

Serum lipid/glucose traits after cholecystectomy from observational and MR study

Table S1. 52 genome-wide significant SNPs In UK Biobank were used as IVs to investigate the causal relationship between cholecystectomy and blood lipid and glucose traits

| SNPs | CHR* | Position | EA* | OA* | Beta | EAF | SE* | F-Stat | P value |
|-------------|------|-----------|-----|-----|----------|----------|----------|----------|----------|
| rs10199034 | 2 | 235935809 | C | G | 0.002441 | 0.226825 | 0.000486 | 25.24066 | 5.10E-07 |
| rs10799476 | 1 | 228603029 | A | C | -0.00209 | 0.302419 | 0.000443 | 22.28211 | 2.40E-06 |
| rs10882890 | 10 | 99048262 | A | G | -0.00221 | 0.622812 | 0.000417 | 28.15487 | 1.10E-07 |
| rs112634731 | 12 | 109292973 | G | A | -0.00382 | 0.068792 | 0.000796 | 23.05946 | 1.60E-06 |
| rs113525652 | 1 | 95604674 | C | T | -0.00354 | 0.083063 | 0.000731 | 23.43042 | 1.30E-06 |
| rs11603634 | 11 | 1136478 | G | A | -0.0022 | 0.503905 | 0.000405 | 29.49634 | 5.60E-08 |
| rs116468765 | 2 | 43908318 | G | A | 0.008453 | 0.02494 | 0.00129 | 42.92637 | 5.70E-11 |
| rs11686966 | 2 | 44047651 | G | C | -0.00634 | 0.024779 | 0.001355 | 21.9242 | 2.80E-06 |
| rs1201467 | 6 | 105432994 | C | G | -0.00386 | 0.104519 | 0.00066 | 34.2879 | 4.80E-09 |
| rs1208280 | 6 | 134165237 | G | A | -0.00216 | 0.398265 | 0.000412 | 27.44448 | 1.60E-07 |
| rs12369071 | 12 | 115789029 | T | G | 0.002065 | 0.27809 | 0.000453 | 20.82569 | 5.00E-06 |
| rs13061117 | 3 | 181186466 | C | T | 0.003365 | 0.090209 | 0.000712 | 22.3161 | 2.30E-06 |
| rs138776098 | 2 | 54903555 | C | T | 0.005121 | 0.038771 | 0.001066 | 23.09568 | 1.50E-06 |
| rs146652454 | 7 | 535398 | T | C | 0.006885 | 0.031145 | 0.001243 | 30.66692 | 3.10E-08 |
| rs150844304 | 15 | 43726625 | C | A | 0.007165 | 0.025812 | 0.00127 | 31.81152 | 1.70E-08 |
| rs17138478 | 17 | 36073320 | A | C | 0.003928 | 0.128841 | 0.000602 | 42.61232 | 6.70E-11 |
| rs1811515 | 2 | 44325917 | C | G | 0.003244 | 0.400945 | 0.000413 | 61.82773 | 3.70E-15 |
| rs2107944 | 7 | 141053519 | G | A | -0.00195 | 0.34061 | 0.000426 | 20.91754 | 4.80E-06 |
| rs2470048 | 8 | 120295405 | T | C | 0.002543 | 0.708173 | 0.000444 | 32.87017 | 9.90E-09 |
| rs28378706 | 2 | 224685334 | C | T | 0.002143 | 0.380942 | 0.000417 | 26.47262 | 2.70E-07 |
| rs28517482 | 2 | 44101538 | T | C | -0.00259 | 0.530457 | 0.000436 | 35.39392 | 2.70E-09 |
| rs2978388 | 8 | 146154001 | T | C | -0.00343 | 0.101031 | 0.000678 | 25.62795 | 4.10E-07 |
| rs3094509 | 17 | 36062299 | G | A | 0.002392 | 0.639268 | 0.000424 | 31.79174 | 1.70E-08 |
| rs332981 | 4 | 172854531 | G | T | -0.00194 | 0.567975 | 0.000407 | 22.81022 | 1.80E-06 |
| rs3793770 | 10 | 102116914 | T | G | -0.00214 | 0.352954 | 0.000423 | 25.55033 | 4.30E-07 |
| rs3862794 | 11 | 72538600 | C | T | 0.003246 | 0.256545 | 0.000462 | 49.42266 | 2.10E-12 |
| rs41276920 | 15 | 90347920 | A | G | -0.00475 | 0.087572 | 0.000713 | 44.41727 | 2.70E-11 |
| rs41281265 | 22 | 40720704 | G | A | 0.002348 | 0.349041 | 0.000424 | 30.59838 | 3.20E-08 |
| rs4150336 | 13 | 103519251 | T | C | 0.005126 | 0.048579 | 0.000936 | 29.98734 | 4.30E-08 |
| rs4331955 | 6 | 93579401 | A | G | -0.00245 | 0.183614 | 0.000522 | 22.14301 | 2.50E-06 |
| rs4346434 | 2 | 44219746 | T | C | -0.00598 | 0.736536 | 0.000459 | 170.1353 | 6.90E-39 |
| rs4681516 | 3 | 149212125 | C | G | -0.00492 | 0.561695 | 0.000407 | 146.3147 | 1.10E-33 |
| rs4881744 | 11 | 1399402 | G | A | 0.002365 | 0.201577 | 0.000504 | 22.04437 | 2.70E-06 |
| rs55780704 | 3 | 149185633 | T | C | 0.006634 | 0.042285 | 0.001008 | 43.30119 | 4.70E-11 |
| rs55971546 | 13 | 103718308 | T | C | 0.00541 | 0.0427 | 0.000997 | 29.46966 | 5.70E-08 |
| rs580477 | 2 | 45071428 | T | C | 0.005049 | 0.03738 | 0.001069 | 22.29988 | 2.30E-06 |
| rs62090594 | 18 | 42383005 | A | G | 0.003516 | 0.079869 | 0.000751 | 21.89845 | 2.90E-06 |
| rs698838 | 2 | 44738763 | T | C | 0.002004 | 0.625104 | 0.000416 | 23.2453 | 1.40E-06 |
| rs714583 | 7 | 107473153 | A | T | -0.00455 | 0.230102 | 0.000488 | 87.09168 | 1.00E-20 |
| rs72931779 | 11 | 69833580 | G | C | 0.00481 | 0.098516 | 0.000677 | 50.44449 | 1.20E-12 |
| rs73192932 | 7 | 85881867 | C | T | -0.00505 | 0.037413 | 0.001062 | 22.5883 | 2.00E-06 |
| rs7337432 | 13 | 52422211 | G | A | -0.00212 | 0.674786 | 0.000432 | 24.10879 | 9.10E-07 |
| rs7564733 | 2 | 235958802 | C | T | 0.002439 | 0.238176 | 0.000475 | 26.36381 | 2.80E-07 |
| rs76818081 | 15 | 57640005 | A | G | 0.007874 | 0.028962 | 0.001337 | 34.7021 | 3.80E-09 |
| rs76862077 | 3 | 59188684 | T | C | 0.005456 | 0.032275 | 0.001155 | 22.30086 | 2.30E-06 |
| rs7993414 | 13 | 103371810 | G | A | -0.00192 | 0.484552 | 0.000403 | 22.56577 | 2.00E-06 |

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|-----------|----|-----------|---|---|----------|----------|----------|----------|----------|
| rs8077886 | 17 | 70058020 | C | T | -0.0035 | 0.108272 | 0.00065 | 29.03423 | 7.10E-08 |
| rs932784 | 13 | 103866575 | A | T | 0.007651 | 0.022017 | 0.001376 | 30.9293 | 2.70E-08 |
| rs9371004 | 6 | 17601853 | C | T | -0.00314 | 0.46429 | 0.000406 | 59.84855 | 1.00E-14 |
| rs9471953 | 6 | 12508653 | G | A | 0.003903 | 0.061084 | 0.000843 | 21.4398 | 3.70E-06 |
| rs9544535 | 13 | 36095039 | G | A | -0.00188 | 0.57346 | 0.000411 | 20.93839 | 4.70E-06 |
| rs9790309 | 3 | 149183177 | A | G | -0.00284 | 0.856098 | 0.000582 | 23.81479 | 1.10E-06 |

*CHR chromosome, EA effect allele, OA other allele, EAF effect allele frequency, SE standard error.

