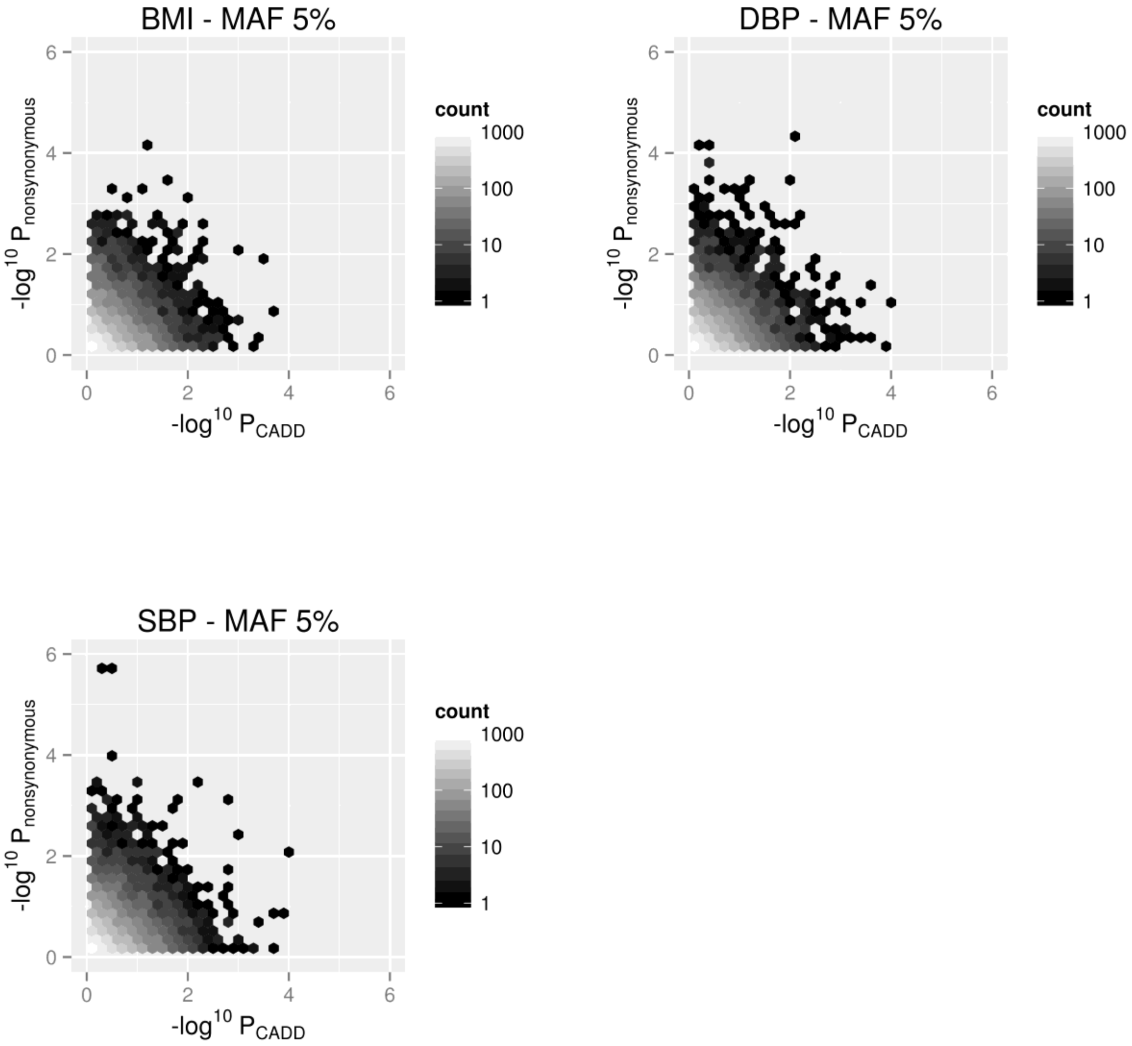
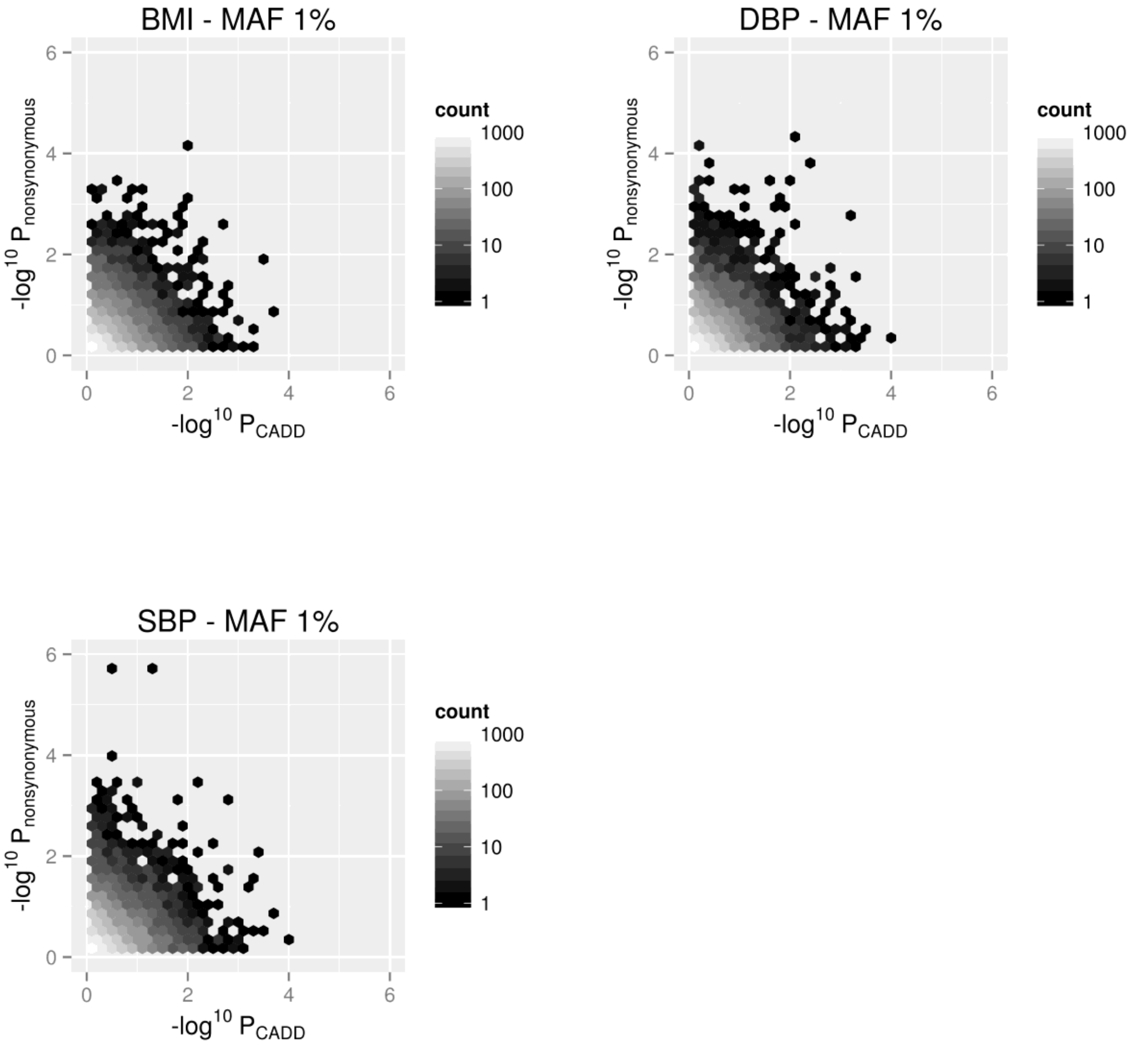
Supporting Information

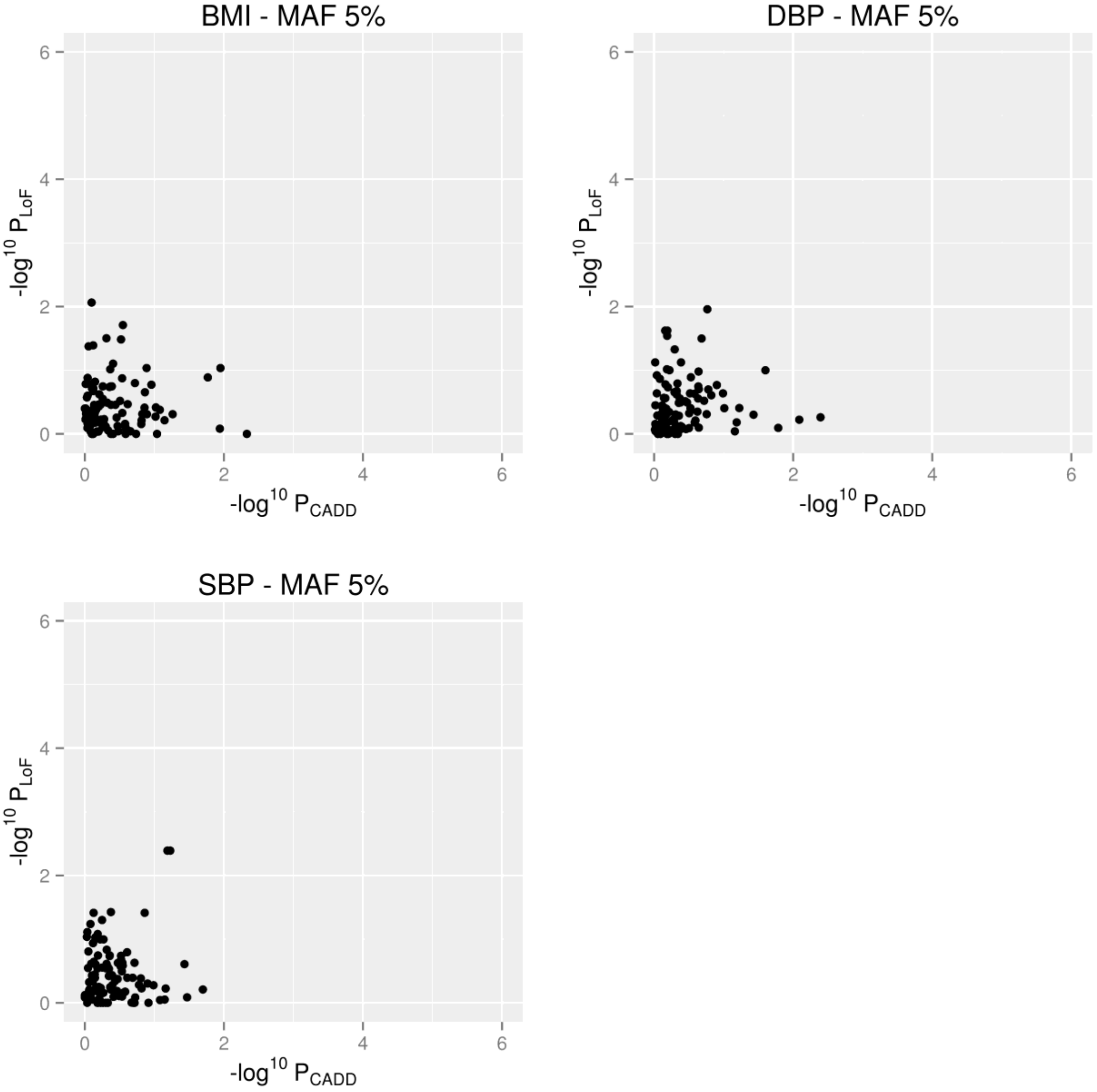
S1 Figure: Gene-based low frequency variant analyses across the genome using SKAT for 3 cardiovascular traits (compared with nonsynonymous filtering)

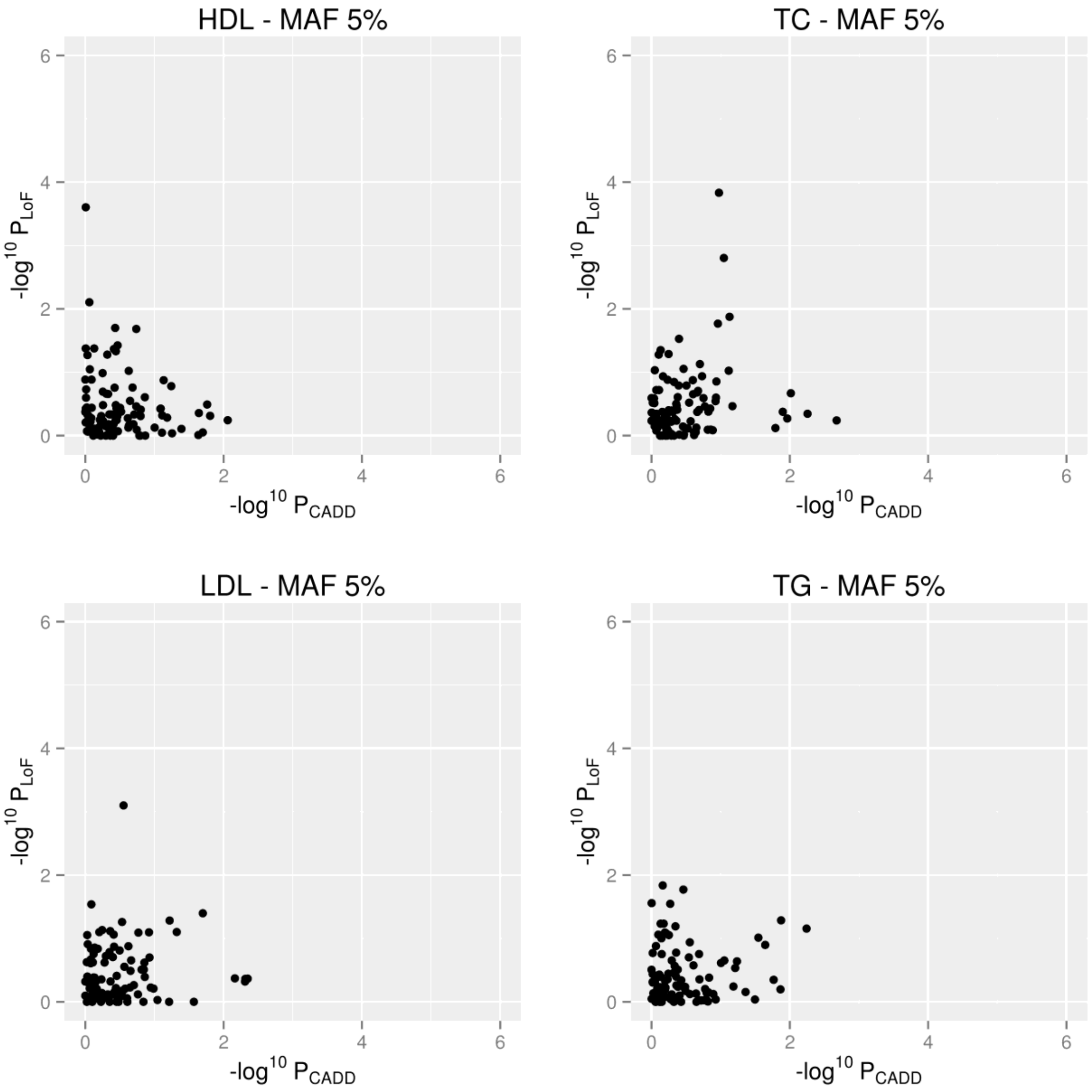


S2 Figure: Gene-based rare variant analyses across the genome using SKAT for 3 cardiovascular traits (compared with nonsynonymous filtering)

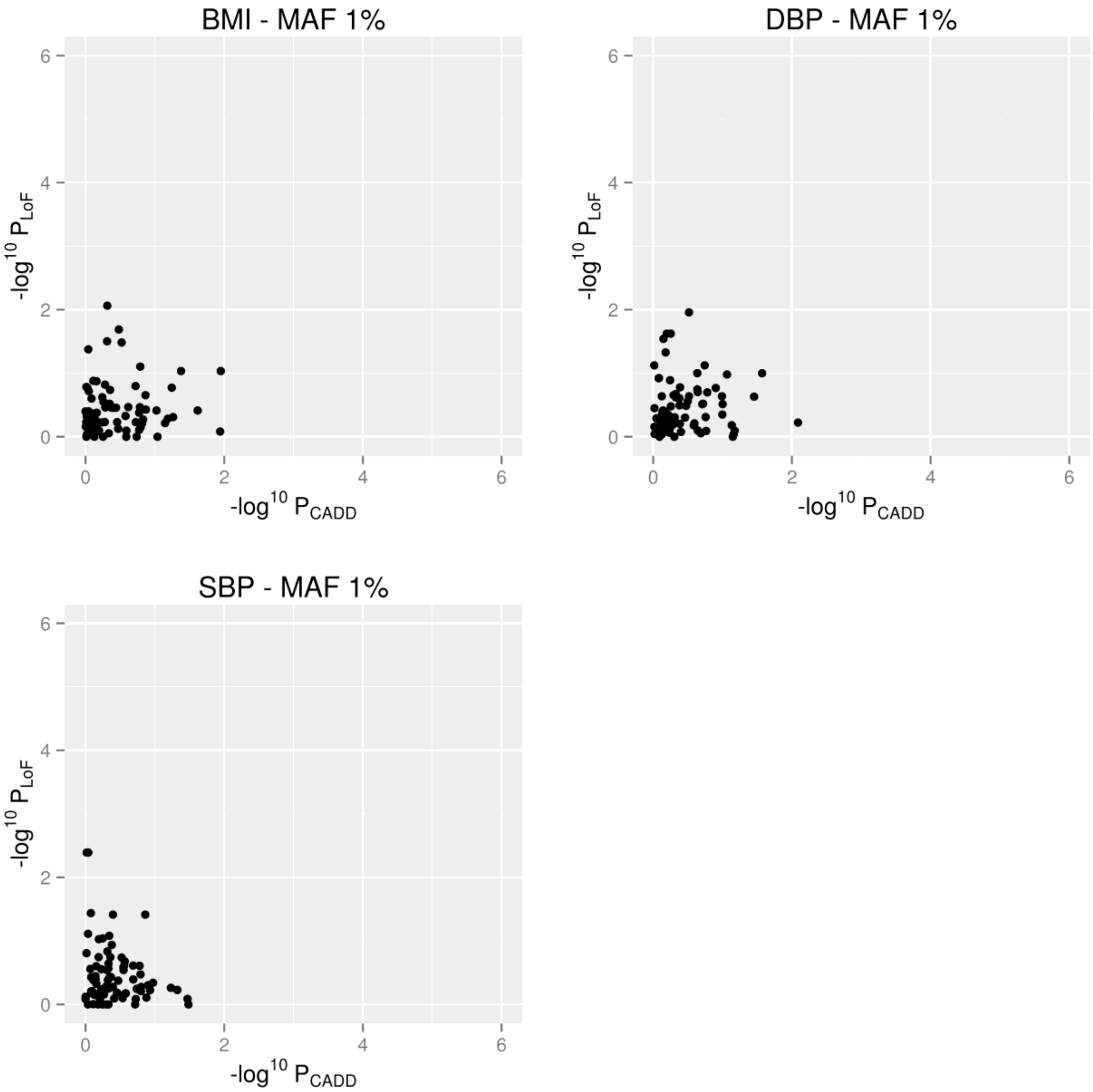


S3 Figure: Gene-based low frequency variant analyses across the genome using SKAT for 7 cardiovascular traits (compared with loss-of-function filtering)




HDL - MAF 5%
TC - MAF 5%
LDL - MAF 5%
TG - MAF 5%
$-\log^{10} P_{LoF}$
$-\log^{10} P_{CADD}$
0
2
4
6

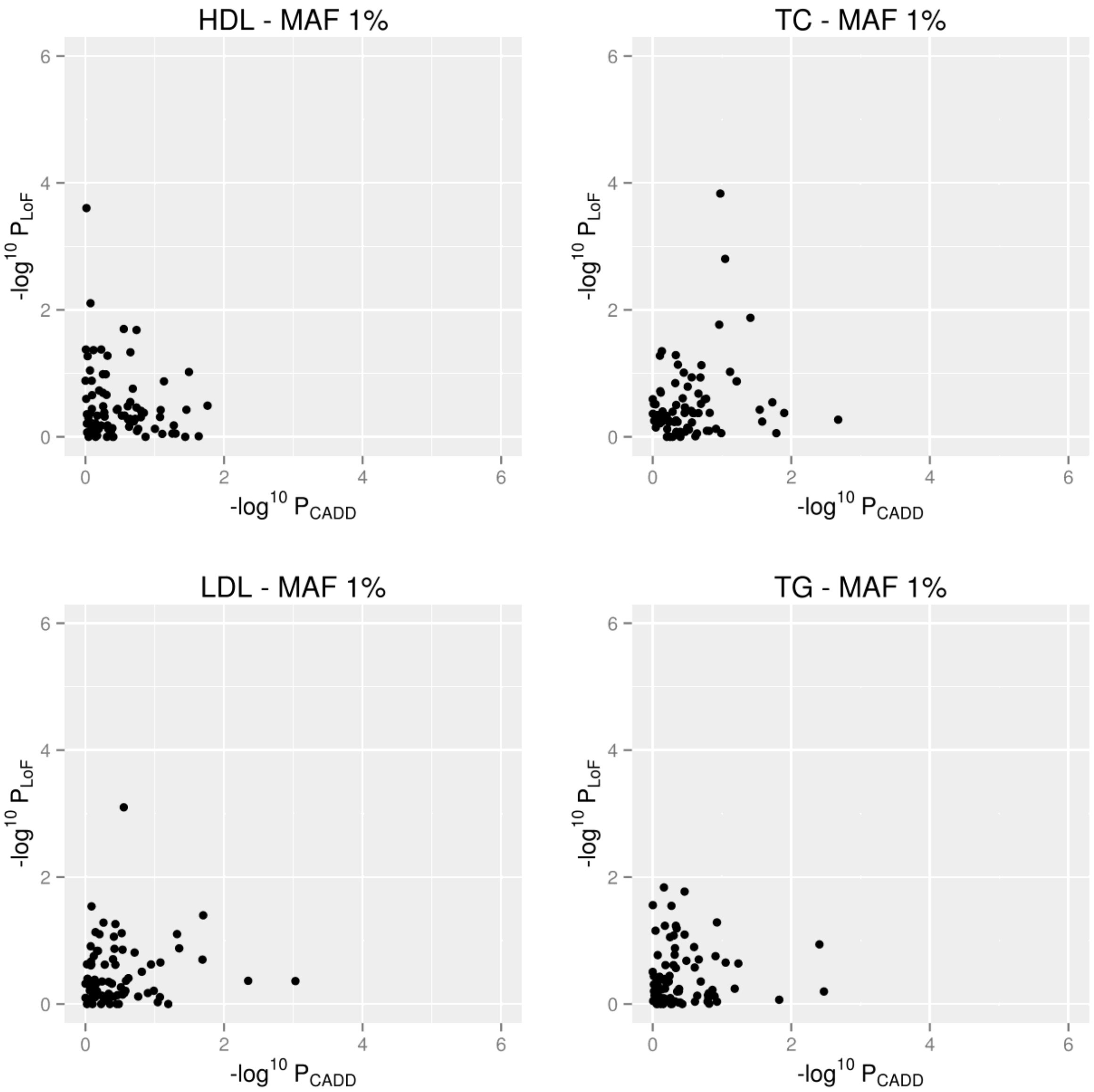
S4 Figure: Gene-based rare variant analyses across the genome using SKAT for 7 cardiovascular traits (compared with loss-of-function filtering)



