# Supplementary Note: Identifying Causal Variants by Fine Mapping Across Multiple Studies

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## 1 Additional simulations

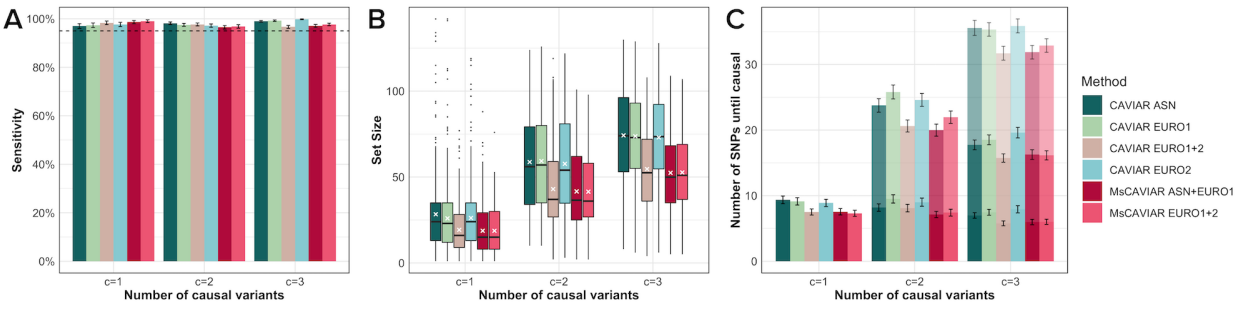


**Fig A. Comparison of the impact of effective sample size increase to modeling heterogeneity.** We simulate summary statistics with c=1, c=2, or c=3 causal variants implanted in 3 loci and 5 heritability levels with 20 replicates each. This is done for 2 different European populations and one Asian sample, all with 9,000 individuals in order to compare the impact leveraging differing LD to the effective sample size increase of meta-analysis. (A) Bar graph displaying the sensitivity of the methods (B) Box plots showing the set sizes returned by the methods. The lines inside the boxes represent the median while the white crosses inside the boxes represent the mean. (C) Bar graph showing the average number of SNPs taken in descending order of posterior inclusion probability (PIP) until 1, 2, or 3 causal SNPs are identified. Stacked bars represent increasing numbers of causal SNPs identified, until the true number of causal SNPs (x-axis) are identified.

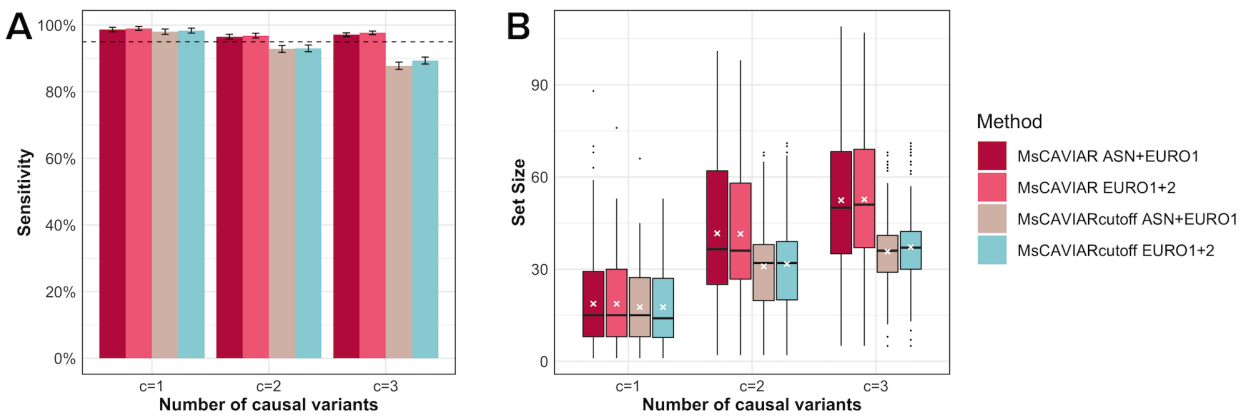


**Fig B. Comparison of sensitivity and set sizes of MsCAVIAR to itself with a PIP cutoff.** We simulated $c \in \{1, 2, 3\}$ causal variants averaging over 20 replications of 3 loci with 5 levels of heritability each. We compare the performance of MsCAVAIR to MsCAVIAR plus a posterior inclusion probability (PIP) threshold of 1%, where any SNPs with a PIP less than 1% is removed from the causal set. (A) Bar graph displaying the sensitivity of the methods. The dashed line reflects the expected posterior probability of recovering all causal SNPs; methods that reach this threshold are considered "well-calibrated". (B) Box plots showing the set sizes returned by the methods.

We performed additional simulations on the data described in the main text ("MsCAVIAR improves fine mapping resolution in a simulation study") including several other approaches. We sampled another population of 9,000 unrelated White British individuals. We then ran MsCAVIAR on the two British populations. We also ran fastGWA on the two European populations to generate stronger summary statistics, and then applied CAVIAR to those statistics (Fig A). We evaluated the effect of applying a "cutoff parameter" to MsCAVIAR's results, in which SNPs with less than 1% posterior probability of being causal were excluded from the causal set (Fig B). We ran simulations in which the causal effect sizes of the SNPs were equal across populations, in order to investigate whether lack of effect size heterogeneity impacted the results (Fig C). Finally, we ran SuSiE [1], a recent fine mapping method, on the Asian population and on the first British population (Fig D). We caution that SuSiE employs a different approach to fine mapping. SuSiE's credible sets differ from the causal sets of the other methods in that SuSiE does not attempt to capture all causal SNPs, so the sensitivity calibration is not directly comparable to the other methods. We focus on the rest of the methods in the following paragraphs, and then return to SuSiE.

MsCAVIAR run on the two British populations performed almost identically to MsCAVIAR run on the Asian and British population. Additionally, CAVIAR run on the two British populations yielded causal set sizes only marginally larger than MsCAVIAR's. Thus, in our simulations, combined population size was a larger factor than ethnic differences in LD. We caution that this may not always be the case in real data.

