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Supplementary tables

Table S1: Association of known urate SNPs ¹ with uric acid in LURIC

| | Gene | Effect allele | EAF | Beta | SE | Pval | Rsqr | Variance explained |
|-----------------------------|------------------|---------------|------|--------|-------|----------|-------|--------------------|
| <i>Non-pleiotropic SNPs</i> | | | | | | | | |
| rs12498742 | <i>SLC2A9</i> | A | 0.77 | 0.295 | 0.051 | 9.92E-09 | - | 1.069% |
| rs478607 | <i>NRXN2</i> | G | 0.15 | 0.06 | 0.061 | 0.324 | 0.997 | 0.032% |
| rs1394125 | <i>UBE2Q2</i> | A | 0.35 | 0.065 | 0.045 | 0.151 | 0.778 | 0.068% |
| rs10821905 | <i>AICF</i> | A | 0.17 | 0.058 | 0.056 | 0.303 | 0.948 | 0.035% |
| rs7188445 | <i>MAF</i> | G | 0.65 | 0.04 | 0.046 | 0.386 | - | 0.025% |
| rs6770152 | <i>SFMBT1</i> | G | 0.42 | 0.022 | 0.043 | 0.612 | 0.999 | 0.008% |
| rs7224610 | <i>HLF</i> | C | 0.42 | 0.017 | 0.044 | 0.693 | 0.997 | 0.005% |
| rs1178977 | <i>BAZ1B</i> | A | 0.83 | 0.007 | 0.057 | 0.906 | 0.95 | 0.001% |
| rs17786744 | <i>STC1</i> | G | 0.41 | -0.023 | 0.044 | 0.6 | 0.985 | 0.009% |
| rs2941484 | <i>HNF4G</i> | T | 0.44 | -0.027 | 0.044 | 0.536 | 0.978 | 0.013% |
| rs653178 | <i>ATXN2</i> | C | 0.54 | -0.035 | 0.043 | 0.417 | 0.998 | 0.022% |
| rs7953704 | <i>B3GNT4</i> | G | 0.54 | -0.017 | 0.043 | 0.697 | 0.966 | 0.005% |
| rs6598541 | <i>IGF1R</i> | A | 0.38 | -0.028 | 0.045 | 0.53 | 0.961 | 0.013% |
| rs7193778 | <i>NFAT5</i> | C | 0.12 | -0.035 | 0.065 | 0.593 | - | 0.009% |
| <i>Pleiotropic SNPs</i> | | | | | | | | |
| rs2231142 | <i>ABCG2</i> | T | 0.11 | 0.177 | 0.068 | 0.01 | 0.954 | 0.220% |
| rs1260326 | <i>GCKR</i> | T | 0.43 | 0.107 | 0.044 | 0.014 | 0.98 | 0.195% |
| rs17632159 | <i>TMEM171</i> | G | 0.7 | 0.101 | 0.046 | 0.029 | 0.981 | 0.155% |
| rs1171614 | <i>SLC16A9</i> | C | 0.88 | 0.081 | 0.066 | 0.222 | 0.559 | 0.049% |
| rs17050272 | <i>INHBB</i> | A | 0.48 | 0.058 | 0.044 | 0.185 | 0.685 | 0.057% |
| rs675209 | <i>RREB1</i> | T | 0.27 | 0.053 | 0.049 | 0.273 | 0.898 | 0.039% |
| rs1165151 | <i>SLC17A1</i> | G | 0.5 | 0.052 | 0.043 | 0.226 | 0.995 | 0.048% |
| rs1471633 | <i>PDZK1</i> | A | 0.9 | 0.036 | 0.071 | 0.609 | 0.987 | 0.009% |
| rs3741414 | <i>INHBC</i> | C | 0.76 | 0.034 | 0.051 | 0.51 | 0.84 | 0.014% |
| rs2078267 | <i>SLC22A11</i> | C | 0.5 | 0.023 | 0.043 | 0.59 | - | 0.010% |
| rs7976059 | <i>ACVR1B-L1</i> | T | 0.34 | 0.016 | 0.046 | 0.732 | 0.896 | 0.004% |
| rs729761 | <i>VEGFA</i> | G | 0.73 | -0.015 | 0.05 | 0.768 | - | 0.003% |
| rs11264341 | <i>TRIM46</i> | C | 0.89 | -0.033 | 0.068 | 0.624 | 0.809 | 0.008% |
| rs10480300 | <i>PRKAG2</i> | T | 0.29 | -0.041 | 0.047 | 0.39 | 0.992 | 0.024% |
| GRS ₂₈ | - | - | - | 0.751 | 0.107 | 3.43E-12 | - | 1.574% |
| GRS ₁₄ | - | - | - | 0.713 | 0.128 | 3.15E-08 | - | 0.997% |
| GRS ₈ | - | - | - | 0.814 | 0.132 | 8.30E-10 | - | 1.226% |

EAF: effect allele frequency; GRS: genetic risk score; Rsqr: measure of imputation quality for imputed SNPs