Table S2. 108 genome-wide significant SNPs In FinnGen were used as IVs to investigate the causal relationship between cholecystectomy and blood lipid and glucose traits

| SNPs | CHR* | Position | EA* | OA* | Beta | EAF | SE* | F-Stat | P value |
|-------------|------|-----------|-----|-----|----------|----------|----------|----------|----------|
| rs12135720 | 1 | 75672495 | G | T | -0.46254 | 0.003305 | 0.085608 | 29.19235 | 6.55E-08 |
| rs263462 | 1 | 86723238 | A | G | 0.109198 | 0.036616 | 0.022852 | 22.83394 | 1.77E-06 |
| rs3790843 | 1 | 200041696 | T | C | 0.052812 | 0.423614 | 0.008877 | 35.39149 | 2.70E-09 |
| rs1629928 | 1 | 245606061 | G | A | 0.045664 | 0.287025 | 0.009707 | 22.13201 | 2.55E-06 |
| rs76592665 | 2 | 39984226 | T | G | -0.06093 | 0.128652 | 0.013169 | 21.40315 | 3.72E-06 |
| rs12470367 | 2 | 41464133 | A | G | 0.046046 | 0.722491 | 0.009799 | 22.07934 | 2.62E-06 |
| rs62140201 | 2 | 41987058 | A | G | 0.149783 | 0.017889 | 0.032284 | 21.52589 | 3.49E-06 |
| rs186890864 | 2 | 42406199 | C | T | 0.240167 | 0.026876 | 0.026017 | 85.21425 | 2.68E-20 |
| rs143949742 | 2 | 42410653 | C | G | 0.213898 | 0.011876 | 0.038163 | 31.4147 | 2.08E-08 |
| rs139199716 | 2 | 42506512 | C | T | 0.193654 | 0.028373 | 0.024993 | 60.03565 | 9.32E-15 |
| rs79693383 | 2 | 42826986 | A | G | 0.070977 | 0.107902 | 0.014015 | 25.64803 | 4.10E-07 |
| rs12615717 | 2 | 42878079 | G | A | 0.106407 | 0.223779 | 0.010408 | 104.5296 | 1.55E-24 |
| rs11690947 | 2 | 43050237 | C | G | -0.09894 | 0.112933 | 0.014229 | 48.34467 | 3.58E-12 |
| rs730803 | 2 | 43056600 | T | G | 0.28261 | 0.016495 | 0.031775 | 79.104 | 5.89E-19 |
| rs13414085 | 2 | 43118875 | A | G | 0.074633 | 0.255252 | 0.009887 | 56.9837 | 4.39E-14 |
| rs2011896 | 2 | 43192747 | G | A | -0.0737 | 0.360721 | 0.009263 | 63.30147 | 1.77E-15 |
| rs75841075 | 2 | 43959696 | A | G | -0.18737 | 0.03149 | 0.026357 | 50.5337 | 1.17E-12 |
| rs61614759 | 2 | 43966363 | A | G | -0.13221 | 0.147441 | 0.012604 | 110.0422 | 9.60E-26 |
| rs55935092 | 2 | 44020807 | G | T | 0.089062 | 0.233584 | 0.010185 | 76.46271 | 2.24E-18 |
| rs75120545 | 2 | 44044357 | T | C | 0.131326 | 0.044953 | 0.0204 | 41.44326 | 1.21E-10 |
| rs71420083 | 2 | 44047252 | A | G | 0.096803 | 0.087747 | 0.015235 | 40.37519 | 2.10E-10 |
| rs11691443 | 2 | 44094498 | T | A | 0.074906 | 0.09175 | 0.014908 | 25.24652 | 5.04E-07 |
| rs187779008 | 2 | 44590590 | G | T | 0.395597 | 0.024937 | 0.02567 | 237.4875 | 1.39E-53 |
| rs163520 | 2 | 44904012 | A | C | -0.13662 | 0.051948 | 0.020461 | 44.58357 | 2.44E-11 |
| rs112266464 | 2 | 44951472 | T | C | 0.178239 | 0.047991 | 0.019874 | 80.43393 | 3.01E-19 |
| rs2921987 | 2 | 45027388 | G | A | 0.098801 | 0.832726 | 0.01193 | 68.59219 | 1.21E-16 |
| rs576479048 | 2 | 45038193 | A | G | 0.230446 | 0.010449 | 0.039855 | 33.43347 | 7.37E-09 |
| rs13399179 | 2 | 45186147 | T | C | 0.088389 | 0.060733 | 0.017873 | 24.45603 | 7.60E-07 |
| rs72799962 | 2 | 45194235 | A | G | 0.129805 | 0.085649 | 0.015202 | 72.90904 | 1.36E-17 |
| rs10208775 | 2 | 45228585 | G | A | 0.116584 | 0.051961 | 0.019115 | 37.19805 | 1.07E-09 |
| rs582384 | 2 | 45669298 | A | C | 0.049829 | 0.604457 | 0.008986 | 30.74902 | 2.94E-08 |
| rs34997129 | 2 | 45708906 | T | C | 0.180582 | 0.027376 | 0.025577 | 49.84979 | 1.66E-12 |
| rs145048510 | 2 | 46089233 | C | G | 0.149561 | 0.032959 | 0.024104 | 38.49948 | 5.48E-10 |
| rs150212157 | 2 | 61808494 | A | G | -0.05912 | 0.155672 | 0.012257 | 23.26222 | 1.41E-06 |
| rs871962 | 3 | 148860828 | A | G | 0.047148 | 0.382407 | 0.008985 | 27.53758 | 1.54E-07 |
| rs79348616 | 3 | 149287571 | T | C | 0.127869 | 0.078752 | 0.016113 | 62.97795 | 2.09E-15 |
| rs76733846 | 3 | 149433851 | G | T | 0.071208 | 0.142828 | 0.01249 | 32.50198 | 1.19E-08 |
| rs79478006 | 3 | 149462775 | T | C | -0.1158 | 0.098232 | 0.0151 | 58.81295 | 1.73E-14 |