When a cutoff parameter was applied to MsCAVIAR, predictably, both the causal set size and recall were reduced. This reduction was proportional to the number of causal SNPs. With one causal SNP, the mean set size was reduced from 18.7 to 17.6 and the recall was reduced from 98.6% to 98%. With two causal SNPs, the mean set size was reduced from 41.6 to 30.9 and the recall was reduced from 96.5% to 92.8%. With three causal SNPs, the mean set size was reduced from 52.4 to 35.7 and the recall was reduced from 97.1% to 87.8%. The cutoff parameter, therefore, can be

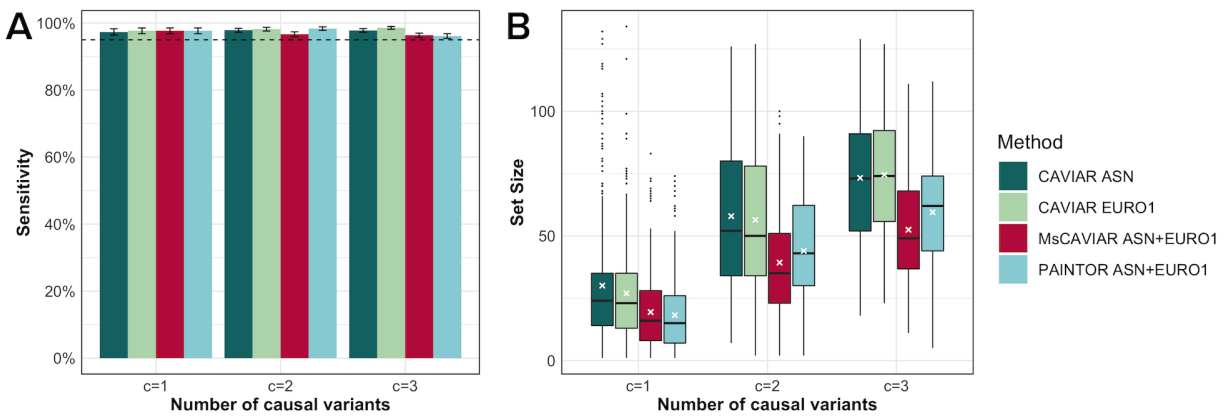


**Fig C. Comparison of sensitivity and set sizes using simulated data with equal effect sizes.** We simulated $c \in \{1, 2, 3\}$ causal variants averaging over 20 replications of 3 loci with 5 levels of heritability each. (A) Bar graph displaying the sensitivity of the methods. The dashed line reflects the expected posterior probability of recovering all causal SNPs; methods that reach this threshold are considered "well-calibrated". (B) Box plots showing the set sizes returned by the methods.

used to limit the causal set size, with the drawback of potentially reducing recall.

When we performed our original simulations except with effect sizes fixed across populations (e.g. no heterogeneity), the results were fairly similar to our main text results. This indicates that, in our simulations, MsCAVIAR's improved performance relative to PAINTOR is not mostly due to explicit modeling of heterogeneity.

SuSiE [1] takes a different approach to fine mapping from the other methods. Instead of returning a causal set, SuSiE returns (potentially multiple) credible sets for a locus, each of which is expected to contain at least one causal SNP. The goal of SuSiE is not to capture all causal variants in a locus, but to return one or more minimal size credible sets, each of which has $\rho$ probability of containing at least one true causal effect. This explains why SuSiE is not well-calibrated according to our causal set definition, which expects all casual variants to be captured with probability $\rho^*$, when there is more than one causal SNP.

It is worth noting, however, that SuSiE's credible set is equivalent to the causal set (as defined by the other methods) when the methods assume that there is only one causal SNP in a locus. In this case, SuSiE applied to our Asian population had a recall of 91% and an average set size of 21.68, while SuSiE applied to the first of our British populations had a recall of 92.3% and an average set size of 20.6. Thus, SuSiE's returned set sizes were smaller than those of CAVIAR applied to individual populations but larger than MsCAVIAR's or PAINTOR's sets.

## 2 MsCAVIAR improves fine mapping resolution in a simulation study

Here, we describe a previous set of simulations that were removed from the main text during the revision process when the simulations now in the main text were developed. We have included them because they can complement our main simulations.

We used two regions from the 1000 Genomes project [2] to generate LD matrices for the SNPs

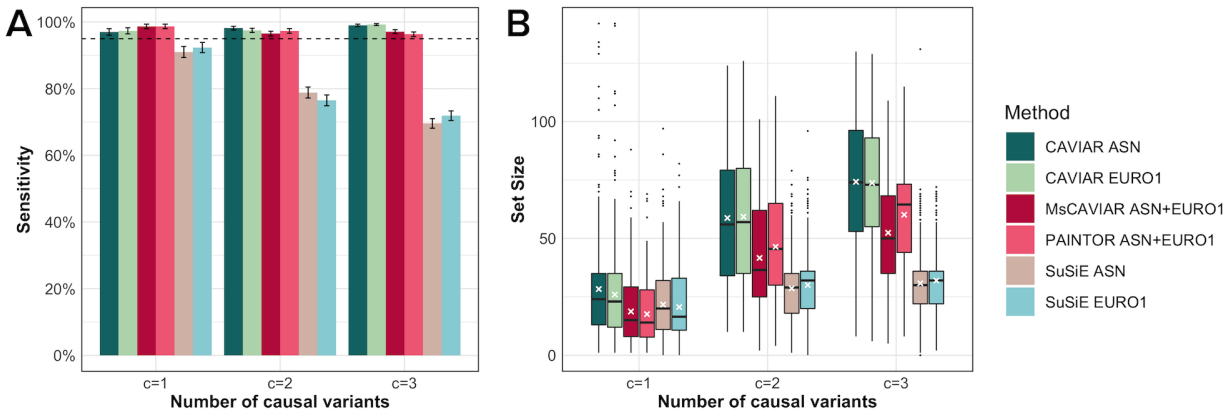


**Fig D. Comparison of sensitivity, set sizes and precision in simulated data (w/ SuSiE).** Comparison of the methods with c=1, c=2, or c=3 causal variants implanted. Results are averaged over three loci and 5 levels of heritability. The simulations are identical to those in the Fig 2 but we now include SuSiE, a fundamentally different method, in the comparison. SuSiE's credible sets differ from the causal sets of the other methods in that SuSiE does not attempt to capture all causal SNPs, so the sensitivity calibration is not directly comparable to the other methods. (A) Bar graphs displaying the sensitivity of the methods. The dashed line reflects the expected posterior probability of recovering all causal SNPs; methods that reach this threshold are considered "well-calibrated". (B) Box plots showing the set sizes returned by the methods. The boxes represent the interquartile range of causal set sizes identified by each tool, the lines inside the boxes represent the median while the white crosses inside the boxes represent the mean.

at that locus for both European and East Asian populations. Out of these loci, we selected one region with relatively low LD, where 20% of the SNP pairs have LD equal to or higher than 0.5, and one region with relatively high LD, where 80% of the SNP pairs have LD equal to or higher than 0.5 (Fig E, LD matrices). These represent easier and more difficult scenarios, respectively, for fine mapping, since LD makes signals more difficult to distinguish. We pruned groups of SNPs that were in perfect LD in one or more of the populations, leaving one SNP for each. After pruning, the low LD matrix contained 48 SNPs and the high LD matrix contained 38 SNPs.