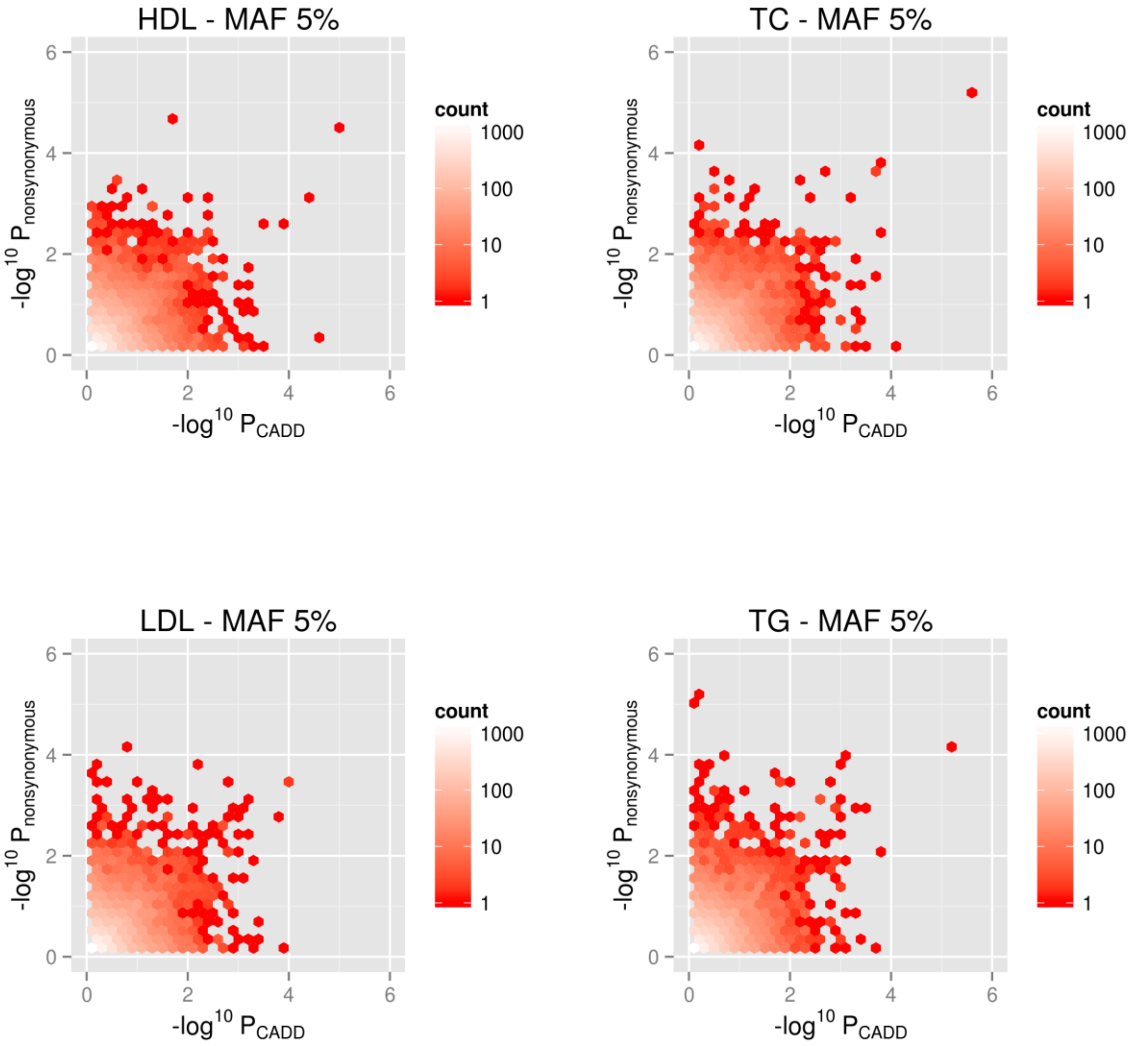
BMI - MAF 1%

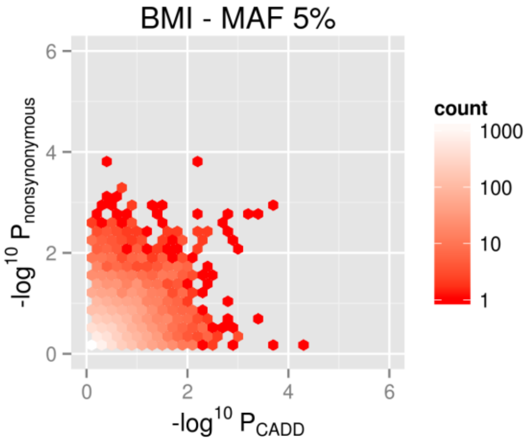
DBP - MAF 1%

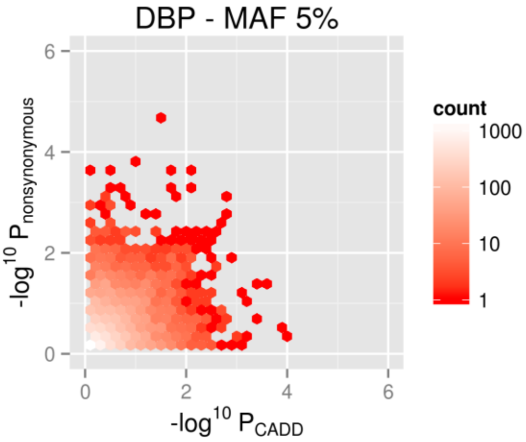
SBP - MAF 1%

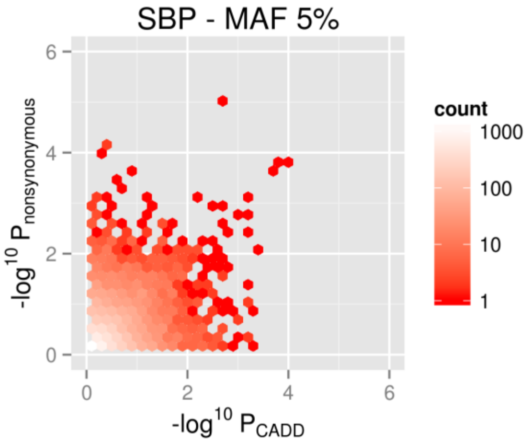

HDL - MAF 1%
TC - MAF 1%
LDL - MAF 1%
TG - MAF 1%
-log10 P_LoF
-log10 P_CADD
0
2
4
6

S5 Figure: Gene-based low frequency variant analyses across the genome using SKAT-O for 7 cardiovascular traits (compared with nonsynonymous filtering)

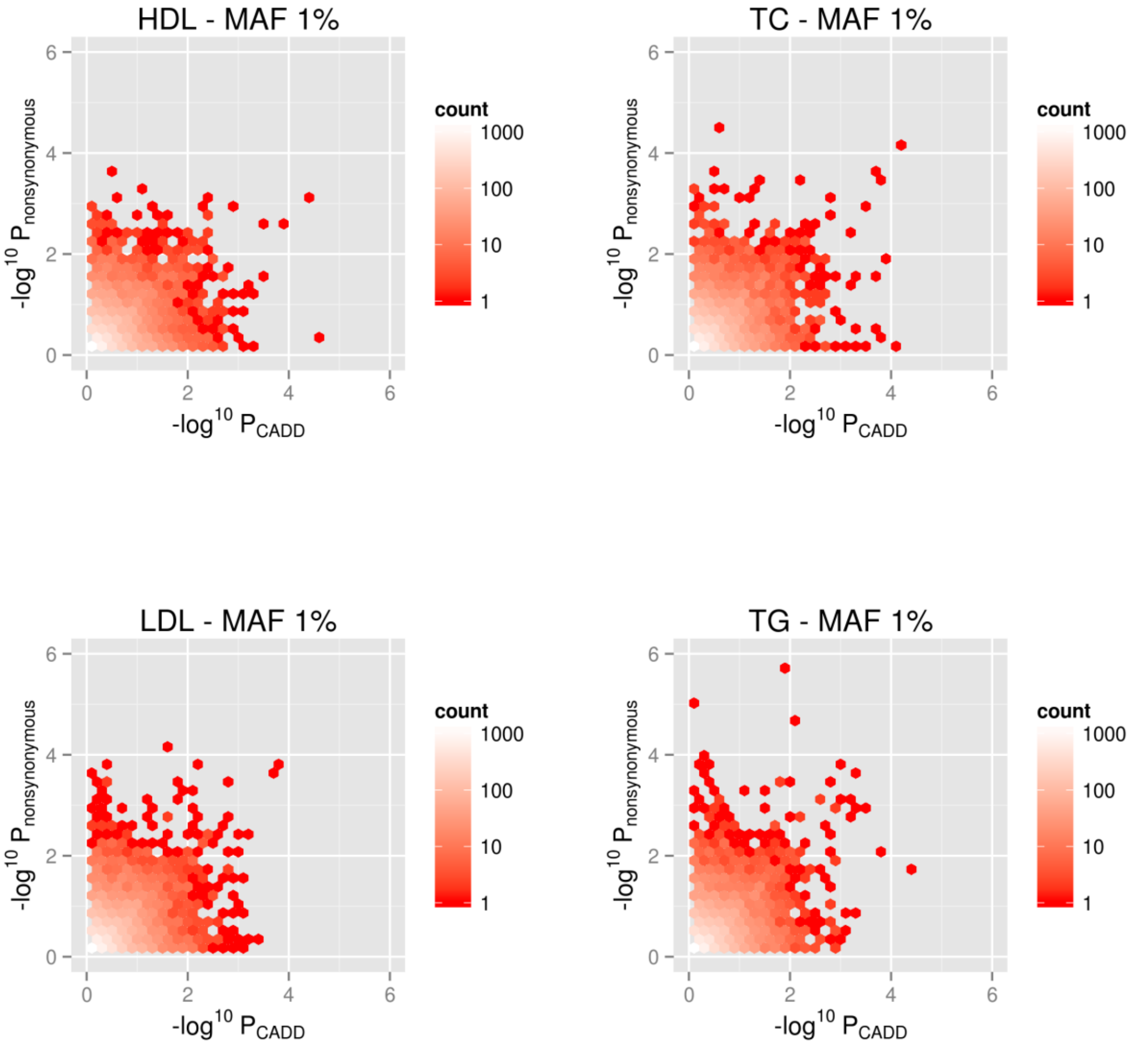


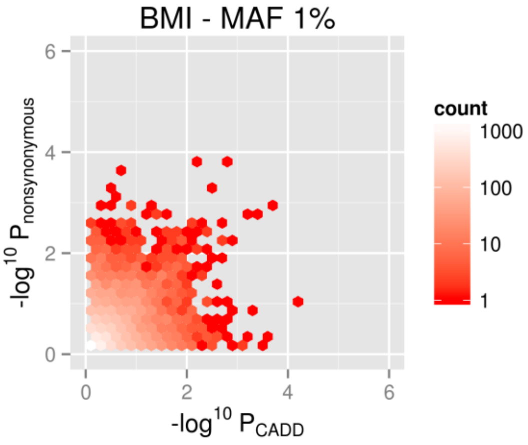

BMI - MAF 5%

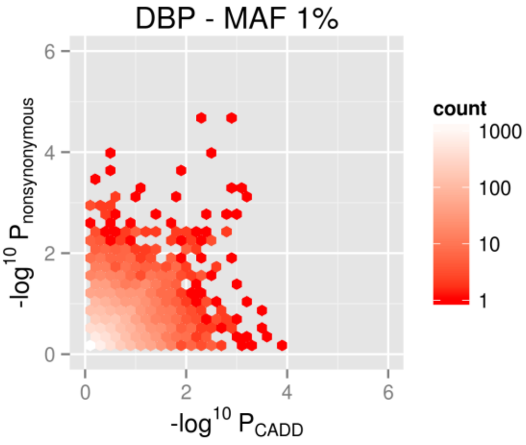

DBP - MAF 5%

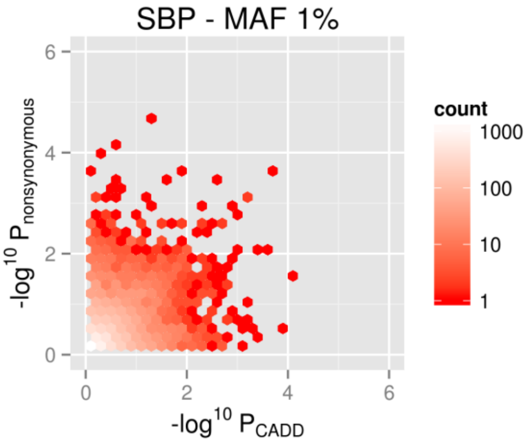

SBP - MAF 5%

S6 Figure: Gene-based rare variant analyses across the genome using SKAT-O for 7 cardiovascular traits (compared with nonsynonymous filtering)

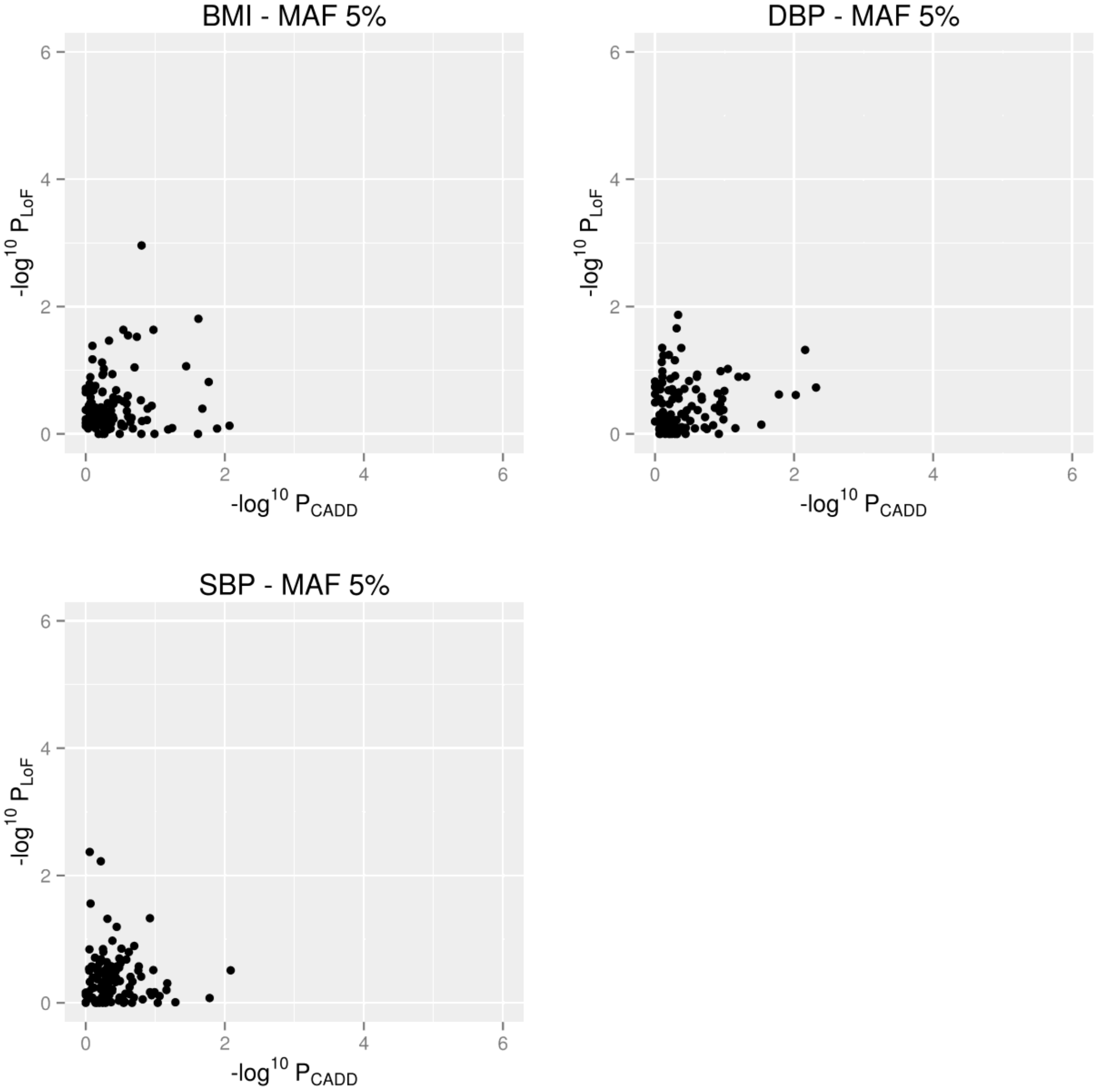


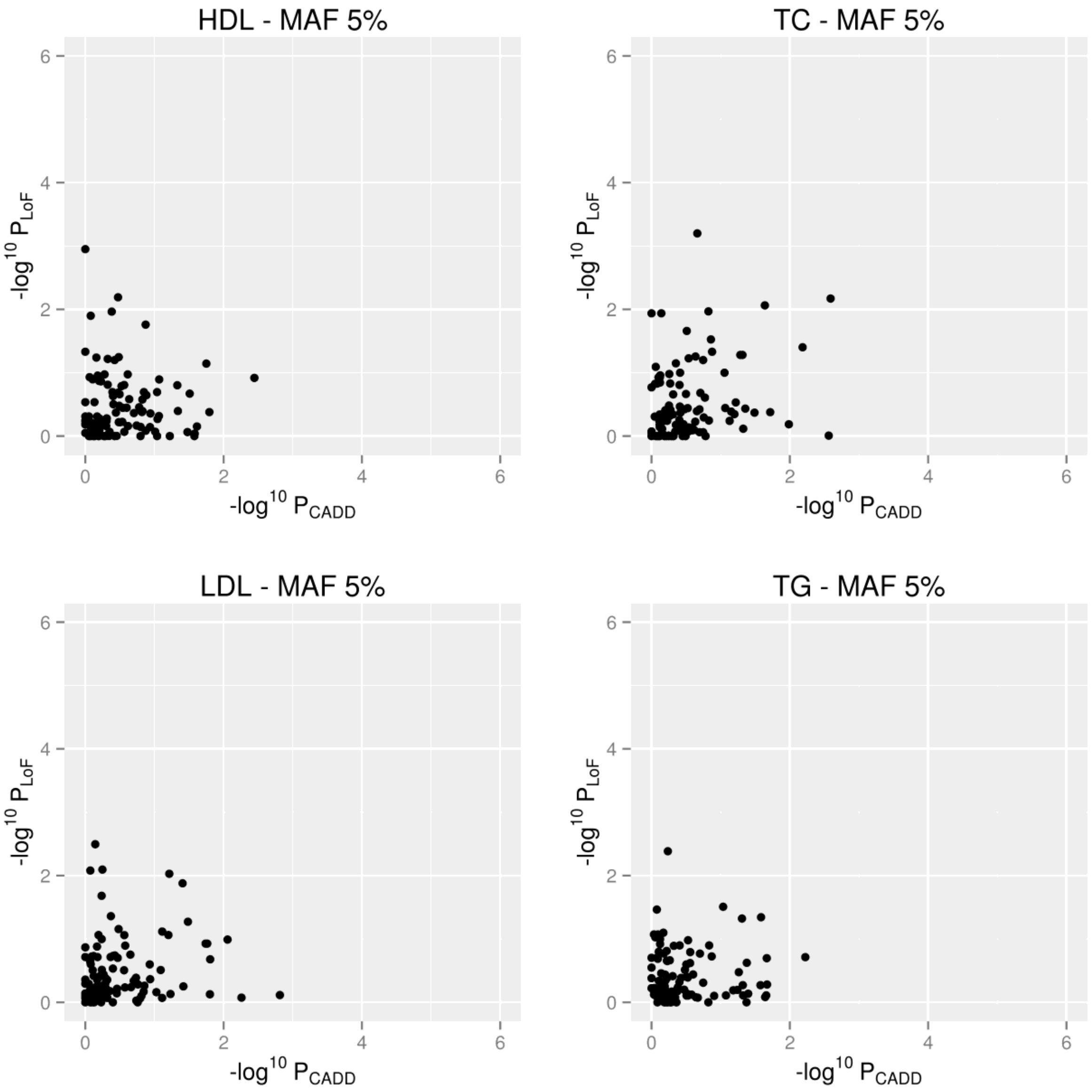

BMI - MAF 1%
-log10 Pnonsynonymous
-log10 PCADD
0
2
4
6
0
2
4
6
count
1000
100
10
1


DBP - MAF 1%
-log10 Pnonsynonymous
-log10 PCADD
0
2
4
6
0
2
4
6
count
1000
100
10
1

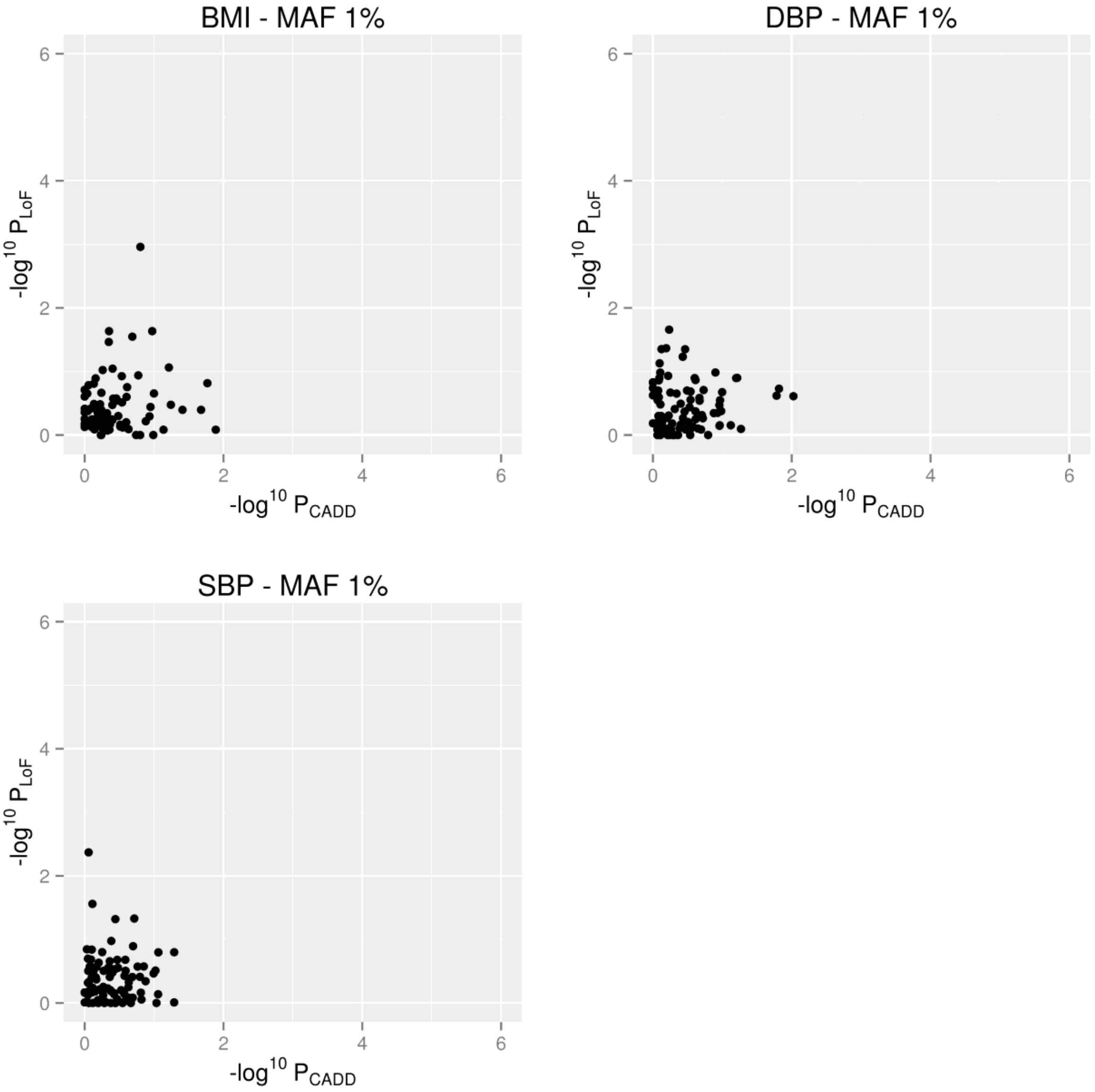

SBP - MAF 1%
-log10 Pnonsynonymous
-log10 PCADD
0
2
4
6
0
2
4
6
count
1000
100
10
1

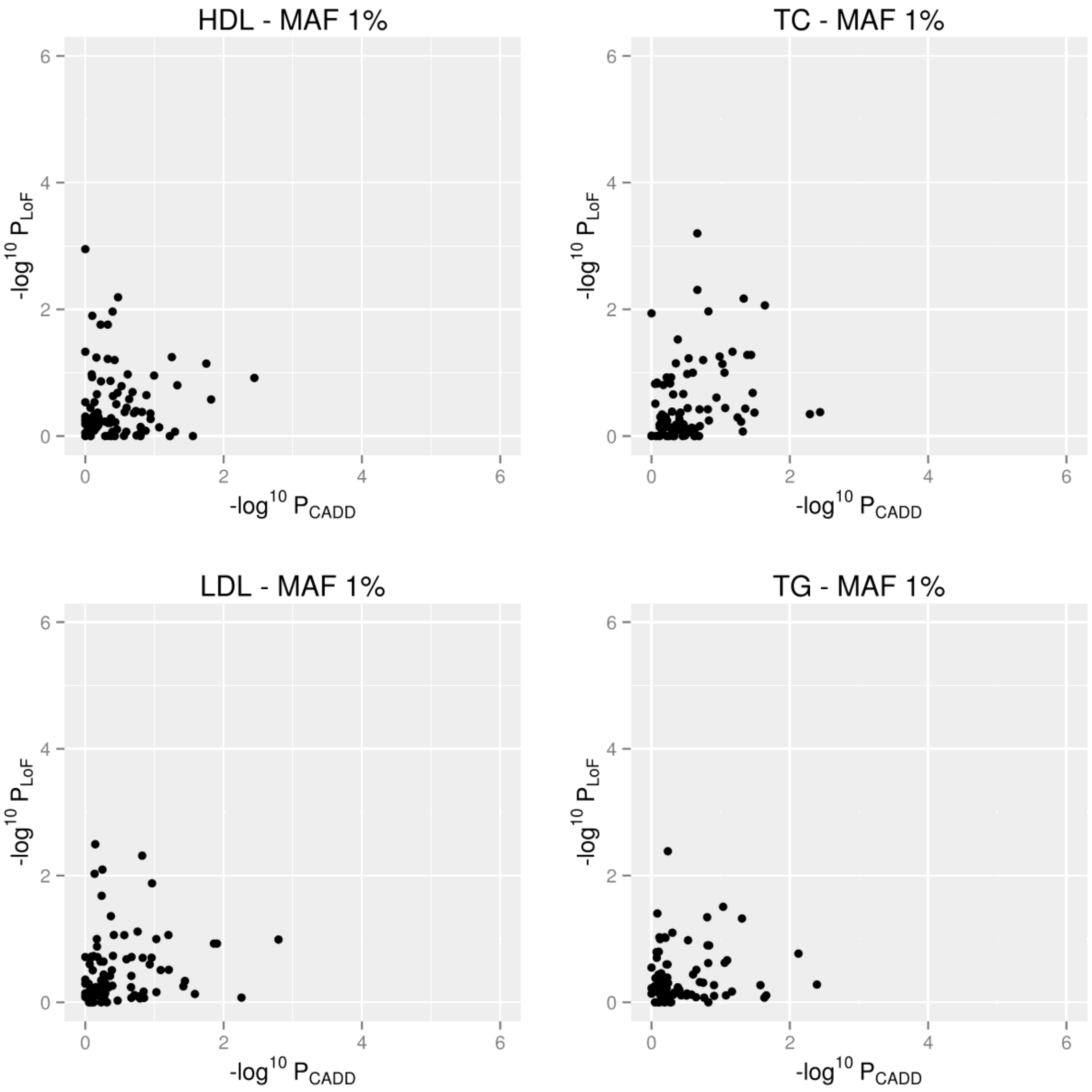
S7 Figure: Gene-based low frequency variant analyses across the genome using SKAT-O for 7 cardiovascular traits (compared with loss-of-function filtering)



