**Table S1:** List of 36 clumped Hb-associated SNPs utilized in construction of Hb-PRS among Male Taiwanese Han Chinese of Taiwan Biobank

|  |  |
| --- | --- |
| **Chr** | **Related Genes and SNPs** |
| 1 | *CHRM3/CHRM3-AS2* (lncRNA) rs891700 |
| 2 | *PRKCE* rs10168349, rs4952800, rs4953318; *STAT1* rs41454245; *BCL2L11* rs616582, rs616130 |
| 3 | *LOC101927995* (ncRNA) rs9862857; *PPM1M* rs11717383 |
| 4 | *MYOZ2* rs2168987 |
| 6 | *LOC101929705* (lncRNA) rs833805; *TRIM38* rs7740793 |
| 7 | *CDHR3* rs11983073; *RUNDC3B* rs1029421 |
| 9 | ***ABO* rs579459**, rs8176741, rs4363269, rs7030248; *CERCAM* rs1009850 |
| 11 | *PRR5L* rs606442 |
| 14 | *NOVA1* rs76420826 |
| 15 | *ACAN* rs112232636 |
| 16 | *RHOT2* rs117821265; *AXIN1* rs11866815; *LUC7L* rs1211375; *HSD17B2* rs72628277 |
| 17 | *MIR22HG* (lncRNA) rs11078597 |
| 18 | *PMAIP1* rs75766249 |
| 20 | *JAG1* rs2423512 |
| 21 | *PSMG1* rs9980212 |
| 22 | *KCTD17/TMPRSS6* rs760719; ***TMPRSS6*** **rs2235321**, rs9619658, rs9607412, **rs228918**; *MPST* rs5756490 |

\*Hb-associated SNPs in bold were found common between Taiwanese Han Chinese and European Whites (i.e., between sex groups or across all sex groups). Chr, chromosome; Hb, hemoglobin; lncRNA, long non-coding RNA; ncRNA, non-coding RNA; PRS, polygenic risk score; SNP, single nucleotide polymorphism.

**Table S2:** List of 58 clumped Hb-associated SNPs utilized in construction of Hb-PRS among Female Taiwanese Han Chinese of Taiwan Biobank

|  |  |
| --- | --- |
| **Chr** | **Related Genes and SNPs** |
| 1 | *ASH1L* rs80142782; *CNN3-DT* (lncRNA) rs78122308, rs11165277; *CAMK1G* rs9430006; *THEMIS2* rs2236074; *DISP1* rs80162998 |
| 2 | *PRKCE* rs10168349, rs4952800, rs4953321; *OSR1* rs7604748 |
| 3 | *POMGNT2* rs938921; *NLGN1* rs619092 |
| 4 | *FAM47E* rs1441920; *AFAP1-AS1* (lncRNA) rs4689851; *AC104619*.2 (lncRNA) rs13128765 |
| 5 | *CTNND2* rs17802003; *TCF7* rs244662 |
| 6 | ***HBS1L*** **rs9376090**; *TMEM63B* rs72858128 |
| 7 | *UNCX* rs10277115; *KIAA0895* rs79300405; *STK31* rs1080935 |
| 8 | *ZNF704* rs72671923 |
| 9 | ***ABO* rs579459**, rs4363269; *AL589923.1* (lncRNA) rs77712720; *GTF3C5* rs2283130; *PUM3* rs10217194, rs4741769; *EPB41L4B* rs7864092 |
| 11 | *FADS1* rs174555; *SBF2/LOC101928008* (lncRNA) rs7946986, rs10500710; *JRKL-AS1* (lncRNA) rs11021624 |
| 14 | *AKAP6* rs1951681; *NPAS3* rs117429775 |
| 15 | ***LIPC* rs1800588** |
| 16 | *AXIN1* rs11866815; *RHOT2* rs117821265; *NPRL3* rs2238367; *CAPN15* rs3213574; *TMEM8A* *(PGAP6)* rs11248931; *DECR2* rs62030830; *PIGQ* rs1981483; *LUC7L* rs1211375; *LOC100134368* (lncRNA) rs11641180; *ITFG3 (FAM234A)* rs3213508; *WWOX* rs11645605; *LMF1* rs72759441 |
| 18 | *SMAD7* rs1873191 |
| 19 | *HNRNPUL1* rs75131890 |
| 21 | *CLDN14/LOC105369301* (ncRNA) rs128494 |
| 22 | ***TMPRSS6*** rs5756504, **rs2235321**, rs9619658, rs9607412, rs1558955, **rs5756515** |

\*Hb-associated SNPs in bold were found common between Taiwanese Han Chinese and European Whites (i.e., between sex groups or across all sex groups). Chr, chromosome; Hb, hemoglobin; lncRNA, long non-coding RNA; ncRNA, non-coding RNA; PRS, polygenic risk score; SNP, single nucleotide polymorphism.

**Table S3:** List of 698 clumped Hb-associated SNPs utilized in construction of Hb-PRS among Male European Whites of UK Biobank