Table S2: Association of urate SNPs with other phenotypes

| SNP | CHR | Effect _Allele | LDL-C | | | HDL-C | | | TC | | | TG | | |
|------------|-----|-------------------|--------|-------|-----------------|--------|-------|----------|--------|-------|-----------------|--------|-------|-----------------|
| | | | BETA | SE | P | BETA | SE | P | BETA | SE | P | BETA | SE | P |
| rs1471633 | 1 | A | 1.454 | 1.443 | 3.14E-01 | -0.121 | 0.452 | 7.89E-01 | 1.330 | 1.639 | 4.17E-01 | -0.005 | 0.020 | 8.17E-01 |
| rs11264341 | 1 | T | 4.070 | 1.389 | 3.43E-03 | 0.305 | 0.436 | 4.85E-01 | 1.471 | 1.580 | 3.52E-01 | -0.008 | 0.020 | 6.99E-01 |
| rs1260326 | 2 | T | -1.120 | 0.895 | 2.11E-01 | 0.101 | 0.281 | 7.19E-01 | 0.399 | 1.016 | 6.95E-01 | 0.073 | 0.013 | 6.26E-09 |
| rs17050272 | 2 | A | -3.850 | 0.897 | 1.82E-05 | -0.284 | 0.282 | 3.14E-01 | -2.757 | 1.021 | 6.95E-03 | 0.021 | 0.013 | 1.02E-01 |
| rs6770152 | 3 | G | -1.147 | 0.889 | 1.97E-01 | -0.076 | 0.279 | 7.84E-01 | -1.350 | 1.010 | 1.82E-01 | -0.008 | 0.013 | 5.34E-01 |
| rs12498742 | 4 | G | -0.579 | 1.055 | 5.83E-01 | 0.178 | 0.331 | 5.91E-01 | -1.459 | 1.198 | 2.23E-01 | -0.011 | 0.015 | 4.68E-01 |
| rs2231142 | 4 | T | -2.339 | 1.394 | 9.34E-02 | 0.477 | 0.437 | 2.75E-01 | -1.829 | 1.584 | 2.48E-01 | -0.014 | 0.020 | 4.79E-01 |
| rs17632159 | 5 | C | -0.398 | 0.950 | 6.76E-01 | 0.052 | 0.298 | 8.62E-01 | 0.189 | 1.079 | 8.61E-01 | 0.009 | 0.013 | 5.24E-01 |
| rs675209 | 6 | T | -0.927 | 0.993 | 3.51E-01 | -0.574 | 0.311 | 6.52E-02 | -2.292 | 1.127 | 4.21E-02 | -0.004 | 0.014 | 7.88E-01 |
| rs1165151 | 6 | G | 0.041 | 0.880 | 9.63E-01 | -0.176 | 0.276 | 5.24E-01 | 0.229 | 0.999 | 8.19E-01 | 0.013 | 0.012 | 3.09E-01 |
| rs729761 | 6 | T | 1.341 | 1.012 | 1.85E-01 | -0.152 | 0.317 | 6.32E-01 | 0.689 | 1.150 | 5.49E-01 | 0.001 | 0.014 | 9.36E-01 |
| rs1178977 | 7 | G | 1.475 | 1.172 | 2.09E-01 | 0.012 | 0.368 | 9.75E-01 | -0.179 | 1.332 | 8.93E-01 | -0.019 | 0.017 | 2.59E-01 |
| rs10480300 | 7 | T | 0.022 | 0.969 | 9.82E-01 | -0.092 | 0.304 | 7.62E-01 | -0.792 | 1.100 | 4.72E-01 | 0.002 | 0.014 | 8.62E-01 |
| rs17786744 | 8 | G | 0.511 | 0.898 | 5.70E-01 | -0.180 | 0.282 | 5.23E-01 | 1.085 | 1.020 | 2.88E-01 | 0.009 | 0.013 | 4.77E-01 |
| rs2941484 | 8 | T | -0.831 | 0.889 | 3.50E-01 | -0.184 | 0.279 | 5.08E-01 | -0.976 | 1.010 | 3.34E-01 | -0.001 | 0.013 | 9.19E-01 |
| rs10821905 | 10 | A | -0.173 | 1.153 | 8.81E-01 | 0.164 | 0.362 | 6.50E-01 | -0.241 | 1.310 | 8.54E-01 | -0.003 | 0.016 | 8.55E-01 |
| rs1171614 | 10 | T | -0.607 | 1.353 | 6.54E-01 | -0.305 | 0.424 | 4.73E-01 | -0.352 | 1.537 | 8.19E-01 | -0.009 | 0.019 | 6.36E-01 |
| rs2078267 | 11 | C | 0.121 | 0.875 | 8.90E-01 | 0.411 | 0.274 | 1.34E-01 | 0.136 | 0.994 | 8.91E-01 | -0.013 | 0.012 | 2.91E-01 |
| rs478607 | 11 | G | 0.426 | 1.240 | 7.32E-01 | 0.015 | 0.389 | 9.70E-01 | -0.145 | 1.409 | 9.18E-01 | -0.003 | 0.017 | 8.78E-01 |
| rs7976059 | 12 | T | -0.646 | 0.939 | 4.92E-01 | 0.155 | 0.294 | 5.99E-01 | -0.349 | 1.067 | 7.44E-01 | -0.011 | 0.013 | 3.90E-01 |
| rs3741414 | 12 | T | 0.223 | 1.040 | 8.30E-01 | 0.101 | 0.326 | 7.56E-01 | 0.313 | 1.180 | 7.91E-01 | 0.020 | 0.015 | 1.64E-01 |
| rs653178 | 12 | T | -0.105 | 0.876 | 9.04E-01 | 0.373 | 0.275 | 1.75E-01 | 0.325 | 0.995 | 7.44E-01 | -0.006 | 0.012 | 6.51E-01 |
| rs7953704 | 12 | A | -0.591 | 0.883 | 5.03E-01 | -0.230 | 0.277 | 4.06E-01 | -1.422 | 1.003 | 1.57E-01 | 0.003 | 0.012 | 8.33E-01 |
| rs1394125 | 15 | A | -0.399 | 0.929 | 6.68E-01 | -0.104 | 0.291 | 7.22E-01 | 0.169 | 1.055 | 8.73E-01 | 0.016 | 0.013 | 2.17E-01 |
| rs6598541 | 15 | A | -1.014 | 0.912 | 2.67E-01 | 0.018 | 0.286 | 9.50E-01 | -1.033 | 1.036 | 3.19E-01 | -0.007 | 0.013 | 6.00E-01 |