Using these LD matrices, we implanted causal SNPs and simulated their non-centrality parameters. In each simulation, we implanted either 1, 2, or 3 causal SNPs. Each causal SNP's true non-centrality parameter $\Lambda$ was drawn according to $\mathcal{N}(5.2, 0.125^2)$. We then drew the non-centrality parameter $\Lambda_i$ for each study $i$ according to $\Lambda_i \sim \mathcal{N}(\Lambda, 0.5)$, and subsequently the summary statistics $S_i$ for each study $i$ according to $S_i \sim \mathcal{N}(\Lambda_i \Sigma_i, \Sigma_i)$. For each number of causal SNPs, we performed 1000 replicate simulations (e.g. re-drawing the causal SNP non-centrality parameters and re-picking the causal SNPs).

Using this data, we compared MsCAVIAR to the trans-ethnic mode of PAINTOR [3] and to CAVIAR [4] and SuSiE [1] run on East Asians and Europeans, individually (Fig E). The SuSiE method is a new approach to fine mapping that has a different model than the other methods, so we first discuss the rest of the methods and then return to SuSiE.

All other methods were run with posterior probability threshold $\rho^* = 0.95$, so methods with 95% or higher sensitivity were considered "well-calibrated" (dashed line in the bar plots). MsCAVIAR's heterogeneity parameter was set to $\tau^2 = 0.5$ (Methods); the sensitivity of MsCAVIAR's performance to different settings of this parameter is shown in the appendix (Fig G). All methods but SuSiE

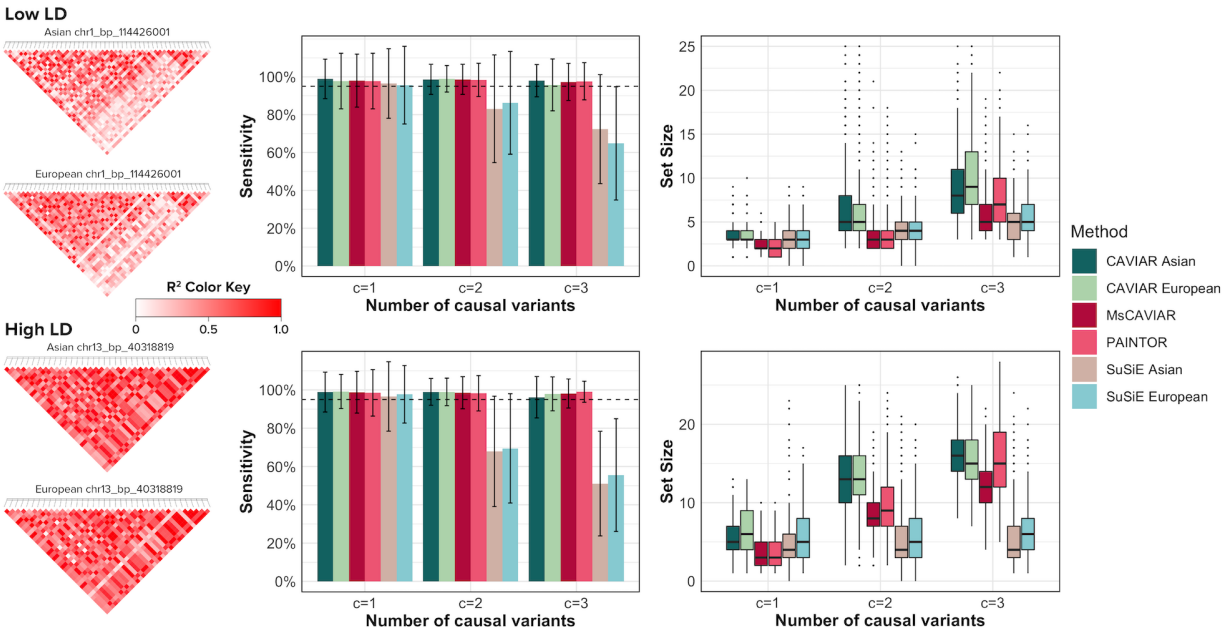


**Fig E. Comparison of sensitivity and set size using simulated data.** Comparison of the methods with c=1, c=2, or c=3 causal variants implanted. Both low LD (top half) and high LD (bottom half) settings were evaluated. The bar plots (left) display the sensitivity of the methods, with standard deviation bars included. The dashed line reflects the expected posterior probability of recovering all causal SNPs; methods that reach this threshold are considered "well-calibrated". The box plots (right) show the set sizes returned by the methods; for SuSiE, this is calculated as the sum of the sizes of credible sets returned. The boxes represent the interquartile range of causal set sizes identified by each tool, the lines inside the boxes represent the median, and the whiskers extend to the non-outlier extremes. Outliers are represented as dots above or below the whiskers. SuSiE's credible sets differ from the causal sets of the other methods in that SuSiE does not attempt to capture all causal SNPs, so the sensitivity calibration is not directly comparable to the other methods.

were well-calibrated in both LD settings (Fig E, bar plots). This is unsurprising since CAVIAR is well-known to be calibrated in the single study setting [4, 5, 6], as is PAINTOR in the trans-ethnic setting [3].

However, when considering the subset of simulations in which each method was able to correctly capture all causal variants (i.e. 100% sensitivity), we observed that MsCAVIAR consistently returns the smallest average set size (Fig E, box plots). MsCAVIAR and PAINTOR return smaller set sizes than CAVIAR run on either population across all settings, highlighting the value of using varying LD patterns in different populations to refine fine-mapping results. MsCAVIAR returned smaller set sizes than PAINTOR with multiple causal variants or high LD. This may be due to MsCAVIAR's explicit modeling of heterogeneity between studies. In both the high LD and multiple causal variants setting, complex and strong correlations between non-causal and causal SNPs are induced, and modeling heterogeneity between studies allows for more effective use of the differing LD structures to disentangle non-causal from causal SNPs.

SuSiE [1] takes a different approach to fine mapping from the other methods. Instead of returning a causal set, SuSiE returns (potentially multiple) credible sets for a locus, each of which is

expected to contain at least one causal SNP. The goal of SuSiE is not to capture all causal variants in a locus, but to return one or more minimal size credible sets, each of which has $\rho$ probability of containing at least one true causal effect. This explains why SuSiE is not well-calibrated according to our causal set definition, which expects all casual variants to be captured with probability $\rho^*$, when there is more than one causal SNP. It is worth noting, however, that SuSiE's credible set is equivalent to the causal set (as defined by the other methods) when the methods assume that there is only one causal SNP in a locus. In this case, all methods are well-calibrated and MsCAVIAR returns the smallest average set size, followed by PAINTOR, then SuSiE, and finally CAVIAR. This finding supports the hypothesis that using trans-ethnic information improves fine mapping resolution.

