**Supplementary material**

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**Figure S1.** Manhattan map for genome-wide association analysis of CysC, SCr, and eGFR in UK Biobank subjects

**Table S1**. Single nucleotide polymorphisms (SNPs) that associated with renal function related phenotypes in UK-biobank subjects

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| SNP | Gene | eGFR(*P-*value) | SCr(*P-*value) | CysC(*P*-value) |
| rs13146355 | *SHROOM3* | 1.308×10-189 | 2.55×10-99 | 7.41×10-266 |
| rs7219624 | *BCAS3* |  | 2.57×10-148 | 6.13×10-47 |
| rs10224002 | *PRKAG2* | 7.24×10-263 | 2.15×10-156 | 3.84×10-84 |
| rs653178 | *SH2B3(ATXN2)* |  |  | 3.49×10-239 |
| rs1153849 | *GATM* | 7.24×10-263 | 2.00×10-226 | 3.11×10-28 |
| rs12917707 | *UMOD* | 8.10×10-162 | 1.50×10-115 | 4.00×10-58 |
| rs316019 | *SLC22A2* | 4.61×10-71 | 1.17×10-41 |  |
| rs3850625 | *CACNC1S* | 2.26×10-55 | 2.60×10-31 |  |
| rs267738 | *CERS2* | 3.26×10-58 | 1.12×10-44 |  |
| rs700233 | *C9* | 2.05×10-83 | 1.32×10-49 | 3.00×10-30 |

**Table S2.** CKD candidate gene loci that selected for genetic risk models

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Number | SNP | Gene | Chr | Base-pair position | MAF(CHB) |
| 1 | rs10277115 | *UNCX* | 7 | 1245559 | 0.34(T) |
| 2 | rs11864909 | *UMOD* | 16 | 20389517 | 0.14(T) |
| 3 | rs16853722 | *MECOM* | 3 | 169432844 | 0.34(C) |
| 4 | rs17319721 | *SHROOM3* | 4 | 76447694 | 0.13(A) |
| 5 | rs17730281 | *WDR72* | 15 | 53615751 | 0.50(A) |
| 6 | rs13146355 | *SHROOM3* | 4 | 76490987 | 0.13(A) |
| 7 | rs2390793 | *LRP2* | 2 | 169348673 | 0.19(T) |
| 8 | rs3770636 | *LRP2* | 2 | 169346323 | 0.22(G) |
| 9 | rs4744712 | *PIP5K1B* | 9 | 68819791 | 0.43(A) |
| 10 | rs504915 | *SLC22A12* | 11 | 64696613 | 0.29(A) |
| 11 | rs881858 | *VEGFA* | 6 | 43838872 | 0.18(G) |
| 12 | rs889472 | *MAF* | 16 | 79612092 | 0.38(A) |
| 13 | rs7219624 | *BCAS3* | 17 | 61382803 | 0.24(G) |
| 14 | rs671 | *ALDH2* | 12 | 111803962 | 0.15(A) |
| 15 | rs3752462 | *MYH* | 22 | 036314138 | 0.30(C) |
| 16 | rs2231142 | *ABCG2* | 4 | 88131171 | 0.28(T) |
| 17 | rs10224002 | *PRKAG2* | 7 | 151717955 | 0.06(G) |
| 18 | rs653178 | *SH2B3(ATXN2)* | 12 | 111569952 | 0.19(T) |
| 19 | rs1153849 | *GATM* | 15 | 45403497 | 0.81(A) |
| 20 | rs12917707 | *UMOD* | 16 | 20356368 | 0.13(T) |
| 21 | rs316019 | *SLC22A2* | 6 | 160249250 | 0.86(C) |
| 22 | rs3850625 | *CACNCA1S* | 1 | 201047168 | 0.04(A) |
| 23 | rs113956264 | *RPL3L* | 16 | 1947003 | 0.03(T) |
| 24 | rs267738 | *CERS2* | 1 | 150968149 | 0.03(G) |
| 25 | rs700233 | *C9* | 5 | 39364452 | 0.07(A) |
| 26 | rs1731274 | *STC1* | 8 | 23908806 | 0.71(A) |
| 27 | rs13038305 | *CST* | 20 | 23629625 | 0.12(T) |

CKD related gene loci were selected base on:(1) With reference to Chinese genotype frequencies, SNP loci with minimum allele frequencies greater than 5% were selected; (2) Consider the physical location distribution of SNP loci in genes. Focus on known biologically significant mutations such as missense mutations in the coding region of the gene; (3) They were significantly associated with CKD in other studies.