| | | | | | | | | | | | | | | |
|-----------|----|---|--------|-------|----------|--------|-------|----------|--------|-------|----------|--------|-------|----------|
| rs7193778 | 16 | C | 2.170 | 1.333 | 1.04E-01 | -0.256 | 0.418 | 5.41E-01 | 1.105 | 1.514 | 4.66E-01 | -0.018 | 0.019 | 3.38E-01 |
| rs7188445 | 16 | A | -0.701 | 0.934 | 4.53E-01 | -0.300 | 0.293 | 3.05E-01 | -0.764 | 1.060 | 4.72E-01 | -0.001 | 0.013 | 9.15E-01 |
| rs7224610 | 17 | C | 1.353 | 0.890 | 1.29E-01 | -0.039 | 0.279 | 8.88E-01 | 0.533 | 1.011 | 5.98E-01 | -0.006 | 0.013 | 6.07E-01 |

| SNP | CHR | Effect_ Allele | BMI | | | FGLU | | | FINS | | | GGT | | |
|------------|-----|-------------------|--------|-------|-----------------|--------|-------|-----------------|--------|-------|-----------------|--------|-------|-----------------|
| | | | BETA | SE | P | BETA | SE | P | BETA | SE | P | BETA | SE | P |
| rs1471633 | 1 | A | 0.042 | 0.169 | 8.03E-01 | -0.016 | 0.010 | 1.13E-01 | -0.073 | 0.028 | 1.00E-02 | -0.045 | 0.034 | 1.84E-01 |
| rs11264341 | 1 | T | 0.024 | 0.163 | 8.83E-01 | 0.017 | 0.010 | 8.27E-02 | 0.025 | 0.027 | 3.68E-01 | 0.010 | 0.033 | 7.51E-01 |
| rs1260326 | 2 | T | -0.007 | 0.105 | 9.46E-01 | -0.010 | 0.006 | 1.18E-01 | -0.012 | 0.018 | 4.92E-01 | 0.051 | 0.021 | 1.53E-02 |
| rs17050272 | 2 | A | -0.093 | 0.105 | 3.76E-01 | -0.007 | 0.006 | 2.99E-01 | -0.014 | 0.018 | 4.36E-01 | 0.038 | 0.021 | 6.74E-02 |
| rs6770152 | 3 | G | -0.031 | 0.104 | 7.63E-01 | 0.003 | 0.006 | 6.29E-01 | -0.001 | 0.018 | 9.57E-01 | 0.002 | 0.021 | 9.32E-01 |
| rs12498742 | 4 | G | 0.060 | 0.123 | 6.25E-01 | -0.004 | 0.008 | 6.26E-01 | 0.007 | 0.021 | 7.47E-01 | 0.006 | 0.025 | 7.97E-01 |
| rs2231142 | 4 | T | -0.327 | 0.163 | 4.48E-02 | -0.020 | 0.010 | 4.99E-02 | -0.049 | 0.027 | 7.40E-02 | -0.060 | 0.033 | 6.39E-02 |
| rs17632159 | 5 | C | -0.056 | 0.111 | 6.12E-01 | 0.008 | 0.007 | 2.69E-01 | -0.011 | 0.019 | 5.57E-01 | -0.008 | 0.022 | 7.35E-01 |
| rs675209 | 6 | T | -0.082 | 0.116 | 4.80E-01 | 0.003 | 0.007 | 6.53E-01 | 0.009 | 0.020 | 6.40E-01 | -0.036 | 0.023 | 1.22E-01 |
| rs1165151 | 6 | G | 0.052 | 0.103 | 6.12E-01 | 0.004 | 0.006 | 5.49E-01 | 0.031 | 0.017 | 7.73E-02 | 0.033 | 0.021 | 1.08E-01 |
| rs729761 | 6 | T | -0.029 | 0.118 | 8.04E-01 | 0.015 | 0.007 | 3.69E-02 | 0.004 | 0.020 | 8.41E-01 | 0.003 | 0.024 | 8.89E-01 |
| rs1178977 | 7 | G | 0.231 | 0.137 | 9.16E-02 | 0.001 | 0.008 | 8.92E-01 | 0.041 | 0.023 | 7.82E-02 | -0.035 | 0.027 | 1.98E-01 |
| rs10480300 | 7 | T | 0.240 | 0.113 | 3.42E-02 | 0.016 | 0.007 | 1.89E-02 | 0.030 | 0.019 | 1.20E-01 | -0.025 | 0.023 | 2.65E-01 |
| rs17786744 | 8 | G | 0.021 | 0.105 | 8.38E-01 | 0.003 | 0.006 | 6.58E-01 | 0.004 | 0.018 | 8.21E-01 | 0.002 | 0.021 | 9.09E-01 |
| rs2941484 | 8 | T | -0.145 | 0.104 | 1.62E-01 | 0.004 | 0.006 | 5.13E-01 | -0.013 | 0.018 | 4.54E-01 | -0.025 | 0.021 | 2.30E-01 |
| rs10821905 | 10 | A | -0.032 | 0.135 | 8.12E-01 | 0.007 | 0.008 | 4.28E-01 | 0.018 | 0.023 | 4.23E-01 | -0.025 | 0.027 | 3.61E-01 |
| rs1171614 | 10 | T | 0.138 | 0.158 | 3.81E-01 | -0.001 | 0.010 | 9.52E-01 | 0.017 | 0.027 | 5.12E-01 | 0.014 | 0.032 | 6.56E-01 |
| rs2078267 | 11 | C | -0.055 | 0.102 | 5.93E-01 | 0.009 | 0.006 | 1.40E-01 | 0.000 | 0.017 | 9.91E-01 | 0.017 | 0.020 | 3.98E-01 |
| rs478607 | 11 | G | -0.177 | 0.145 | 2.22E-01 | 0.006 | 0.009 | 5.10E-01 | 0.008 | 0.024 | 7.56E-01 | 0.049 | 0.029 | 9.31E-02 |
| rs7976059 | 12 | T | -0.172 | 0.110 | 1.17E-01 | -0.008 | 0.007 | 2.54E-01 | -0.039 | 0.019 | 3.58E-02 | -0.005 | 0.022 | 8.03E-01 |

