbour match	72.6	0.091478	0.001102	0.659531	0.000635	0	0	71.8	0
1000	0.1	4	Nearest neighbour match	16.2	NA	NA	NA	NA	NA	NA	NA	NA
1000	0.1	5	Nearest neighbour match	0.1	NA	NA	NA	NA	NA	NA	NA	NA
100	0.1	1	Nearest neighbour match	67.4	0.213431	0.001355	0.754876	0.000825	0	0	66.1	0
100	0.1	2	Nearest neighbour match	29.2	0.286568	0.002642	0.635487	0.001787	0.100301	0.100251	28.78636	0.100251
100	0.1	3	Nearest neighbour match	6.2	NA	NA	NA	NA	NA	NA	NA	NA
100	0.1	4	Nearest neighbour match	0.9	NA	NA	NA	NA	NA	NA	NA	NA
100	0.1	5	Nearest neighbour match	0	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.1	1	Caliper match	100	0.002304	3.40E-05	0.026963	2.08E-05	100	0	96	0
1.00E+05	0.1	2	Caliper match	100	-0.05242	5.18E-05	0.06083	4.16E-05	100	0	87.4	0
1.00E+05	0.1	3	Caliper match	100	-0.13858	0.000101	0.145884	8.98E-05	100	0	72.7	0
1.00E+05	0.1	4	Caliper match	100	-0.20208	0.000212	0.237302	0.000171	97.3	0.512552	87.3	0.512552
1.00E+05	0.1	5	Caliper match	42.5	0.107365	0.001568	0.569903	0.000848	0	0	42.5	0
10000	0.1	1	Caliper match	100	-0.00212	0.0001	0.079867	6.06E-05	100	0	97.7	0
10000	0.1	2	Caliper match	100	-0.05135	0.000165	0.138374	0.000103	100	0	96.5	0
10000	0.1	3	Caliper match	100	-0.15288	0.000322	0.278344	0.000223	77.6	1.318423	95.3	1.318423
10000	0.1	4	Caliper match	96.2	-0.22753	0.000716	0.572583	0.000462	0.7	0.263647	95.7	0.263647
10000	0.1	5	Caliper match	0.9	NA	NA	NA	NA	NA	NA	NA	NA

Supp table 2b: Simulation results for exposure probability of 0.1 (continued from 2a, continues in 2c)