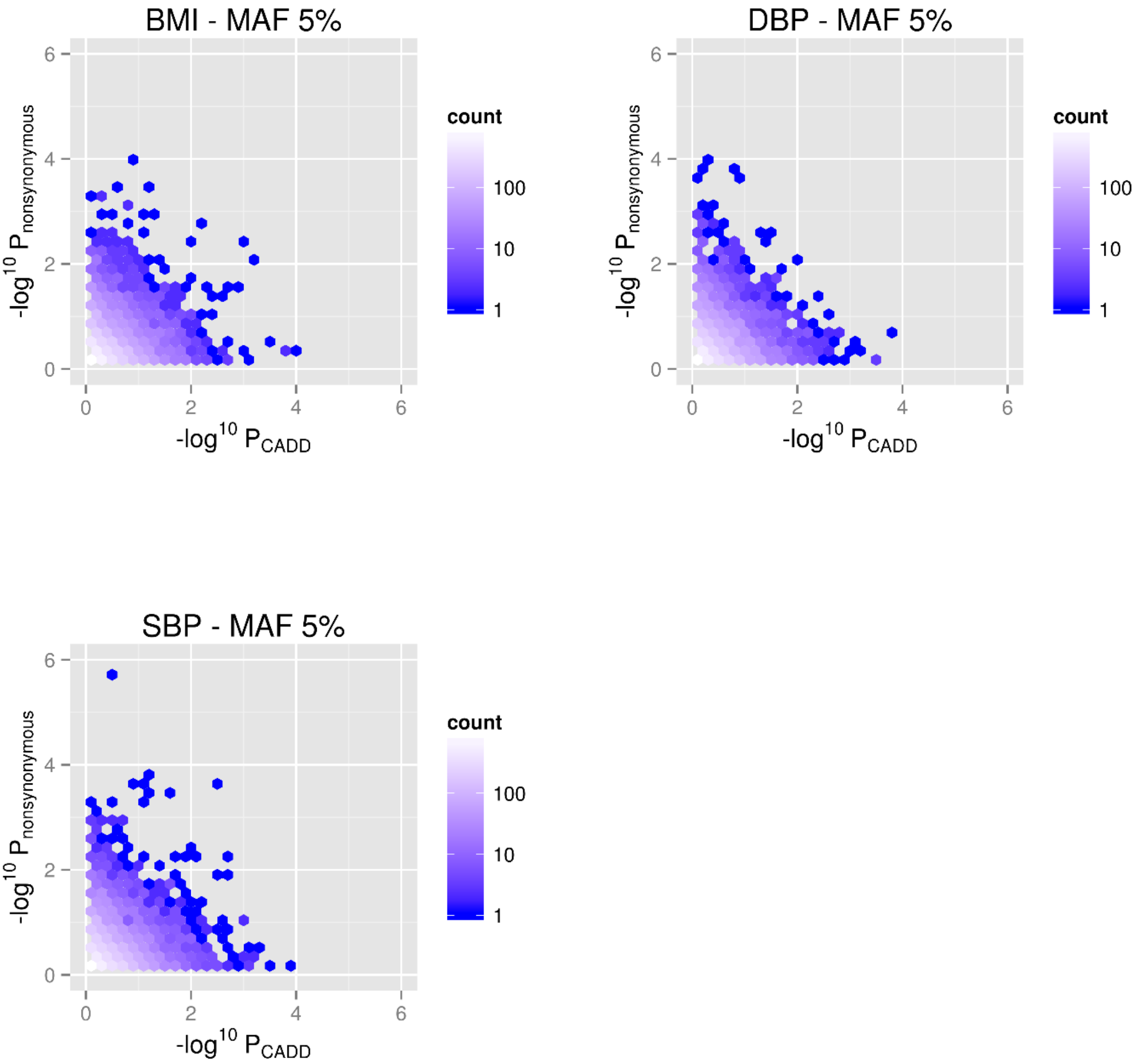

HDL - MAF 5%
TC - MAF 5%
LDL - MAF 5%
TG - MAF 5%
$-\log^{10} P_{LoF}$
$-\log^{10} P_{CADD}$
0
2
4
6

S8 Figure: Gene-based rare variant analyses across the genome using SKAT-O for 7 cardiovascular traits (compared with loss-of-function filtering)




HDL - MAF 1%
TC - MAF 1%
LDL - MAF 1%
TG - MAF 1%
$-\log^{10} P_{LoF}$
$-\log^{10} P_{CADD}$
0
2
4
6

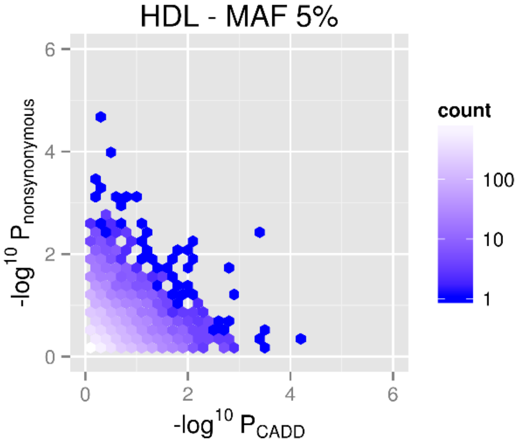
S9 Figure: Gene-based low frequency variant analyses across the genome using MiST for 7 cardiovascular traits (compared with nonsynonymous filtering)

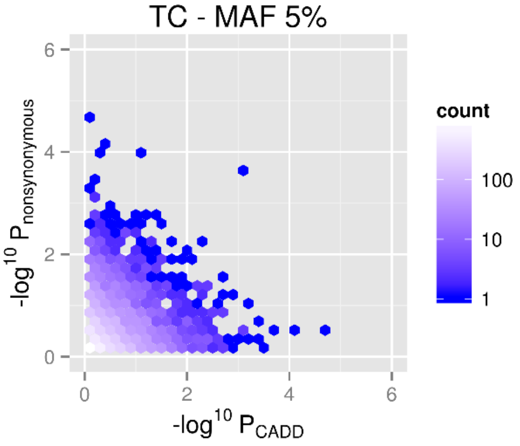


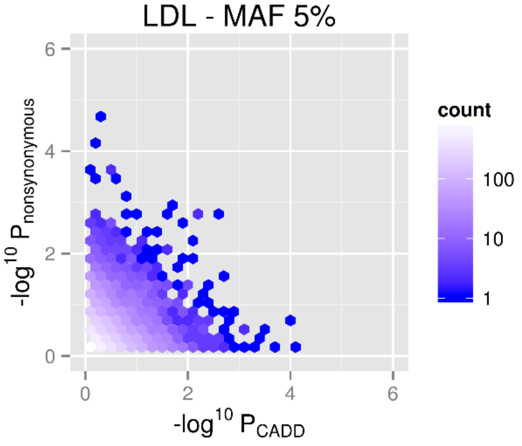
BMI - MAF 5%

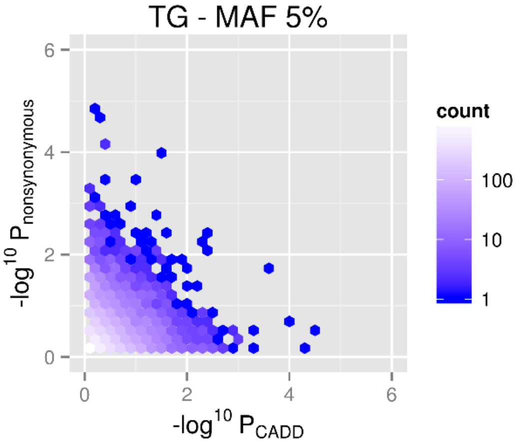
DBP - MAF 5%

SBP - MAF 5%

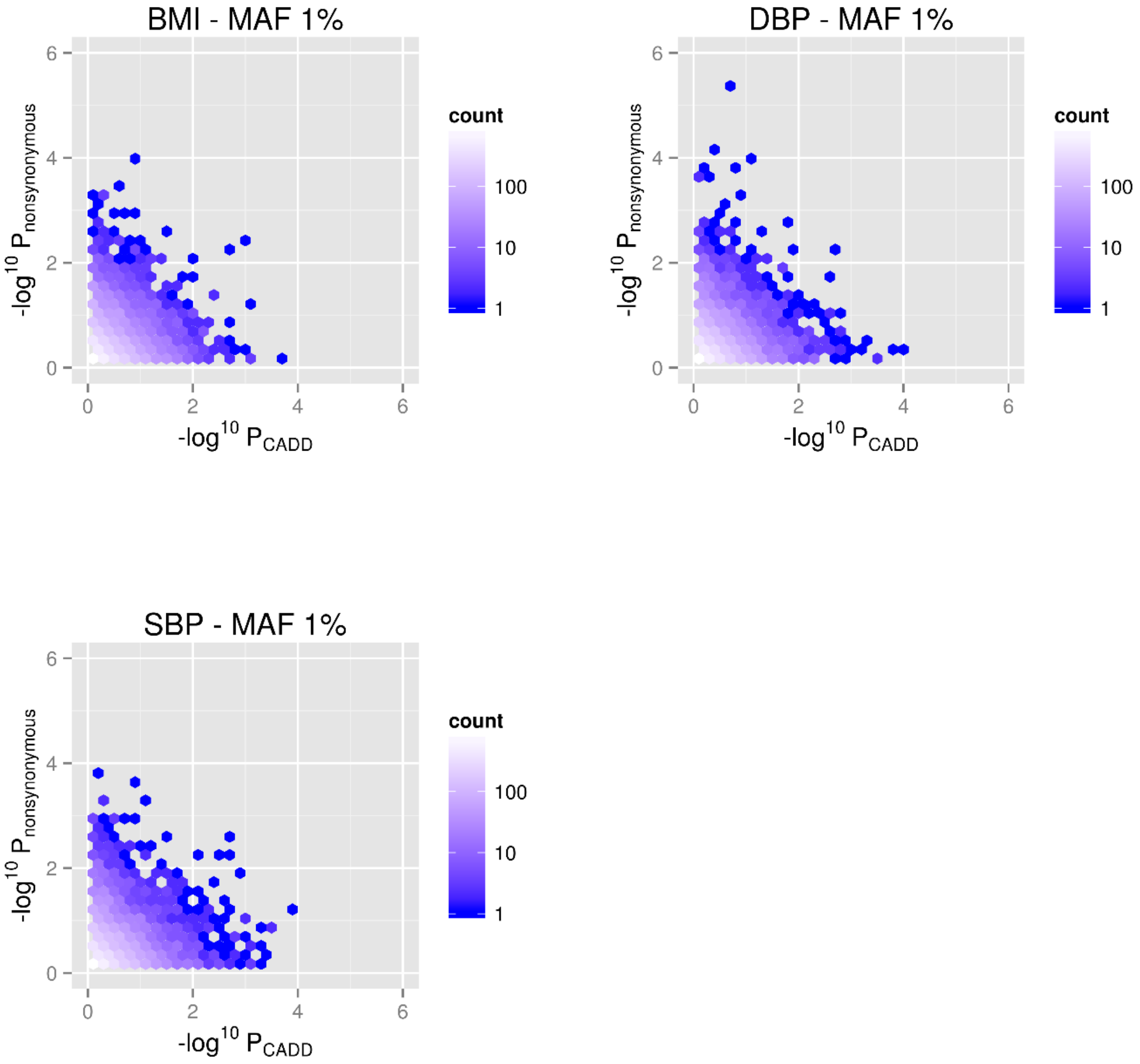

HDL - MAF 5%
-log10 P nonsynonymous
-log10 P CADD
0
2
4
6
count
100
10
1

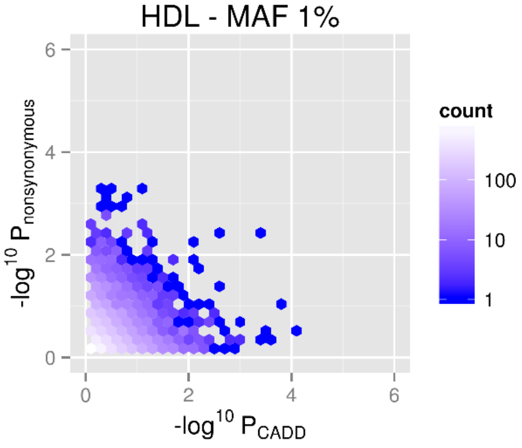

TC - MAF 5%
-log10 P nonsynonymous
-log10 P CADD
0
2
4
6
count
100
10
1

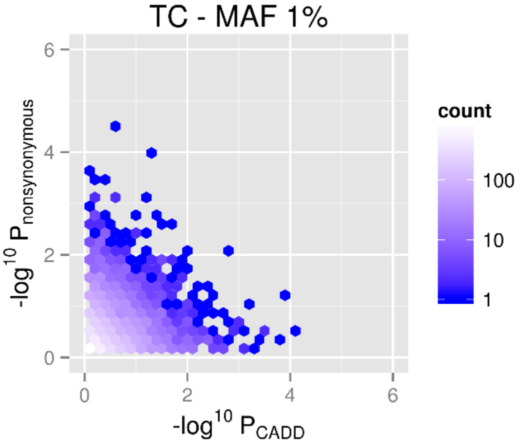

LDL - MAF 5%
-log10 P nonsynonymous
-log10 P CADD
0
2
4
6
count
100
10
1

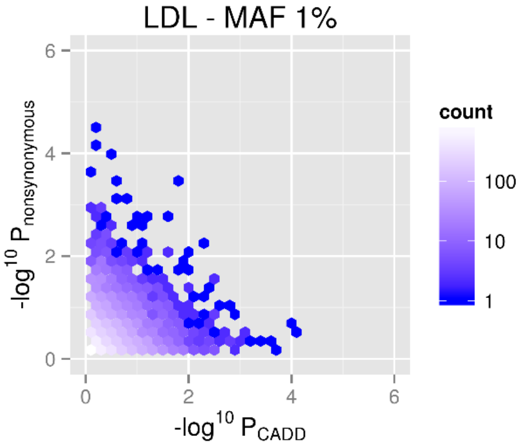

TG - MAF 5%
-log10 P nonsynonymous
-log10 P CADD
0
2
4
6
count
100
10
1

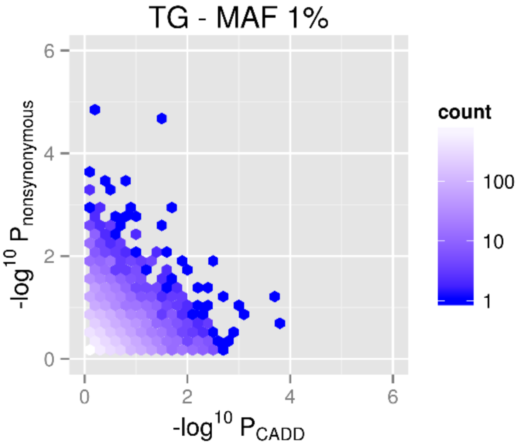
S10 Figure: Gene-based rare variant analyses across the genome using MiST for 7 cardiovascular traits (compared with nonsynonymous filtering)



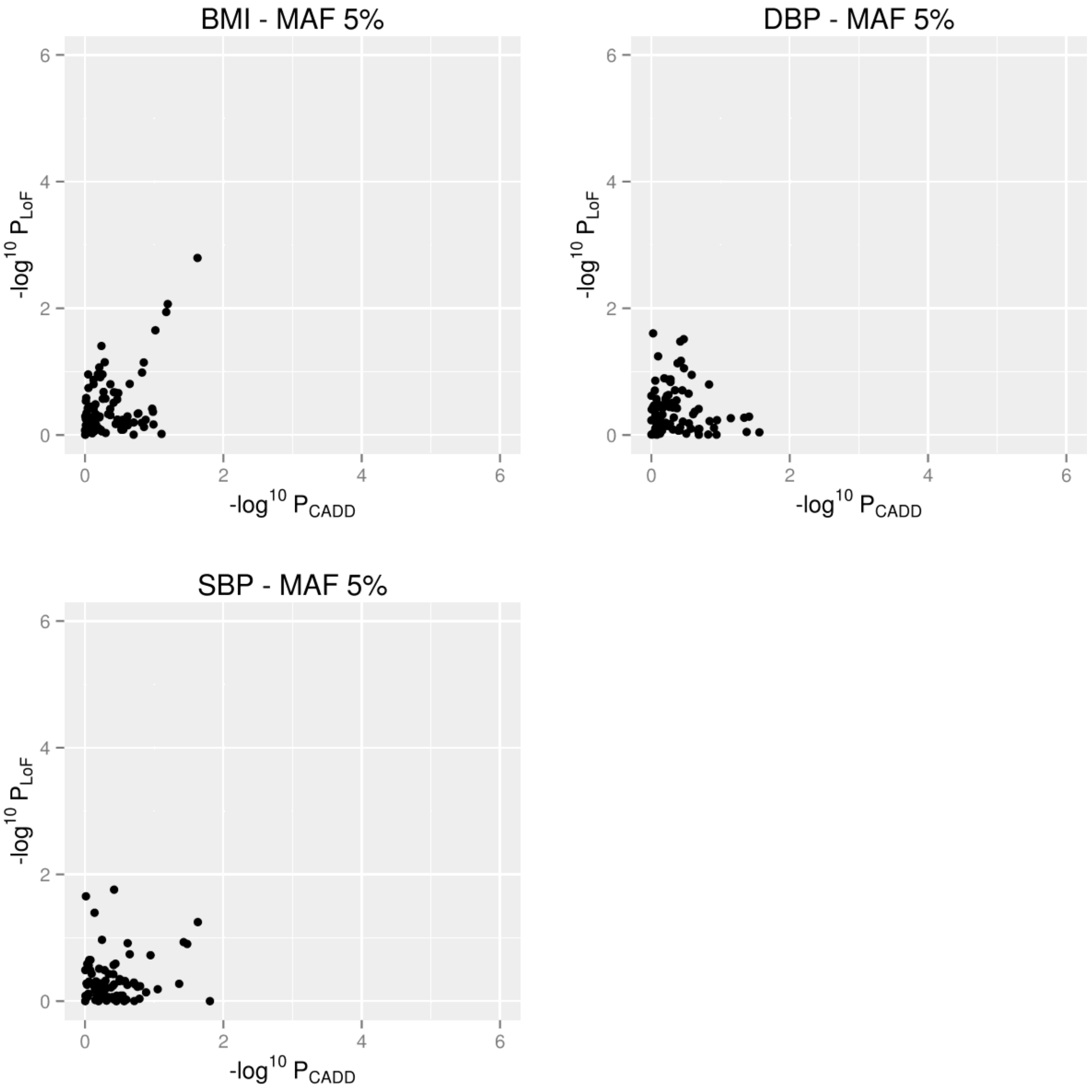

HDL - MAF 1%
-log10 P nonsynonymous
-log10 P CADD
0
2
4
6
count
100
10
1

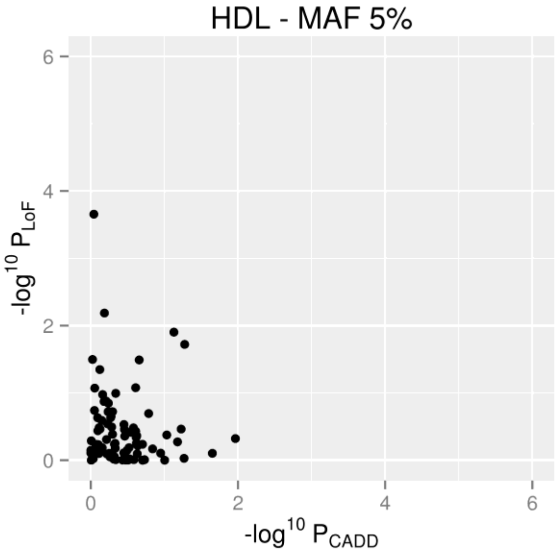

TC - MAF 1%
-log10 P nonsynonymous
-log10 P CADD
0
2
4
6
count
100
10
1

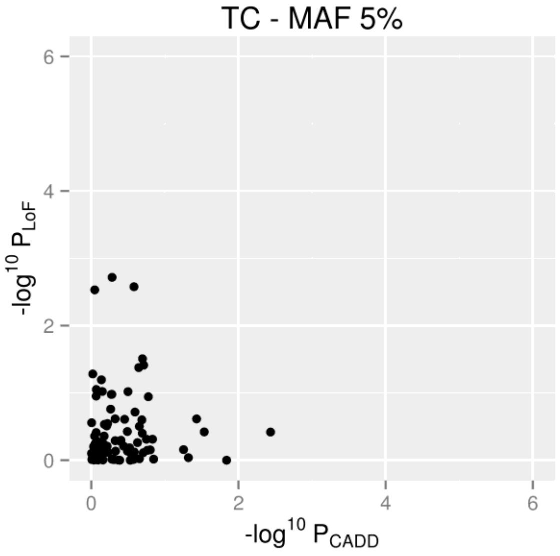

LDL - MAF 1%
-log10 P nonsynonymous
-log10 P CADD
0
2
4
6
count
100
10
1

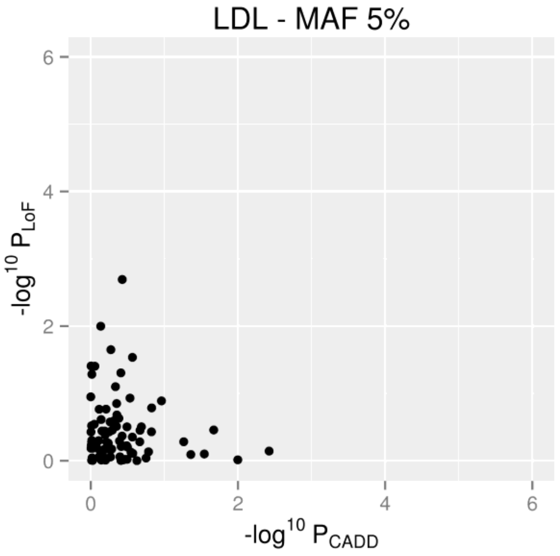

TG - MAF 1%
-log10 P nonsynonymous
-log10 P CADD
0
2
4
6
count
100
10
1

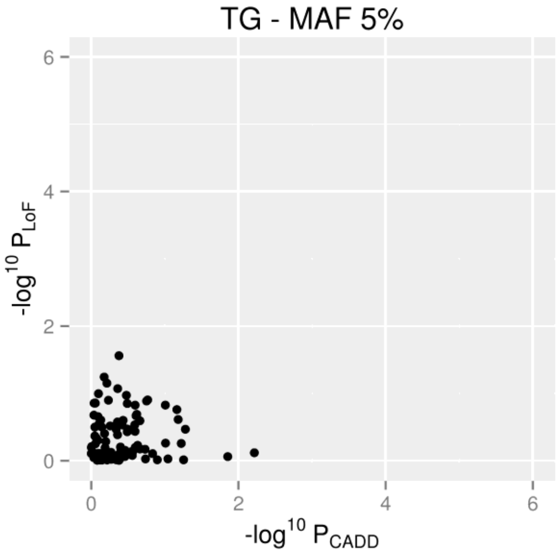
S11 Figure: Gene-based low frequency variant analyses across the genome using MiST for 7 cardiovascular traits (compared with loss-of-function filtering)