**Table S3.** Univariate Cox regression analyses for non-genetic risk factors

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Characteristics | β | SE | χ2 | RR | 95%*CI* | *P-value* |
| Age, year |  |  |  |  |  |  |
| <50 | 1(ref.) |  |  | 1(ref.) |  |  |
| 50-59 | -0.055 | 0.563 | 0.009 | 0.947 | 0.314-2.852 | 0.992 |
| 60-69 | 0.798 | 0.529 | 2.276 | 2.220 | 0.788-6.257 | 0.031 |
| 70-79 | 1.943 | 0.522 | 13.829 | 6.979 | 2.507-19.43 | 0.000 |
| 80-100 | 2.961 | 0.550 | 28.997 | 19.314 | 6.574-26.74 | 0.000 |
| Age as a continuous variable | 0.110 | 0.011 | 15.163 | 1.116 | 1.093-1.140 | 0.000 |
| Sex |  |  |  |  |  |  |
| Male | 1(ref.) |  |  | 1(ref.) |  |  |
| Female | 0.244 | 0.199 | 1.499 | 1.276 | 0.864-1.886 | 0.221 |
| Type II diabetes |  |  |  |  |  |  |
| Without | 1(ref.) |  |  | 1(ref.) |  |  |
| With | 0.486 | 0.330 | 2.168 | 1.626 | 0.851-3.108 | 0.041 |
| FPG as a continuous variable | 0.168 | 0.073 | 5.325 | 1.183 | 1.026-1.364 | 0.021 |
| TC(mmol/L) |  |  |  |  |  |  |
| <4.4 | 1(ref.) |  |  | 1(ref.) |  |  |
| 4.4-5.0 | 0.139 | 0.288 | 0.233 | 1.149 | 0.654-2.021 | 0.629 |
| 5.1-5.5 | 0.316 | 0.297 | 1.131 | 1.372 | 0.766-2.457 | 0.288 |
| >5.5 | 0.688 | 0.279 | 6.086 | 1.989 | 1.152-3.400 | 0.121 |
| TC as a continuous variable | 0.248 | 0.097 | 6.586 | 1.282 | 1.060-1.550 | 0.010 |
| TG(mmol/L) |  |  |  |  |  |  |
| <1.05 | 1(ref.) |  |  | 1(ref.) |  |  |
| 1.05-1.45 | -0.337 | 0.266 | 1.600 | 0.714 | 0.424-1.203 | 0.206 |
| 1.46-2.08 | 0.024 | 0.250 | 0.009 | 1.024 | 0.627-1.672 | 0.924 |
| >2.08 | -0.117 | 0.256 | 0.209 | 0.889 | 0.538-1.470 | 0.648 |
| TG as a continuous variable | 0.034 | 0.064 | 0.284 | 1.035 | 0.913-1.173 | 0.594 |
| Hyperuricemia |  |  |  |  |  |  |
| Without | 1(ref.) |  |  |  |  |  |
| With | 0.378 | 0.232 | 2.657 | 1.46 | 0.926-2.300 | 0.103 |
| BUN(mmol/L) |  |  |  |  |  |  |
| <4.7 | 1(ref.) |  |  | 1(ref.) |  |  |
| 4.7-5.35 | 0.747 | 0.358 | 4.356 | 2.110 | 1.047-4.254 | 2.773 |
| 5.36-6.1 | 1.020 | 0.348 | 8.568 | 2.773 | 1.401-5.488 | 0.501 |
| >6.1 | 1.714 | 0.334 | 26.284 | 5.552 | 2.883-10.69 | 0.000 |
| BUN as a continuous variable | 0.437 | 0.077 | 32.131 | 1.547 | 1.331-1.799 | 0.000 |
| SCr(μmmol/L) |  |  |  |  |  |  |
| <74 | 1(ref.) |  |  | 1(ref.) |  |  |