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|-------------|----|-----------|---|---|----------|----------|----------|----------|----------|
| rs62272019 | 3 | 149478444 | T | C | 0.238694 | 0.092667 | 0.014488 | 271.4314 | 5.54E-61 |
| rs78815523 | 3 | 149580110 | T | C | -0.08383 | 0.108285 | 0.014453 | 33.64538 | 6.61E-09 |
| rs66498012 | 3 | 149680106 | A | G | -0.05569 | 0.271609 | 0.009898 | 31.65586 | 1.84E-08 |
| rs79469600 | 3 | 150067426 | G | A | 0.097206 | 0.044549 | 0.021056 | 21.31196 | 3.90E-06 |
| rs4681199 | 3 | 150277525 | G | A | 0.046922 | 0.45868 | 0.008932 | 27.59618 | 1.49E-07 |
| rs843372 | 3 | 184278425 | T | C | -0.04947 | 0.717723 | 0.009651 | 26.2785 | 2.96E-07 |
| rs6448619 | 4 | 28970411 | T | C | 0.043375 | 0.318083 | 0.009366 | 21.44589 | 3.64E-06 |
| rs13126112 | 4 | 94918869 | T | C | 0.057621 | 0.158958 | 0.011865 | 23.58535 | 1.19E-06 |
| rs13104082 | 4 | 115022856 | G | A | -0.08689 | 0.943807 | 0.018729 | 21.52174 | 3.50E-06 |
| rs2016239 | 4 | 166098443 | C | G | -0.04357 | 0.491819 | 0.008818 | 24.4102 | 7.79E-07 |
| rs16891958 | 5 | 33933857 | T | C | 0.484143 | 0.001452 | 0.10247 | 22.32307 | 2.30E-06 |
| rs1320308 | 5 | 76875427 | C | A | 0.044883 | 0.67384 | 0.009403 | 22.78335 | 1.81E-06 |
| rs181090787 | 5 | 82866204 | T | A | -0.18289 | 0.015269 | 0.038635 | 22.40855 | 2.20E-06 |
| rs375844484 | 5 | 114274349 | A | G | -0.12947 | 0.028078 | 0.027544 | 22.09382 | 2.60E-06 |
| rs9396788 | 6 | 17676239 | G | A | -0.06873 | 0.367114 | 0.009116 | 56.84143 | 4.72E-14 |
| rs182978364 | 6 | 29754228 | A | G | -0.17821 | 0.018013 | 0.035047 | 25.85708 | 3.68E-07 |
| rs735286 | 6 | 43776884 | T | C | 0.050626 | 0.232783 | 0.010271 | 24.29688 | 8.26E-07 |
| rs4629659 | 6 | 84683238 | T | C | -0.04255 | 0.495475 | 0.008731 | 23.74789 | 1.10E-06 |
| rs375716154 | 6 | 102757915 | C | T | -0.06599 | 0.158104 | 0.012223 | 29.15184 | 6.69E-08 |
| rs78956178 | 6 | 105041334 | G | T | -0.10474 | 0.058193 | 0.019308 | 29.42864 | 5.80E-08 |
| rs9487939 | 6 | 112644625 | C | A | 0.0524 | 0.271382 | 0.009868 | 28.19629 | 1.10E-07 |
| rs78686882 | 7 | 6743309 | T | C | 0.070123 | 0.090573 | 0.015104 | 21.55417 | 3.44E-06 |
| rs75128707 | 7 | 27869731 | T | C | -0.1198 | 0.033 | 0.025352 | 22.32987 | 2.30E-06 |
| rs73135307 | 7 | 74455527 | G | C | -0.09258 | 0.061309 | 0.018799 | 24.25437 | 8.44E-07 |
| rs60851079 | 7 | 87017091 | T | C | -0.08359 | 0.112321 | 0.014113 | 35.08268 | 3.16E-09 |
| rs116979197 | 7 | 87359731 | G | A | -0.12237 | 0.040236 | 0.023094 | 28.07916 | 1.16E-07 |
| rs12154319 | 7 | 87559241 | A | G | -0.30817 | 0.009651 | 0.048505 | 40.36354 | 2.11E-10 |
| rs2188251 | 7 | 88574992 | C | G | 0.082791 | 0.912697 | 0.015881 | 27.17812 | 1.86E-07 |
| rs73194916 | 7 | 88617367 | T | C | -0.07655 | 0.080299 | 0.016423 | 21.72978 | 3.14E-06 |
| rs75741381 | 7 | 101166177 | G | C | -0.06547 | 0.15219 | 0.012343 | 28.13546 | 1.13E-07 |
| rs714582 | 7 | 107832881 | A | G | -0.08385 | 0.295045 | 0.009707 | 74.62879 | 5.68E-18 |
| rs193067613 | 7 | 119273716 | A | T | -0.06696 | 0.126165 | 0.013498 | 24.60706 | 7.03E-07 |
| rs117920913 | 8 | 1043637 | C | A | 0.46571 | 0.001701 | 0.093693 | 24.70677 | 6.68E-07 |
| rs117018004 | 8 | 11298452 | A | G | -0.13669 | 0.02507 | 0.029237 | 21.85926 | 2.93E-06 |
| rs74707612 | 8 | 23383264 | T | C | 0.168733 | 0.014761 | 0.034835 | 23.46191 | 1.27E-06 |
| rs75745670 | 8 | 58145023 | T | G | -0.08244 | 0.085982 | 0.016199 | 25.89843 | 3.60E-07 |
| rs16894137 | 8 | 95934063 | C | T | 0.080856 | 0.130545 | 0.012803 | 39.88651 | 2.69E-10 |
| rs2468191 | 8 | 119222029 | A | G | 0.040684 | 0.583063 | 0.008896 | 20.91532 | 4.80E-06 |
| rs113828886 | 9 | 7384055 | T | C | -0.14886 | 0.024132 | 0.030248 | 24.21887 | 8.60E-07 |
| rs7039251 | 9 | 133025870 | A | T | 0.041543 | 0.463642 | 0.008804 | 22.268 | 2.37E-06 |
| rs11012722 | 10 | 21483238 | G | A | 0.046759 | 0.290648 | 0.009617 | 23.64108 | 1.16E-06 |
| rs147037994 | 10 | 29737565 | T | C | 0.165288 | 0.015178 | 0.034759 | 22.613 | 1.98E-06 |
| rs6584349 | 10 | 100182799 | G | A | 0.061531 | 0.126047 | 0.013075 | 22.14611 | 2.53E-06 |
| rs1502593 | 10 | 100349445 | A | G | -0.04628 | 0.470589 | 0.008792 | 27.70291 | 1.41E-07 |
| rs7104956 | 11 | 993745 | G | C | -0.0611 | 0.19195 | 0.011371 | 28.87821 | 7.71E-08 |
| rs35779873 | 11 | 1197482 | T | C | 0.046456 | 0.242253 | 0.010177 | 20.83888 | 5.00E-06 |
| rs10831930 | 11 | 12971602 | T | C | 0.047218 | 0.309277 | 0.009877 | 22.85428 | 1.75E-06 |
| rs11023658 | 11 | 15624182 | G | A | -0.17443 | 0.017996 | 0.034887 | 24.99914 | 5.74E-07 |
| rs61898562 | 11 | 61909033 | T | C | -0.14976 | 0.02612 | 0.029028 | 26.61474 | 2.48E-07 |

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|-------------|----|-----------|---|---|----------|----------|----------|----------|----------|
| rs17421328 | 11 | 70017223 | T | C | 0.107614 | 0.072358 | 0.01647 | 42.6903 | 6.41E-11 |
| rs76726250 | 11 | 70189554 | T | G | 0.098054 | 0.046827 | 0.020383 | 23.14224 | 1.50E-06 |
| rs556153 | 11 | 107802902 | C | T | 0.049348 | 0.463267 | 0.00876 | 31.73485 | 1.77E-08 |
| rs75497660 | 12 | 14984781 | T | A | 0.061232 | 0.156109 | 0.011881 | 26.56336 | 2.55E-07 |
| rs2146990 | 13 | 102814632 | C | G | -0.07753 | 0.65365 | 0.009137 | 72.00915 | 2.14E-17 |
| rs16961281 | 13 | 103066474 | A | G | -0.10946 | 0.09983 | 0.014948 | 53.61946 | 2.43E-13 |
| rs862135 | 14 | 56783060 | A | G | -0.04424 | 0.710884 | 0.009618 | 21.16086 | 4.22E-06 |
| rs62041381 | 16 | 52831633 | C | A | 0.158127 | 0.018939 | 0.031273 | 25.56644 | 4.27E-07 |
| rs7193671 | 16 | 85201484 | C | G | 0.045923 | 0.712696 | 0.009755 | 22.16238 | 2.51E-06 |
| rs75532121 | 17 | 56047927 | A | G | -0.14775 | 0.023983 | 0.030414 | 23.60008 | 1.19E-06 |
| rs28537992 | 17 | 79927531 | T | G | 0.072358 | 0.119478 | 0.013341 | 29.41557 | 5.84E-08 |
| rs140864352 | 18 | 14396062 | C | T | 0.136064 | 0.028486 | 0.025608 | 28.2307 | 1.08E-07 |
| rs554790528 | 18 | 26973074 | C | T | 0.099073 | 0.043397 | 0.021188 | 21.86389 | 2.93E-06 |
| rs1032916 | 18 | 77767543 | G | A | 0.045234 | 0.282091 | 0.009665 | 21.90601 | 2.86E-06 |
| rs9676730 | 19 | 32176163 | A | G | 0.044932 | 0.487821 | 0.008774 | 26.2247 | 3.04E-07 |
| rs7246984 | 19 | 33077764 | T | C | -0.06331 | 0.130289 | 0.013185 | 23.05669 | 1.57E-06 |
| rs67165745 | 19 | 47420724 | A | C | -0.124 | 0.03661 | 0.024379 | 25.87005 | 3.65E-07 |
| rs117549631 | 19 | 47988536 | T | C | -0.12964 | 0.034536 | 0.025164 | 26.54045 | 2.58E-07 |
| rs2425622 | 20 | 44149792 | G | A | 0.04584 | 0.574535 | 0.008908 | 26.48287 | 2.66E-07 |
| rs374283213 | 20 | 44672053 | T | C | 0.130455 | 0.026024 | 0.028225 | 21.36318 | 3.80E-06 |
| rs117296576 | 20 | 44697510 | A | T | 0.124031 | 0.035328 | 0.023284 | 28.37537 | 9.99E-08 |

*CHR chromosome, EA effect allele, OA other allele, EAF effect allele frequency, SE standard error.

Table S3. Heterogeneity and pleiotropy test in the primary MR analysis

| | UK Biobank | | | FinnGen | | |
|-----------------|--------------------------|-----------------|------------------------------------|--------------------------|-------------------|------------------------------------|
| | Cochran's Q test for IVW | Pleiotropy test | Global Test from MR-PRESSO results | Cochran's Q test for IVW | Pleiotropy test | Global Test from MR-PRESSO results |
| LDL | 1.55E-44 | 0.6794916 | < 0.001 | 4.60E-56 | 0.8970017 | < 0.001 |
| HDL | 7.71E-113 | 0.4352173 | < 0.001 | 9.94E-18 | 0.01004672 | 0.085 |
| TC | 1.04E-53 | 0.4356993 | < 0.001 | 2.27E-52 | 0.9150016 | < 0.001 |
| TG | 2.62E-192 | 0.6036673 | < 0.001 | 2.10E-25 | 0.01152794 | < 0.001 |
| Fasting Glucose | 0.1258829 | 0.5840239 | 0.241 | 0.1941064 | 0.06259374 | 0.706 |
| Fasting Insulin | 0.003960247 | 0.8520083 | 0.107 | 0.6700269 | 0.2420156 | 0.726 |
| HbA1C | 0.5202533 | 0.2311212 | 0.435 | 0.1941064 | 0.06259374 | 0.278 |

Value in bold means significant.