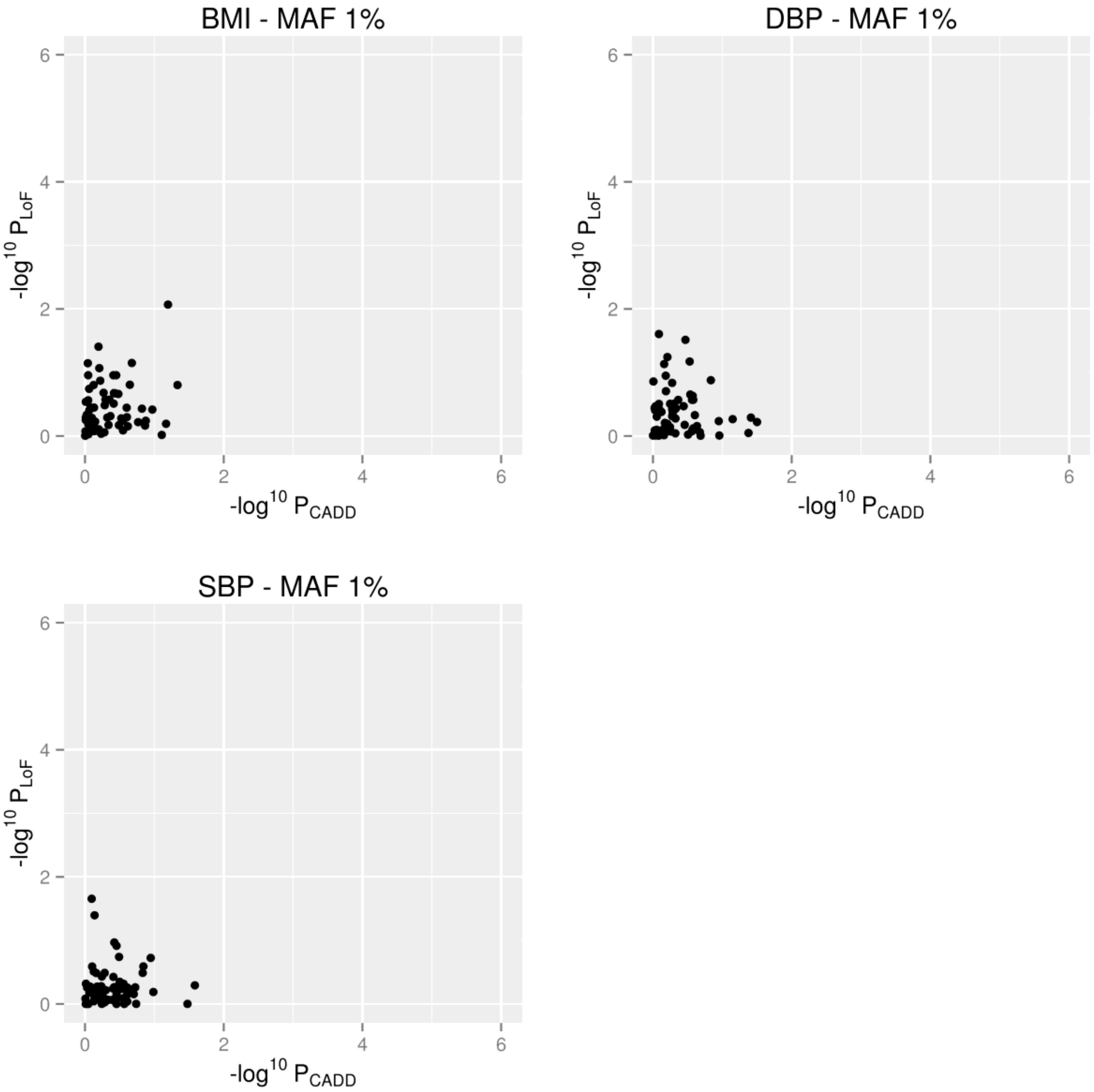

HDL - MAF 5%

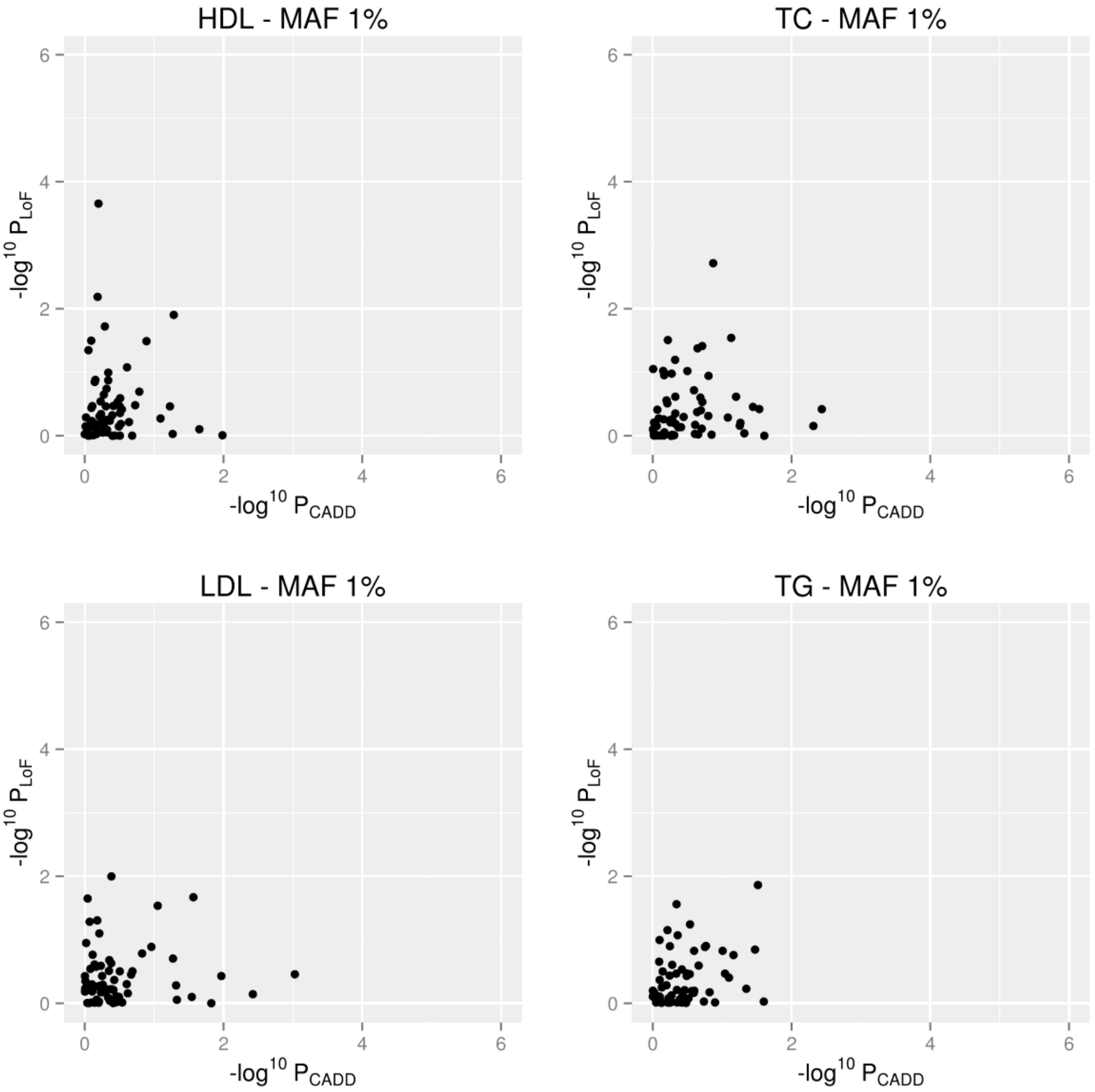

TC - MAF 5%


LDL - MAF 5%


TG - MAF 5%

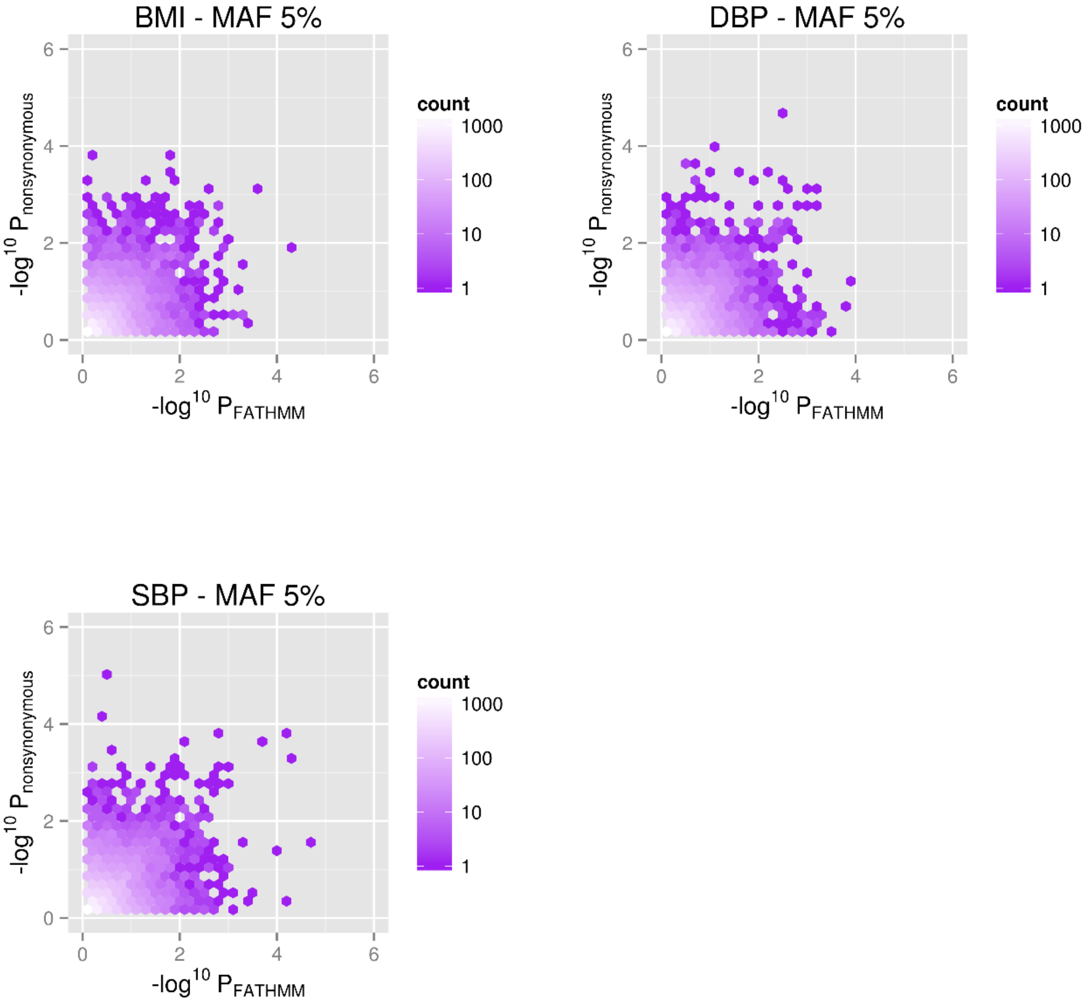
S12 Figure: Gene-based rare variant analyses across the genome using MiST for 7 cardiovascular traits (compared with loss-of-function filtering)

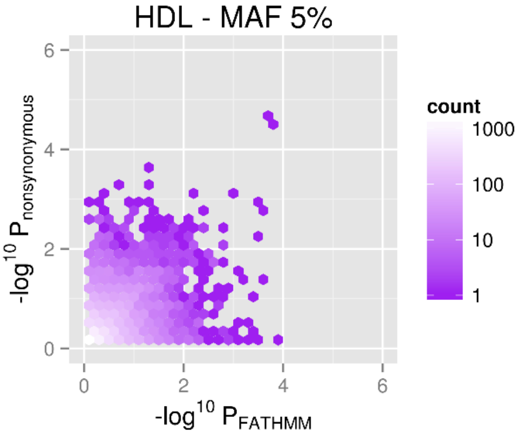


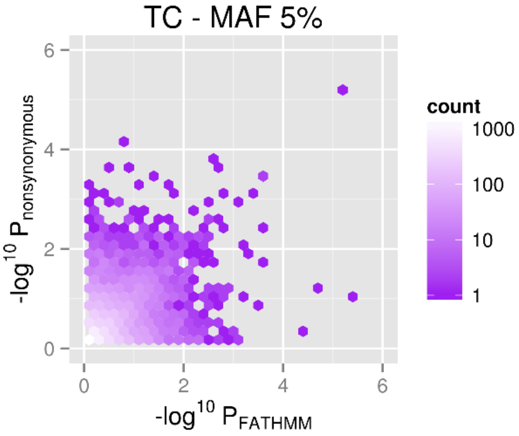

HDL - MAF 1%
TC - MAF 1%
LDL - MAF 1%
TG - MAF 1%
$-\log^{10} P_{LoF}$
$-\log^{10} P_{CADD}$
0
2
4
6

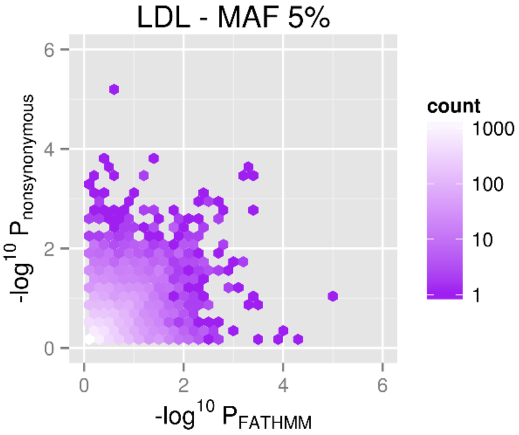
FATHMM-MKL tests

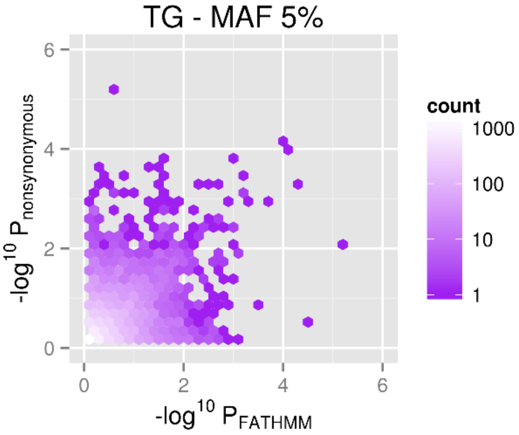
S13 Figure: Gene-based low frequency variant analyses across the genome using SKAT-O for 7 cardiovascular traits (compared with nonsynonymous filtering)



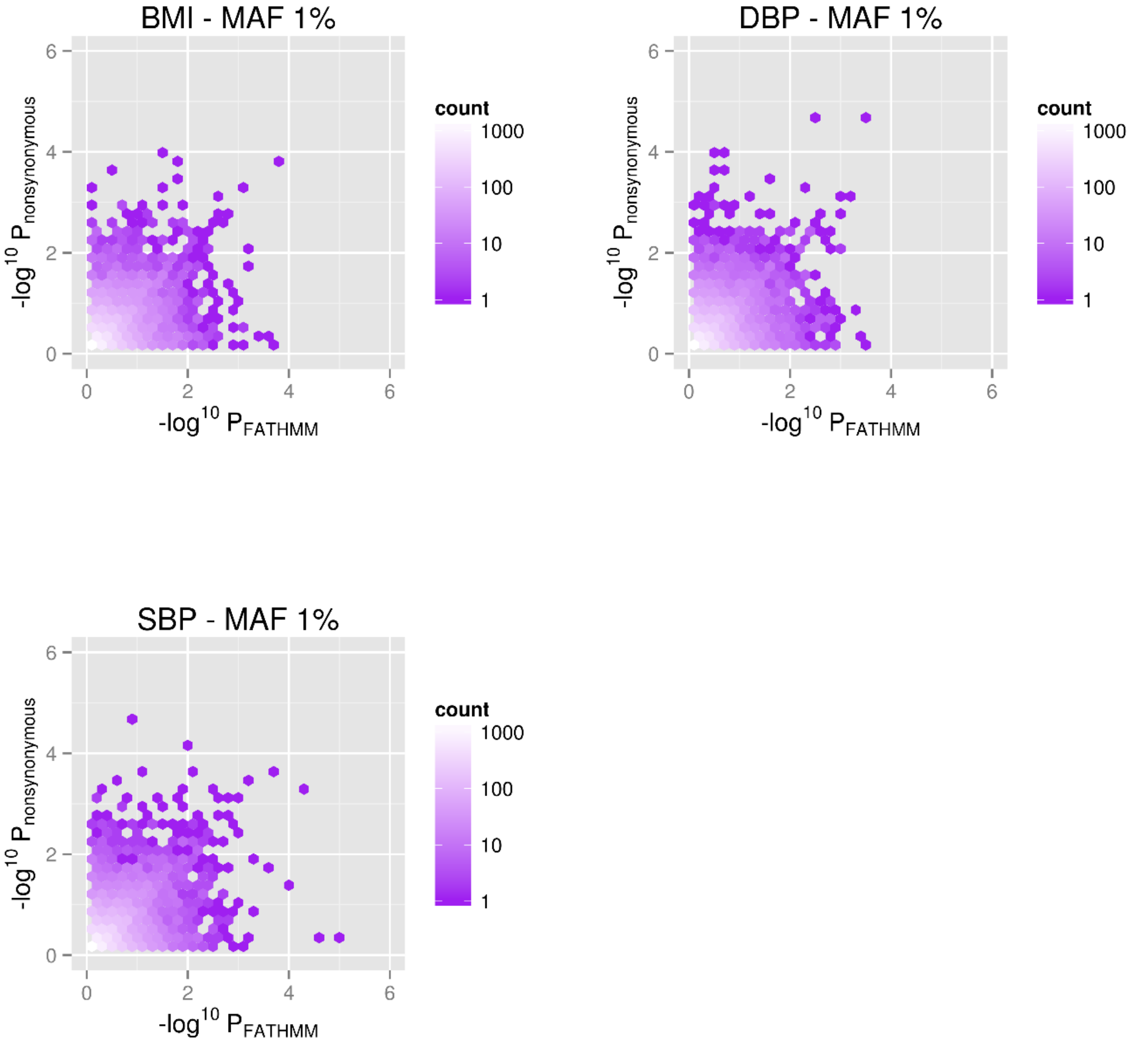

HDL - MAF 5%
count
1000
100
10
1
0
2
4
6
0
2
4
6
$-\log^{10} P_{\mathrm{nonsynonymous}}$
$-\log^{10} P_{\mathrm{FATHMM}}$

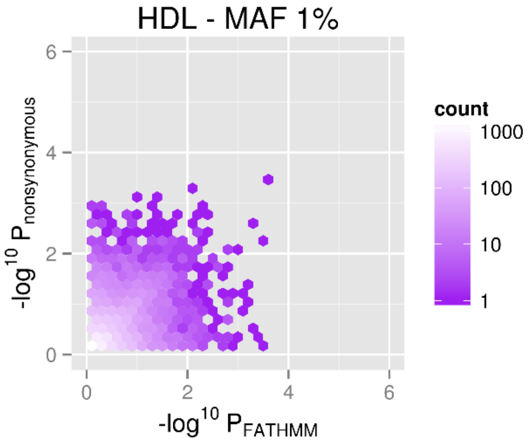

TC - MAF 5%
count
1000
100
10
1
0
2
4
6
0
2
4
6
$-\log^{10} P_{\mathrm{nonsynonymous}}$
$-\log^{10} P_{\mathrm{FATHMM}}$

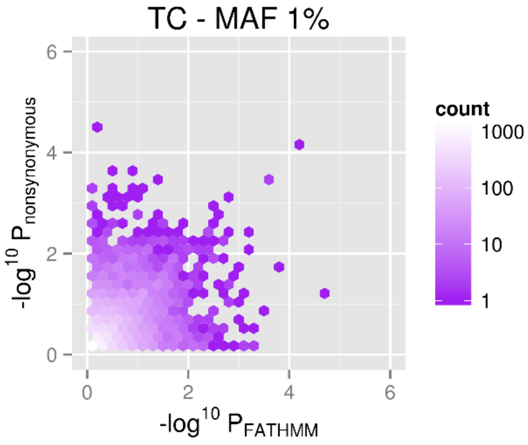

LDL - MAF 5%
count
1000
100
10
1
0
2
4
6
0
2
4
6
$-\log^{10} P_{\mathrm{nonsynonymous}}$
$-\log^{10} P_{\mathrm{FATHMM}}$

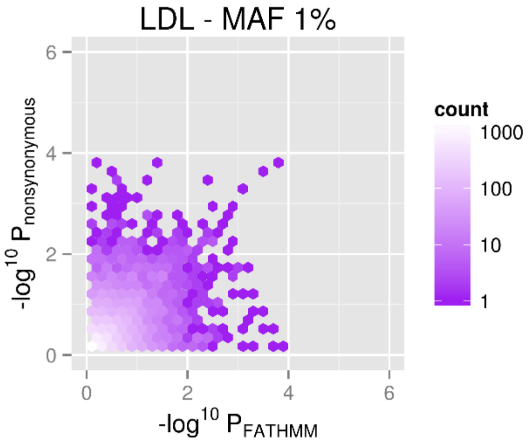

TG - MAF 5%
count
1000
100
10
1
0
2
4
6
0
2
4
6
$-\log^{10} P_{\mathrm{nonsynonymous}}$
$-\log^{10} P_{\mathrm{FATHMM}}$

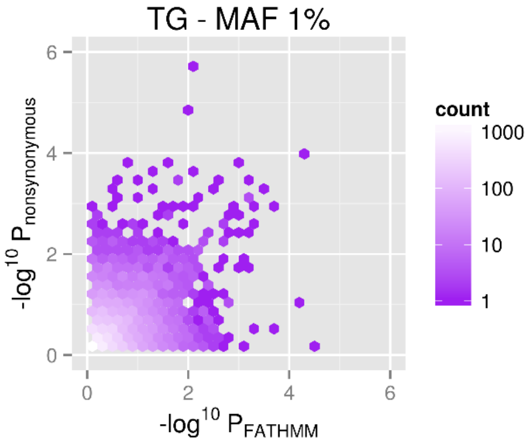
S14 Figure: Gene-based rare variant analyses across the genome using SKAT-O for 7 cardiovascular traits (compared with nonsynonymous filtering)



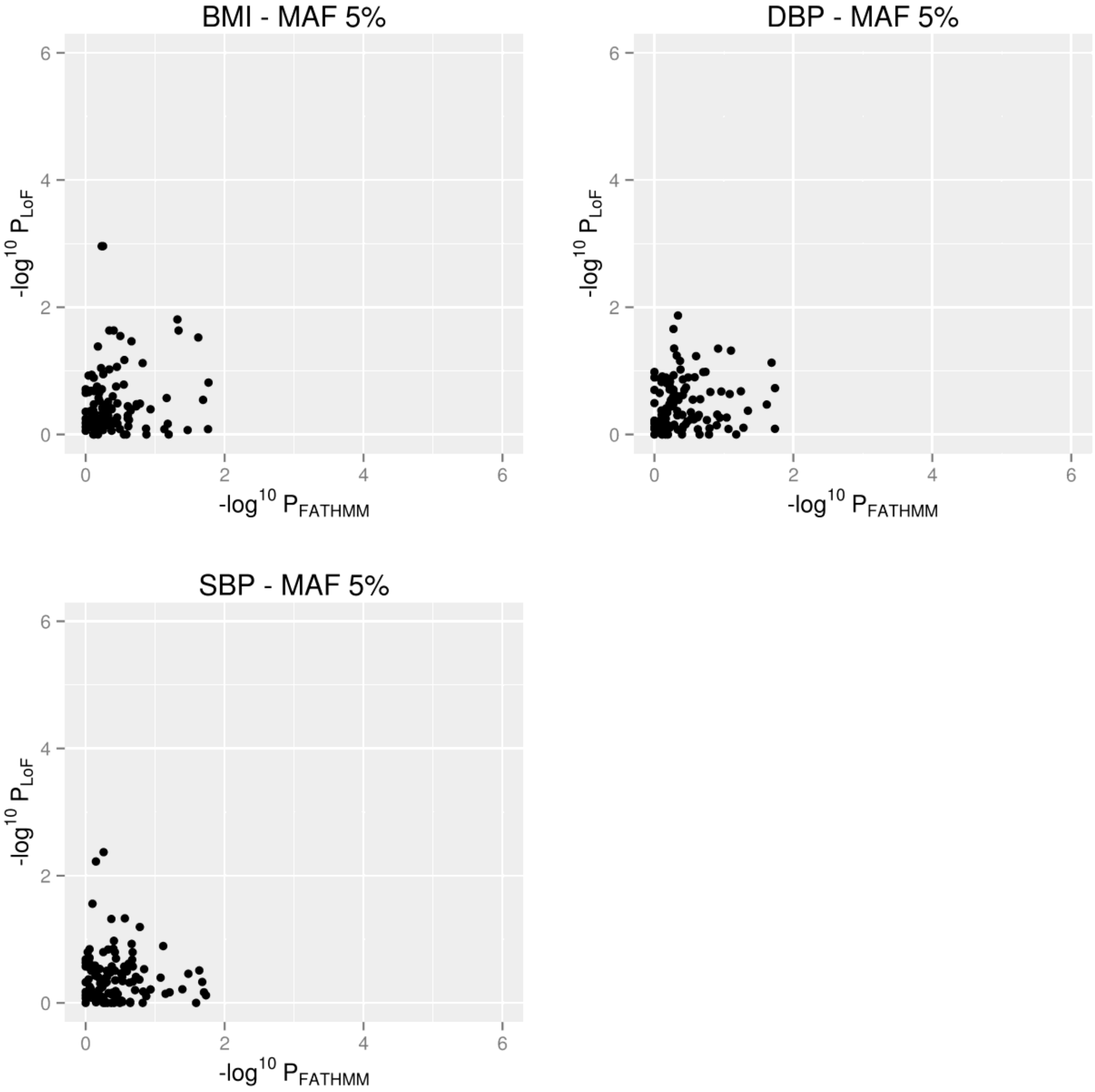

HDL - MAF 1%
$-\log^{10} P_{\mathrm{nonsynonymous}}$
$-\log^{10} P_{\mathrm{FATHMM}}$
0
2
4
6
count
1000
100
10
1