n	Exposure probability	PS overlap scenario	Method	Convergence (%)	Bias	SE bias	Absolute error	SE absolute error	Power (%)	SE Power	Coverage (%)	SE coverage
1000	0.1	1	Caliper match	100	-0.00785	0.000358	0.281603	0.00022	70.1	1.447753	96.9	1.447753
1000	0.1	2	Caliper match	99.7	-0.10773	0.000586	0.458602	0.000378	5.8	0.739162	98.5	0.739162
1000	0.1	3	Caliper match	72.2	0.08761	0.001073	0.640345	0.000615	0	0	71.9	0
1000	0.1	4	Caliper match	13.4	NA	NA	NA	NA	NA	NA	NA	NA
1000	0.1	5	Caliper match	0	NA	NA	NA	NA	NA	NA	NA	NA
100	0.1	1	Caliper match	59.8	0.211592	0.001479	0.752363	0.000853	0	0	59.7	0
100	0.1	2	Caliper match	23.7	NA	NA	NA	NA	NA	NA	NA	NA
100	0.1	3	Caliper match	3.7	NA	NA	NA	NA	NA	NA	NA	NA
100	0.1	4	Caliper match	0.5	NA	NA	NA	NA	NA	NA	NA	NA
100	0.1	5	Caliper match	0	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.1	1	IPTW	100	-0.02878	2.95E-05	0.033615	2.39E-05	100	0	87.8	0
1.00E+05	0.1	2	IPTW	100	0.012763	6.81E-05	0.05423	4.31E-05	100	0	93.7	0
1.00E+05	0.1	3	IPTW	100	0.076698	0.000244	0.205244	0.000152	96.4	0.589101	85.2	0.589101
1.00E+05	0.1	4	IPTW	100	0.437139	0.000734	0.698854	0.000491	15.8	1.153412	65.3	1.153412
1.00E+05	0.1	5	IPTW	96.4	5.247144	0.003104	5.452763	0.002695	76.4	1.342773	11.7	1.342773
10000	0.1	1	IPTW	100	-0.0302	9.44E-05	0.079833	5.86E-05	100	0	95.8	0
10000	0.1	2	IPTW	100	0.026554	0.000204	0.161412	0.000128	99.2	0.281709	93.1	0.281709
10000	0.1	3	IPTW	100	0.263692	0.000652	0.553033	0.000434	26.8	1.400628	76.9	1.400628
10000	0.1	4	IPTW	99.8	1.242227	0.001565	1.603137	0.00119	19.6	1.255325	54.3	1.255325
10000	0.1	5	IPTW	27.4	4.640378	0.010549	5.066658	0.007481	21.9	1.307819	3.5	1.307819
1000	0.1	1	IPTW	100	0.00733	0.000331	0.261345	0.000202	81.8	1.220147	95.6	1.220147
1000	0.1	2	IPTW	100	0.149046	0.00066	0.52233	0.00043	16.8	1.182269	90.3	1.182269
1000	0.1	3	IPTW	93.7	0.92096	0.001796	1.468067	0.001318	13	1.063485	62.2	1.063485
1000	0.1	4	IPTW	50.8	1.744638	0.004728	2.473204	0.003229	16.5	1.173776	22.9	1.173776
1000	0.1	5	IPTW	2.5	NA	NA	NA	NA	NA	NA	NA	NA

Supp table 2c: Simulation results for exposure probability of 0.1 (continued from 2b, continues in 2d)

n	Exposure probability	PS overlap scenario	Method	Convergence (%)	Bias	SE bias	Absolute error	SE absolute error	Power (%)	SE Power	Coverage (%)	SE coverage
100	0.1	1	IPTW	89.4	0.225603	0.001342	0.963315	0.000838	0.7	0.263647	80.7	0.263647
100	0.1	2	IPTW	57.8	-0.02142	0.002416	1.117318	0.001448	0.902708	0.299542	50.75226	0.299542
100	0.1	3	IPTW	22.6	NA	NA	NA	NA	NA	NA	NA	NA
100	0.1	4	IPTW	5.2	NA	NA	NA	NA	NA	NA	NA	NA
100	0.1	5	IPTW	0	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.1	1	Logistic regression	100	-9.81E-06	2.04E-05	0.016516	1.20E-05	100	0	94.7	0
1.00E+05	0.1	2	Logistic regression	100	0.000273	2.65E-05	0.021145	1.59E-05	100	0	94.7	0
1.00E+05	0.1	3	Logistic regression	100	0.000797	4.25E-05	0.033952	2.55E-05	100	0	93.8	0
1.00E+05	0.1	4	Logistic regression	100	0.004359	7.37E-05	0.058738	4.46E-05	100	0	94.8	0
1.00E+05	0.1	5	Logistic regression	96.4	0.042781	0.000322	0.246071	0.000202	80.1	1.262533	92.6	1.262533
10000	0.1	1	Logistic regression	100	-0.00238	5.96E-05	0.04782	3.55E-05	100	0	96.2	0
10000	0.1	2	Logistic regression	100	0.003365	8.24E-05	0.067052	4.79E-05	100	0	96	0
10000	0.1	3	Logistic regression	100	0.009326	0.000131	0.104426	7.97E-05	100	0	94.9	0
10000	0.1	4	Logistic regression	99.8	0.033202	0.000253	0.192134	0.000168	93.9	0.756829	95.4	0.756829
10000	0.1	5	Logistic regression	27.4	-0.66785	0.000682	0.66799	0.00068	0	0	23.9	0
1000	0.1	1	Logistic regression	100	0.01625	0.000205	0.161587	0.000127	99.6	0.1996	94.8	0.1996
1000	0.1	2	Logistic regression	100	0.013902	0.000266	0.208961	0.000166	93.9	0.756829	95.8	0.756829
1000	0.1	3	Logistic regression	93.7	0.049017	0.000422	0.313274	0.000262	54	1.576071	90.1	1.576071
1000	0.1	4	Logistic regression	50.8	-0.33885	0.000682	0.395634	0.00055	0.7	0.263647	46.1	0.263647
1000	0.1	5	Logistic regression	2.7	NA	NA	NA	NA	NA	NA	NA	NA
100	0.1	1	Logistic regression	89.4	-0.02653	0.000728	0.520035	0.000439	4.4	0.648568	85	0.648568
100	0.1	2	Logistic regression	57.8	-0.36494	0.001063	0.578257	0.000725	1.2	0.344325	52.2	0.344325
100	0.1	3	Logistic regression	22.9	NA	NA	NA	NA	NA	NA	NA	NA
100	0.1	4	Logistic regression	6.2	NA	NA	NA	NA	NA	NA	NA	NA
100	0.1	5	Logistic regression	0	NA	NA	NA	NA	NA	NA	NA	NA