| 74-83 | 0.562 | 0.308 | 3.337 | 1.755 | 0.960-3.209 | 0.068 |
| 83.1-93 | 0.284 | 0.335 | 0.715 | 1.328 | 0.688-2.563 | 0.398 |
| >93 | 1.594 | 0.287 | 30.924 | 4.925 | 2.808-8.638 | 0.000 |
| SCr as a continuous variable | 0.051 | 0.008 | 46.272 | 1.053 | 1.037-1.069 | 0.000 |
| SUA(μmmol/L) |  |  |  |  |  |  |
| <281 | 1(ref.) |  |  | 1(ref.) |  |  |
| 281-331 | 0.289 | 0.27 | 1.141 | 1.335 | 0.786-2.662 | 0.285 |
| 331.1-383.75 | 0.317 | 0.276 | 1.318 | 1.373 | 0.799-2.358 | 0.251 |
| >383.75 | 0.469 | 0.265 | 3.123 | 1.598 | 0.950-2.687 | 0.027 |
| SUA as a continuous variable | 0.002 | 0.001 | 3.027 | 1.002 | 1.000-1.004 | 0.082 |
| TP(g/L) |  |  |  |  |  |  |
| <73 | 1(ref.) |  |  | 1(ref.) |  |  |
| 73-75 | -0.168 | 0.263 | 0.406 | 0.845 | 0.505-1.417 | 0.524 |
| 75.1-78 | 0.008 | 0.261 | 0.001 | 1.008 | 0.604-1.683 | 0.974 |
| >78 | 0.261 | 0.265 | 0.965 | 1.298 | 0.772-2.183 | 0.326 |
| TP as a continuous variable | 0.031 | 0.022 | 2.072 | 1.032 | 0.989-1.077 | 0.150 |
| ALB(g/L) |  |  |  |  |  |  |
| <44 | 1(ref.) |  |  | 1(ref.) |  |  |
| 44-46 | 0.097 | 0.259 | 0.142 | 1.102 | 0.664-1.830 | 0.707 |
| 46.1-47 | 0.273 | 0.299 | 0.836 | 1.314 | 0.732-2.361 | 0.360 |
| >47 | -0.175 | 0.302 | 0.335 | 0.840 | 0.465-1.517 | 0.563 |
| ALB as a continuous variable | -0.035 | 0.035 | 0.988 | 0.965 | 0.901-1.035 | 0.320 |
| GLB(g/L) |  |  |  |  |  |  |
| <27 | 1(ref.) |  |  | 1(ref.) |  |  |
| 27-29 | -0.262 | 0.294 | 0.797 | 0.769 | 0.432-1.368 | 0.372 |
| 29.1-32 | -0.081 | 0.312 | 0.067 | 0.922 | 0.501-1.699 | 0.796 |
| >32 | 0.463 | 0.305 | 2.306 | 1.589 | 0.874-2.887 | 0.129 |
| GLB as a continuous variable | 0.067 | 0.026 | 6.550 | 1.069 | 1.016-1.125 | 0.010 |
| ALI(IU/L) |  |  |  |  |  |  |
| <20 | 1(ref.) |  |  | 1(ref.) |  |  |
| 20-24 | -0.428 | 0.248 | 2.974 | 0.652 | 0.400-1.060 | 0.085 |
| 24.1-32 | -0.307 | 0.247 | 1.555 | 0.735 | 0.454-1.192 | 0.212 |
| >32 | -0.650 | 0.281 | 5.348 | 0.522 | 0.301-0.906 | 0.021 |
| ALT as a continuous variable | -0.031 | 0.012 | 7.117 | 0.969 | 0.947-0.992 | 0.008 |
| TBIL(μmol/L) |  |  |  |  |  |  |
| <11 | 1(ref.) |  |  | 1(ref.) |  |  |
| 11-14.2 | -0.382 | 0.240 | 2.529 | 0.683 | 0.426-1.093 | 0.112 |
| 14.3-17.5 | -0.479 | 0.255 | 3.542 | 0.619 | 0.376-1.020 | 0.060 |