Serum lipid/glucose traits after cholecystectomy from observational and MR study

Table S4. IVs and Outliers in UK Biobank for lipid traits detected via RadialMR package

| | SNP | TC | LDL-C | HDL-C | TG |
|----|-------------|---------|---------|---------|---------|
| 1 | rs10199034 | Outlier | Outlier | Variant | Outlier |
| 2 | rs10799476 | Variant | Variant | Outlier | Variant |
| 3 | rs10882890 | Outlier | Variant | Variant | Variant |
| 4 | rs112634731 | Variant | Variant | Variant | Variant |
| 5 | rs113525652 | Outlier | Outlier | Variant | Outlier |
| 6 | rs11603634 | Outlier | Outlier | Outlier | Variant |
| 7 | rs116468765 | Outlier | Outlier | Variant | Variant |
| 8 | rs11686966 | Outlier | Outlier | Outlier | Outlier |
| 9 | rs1201467 | Variant | Variant | Variant | Variant |
| 10 | rs1208280 | Outlier | Outlier | Variant | Outlier |
| 11 | rs12369071 | Variant | Variant | Variant | Variant |
| 12 | rs13061117 | Variant | Variant | Variant | Variant |
| 13 | rs138776098 | Variant | Variant | Outlier | Variant |
| 14 | rs146652454 | Outlier | Variant | Variant | Variant |
| 15 | rs150844304 | Outlier | Variant | Outlier | Outlier |
| 16 | rs17138478 | Variant | Variant | Variant | Variant |
| 17 | rs1811515 | Outlier | Outlier | Variant | Variant |
| 18 | rs2107944 | Outlier | Outlier | Variant | Variant |
| 19 | rs2470048 | Variant | Variant | Variant | Outlier |
| 20 | rs28378706 | Variant | Variant | Outlier | Variant |
| 21 | rs28517482 | Outlier | Outlier | Variant | Outlier |
| 22 | rs2978388 | Variant | Variant | Variant | Variant |
| 23 | rs3094509 | Variant | Variant | Variant | Variant |
| 24 | rs332981 | Variant | Variant | Variant | Variant |
| 25 | rs3793770 | Outlier | Outlier | Variant | Variant |
| 26 | rs3862794 | Variant | Variant | Variant | Variant |
| 27 | rs41276920 | Outlier | Outlier | Outlier | Outlier |
| 28 | rs41281265 | Variant | Variant | Outlier | Outlier |
| 29 | rs4150336 | Outlier | Outlier | Outlier | Variant |
| 30 | rs4331955 | Variant | Variant | Variant | Variant |
| 31 | rs4346434 | Outlier | Outlier | Outlier | Outlier |
| 32 | rs4681516 | Outlier | Outlier | Variant | Outlier |
| 33 | rs4881744 | Variant | Variant | Variant | Variant |
| 34 | rs55780704 | Outlier | Outlier | Outlier | Outlier |
| 35 | rs55971546 | Variant | Variant | Variant | Variant |
| 36 | rs580477 | Outlier | Outlier | Variant | Variant |
| 37 | rs62090594 | Variant | Variant | Variant | Variant |
| 38 | rs698838 | Outlier | Variant | Outlier | Variant |
| 39 | rs714583 | Variant | Variant | Variant | Variant |
| 40 | rs72931779 | Outlier | Outlier | Outlier | Outlier |
| 41 | rs73192932 | Outlier | Outlier | Variant | Variant |
| 42 | rs7337432 | Variant | Variant | Variant | Variant |
| 43 | rs7564733 | Variant | Variant | Variant | Variant |
| 44 | rs76818081 | Variant | Variant | Outlier | Variant |
| 45 | rs76862077 | Variant | Variant | Variant | Variant |
| 46 | rs7993414 | Outlier | Outlier | Variant | Outlier |
| 47 | rs8077886 | Variant | Variant | Outlier | Outlier |
| 48 | rs932784 | Variant | Variant | Outlier | Variant |
| 49 | rs9371004 | Variant | Variant | Variant | Variant |
| 50 | rs9471953 | Variant | Variant | Variant | Variant |
| 51 | rs9544535 | Variant | Variant | Outlier | Outlier |
| 52 | rs9790309 | Variant | Variant | Outlier | Outlier |

Serum lipid/glucose traits after cholecystectomy from observational and MR study

Table S5. IVs and Outliers in FinnGen for lipid traits detected via RadialMR package

| | SNP | TC | LDL | HDL | TG |
|----|-------------|---------|---------|---------|---------|
| 1 | rs10208775 | Variant | Variant | Variant | Variant |
| 2 | rs1032916 | Variant | Variant | Variant | Variant |
| 3 | rs10831930 | Variant | Variant | Variant | Variant |
| 4 | rs11012722 | Variant | Variant | Outlier | Outlier |
| 5 | rs11023658 | Variant | Variant | Variant | Outlier |
| 6 | rs112266464 | Variant | Variant | Variant | Variant |
| 7 | rs113828886 | Variant | Variant | Variant | Variant |
| 8 | rs11690947 | Outlier | Outlier | Variant | Variant |
| 9 | rs11691443 | Outlier | Outlier | Variant | Variant |
| 10 | rs116979197 | Variant | Variant | Variant | Variant |
| 11 | rs117018004 | Variant | Variant | Variant | Variant |
| 12 | rs117296576 | Outlier | Variant | Outlier | Variant |
| 13 | rs117549631 | Outlier | Variant | Variant | Variant |
| 14 | rs117920913 | Variant | Variant | Outlier | Variant |
| 15 | rs12135720 | Variant | Variant | Variant | Variant |
| 16 | rs12154319 | Variant | Outlier | Variant | Variant |
| 17 | rs12470367 | Variant | Variant | Outlier | Outlier |
| 18 | rs12615717 | Variant | Variant | Variant | Variant |
| 19 | rs13104082 | Variant | Outlier | Outlier | Variant |
| 20 | rs13126112 | Variant | Variant | Variant | Variant |
| 21 | rs1320308 | Variant | Variant | Variant | Variant |
| 22 | rs13399179 | Variant | Variant | Outlier | Variant |
| 23 | rs13414085 | Outlier | Outlier | Variant | Variant |
| 24 | rs139199716 | Variant | Variant | Variant | Variant |
| 25 | rs140864352 | Variant | Variant | Variant | Variant |
| 26 | rs143949742 | Variant | Variant | Variant | Variant |
| 27 | rs145048510 | Variant | Variant | Variant | Variant |
| 28 | rs147037994 | Variant | Variant | Variant | Variant |
| 29 | rs150212157 | Variant | Variant | Variant | Variant |
| 30 | rs1502593 | Outlier | Outlier | Variant | Variant |
| 31 | rs1629928 | Variant | Variant | Variant | Variant |
| 32 | rs163520 | Variant | Variant | Variant | Variant |
| 33 | rs16891958 | Variant | Variant | Variant | Variant |
| 34 | rs16894137 | Variant | Variant | Outlier | Variant |
| 35 | rs16961281 | Outlier | Outlier | Variant | Outlier |
| 36 | rs17421328 | Outlier | Outlier | Outlier | Outlier |
| 37 | rs181090787 | Variant | Variant | Variant | Variant |
| 38 | rs182978364 | Variant | Variant | Variant | Variant |
| 39 | rs186890864 | Outlier | Outlier | Variant | Variant |
| 40 | rs187779008 | Variant | Variant | Variant | Variant |
| 41 | rs193067613 | Variant | Variant | Variant | Variant |
| 42 | rs2011896 | Outlier | Outlier | Variant | Variant |
| 43 | rs2016239 | Variant | Variant | Variant | Variant |
| 44 | rs2146990 | Outlier | Outlier | Variant | Outlier |
| 45 | rs2188251 | Outlier | Outlier | Variant | Outlier |
| 46 | rs2425622 | Variant | Variant | Outlier | Variant |
| 47 | rs2468191 | Variant | Variant | Variant | Outlier |