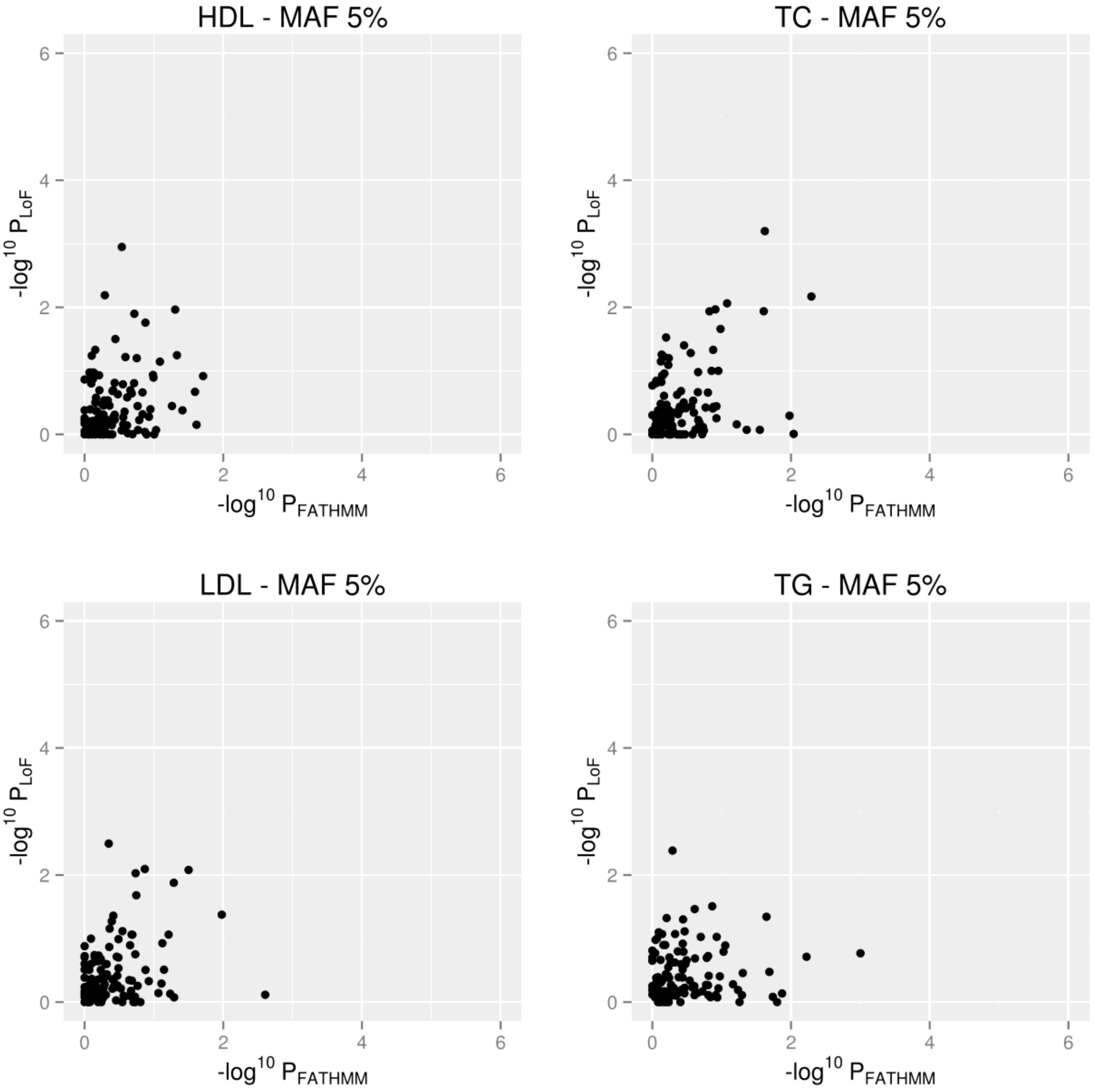

TC - MAF 1%
$-\log^{10} P_{\mathrm{nonsynonymous}}$
$-\log^{10} P_{\mathrm{FATHMM}}$
0
2
4
6
count
1000
100
10
1


LDL - MAF 1%
$-\log^{10} P_{\mathrm{nonsynonymous}}$
$-\log^{10} P_{\mathrm{FATHMM}}$
0
2
4
6
count
1000
100
10
1

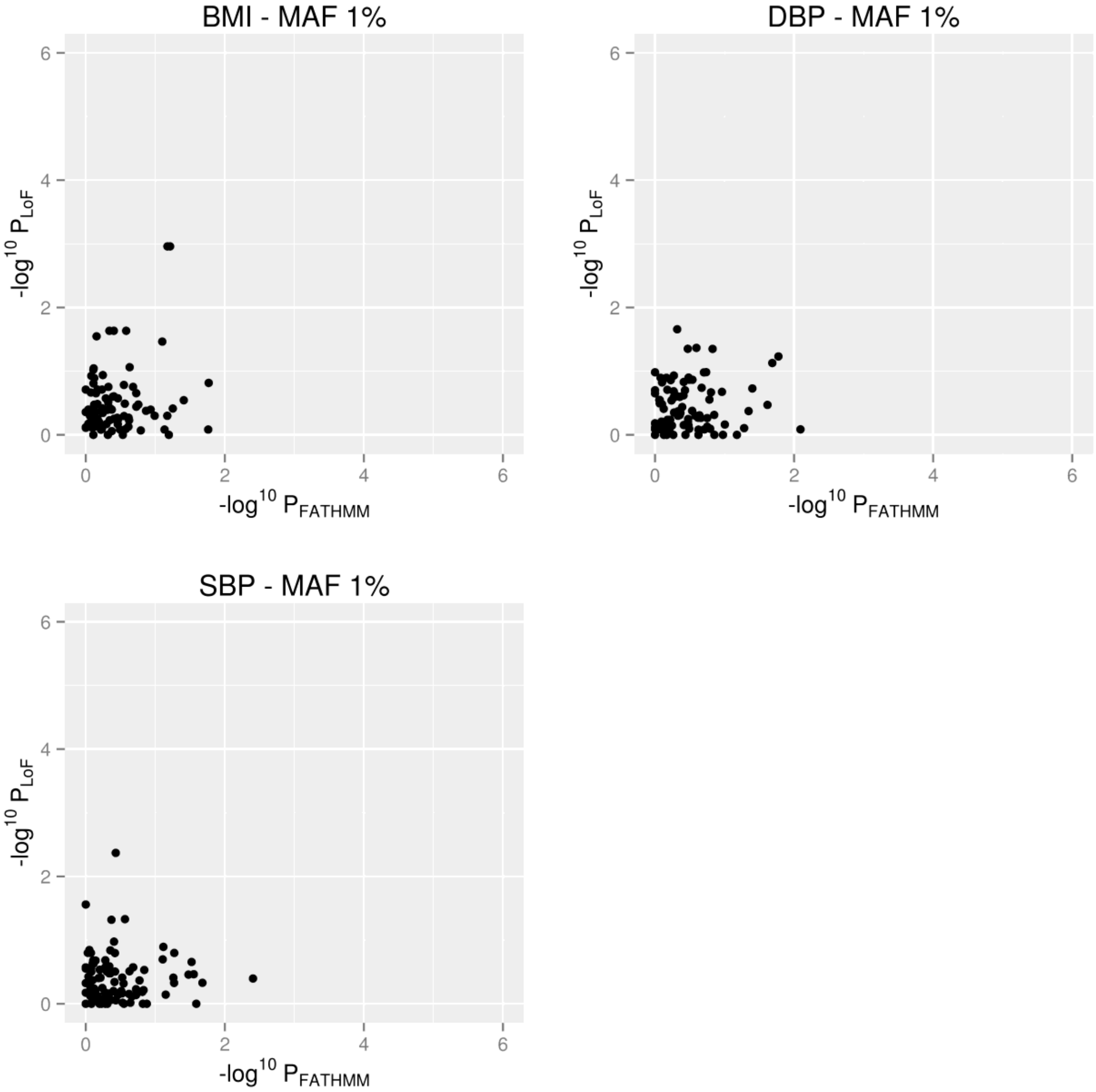

TG - MAF 1%
$-\log^{10} P_{\mathrm{nonsynonymous}}$
$-\log^{10} P_{\mathrm{FATHMM}}$
0
2
4
6
count
1000
100
10
1

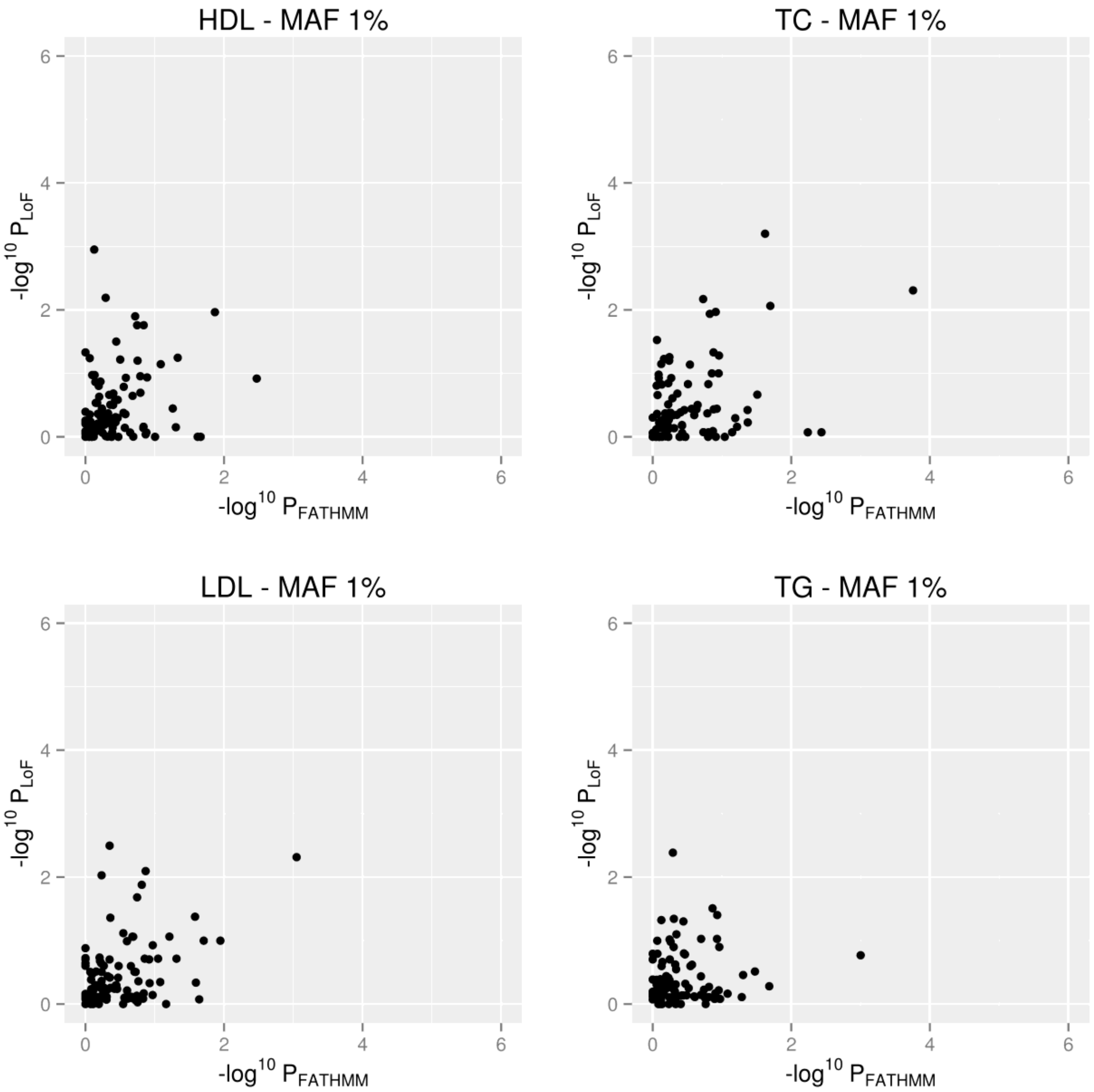
S15 Figure: Gene-based low frequency variant analyses across the genome using SKAT-O for 7 cardiovascular traits (compared with loss-of-function filtering)



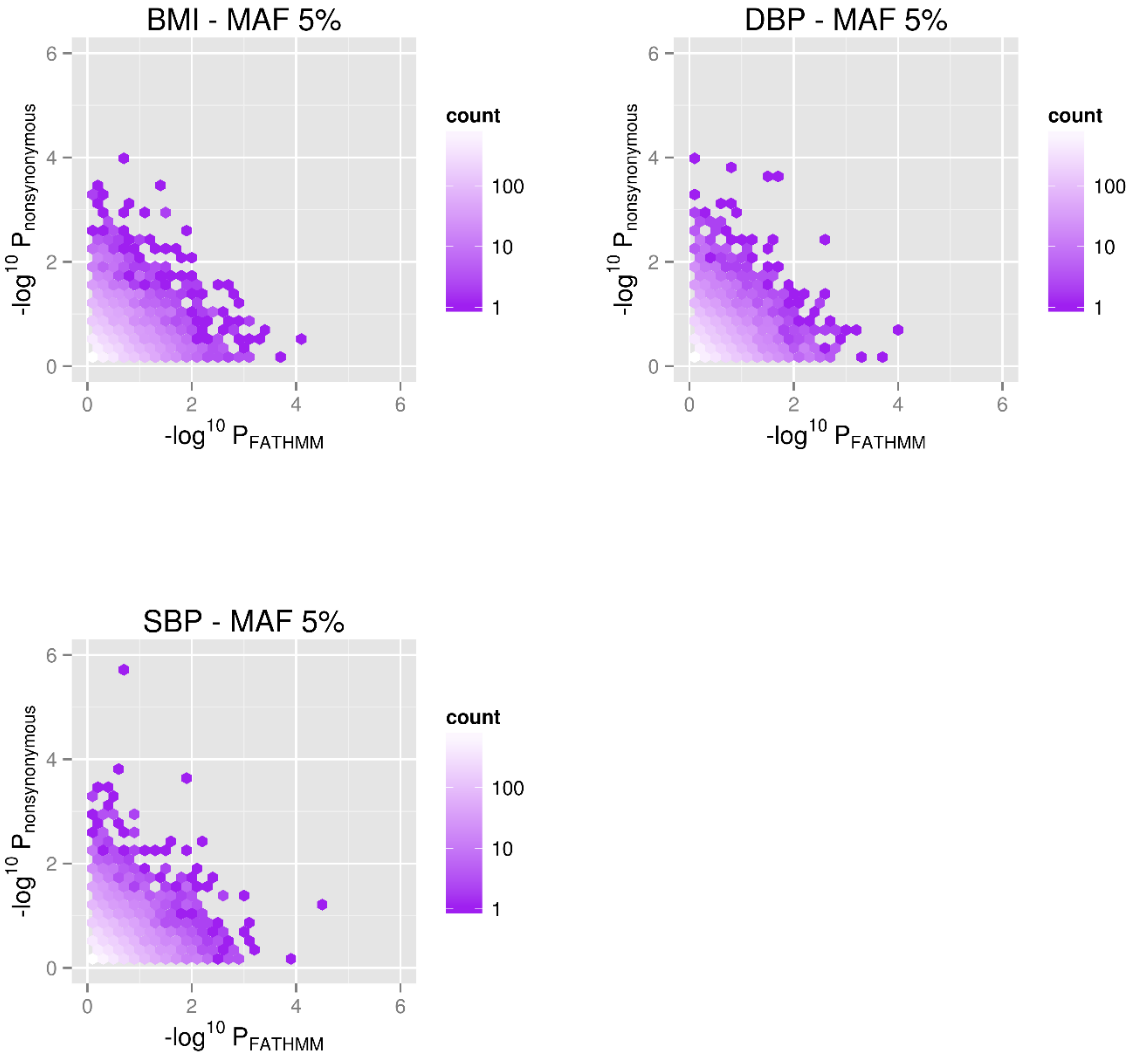

HDL - MAF 5%
TC - MAF 5%
LDL - MAF 5%
TG - MAF 5%
$-\log^{10} P_{LoF}$
$-\log^{10} P_{FATHMM}$
0
2
4
6

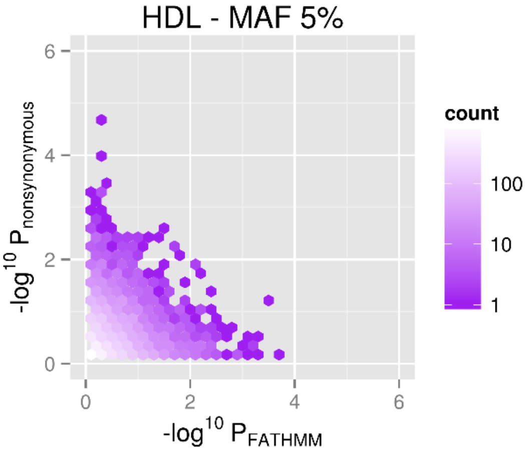
S16 Figure: Gene-based rare variant analyses across the genome using SKAT-O for 7 cardiovascular traits (compared with loss-of-function filtering)

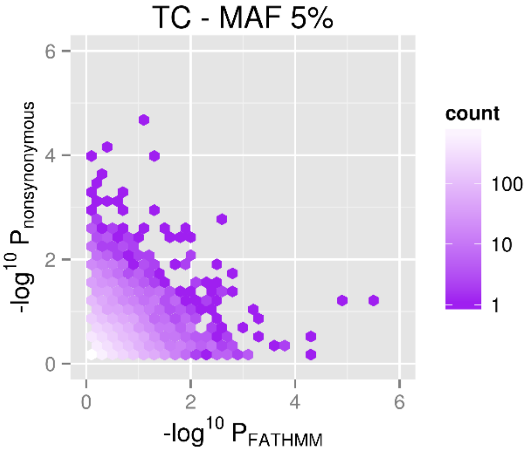


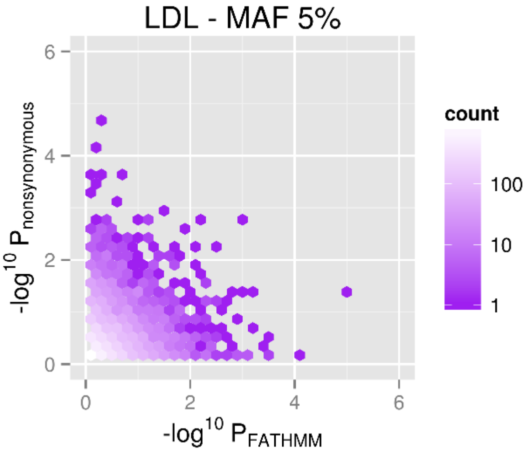

HDL - MAF 1%
TC - MAF 1%
LDL - MAF 1%
TG - MAF 1%
$-\log^{10} P_{LoF}$
$-\log^{10} P_{FATHMM}$
0
2
4
6

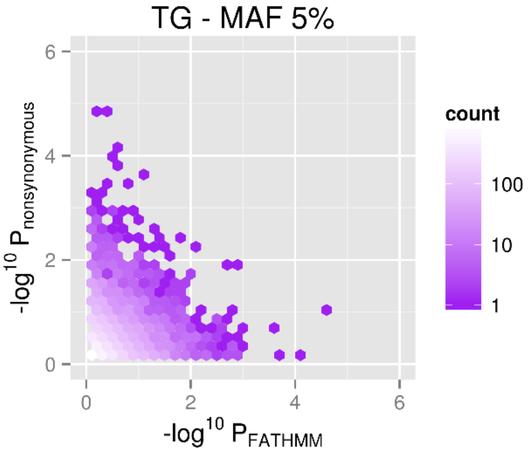
S17 Figure: Gene-based low frequency variant analyses across the genome using MiST for 7 cardiovascular traits (compared with nonsynonymous filtering)