| >17.5 | -0.549 | 0.261 | 4.428 | 0.578 | 0.346-0.963 | 0.035 |
| TBIL as a continuous variable | -0.051 | 0.022 | 5.405 | 0.950 | 0.911-0.992 | 0.02 |
| DBIL(μmol/L) |  |  |  |  |  |  |
| <1.4 | 1(ref.) |  |  | 1(ref.) |  |  |
| 1.4-2.1 | -0.145 | 0.272 | 0.283 | 0.865 | 0.507-1.475 | 0.595 |
| 2.2-3.0 | 0.064 | 0.265 | 0.058 | 1.066 | 0.634-1.794 | 0.809 |
| >3.0 | 0.492 | 0.255 | 3.730 | 1.636 | 0.993-2.697 | 0.053 |
| TBIL as a continuous variable | 0.200 | 0.071 | 7.868 | 1.221 | 1.062-1.405 | 0.005 |
| Hypertension |  |  |  |  |  |  |
| Without | 1(ref.) |  |  | 1(ref.) |  |  |
| With | -0.138 | 0.240 | 0.329 | 0.871 | 0.544-1.395 | 0.566 |
| Obesity |  |  |  |  |  |  |
| Without | 1(ref.) |  |  | 1(ref.) |  |  |
| With | 0.220 | 0.183 | 1.444 | 1.245 | 0.871-1.782 | 0.230 |
| CysC(mg/L) |  |  |  |  |  |  |
| <0.78 | 1(ref.) |  |  | 1(ref.) |  |  |
| 0.78-1.0 | 0.786 | 0.340 | 5.347 | 2.194 | 1.127-4.271 | 0.021 |
| 1.01-1.32 | 1.100 | 0.325 | 11.453 | 3.003 | 1.588-5.677 | 0.001 |
| >1.32 | 1.401 | 0.314 | 19.852 | 4.058 | 2.192-7.516 | 0.000 |
| CysC as a continuous variable | 0.008 | 0.003 | 7.262 | 1.008 | 1.002-1.014 | 0.007 |
| TGF-β(pg/mL) |  |  |  |  |  |  |
| <8.36 | 1(ref.) |  |  | 1(ref.) |  |  |
| 8.36-12.84 | 1.748 | 0.769 | 5.170 | 5.743 | 1.273-5.916 | 0.023 |
| 12.85-18.42 | 3.331 | 0.724 | 21.194 | 27.978 | 6.774-9.553 | 0.000 |
| >18.42 | 3.877 | 0.719 | 29.089 | 48.282 | 9.801-17.548 | 0.000 |
| TGF-β as a continuous variable | 0.235 | 0.024 | 17.606 | 1.265 | 1.207-1.325 | 0.000 |
| NGAL(μmol/L) |  |  |  |  |  |  |
| <12.34 | 1(ref.) |  |  | 1(ref.) |  |  |
| 12.34-14.96 | -0.911 | 0.239 | 14.524 | 0.402 | 0.252-0.642 | 0.000 |
| 14.97-18.04 | -1.358 | 0.273 | 24.769 | 0.257 | 0.151-0.439 | 0.000 |
| >18.04 | -1.116 | 0.254 | 19.397 | 0.327 | 0.199-0.538 | 0.000 |
| NGAL as a continuous variable | -0.057 | 0.019 | 9.222 | 0.945 | 0.911-0.980 | 0.002 |
| ADMA(μg/L) |  |  |  |  |  |  |
| <60.04 | 1(ref.) |  |  | 1(ref.) |  |  |
| 60.04-89.86 | 1.650 | 0.550 | 8.991 | 5.206 | 1.771-5.307 | 0.003 |
| 89.87-122.06 | 3.172 | 0.518 | 17.570 | 23.866 | 8.654-10.816 | 0.000 |
| >122.06 | 2.456 | 0.527 | 21.730 | 11.655 | 4.151-9.730 | 0.000 |
| ADMA as a continuous variable | 0.003 | 0.001 | 12.691 | 1.003 | 1.002-1.005 | 0.000 |