Serum lipid/glucose traits after cholecystectomy from observational and MR study

| | | | | | |
|----|-------------|---------|---------|---------|---------|
| 48 | rs263462 | Variant | Variant | Variant | Variant |
| 49 | rs28537992 | Outlier | Outlier | Variant | Variant |
| 50 | rs2921987 | Variant | Variant | Outlier | Variant |
| 51 | rs34997129 | Variant | Variant | Variant | Variant |
| 52 | rs35779873 | Variant | Variant | Variant | Variant |
| 53 | rs374283213 | Variant | Variant | Variant | Variant |
| 54 | rs375716154 | Variant | Variant | Variant | Variant |
| 55 | rs375844484 | Variant | Variant | Variant | Variant |
| 56 | rs3790843 | Variant | Variant | Variant | Variant |
| 57 | rs4629659 | Variant | Variant | Variant | Variant |
| 58 | rs4681199 | Variant | Variant | Outlier | Outlier |
| 59 | rs554790528 | Variant | Variant | Variant | Variant |
| 60 | rs556153 | Variant | Variant | Variant | Variant |
| 61 | rs55935092 | Outlier | Outlier | Outlier | Outlier |
| 62 | rs576479048 | Variant | Outlier | Variant | Variant |
| 63 | rs582384 | Variant | Variant | Variant | Variant |
| 64 | rs60851079 | Outlier | Outlier | Variant | Variant |
| 65 | rs61614759 | Outlier | Outlier | Variant | Variant |
| 66 | rs61898562 | Variant | Variant | Outlier | Outlier |
| 67 | rs62041381 | Variant | Variant | Variant | Variant |
| 68 | rs62140201 | Variant | Variant | Variant | Variant |
| 69 | rs62272019 | Outlier | Outlier | Variant | Outlier |
| 70 | rs6448619 | Outlier | Variant | Variant | Outlier |
| 71 | rs6584349 | Outlier | Variant | Outlier | Outlier |
| 72 | rs66498012 | Outlier | Outlier | Variant | Outlier |
| 73 | rs67165745 | Variant | Variant | Outlier | Variant |
| 74 | rs7039251 | Variant | Variant | Variant | Variant |
| 75 | rs7104956 | Outlier | Outlier | Variant | Variant |
| 76 | rs71420083 | Outlier | Outlier | Outlier | Variant |
| 77 | rs714582 | Variant | Variant | Variant | Variant |
| 78 | rs7193671 | Variant | Variant | Variant | Outlier |
| 79 | rs7246984 | Outlier | Outlier | Variant | Variant |
| 80 | rs72799962 | Variant | Variant | Variant | Outlier |
| 81 | rs730803 | Variant | Variant | Variant | Variant |
| 82 | rs73135307 | Variant | Variant | Variant | Outlier |
| 83 | rs73194916 | Outlier | Variant | Variant | Variant |
| 84 | rs735286 | Variant | Variant | Variant | Variant |
| 85 | rs74707612 | Variant | Variant | Variant | Variant |
| 86 | rs75120545 | Outlier | Outlier | Variant | Outlier |
| 87 | rs75128707 | Variant | Variant | Variant | Variant |
| 88 | rs75497660 | Variant | Variant | Variant | Variant |
| 89 | rs75532121 | Variant | Variant | Variant | Variant |
| 90 | rs75741381 | Variant | Variant | Outlier | Outlier |
| 91 | rs75745670 | Outlier | Outlier | Variant | Outlier |
| 92 | rs75841075 | Outlier | Outlier | Variant | Variant |
| 93 | rs76592665 | Variant | Variant | Variant | Variant |
| 94 | rs76726250 | Variant | Variant | Variant | Outlier |
| 95 | rs76733846 | Variant | Outlier | Variant | Variant |
| 96 | rs78686882 | Variant | Variant | Variant | Variant |

Serum lipid/glucose traits after cholecystectomy from observational and MR study

| | | | | | |
|-----|------------|---------|---------|---------|---------|
| 97 | rs78815523 | Variant | Variant | Variant | Variant |
| 98 | rs78956178 | Variant | Outlier | Variant | Variant |
| 99 | rs79348616 | Variant | Variant | Variant | Variant |
| 100 | rs79469600 | Variant | Variant | Variant | Variant |
| 101 | rs79478006 | Variant | Variant | Variant | Variant |
| 102 | rs79693383 | Variant | Variant | Variant | Variant |
| 103 | rs843372 | Outlier | Outlier | Outlier | Outlier |
| 104 | rs862135 | Variant | Variant | Variant | Variant |
| 105 | rs871962 | Variant | Variant | Variant | Variant |
| 106 | rs9396788 | Variant | Variant | Variant | Variant |
| 107 | rs9487939 | Variant | Variant | Variant | Outlier |
| 108 | rs9676730 | Variant | Variant | Variant | Variant |

Table S6. Heterogeneity and pleiotropy test in the repeated MR analysis for lipid traits after outlier removal

| | UK Biobank | | | FinnGen | | |
|-------|--------------------------|-----------------|------------------------------------|--------------------------|-----------------|------------------------------------|
| | Cochran's Q test for IVW | Pleiotropy test | Global Test from MR-PRESSO results | Cochran's Q test for IVW | Pleiotropy test | Global Test from MR-PRESSO results |
| LDL-C | 0.09579939 | 0.571592 | 0.102 | 0.6165756 | 0.3583751 | 0.458 |
| HDL-C | 0.5505367 | 0.5941352 | 0.0575 | 0.4749689 | 0.2541208 | 0.431 |
| TC | 0.08498349 | 0.4487776 | 0.104 | 0.6365185 | 0.8969529 | 0.564 |
| TG | 0.3341356 | 0.4445664 | 0.375 | 0.8091941 | 0.1992355 | 0.355 |

Serum lipid/glucose traits after cholecystectomy from observational and MR study

Table S7. Association between genetically predicted cholecystectomy and blood lipid traits in UK Biobank

| exposure | outcome | method | n SNP | b | se | pval | lo_ci | up_ci | or | or_lci95 | or_uci95 |
|-----------------|---------|---------------------------|-------|----------|----------|----------|----------|----------|----------|----------|----------|
| cholecystectomy | TC | MR Egger | 29 | 0.162857 | 0.407652 | 0.692668 | -0.63614 | 0.961855 | 1.176868 | 0.529331 | 2.616545 |
| cholecystectomy | TC | Weighted median | 29 | -0.0382 | 0.171731 | 0.823978 | -0.37479 | 0.298395 | 0.962522 | 0.687433 | 1.347694 |
| cholecystectomy | TC | Inverse variance weighted | 29 | -0.13296 | 0.133421 | 0.318985 | -0.39447 | 0.128545 | 0.8755 | 0.67404 | 1.137173 |
| cholecystectomy | TC | Simple mode | 29 | 0.41667 | 0.401746 | 0.308541 | -0.37075 | 1.204093 | 1.516902 | 0.690215 | 3.333733 |
| cholecystectomy | TC | Weighted mode | 29 | 0.272529 | 0.368446 | 0.465655 | -0.44962 | 0.994683 | 1.313282 | 0.637868 | 2.703868 |
| cholecystectomy | LDL-C | MR Egger | 32 | -0.07519 | 0.380244 | 0.844579 | -0.82047 | 0.670088 | 0.927566 | 0.440225 | 1.954409 |
| cholecystectomy | LDL-C | Weighted median | 32 | -0.17723 | 0.17479 | 0.310595 | -0.51982 | 0.165356 | 0.837585 | 0.594627 | 1.179813 |
| cholecystectomy | LDL-C | Inverse variance weighted | 32 | -0.27896 | 0.131508 | 0.033903 | -0.53671 | -0.0212 | 0.756573 | 0.584668 | 0.979022 |
| cholecystectomy | LDL-C | Simple mode | 32 | 0.085182 | 0.352448 | 0.810615 | -0.60562 | 0.77598 | 1.088915 | 0.545738 | 2.17272 |
| cholecystectomy | LDL-C | Weighted mode | 32 | -0.0551 | 0.37583 | 0.884391 | -0.79173 | 0.681527 | 0.946391 | 0.453062 | 1.976895 |
| cholecystectomy | HDL-C | MR Egger | 33 | -0.43975 | 0.351313 | 0.220031 | -1.12832 | 0.248824 | 0.644198 | 0.323575 | 1.282516 |
| cholecystectomy | HDL-C | Weighted median | 33 | -0.27597 | 0.158023 | 0.080747 | -0.58569 | 0.033759 | 0.758838 | 0.55672 | 1.034336 |
| cholecystectomy | HDL-C | Inverse variance weighted | 33 | -0.26024 | 0.11074 | 0.018773 | -0.47729 | -0.04319 | 0.770866 | 0.620462 | 0.95773 |
| cholecystectomy | HDL-C | Simple mode | 33 | -0.41373 | 0.32258 | 0.208862 | -1.04598 | 0.218531 | 0.661182 | 0.351346 | 1.244248 |
| cholecystectomy | HDL-C | Weighted mode | 33 | -0.37801 | 0.259028 | 0.154217 | -0.88571 | 0.129683 | 0.685222 | 0.412422 | 1.138467 |
| cholecystectomy | TG | MR Egger | 35 | 0.740345 | 0.307647 | 0.021866 | 0.137356 | 1.343334 | 2.096658 | 1.147237 | 3.831796 |
| cholecystectomy | TG | Weighted median | 35 | 0.611595 | 0.160558 | 0.000139 | 0.296902 | 0.926288 | 1.843369 | 1.345683 | 2.525119 |
| cholecystectomy | TG | Inverse variance weighted | 35 | 0.518493 | 0.110892 | 2.93E-06 | 0.301144 | 0.735842 | 1.679494 | 1.351404 | 2.087238 |
| cholecystectomy | TG | Simple mode | 35 | 0.775825 | 0.336486 | 0.027358 | 0.116313 | 1.435337 | 2.172384 | 1.123348 | 4.20106 |
| cholecystectomy | TG | Weighted mode | 35 | 0.727329 | 0.303211 | 0.022082 | 0.133035 | 1.321622 | 2.069544 | 1.14229 | 3.749499 |

