Table S1. The confounders excluded in the Mendelian Randomization.

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| **Confounders** | **Outcomes \*** | **Traits label in GWAS Catalog †** | **Reported traits ‡** |
| Aging | Esophageal cancer, Gastric cancer, Colorectal cancer, Hepatocarcinoma, Pancreatic cancer | aging | Aging; Aging (facial); Aging (time to death); Aging (time to event); Aging traits; Biological age (BioAge); Biological age (PhenoAge); DNA methylation GrimAge acceleration; DNA methylation Hannum age acceleration; DNA methylation PhenoAge acceleration; Differential aging (cerebellum); Differential aging (frontal cortex); Differential aging in older adults (cerebellum); Differential aging in older adults (frontal cortex); Differential aging in younger adults (frontal cortex); Epigenetic age acceleration in alcohol use disorder; Extrinsic epigenetic age acceleration; Intrinsic epigenetic age acceleration; Residual cognition |
| BMI | Esophageal cancer, Gastric cancer, Colorectal cancer, Hepatocarcinoma, Pancreatic cancer | body mass index | Adult onset asthma and/or BMI; Age-related disease endophenotypes; Age-related diseases, mortality and associated endophenotypes; Alanine aminotransferase levels x BMI interaction; Alzheimer's disease or BMI (pleiotropy); Alzheimer's disease or cardiovascular risk factors (pleiotropy); Aspartate aminotransferase levels x BMI interaction; BMI (adjusted for smoking behaviour); BMI (smoking interaction); BMI at 1 year old; BMI at 1.5 years old; BMI at 2 years old; BMI at 3 months old; BMI at 3 years old; BMI at 5 years old; BMI at 6 months old; BMI at 6 weeks old; BMI at 7 years old; BMI at 8 months old; BMI at 8 years old; BMI at birth; BMI in adult survivors of childhood acute lymphoblastic leukemia; BMI in adult survivors of childhood acute lymphoblastic leukemia not treated with cranial radiation; BMI in adult survivors of childhood acute lymphoblastic leukemia treated with cranial radiation; BMI in non-smokers; BMI in smokers; BMI x environmental factors (excluding physical activity) interaction; BMI x SSRI defined daily dose interaction in schizophrenia or bipolar disorder; BMI x SSRI levels (escitalopram or citalopram) interaction in schizophrenia or bipolar disorder; BMI x SSRI levels interaction in schizophrenia or bipolar disorder; BMI x dairy intake interaction (1df interaction test); BMI x environmental factors (including physical activity) interaction; Barrett's esophagus x BMI interaction; Biomedical quantitative traits; Bipolar disorder (body mass index interaction); Bipolar disorder or body mass index; Birth weight or body mass index (pleiotropy); Body mass in chronic obstructive pulmonary disease; Body mass index; Body mass index (smoking years interaction); Body mass index (SNP x SNP interaction); Body mass index (adult); Body mass index (age <50); Body mass index (age>50); Body mass index (alcohol intake interaction); Body mass index (dietary energy interaction); Body mass index (education interaction); Body mass index (ever vs never smoking interaction); Body mass index (joint analysis main effects and physical activity interaction); Body mass index (joint analysis main effects and smoking interaction); Body mass index (physical activity interaction); Body mass index (recreational physical activity interaction); Body mass index (sex interaction); Body mass index and HDL-C (pairwise); Body mass index and LDL-C (pairwise); Body mass index and cholesterol (psychopharmacological treatment); Body mass index and coronary artery disease (pairwise); Body mass index and diastolic blood pressure (bivariate analysis); Body mass index and fasting glucose (pairwise); Body mass index and fasting insulin (pairwise); Body mass index and fat mass; Body mass index and systole blood pressure (pairwise); Body mass index and systolic blood pressure (bivariate analysis); Body mass index and triglycerides (pairwise); Body mass index and type 2 diabetes (pairwise); Body mass index and waist-hip ratio (pleiotropy); Body mass index in asthmatics; Body mass index in non-asthmatics; Body mass index in physically active individuals; Body mass index in physically inactive individuals; Body mass index variance; Body mass index x age interaction; Body mass index x sex interaction; Body mass index x sex x age interaction; Body mass index x sex x age interaction (4df test); Body morphological traits (multivariate analysis); Cardiometabolic traits; Childhood body mass index; Colorectal cancer x BMI interaction (2df); Coronary artery disease and/or body mass index (pleiotropy); Esophageal adenocarcinoma x BMI interaction; Fasting blood glucose (BMI interaction); Fasting blood insulin (BMI interaction); Fibrinogen levels (smoking status, alcohol consumption or body mass index interaction); Homeostasis model assessment of insulin resistance x BMI interaction; Hyperglycemia x BMI interaction; Hyperinsulinemia x BMI interaction; Major psychiatric disorders or BMI (pleiotropy); Modified Stumvoll Insulin Sensitivity Index (BMI interaction); Modified Stumvoll Insulin Sensitivity Index (model adjusted for BMI); Multiple sclerosis and body mass index (pleiotropy); Nonatopic asthma and/or BMI; Normal body mass index vs. thin; Obesity-related traits; Physiological traits; Preterm birth (maternal effect) (maternal pre-pregnancy BMI interaction); Quantitative traits; Stroke and BMI (pleiotropy); Urate levels (BMI interaction); Visceral adipose tissue adjusted for BMI; Visceral adipose tissue/subcutaneous adipose tissue ratio adjusted for BMI |