| | | | | | | | | | | | | | | |
|-----------|----|---|--------|-------|-----------------|--------|-------|----------|--------|-------|----------|--------|-------|----------|
| rs3741414 | 12 | T | 0.275 | 0.121 | 2.36E-02 | 0.011 | 0.007 | 1.27E-01 | 0.023 | 0.020 | 2.61E-01 | -0.008 | 0.024 | 7.47E-01 |
| rs653178 | 12 | T | 0.133 | 0.102 | 1.94E-01 | -0.006 | 0.006 | 3.02E-01 | 0.001 | 0.017 | 9.31E-01 | 0.003 | 0.020 | 8.67E-01 |
| rs7953704 | 12 | A | 0.059 | 0.103 | 5.68E-01 | 0.006 | 0.006 | 3.77E-01 | 0.019 | 0.017 | 2.77E-01 | -0.001 | 0.021 | 9.78E-01 |
| rs1394125 | 15 | A | 0.090 | 0.108 | 4.07E-01 | -0.004 | 0.007 | 5.00E-01 | 0.002 | 0.018 | 9.08E-01 | 0.009 | 0.022 | 6.67E-01 |
| rs6598541 | 15 | A | 0.186 | 0.107 | 8.11E-02 | 0.007 | 0.007 | 2.73E-01 | 0.003 | 0.018 | 8.50E-01 | 0.000 | 0.021 | 9.90E-01 |
| rs7193778 | 16 | C | 0.093 | 0.156 | 5.51E-01 | 0.011 | 0.010 | 2.44E-01 | -0.036 | 0.026 | 1.69E-01 | 0.013 | 0.031 | 6.80E-01 |
| rs7188445 | 16 | A | -0.004 | 0.109 | 9.69E-01 | 0.000 | 0.007 | 1.00E+00 | -0.012 | 0.018 | 5.04E-01 | -0.009 | 0.022 | 6.88E-01 |
| rs7224610 | 17 | C | -0.037 | 0.104 | 7.20E-01 | -0.009 | 0.006 | 1.48E-01 | -0.029 | 0.018 | 9.70E-02 | -0.028 | 0.021 | 1.85E-01 |