Supp table 2d: Simulation results for exposure probability of 0.1 (continued from 2c)

n	Exposure probability	PS overlap scenario	Method	Convergence (%)	Bias	SE bias	Absolute error	SE absolute error	Power (%)	SE Power	Coverage (%)	SE coverage
1.00E+05	0.5	1	PS covariate	100	-0.03559	1.71E-05	0.035727	1.68E-05	100	0	50.8	0
1.00E+05	0.5	2	PS covariate	100	-0.13116	2.53E-05	0.131164	2.53E-05	100	0	0	0
1.00E+05	0.5	3	PS covariate	100	-0.1075	3.90E-05	0.107533	3.89E-05	100	0	31	0
1.00E+05	0.5	4	PS covariate	100	-0.01191	6.72E-05	0.0544	4.12E-05	100	0	98.1	0
1.00E+05	0.5	5	PS covariate	8.8	NA	NA	NA	NA	NA	NA	NA	NA
10000	0.5	1	PS covariate	100	-0.03726	5.29E-05	0.052802	3.74E-05	100	0	93.4	0
10000	0.5	2	PS covariate	100	-0.13196	8.04E-05	0.135177	7.49E-05	100	0	67.8	0
10000	0.5	3	PS covariate	100	-0.10398	0.00013	0.136964	9.40E-05	100	0	89.6	0
10000	0.5	4	PS covariate	98.7	-0.00621	0.000205	0.160355	0.000125	98.1	0.431729	97	0.431729
10000	0.5	5	PS covariate	31	-0.31753	0.01876	0.992339	0.018513	0.5	0.223047	30.4	0.223047
1000	0.5	1	PS covariate	100	-0.03414	0.000166	0.135533	0.000101	100	0	97.3	0
1000	0.5	2	PS covariate	100	-0.11593	0.00025	0.220191	0.000165	95.2	0.675988	95.8	0.675988
1000	0.5	3	PS covariate	100	-0.10236	0.000417	0.336131	0.000267	41.8	1.559731	96.3	1.559731
1000	0.5	4	PS covariate	90.1	-0.09989	0.000945	0.634292	0.00064	0.2	0.14128	87.9	0.14128
1000	0.5	5	PS covariate	9.3	NA	NA	NA	NA	NA	NA	NA	NA
100	0.5	1	PS covariate	100	-0.04522	0.000569	0.440748	0.000362	1.2	0.344325	98.3	0.344325
100	0.5	2	PS covariate	95.8	-0.24232	0.001052	0.786767	0.000704	0	0	93.9	0
100	0.5	3	PS covariate	62.3	-1.71912	0.013928	2.1133	0.013787	0.1001	0.10005	61.06106	0.10005
100	0.5	4	PS covariate	20.9	NA	NA	NA	NA	NA	NA	NA	NA
100	0.5	5	PS covariate	0	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.5	1	Nearest neighbour match	100	-0.01783	2.41E-05	0.02449	1.73E-05	100	0	75.3	0
1.00E+05	0.5	2	Nearest neighbour match	100	-0.08936	3.59E-05	0.089558	3.54E-05	100	0	18.4	0
1.00E+05	0.5	3	Nearest neighbour match	100	-0.18261	8.42E-05	0.184139	8.08E-05	100	0	17.8	0
1.00E+05	0.5	4	Nearest neighbour match	100	-0.29783	0.000276	0.356013	0.000195	99.3	0.263647	25.6	0.263647
1.00E+05	0.5	5	Nearest neighbour match	79.9	-0.93885	0.001231	1.173077	0.00086	4.3	0.64149	63.1	0.64149