Serum lipid/glucose traits after cholecystectomy from observational and MR study

Table S8. Association between genetically predicted cholecystectomy and blood lipid traits in FinnGen

| exposure | outcome | method | nsnp | b | se | pval | lo_ci | up_ci | or | or_lci95 | or_uci95 |
|-----------------|---------|---------------------------|------|----------|----------|----------|----------|-----------|----------|----------|----------|
| cholecystectomy | TC | MR Egger | 78 | -0.01007 | 0.005483 | 0.070091 | -0.02082 | 0.000673 | 0.989978 | 0.979397 | 1.000674 |
| cholecystectomy | TC | Weighted median | 78 | -0.00505 | 0.00518 | 0.329495 | -0.0152 | 0.005101 | 0.994962 | 0.984912 | 1.005114 |
| cholecystectomy | TC | Inverse variance weighted | 78 | -0.00948 | 0.003045 | 0.001849 | -0.01545 | -0.003512 | 0.990565 | 0.984671 | 0.996494 |
| cholecystectomy | TC | Simple mode | 78 | 0.00987 | 0.011596 | 0.39732 | -0.01286 | 0.032597 | 1.009919 | 0.987225 | 1.033134 |
| cholecystectomy | TC | Weighted mode | 78 | -0.0017 | 0.007792 | 0.828125 | -0.01697 | 0.013574 | 0.998304 | 0.983174 | 1.013667 |
| cholecystectomy | LDL-C | MR Egger | 77 | -0.01434 | 0.00582 | 0.016065 | -0.02574 | -0.002928 | 0.985767 | 0.974586 | 0.997076 |
| cholecystectomy | LDL-C | Weighted median | 77 | -0.0034 | 0.005264 | 0.517786 | -0.01372 | 0.006912 | 0.996602 | 0.986373 | 1.006936 |
| cholecystectomy | LDL-C | Inverse variance weighted | 77 | -0.00986 | 0.003224 | 0.00223 | -0.01618 | -0.003539 | 0.990191 | 0.983954 | 0.996467 |
| cholecystectomy | LDL-C | Simple mode | 77 | 0.002975 | 0.011985 | 0.804656 | -0.02052 | 0.026466 | 1.002979 | 0.979692 | 1.026819 |
| cholecystectomy | LDL-C | Weighted mode | 77 | 0.00116 | 0.008651 | 0.893708 | -0.0158 | 0.018116 | 1.00116 | 0.984328 | 1.018281 |
| cholecystectomy | HDL-C | MR Egger | 88 | -0.00025 | 0.005546 | 0.964164 | -0.01112 | 0.01062 | 0.99975 | 0.988942 | 1.010676 |
| cholecystectomy | HDL-C | Weighted median | 88 | -0.00252 | 0.004391 | 0.565337 | -0.01113 | 0.006082 | 0.997479 | 0.988931 | 1.0061 |
| cholecystectomy | HDL-C | Inverse variance weighted | 88 | -0.00567 | 0.002906 | 0.050862 | -0.01137 | 2.14E-05 | 0.994342 | 0.988694 | 1.000021 |
| cholecystectomy | HDL-C | Simple mode | 88 | 0.000406 | 0.009707 | 0.966748 | -0.01862 | 0.019431 | 1.000406 | 0.981553 | 1.019621 |
| cholecystectomy | HDL-C | Weighted mode | 88 | -0.00161 | 0.007697 | 0.835045 | -0.01669 | 0.013479 | 0.998394 | 0.983444 | 1.01357 |
| cholecystectomy | TG | MR Egger | 78 | -0.00789 | 0.008372 | 0.349189 | -0.0243 | 0.008523 | 0.992144 | 0.975996 | 1.00856 |
| cholecystectomy | TG | Weighted median | 78 | -0.00434 | 0.00501 | 0.386159 | -0.01416 | 0.005478 | 0.995668 | 0.985939 | 1.005493 |
| cholecystectomy | TG | Inverse variance weighted | 78 | 0.006904 | 0.004754 | 0.146367 | -0.00241 | 0.016221 | 1.006928 | 0.99759 | 1.016354 |
| cholecystectomy | TG | Simple mode | 78 | -0.00989 | 0.011363 | 0.38686 | -0.03216 | 0.012383 | 0.99016 | 0.96835 | 1.01246 |
| cholecystectomy | TG | Weighted mode | 78 | -0.00865 | 0.007863 | 0.274712 | -0.02406 | 0.006762 | 0.991387 | 0.976224 | 1.006785 |

Serum lipid/glucose traits after cholecystectomy from observational and MR study

Table S9. Association between genetically predicted cholecystectomy and blood glucose traits in UK Biobank

| exposure | outcome | method | n SNP | b | se | pval | lo_ci | up_ci | or | or_lci95 | or_uci95 |
|-----------------|-----------------|---------------------------|-------|----------|----------|----------|----------|----------|----------|----------|----------|
| cholecystectomy | Fasting Glucose | MR Egger | 19 | 1.022421 | 0.999849 | 0.320841 | -0.93728 | 2.982125 | 2.779917 | 0.391691 | 19.72969 |
| cholecystectomy | Fasting Glucose | Weighted median | 19 | 0.364355 | 0.475288 | 0.443321 | -0.56721 | 1.29592 | 1.439585 | 0.567105 | 3.654356 |
| cholecystectomy | Fasting Glucose | Inverse variance weighted | 19 | 0.5054 | 0.369058 | 0.170864 | -0.21795 | 1.228754 | 1.657649 | 0.804162 | 3.416971 |
| cholecystectomy | Fasting Glucose | Simple mode | 19 | -0.05876 | 0.857526 | 0.94613 | -1.73951 | 1.621996 | 0.942938 | 0.175607 | 5.063187 |
| cholecystectomy | Fasting Glucose | Weighted mode | 19 | 0.24792 | 0.556778 | 0.661429 | -0.84337 | 1.339205 | 1.281357 | 0.43026 | 3.81601 |
| cholecystectomy | Fasting Insulin | MR Egger | 19 | 0.338647 | 1.26738 | 0.792528 | -2.14542 | 2.822711 | 1.403048 | 0.117019 | 16.8224 |
| cholecystectomy | Fasting Insulin | Weighted median | 19 | 0.343181 | 0.491155 | 0.484725 | -0.61948 | 1.305844 | 1.409424 | 0.538223 | 3.690804 |
| cholecystectomy | Fasting Insulin | Inverse variance weighted | 19 | 0.116074 | 0.46202 | 0.801635 | -0.78949 | 1.021634 | 1.123079 | 0.454078 | 2.777729 |
| cholecystectomy | Fasting Insulin | Simple mode | 19 | 0.446577 | 1.103343 | 0.690431 | -1.71597 | 2.609129 | 1.562953 | 0.179788 | 13.58721 |
| cholecystectomy | Fasting Insulin | Weighted mode | 19 | 0.380697 | 0.560213 | 0.505431 | -0.71732 | 1.478715 | 1.463304 | 0.488058 | 4.387304 |
| cholecystectomy | HbA1c | MR Egger | 19 | 1.013599 | 0.910318 | 0.281009 | -0.77062 | 2.797822 | 2.755501 | 0.462725 | 16.40886 |
| cholecystectomy | HbA1c | Weighted median | 19 | 0.233157 | 0.503369 | 0.643226 | -0.75345 | 1.21976 | 1.26258 | 0.470742 | 3.386374 |
| cholecystectomy | HbA1c | Inverse variance weighted | 19 | -0.03074 | 0.348675 | 0.929749 | -0.71414 | 0.652663 | 0.969728 | 0.489612 | 1.92065 |
| cholecystectomy | HbA1c | Simple mode | 19 | -1.29551 | 0.919072 | 0.175705 | -3.09689 | 0.505868 | 0.273757 | 0.045189 | 1.658424 |
| cholecystectomy | HbA1c | Weighted mode | 19 | 0.421642 | 0.590219 | 0.484153 | -0.73519 | 1.578472 | 1.524463 | 0.479415 | 4.847542 |

Table S10. Association between genetically predicted cholecystectomy and blood glucose traits in FinnGen