| SNP | CHR | Effect_Allele | SBP | | | DBP | | | hsCRP | | |
|------------|-----|---------------|--------|-------|-----------------|--------|-------|-----------------|--------|-------|----------|
| | | | BETA | SE | P | BETA | SE | P | BETA | SE | P |
| rs1471633 | 1 | A | -0.278 | 0.987 | 7.78E-01 | 0.216 | 0.478 | 6.52E-01 | -0.015 | 0.056 | 7.83E-01 |
| rs11264341 | 1 | T | -0.487 | 0.952 | 6.09E-01 | -0.450 | 0.461 | 3.29E-01 | -0.002 | 0.054 | 9.76E-01 |
| rs1260326 | 2 | T | 0.561 | 0.612 | 3.60E-01 | 0.382 | 0.296 | 1.97E-01 | 0.058 | 0.035 | 9.54E-02 |
| rs17050272 | 2 | A | -0.765 | 0.615 | 2.14E-01 | -0.542 | 0.298 | 6.91E-02 | 0.053 | 0.035 | 1.27E-01 |
| rs6770152 | 3 | G | -0.654 | 0.608 | 2.82E-01 | -0.055 | 0.295 | 8.53E-01 | 0.028 | 0.034 | 4.18E-01 |
| rs12498742 | 4 | G | 0.373 | 0.721 | 6.05E-01 | 0.417 | 0.350 | 2.32E-01 | 0.038 | 0.041 | 3.49E-01 |
| rs2231142 | 4 | T | 0.013 | 0.954 | 9.89E-01 | -0.041 | 0.462 | 9.29E-01 | -0.081 | 0.054 | 1.35E-01 |
| rs17632159 | 5 | C | -1.529 | 0.649 | 1.86E-02 | -0.918 | 0.314 | 3.53E-03 | 0.064 | 0.037 | 8.32E-02 |
| rs675209 | 6 | T | -0.502 | 0.679 | 4.60E-01 | -0.652 | 0.329 | 4.74E-02 | -0.005 | 0.038 | 8.97E-01 |
| rs1165151 | 6 | G | -1.384 | 0.601 | 2.14E-02 | -0.609 | 0.291 | 3.65E-02 | 0.013 | 0.034 | 7.10E-01 |
| rs729761 | 6 | T | 1.086 | 0.692 | 1.17E-01 | 0.243 | 0.335 | 4.69E-01 | 0.007 | 0.039 | 8.61E-01 |
| rs1178977 | 7 | G | -0.945 | 0.802 | 2.39E-01 | -0.253 | 0.389 | 5.15E-01 | -0.064 | 0.045 | 1.59E-01 |
| rs10480300 | 7 | T | 1.450 | 0.662 | 2.86E-02 | 0.727 | 0.321 | 2.35E-02 | 0.035 | 0.037 | 3.56E-01 |
| rs17786744 | 8 | G | -0.659 | 0.614 | 2.83E-01 | -0.335 | 0.298 | 2.60E-01 | 0.058 | 0.035 | 9.63E-02 |
| rs2941484 | 8 | T | 0.465 | 0.608 | 4.44E-01 | 0.245 | 0.295 | 4.05E-01 | 0.023 | 0.034 | 5.10E-01 |
| rs10821905 | 10 | A | -0.018 | 0.789 | 9.81E-01 | 0.129 | 0.382 | 7.36E-01 | -0.002 | 0.045 | 9.69E-01 |
| rs1171614 | 10 | T | -2.024 | 0.924 | 2.87E-02 | -0.739 | 0.448 | 9.92E-02 | -0.010 | 0.052 | 8.45E-01 |

| | | | | | | | | | | | |
|-----------|----|---|--------|-------|-----------------|--------|-------|----------|--------|-------|----------|
| rs2078267 | 11 | C | 1.227 | 0.598 | 4.02E-02 | 0.476 | 0.290 | 1.01E-01 | 0.023 | 0.034 | 5.05E-01 |
| rs478607 | 11 | G | 0.479 | 0.848 | 5.73E-01 | -0.099 | 0.411 | 8.09E-01 | 0.048 | 0.048 | 3.19E-01 |
| rs7976059 | 12 | T | 0.035 | 0.642 | 9.56E-01 | -0.272 | 0.311 | 3.82E-01 | 0.038 | 0.036 | 2.97E-01 |
| rs3741414 | 12 | T | 0.354 | 0.711 | 6.19E-01 | 0.052 | 0.345 | 8.80E-01 | 0.010 | 0.040 | 7.99E-01 |
| rs653178 | 12 | T | -0.388 | 0.599 | 5.17E-01 | -0.466 | 0.290 | 1.09E-01 | 0.012 | 0.034 | 7.22E-01 |
| rs7953704 | 12 | A | -0.306 | 0.604 | 6.13E-01 | -0.477 | 0.293 | 1.04E-01 | 0.001 | 0.034 | 9.86E-01 |
| rs1394125 | 15 | A | 0.708 | 0.635 | 2.65E-01 | 0.094 | 0.307 | 7.60E-01 | -0.024 | 0.036 | 5.02E-01 |
| rs6598541 | 15 | A | 0.646 | 0.624 | 3.00E-01 | -0.022 | 0.302 | 9.42E-01 | 0.007 | 0.035 | 8.49E-01 |
| rs7193778 | 16 | C | 0.420 | 0.912 | 6.45E-01 | -0.302 | 0.442 | 4.94E-01 | -0.064 | 0.051 | 2.16E-01 |
| rs7188445 | 16 | A | -0.095 | 0.639 | 8.82E-01 | -0.104 | 0.309 | 7.36E-01 | 0.001 | 0.036 | 9.86E-01 |
| rs7224610 | 17 | C | -0.209 | 0.609 | 7.31E-01 | 0.042 | 0.295 | 8.88E-01 | -0.021 | 0.034 | 5.34E-01 |

Table S3: Medication according to quartiles of GRS₈

| | GRS ₈ | | | | | P value* |
|--------------------------------------|------------------|------------------------|----------------------------|----------------------------|----------------------|----------|
| | All patients | 1st quartile (<= 0.63) | 2nd quartile (0.64 - 0.94) | 3rd quartile (0.95 - 1.03) | 4th quartile (1.04+) | |
| Diuretics (%) | 29.0 | 29.8 | 28.0 | 27.9 | 30.5 | 0.107 |
| ACE-inhibitors (%) | 53.6 | 54.1 | 50.2 | 54.1 | 56.5 | 0.34 |
| Beta-blockers (%) | 63.2 | 64.9 | 61.5 | 62.6 | 64.3 | 0.479 |
| Calcium antagonist (%) | 15.9 | 16.5 | 15.1 | 16.4 | 15.9 | 0.868 |
| Glucocorticoids (%) | 2.2 | 2.1 | 2.2 | 2.0 | 2.4 | 0.939 |
| Aspirin/other antiplatelet agent (%) | 71.3 | 71.1 | 70.8 | 69.9 | 74.0 | 0.339 |
| Oral antidiabetics (%) | 8.4 | 9.2 | 8.5 | 8.1 | 7.8 | 0.805 |
| Insulin (%) | 6.1 | 6.5 | 7.0 | 4.8 | 6.1 | 0.171 |
| Statins (%) | 47.3 | 47.5 | 46.0 | 47.4 | 48.7 | 0.782 |