|  |  |
| --- | --- |
| **Chr** | **Related Genes and SNPs** |
| 1 | *ATP2B4* rs4951070; *PROX1* rs4282786; *PROX1-AS1* (lncRNA)/*PROX1* rs340874; *PROX1-AS1* (lncRNA) rs111948736; *PIK3R3* rs12090501, rs785467, rs12029005; *MAST2* rs785479; *CCDC17* rs3014238; *EXOC8* rs10489609; *EGLN1* rs2808595; *MTX1* rs760077; *PRDM16* rs112206206; *TRIM58* rs3811444; *LRRC47* rs6667255; *LEPROT/LEPR* rs3934256, rs7531110, rs17412403, rs6656451; *PRDX1* rs12133294; *TIE1* rs2282226; *DNM3* rs10489297, rs572802, rs11584664; *RPRD2* rs115584674; *SZT2* rs839758; *NSUN4* rs3737744; *EPB41* rs57051210; *CDC20* rs11210838; *ST3GAL3* rs11587515; *MPL* rs11576614; *ATP13A2* rs3738814; *FCGR2A* rs1801274; *MFAP2* rs2311528; *PDE4B* rs1577844; *CDC14A* rs630646; *FAM89A* rs4074493; *LINC01389* (lncRNA) rs10437097; *SLC6A17* rs11811388 |
| 2 | ***PRKCE*** rs71422190, rs12623399, **rs10495928**, rs3768735, rs10495930, rs113797384, rs11690961, rs281473, rs921183, rs57322816, rs2594494, rs6742742, rs13405039, rs55639402, rs34496377, rs4952798, rs10171092, rs7601785, rs11686522; *PSD4* rs752590; *PAX8* rs72831838; *TFCP2L1* rs11677172, rs6723509; *LOC105377632* (ncRNA) rs7599954; *GCKR* rs780094; *GPN1* rs3749147; *TTLL4* rs3731877; *ALPI* rs790022; *ZNF142* rs10187066; *ITGB6* rs16844875; *LOC101928278* (ncRNA) rs1861630; *CYP27A1* rs6436090; *LOC101929763* *(LINC02580)* (lncRNA) rs67929940; *AC096666.1* (lncRNA) rs16824898; *PSME4* rs7569370; *HPCAL1* rs4669566; *CTDSP1* rs921968; *EPAS1* rs6758592; *GALNT14* rs10179187 |
| 3 | *SYN2* rs73813126; *CTDSPL* rs74878094; *PPARG* rs60290266; *MECOM* rs419076, rs7613621, rs6774494; *ARHGEF3* rs3772219, rs4407379; *TNK2* rs56260729, rs4927791; *FGF12* rs112154005; *TFRC* rs7627706; *MKRN2OS/MKRN2* rs2633443; *LINC01991* (lncRNA) rs763342, rs2248422, rs9810106; *RAF1* rs9817675; *AADACL2* rs9834244; *LOC647323* *(LINC02026)* (lncRNA) rs9814612, rs1873407; *MITF* rs10510988; *MYRIP* rs6776146; *ABHD6* rs4681675, rs3773004; *AHSG* rs4917; *C3orf43* *(SMCO1)* rs7629990 |
| 4 | *KLHL8* rs10006766; *MMAA* rs11939702; *TIGD2* rs17015027; *SMAD1* rs959641; *C4orf19* rs10026105 |
| 5 | *NREP* rs77080560; *ITGA1* rs2279587; *PTGER4* rs1505991; *PPARGC1B* rs17710855; *CARMN* (lncRNA) rs72840216; *VCAN* rs2591455; *LINC01951* (lncRNA) rs11741337; *ABLIM3* rs13174812 |
| 6 | *SLC17A2* rs80215559, rs2071298, rs199741, rs199736, rs2071300; *SLC17A2* rs17342717, rs17270561; *LRRC16A* *(CARMIL1)* rs2274089, rs72828723, rs55946641, rs13203202, rs12526480, rs1012899, rs9461183, rs368638; *LRRC16A* *(CARMIL1)/LOC101928699*\* rs79693813, rs913455, rs55731467, rs2328881, rs12192665, rs77042711, rs12153885, rs9379764, rs9467515; *HFE* rs1799945, rs2794720, rs17596719, rs2071303; *ZSCAN31* rs35814746, rs67340775, rs213240, rs7772827; *SCGN* rs932316, rs4711092, rs1074707, rs4712955, rs6935832; *TRIM38* rs12216125, rs13212534, rs169219; *GPX5* rs11757235; *BTN1A1* rs13194984, rs3736780; *TRNAW9 (TRW-CCA3-1)* (tRNA) rs9467704, rs9467703; *HIST1H2BC (H2BC4)* rs13200797, rs198823; *BTN3A1* rs41266839, rs1741738, rs10456045, rs3799378, rs1796520; *TRNAS10 (TRS-AGA2-2)* (tRNA) rs7749305, rs7761966; *TRNAA10 (TRA-TGC5-1)* (tRNA) rs3118362; *HIST1H3J (H3C12)* rs200973; *HIST1H1B (H1-5)* rs200953, rs200951; *HIST1H2BO (H2BC17)* rs13218875, rs731132; *SLC17A4* rs4712972; *LOC101928743* (ncRNA) rs9467714, rs9358929, rs9358928, rs9467715; *TRNAA13 (TRA-AGC2-1)* (tRNA) rs3118357; *HLA-DMA* rs1480380; *CFB* rs1270942; *HLA-DRA* rs3135394, rs9501626, rs3135338, rs1041885; *TRNAY7 (TRY-GTA3-1)* (tRNA) rs9393735; *NOTCH4* rs3132956, rs374205, rs377763, rs424232, rs412657, rs507778; *HLA-DRB1* rs9270493, rs502771, rs615672, rs9269831, rs3021304; *SLC17A3* rs56027330, rs4712976, rs12664474; *ATP6V1G2-DDX39B* (lncRNA)/*ATP6V1G2* rs9267488; *ATP6V1G2-DDX39B* (lncRNA)/*DDX39B* rs3093974; *RNF39* rs9261290; *BTNL2* rs28366191, rs2395165, rs3135363, rs2395166; *TRNAA8 (TRA-AGC5-1)* (tRNA) rs7775835; *SNORD32B* (snoRNA) rs926552; *TRNAS16 (TRS-GCT6-1)* (tRNA) rs994379; ***HBS1L*** rs9494145, **rs9376090**, rs76267242, rs6569992, rs10457631; *HCG27* (lncRNA) rs3132510, rs3130474, rs3130953; *HLA-DQA2* rs28371355; *BTN3A2* rs72841509, rs11758089, rs12199613, rs1985732; *TRNAS13 (TRS-GCT5-1)* (tRNA) rs1233708; *HIST1H3G (H3C8)* rs11759682; *HIST1H4G (H4C7)* rs41266821; *HLA-DOB* rs9276731, rs4947350, rs3948793, rs2857161, rs9276726; *HCP5* (lncRNA) rs3128987, rs2596454; *HIST1H3I (H3C11)* rs200956; *DPCR1 (MUCL3)* rs3132580; *TNXB* rs1150758; *LINC00243* (lncRNA) rs3130641, rs3131064, rs3094111; *HLA-B* rs2507997, rs2596503, rs2523608, rs2156875; *RNF5* rs3130349; *LOC101929111 (LINC01149)* (lncRNA) rs2516470, rs3128982, rs3131622, rs2263316, rs2395004; *POLH* rs9296418; *TRNAL16 (TRL-TAA2-1)* (tRNA) rs2056925, rs9295740; *TNF* rs1800629; *PSORS1C1* rs3130564, rs3130552, rs3130553, rs2285803; *PSORS1C1/CDSN* rs3130989; *PSORS1C1/PSORS1C2* rs3130573; *TRNAF9 (TRF-GAA4-1)* (tRNA) rs209181; *RREB1* rs74640935, rs12192672, rs76052955, rs9379077, rs2714341, rs2714346, rs2256596, rs2842358; *TRNAR10* *(TRR-ACG2-3)* (tRNA) rs13219354; *LINC01015* (lncRNA) rs1233478; *GPX6* rs722788; *TRNAA38 (TRA-CGC5-1)* (tRNA) rs6939576, rs1319075; *TRNAA28 (TRA-AGC3-1)* (tRNA) rs36103239; *TRNAV7 (TRV-AAC1-5)* (tRNA) rs4713120; *TRIM31* rs9261387, rs2523986, rs2523990, rs9261424; *OR2J2* rs3129152, rs3130740; *VEGFA* rs699947, rs25648; *ZKSCAN4* rs9295768; *TRNAA19 (TRA-TGC1-1)* (tRNA) rs9257182; *HIST1H1D (H1-3)* rs16891464; *LOC101929072 (MICA-AS1)* (lncRNA) rs2251396; *C6orf10 (TSBP1)* rs9268135, rs6910668, rs3129943, rs926070, rs17422727, rs3129907, rs1003879, rs2050190, rs2273017; *TRIM26* rs2517618, rs1345229, rs3132668; NCR3 rs2857595, rs2857596; BAG6 rs3130048, rs805303; *HIST1H2AC (H2AC6)* rs2856646; *OR12D3* rs6934993, rs9257802, rs10807053; *HLA-DQA1* rs9271489, rs9271824, rs5004277; *TRNAI4 (TRI-AAT2-1)* (tRNA) rs9348772; *CCHCR1* rs1265086, rs1265078, rs130068; *MICB* rs3132469, rs3131633, *LOC100294145* (ncRNA) rs9276915, rs2857218; *HCG22* rs2517527, rs2517534, rs2523864, rs2844645; *C6orf15* rs2233956, rs2535296, rs2517529, rs1265052; *TRNAV20 (TRV-CAC9-1)* (tRNA) rs9379960; *EHMT2* rs652888; *PSORS1C3* (lncRNA) rs887465; *TRIM10* rs3094134, rs12212092; *C6orf48 (SNHG32)* (lncRNA) rs2471980; *HIST1H4C (H4C3)* rs198853; *PRSS16* rs2295603; *BTN3A3* rs2237236; *ZNF322* rs7740197; *TRNAQ21 (TRQ-CTG2-1)* (tRNA) rs6915987; *TRNAI1 (TRI-AAT9-1)* (tRNA) rs7759694; *BTN2A1* rs9358945; *TRNAK19 (TRK-TTT6-1)* (tRNA) rs9461366; *MUC22* rs2517544, rs2844670; *POLR1C* rs9357429; *DDAH2* rs805304; *LY6G5C* rs3115667; *HLA-DQB1* rs6906021; *LTA* rs2071590; *HIST1H2BJ (H2BC11)* rs7745603; *HIST1H1E (H1-4)* rs806973; *PSMB9* rs9276815; *MICD/HCG9* (lncRNA) rs2735076; *HCG9* (lncRNA) rs2394251; *HLA-DQB2* rs2857211; *ZNF184* rs7772160; *ZNF165* rs203878; *TRNAA29 (TRA-CGC1-1)* (tRNA) rs1884947; *OR2J3* rs3130766; *PBX2* rs204993; *TRNAV18 (TRV-AAC6-1)* (tRNA) rs1233572, rs880638; *SCAND3 (ZBED9)* rs418092; *TRNAA41 (TRA-AGC13-1)* (tRNA) rs2498399; *HSPA1L/HSPA1A* rs1043618; *TRIM15* rs2844787; *HLA-C* rs7759127, rs2894202, rs2894186, rs6923313; *LINC02571* (lncRNA) rs3094682, rs396243, rs3915971; *TRNAD9 (TRD-GTC3-1)* (tRNA) rs12197514; *NFKBIL1* rs2857605, rs2239707; *TRNAS5 (TRS-GCT2-1)* (tRNA) rs4559087; *TRNAM1 (TRX-CAT1-2)* (tRNA) rs9379842, rs10946810; *VARS (VARS1)* rs2736426; *RSPO3* rs9491696, rs6569474; *TAP2* rs2071465, rs2239701; *LOC105375005* (ncRNA) rs1033568; *HIST1H2AA (H2AC1)* rs9467583; *PTP4A1* rs1923521; *HIST1H2BH (H2BC9)* rs6935954; *GMPR* rs1042391; *ZKSCAN3* rs6922111; *HLA-F-AS1* (lncRNA) rs1736913; *IER3* rs2535319; *TRIM40* rs2107202; *COL11A2* rs9277935, rs2254287*; HLA-DPB1* rs3128965; *HLA-E* rs3131115; *POU5F1* rs9263804; *SSR1* rs10004; *HCG24* (lncRNA) rs3116971; *GMDS* rs11242732, rs234944; *ABCF1* rs1264431; *CASC15* (lncRNA) rs4712653, rs9393228, rs1207775; *CASC15* (lncRNA)/*CASC14 (NBAT1)* (lncRNA) rs6939340, rs9460707, rs6934891; *PRKN* rs9458501; *NKAIN2* rs2689888; *PDE10A* rs13217316; *CAGE1* rs9505168; *LOC105377882* (ncRNA) rs4706304 |
| 7 | *PRKAG2* rs10224002, rs56148928, rs6967507, rs6947064, rs2374270, rs28533208, rs4726086, rs62478183; *GIGYF1* rs56148928; *USP42* rs55962331, rs2107853; *CYTH3* rs6463537; *PRKAR1B* rs9719145, rs62431456, rs62432166; *ZNF804B* rs73202737, rs2189055, rs73204774; *EIF2AK1/ANKRD61* rs12334093; *DAGLB* rs836534; *ZCWPW1* rs7783159; *ZNF679* rs35638959; *MYL10* rs4602817; *KPNA7* rs10953283, rs62473013; *SEMA3C* rs1358503 |
| 8 | *SMIM19* rs2974359; *COL22A1* rs67263012; *SLC20A2* rs55840085, rs6988165, rs2978456; *TDRP* rs2290072, rs3735918, rs55785048; *TRPS1* rs3779881, rs800897; *FAM135B* rs55976017, rs7015202, rs11166827; *LOC105375739* (ncRNA) rs10088262; *FBXO25* rs3735923; *LINC01609* (lncRNA) rs76622126; *DPY19L4* rs9643349, rs13267007; *RB1CC1* rs2884945; *ZHX2* rs3802266; *PLEKHA2* rs7386365; *NECAB1* rs35918434; *LOC100288748* (lncRNA) rs10504938; *LOC101926977* (ncRNA) rs1426172; *HAS2-AS1* (lncRNA) rs3910553; *ESRP1* rs72676907 |
| 9 | ***ABO*** rs507666, **rs8176749**, rs7853989, rs687621, rs8176720; *C9orf96 (STKLD1)* rs41302673, rs3124747; *SURF4* rs56343119; *ADAMTS13* rs4962153; *OBP2B* rs7864821; *SLC2A6* rs73553519; *ZNF462* rs7027110; *LOC100505478 (TEX48)* rs78996265; *GLIS3* rs72693873; *RALGDS* rs11244009; *DCAF12* rs10971956 |
| 10 | *HK1* rs16926246, rs7909192, rs7072268, rs2084274; *HKDC1* rs12359891; *LINC02561* (lncRNA) rs72778452; *BICC1* rs1658457; *CXCL12* rs4948877, rs266100; *CTBP2* rs2949371, rs3781445; *LRMDA* rs4745785; *ACSL5* rs1926564; *ZNF438* rs10160116; *AKR1C3* rs11252918; *ATRNL1* rs11197481; *FRMD4A* rs55830730; *OAT* rs2361610 |
| 11 | *SBF2* rs56352102, rs16907334, rs35815123, rs7938570; *CAND1.11* (lncRNA) rs7129220; *FADS1* rs174548; *MYRF* rs108499; *NLRP6* rs17156153; *FEN1* rs4246215; *ST5 (DENND2B)* rs3794153; *MRVI1 (IRAG1)* rs7940646, rs4909947; *AMPD3* rs72859103, rs7416; *NELL1* rs16907672; *SWAP70* rs2649048, rs12223505; *RRM1* rs12806698; *NUP98* rs10767588; *OR4B1* rs10769322; *LOC105369381* (ncRNA) rs1791936 |
| 12 | *ATXN2* rs653178, rs1029388; *BRAP* rs11065987; *PTPN11* rs2079175, rs2301756, rs11066301; *NAA25* rs7965087, rs4767364; *TRAFD1* rs17630235; *ACAD10* rs4766897; *ALDH2* rs4646777, rs2238151; *CUX2* rs1265565, rs79592135, rs10849937, rs4766558, rs10849931, rs4766568, rs7297186, rs3809291, rs7970490, rs4766567, rs4378452, rs2106410; *PFKM* rs4760682; *OR10AD1* rs11168459, rs4760622; *CACNA1C* rs35407591; *RPH3A* rs10744782; *GPRC5A* rs12811512; *ETV6* rs2856319; *IFT81* rs11065340; *RPH3A* rs7132088; *MIR1302-1* (miRNA) rs3803064; *KSR2* rs73208197; *CCND2* rs10849018; *ALG10* rs11053075; *CPNE8* rs10506126; *PAH* rs937475 |
| 13 | *STARD13* rs9536654, rs2858813, rs797194, rs652184, rs9315204; *GAS6* rs6602910; *MED4* rs1571256; *LINC00427* (lncRNA) rs60264756 |
| 14 | *ESR2* rs7157428, rs12435857; *TEX22* rs74541291; *GPATCH2L* rs2121074; *BCL11B* rs7151737; *ZFYVE1* rs1007934; *LINC02291* (lncRNA) rs17583994; *LOC107987211* rs74093831 |
| 15 | *UBR1* rs62020698; *DNAJA4* rs11856774, rs3169166; *NRG4* rs8024155; *ACSBG1* rs80071140, rs4887019; *ZNF106* rs74009095, rs12440118, rs4924678; *LINC02248* (lncRNA) rs4545787; *WDR72* rs16966245, rs491567; *TPM1* rs72743223; *WDR61* rs4887029; *FBXL22* rs8035931; *GLDN* rs2446417; *SMAD3* rs17228212; *BLM* rs7162960; *EIF2AK4* rs566792 |
| 16 | *PSKH1* rs16942887; *PIEZO1* rs57374020, rs78579285, rs2879906; *PKD1L3* rs74343175; *NFATC3* rs74024145; *TBX6* rs3809627; *DEF8* rs7192165; *ADCY9* rs387212; *CDK10* rs12924572; *DPEP1* rs164749; *PAPD5 (TENT4B)* rs8055697; *SPIRE2* rs8060934; *NPRL3* rs7185768; *DUS2* rs2285912; *IRX6* rs24117; *TERF2* rs3785073; *CACNG3* rs4787433; *COG8* rs3759979 |
| 17 | *PLEKHM1* rs5026246; *ARHGAP27* rs12939187; *MAPT* rs8070723, rs1001945; *ARL17A/LRRC37A2* rs145809511; *CRHR1* rs117615688, rs9303521; *WNT3* rs916888, rs199501; *BCAS3* rs7214149; *GOSR2* rs17608766, rs197920; *LOC100996660* (ncRNA) rs11656267; *GCGR* rs144150986; *P4HB* rs35788525; *LRRC37A2*/*LOC101927060* (ncRNA) rs4968295, rs2316758; *LRRC37A2* rs8079694, rs6504635; *HEATR6* rs3744375; *PLXDC1* rs11650037; *FAAP100* rs11552304 |
| 18 | *PIEZO2* rs55646160; *GREB1L* rs62089245; *MBP* rs470970, rs17660901 |
| 19 | *DOT1L* rs3803915, rs12986413, rs12976923, rs12983546, rs3815145, rs3815308; *SH3GL1* rs732716; *TDRD12* rs58026555; *PTBP1* rs123698; *CHAF1A* rs2230636; *AP3D1* rs2238610; *ANKRD27* rs405858, rs12462871, rs2287669; *ZNF71* rs10405623; *QPCTL* rs2302593; *SNRPD2* rs10403723; *LILRA4* rs8102662 |
| 20 | *PCMTD2* rs75501408; *CDH4* rs6061618; *LOC100505664* (ncRNA) rs11698127; *MIR1*-*1HG* (lncRNA) rs6062234, rs35271296 |
| 21 | *LOC105369301* (ncRNA) rs218642; *NRIP1* rs2229742; *ITSN1* rs2834285, rs3787717; *ATP5O* rs2834297; *BACH1* rs372883, rs407712; *LOC105372789* (ncRNA)/*LOC105372790* (ncRNA) rs2834345; *LOC101928126* (lncRNA) rs2834323; *ATP5PO* rs2834298; *LINC00649* (lncRNA) rs13049489 |
| 22 | ***TMPRSS6*** **rs4820268**, rs881144, **rs2235321**, rs2543515, rs7286184, rs855788, rs73160055, rs17750152, **rs228918**, **rs5756515**; *MPST* rs3753145; *WNT7B* rs9330813, rs28605102, rs28663466; *TEX33* rs2413447, rs743749; *PNPLA3* rs738409; *FBLN1* rs75939739; *LOC100506241* *(LL22NC01-81G9.3)* (lncRNA) rs17749540; *A4GALT* rs5758896, rs34091628; *PARVB* rs2073080; *XBP1* rs2239815 |

