

| Dataset      | Releases<br>(1 <sup>st</sup> , 2 <sup>nd</sup> ) | Univariate<br>$p$ -Value<br>Threshold<br>(1 <sup>st</sup> , 2 <sup>nd</sup> ) | New<br>Multivariate<br>SNPs in 1 <sup>st</sup> | Lower<br>Univariate<br>$p$ -Value in 2 <sup>nd</sup> | Below 2 <sup>nd</sup><br>Univariate<br>Threshold |
|--------------|--|---|--|--|--|
| GlobalLipids | 2010, 2013                                       | $5 \times 10^{-8}$ , $5 \times 10^{-8}$                                       | 19   | 14   | 11   |
| GIANT        | 2010, 2014/5                                     | $5 \times 10^{-8}$ , $5 \times 10^{-8}$                                       | 60   | 59   | 51   |
| HaemgenRBC   | 2012, 2016                                       | $1 \times 10^{-8}$ , $8.31 \times 10^{-9}$                                    | 16   | 11   | 6  |

**S5 Table. Replication of New Multivariate Associations.**

Shown are example metrics of how well our new multivariate associations replicate in datasets that allow such an evaluation. Specifically, for three of the studies used (GlobalLipids, GIANT, and HaemgenRBC), there are multiple dataset releases. To examine how well our new multivariate **bmss** associations replicate, we compared the results from the first releases (“1<sup>st</sup>”) with the univariate GWAS associations of the second releases (“2<sup>nd</sup>”). In essence, each of these approaches aim to increase power – one by using a multivariate approach (**bmss**) and the other by increasing sample size (the 2<sup>nd</sup> releases) – thus allowing us to compare the results against one another. Univariate  $p$ -Value Threshold: univariate GWAS significance  $p$ -value thresholds used by the original publication(s) for both the earlier (1<sup>st</sup>) and later (2<sup>nd</sup>) releases. New Multivariate SNPs in 1<sup>st</sup>: number of new multivariate associations from the earlier release. Lower Univariate  $p$ -Value in 2<sup>nd</sup>: number of new multivariate associations from the earlier release that also have lower univariate  $p$ -values in the later release. Below 2<sup>nd</sup> Univariate Threshold: number of new multivariate associations from the earlier release that also cross the later release’s univariate GWAS significance threshold.