Supp table 3a: Simulation results for exposure probability of 0.5 (continues in 3b)

n	Exposure probability	PS overlap scenario	Method	Convergence (%)	Bias	SE bias	Absolute error	SE absolute error	Power (%)	SE Power	Coverage (%)	SE coverage
10000	0.5	1	Nearest neighbour match	100	-0.01903	7.39E-05	0.06022	4.69E-05	100	0	86.5	0
10000	0.5	2	Nearest neighbour match	100	-0.09097	0.000116	0.120106	8.58E-05	100	0	77.1	0
10000	0.5	3	Nearest neighbour match	100	-0.20595	0.000263	0.277617	0.000186	97.7	0.474036	66.1	0.474036
10000	0.5	4	Nearest neighbour match	100	-0.47674	0.000636	0.634051	0.000479	38.4	1.537999	70.2	1.537999
10000	0.5	5	Nearest neighbour match	11	NA	NA	NA	NA	NA	NA	NA	NA
1000	0.5	1	Nearest neighbour match	100	-0.02525	0.00024	0.186378	0.000153	99.2	0.281709	86.8	0.281709
1000	0.5	2	Nearest neighbour match	100	-0.13781	0.000376	0.315417	0.000247	79	1.288022	89.1	1.288022
1000	0.5	3	Nearest neighbour match	98	-0.3375	0.000781	0.651652	0.000535	9.5	0.927227	89.8	0.927227
1000	0.5	4	Nearest neighbour match	45.6	0.151331	0.002158	0.729368	0.001485	0.6	0.244213	43.7	0.244213
1000	0.5	5	Nearest neighbour match	0.1	NA	NA	NA	NA	NA	NA	NA	NA
100	0.5	1	Nearest neighbour match	97.4	-0.10068	0.000821	0.637978	0.000505	2.2	0.463853	89.3	0.463853
100	0.5	2	Nearest neighbour match	72.5	0.076048	0.00123	0.720246	0.000732	0.4	0.1996	70	0.1996
100	0.5	3	Nearest neighbour match	22.2	NA	NA	NA	NA	NA	NA	NA	NA
100	0.5	4	Nearest neighbour match	2	NA	NA	NA	NA	NA	NA	NA	NA
100	0.5	5	Nearest neighbour match	0	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.5	1	Caliper match	100	-0.00953	2.07E-05	0.01858	1.32E-05	100	0	95.5	0
1.00E+05	0.5	2	Caliper match	100	-0.0929	3.10E-05	0.092941	3.09E-05	100	0	19.7	0
1.00E+05	0.5	3	Caliper match	100	-0.16837	6.14E-05	0.168492	6.10E-05	100	0	26.2	0
1.00E+05	0.5	4	Caliper match	100	-0.22996	0.000142	0.235591	0.000132	100	0	64.1	0
1.00E+05	0.5	5	Caliper match	74.4	-0.07988	0.000986	0.60845	0.00056	0	0	74.2	0
10000	0.5	1	Caliper match	100	-0.01288	6.62E-05	0.054229	4.01E-05	100	0	96.9	0
10000	0.5	2	Caliper match	100	-0.09723	0.0001	0.113426	8.13E-05	100	0	87.1	0
10000	0.5	3	Caliper match	100	-0.16976	0.000205	0.218036	0.000153	98.9	0.329833	88.5	0.329833
10000	0.5	4	Caliper match	99.9	-0.27877	0.000488	0.436021	0.000354	29.1	1.436381	94.9	1.436381
10000	0.5	5	Caliper match	2.9	NA	NA	NA	NA	NA	NA	NA	NA