\*Hb-associated SNPs in bold were found common between European Whites and Taiwanese Han Chinese (i.e., between sex groups or across all sex groups). Chr, chromosome; Hb, hemoglobin; lncRNA, long non-coding RNA; miRNA, microRNA; ncRNA, non-coding RNA; PRS, polygenic risk score; snoRNA, small nucleolar RNA; SNP, single nucleotide polymorphism; tRNA, transfer RNA.

**Table S4:** List of 805 clumped Hb-associated SNPs utilized in construction of Hb-PRS among Female European Whites of UK Biobank

|  |  |
| --- | --- |
| **Chr** | **Related Genes and SNPs** |
| 1 | *MTX1* rs760077; *PROX1* rs4282786; *E2F2* rs12144921; *EGLN1* rs6677989; *MUC1* rs4072037; *HSPB7* rs12725641, rs945420; *CLIC4* rs4601530; *MAST2* rs785479; *KDM4A* rs660899; *GALNT2* rs4846914; *TIE1* rs1209384; *SZT2* rs2782643; *FLVCR1* rs7528119; *TNFRSF8* rs2486316; *PTPRF* rs2842185; *USH2A* rs10864216; *OLFML2B* rs2880058; *NOS1AP* rs12143842; *LOC149351* *(LINC02609)* (lncRNA) rs11578876 |
| 2 | ***PRKCE*** rs71422190, rs12623399, **rs10495928**, rs10495930, rs11690961, rs3768735, rs113797384, rs7601785, rs11686522; *TFCP2L1* rs11677172; *PAIP2B* rs115883483; *ATOH8* rs6706567; *ZFP36L2* rs77030801, rs35266644; *ASXL2* rs6729339, rs34579290; *DTNB* rs28407131, rs7582059; *LNPK* rs34897061; *RQCD1 (CNOT9)* rs589967; *TTLL4* rs3731876; *PAX8* rs6734610; *LOC100129455* (ncRNA) rs2592394; *ERMN* rs13028288; *LINC00299* (lncRNA) rs76281458; *HAGLR* (lncRNA)/*HAGLROS* (lncRNA) rs2072590; *LOC101929763 (LINC02580)* (lncRNA) rs756110; *SFTPB* rs59494763; *SNED1* rs34586607; *LINC00607* (lncRNA) rs13427941; *COMMD1* rs17514412; *THSD7B* rs10197612; *AGAP1* rs13014851; *LOC728730 (MAP4K3-DT)* (lncRNA) rs887970; *TMEM194B (NEMP2)* rs4439990; *B3GNT2* rs79813025; *CCT4* rs76248080; *ATG16L1* rs3792109; *LOC105374329* (ncRNA) rs6756785; *TMEM178A* rs2716716 |
| 3 | *STAB1* rs1010553, rs4434138, rs731831; *LIPH* rs74474250; *PBRM1* rs13083798, rs2251219; *MITF* rs6805563; *PPARG* rs60290266, rs62243565, rs2960422; *GLYCTK* rs9311474; *PHF7* rs13094687; *ULK4* rs73071203; *ITIH3* rs3617; *DNAH1* rs4687612; *TWF2* rs353547; *ALAS1* rs352169; *ITIH4* rs2071042; *PRKCD* rs3821690, rs12490645; *LRIG1* rs6793110; *SLC25A26* rs782722; *DCP1A* rs62250805, rs62257007; *C3orf20* rs6765537, rs11710203; *CAND2* rs4684883; *NR1I2* rs2461823; *CNTN4* rs13088710 |
| 4 | *SLC39A8* rs13107325; *FGF5* rs16998073; *FRAS1* rs55860532; *LRBA* rs115370855; *SMIM14* rs7673664; *N4BP2* rs17619392; *ARHGAP10* rs2358182, rs7697204 |
| 5 | *RGS14* rs4075958; *NR3C1* rs10482633; *SLC25A46* rs381661; *PCDHB5* rs56197059; *HK3* rs539822; *MRPS27* rs9293282; *CAST* rs13184900; *CAMK4* rs11960269; *HSPB3* rs62354468; *ADRB2* rs10875641 |
| 6 | *SLC17A2* rs80215559, rs6932113, rs7748167, rs199741, rs2071300; *SLC17A1* rs17342717, rs17270561; *LRRC16A (CARMIL1)* rs2274089, rs72828723, rs55946641, rs78114836, rs13203202, rs35676593, rs7760067, rs12526480, rs419563, rs742132, rs1012899, rs368638, rs9461183; *LRRC16A (CARMIL1)/LOC101928699*\* rs79693813, rs55731467, rs12192665, rs77042711, rs9379764, rs12153885, rs2328881, rs913455, rs927984, rs969645, rs9461167; *HFE* rs1799945, rs17596719, rs2071303; *SCGN* rs932316, rs4711092, rs1074707, rs6935832, rs4712955; *ZKSCAN3* rs71559077, rs11751928; *ZSCAN31/ZKSCAN3* rs1474589; *TRNAA10 (TRA-TGC5-1)* (tRNA) rs3118362; *TRIM38* rs12216125, rs13212534, rs169219, rs199725; *HIST1H4B (H4C2)* rs3752419; *BTN3A2* rs36085954, rs9393714, rs12199613, rs1985732, rs11758089; *TRIM31* rs9261387; *TRIM31/TRIM31-AS1* (lncRNA) rs3132679, rs9261407, rs2523990; *TRIM31-AS1* (lncRNA) rs2517597, rs9261431, rs1015465; *FAM65B (RIPOR2)* rs12193223, rs12194442, rs370748, rs303880, rs7743187; *SLC17A3* rs523383, rs56027330, rs4712976, rs12664474; *TRIM10* rs3094134, rs2517645; ***HBS1L* rs7775698**, rs9494145, rs6569992, rs72974176, rs76267242, rs10484494, rs10457631, rs9494139, rs6940258, rs1135205; *TRNAS16 (TRS-GCT6-1)* (tRNA) rs994379; *BTN3A1* rs41266839, rs1741738, rs3799378, rs10456045, rs742090; *HIST1H4G (H4C7)* rs41266821; *SLC17A4* rs4712972; *LOC101928743* (ncRNA) rs9467714, rs9358929, rs9467715, rs9358928, rs6930616, rs2179152, rs7755741; *GPX6* rs722788, rs434112; *TRNAS10 (TRS-AGA2-2)* (tRNA) rs7749305; *PPT2-EGFL8* (lncRNA)/*EGFL8* rs41268924; *HIST1H4C (H4C3)* rs2229768; *EHMT2* rs2844456, rs7743807; *MDC1* rs3094093; *HIST1H3G (H3C8)* rs11759682; *HCP5* (lncRNA) rs2255223, rs2255221, rs3131618; *AIF1* rs34451818; *ZSCAN12* rs2232423, rs2232422; *NOTCH4* rs8192575, rs3134942, rs374205, rs377763, rs715299, rs915894, rs3134931, rs2395106, rs483574; *HIST1H2AK (H2AC15)* rs34706883; *ABCF1* rs3132611, rs3132610; *TRNAA2 (TRA-AGC11-1)* (tRNA) rs13214027; *OR2B6* rs7767176; *BAG6* rs743400, rs3117583, rs3130048; *HIST1H2AM (H2AC17)* rs200968; *LINC00243* (lncRNA) rs3129988, rs3094123, rs3130648, rs3130654, rs3130787, rs2250264; *TRIM15* rs9261536, rs2844787; *ZSCAN26* rs1419183, rs2179174; *C6orf10 (TSBP1)* rs9268219, rs28366175, rs3117111, rs3129949, rs4348357, rs9268220, rs521828, rs9268199, rs9268213, rs3129945, rs910050, rs9268103, rs1003879, rs17422727, rs2273017, rs2050190; *HIST1H3I (H3C11)* rs200956; *VEGFA* rs62401198, rs943072, rs699947; *LINC01015* (lncRNA) rs1233478, rs3094564, rs3130855; *HIST1H3C (H3C3)* rs7756117; *AGPAT1* rs1269839; *OR12D3* rs9257802, rs9257794; *HCG27* (lncRNA) rs3132510, rs3130474; *ZNRD1 (POLR1H)* rs8321; *HIST1H2BN (H2BC15)* rs200994; *HLA-B* rs2507997, rs2596503, rs2156875; *LOC101929111* *(LINC01149)* (lncRNA) rs2516470, rs3131622, rs3099836; *ZKSCAN4* rs1736904, rs2185955; *MSH5-SAPCD1* (lncRNA)/*MSH5* rs3117575; *TRIM40* rs1419675, rs3132676, rs2523995; *OR2B2* rs149878, rs731132; *PSORS1C1* rs3130564, rs3130552, rs3130989; *HCG17* (lncRNA)/*HCG18* (lncRNA) rs1048664; *HCG17* (lncRNA)/*HLA-L* rs2021107; *PRSS16* rs4452638; *MICD/HCG9* (lncRNA) rs2735076; *HLA-DQA1* rs9271541, rs9271489, rs9272105; *NCR3* rs2857596, rs2857595; *ZNF322* rs148210763, rs1027204; *TRNAS13 (TRS-GCT5-1)* (tRNA) rs1233708; *OR2J3* rs3129106; *HIST1H4A* *(H4C1)* rs75397441; *BTNL2* rs2395165, rs2395166; *HIST1H3F (H3C7)* rs11759720; *BTN1A1* rs2093169; *TRNAL16 (TRL-TAA2-1)* (tRNA) rs2056925; *HIST1H2AC (H2AC6)* rs707901, rs2856646; *EDN1* rs1629862, rs2070699, rs10947946; *DDR1* rs3132572; *TRNAF9 (TRF-GAA4-1)* (tRNA) rs209181; *ZKSCAN8* rs1890809; *HLA-DOB* rs3948793, rs2621383; *TRNAA28* *(TRA-AGC3-1)* (tRNA) rs36103239; *ZFP57* rs3870968, rs445150; *MICB* rs2534674, rs3132469, rs9267404; *DPCR1 (MUCL3)* rs3131921; *HLA-DRB1* rs502771, rs615672, rs9269822, rs9269910, rs3021304; *TRNAS17 (TRS-GCT4-1)* (tRNA) rs6901724; *C6orf15* rs2517448, rs1265053, rs2517529, rs2233974, rs2233956; *TRNAA29 (TRA-CGC1-1)* (tRNA) rs1884947; *ABHD16A* rs1475865; *HLA-F-AS1* (lncRNA)/*MICE* rs9258224; *HLA-F-AS1* (lncRNA) rs1736913; *HIST1H2BH* *(H2BC9)* rs809871; *LOC101929072 (MICA-AS1)* (lncRNA) rs2251396; *LOC100131289* (lncRNA) rs9295747; *HIST1H4D* *(H4C4)* rs6906367; *TRNAI20 (TRI-AAT5-2)* (tRNA) rs911186, rs13194053; *HIST1H1E (H1-4)* rs806973; *CCHCR1* rs1265086; *GSTA1* rs6917325; *TRNAA19 (TRA-TGC1-1)* (tRNA) rs9257182; *NFKBIL1* rs2071591; *L3MBTL3* rs13209890, rs9388768; *HIST1H2BF (H2BC7)* rs806794; *TRNAA38 (TRA-CGC5-1)* (tRNA) rs6939576; *SFTA2* rs2253588; *GABBR1* rs3025642, rs29221; *HIST1H4F (H4C6)* rs9358913; *HLA-DRA* rs3129867, rs2239806, rs3135344, rs9268633; *GSTA5* rs4715354, rs13219949; *GNL1* rs2534804; *LTA* rs2071590; *TRNAV20 (TRV-CAC9-1)* (tRNA) rs9379960; *HCG22* rs2523864, rs2844645; *TRNAK19 (TRK-TTT6-1)* (tRNA) rs9461366; *HIST1H2BC (H2BC4)* rs198823; *PRSS16* rs2295603; *TRNAL28 (TRL-CAA2-1)* (tRNA) rs6456799; *RSPO3* rs72961013, rs6932207, rs9968920; *HLA-A* rs7745413; *HLA-E* rs3131115; *HCG9* (lncRNA) rs2394250, rs2246638, rs2246642, rs3823374, rs2735071; *HIST1H2AA (H2AC1)* rs9467583; *MICA* rs3094584; *MUC22* rs2517544; *GPSM3* rs3134605; *CDK19* rs12208594; *VARS (VARS1)* rs2736426; *OR2J2* rs3130740; *GSTA3* rs62412923; *PBX2* rs204993; *IER3* rs2535319; *MOG* rs3129073, rs2535260, rs1233367; *GMDS* rs11242732, rs234944; *TSBP1-AS1* (lncRNA) rs424232, rs507778, rs412657; *PSMB9* rs6938130; *PIM1* rs9357237, rs55866815; *MUC21* rs1634731; *C6orf47* rs805262; *COL11A2* rs79131379; *LST1* rs2256974; *ZSCAN23* rs13190937; *GMPR* rs4716056, rs9396650; *QKI* rs783140; *BACH2* rs79786487; *SRSF3* rs9380580; *IYD* rs1033446; *ALDH8A1* rs9321479; *GTF2H4* rs1264309; *KCNK5* rs2815104; *LOC100132354 (LINC01512)* (lncRNA) rs1003167; *PLEKHG1* rs6919129; *MYO6* rs2748940; *PNRC1* rs1573857 |
| 7 | *GIGYF1* rs56148928; *PRKAG2* rs10224002, rs6967507, rs2374270, rs6947064, rs4726086, rs2538045, rs2538038; *EPO* rs1617640; *UNCX* rs6950388, rs12702509, rs4724805; *ZAN* rs2293767, rs10953303; *TFR2* rs4434553; *ZC3HC1* rs11556924, rs12536542, rs1464890; *EPHB4* rs2571607; *UBE2H* rs62491541; *STRIP2* rs17553578; *NYAP1* rs12539172; *AP1S1* rs34699890; *LRCH4* rs909152; *SERPINE1* rs13238709; *PDE1C* rs6955875; *TRG-AS1* (lncRNA) rs1006867; *TMEM176B* rs3757410 |
| 8 | *ZBTB10* rs76592669; *LOC157273* (lncRNA) rs2126259, rs6984305, rs11779870; *GPAT4* rs34733644; *DPY19L4* rs9643349; *DLC1* rs2119910; *NDUFAF6* rs2923814; *NAT2* rs10103029, rs1495741; *HNF4G* rs1464093; *ERICH1-AS1* *(DLGAP2)/DLGAP2* rs17740640; *PENK* rs111273977; *KIAA1456 (TRMT9B)* rs12677529; *MIR4471* (miRNA) rs16898310; *ZC2HC1A/IL7* rs7010897; *RNF19A* rs1371867; *MSC* rs10096875; *ZFPM2* rs6995272; *DLGAP2* rs9650539; *STC1* rs218871 |
| 9 | ***ABO* rs8176749**, rs507666, rs7853989, rs612169, rs8176720, rs581107, rs688976, rs512770; *SURF4* rs56343119; *C9orf96* *(STKLD1)* rs41302673, rs3124747; *ADAMTS13* rs4962153, rs3124776, rs2301612; *OBP2B* rs11244035, rs7864821; *ENG* rs4837197, rs12379490, rs41432051; *AK1* rs4226; *ST6GALNAC4* rs3818509; *SLC2A6* rs2073935; *GBGT1* rs6597604, rs6597604; *MED22* rs7870707; *GLIS3* rs10814852; *EXD3* rs28374197, rs11534411; *GNG10* rs12353546; *RGS3* rs41305473; *NELFB* rs78469234; *SURF6* rs10793964; *FAM166A* rs9802950; *RPL12* rs1139400; *NIBAN2* rs2244830; *UAP1L1* rs7037849; *SLC2A8* rs3824414; *POLE3* rs14419; *SLC24A2* rs10757124; *CDC37L1* rs10974736; *DELEC1* (lncRNA) rs10114224; *C9orf66 (DOCK8-AS1)* (lncRNA)/*DOCK8* rs636922; *DOCK8* rs506121; *GTF3C5* rs2905095;  *BANCR* (lncRNA) rs10867296; *CCDC171* rs10962128 |