## 3 MsCAVIAR is well-calibrated with different population sizes between studies

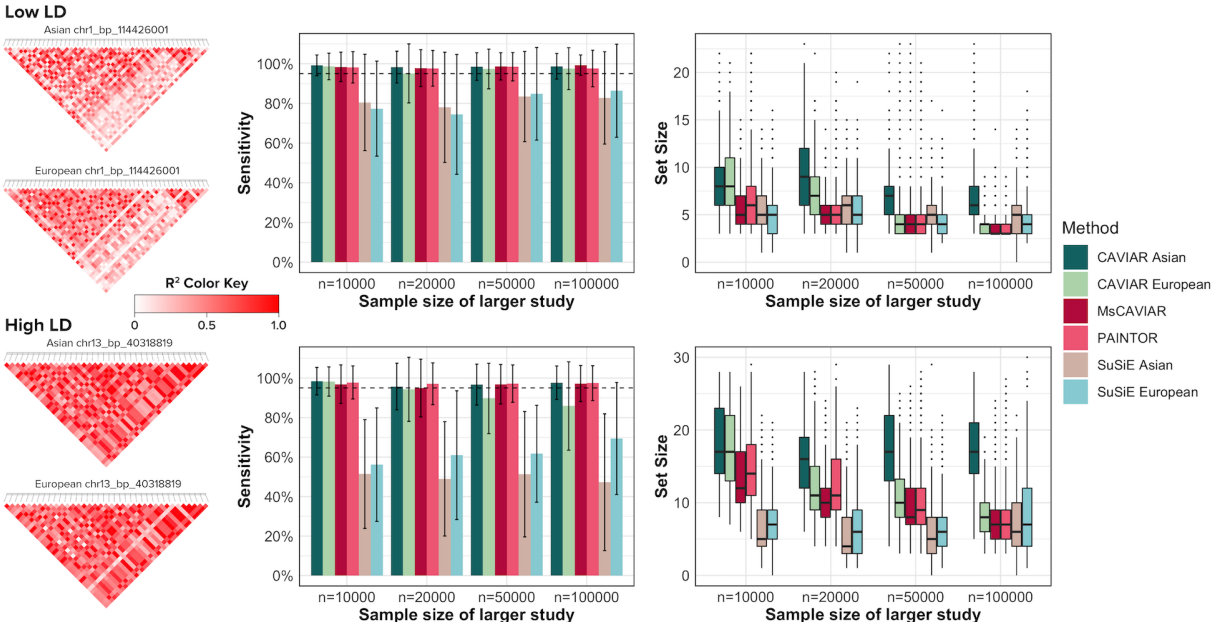


**Fig F. Comparison of sensitivity and set size using simulated studies with unequal sample sizes.** Comparison of the methods with 3 causal variants implanted and imbalanced sample sizes. The size of the Asian population was fixed at 10,000, while the European study was set to be 1, 2, 5, or 10 times larger. Both low LD (top half) and high LD (bottom half) settings were evaluated. The bar plots (left) display the sensitivity of the methods, with standard deviation bars included. The dashed line reflects the expected posterior probability of recovering all causal SNPs; methods that reach this threshold are considered "well-calibrated". The box plots (right) show the set sizes returned by the methods; for SuSiE, this is calculated as the sum of the sizes of credible sets returned. The boxes represent the interquartile range of causal set sizes identified by each tool, the lines inside the boxes represent the median, and the whiskers extend to the non-outlier extremes. Outliers are represented as dots above or below the whiskers. SuSiE's credible sets differ from the causal sets of the other methods in that SuSiE does not attempt to capture all causal SNPs, so the sensitivity calibration is not directly comparable to the other methods.

It is possible that input studies can have different sample sizes, in which case the non-centrality parameters of their SNPs are expected to be different proportionally to sample size, in addition to heterogeneity. We tested whether MsCAVIAR would still be well-calibrated in this setting, and compared it again with trans-ethnic PAINTOR and with CAVIAR and SuSiE run on the individual populations (Fig F). The caveats with SuSiE discussed in the previous section also apply here, so we omit it from further discussion and refer readers to the appendix.

In order to evaluate performance under this scenario in a simulation study, we used the same LD matrices from the previous section, but now varied the population size for one of the studies. We fixed the population size of the Asian study at 10,000 individuals, and varied the European study to have population sizes of 1, 2, 5, or 10 times that of the Asian study. Consequently, the effect sizes of causal SNPs in the European study were larger than those of the corresponding SNPs in the Asian study by a factor of $\sqrt{1}$, $\sqrt{2}$, $\sqrt{5}$, and $\sqrt{10}$ (Methods). For the sake of sufficient statistical power, we ensured that the causal variants in the smaller study were still statistically significant genome-wide. 1000 simulation replicates were run for each LD setting. In each simulation, we implanted three causal SNPs and simulated their effect sizes, with the association statistics of non-causal SNPs being based on their correlation with causal SNPs (Methods). All methods were run with posterior probability threshold $\rho^* = 0.95$, so methods with 95% or higher sensitivity were considered "well-calibrated" (dashed line in the bar plots). MsCAVIAR was run with its heterogeneity parameter set at $\tau^2 = 0.5$ (Methods).

Once again, MsCAVIAR was well-calibrated and generally returned the smallest causal set sizes. As the sample size differences grew, the difference between MsCAVIAR, CAVIAR on Europeans, and PAINTOR tended to diminish. This is likely due to the fact that we required SNPs to be genome-wide significant in the smaller study, such that the larger study had very large effect sizes for causal SNPs when there was a significant sample size imbalance, making the fine mapping problem easier. Reinforcing this interpretation is the fact that CAVIAR on Asians had consistently much larger causal set sizes than the other methods when the sample size imbalance was large.

All methods (exempting SuSiE) were well-calibrated in the low LD setting, but we observed that as the sample size increases with high LD that CAVIAR's calibration on the larger population decreases. This is likely due to the extremity of the situation, with exceptionally large effect sizes in combination with the high LD setting. We again, note that SuSiE's miscalibration is due to fundamental differences between SuSiE and the other methods.

# 4 Effects of heterogeneity parameter on MsCAVIAR

To examine the effects of mismatched true and model heterogeneity on MsCaviar results, we first simulated our studies with different "true heterogeneity" $\tau^2$. We used two regions from the 1000 Genomes project [2] to generate a high LD matrix and low LD matrix. For the low LD matrix, 20% of the SNPs have LD equal to or higher than 0.5, while the region with relatively high LD have 80% of the SNPs with LD equal to or higher than 0.5. We pruned groups of SNPs that were in perfect LD in one or more of the populations, leaving one SNP for each. The low LD matrix contains 48 SNPs, and the high LD matrix contained 38 SNPs Using these two matrices LD matrices, we implanted causal SNPs and simulated their effect sizes. In each simulation, we implanted either 1, 2, or 3 causal SNPs.