| Physical activity | Esophageal cancer, Gastric cancer, Colorectal cancer, Hepatocarcinoma, Pancreatic cancer | physical activity measurement | Accelerometer-based physical activity measurement (average acceleration); Accelerometer-based physical activity measurement (fraction of time with accelerations >425 milli-gravities); Activity variability during wake; BMI x environmental factors (including physical activity) interaction; Body mass index; Body mass index (joint analysis main effects and physical activity interaction); Body mass index (physical activity interaction); Body mass index (recreational physical activity interaction); DIastolic blood pressure x physical activity interaction (2df); Diastolic blood pressure x physical activity interaction (1df); Homeostasis model assessment of insulin resistance x physical activity interaction; Hyperglycemia x physical activity interaction; Hyperinsulinemia x physical activity interaction; Moderate to vigorous physical activity levels; Physical activity (moderate intensity activity duration); Physical activity (overall physical activity time); Physical activity (walking duration); Sedentary behaviour duration; Strenuous sports or other exercises; Systolic blood pressure x physical activity interaction (1df); Systolic blood pressure x physical activity interaction (2df); Vigorous physical activity; Waist circumference adjusted for BMI (joint analysis main effects and physical activity interaction); Waist circumference adjusted for BMI (physical activity interaction); Waist-to-hip circumference ratio (recreational physical activity interaction); Waist-to-hip ratio adjusted for BMI (joint analysis for main effect and physical activity interaction); Waist-to-hip ratio adjusted for BMI (physical activity interaction); Waist-to-hip ratio adjusted for body mass index |
| Physical activity | Esophageal cancer, Gastric cancer, Colorectal cancer, Hepatocarcinoma, Pancreatic cancer | physical activity | Diastolic blood pressure x physical activity (least active quartile vs others) interaction (1df); Diastolic blood pressure x physical activity (least active quartile vs others) interaction (2df); Diastolic blood pressure x physical activity (least vs most active quartile) interaction (1df); Diastolic blood pressure x physical activity (least vs most active quartile) interaction (2df); Diastolic blood pressure x physical activity (less vs more active half) interaction (1df); Diastolic blood pressure x physical activity (less vs more active half) interaction (2df); HDL cholesterol x physical activity interaction (1df test); HDL cholesterol x physical activity interaction (2df test); LDL cholesterol x physical activity interaction (1df test); LDL cholesterol x physical activity interaction (2df test); Obesity-related traits; Systolic blood pressure x physical activity (least active quartile vs others) interaction (1df); Systolic blood pressure x physical activity (least active quartile vs others) interaction (2df); Systolic blood pressure x physical activity (least vs most active quartile) interaction (1df); Systolic blood pressure x physical activity (least vs most active quartile) interaction (2df); Systolic blood pressure x physical activity (less vs more active half) interaction (1df); Systolic blood pressure x physical activity (less vs more active half) interaction (2df); Triglycerides x physical activity interaction (1df test); Triglycerides x physical activity interaction (2df test) |
| Smoking | Esophageal cancer, Gastric cancer, Colorectal cancer, Hepatocarcinoma, Pancreatic cancer | smoking behaviour measurement | Anxiety x maternal smoking during pregnancy interaction; Bioavailable testosterone levels x smoking behaviour (cigarettes smoked per day) interaction; Blood pressure (smoking interaction); Body mass index (smoking years interaction); Body mass index (ever vs never smoking interaction); Carotid plaque burden (smoking interaction); Current cigarettes per day in chronic obstructive pulmonary disease; Depression x maternal smoking during pregnancy interaction; Diastolic blood pressure (cigarette smoking interaction); Estradiol levels x smoking behaviour (cigarettes smoked per day) interaction; Lifetime average cigarettes per day in chronic obstructive pulmonary disease; Lifetime smoking index; Pulmonary function (smoking interaction); Sex hormone-binding globulin levels x smoking behaviour (cigarettes smoked per day) interaction; Smoking quantity; Smoking status (daily vs non-daily); Smoking status (heavy vs light); Systolic blood pressure (cigarette smoking interaction); Testosterone levels x smoking behaviour (cigarettes smoked per day) interaction; Waist-to-hip circumference ratio (ever vs never smoking interaction); Waist-to-hip circumference ratio (smoking years interaction) |
| Alcohol consumption | Esophageal cancer, Gastric cancer, Colorectal cancer, Hepatocarcinoma, Pancreatic cancer | alcohol consumption | Acohol consumption; Alcohol drinker status |
| Barrett's esophagus | Esophageal cancer | Barrett's esophagus | Barrett's esophagus |
| Gastroesophageal reflux disease | Esophageal cancer | gastroesophageal reflux disease | Gastroesophageal reflux disease |
| Helicobacter pylori | Gastric cancer | Helicobacter pylori | Helicobacter pylori |
| Atrophic gastritis | Gastric cancer | Atrophic gastritis | Atrophic gastritis; Gastric atrophy; Severe gastric atrophy |
| Adenomatous colon polyp | Colorectal cancer | rectal or colon adenoma polyps | Rectal or colon adenoma polyps |
| Inflammatory bowel disease | Colorectal cancer | Inflammatory bowel disease | Crohn's disease; ulcerative colitis; Inflammatory bowel disease |
| Cirrhosis of liver | Hepatocarcinoma | cirrhosis of liver | Cirrhosis of liver |
| Viral hepatitis | Hepatocarcinoma | viral hepatitis | Viral hepatitis |
| Chronic pancreatitis | Pancreatic cancer | chronic pancreatitis | Chronic pancreatitis |

\* the confounders associated variants were excluded when the listed traits as outcomes in MR.

† the trait label used in the NHGRI-EBI GWAS Catalog.

‡ the trait names based on auther language and taken into acount study design.

BMI, body mass index; GWAS, genome-wide association study