| 10 | *HK1* rs16926246, rs4746839, rs7909192, rs7072268, rs35932296; *GDF2* rs34130368; *PGAM1* rs60890987; *ADAM12* rs80314400, rs7075337; *SLC16A9* rs12356193; *C10orf71-AS1* (lncRNA) rs12411581; *PFKP* rs7393395; *PLEKHS1* rs3127078; *PITRM1* rs7916396 |
| 11 | *CAND1.11* (lncRNA) rs72852812; *FADS2* rs174583, rs174591, rs61897793, rs174611, rs174609; *LOC101928338* (ncRNA) rs963837, rs628093; *MYRF* rs108499, rs509360; *DCDC5 (DCDC1)* rs163884, rs273613; *RAB3IL1* rs174479; *NRIP3* rs7479407; *MPPED2-AS1* (lncRNA) rs294348; *ST5 (DENND2B)* rs2742552, rs10840128; *FADS3* rs1000778, rs174455; *SBF2* rs1822295, rs7938543, rs2403259; *AP003174.1* (lncRNA) rs11215599; *BDNF-AS* (lncRNA) rs16960959; *WT1* rs16921914; *MIR4491* (miRNA) rs1893990, rs12365324; *PSMC3* rs11600581; *SPI1* rs72896066; *PICALM* rs3844143; *NUP98* rs10767588; *PDGFD* rs11226142; *ZBTB16* rs2519193 |
| 12 | *SH2B3* rs3184504; *BRAP* rs11065987; *TRAFD1* rs17630235; *PTPN11* rs11066301, rs58116261, rs2301756; *MAPKAPK5* rs16941724; *ACAD10* rs4766897, rs627308; *HECTD4* rs57866673; *ATXN2* rs657197; *PFKM* rs4760682; *CUX2* rs1265565, rs16941264, rs4378452, rs10849937, rs1265566, rs7297186, rs4766540, rs7970490, rs10849933, rs916683, rs6490029, rs4766567, rs10774613, rs10849931; *GPRC5A* rs12811512, rs11055137; *ALDH2* rs2238151; *OR10AD1* rs79054759, rs61941006; *FAM109A (PHETA1)* rs3809272; *NAA25* rs4767364; *H1FNT (H1-7)* rs2054905; *COL2A1* rs11168351, rs12308909, rs1793923; *LOC100131138 (LINC01405)* (lncRNA) rs1056620; *MYL2* rs6489835; *SETD1B* rs1678960; *HNF1A* rs2259816; *PSMD9* rs2230681; *SLC8B1* rs73192857; *SENP1* rs4258439; *TMEM106C* rs2286024, rs4760674; *RASAL1* rs73207101; *IQCD* rs34767568; *TBX3* rs6489973 |
| 13 | *GAS6-AS1* (lncRNA)/*GAS6* rs9577924, rs7331124, rs12860172; *GAS6* rs6602910; *LINC00462* (lncRNA) rs9568051, rs1009718; *RB1/PPP1R26P1* rs3825417; *CYSLTR2* rs12585234; *RCBTB2* rs990814, rs1536394; *ITM2B* rs9534996; *TRPC4* rs7991324; *GPC5* rs345491; *LINC00423* (lncRNA) rs4941700; *MTIF3* rs7334690; *STK24* rs912330 |
| 14 | *RALGAPA1* rs113670117 |
| 15 | *TP53BP1* rs999047, rs2242067; *MFAP1* rs3825783; *MAP1A* rs2245715; *LCMT2* rs3742970, rs1095386; *FMN1* rs75411053, rs71462837, rs345748; ***LIPC* rs1800588**, rs2043085, rs10468017, rs11857386; *SPPL2A* rs12911654; *AP4E1* rs2306333; *UBE2Q2* rs1394125; *TRPM7* rs11635825; *CYP19A1/MIR4713HG* (lncRNA) rs12439137; *SPRED1* rs972091; *STARD9* rs7168835; *HAUS2* rs12439377; *ZNF106* rs4924678; *TEX9* rs72740533; *ADAMTS7* rs113052063, rs8034658; *RFX7* rs72740509; *SMAD6* rs7497064, rs2439385; *CSNK1G1* rs8034754; *IREB2* rs4436747; *CHRNA5* rs11637635; *CHRNB4* rs950776; *PSMA4* rs8053; *CHRNA3* rs8025188; *HMG20A* rs7178572 |
| 16 | *ACSF3* rs72819315; *LUC7L* rs7197253; *ANKRD11* rs72821345; *GSE1/LOC727710*\* rs72821345; *DPEP1* rs72821345, rs12930346, rs391773; *CDK10* rs12924138; *SPIRE2* rs12924138, rs8060934; *CTU2* rs4782321; *CASC16* (lncRNA) rs4594251; *PIEZO1* rs4594251, rs9788969; *PIEZO1*/*LOC100289580* (lncRNA) rs13333358, rs726884; *FANCA* rs3743860, rs2238526; *LOC102723323* (ncRNA) rs4784307 |
| 17 | *CRHR1* rs62057061, rs9303521; *PLEKHM1* rs55663797, rs5026246, rs62065400; *NSF* rs199533; *HDAC5* rs8065686; *WNT3* rs916888, rs9890413, rs11657305; *ABCA10* rs2886232, rs72631343; *AC091059.1* (lncRNA) rs34557869; *SMURF2* rs34557869; *METRNL* rs7223467; *PFAS* rs4791641; *ARHGEF15* rs4791641, rs3744647; *ODF4* rs12945939, rs60312514; *ENDOV* rs41300752; *CORO6* rs13723; *SPECC1* rs62066348, rs62066348; *ARSG* rs34497818; *TMEM95* rs34755955 |
| 18 | *CTIF* rs9960798; *SMAD7* rs4464148; *PSTPIP2* rs4890613; *PTPN2* rs7234029; *LOC101927548* (ncRNA) rs7240035; *LOC107985179* (ncRNA) rs1454738; *ZBTB7C* rs6507806; *IMPA2* rs627965; *CDH20* rs723769; *RNF125* rs12454708 |
| 19 | *CEBPA* rs78744187; *PTBP1* rs13169, rs112763660, rs123698, rs62131354; *DOT1L* rs12986413, rs12976923, rs3815308, rs12983546, rs3815145, rs1003531; *AP3D1* rs2238610, rs34615083; *ZNF616* rs8100114; *ZSCAN5A/LOC100506374* (*EDDM13*) rs758758, rs11882259; *PLPPR3* rs602186; *EXOC3L2* rs11083767; *LTBP4* rs1051303, rs2303729; *HDGFRP2* (*HDGFL2*) rs7249084; *PLIN4* rs16989695; *QPCTL* rs2302593; *RSPH6A* rs12463359; *LOC101927411* (*LINC01782*) (lncRNA) rs3943790; *MEIOSIN* rs10422883; *ZNF536* rs73019621; *ZBTB45* rs73066251; *NCAN* rs10402294; *GNG7* rs72989164; *SULT2A1* rs4149452; *ZNF83* rs8106200; *BCAM* rs1871045 |
| 20 | *CYP24A1* rs2585414; *TP53INP2* rs6129156 |
| 21 | *CHAF1B* rs35705526; *CLDN14* rs2835354, rs219757, rs2071050; *LOC101927745* (ncRNA) rs1040360, rs2823285, rs34814096, rs62218374; *PRDM15* rs76291974; *DOP1B* rs41418546; *ATP5O* rs2834297; SIM2 rs2252821; *LOC105369292* (lncRNA) rs4817754; *LOC101928126* (lncRNA) rs2834318; *SLC19A1* rs77632903 |
| 22 | ***TMPRSS6*** **rs2413450**, **rs2235321**, rs881144, rs2543515, rs855788, rs7286184, rs73160055, **rs228918**, rs17750152, **rs5756515**, rs228906; *TST* rs4764; *MPST* rs3753145; *KCTD17* rs130627; *TEX33* rs1573672, rs2413447; *PNPLA3* rs738409; *SAMM50* rs3761472; *FBLN1* rs2016518; *LOC100506737* (*LINC01589*) (lncRNA) rs17564843; *WNT7B* rs17564843, rs28663466; *LOC100506241* (*LL22NC01-81G9.3*) (lncRNA) rs17749540; *IL2RB* rs5750383; *A4GALT* rs5758896, rs738526; *PARVB* rs2073080; *CBX6* rs760481 |