Each casual SNP's true overall non-centrality parameter $\Lambda$ was drawn according to $\mathcal{N}(5.2, 0.125^2)$. The study specific non-centrality parameter $\Lambda_i$ for each study $i$ was drawn according to $\Lambda_i \sim \mathcal{N}(\Lambda, \tau^2)$, where $\tau^2 = 0.5$, 1, or 2. For each model configuration, we performed 1000 replicate simulations (e.g. re-drawing the causal SNP effect sizes and re-picking the causal SNPs). We then

ran MsCAVIAR with different modeled heterogeneity settings, $\tau^2 = 0.5$, 1, or 2, on the simulations with the various true heterogeneity settings (Fig G). MsCAVIAR was well-calibrated and maintained similar set sizes even when the modeled heterogeneity did not match the true heterogeneity, indicating that MsCAVIAR is fairly robust to small mis-specifications of the $\tau^2$ parameter.

## 5 Out-of-sample LD matrices degrade the accuracy of fine-mapping

The methods CAVIAR [4], PAINTOR [3], and MsCAVIAR are designed such that they only require the z-scores as summary data and may use an external LD matrix representative of the samples for fine-mapping. Previous work has shown that this approach is underpowered [7]. In the results section "MsCAVIAR improves fine mapping resolution in a simulation study" we provide each fine-mapping method the LD matrices generated in-sample. Here, we simulate data in an almost identical fashion, but we generate the input LD matrices using the 1000 Genomes Project [2] to demonstrate the impact of the out-of-sample LD matrices on our fine-mapping results. We exclude SuSiE [1] from this set of analyses as the method was not designed to accept summary data.

For the results shown in Fig H, we use two sets of 9,000 unrelated individuals from the UK Biobank with European and Asian ancestry and then identify the corresponding populations in 1000 Genomes Project to generate the out-of-sample LD matrices. For the 9,000 UK Biobank samples with European ancestry, we select the 503 samples in the super population "EUR" in the 1000 Genomes Project as the reference sample. For the individuals with Asian ancestry, we needed to use two super populations "SAS" and "EAS" due to the UK Biobank sample containing 1600 individuals with Chinese ancestry, 5900 individuals with Indian ancestry, and 1800 individuals with other Asian ancestry. We generate our representative sample using all 489 "SAS" individuals and 123 "EAS" individuals sampled across subpopulations. This sub-sampling was done to approximate the proportion of individuals with Chinese and Indian ancestry. We note that while our example of out-of-sample LD for Asian ancestry is more extreme than when only 1 "super population" is used, it highlights how the accuracy of the out-of-sample LD impacts fine-mapping.

We looked at the three loci with low, medium, and high LD described in "MsCAVIAR improves fine mapping resolution in a simulation study" and retained the SNPs with MAF $> 0.05$ in the two samples generated from the 1000 Genomes Project. This resulted in 144, 125, and 149 SNPs for the low, medium, and high LD loci, respectively. Using this set of SNPs, we simulate the causal variants identically to the process described in the main results section referenced above. The only difference was that we provide the LD matrices generated from the 1000 Genomes samples to the methods instead of their in-sample LD matrices.

In the results shown in Fig H, we compare MsCAVIAR to trans-ethnic PAINTOR [3] and to CAVIAR [4] run on the Asian and European populations, separately. We average the results over the set of simulations for each number of causal SNPs: 1, 2, and 3. All methods were run using $\rho^* = 0.95$ as the posterior probability threshold; therefore methods were considered "well-calibrated" if their sensitivity was at least 95% (dashed line in Fig HA), and we set MsCAVIAR's heterogeneity parameter to $\tau^2 = 0.52$ (see Methods). We evaluated the precision of the methods in Fig HB where we show the causal set size. This metric is informative when the method returns the causal variant(s) because then fewer non-causal variants or "false positives" are being returned in the set.

When there is only 1 causal SNP, all methods are well-calibrated; however, only CAVIAR when analyzing European samples is well-calibrated when there are 3 causal SNPs and is slightly below the threshold for 2 implanted causal variants (94.3%). All other methods see a serious degradation in their sensitivity. This decrease in performance is a result of a poor approximation to the LD