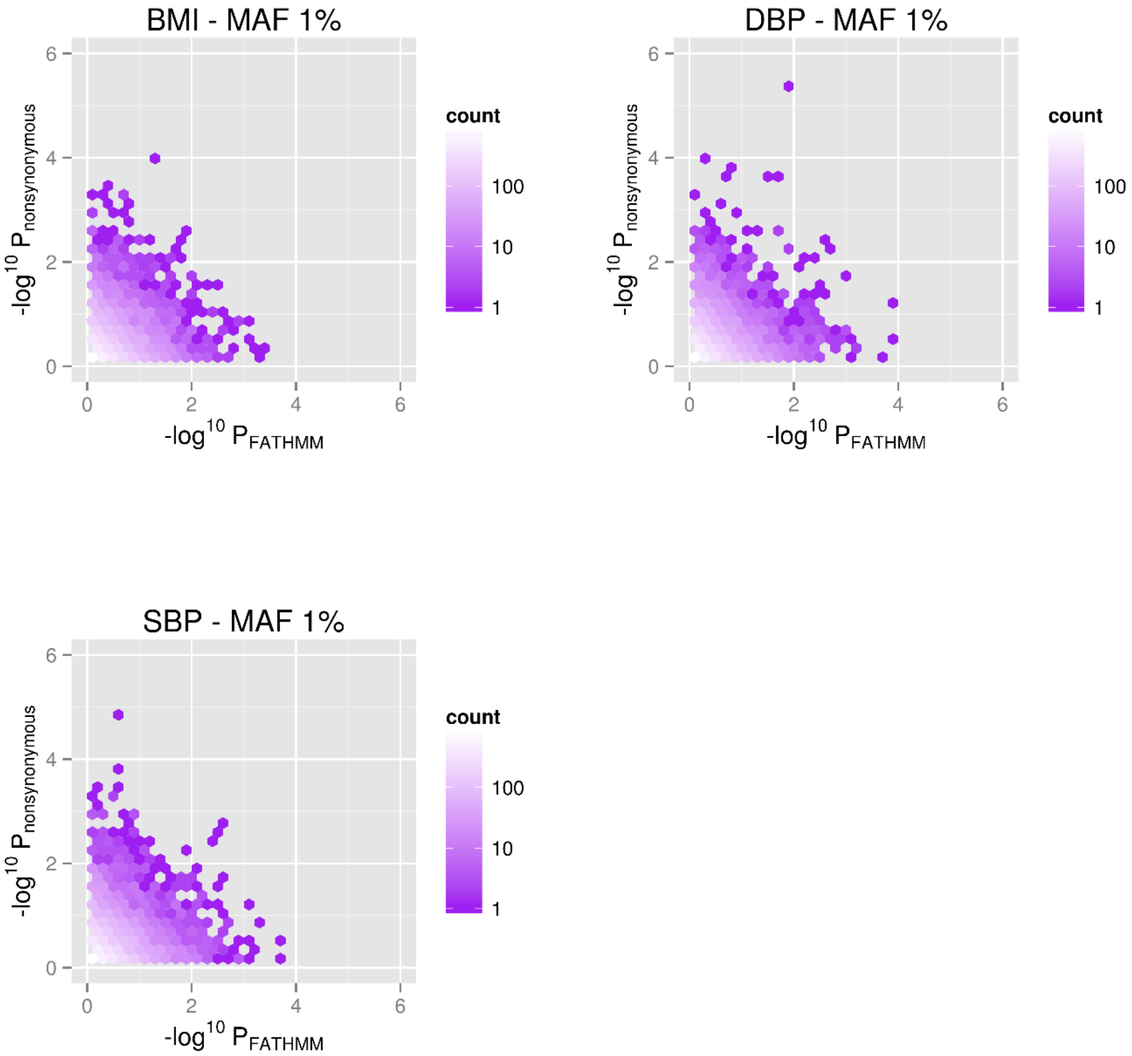

HDL - MAF 5%
-log10 P nonsynonymous
-log10 P FATHMM
0
2
4
6
count
100
10
1

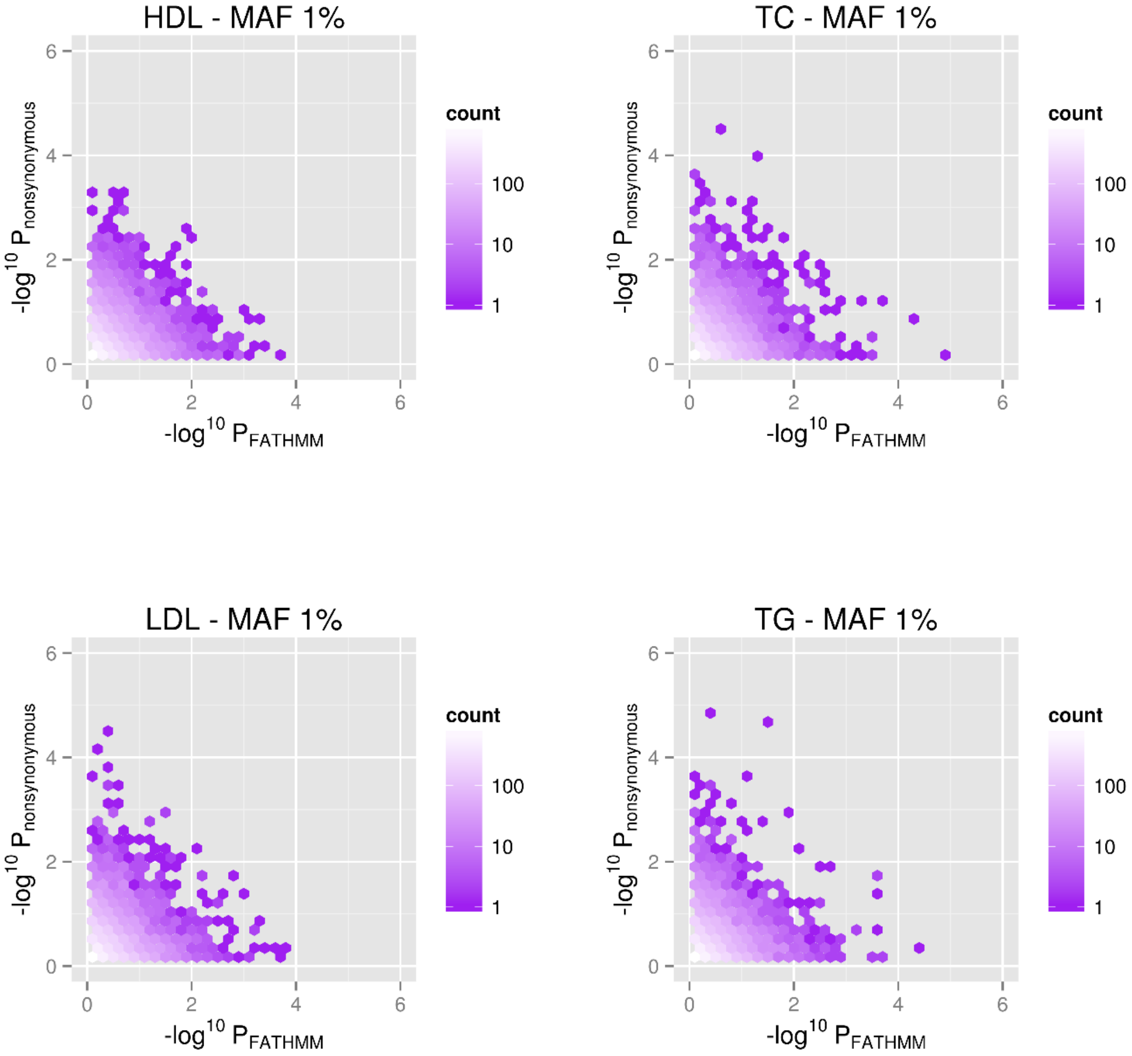

TC - MAF 5%
-log10 P nonsynonymous
-log10 P FATHMM
0
2
4
6
count
100
10
1


LDL - MAF 5%
-log10 P nonsynonymous
-log10 P FATHMM
0
2
4
6
count
100
10
1

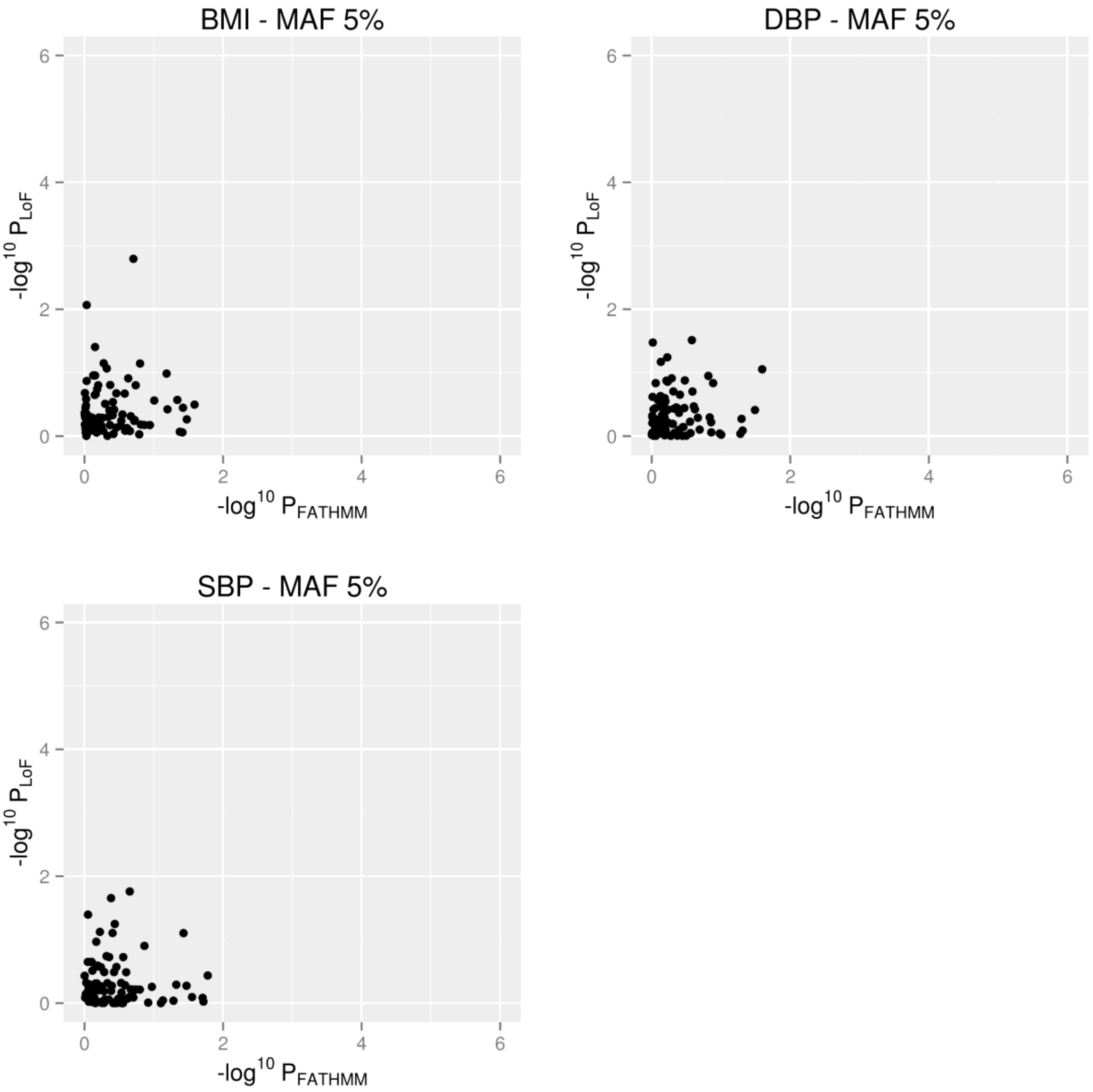

TG - MAF 5%
-log10 P nonsynonymous
-log10 P FATHMM
0
2
4
6
count
100
10
1

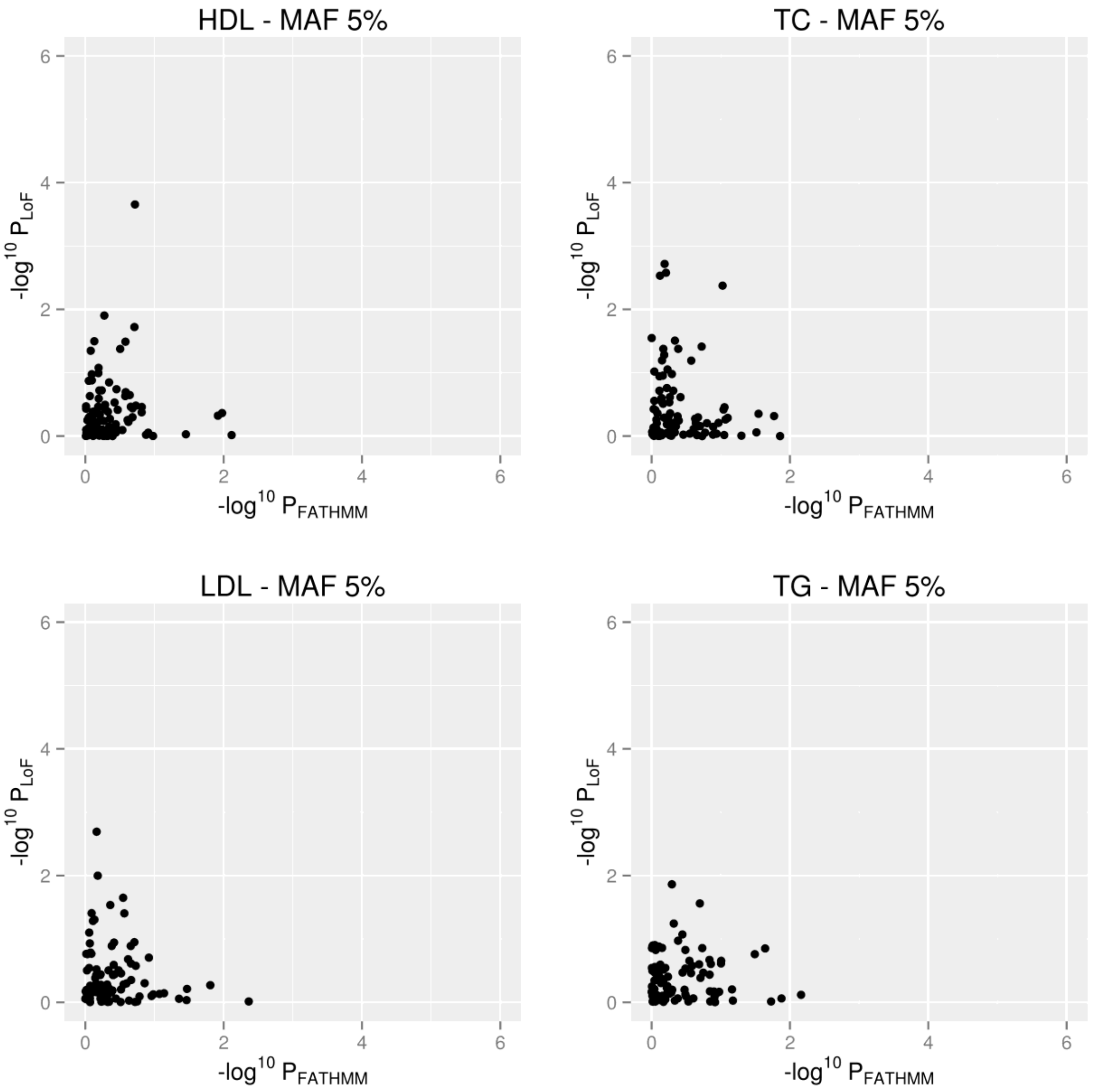
S18 Figure: Gene-based rare variant analyses across the genome using MiST for 7 cardiovascular traits (compared with nonsynonymous filtering)



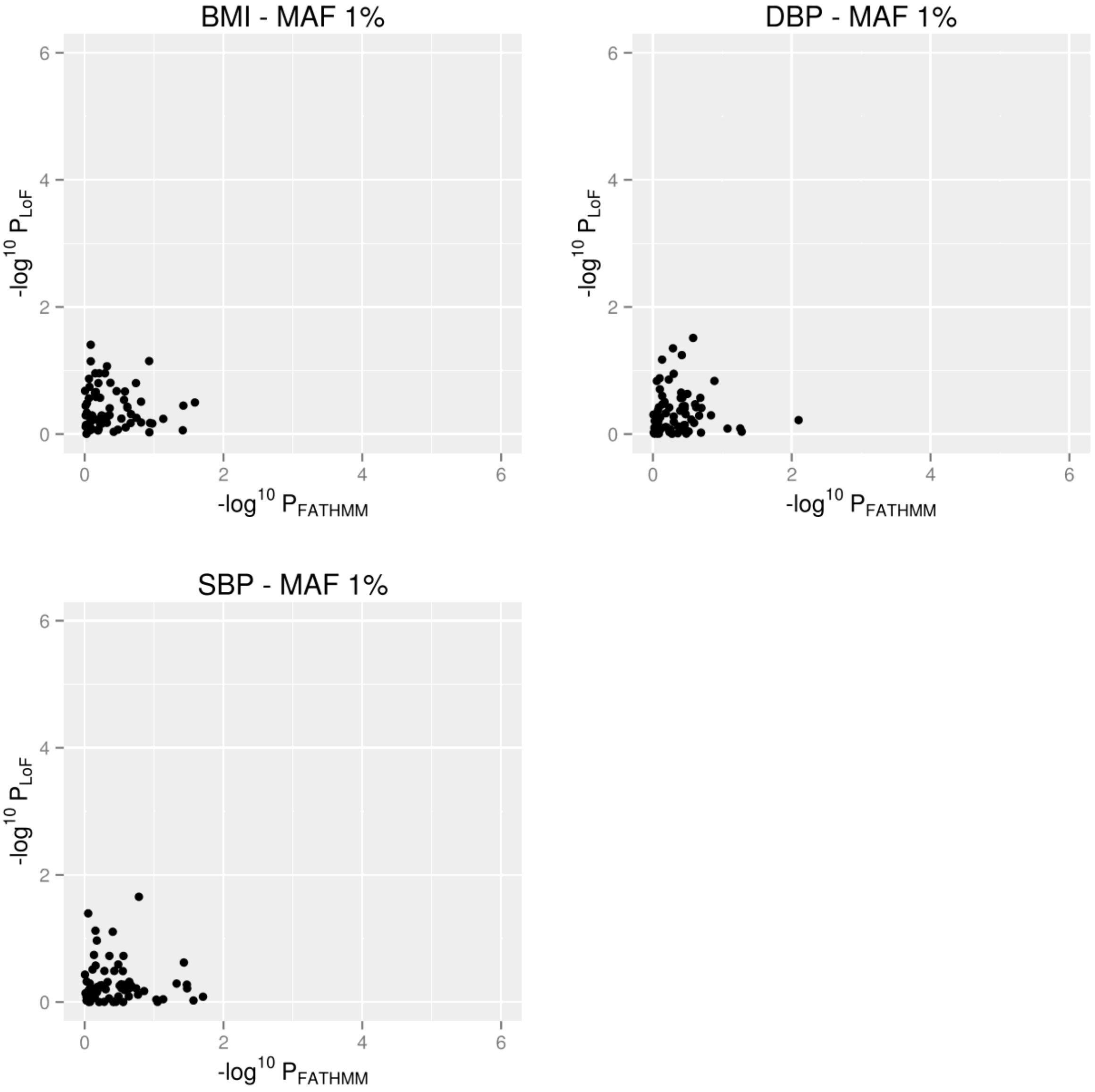

HDL - MAF 1%
TC - MAF 1%
LDL - MAF 1%
TG - MAF 1%
$-\log^{10} P_{nonsynonymous}$
$-\log^{10} P_{FATHMM}$
0
2
4
6
count
100
10
1

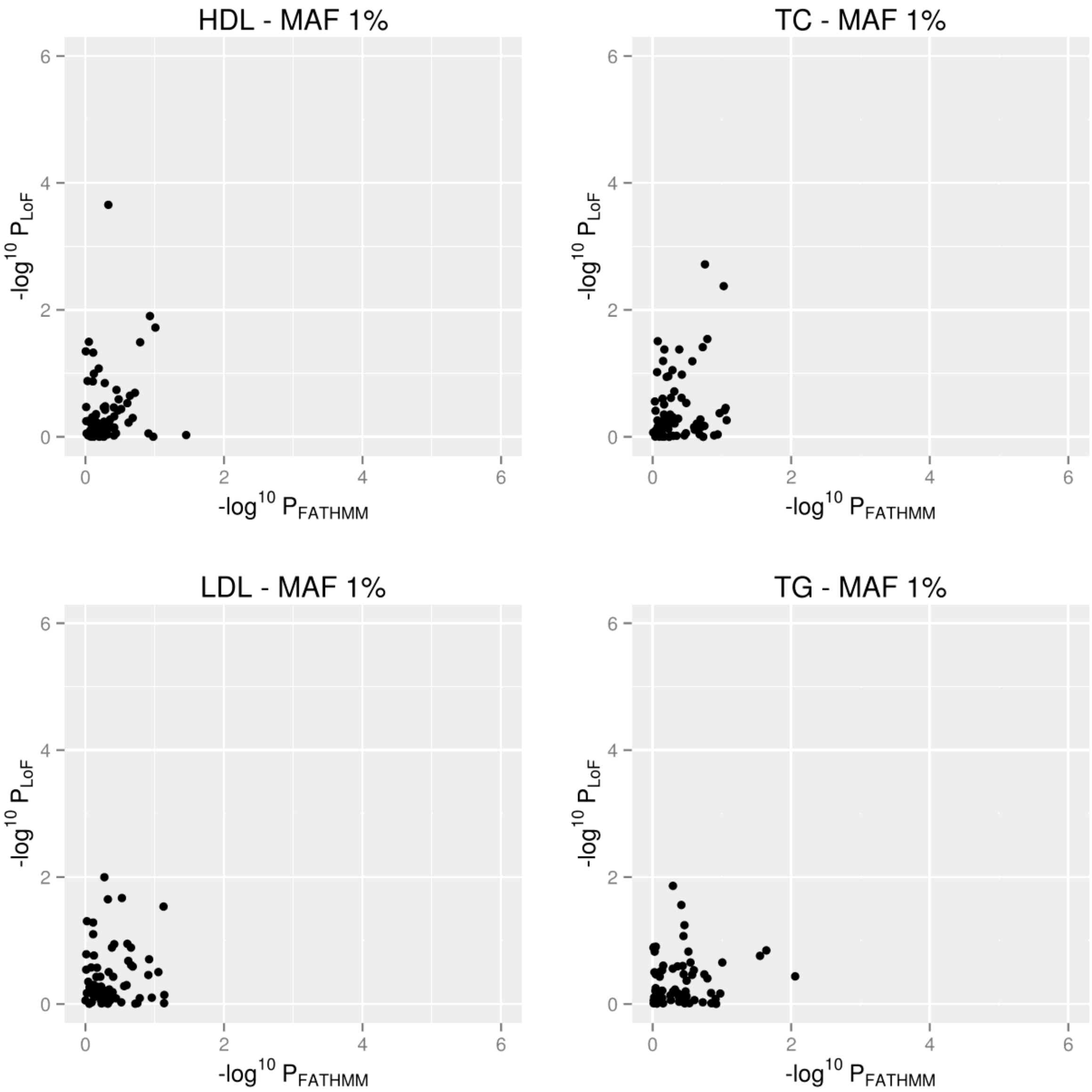
S19 Figure: Gene-based low frequency variant analyses across the genome using MiST for 7 cardiovascular traits (compared with loss-of-function filtering)




HDL - MAF 5%
TC - MAF 5%
LDL - MAF 5%
TG - MAF 5%
-log10 P_LoF
-log10 P_FATHMM
0
2
4
6

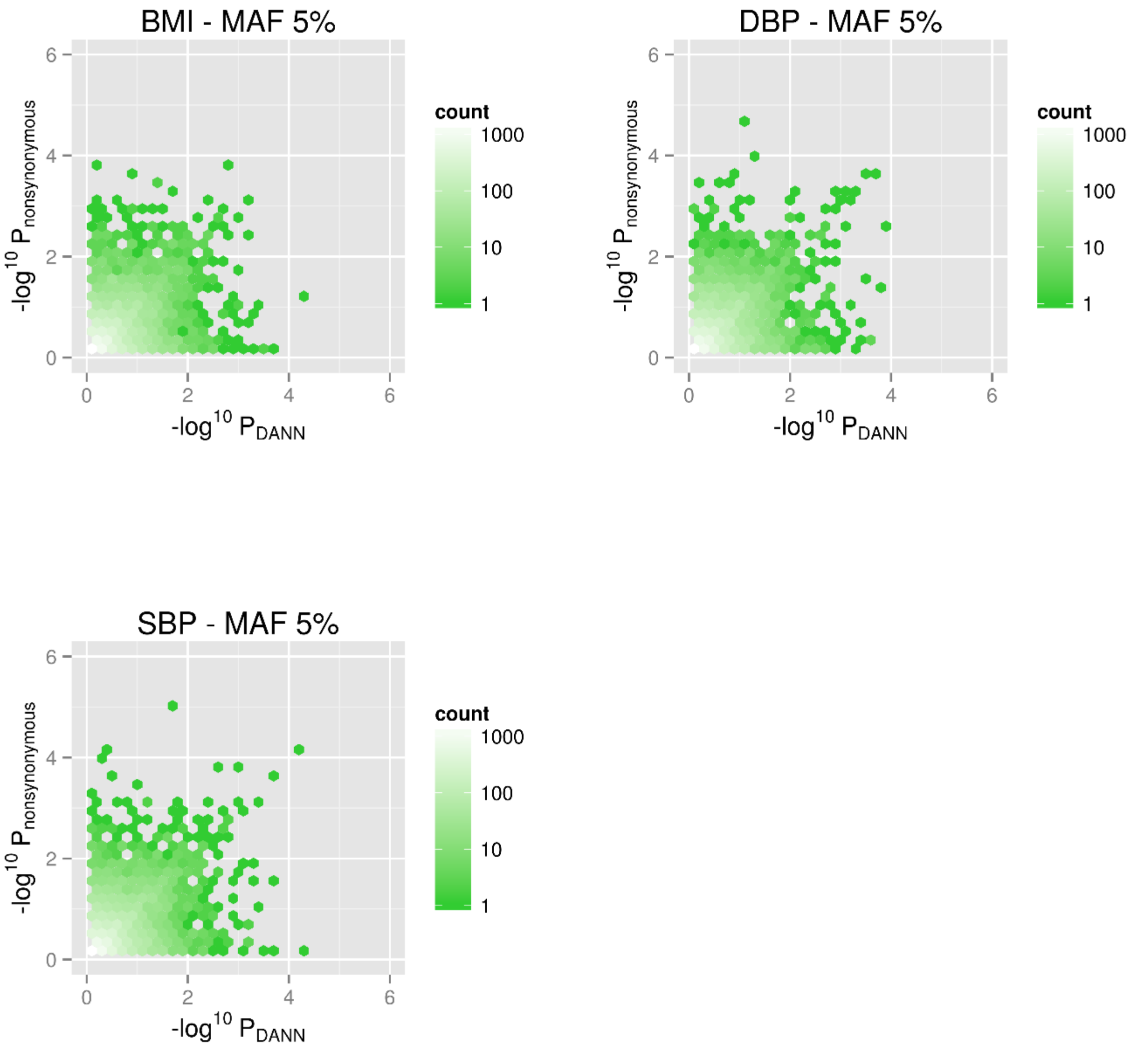
S20 Figure: Gene-based rare variant analyses across the genome using MiST for 7 cardiovascular traits (compared with loss-of-function filtering)

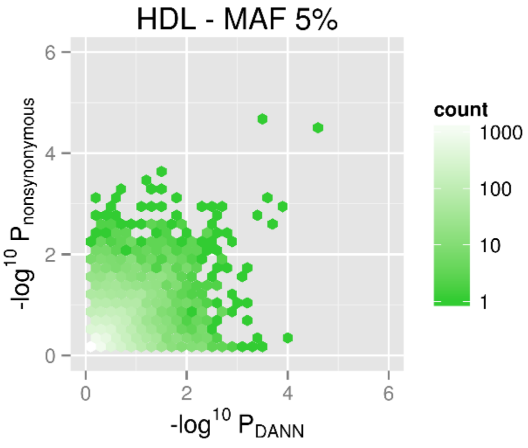


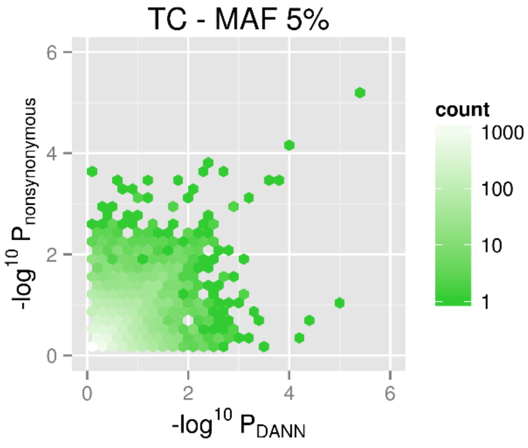

HDL - MAF 1%
TC - MAF 1%
LDL - MAF 1%
TG - MAF 1%
$-\log^{10} P_{LoF}$
$-\log^{10} P_{FATHMM}$
0
2
4
6

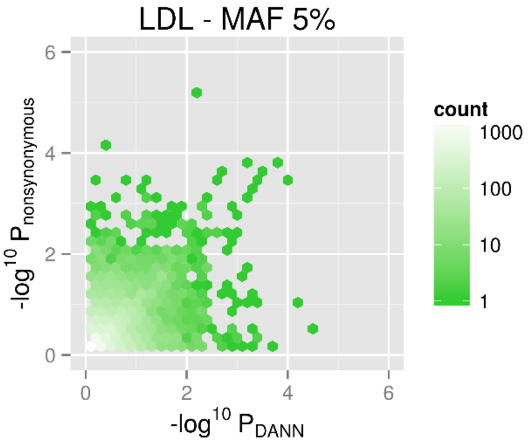
DANN tests

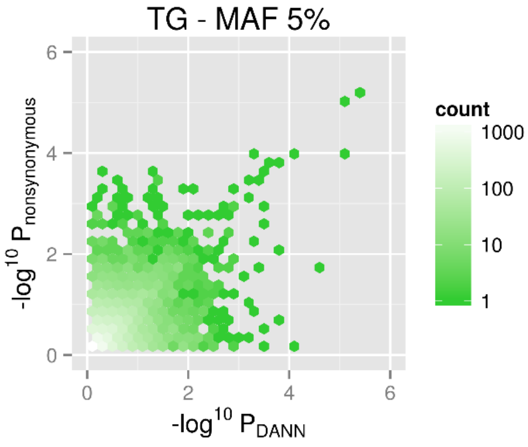
S21 Figure: Gene-based low frequency variant analyses across the genome using SKAT-O for 7 cardiovascular traits (compared with nonsynonymous filtering)