**Material S1.** Four CKDNGRS models that constructed with 5 selected non-genetic risk factors

CKDNGRS1=1.84×S1+1.137×S2 (1)

CKDNGRS2=1.84×S1+1.137×S2+0.84×S3 (2)

CKDNGRS3=1.84×S1+1.137×S2+0.84×S3+0.497×S4 (3)

CKDNGRS4=1.84×S1+1.137×S2+0.84×S3+0.497×S4+0.603×S5 (4)

In the formula above, S1=Normal high value of TGF-β(0: <1.011pg/ml; 1: ≥1.011pg/ml), S2=Normal high value of ADMA(0: <0.019μmol/L; 1: ≥0.019μmol/L), S3=Diabetes(0: with; 1: without), S4=Normal high value of BUN(0: <5.9mmol/L; 1: ≥5.9mmol/L), S5= The elderly(0: <60years; 1: ≥60years).

**Table S4.** Logistic regression analyses for different CKD NGRS models

|  |  |  |  |
| --- | --- | --- | --- |
| NGRS model | OR | 95%*CI* | *P-*value |
| NGRS1 | 3.634 | 2.723-4.850 | <0.001 |
| NGRS2 | 3.703 | 2.775-4.942 | <0.001 |
| NGRS3 | 3.917 | 2.910-5.273 | <0.001 |
| NGRS4 | 4.113 | 3.039-5.566 | <0.001 |

**Table S5.** Comparison of predictive powers of different CKD NGRS models

|  |  |  |  |
| --- | --- | --- | --- |
| NGRS model | AUC | 95%*CI* | *P-*value |
| NGRS1 | 0.831 | 0.782-0.879 | <0.001 |
| NGRS2 | 0.841 | 0.794-0.888 | <0.001 |
| NGRS3 | 0.865 | 0.822-0.907 | <0.001 |
| NGRS4 | 0.889 | 0.851-0.925 | <0.001 |

**Table S6**. Hardy-Weinberg Equilibrium tests for 27 CKD candidate gene loci

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| No. | SNP | Gene | Detectable rate (%) | HWE  (*P*-value) | HWE  (*P*-value)  case | HWE  (*P*-value)  control |
| 1 | rs10277115 | *UNCX* | 99 | 0.9057 | 0.6799 | 0.6623 |
| 2 | rs11864909 | *UMOD* | 100 | 0.1424 | 0.6769 | 0.1526 |
| 3 | rs16853722 | *MECOM* | 100 | 0.8961 | 0.6682 | 1 |
| 4 | rs17319721 | *SHROOM3* | 100 | 0.265 | 0.2798 | 0.6854 |
| 5 | rs17730281 | *WDR72* | 100 | 0.8107 | 1 | 0.7659 |
| 6 | rs13146355 | *SHROOM3* | 100 | 0.6063 | 0.7908 | 0.3722 |
| 7 | rs2390793 | *LRP2* | 100 | 0.1469 | 0.1907 | 0.3899 |
| 8 | rs3770636 | *LRP2* | 100 | 0.1548 | 0.1581 | 0.4098 |
| 9 | rs4744712 | *PIP5K1B* | 100 | 0.01657a | 0.07832 | 0.1223 |
| 10 | rs504915 | *SLC22A12* | 100 | 1 | 0.5841 | 0.6028 |
| 11 | rs881858 | *VEGFA* | 100 | 0.5277 | 0.7422 | 0.2659 |
| 12 | rs889472 | *MAF* | 100 | 0.02745b | 0.843 | 0.01043c |
| 13 | rs7219624 | *BCAS3* | 100 | 1 | 0.5978 | 0.7252 |
| 14 | rs671 | *ALDH2* | 100 | 0.2466 | 1 | 0.1922 |
| 15 | rs3752462 | *MYH9* | 100 | 0.3728 | 0.8094 | 0.1806 |
| 16 | rs2231142 | *ABCG2* | 100 | 0.6961 | 0.252 | 0.752 |
| 17 | rs10224002 | *PRKAG2* | 100 | 1 | 1 | 1 |
| 18 | rs653178 | *SH2B3(ATXN2)* | 100 | 1 | 1 | 1 |
| 19 | rs1153849 | *GATM* | 100 | 0.1278 | 1 | 0.1189 |
| 20 | rs12917707 | *UMOD* | 99 | 1 | 1 | 1 |
| 21 | rs316019 | *SLC22A2* | 100 | 1 | 1 | 1 |
| 22 | rs3850625 | *CACNCA1S* | 100 | 1 | 1 | 1 |
| 23 | rs113956264 | *RPL3L* | 100 | 1 | 1 | 1 |
| 24 | rs267738 | *CERS2* | 100 | 1 | 1 | 1 |
| 25 | rs700233 | *C9* | 100 | 0.4888 | 0.4642 | 0.2261 |
| 26 | rs1731274 | *STC1* | 99 | 1 | 0.7763 | 1 |
| 27 | rs13038305 | *CST* | 100 | 0.4426 | 0.6876 | 0.7468 |

a,b,c*P*<0.05, therefore the two SNPs (rs4744712 and rs889472) didn’t pass Hardy-Weinberg equilibrium test.