\*Hb-associated SNPs in bold were found common between European Whites and Taiwanese Han Chinese (i.e., between sex groups or across all sex groups). Chr, chromosome; Hb, hemoglobin; lncRNA, long non-coding RNA; miRNA, microRNA; ncRNA, non-coding RNA; PRS, polygenic risk score; SNP, single nucleotide polymorphism; tRNA, transfer RNA.

**Table S5:** Means and standard deviations of Hb-PRS and beta coefficients regressing Hb on Hb-GRS by sex and by ethnic group: Taiwanese Han Chinese of Taiwan Biobank and European Whites of UK Biobank

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Hb-PRS** | **Hb (g/dL) per unit change of Hb-PRS** | | | | |
|  | **Mean ± S.D. (Range)** | **Coefficient** | **SE** | **F** | ***p*** | **r2** |
| Taiwanese Han Chinese (*N*=61,352) |  |  |  |  |  |  |
| Males (*n*=19,012) | 0.0391 ± 0.005 (0.0193-0.0554) | 36.85 | 1.83 | 404.0 | **<0.0001** | 0.0208 |
| Females (*n*=42,340) | 0.0301 ± 0.003 (0.0164-0.0396) | 62.00 | 2.41 | 659.5 | **<0.0001** | 0.0153 |
| European Whites (*N*=271,366) |  |  |  |  |  |  |
| Males (*n*=128,549) | 0.0157 ± 0.002 (0.0082-0.0212) | 62.01 | 1.61 | 1,478.9 | **<0.0001** | 0.0114 |
| Females (*n*=142,817) | 0.0127 ± 0.001 (0.0071-0.0180) | 97.84 | 2.05 | 2,284.7 | **<0.0001** | 0.0157 |

|  |  |
| --- | --- |
|  |  |
|  |  |

**Figure S1:** Overlay histograms of sex-specific Hb-PRSs (top) and scatterplots of sex-specific Hb concentration against Hb-PRSs (bottom) among Taiwanese Han Chinese of TWB (*N*=61,352) and European Whites of UKB (*N*=271,366).