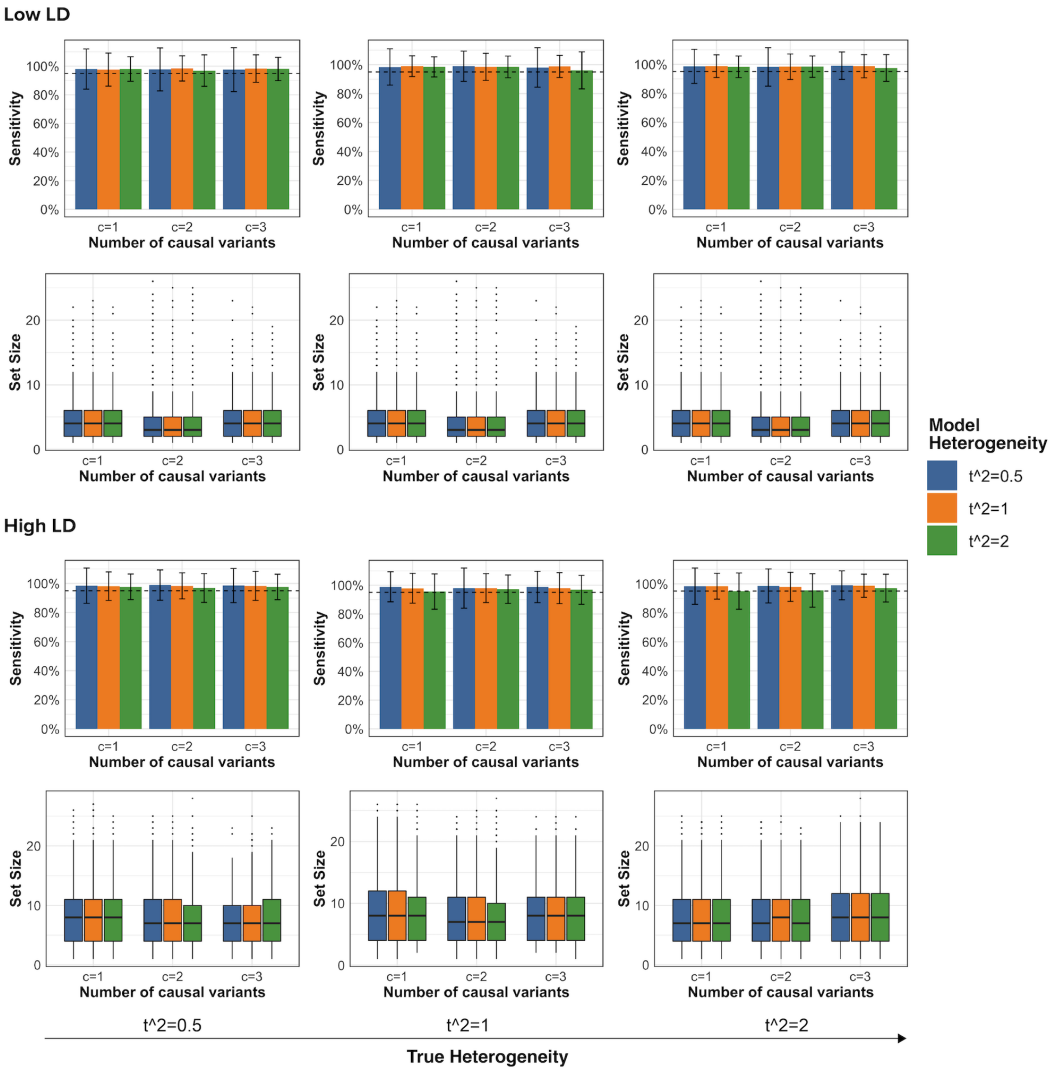


**Fig G. Evaluation of the sensitivity and set sizes of MsCAVIAR results under mis-specified heterogeneity parameters.** Each column of plots shows a different "True Heterogeneity" value $\tau^2$ used to simulate Z-scores of causal variants. Different-colored bars/boxes correspond to different values of $\tau^2$ used internally in MsCAVIAR's model, referred to as the "Model Heterogeneity". The model is mis-specified when the Model Heterogeneity does not match the True Heterogeneity. The first two rows of plots are based on a low LD locus, and the bottom two rows are based on a high LD locus. The bar plots (1st and 3rd rows) display the sensitivity of the results, with standard deviation bars included. The dashed line reflects the expected posterior probability of recovering all causal SNPs; methods that reach this threshold are considered "well-calibrated". The box plots (2nd and 4th rows) show the set sizes returned by MsCAVIAR. The boxes represent the interquartile range of causal set sizes identified by each tool, the lines inside the boxes represent the median, and the whiskers extend to the non-outlier extremes. Outliers are represented as dots above or below the whiskers. Simulations were performed with c=1, c=2, or c=3 causal variants.

matrix for individuals with Asian ancestry. When the out-of-sample LD accurately reflects the sample, as is the case for European ancestry, CAVIAR returns results comparable to when an in-

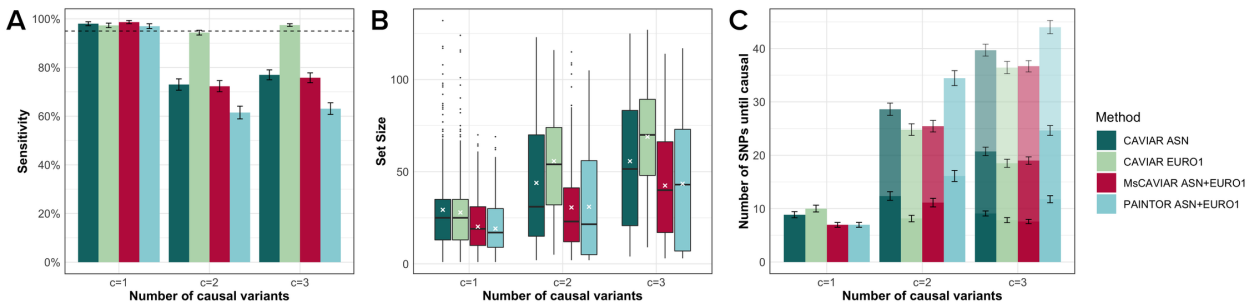


**Fig H. Comparison of sensitivity, precision, and set sizes using simulated data and out-of-sample LD matrices.** We compare MsCAVIAR, PAINTOR, and CAVIAR with $c \in \{1, 2, 3\}$ causal variants averaging over 3 loci and 5 levels of heritability with 20 replicates for each value of $c$. (A) Bar graph indicating the sensitivity of the method and the expected posterior probability, $\rho$, of recovering all causal SNPs represented as a dashed line. (B) Box plots showing the average set sizes each method returns. Each box is the interquartile range of causal set sizes. The middle black line represents the median and the white crosses indicating the mean. (C) Bar graph displaying the average number of SNPs in descending order of posterior inclusion probability (PIP) until 1,2, or 3 causal SNPs is identified. Stacked bars represent increasing numbers of causal SNPs identified until the true number of causal SNPs (x-axis) are identified.

sample LD matrix is provided. For MsCAVIAR and PAINTOR, however, we see incorporating two populations does not help when one sample's LD is poorly approximated. Though the set sizes are smaller in Fig H, the specificity is also lower than either run of CAVIAR. While MsCAVIAR and PAINTOR are both poorly calibrated, we see that MsCAVIAR is more robust to the out-of-sample LD than PAINTOR. Further work would need to be done to explore this phenomenon.

At present, we encourage users to use the in-sample LD matrix whenever possible. If this is not a possibility, we advise the user to interpret their results with the understanding the out-of-sample LD may fail to provide well-calibrated results, and the quality of results depend how well the out-of-sample LD approximates the in-sample LD. Future work could also enable the method to incorporate the sufficient summary data described in [7].

## 6 Loci and set sizes for the real data fine-mapping analysis.

Below we include a table of the real data results. The first column is the list of regions fine-mapped. The remaining four columns is the number of SNPs returned by each method's causal set. The methods in order are: CAVIAR on Biobank Japan (BBJ) "CAVIAR-Asian", CAVIAR on UK Biobank (UKB) "CAVIAR-Euro", PAINTOR, and MsCAVIAR. The last two methods fine-map utilizing data from both BBJ and UKB.

| LOCUS | CAVIAR-Asian | CAVIAR-Euro | PAINTOR | MsCAVIAR |
|---|---|---|---|---|
| chr10:113440329-114440329 | 83 | 52 | 58 | 61 |
| chr10:115286236-116286236 | 31 | 16 | 18 | 10 |
| chr10:122398697-123398697 | 97 | 85 | 53 | 102 |
| chr10:33136099-34136099 | 230 | 32 | 48 | 20 |
| chr10:45522005-46522005 | 59 | 48 | 38 | 34 |
| chr10:64552205-65552205 | 275 | 249 | 230 | 238 |