* ANOVA

Table S4: Spearman's correlation of genetically predicted uric acid with biomarkers

| | Genetically predicted uric acid | |
|---|---------------------------------|-----------|
| | rs | P |
| Uric acid (mg/dl) | 0.112 | 5.886E-10 |
| age (yr) | 0.016 | 0.370 |
| body mass index (kg/m ²) | -0.010 | 0.596 |
| eGFR (ml/min/1.73m ²) | -0.007 | 0.682 |
| Systolic blood pressure (mmHg) | -0.013 | 0.457 |
| Diastolic blood pressure (mmHg) | -0.016 | 0.381 |
| Fasting glucose (mg/dL) | -0.001 | 0.939 |
| LDL cholesterol (mg/dL) | -0.002 | 0.911 |
| HDL cholesterol (mg/dL) | -0.010 | 0.598 |
| Triglycerides (mg/dL) | 0.017 | 0.337 |
| High sensitive C-reactive protein(mg/L) | -0.010 | 0.595 |

Table S5: Association SLC2A9 SNP rs7442295 with mortality, cardiovascular mortality and sudden cardiac death

| | CHR (95%CI) | Pval* |
|--------------------------|------------------|-------|
| Model 1 | | |
| All-cause mortality | 1.06(0.73-1.53) | 0.778 |
| Cardiovascular mortality | 1.58(0.97-2.59) | 0.067 |
| Sudden Cardiac Death | 2.10(0.96-4.58) | 0.062 |
| Model 2 | | |
| All-cause mortality | 1.03 (0.71-1.50) | 0.882 |
| Cardiovascular mortality | 1.55(0.95-2.55) | 0.082 |
| Sudden Cardiac Death | 1.92(0.88-4.21) | 0.101 |
| Model 3 | | |
| All-cause mortality | 1.13 (0.78-1.65) | 0.518 |
| Cardiovascular mortality | 1.82 (1.11-3.0) | 0.018 |
| Sudden Cardiac Death | 2.20(1.00-4.81) | 0.049 |
| Model 4 | | |
| All-cause mortality | 1.13 (0.77-1.64) | 0.532 |
| Cardiovascular mortality | 1.82 (1.10-3.0) | 0.019 |
| Sudden Cardiac Death | 2.45 (1.12-5.39) | 0.026 |

* after Bonferroni correction for 3 test P < 0.017 would be considered significant

Model 1: unadjusted

Model 2: adjusted for age, sex

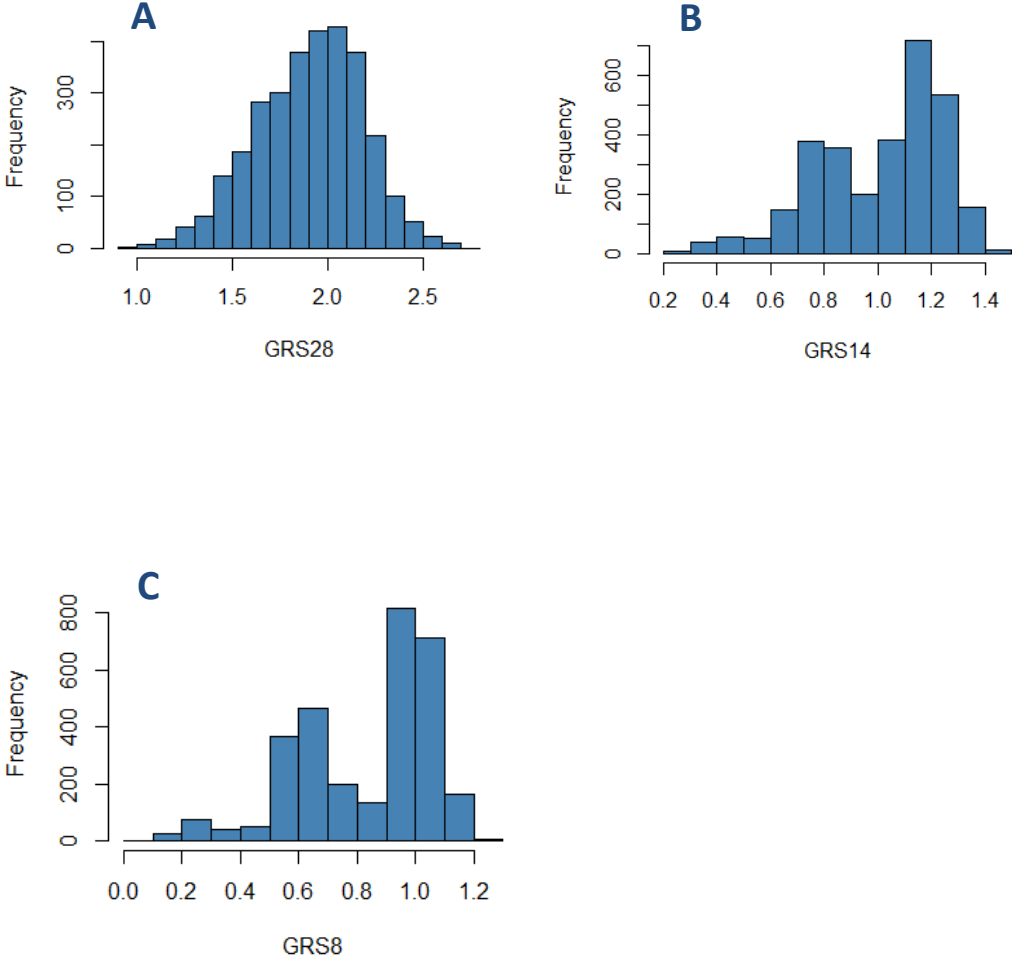
Model 3: additionally adjusted for LDL-C, HDL-C, smoking, bmi, diabetes, hypertension, eGFR, TG, friesinger score ², hsCRP

