Supplementary Material

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gwas id** | **Trait** | **Sample size** | **Number of SNPs** | **Population** | **PMID** |
| ebi-a-GCST90012115 | Age-related hearing impairment (MTAG) | 330,759 | 10,858,770 | European | 32986727 |
| ebi-a-GCST90010147 | Kidney Injury Molecule levels | 1,301 | 18,166,693 | European | 33303764 |
| finn-b-N14\_OTHETNASKIDUR | Other specified disorders of kidney and ureter | 217609 | 16,380,462 | European |  |

**Table S1 Summary of the GWAS included in this study**

**Table S2 Data** **Quantization rule**

|  |  |  |
| --- | --- | --- |
| **variable** | **pre-quantification** | **post-quantification** |
| self\_reported\_better\_ear | no /don't know | 0 |
|  | yes, left ear | 1 |
|  | yes, right ear | 2 |
| excessive\_cerumen\_left\_ear | no | 0 |
| impacted\_cerumen\_left\_ear |
| otoscopy\_left\_ear |
| collapsing\_ear\_canals\_left\_ear |
| normal\_otoscopy\_right\_ear | yes | 1 |
| excessive\_cerumen\_right\_ear |
| impacted\_cerumen\_right\_ear |
| collapsing\_ear\_canals\_right\_ear |
| sex | Female | 0 |
|  | Male | 1 |
| eth1 | Mexican American | 1 |
|  | Non-Hispanic Black | 2 |
|  | Non-Hispanic white | 3 |
|  | Other Hispanic | 4 |
|  | Other Race-Including lulti-Racial | 5 |
| country\_of\_birth | Born Elsewhere | 1 |
|  | VBorn in 50 Us States or Washington, DC | 2 |
|  | Born in Mexico | 3 |
|  | Born in Other Non-Spanish gpeaking Country | 4 |
|  | Born in Other Spanish Speaking Country | 5 |
|  | 0thers | 6 |
| citizenship | Not a citizen of the US | 1 |
|  | Citizen by birth or naturalization | 2 |
| household\_size | 7 or more people in the Household | 7 |
| edu | 10th Grade | 1 |
|  | 11th Grade | 2 |
|  | 12th Grade, No Diploma | 3 |
|  | 1st grade | 4 |
|  | 2nd grade | 5 |
|  | 3rd grade | 6 |
|  | 4th Grade | 7 |
|  | 5th Grade | 8 |
|  | 6th Grade | 9 |
|  | 7th Grade | 10 |
|  | 8th Grade | 11 |
|  | 9-11th Grade (Includes 12th grade with no diploma) | 12 |
|  | 9th Grade | 13 |
|  | College Graduate or above | 14 |
|  | GED or Equivalent | 15 |
|  | High School Grad/GED or Equivalent | 16 |
|  | High School Graduate | 17 |
|  | High school graduate/GED or equivalent | 18 |
|  | Less Than 5th Grade | 19 |
|  | Less Than 9th Grade | 20 |
|  | More than high school | 21 |
|  | Never attended / kindergarten only | 22 |
|  | Some College or AA degree | 23 |