| LOCUS | CAVIAR-Asian | CAVIAR-Euro | PAINTOR | MsCAVIAR |
|---|---|---|---|---|
| chr10:88011326-89011326 | 88 | 77 | 54 | 63 |
| chr10:94314710-95314710 | 148 | 15 | 22 | 6 |
| chr10:94816037-95816037 | 112 | 7 | 17 | 4 |
| chr10:99269388-100269388 | 66 | 57 | 57 | 55 |
| chr11:109470749-110470749 | 72 | 65 | 62 | 62 |
| chr11:115908029-116908029 | 9 | 6 | 6 | 5 |
| chr11:117920241-118920241 | 54 | 46 | 44 | 38 |
| chr11:122014403-123014403 | 97 | 59 | 58 | 43 |
| chr11:125725876-126725876 | 143 | 50 | 47 | 18 |
| chr11:13837575-14837575 | 254 | 151 | 118 | 93 |
| chr11:14365399-15365399 | 137 | 112 | 105 | 71 |
| chr11:27248493-28248493 | 121 | 101 | 90 | 90 |
| chr11:45413607-46413607 | 15 | 13 | 15 | 12 |
| chr11:46228966-47228966 | 170 | 57 | 16 | 24 |
| chr11:46837383-47837383 | 396 | 82 | 81 | 73 |
| chr11:47398535-48398535 | 248 | 34 | 49 | 36 |
| chr11:47944711-48944711 | 71 | 9 | 4 | 9 |
| chr11:61092362-62092362 | 44 | 6 | 25 | 6 |
| chr11:63504723-64504723 | 23 | 14 | 18 | 16 |
| chr11:64973798-65973798 | 100 | 62 | 65 | 64 |
| chr11:65566993-66566993 | 35 | 27 | 33 | 28 |
| chr11:68116074-69116074 | 55 | 51 | 50 | 46 |
| chr11:74952486-75952486 | 143 | 116 | 110 | 100 |
| chr12:109371179-110371179 | 232 | 177 | 19 | 28 |
| chr12:110558188-111558188 | 64 | 88 | 35 | 65 |
| chr12:111218231-112218231 | 10 | 172 | 5 | 7 |
| chr12:112091686-113091686 | 16 | 27 | 27 | 19 |
| chr12:112819105-113819105 | 6 | 90 | 10 | 4 |
| chr12:120916622-121916622 | 159 | 110 | 94 | 96 |
| chr12:122688475-123688475 | 129 | 31 | 19 | 19 |
| chr12:123236084-124236084 | 430 | 253 | 128 | 249 |
| chr12:123909502-124909502 | 98 | 56 | 6 | 17 |
| chr12:124765201-125765201 | 19 | 6 | 4 | 5 |
| chr12:19970199-20970199 | 75 | 9 | 19 | 9 |
| chr12:53233529-54233529 | 33 | 23 | 25 | 17 |
| chr12:56831741-57831741 | 42 | 19 | 29 | 28 |
| chr12:57339173-58339173 | 46 | 20 | 16 | 15 |
| chr12:57922642-58922642 | 36 | 33 | 34 | 33 |
| chr12:6163964-7163964 | 89 | 81 | 79 | 69 |
| chr12:70973887-71973887 | 17 | 14 | 16 | 14 |
| chr12:8595905-9595905 | 83 | 51 | 42 | 54 |
| chr14:102747844-103747844 | 22 | 17 | 16 | 10 |
| chr14:104758892-105758892 | 33 | 8 | 26 | 8 |
| chr14:68649372-69649372 | 29 | 28 | 30 | 26 |
| chr14:73750126-74750126 | 30 | 22 | 25 | 19 |
| chr14:74860906-75860906 | 367 | 320 | 236 | 283 |
| chr14:81135888-82135888 | 50 | 49 | 47 | 39 |

| LOCUS | CAVIAR-Asian | CAVIAR-Euro | PAINTOR | MsCAVIAR |
|---|---|---|---|---|
| chr15:23444489-24444489 | 25 | 21 | 21 | 21 |
| chr15:42599550-43599550 | 99 | 83 | 55 | 45 |
| chr15:57703414-58703414 | 8 | 6 | 5 | 3 |
| chr15:58223939-59223939 | 5 | 3 | 6 | 3 |
| chr15:59004897-60004897 | 30 | 52 | 20 | 14 |
| chr15:62844167-63844167 | 18 | 12 | 16 | 12 |
| chr15:74212937-75212937 | 219 | 191 | 171 | 189 |
| chr15:74964992-75964992 | 51 | 42 | 42 | 40 |
| chr16:53303187-54303187 | 59 | 45 | 47 | 40 |
| chr16:55410194-56410194 | 51 | 8 | 6 | 5 |
| chr16:55918284-56918284 | 50 | 10 | 7 | 7 |
| chr16:56995026-57995026 | 4 | 3 | 5 | 6 |
| chr16:66898369-67898369 | 57 | 38 | 48 | 43 |
| chr16:67472194-68472194 | 301 | 154 | 8 | 94 |
| chr16:68059767-69059767 | 302 | 111 | 5 | 82 |
| chr16:74682354-75682354 | 311 | 295 | 254 | 286 |
| chr16:81034790-82034790 | 86 | 17 | 21 | 19 |
| chr17:37310218-38310218 | 287 | 111 | 42 | 110 |
| chr17:37844485-38844485 | 192 | 94 | 58 | 91 |
| chr17:40281561-41281561 | 196 | 182 | 64 | 66 |
| chr17:41426126-42426126 | 22 | 7 | 7 | 6 |
| chr17:66323805-67323805 | 129 | 36 | 27 | 19 |
| chr17:6962969-7962969 | 34 | 30 | 28 | 22 |
| chr17:75898130-76898130 | 157 | 112 | 124 | 97 |
| chr17:7590908-8590908 | 32 | 25 | 27 | 23 |
| chr18:19166877-20166877 | 147 | 137 | 140 | 138 |
| chr18:46078242-47078242 | 49 | 5 | 12 | 4 |
| chr18:46609955-47609955 | 7 | 13 | 7 | 6 |
| chr18:47132322-48132322 | 24 | 15 | 6 | 7 |
| chr18:57413965-58413965 | 65 | 41 | 48 | 33 |
| chr19:10850488-11850488 | 28 | 14 | 19 | 8 |
| chr19:33396432-34396432 | 65 | 30 | 40 | 27 |
| chr19:44911941-45911941 | 6 | 3 | 5 | 3 |
| chr19:45884830-46884830 | 72 | 45 | 39 | 41 |
| chr19:51841757-52841757 | 291 | 204 | 100 | 149 |
| chr19:54300500-55300500 | 14 | 14 | 6 | 11 |
| chr19:7011798-8011798 | 16 | 13 | 13 | 11 |
| chr19:7929323-8929323 | 46 | 6 | 7 | 5 |
| chr1:109166352-110166352 | 41 | 16 | 25 | 15 |
| chr1:109732983-110732983 | 85 | 12 | 7 | 7 |
| chr1:178013895-179013895 | 193 | 138 | 127 | 123 |
| chr1:181671957-182671957 | 77 | 67 | 70 | 63 |
| chr1:219182178-220182178 | 24 | 19 | 19 | 15 |
| chr1:220470028-221470028 | 51 | 24 | 30 | 19 |
| chr1:229797778-230797778 | 177 | 19 | 11 | 23 |
| chr1:230323363-231323363 | 53 | 6 | 22 | 6 |
| chr1:23210475-24210475 | 26 | 19 | 21 | 18 |