Model 4: additionally adjusted for medication use (diuretics, ACE-inhibitors, beta-blockers, calcium-antagonists, statins, acetyl salicylic acid, oral antidiabetics, insulin)

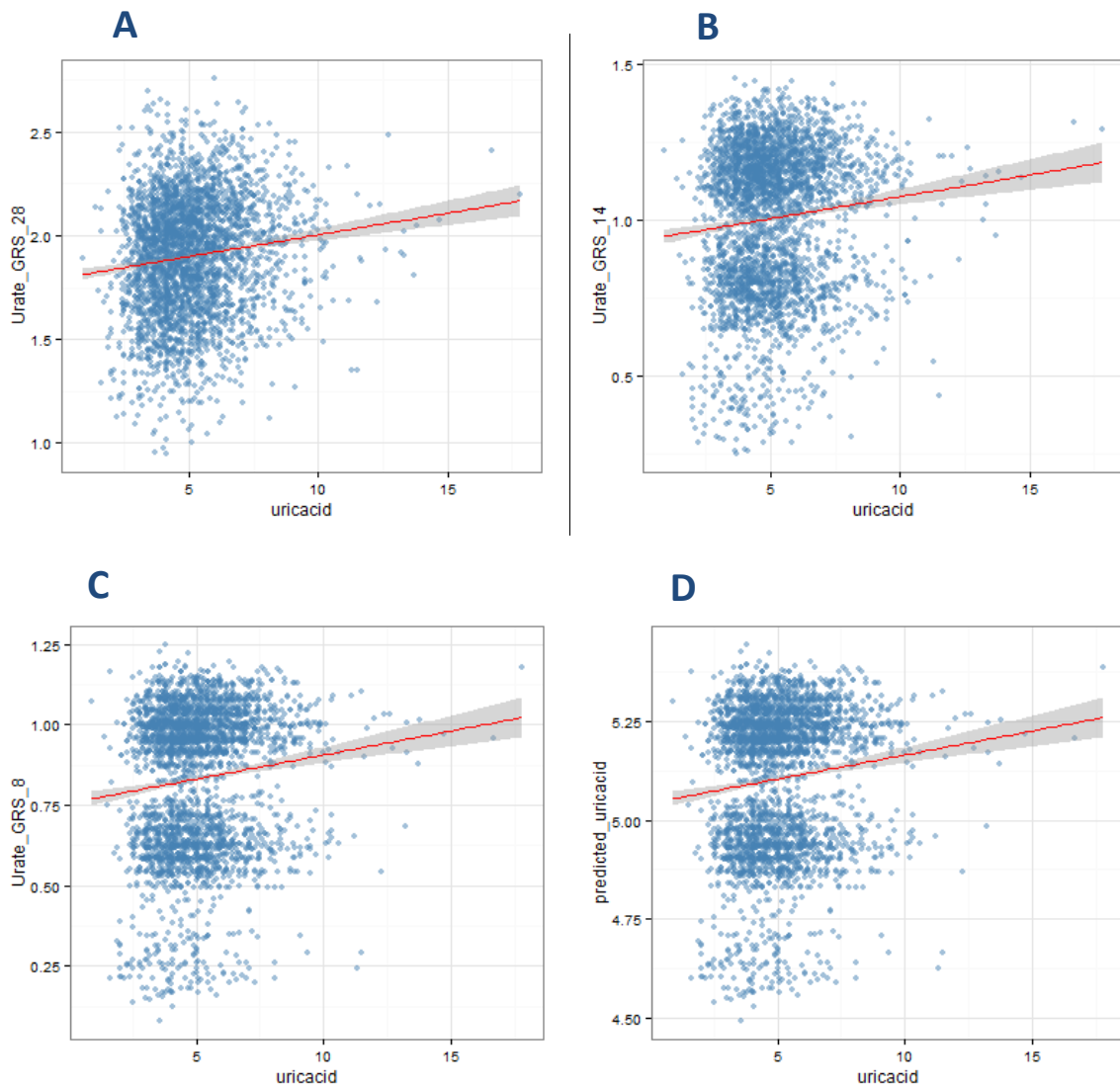
Table S6: Causal odds ratio for left ventricular hypertrophy

| | Uric acid | | Predicted uric acid | |
|--|------------------|--------|---------------------|-------|
| | OR (95% CI) | P | COR (95% CI) | P |
| Left ventricular hypertrophy (ECG) | 1.13 (1.05-1.21) | 0.001 | 0.94 (0.47-1.87) | 0.856 |
| Left ventricular wall thickness > 12 mm (Echo) | 1.17 (1.11-1.24) | <0.001 | 0.89 (0.56-1.41) | 0.611 |

Supplementary figures



Supplementary figure 1: Histograms of GRS28 (A), GRS14 (B) and GRS8 (C).