Supp table 3b: Simulation results for exposure probability of 0.5 (continued from 3a, continues in 3c)

n	Exposure probability	PS overlap scenario	Method	Convergence (%)	Bias	SE bias	Absolute error	SE absolute error	Power (%)	SE Power	Coverage (%)	SE coverage
1000	0.5	1	Caliper match	100	-0.01122	0.000229	0.179753	0.000142	99	0.314643	96.6	0.314643
1000	0.5	2	Caliper match	100	-0.09563	0.000347	0.279412	0.000227	71.5	1.427498	96.5	1.427498
1000	0.5	3	Caliper match	97.8	-0.18793	0.000751	0.591511	0.000484	0.7	0.263647	96.5	0.263647
1000	0.5	4	Caliper match	30.8	0.151155	0.002122	0.571359	0.001137	0	0	30.8	0
1000	0.5	5	Caliper match	0	NA	NA	NA	NA	NA	NA	NA	NA
100	0.5	1	Caliper match	81.6	0.101127	0.001072	0.707704	0.000642	0	0	80.9	0
100	0.5	2	Caliper match	48.4	0.173271	0.001677	0.691049	0.000947	0	0	48.4	0
100	0.5	3	Caliper match	7.7	NA	NA	NA	NA	NA	NA	NA	NA
100	0.5	4	Caliper match	0.5	NA	NA	NA	NA	NA	NA	NA	NA
100	0.5	5	Caliper match	0	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.5	1	IPTW	100	6.32E-05	1.59E-05	0.012734	9.50E-06	100	0	97.7	0
1.00E+05	0.5	2	IPTW	100	-0.00164	2.94E-05	0.023238	1.81E-05	100	0	96.7	0
1.00E+05	0.5	3	IPTW	100	-0.00382	0.000143	0.112017	8.92E-05	99.6	0.1996	92.4	0.1996
1.00E+05	0.5	4	IPTW	100	0.19742	0.000576	0.482599	0.00037	46.1	1.576322	72.8	1.576322
1.00E+05	0.5	5	IPTW	100	4.582742	0.002293	4.727789	0.001977	79.6	1.2743	10.7	1.2743
10000	0.5	1	IPTW	100	-0.00156	4.92E-05	0.039781	2.89E-05	100	0	98.5	0
10000	0.5	2	IPTW	100	0.004651	9.24E-05	0.072758	5.71E-05	100	0	96.8	0
10000	0.5	3	IPTW	100	0.07874	0.000388	0.307416	0.000249	82	1.214907	84.8	1.214907
10000	0.5	4	IPTW	100	0.801685	0.001135	1.154034	0.000773	13.2	1.070402	53.4	1.070402
10000	0.5	5	IPTW	64.8	5.905272	0.003264	5.986807	0.002889	58.7	1.55702	4	1.55702
1000	0.5	1	IPTW	100	0.00359	0.000153	0.123231	9.06E-05	100	0	98.4	0
1000	0.5	2	IPTW	100	0.04	0.000289	0.225889	0.000184	89.6	0.965319	96.1	0.965319
1000	0.5	3	IPTW	100	0.429436	0.000914	0.784555	0.000636	7.3	0.822624	74.6	0.822624
1000	0.5	4	IPTW	90.2	2.281712	0.002063	2.544733	0.001641	40.2	1.550471	33.3	1.550471
1000	0.5	5	IPTW	9.5	NA	NA	NA	NA	NA	NA	NA	NA