**Table S3.** **Details of each SNP in Mendelian randomization (Because of the large amount of data, see excel table)**

**Table S4.** **Causal evaluation results of five methods of Mendelian randomization**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **outcome** | **exposure** | **method** | **nsnp** | **b** | **se** | **pval** | **or** | **or\_lci95** | **or\_uci95** |
| Kidney Injury Molecule levels | Age-related hearing impairment (MTAG) | MR Egger | 28 | -0.024075602 | 2.771438747 | 0.993135145 | 0.976211903 | 0.004270196 | 223.1723499 |
| Kidney Injury Molecule levels | Age-related hearing impairment (MTAG) | Weighted median | 28 | 1.145948034 | 0.712989463 | 0.108000854 | 3.145421911 | 0.77762466 | 12.72294913 |
| Kidney Injury Molecule levels | Age-related hearing impairment (MTAG) | Inverse variance weighted | 28 | 1.115550883 | 0.537360621 | 0.037895632 | 3.051248596 | 1.064307195 | 8.747585319 |
| Kidney Injury Molecule levels | Age-related hearing impairment (MTAG) | Simple mode | 28 | 0.950453742 | 1.240896043 | 0.450355796 | 2.586883171 | 0.227250464 | 29.44752857 |
| Kidney Injury Molecule levels | Age-related hearing impairment (MTAG) | Weighted mode | 28 | 0.871012682 | 1.104668023 | 0.437282536 | 2.38932926 | 0.274134438 | 20.82516284 |
| Other specified disorders of kidney and ureter | Age-related hearing impairment (MTAG) | MR Egger | 28 | 4.708980206 | 3.915577482 | 0.239958667 | 110.9389674 | 0.051532033 | 238831.1442 |
| Other specified disorders of kidney and ureter | Age-related hearing impairment (MTAG) | Weighted median | 28 | 1.104495336 | 1.345847192 | 0.41183472 | 3.01770116 | 0.215808215 | 42.19728292 |
| Other specified disorders of kidney and ureter | Age-related hearing impairment (MTAG) | Inverse variance weighted | 28 | 2.160246201 | 0.920863637 | 0.018981631 | 8.673272764 | 1.42668486 | 52.72759426 |
| Other specified disorders of kidney and ureter | Age-related hearing impairment (MTAG) | Simple mode | 28 | 0.077941179 | 2.600053818 | 0.97630608 | 1.081059067 | 0.006616662 | 176.6281475 |
| Other specified disorders of kidney and ureter | Age-related hearing impairment (MTAG) | Weighted mode | 28 | 0.006925104 | 2.35683832 | 0.99767718 | 1.006949138 | 0.009927188 | 102.1383442 |

**Table S5. Mendelian randomization results for heterogeneity and horizontal pleiotropy**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **id.exposure** | **id.outcome** | **outcome** | **exposure** | **method** | **Q** | **Q\_df** | **Q\_pval** | **egger\_intercept** | **se** | **pval** |
| ebi-a-GCST90012115 | ebi-a-GCST90010147 | Kidney Injury Molecule levels | Age-related hearing impairment (MTAG) | MR Egger | 12.74782638 | 26 | 0.986106877 | 0.018626354 | 0.044437509 | 0.678543266 |
| ebi-a-GCST90012115 | finn-b-N14\_OTHETNASKIDUR | Other specified disorders of kidney and ureter | Age-related hearing impairment (MTAG) | MR Egger | 25.18676288 | 26 | 0.508423976 | -0.043539675 | 0.065013162 | 0.508949934 |

**Table S6. Optimal parameters of nine machine learning models after hyperparameter optimization**

|  |  |
| --- | --- |
| **Model** | **parameter** |
| SVM | C:0.9  Decision Function Shape: ovo  Degree : 2.0  Kernel Type: poly  Probability: TRUE |
| RandomForest | Criterion: gini  Maximum Depth of Trees: 11.0  Maximum Number of Leaf Nodes: 92.0  Number of Trees: 391.0 |
| Logistic Regression | Penalty: l1  Solver: liblinear |
| K-Nearest Neighbors | Number of Neighbors: 18.0  Leaf Size: 17.0 |
| GradientBoosting | Maximum Depth of Trees: 4.0  Number of Trees: 250.0  Learning Rate: 0.2  Loss Function: deviance  Maximum Number of Features: auto  Minimum Number of Samples Required to Split a Node: 2.0  Minimum Number of Samples Required to be at a Leaf Node: 1.0 |
| LGBM | Maximum Depth of Trees: 4.0  Learning Rate: 0.05625  Bagging Fraction: 0.84  Bagging Frequency: 8.0  Feature Fraction: 0.7  Lambda L1: 8.1  Lambda L2: 2.1  Number of Leaves: 21.0 |
| Decision Tree | Criterion: gini  Maximum Depth of Trees: 13.0  Maximum Number of Leaf Nodes: 12.0 |
| AdaBoost | Number of Trees: 1.0 |
| CatBoost | Learning Rate: Approximately 0.0116  Depth of Trees: 5.0  Random Strength: 3.0 |