**Table S7**. Logistic regression analyses of CKD related candidate gene SNPs

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| No. | SNP | β | SE | χ2 | OR | 95%*CI* | *P-*value | *P-*value  ranking |
| 1 | rs10277115 | -0.033 | 0.174 | 0.035 | 0.968 | 0.688-1.362 | 0.851 | 22 |
| 2 | rs11864909 | -0.286 | 0.228 | 1.567 | 0.752 | 0.481-1.175 | 0.211 | 4 |
| 3 | rs16853722 | 0.147 | 0.181 | 0.664 | 1.159 | 0.813-1.652 | 0.415 | 12 |
| 4 | rs17319721 | 0.577 | 0.251 | 5.288 | 1.781 | 1.089-2.913 | 0.021 | 1 |
| 5 | rs17730281 | -0.012 | 0.176 | 0.004 | 0.988 | 0.700-1.396 | 0.947 | 24 |
| 6 | rs13146355 | 0.228 | 0.203 | 1.255 | 1.256 | 0.843-1.870 | 0.263 | 7 |
| 7 | rs2390793 | -0.155 | 0.243 | 0.409 | 0.856 | 0.532-1.378 | 0.522 | 15 |
| 8 | rs3770636 | -0.234 | 0.246 | 0.907 | 0.791 | 0.489-1.281 | 0.341 | 10 |
| 9 | rs504915 | -0.178 | 0.196 | 0.822 | 0.837 | 0.570-1.229 | 0.365 | 11 |
| 10 | rs881858 | 0.253 | 0.233 | 1.175 | 1.288 | 0.815-2.034 | 0.278 | 8 |
| 11 | rs7219624 | 0.026 | 0.267 | 0.010 | 1.026 | 0.608-1.734 | 0.922 | 23 |
| 12 | rs671 | -0.362 | 0.247 | 2.154 | 0.696 | 0.429-1.129 | 0.142 | 3 |
| 13 | rs3752462 | 0.225 | 0.199 | 1.281 | 1.252 | 0.848-1.849 | 0.258 | 6 |
| 14 | rs2231142 | -0.074 | 0.185 | 0.163 | 0.928 | 0.646-1.333 | 0.687 | 19 |
| 15 | rs10224002 | 0.182 | 0.387 | 0.222 | 1.200 | 0.562-2.561 | 0.637 | 18 |
| 16 | rs653178 | 1.099 | 0.921 | 1.423 | 3.000 | 0.493-18.24 | 0.233 | 5 |
| 17 | rs1153849 | -0.240 | 0.234 | 1.048 | 0.787 | 0.497-1.245 | 0.306 | 9 |
| 18 | rs12917707 | 0.683 | 1.007 | 0.460 | 1.980 | 0.275-14.26 | 0.498 | 13 |
| 19 | rs316019 | 0.053 | 0.272 | 0.038 | 1.054 | 0.619-1.795 | 0.845 | 21 |
| 20 | rs3850625 | -0.247 | 0.423 | 0.343 | 0.781 | 0.341-1.787 | 0.558 | 17 |
| 21 | rs113956264 | 0.298 | 0.479 | 0.389 | 1.348 | 0.527-3.445 | 0.533 | 16 |
| 22 | rs267738 | -0.019 | 0.432 | 0.002 | 0.981 | 0.421-2.287 | 0.964 | 25 |
| 23 | rs700233 | -0.183 | 0.313 | 0.340 | 0.833 | 0.451-1.539 | 0.056 | 2 |
| 24 | rs1731274 | -0.133 | 0.202 | 0.434 | 0.876 | 0.590-1.300 | 0.510 | 14 |
| 25 | rs13038305 | 0.091 | 0.261 | 0.121 | 1.095 | 0.657-1.824 | 0.728 | 20 |

**Table S8.** GRS models including different SNP loci that related to CKD

|  |  |  |
| --- | --- | --- |
| GRS model |  | Included SNP loci number |
| CKDGRS4 |  | 4,23,12,2 |
| CKDGRS5 |  | 4,23,12,2,16 |
| CKDGRS6 |  | 4,23,12,2,16,13 |
| CKDGRS7 |  | 4,23,12,2,16,13,6 |
| CKDGRS8 |  | 4,23,12,2,16,13,6,10 |
| CKDGRS9 |  | 4,23,12,2,16,13,6,10,17 |
| CKDGRS10 |  | 4,23,12,2,16,13,6,10,17,8 |
| CKDGRS11 |  | 4,23,12,2,16,13,6,10,17,8,9 |
| CKDGRS12 |  | 4,23,12,2,16,13,6,10,17,8,9,3 |
| CKDGRS13 |  | 4,23,12,2,16,13,6,10,17,8,9,3,18 |
| CKDGRS14 |  | 4,23,12,2,16,13,6,10,17,8,9,3,18,24 |
| CKDGRS15 |  | 4,23,12,2,16,13,6,10,17,8,9,3,18,24,7 |
| CKDGRS16 |  | 4,23,12,2,16,13,6,10,17,8,9,3,18,24,7,21 |
| CKDGRS17 |  | 4,23,12,2,16,13,6,10,17,8,9,3,18,24,7,21,20 |