Supp table 3c: Simulation results for exposure probability of 0.5 (continued from 3c, continues in 3d)

n	Exposure probability	PS overlap scenario	Method	Convergence (%)	Bias	SE bias	Absolute error	SE absolute error	Power (%)	SE Power	Coverage (%)	SE coverage
100	0.5	1	IPTW	100	0.014764	0.00055	0.419714	0.000356	3.9	0.612201	97.4	0.612201
100	0.5	2	IPTW	95.8	0.240202	0.001013	0.783595	0.000647	0	0	89	0
100	0.5	3	IPTW	62.6	0.774853	0.002299	1.344331	0.001484	1.101101	0.330162	48.84885	0.330162
100	0.5	4	IPTW	21.4	NA	NA	NA	NA	NA	NA	NA	NA
100	0.5	5	IPTW	0	NA	NA	NA	NA	NA	NA	NA	NA
1.00E+05	0.5	1	Logistic regression	100	0.000654	1.44E-05	0.011603	8.53E-06	100	0	94.5	0
1.00E+05	0.5	2	Logistic regression	100	6.37E-05	1.72E-05	0.013656	1.05E-05	100	0	94.1	0
1.00E+05	0.5	3	Logistic regression	100	-0.00012	2.50E-05	0.019946	1.51E-05	100	0	94.6	0
1.00E+05	0.5	4	Logistic regression	100	0.002124	4.28E-05	0.034085	2.60E-05	100	0	94.9	0
1.00E+05	0.5	5	Logistic regression	100	0.026317	0.000181	0.140248	0.000118	99.1	0.298647	94.7	0.298647
10000	0.5	1	Logistic regression	100	0.000144	4.44E-05	0.035327	2.68E-05	100	0	94	0
10000	0.5	2	Logistic regression	100	0.000263	5.33E-05	0.042899	3.17E-05	100	0	95.1	0
10000	0.5	3	Logistic regression	100	0.003195	7.94E-05	0.064151	4.68E-05	100	0	95.6	0
10000	0.5	4	Logistic regression	100	0.012328	0.000134	0.104885	8.36E-05	99.9	0.09995	95.9	0.09995
10000	0.5	5	Logistic regression	64.8	-0.16349	0.000365	0.220438	0.000285	41.2	1.556458	60.1	1.556458
1000	0.5	1	Logistic regression	100	0.001655	0.000138	0.109866	8.37E-05	100	0	95.4	0
1000	0.5	2	Logistic regression	100	0.012929	0.000171	0.137438	0.000102	100	0	95.7	0
1000	0.5	3	Logistic regression	100	0.024236	0.000258	0.203358	0.000161	94.2	0.739162	96.5	0.739162
1000	0.5	4	Logistic regression	90.2	0.045674	0.000429	0.31047	0.00026	51.9	1.579997	86.4	1.579997
1000	0.5	5	Logistic regression	9.9	NA	NA	NA	NA	NA	NA	NA	NA
100	0.5	1	Logistic regression	100	0.001625	0.000474	0.371008	0.000296	42.6	1.563726	93.7	1.563726
100	0.5	2	Logistic regression	94.6	-0.00433	0.000644	0.485514	0.000389	14.4	1.110243	87.2	1.110243
100	0.5	3	Logistic regression	59.7	-0.21994	0.001148	0.579225	0.000715	2.5	0.49371	52.9	0.49371
100	0.5	4	Logistic regression	22.1	NA	NA	NA	NA	NA	NA	NA	NA
100	0.5	5	Logistic regression	1.8	NA	NA	NA	NA	NA	NA	NA	NA

Supp table 3d: Simulation results for exposure probability of 0.5 (continued from 3c)