| exposure | outcome | method | n SNP | b | se | pval | lo_ci | up_ci | or | or_lci95 | or_uci95 |
|-----------------|-----------------|---------------------------|-------|----------|----------|----------|----------|----------|----------|----------|----------|
| cholecystectomy | Fasting Glucose | MR Egger | 26 | 0.045313 | 0.034417 | 0.200406 | -0.02214 | 0.112769 | 1.046355 | 0.9781 | 1.119374 |
| cholecystectomy | Fasting Glucose | Weighted median | 26 | 0.023215 | 0.017837 | 0.193079 | -0.01175 | 0.058176 | 1.023487 | 0.988323 | 1.059902 |
| cholecystectomy | Fasting Glucose | Inverse variance weighted | 26 | 0.022497 | 0.01224 | 0.066064 | -0.00149 | 0.046488 | 1.022752 | 0.998508 | 1.047585 |
| cholecystectomy | Fasting Glucose | Simple mode | 26 | 0.050603 | 0.037215 | 0.186053 | -0.02234 | 0.123544 | 1.051905 | 0.977909 | 1.1315 |
| cholecystectomy | Fasting Glucose | Weighted mode | 26 | 0.052287 | 0.035195 | 0.149878 | -0.0167 | 0.121269 | 1.053678 | 0.983443 | 1.128929 |
| cholecystectomy | Fasting Insulin | MR Egger | 26 | 0.045187 | 0.034652 | 0.204604 | -0.02273 | 0.113105 | 1.046223 | 0.977524 | 1.11975 |
| cholecystectomy | Fasting Insulin | Weighted median | 26 | 0.001597 | 0.01769 | 0.928048 | -0.03308 | 0.036271 | 1.001599 | 0.967465 | 1.036936 |
| cholecystectomy | Fasting Insulin | Inverse variance weighted | 26 | 0.00632 | 0.012288 | 0.607033 | -0.01776 | 0.030404 | 1.00634 | 0.982392 | 1.030871 |
| cholecystectomy | Fasting Insulin | Simple mode | 26 | 0.002309 | 0.033902 | 0.946233 | -0.06414 | 0.068756 | 1.002312 | 0.937876 | 1.071175 |
| cholecystectomy | Fasting Insulin | Weighted mode | 26 | 0.010934 | 0.026711 | 0.685768 | -0.04142 | 0.063287 | 1.010994 | 0.959427 | 1.065332 |
| cholecystectomy | HbA1c | MR Egger | 24 | 0.075444 | 0.040394 | 0.075181 | -0.00373 | 0.154616 | 1.078363 | 0.996279 | 1.167209 |
| cholecystectomy | HbA1c | Weighted median | 24 | 0.020503 | 0.018968 | 0.279749 | -0.01668 | 0.057681 | 1.020714 | 0.983463 | 1.059377 |
| cholecystectomy | HbA1c | Inverse variance weighted | 24 | 0.001359 | 0.015184 | 0.928699 | -0.0284 | 0.031119 | 1.00136 | 0.971998 | 1.031608 |
| cholecystectomy | HbA1c | Simple mode | 24 | 0.01519 | 0.034903 | 0.667465 | -0.05322 | 0.083601 | 1.015306 | 0.948171 | 1.087195 |
| cholecystectomy | HbA1c | Weighted mode | 24 | 0.020044 | 0.027626 | 0.475447 | -0.0341 | 0.074191 | 1.020246 | 0.966471 | 1.077012 |

Serum lipid/glucose traits after cholecystectomy from observational and MR study

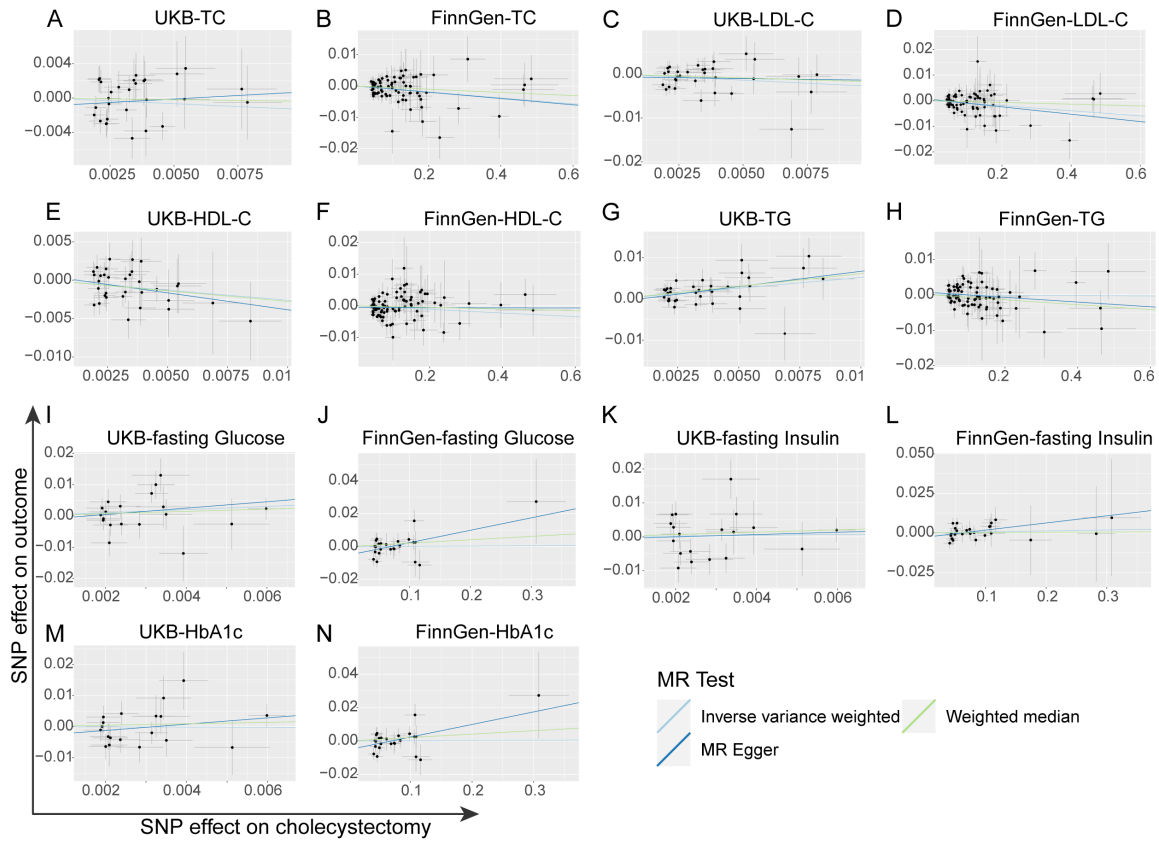
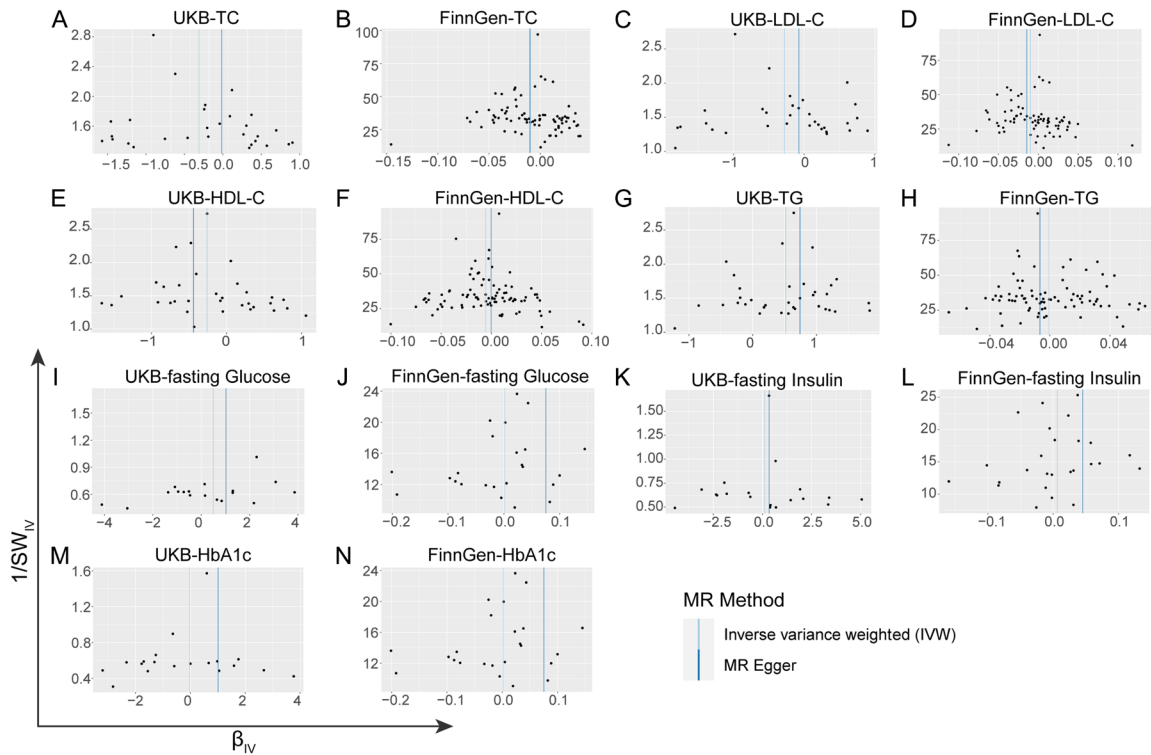


Figure S1. Scatter plots of MR results from UK biobank and FinnGen datasets. Abbreviations: UKB, UK biobank; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; HbA1c, hemoglobin A1c; IVW method, Inverse Variance Weighted method; MR, Mendelian randomization; SNP, single nucleotide polymorphism.



Serum lipid/glucose traits after cholecystectomy from observational and MR study

Figure S2. Funnel plots of MR results from UK biobank and FinnGen datasets. Abbreviations: UKB, UK biobank; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; HbA1c, hemoglobin A1c; IVW method, Inverse Variance Weighted method; MR, Mendelian randomization; SNP, single nucleotide polymorphism.