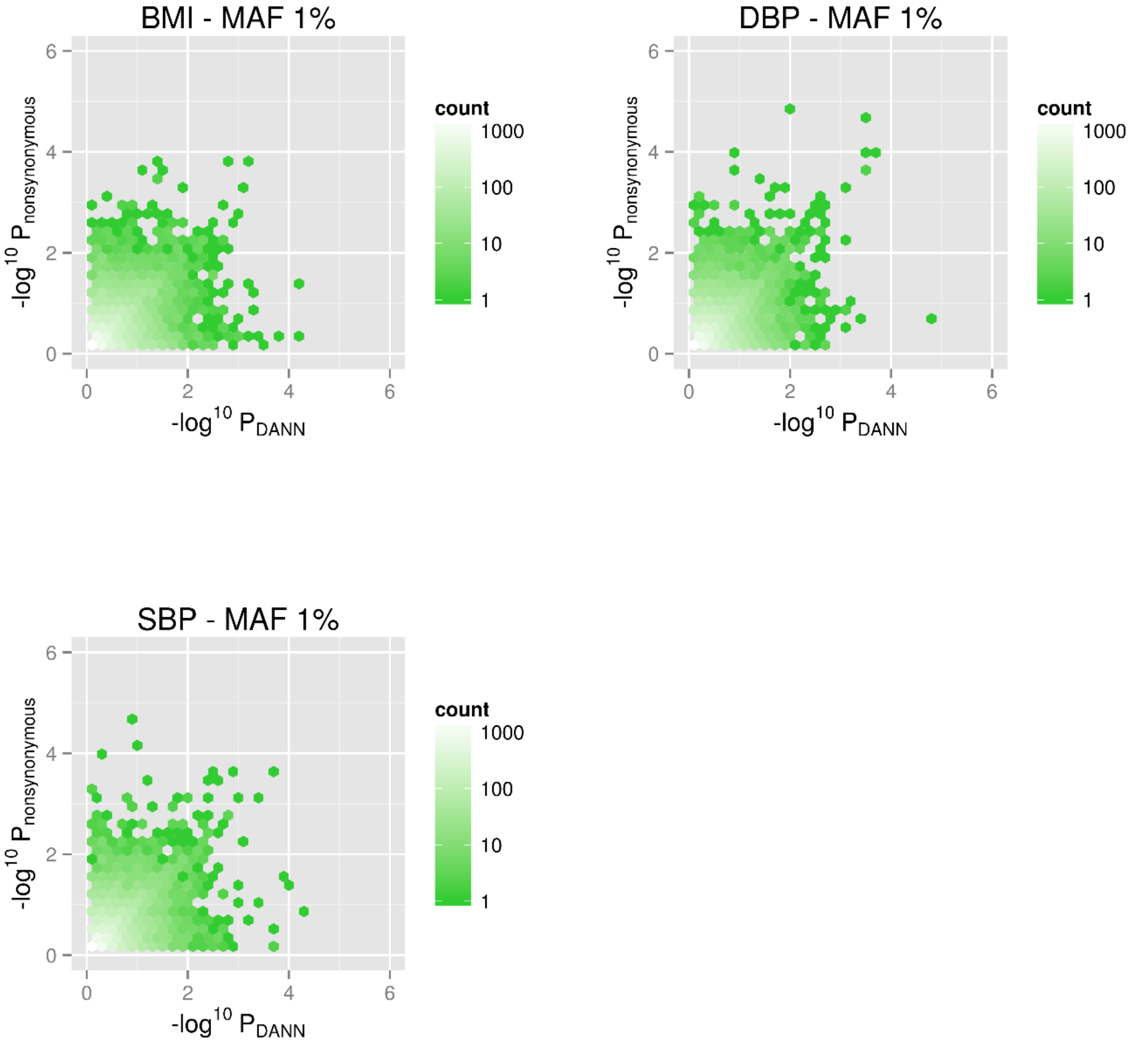

HDL - MAF 5%

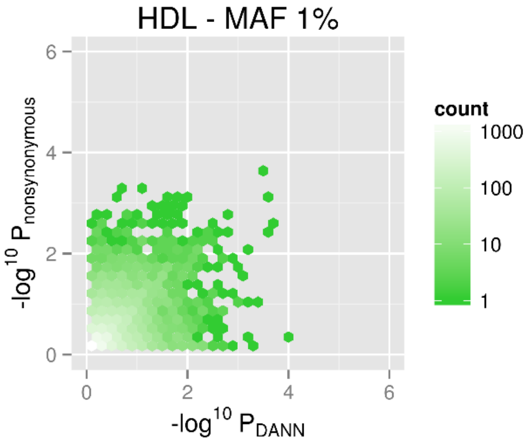

TC - MAF 5%

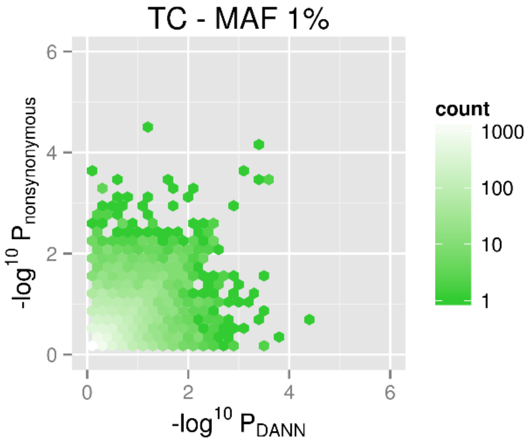

LDL - MAF 5%

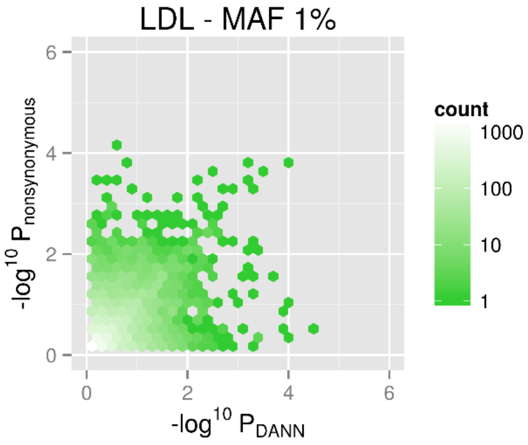

TG - MAF 5%

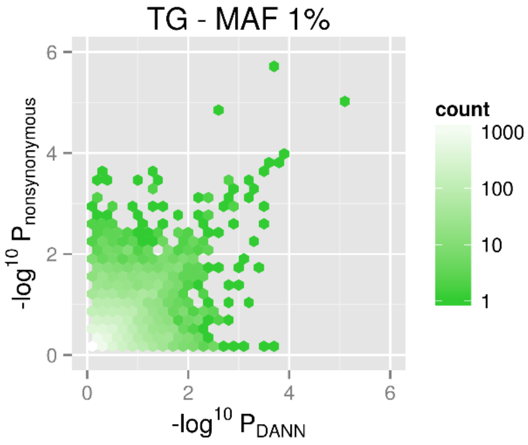
S22 Figure: Gene-based rare variant analyses across the genome using SKAT-O for 7 cardiovascular traits (compared with nonsynonymous filtering)



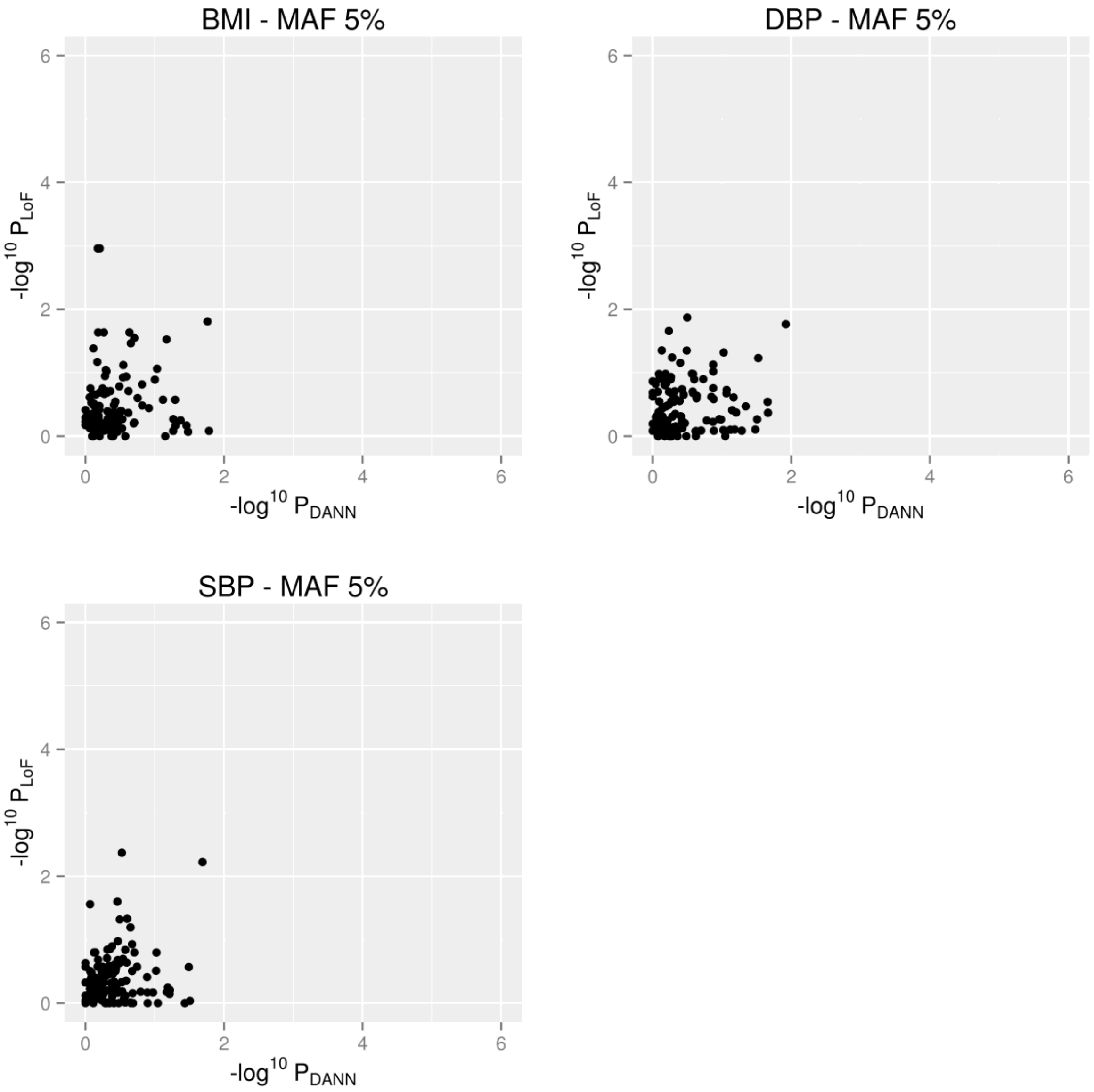

HDL - MAF 1%
-log10 P nonsynonymous
-log10 P DANN
0
2
4
6
count
1000
100
10
1

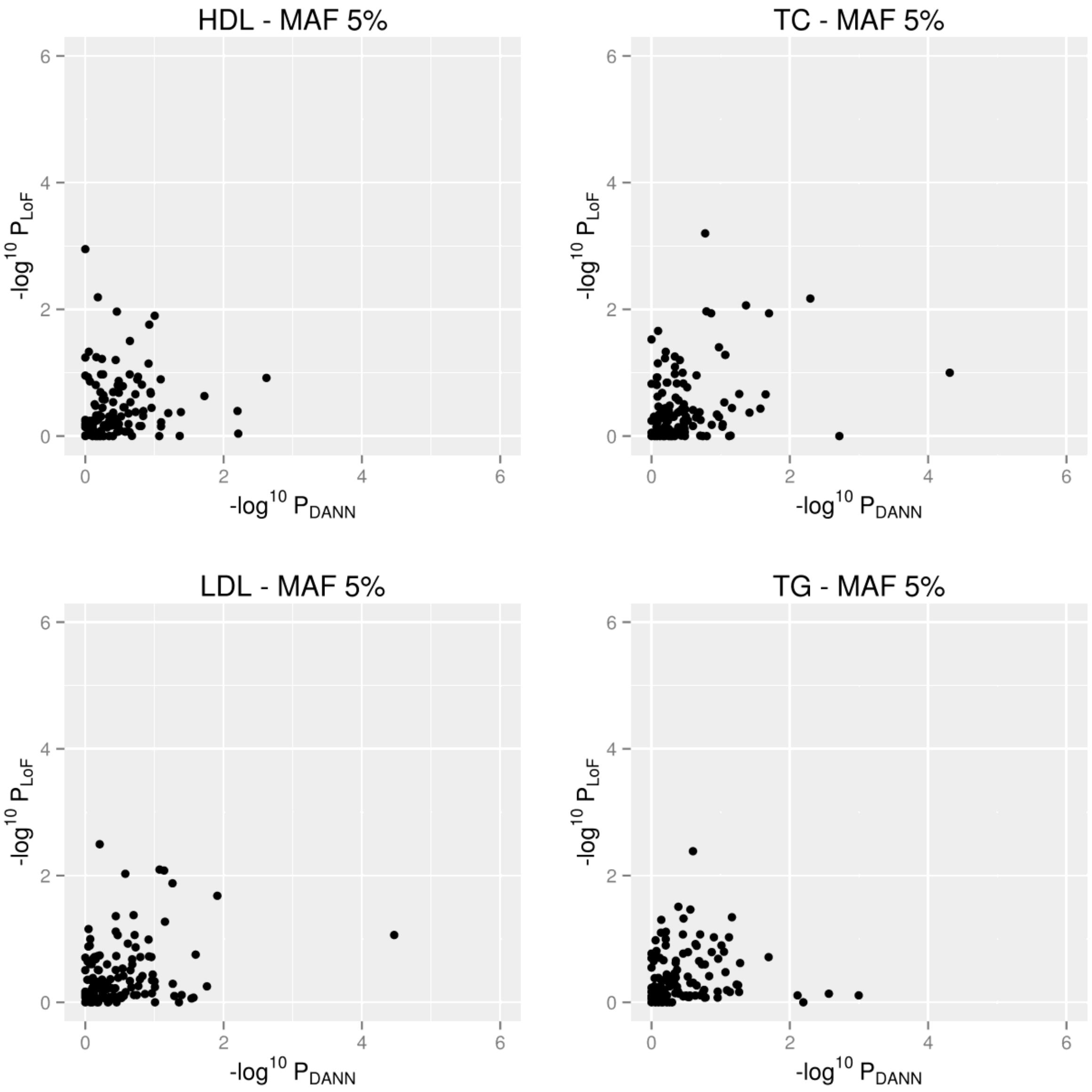

TC - MAF 1%
-log10 P nonsynonymous
-log10 P DANN
0
2
4
6
count
1000
100
10
1


LDL - MAF 1%
-log10 P nonsynonymous
-log10 P DANN
0
2
4
6
count
1000
100
10
1

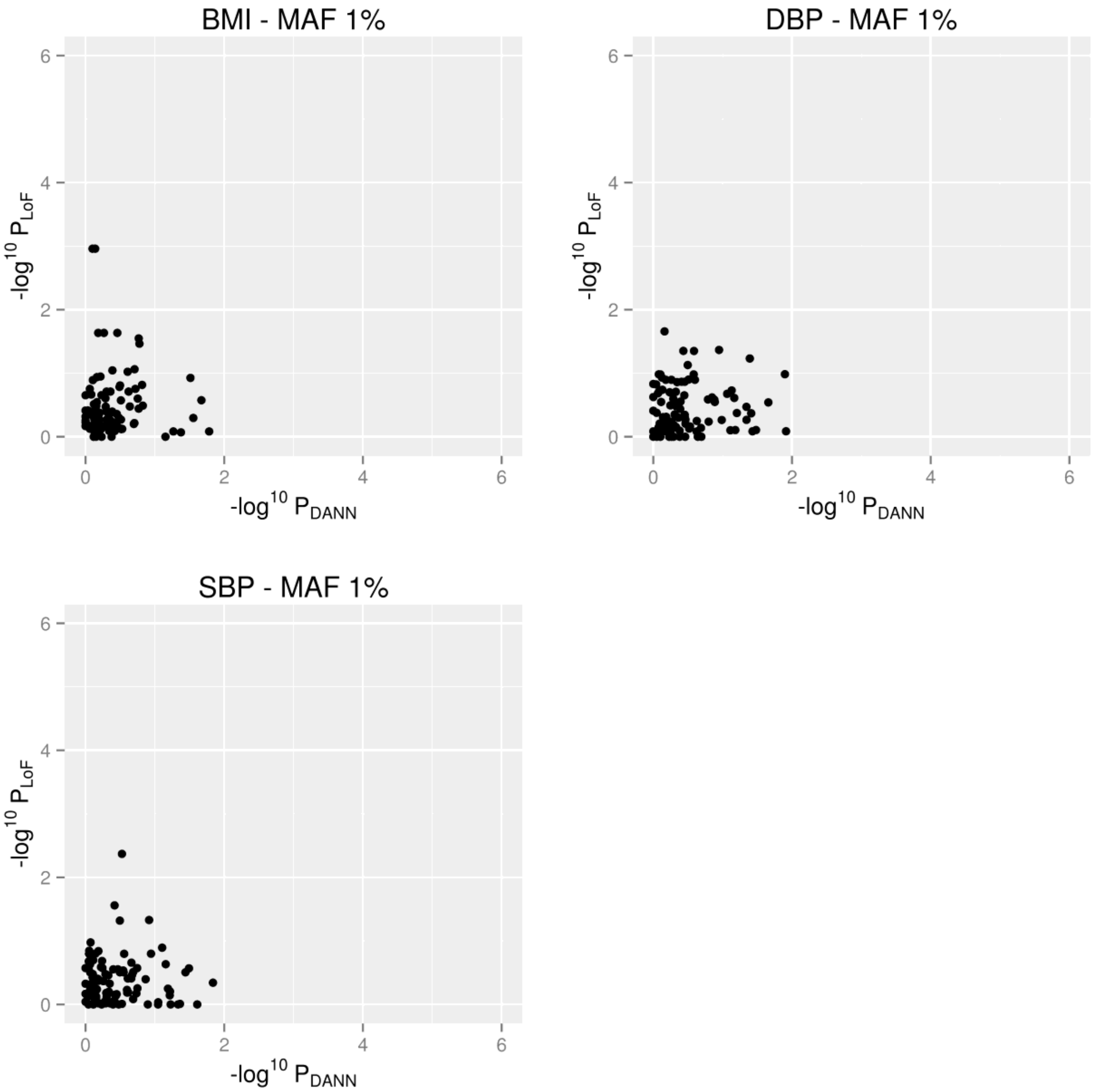

TG - MAF 1%
-log10 P nonsynonymous
-log10 P DANN
0
2
4
6
count
1000
100
10
1

S23 Figure: Gene-based low frequency variant analyses across the genome using SKAT-O for 7 cardiovascular traits (compared with loss-of-function filtering)

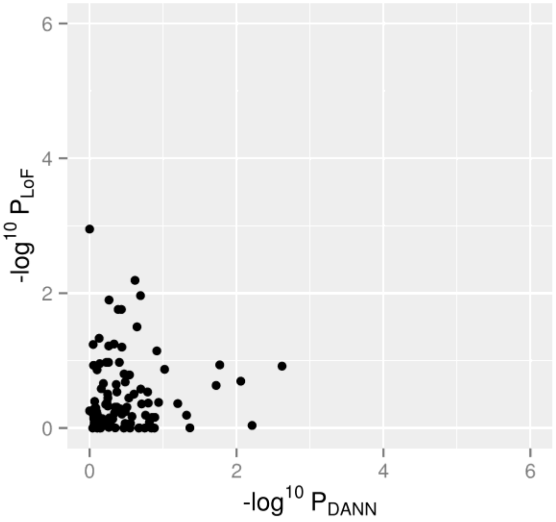



HDL - MAF 5%
TC - MAF 5%
LDL - MAF 5%
TG - MAF 5%
$-\log^{10} P_{LoF}$
$-\log^{10} P_{DANN}$
0
2
4
6

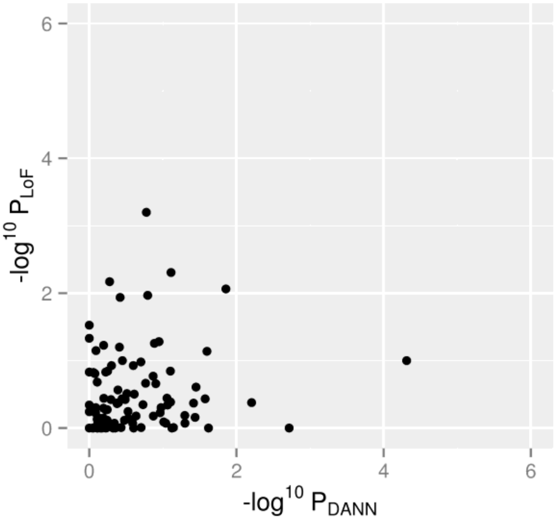
S24 Figure: Gene-based rare variant analyses across the genome using SKAT-O for 7 cardiovascular traits (compared with loss-of-function filtering)



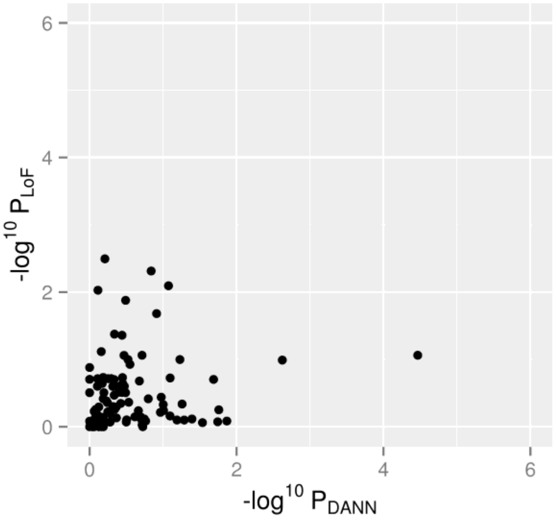
HDL - MAF 1%



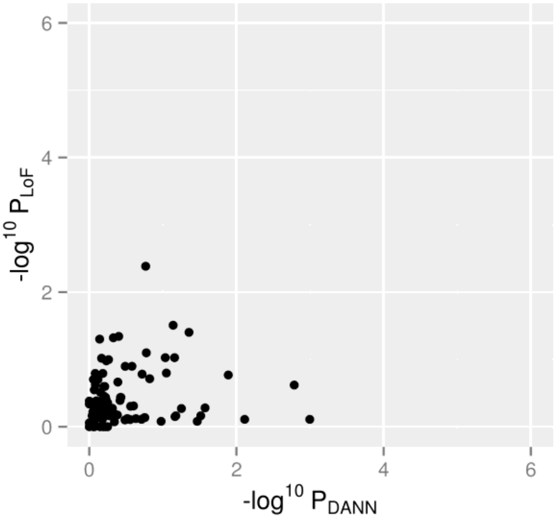
TC - MAF 1%



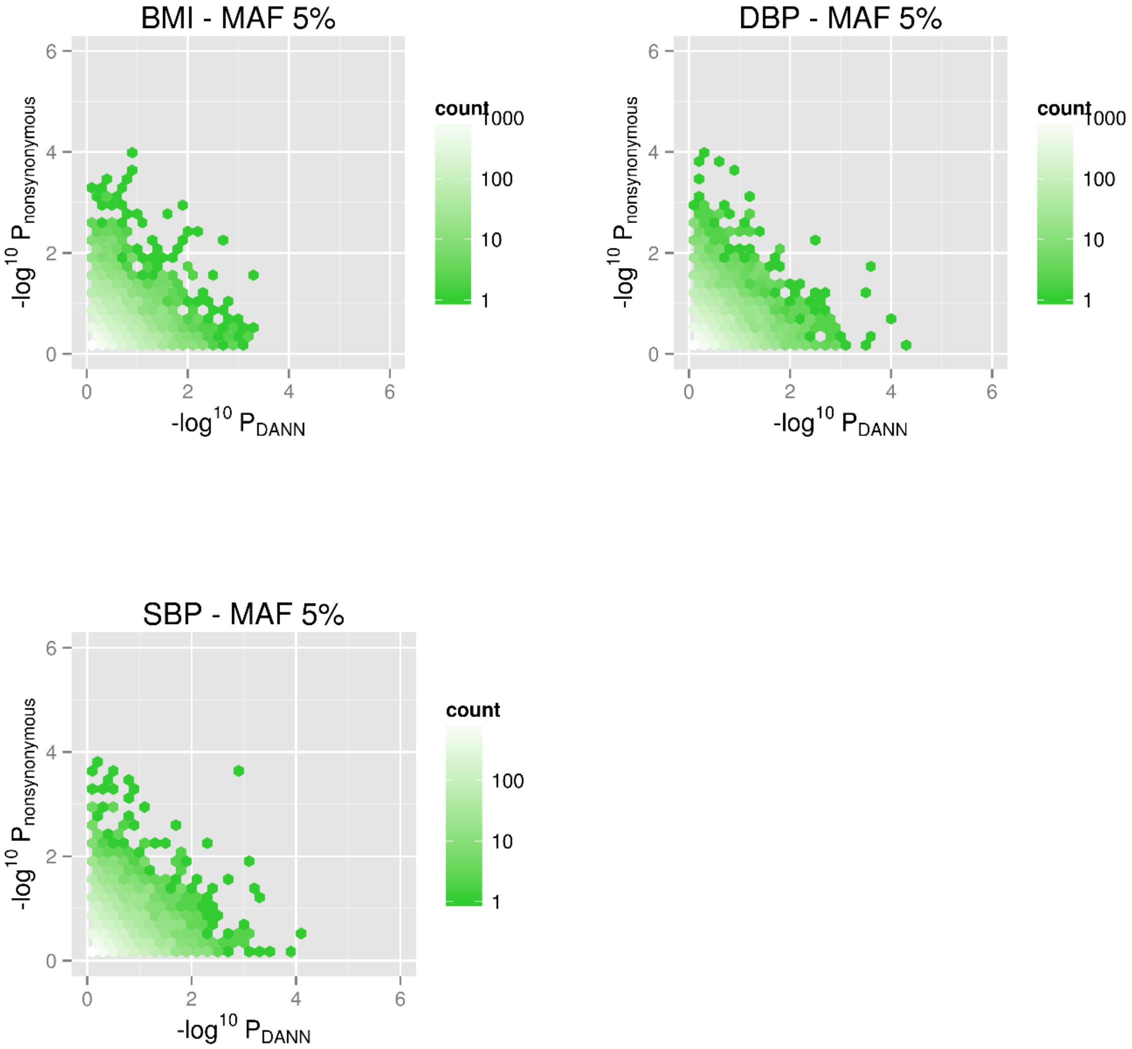
LDL - MAF 1%

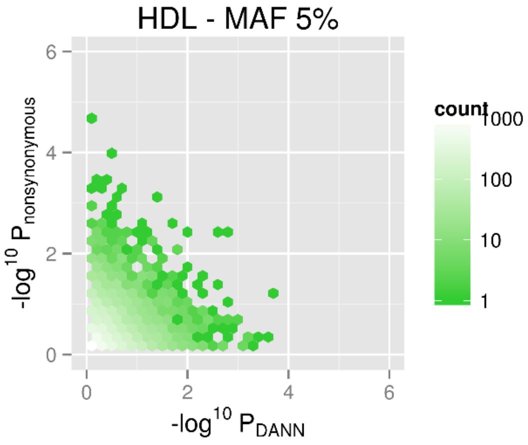


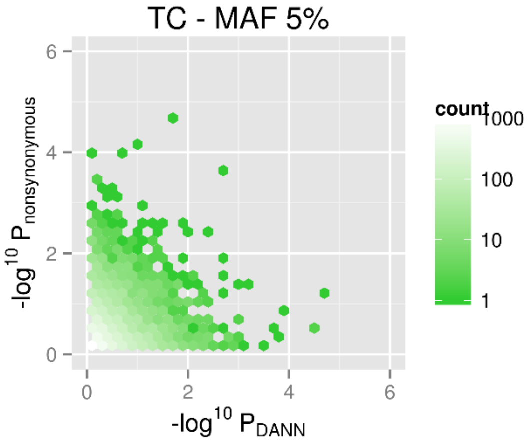
TG - MAF 1%

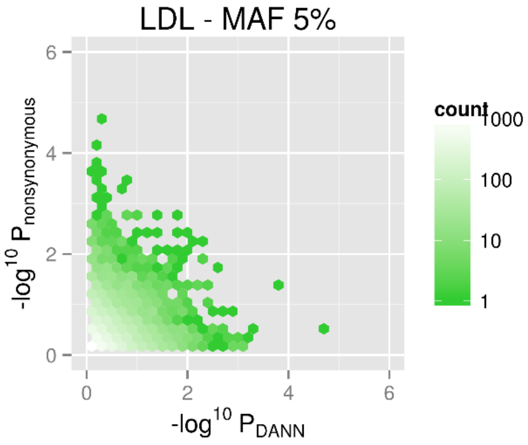


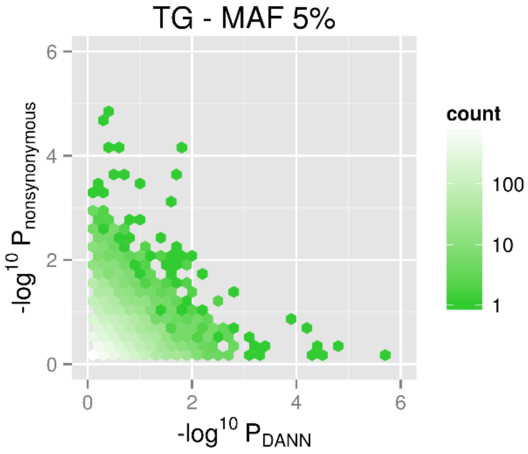
S25 Figure: Gene-based low frequency variant analyses across the genome using MiST for 7 cardiovascular traits (compared with nonsynonymous filtering)