| LOCUS | CAVIAR-Asian | CAVIAR-Euro | PAINTOR | MsCAVIAR |
|---|---|---|---|---|
| chr1:39503410-40503410 | 183 | 103 | 84 | 115 |
| chr1:435222-1435222 | 13 | 8 | 11 | 8 |
| chr1:65573952-66573952 | 23 | 14 | 18 | 12 |
| chr2:-216206-783794 | 73 | 64 | 52 | 55 |
| chr1:93358292-94358292 | 274 | 156 | 48 | 56 |
| chr20:17096155-18096155 | 70 | 53 | 50 | 31 |
| chr20:44051855-45051855 | 75 | 10 | 4 | 12 |
| chr20:45840596-46840596 | 138 | 7 | 12 | 7 |
| chr20:50746378-51746378 | 48 | 44 | 42 | 41 |
| chr20:61847191-62847191 | 255 | 183 | 9 | 87 |
| chr21:45771452-46771452 | 122 | 127 | 71 | 61 |
| chr21:46399279-47399279 | 60 | 52 | 51 | 47 |
| chr22:21425017-22425017 | 69 | 68 | 68 | 68 |
| chr22:29924863-30924863 | 260 | 206 | 187 | 188 |
| chr22:30425616-31425616 | 217 | 170 | 128 | 159 |
| chr22:38099857-39099857 | 31 | 23 | 24 | 16 |
| chr22:38610124-39610124 | 33 | 24 | 29 | 23 |
| chr2:100295962-101295962 | 60 | 59 | 4 | 49 |
| chr2:134763081-135763081 | 96 | 85 | 81 | 76 |
| chr2:135407088-136407088 | 60 | 59 | 57 | 53 |
| chr2:135907479-136907479 | 26 | 24 | 24 | 22 |
| chr2:136507429-137507429 | 21 | 19 | 20 | 18 |
| chr2:165055539-166055539 | 144 | 73 | 55 | 61 |
| chr2:173416114-174416114 | 78 | 57 | 67 | 50 |
| chr2:19871772-20871772 | 13 | 10 | 12 | 10 |
| chr2:20731524-21731524 | 105 | 24 | 32 | 27 |
| chr2:211040507-212040507 | 64 | 55 | 46 | 40 |
| chr2:226599180-227599180 | 218 | 61 | 107 | 139 |
| chr2:241737902-242737902 | 105 | 87 | 71 | 75 |
| chr2:48462291-49462291 | 31 | 26 | 29 | 23 |
| chr3:11851223-12851223 | 365 | 79 | 32 | 69 |
| chr3:135380410-136380410 | 130 | 100 | 91 | 103 |
| chr3:135904095-136904095 | 163 | 130 | 115 | 123 |
| chr3:156298732-157298732 | 46 | 23 | 35 | 24 |
| chr3:184782232-185782232 | 66 | 55 | 64 | 60 |
| chr3:185322353-186322353 | 92 | 10 | 29 | 10 |
| chr3:46425539-47425539 | 152 | 126 | 110 | 112 |
| chr3:47221512-48221512 | 67 | 66 | 57 | 55 |
| chr3:49524027-50524027 | 249 | 163 | 164 | 100 |
| chr4:102181041-103181041 | 23 | 14 | 19 | 12 |
| chr4:102688709-103688709 | 24 | 10 | 16 | 12 |
| chr4:25550450-26550450 | 11 | 3 | 7 | 3 |
| chr4:39288949-40288949 | 91 | 77 | 68 | 59 |
| chr4:470112-1470112 | 63 | 56 | 50 | 44 |
| chr4:54998781-55998781 | 25 | 20 | 23 | 21 |
| chr4:68861445-69861445 | 29 | 25 | 27 | 24 |
| chr4:86973776-87973776 | 133 | 101 | 100 | 84 |

| LOCUS | CAVIAR-Asian | CAVIAR-Euro | PAINTOR | MsCAVIAR |
|---|---|---|---|---|
| chr4:87518991-88518991 | 242 | 68 | 103 | 89 |
| chr4:89230074-90230074 | 111 | 65 | 78 | 65 |
| chr4:99761577-100761577 | 160 | 110 | 100 | 83 |
| chr5:103434169-104434169 | 44 | 35 | 26 | 23 |
| chr5:110726812-111726812 | 79 | 73 | 69 | 63 |
| chr5:126850549-127850549 | 49 | 35 | 21 | 19 |
| chr5:157499022-158499022 | 122 | 109 | 71 | 87 |
| chr5:55304552-56304552 | 88 | 9 | 6 | 9 |
| chr5:74503678-75503678 | 78 | 58 | 49 | 41 |
| chr7:551664-1551664 | 195 | 85 | 65 | 51 |
| chr7:106289152-107289152 | 63 | 41 | 46 | 34 |
| chr7:129938531-130938531 | 70 | 31 | 37 | 29 |
| chr7:150040196-151040196 | 407 | 203 | 105 | 187 |
| chr7:17420253-18420253 | 359 | 230 | 221 | 252 |
| chr7:25897239-26897239 | 73 | 54 | 53 | 48 |
| chr7:35710924-36710924 | 114 | 80 | 86 | 75 |
| chr7:49806810-50806810 | 32 | 32 | 34 | 30 |
| chr7:5970622-6970622 | 111 | 82 | 54 | 66 |
| chr7:72539406-73539406 | 117 | 68 | 90 | 78 |
| chr7:79842775-80842775 | 148 | 173 | 68 | 69 |
| chr8:103383630-104383630 | 45 | 2 | 35 | 11 |
| chr8:116103103-117103103 | 216 | 113 | 24 | 110 |
| chr8:12123463-13123463 | 24 | 21 | 24 | 22 |
| chr8:8683358-9683358 | 96 | 10 | 24 | 9 |
| chr8:121367780-122367780 | 79 | 70 | 15 | 25 |
| chr8:125980367-126980367 | 73 | 36 | 40 | 27 |
| chr8:143806597-144806597 | 58 | 35 | 40 | 33 |
| chr8:18751679-19751679 | 13 | 7 | 5 | 4 |
| chr8:19324667-20324667 | 55 | 24 | 6 | 18 |
| chr8:19941920-20941920 | 10 | 3 | 6 | 3 |
| chr8:70838185-71838185 | 325 | 314 | 298 | 285 |
| chr8:9277873-10277873 | 51 | 12 | 24 | 9 |
| chr9:106574213-107574213 | 8 | 22 | 9 | 14 |
| chr9:107161742-108161742 | 6 | 3 | 5 | 3 |
| chr9:123131225-124131225 | 109 | 121 | 70 | 103 |
| chr9:139487756-140487756 | 38 | 32 | 33 | 31 |
| chr9:14804782-15804782 | 52 | 11 | 14 | 10 |
| chr9:94882297-95882297 | 121 | 101 | 98 | 96 |

**Table A. Loci and causal set sizes for the trans-biobank High Density Lipoprotein fine mapping analysis.** Each row is a fine mapping locus, and the columns represent the number of SNPs in the causal sets returned by each method.

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