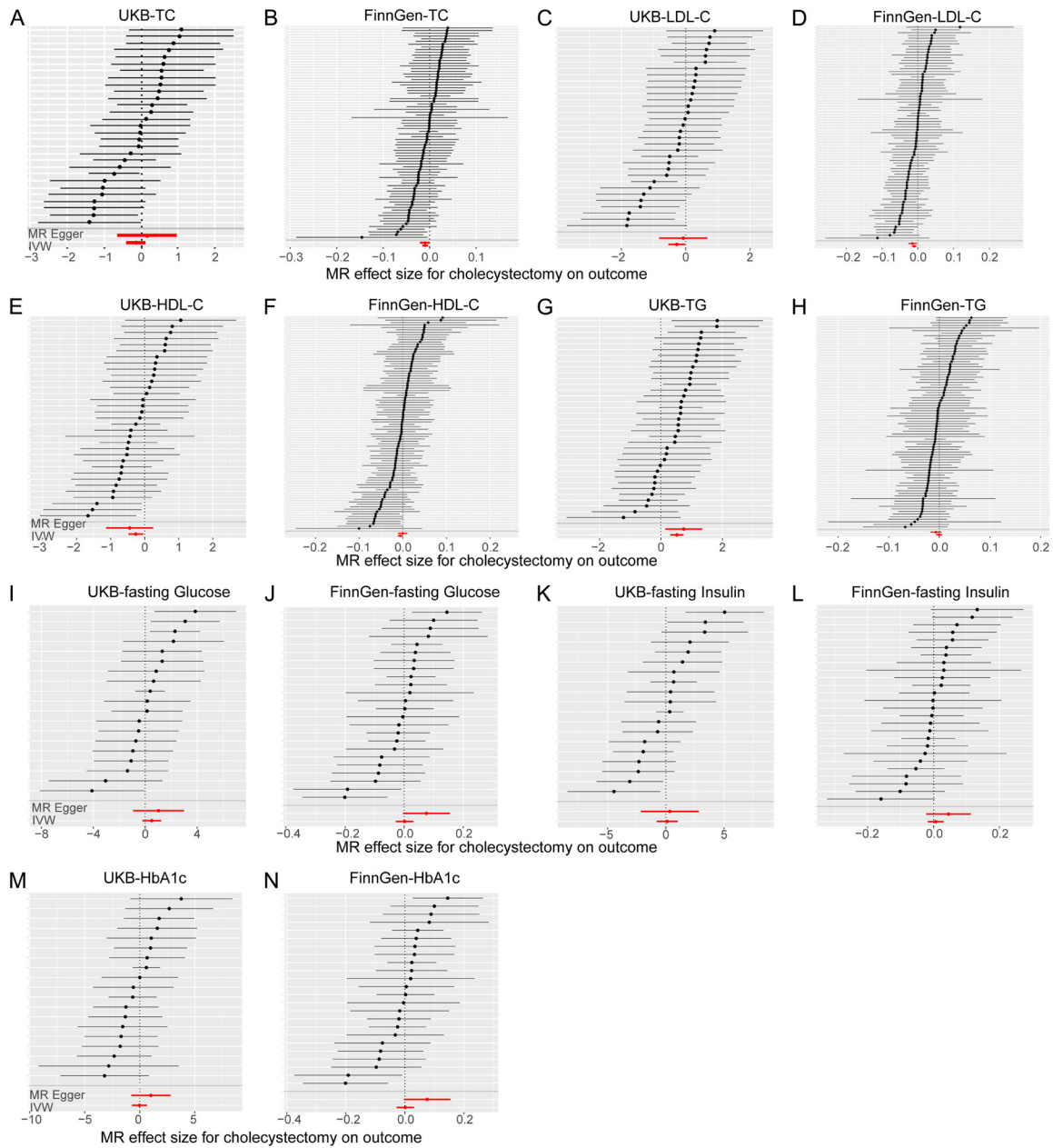


Figure S3. Forest plots of MR results from UK biobank and FinnGen datasets. Abbreviations: UKB, UK biobank; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; HbA1c, hemoglobin A1c; IVW method, Inverse Variance Weighted method; MR, Mendelian randomization; SNP, single nucleotide polymorphism.

Serum lipid/glucose traits after cholecystectomy from observational and MR study

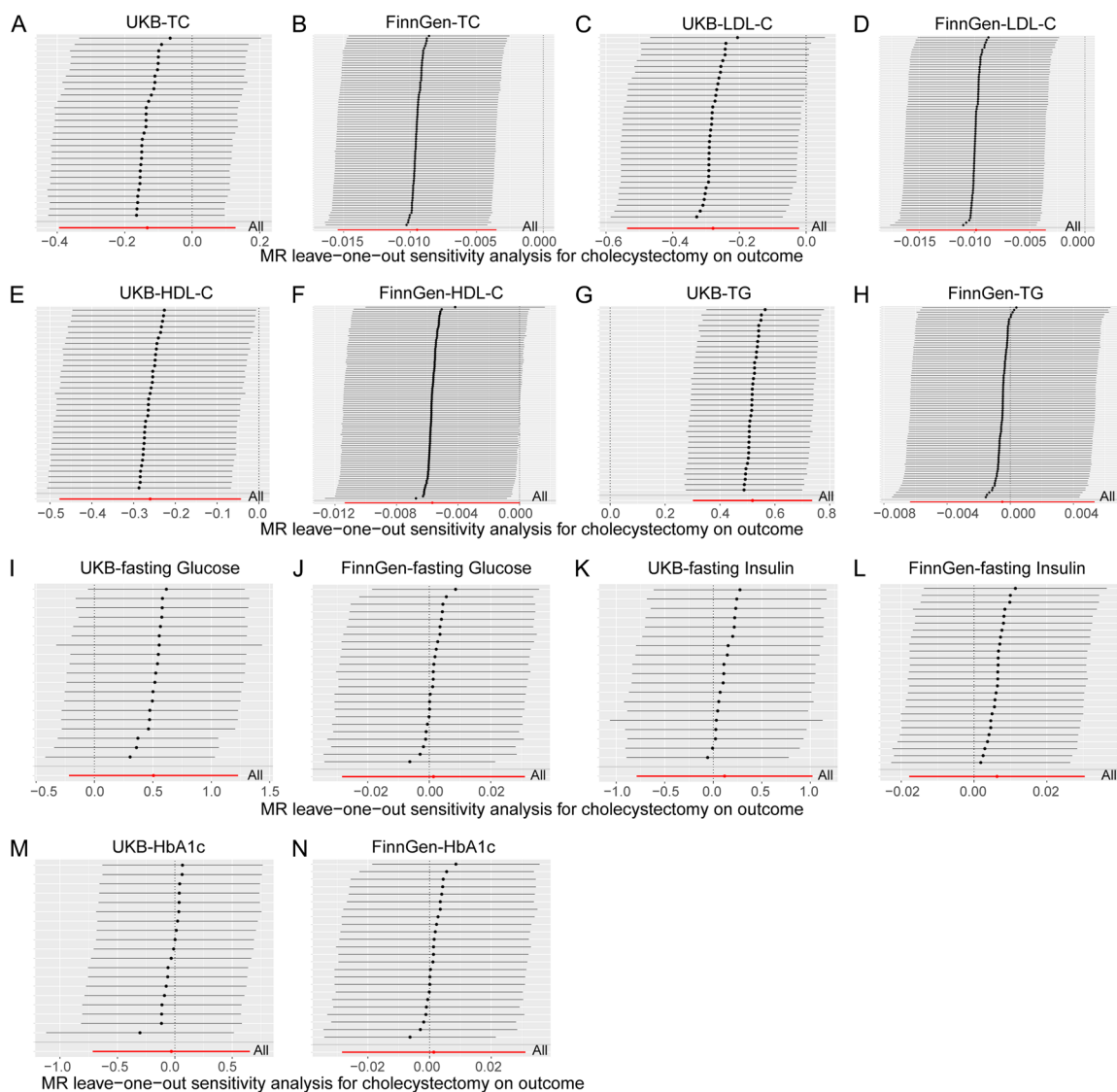


Figure S4. Leave-one-out plots of MR results from UK biobank and FinnGen datasets. Abbreviations: UKB, UK bio-bank; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; HbA1c, hemoglobin A1c; IVW method, Inverse Variance Weighted method; MR, Mendelian randomization; SNP, single nucleotide polymorphism.

Table S11. Results of heterogeneity test to combine Mendelian randomization estimates.

| Source | Estimates | I ² statistic | Q statistic | Specific Model |
|--------|-----------------|--------------------------|-------------|---------------------|
| GCLC | LDL | 0.761 | 0.0408 | Random-effect model |
| GCLC | HDL | 0.811 | 0.0216 | Random-effect model |
| GCLC | TC | 0 | 0.3548 | Common-effect model |
| GCLC | TG | 0.953 | < 0.0001 | Random-effect model |
| MAGIC | Fasting Glucose | 0.415 | 0.191 | Common-effect model |
| MAGIC | Fasting Insulin | 0 | 0.8123 | Common-effect model |
| MAGIC | HbA1C | 0 | 0.9267 | Common-effect model |