Supplementary figure 2: Scatter plots of GRS28 (A), GRS14(B), GRS8 (C) and genetically predicted uric acid concentration (D) versus measured uric acid concentration. Regression lines are drawn in red.

Supplementary text

Calculation of genetic risk scores

All 28 SNPs used to calculate the GRS were coded in a way that the allele that was associated with increased uric acid concentration in the meta-analysis by Köttgen et al. was counted. The coded allele for each SNP is shown in **Supplementary table 1**. Weighted genetic risk scores were calculated by multiplying the number of uric acid increasing alleles of each SNP with the respective beta coefficient from the published meta-analysis and then taking the sum of all values. For some SNPs we detected an opposite effect on uric acid concentration in our study as compared to the meta-analysis. But it should be noted that these effects were not statistically significant and could be due to chance. GRS28 includes all SNPs from the meta-analysis, GRS14 only SNPs that were not associated with confounders in LURIC and GRS8 only those SNPs from GRS14 that showed an effect on uric acid concentration directionally in accordance to the meta-analysis.

GRS28

$$\begin{aligned} \text{GRS28} = & \text{rs11264341} * 0.05 + \text{rs1471633} * 0.059 + \text{rs6770152} * 0.044 + \text{rs12498742} * 0.373 + \\ & \text{rs17632159} * 0.039 + \text{rs675209} * 0.061 + \text{rs10480300} * 0.035 + \text{rs17786744} * 0.029 + \\ & \text{rs2941484} * 0.044 + \text{rs10821905} * 0.057 + \text{rs2078267} * 0.073 + \text{rs478607} * 0.047 + \\ & \text{rs7976059} * 0.032 + \text{rs7224610} * 0.042 + \text{rs2231142} * 0.217 + \text{rs1260326} * 0.074 + \\ & \text{rs1171614} * 0.047 + \text{rs1394125} * 0.043 + \text{rs17050272} * 0.035 + \text{rs1165151} * 0.091 + \\ & \text{rs7188445} * 0.032 + \text{rs3741414} * 0.072 + \text{rs1178977} * 0.047 + \text{rs729761} * 0.047 + \text{rs653178} \\ & * 0.035 + \text{rs7953704} * 0.029 + \text{rs6598541} * 0.043 + \text{rs7193778} * 0.046 \end{aligned}$$

GRS14

$$\begin{aligned} \text{GRS14} = & \text{rs6770152} * 0.044 + \text{rs12498742} * 0.373 + \text{rs17786744} * 0.029 + \text{rs2941484} * 0.044 + \\ & \text{rs10821905} * 0.057 + \text{rs478607} * 0.047 + \text{rs7224610} * 0.042 + \text{rs1394125} * 0.043 + \\ & \text{rs7188445} * 0.032 + \text{rs1178977} * 0.047 + \text{rs653178} * 0.035 + \text{rs7953704} * 0.029 + \\ & \text{rs6598541} * 0.043 + \text{rs7193778} * 0.046 \end{aligned}$$

GRS8

$$\begin{aligned} \text{GRS8} = & \text{rs6770152} * 0.044 + \text{rs12498742} * 0.373 + \text{rs10821905} * 0.057 + \text{rs478607} * 0.047 + \\ & \text{rs7224610} * 0.042 + \text{rs1394125} * 0.043 + \text{rs7188445} * 0.032 + \text{rs1178977} * 0.047 \end{aligned}$$

Regression on measured uric acid concentration

Independent: genetically predicted uric acid

Measured uric acid = $0.9949 * \text{genetically predicted uric acid} + 0.02686$

Residual standard error: 1.677 on 3053 degrees of freedom

Multiple R-squared: 0.01209, Adjusted R-squared: 0.01177

F-statistic: 37.36 on 1 and 3053 DF, p-value: $1.105e-09$

Independent: GRS28

Measured uric acid = $0.7508 * \text{GRS28} + 3.6781$

Residual standard error: 1.673 on 3053 degrees of freedom

Multiple R-squared: 0.01574, Adjusted R-squared: 0.01542

F-statistic: 48.82 on 1 and 3053 DF, p-value: $3.43e-12$

Independent: GRS14

Measured uric acid = $0.7144 * \text{GRS14} + 4.3862$

Residual standard error: 1.678 on 3053 degrees of freedom

Multiple R-squared: 0.01, Adjusted R-squared: 0.009677

F-statistic: 30.84 on 1 and 3053 DF, p-value: $3.037e-08$

Independent: GRS8

Measured uric acid = $0.8094 * \text{GRS8} + 4.4322$

Residual standard error: 1.677 on 3053 degrees of freedom

Multiple R-squared: 0.01209, Adjusted R-squared: 0.01177

F-statistic: 37.36 on 1 and 3053 DF, p-value: $1.105e-09$

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