**Material S2**. GRS models including different SNPs that related to CKD

CKDGRS4=0.577×rs17319721Gi+(-0.183)×rs700233Gi+(-0.362)×rs671Gi+(-0.286)×rs11864909Gi

CKDGRS5=0.577×rs17319721Gi+(-0.183)×rs700233Gi+(-0.362)×rs671Gi+(-0.286)×rs11864909Gi+1.099×rs653178Gi

CKDGRS6=0.577×rs17319721Gi+(-0.183)×rs700233Gi+(-0.362)×rs671Gi+(-0.286)×rs11864909Gi+1.099×rs653178Gi+0.255×rs3752462Gi

CKDGRS7=0.577×rs17319721Gi+(-0.183)×rs700233Gi+(-0.362)×rs671Gi+(-0.286)×rs11864909Gi+1.099×rs653178Gi+0.255×rs3752462Gi+0.228×rs13146355Gi

CKDGRS8=0.577×rs17319721Gi+(-0.183)×rs700233Gi+(-0.362)×rs671Gi+(-0.286)×rs11864909Gi+1.099×rs653178Gi+0.255×rs3752462Gi+0.228×rs13146355Gi+0.253×rs881858Gi

CKDGRS9=0.577×rs17319721Gi+(-0.183)×rs700233Gi+(-0.362)×rs671Gi+(-0.286)×rs11864909Gi+1.099×rs653178Gi+0.255×rs3752462Gi+0.228×rs13146355Gi+0.253×rs881858Gi+(-0.24)×rs1153849Gi

CKDGRS10=0.577×rs17319721Gi+(-0.183)×rs700233Gi+(-0.362)×rs671Gi+(-0.286)×rs11864909Gi+1.099×rs653178Gi+0.255×rs3752462Gi+0.228×rs13146355Gi+0.253×rs881858Gi+(-0.24)×rs1153849Gi+(-0.234)×3770636Gi

CKDGRS11=0.577×rs17319721Gi+(-0.183)×rs700233Gi+(-0.362)×rs671Gi+(-0.286)×rs11864909Gi+1.099×rs653178Gi+0.255×rs3752462Gi+0.228×rs13146355Gi+0.253×rs881858Gi+(-0.24)×rs1153849Gi+(-0.234)×3770636Gi+(-0.178)×rs504915Gi

CKDGRS12=0.577×rs17319721Gi+(-0.183)×rs700233Gi+(-0.362)×rs671Gi+(-0.286)×rs11864909Gi+1.099×rs653178Gi+0.255×rs3752462Gi+0.228×rs13146355Gi+0.253×rs881858Gi+(-0.24)×rs1153849Gi+(-0.234)×3770636Gi+(-0.178)×rs504915Gi+0.149×rs16853722Gi

CKDGRS13=0.577×rs17319721Gi+(-0.183)×rs700233Gi+(-0.362)×rs671Gi+(-0.286)×rs11864909Gi+1.099×rs653178Gi+0.255×rs3752462Gi+0.228×rs13146355Gi+0.253×rs881858Gi+(-0.24)×rs1153849Gi+(-0.234)×3770636Gi+(-0.178)×rs504915Gi+0.149×rs16853722Gi+0.683×rs12917707Gi

CKDGRS14=0.577×rs17319721Gi+(-0.183)×rs700233Gi+(-0.362)×rs671Gi+(-0.286)×rs11864909Gi+1.099×rs653178Gi+0.255×rs3752462Gi+0.228×rs13146355Gi+0.253×rs881858Gi+(-0.24)×rs1153849Gi+(-0.234)×3770636Gi+(-0.178)×rs504915Gi+0.149×rs16853722Gi+0.683×rs12917707Gi+(-0.133)×rs1731274Gi