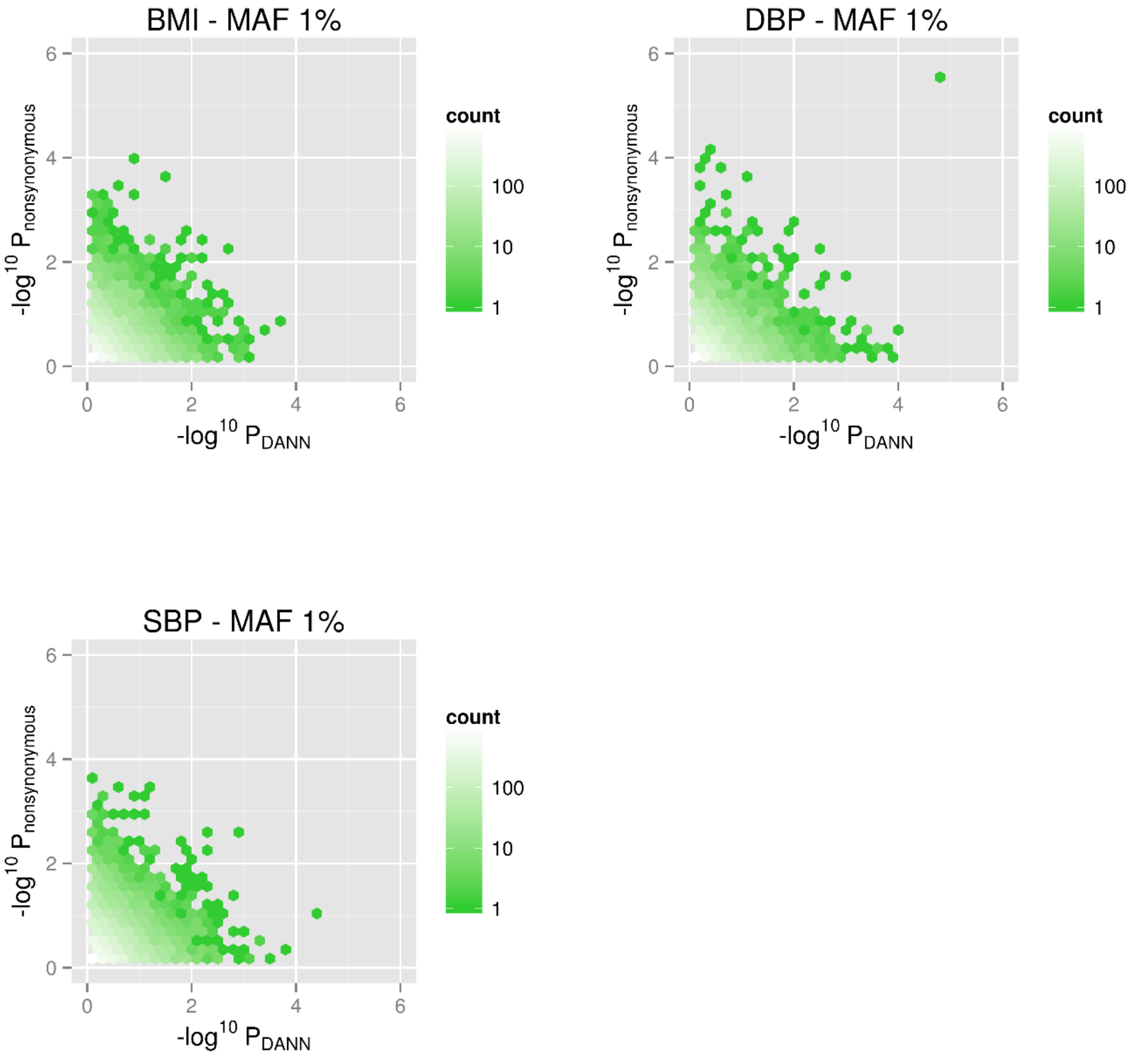

HDL - MAF 5%
$-\log^{10} P_{nonsynonymous}$
$-\log^{10} P_{DANN}$
0
2
4
6
0
2
4
6
count
1000
100
10
1

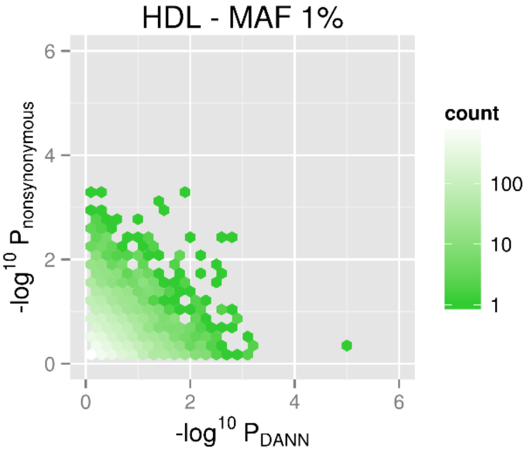

TC - MAF 5%
$-\log^{10} P_{nonsynonymous}$
$-\log^{10} P_{DANN}$
0
2
4
6
0
2
4
6
count
1000
100
10
1

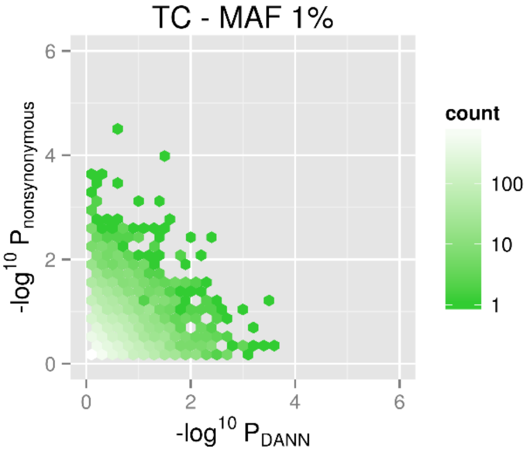

LDL - MAF 5%
$-\log^{10} P_{nonsynonymous}$
$-\log^{10} P_{DANN}$
0
2
4
6
0
2
4
6
count
1000
100
10
1

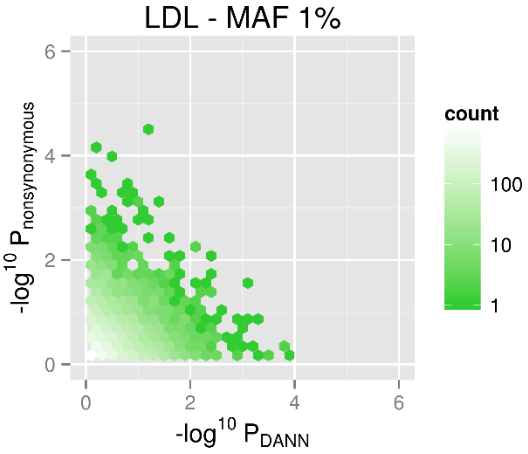

TG - MAF 5%
$-\log^{10} P_{nonsynonymous}$
$-\log^{10} P_{DANN}$
0
2
4
6
0
2
4
6
count
100
10
1

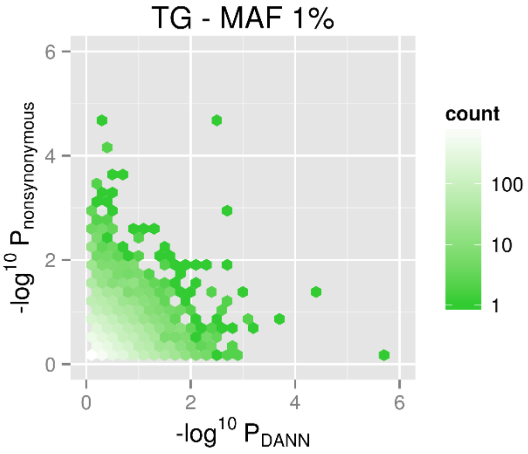
S26 Figure: Gene-based rare variant analyses across the genome using MiST for 7 cardiovascular traits (compared with nonsynonymous filtering)



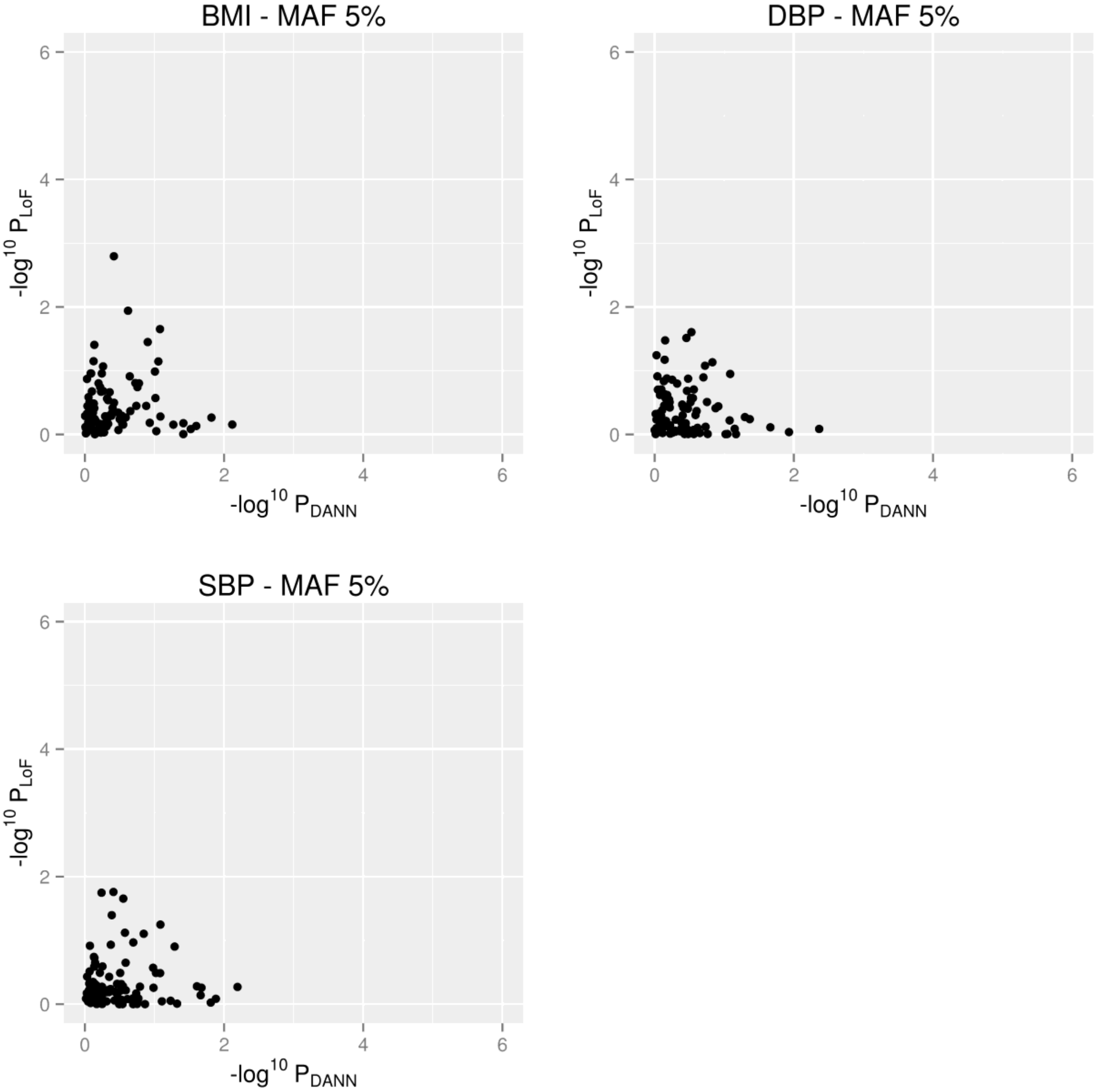

HDL - MAF 1%
-log10 P nonsynonymous
-log10 P DANN
0
2
4
6
count
100
10
1

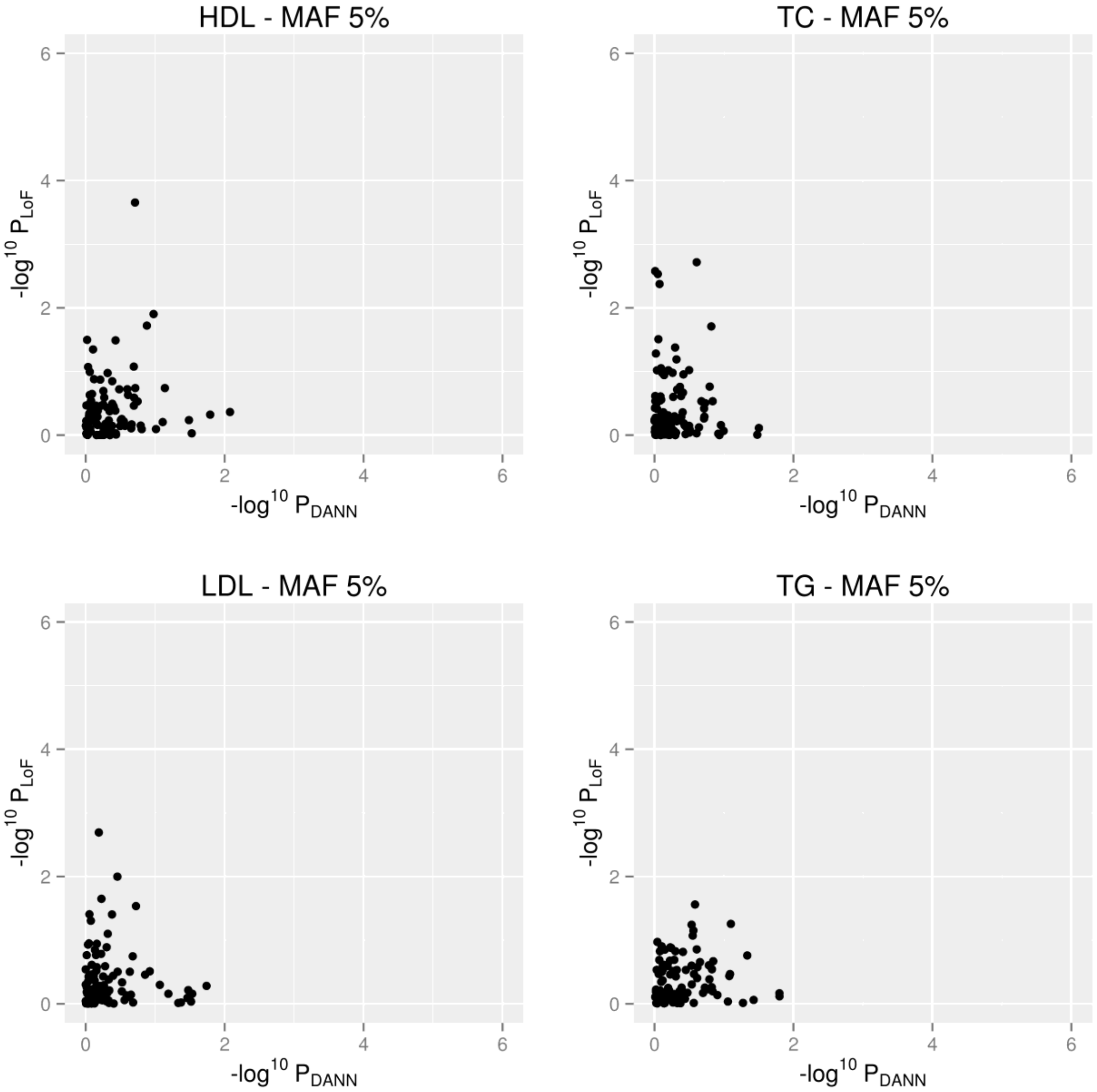

TC - MAF 1%
-log10 P nonsynonymous
-log10 P DANN
0
2
4
6
count
100
10
1


LDL - MAF 1%
-log10 P nonsynonymous
-log10 P DANN
0
2
4
6
count
100
10
1

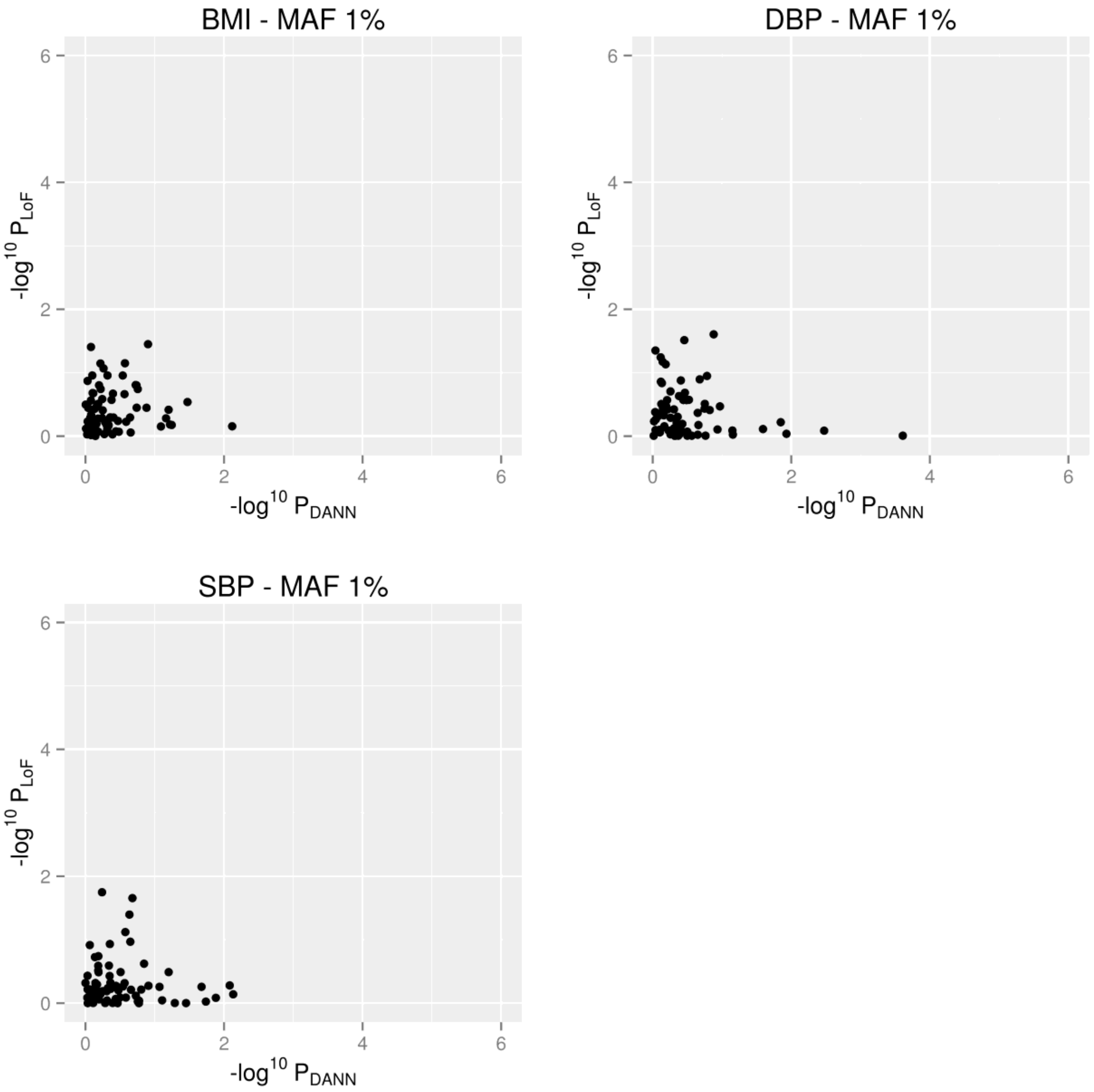

TG - MAF 1%
-log10 P nonsynonymous
-log10 P DANN
0
2
4
6
count
100
10
1

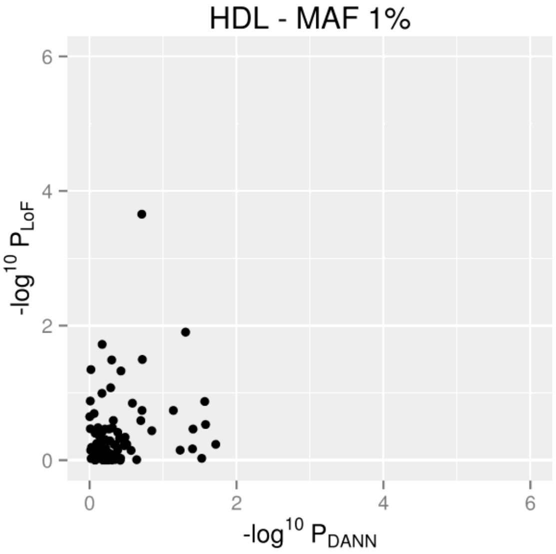
S27 Figure: Gene-based low frequency variant analyses across the genome using MiST for 7 cardiovascular traits (compared with loss-of-function filtering)

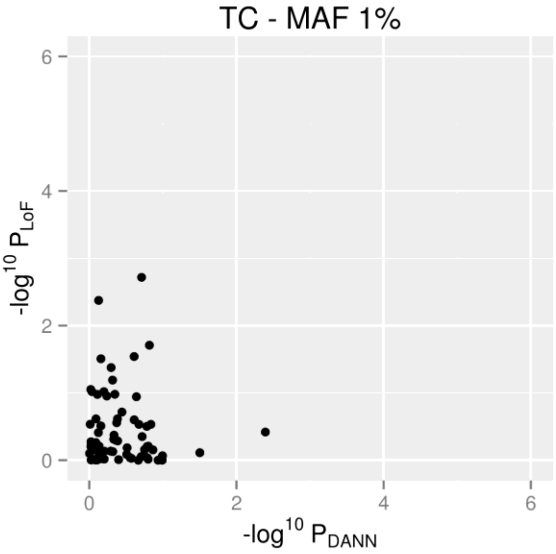


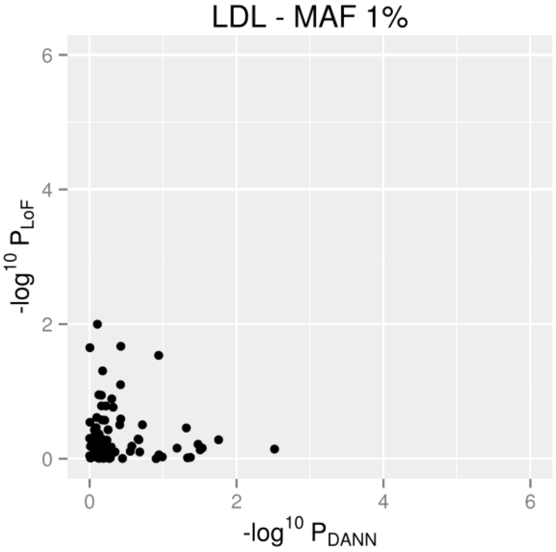

HDL - MAF 5%
TC - MAF 5%
LDL - MAF 5%
TG - MAF 5%
$-\log^{10} P_{LoF}$
$-\log^{10} P_{DANN}$
0
2
4
6

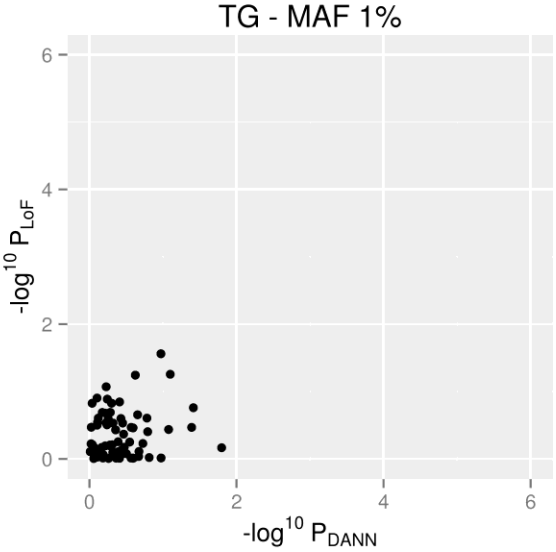
S28 Figure: Gene-based rare variant analyses across the genome using MiST for 7 cardiovascular traits (compared with loss-of-function filtering)




HDL - MAF 1%


TC - MAF 1%


LDL - MAF 1%


TG - MAF 1%