CKDGRS15=0.577×rs17319721Gi+(-0.183)×rs700233Gi+(-0.362)×rs671Gi+(-0.286)×rs11864909Gi+1.099×rs653178Gi+0.255×rs3752462Gi+0.228×rs13146355Gi+0.253×rs881858Gi+(-0.24)×rs1153849Gi+(-0.234)×3770636Gi+(-0.178)×rs504915Gi+0.149×rs16853722Gi+0.683×rs12917707Gi+(-0.133)×rs1731274Gi+(-0.155)×rs2390793Gi

CKDGRS16=0.577×rs17319721Gi+(-0.183)×rs700233Gi+(-0.362)×rs671Gi+(-0.286)×rs11864909Gi+1.099×rs653178Gi+0.255×rs3752462Gi+0.228×rs13146355Gi+0.253×rs881858Gi+(-0.24)×rs1153849Gi+(-0.234)×3770636Gi+(-0.178)×rs504915Gi+0.149×rs16853722Gi+0.683×rs12917707Gi+(-0.133)×rs1731274Gi+(-0.155)×rs2390793Gi+0.298×rs113956264Gi

CKDGRS17=0.577×rs17319721Gi+(-0.183)×rs700233Gi+(-0.362)×rs671Gi+(-0.286)×rs11864909Gi+1.099×rs653178Gi+0.255×rs3752462Gi+0.228×rs13146355Gi+0.253×rs881858Gi+(-0.24)×rs1153849Gi+(-0.234)×3770636Gi+(-0.178)×rs504915Gi+0.149×rs16853722Gi+0.683×rs12917707Gi+(-0.133)×rs1731274Gi+(-0.155)×rs2390793Gi+0.298×rs113956264Gi+(-0.247)×rs3850625Gi

**Table S9.** Logistic regression analyses for GRS models

|  |  |  |  |
| --- | --- | --- | --- |
| GRS model | OR | 95%*CI* | *P-*value |
| CKDGRS4 | 2.785 | 1.429-5.427 | 0.003 |
| CKDGRS5 | 2.760 | 1.486-5.126 | 0.001 |
| CKDGRS6 | 2.703 | 1.508-4.846 | 0.001 |
| CKDGRS7 | 2.252 | 1.371-2.698 | 0.001 |
| CKDGRS8 | 2.272 | 1.403-3.680 | 0.001 |
| CKDGRS9 | 2.331 | 1.447-3.752 | 0.000 |
| CKDGRS10 | 2.340 | 1.468-3.731 | 0.000 |
| CKDGRS11 | 2.368 | 1.493-3.757 | 0.000 |
| CKDGRS12 | 2.422 | 1.530-3.834 | 0.000 |
| CKDGRS13 | 2.409 | 1.534-3.785 | 0.000 |
| CKDGRS14 | 2.363 | 1.518-3.679 | 0.000 |
| CKDGRS15 | 2.263 | 1.477-3.466 | 0.000 |
| CKDGRS16 | 2.324 | 1.515-3.566 | 0.000 |
| CKDGRS17 | 2.334 | 1.521-3.581 | 0.000 |

**Table S10**. Comparison of predictive powers of different GRS models

|  |  |  |  |
| --- | --- | --- | --- |
| GRS model | AUC | 95%*CI* | *P-*value |
| CKDGRS4 | 0.593 | 0.526-0.661 | 0.007 |
| CKDGRS5 | 0.594 | 0.526-0.662 | 0.007 |
| CKDGRS6 | 0.603 | 0.534-0.673 | 0.003 |
| CKDGRS7 | 0.589 | 0.521-0.658 | 0.010 |
| CKDGRS8 | 0.599 | 0.531-0.667 | 0.004 |
| CKDGRS9 | 0.613 | 0.546-0.680 | 0.001 |
| CKDGRS10 | 0.621 | 0.555-0.687 | 0.001 |
| CKDGRS11 | 0.628 | 0.562-0.695 | 0.000 |
| CKDGRS12 | 0.633 | 0.567-0.699 | 0.000 |
| CKDGRS13 | 0.638 | 0.572-0.704 | 0.000 |
| CKDGRS14 | 0.643 | 0.578-0.709 | 0.000 |
| CKDGRS15 | 0.640 | 0.575-0.706 | 0.000 |
| CKDGRS16 | 0.637 | 0.571-0.703 | 0.000 |
| CKDGRS17 | 0.642 | 0.576-0.707 | 0.000 |



**Figure S1.** Manhattan map for genome-wide association analysis of CysC, SCr, and eGFR in UK Biobank subjects