**Table S6:** Characteristics of subjects in Taiwan Biobank (*N*=61,352) across quintiles of Hb-PRS

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Variables** | **All** | **Q1** | **Q2** | **Q3** | **Q4** | **Q5** | ***P*-trend** |
| **Males, *n*** | 19,012 | 3,802 | 3,803 | 3,802 | 3,803 | 3,802 |  |
| Hemoglobin, g/dL | 15.04 ± 1.21 | 14.79 ± 1.21 | 14.98 ± 1.21 | 15.04 ± 1.16 | 15.11 ± 1.20 | 15.28 ± 1.20 | **<0.0001** |
| Anemia (Hb <13.0 g/dL), % | 917 (4.8) | 264 (7.0) | 202 (5.3) | 161 (4.2) | 168 (4.4) | 122 (3.2) | **<0.0001** |
| Age, y | 50.8 ± 11.2 | 50.8 ± 11.3 | 51.0 ± 11.1 | 50.9 ± 11.3 | 50.8 ± 11.1 | 50.7 ± 11.3 | 0.3543 |
| 30-39 y, % | 4,008 (21.1) | 820 (21.6) | 770 (20.3) | 811 (21.3) | 799 (21.0) | 808 (21.3) |  |
| 40-49 y, % | 4,230 (22.3) | 817 (21.5) | 839 (22.1) | 854 (22.5) | 871 (22.9) | 849 (22.3) |  |
| 50-59 y, % | 5,471 (28.8) | 1,075 (28.3) | 1,132 (29.8) | 1,048 (27.6) | 1,099 (28.9) | 1,117 (29.4) |  |
| 60-70 y, % | 5,296 (27.9) | 1,088 (28.6) | 1,062 (27.9) | 1,088 (28.6) | 1,032 (27.2) | 1,026 (27.0) |  |
| Weight, kg | 73.1 ± 11.8 | 72.8 ± 11.6 | 72.9 ± 11.8 | 73.0 ± 11.6 | 73.3 ± 12.0 | 73.5 ± 11.9 | **0.0123** |
| Body mass index, kg/m2 | 25.4 ± 3.5 | 25.3 ± 3.5 | 25.4 ± 3.5 | 25.4 ± 3.5 | 25.5 ± 3.6 | 25.5 ± 3.5 | **0.0122** |
| Waist circumference, cm | 88.3 ± 9.4 | 88.0 ± 9.4 | 88.1 ± 9.3 | 88.2 ± 9.3 | 88.5 ± 9.6 | 88.5 ± 9.3 | **0.0112** |
| Waist-hip ratio | 0.904 ± 0.06 | 0.903 ± 0.06 | 0.904 ± 0.06 | 0.904 ± 0.06 | 0.906 ± 0.06 | 0.905 ± 0.06 | **0.0199** |
| Systolic blood pressure, mm Hg | 127.0 ± 16.8 | 126.6 ± 16.7 | 126.9 ± 16.7 | 126.9 ± 16.8 | 127.1 ± 17.0 | 127.4 ± 17.0 | **0.0320** |
| Diastolic blood pressure, mm Hg | 78.6 ± 10.6 | 78.2 ± 10.4 | 78.4 ± 10.5 | 78.6 ± 10.7 | 78.8 ± 10.8 | 79.0 ± 10.7 | **0.0004** |
| Fasting blood glucose, mg/dL | 99.6 ± 23.6 | 99.4 ± 24.4 | 99.0 ± 20.2 | 100.0 ± 24.8 | 99.9 ± 24.1 | 99.9 ± 24.4 | 0.0934 |
| Glycated hemoglobin, % | 5.91 ± 0.93 | 5.93 ± 0.96 | 5.88 ± 0.83 | 5.93 ± 0.98 | 5.91 ± 0.92 | 5.90 ± 0.98 | 0.7050 |
| Triglycerides, mg/dL | 140.0 ± 119.7 | 139.4 ± 128.0 | 137.9 ± 115.7 | 135.5 ± 102.4 | 141.9 ± 111.8 | 145.1 ± 137.1 | **0.0005** |
| Total cholesterol, mg/dL | 191.6 ± 35.0 | 192.2 ± 35.0 | 191.5 ± 34.7 | 191.3 ± 34.7 | 191.4 ± 34.7 | 191.0 ± 35.7 | **0.0289** |
| LDL-cholesterol, mg/dL | 120.8 ± 31.3 | 121.9 ± 31.7 | 121.0 ± 31.3 | 120.8 ± 31.3 | 120.6 ± 31.3 | 119.6 ± 31.0 | **0.0017** |
| HDL-cholesterol, mg/dL | 47.9 ± 11.1 | 48.0 ± 11.0 | 48.0 ± 11.3 | 48.0 ± 11.1 | 47.7 ± 11.1 | 47.8 ± 11.1 | 0.2137 |
| Uric acid, mg/dL | 6.42 ± 1.37 | 6.41 ± 1.39 | 6.40 ± 1.36 | 6.42 ± 1.35 | 6.44 ± 1.35 | 6.44 ± 1.37 | 0.1744 |
| Smoking status |  |  |  |  |  |  | **0.0129** |
| Never smoked | 10,178 (53.6) | 2,041 (53.7) | 1,992 (52.4) | 2,006 (52.8) | 2,040 (53.7) | 2,099 (55.2) |  |
| Stopped smoked | 4,722 (24.9) | 959 (25.2) | 985 (25.9) | 985 (25.9) | 902 (23.7) | 891 (23.5) |  |
| Occasionally smoking | 121 (0.6) | 20 (0.53) | 38 (1.00) | 24 (0.63) | 19 (0.50) | 20 (0.53) |  |
| Currently smoking | 3,984 (21.0) | 780 (20.5) | 788 (20.7) | 786 (20.7) | 840 (22.1) | 790 (20.8) |  |
| Alcohol drinking status |  |  |  |  |  |  | 0.5537 |
| Stopped drinking | 1,092 (5.8) | 199 (5.2) | 222 (5.8) | 211 (5.6) | 229 (6.0) | 231 (6.1) |  |
| Occasionally drinking | 15,381 (80.9) | 3,121 (82.1) | 3,056 (80.4) | 3,081 (81.1) | 3,052 (80.3) | 3,071 (80.8) |  |
| Currently drinking | 2,532 (13.3) | 480 (12.6) | 525 (13.8) | 509 (13.4) | 520 (13.7) | 498 (13.1) |  |
| Physical activity |  |  |  |  |  |  | 0.2042 |
| With regular exercise | 8,286 (43.6) | 1,662 (43.8) | 1,701 (44.7) | 1,656 (43.6) | 1,632 (42.9) | 1,635 (43.0) |  |
| **Females, *n*** | 42,340 | 8,468 | 8,466 | 8,470 | 8,468 | 8,468 |  |
| Hemoglobin, g/dL | 13.01 ± 1.27 | 12.78 ± 1.26 | 12.93 ± 1.26 | 13.04 ± 1.26 | 13.11 ± 1.26 | 13.21 ± 1.25 | **<0.0001** |
| Anemia (Hb <12.0 g/dL), % | 6,503 (15.4) | 1,706 (20.2) | 1,415 (16.7) | 1,240 (14.6) | 1,129 (13.3) | 1,013 (12.0) | **<0.0001** |
| Age, y | 50.3 ± 10.4 | 50.4 ± 10.5 | 50.3 ± 10.4 | 50.4 ± 10.4 | 50.3 ± 10.3 | 50.4 ± 10.4 | 0.6924 |
| 30-39 y, % | 8,305 (19.6) | 1,691 (20.0) | 1,669 (19.7) | 1,645 (19.4) | 1,657 (19.6) | 1,643 (19.4) |  |
| 40-49 y, % | 9,965 (23.5) | 1,918 (22.7) | 2,039 (24.1) | 1,992 (23.5) | 1,981 (23.4) | 2,035 (24.0) |  |
| 50-59 y, % | 14,658 (34.6) | 2,954 (34.9) | 2,891 (34.2) | 2,899 (34.3) | 3,010 (35.6) | 2,904 (34.3) |  |
| 60-70 y, % | 9,400 (22.2) | 1,905 (22.5) | 1,866 (22.0) | 1,928 (22.8) | 1,818 (21.5) | 1,883 (22.2) |  |
| Had menopause, % | 21,685 (51.2) | 4,383 (51.8) | 4,291 (50.7) | 4,319 (51.0) | 4,323 (51.1) | 4,369 (51.6) | 0.8361 |
| Age at menopause, y | 46.0 ± 13.2 | 46.2 ± 13.0 | 45.9 ± 13.5 | 46.1 ± 13.2 | 46.0 ± 13.2 | 46.0 ± 13.3 | 0.8031 |
| Weight, kg | 58.6 ± 9.8 | 58.5 ± 9.8 | 58.6 ± 9.8 | 58.4 ± 9.7 | 58.6 ± 9.9 | 58.7 ± 10.0 | 0.2311 |
| Body mass index, kg/m2 | 23.6 ± 3.7 | 23.6 ± 3.7 | 23.6 ± 3.7 | 23.6 ± 3.7 | 23.6 ± 3.7 | 23.7 ± 3.8 | 0.1888 |
| Waist circumference, cm | 80.9 ± 9.6 | 80.9 ± 9.6 | 80.8 ± 9.7 | 80.8 ± 9.6 | 80.8 ± 9.6 | 81.0 ± 9.7 | 0.5908 |
| Waist-hip ratio | 0.849 ± 0.07 | 0.850 ± 0.07 | 0.848 ± 0.07 | 0.849 ± 0.07 | 0.848 ± 0.07 | 0.849 ± 0.07 | 0.1821 |
| Systolic blood pressure, mm Hg | 117.6 ± 18.0 | 117.4 ± 17.8 | 117.6 ± 17.9 | 117.7 ± 18.2 | 117.5 ± 17.9 | 117.9 ± 18.3 | 0.0901 |
| Diastolic blood pressure, mm Hg | 71.1 ± 10.2 | 70.8 ± 10.0 | 71.0 ± 10.1 | 71.2 ± 10.3 | 71.3 ± 10.2 | 71.3 ± 10.3 | **0.0002** |
| Fasting blood glucose, mg/dL | 94.2 ± 18.8 | 94.2 ± 18.8 | 94.3 ± 18.5 | 94.2 ± 18.6 | 94.3 ± 19.0 | 94.0 ± 19.1 | 0.4432 |
| Glycated hemoglobin, % | 5.77 ± 0.75 | 5.79 ± 0.76 | 5.79 ± 0.77 | 5.77 ± 0.73 | 5.76 ± 0.74 | 5.76 ± 0.74 | **<0.0001** |
| Triglycerides, mg/dL | 104.0 ± 71.7 | 104.6 ± 75.6 | 102.7 ± 71.0 | 103.6 ± 70.4 | 103.7 ± 68.3 | 105.5 ± 72.9 | **0.0430** |
| Total cholesterol, mg/dL | 198.6 ± 35.9 | 199.3 ± 36.1 | 198.1 ± 35.7 | 198.9 ± 36.0 | 198.4 ± 35.7 | 198.0 ± 35.6 | 0.0729 |
| LDL-cholesterol, mg/dL | 120.7 ± 31.8 | 121.1 ± 31.8 | 120.3 ± 31.7 | 120.7 ± 31.9 | 120.8 ± 31.8 | 120.4 ± 31.6 | 0.4871 |
| HDL-cholesterol, mg/dL | 58.2 ± 13.2 | 58.1 ± 13.1 | 58.2 ± 13.2 | 58.4 ± 13.3 | 58.2 ± 13.2 | 58.0 ± 13.3 | 0.6839 |
| Uric acid, mg/dL | 4.88 ± 1.13 | 4.87 ± 1.13 | 4.87 ± 1.13 | 4.87 ± 1.11 | 4.89 ± 1.13 | 4.91 ± 1.15 | **0.0079** |
| Smoking status |  |  |  |  |  |  | 0.5040 |
| Never smoked | 40,095 (94.7) | 8,041 (95.0) | 8,027 (94.8) | 8,009 (94.6) | 7,988 (94.4) | 8,030 (94.9) |  |
| Stopped smoked | 967 (2.3) | 184 (2.2) | 205 (2.4) | 188 (2.2) | 206 (2.4) | 184 (2.2) |  |
| Occasionally smoking | 39 (0.09) | 6 (0.07) | 8 (0.09) | 8 (0.09) | 5 (0.06) | 12 (0.14) |  |
| Currently smoking | 1,227 (2.9) | 237 (2.8) | 225 (2.7) | 259 (3.1) | 267 (3.2) | 239 (2.8) |  |
| Alcohol drinking status |  |  |  |  |  |  | 0.9006 |
| Stopped drinking | 349 (0.8) | 64 (0.8) | 80 (1.0) | 66 (0.8) | 70 (0.8) | 69 (0.8) |  |
| Occasionally drinking | 41,216 (97.4) | 8,258 (97.5) | 8,236 (97.3) | 8,246 (97.4) | 8,231 (97.2) | 8,245 (97.4) |  |
| Currently drinking | 762 (1.8) | 146 (1.7) | 149 (1.8) | 152 (1.8) | 164 (1.9) | 151 (1.8) |  |
| Physical activity |  |  |  |  |  |  | 0.8738 |
| With regular exercise | 17,204 (40.7) | 3,426 (40.5) | 3,405 (40.2) | 3,500 (41.4) | 3,472 (41.0) | 3,401 (40.2) |  |

Continuous variables are presented as mean ± s.d., whereas categorical characteristics are in *n* (%).

**Table S7:** Characteristics of subjects in UK Biobank (*N*=271,366) across quintiles of Hb-PRS

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Variables** | **All** | **Q1** | **Q2** | **Q3** | **Q4** | **Q5** | ***P*-trend** |
| **Males, *n*** | 128,549 | 25,709 | 25,710 | 25,712 | 25,709 | 25,709 |  |
| Hemoglobin, g/dL | 15.03 ± 0.98 | 14.91 ± 0.98 | 14.94 ± 0.98 | 15.00 ± 0.97 | 15.08 ± 0.97 | 15.21 ± 0.97 | **<0.0001** |
| Anemia (Hb <13.0 g/dL), % | 2,841 (2.2) | 732 (2.9) | 644 (2.5) | 554 (2.2) | 498 (1.9) | 413 (1.6) | **<0.0001** |
| Age, y | 56.6 ± 8.1 | 56.5 ± 8.1 | 56.5 ± 8.1 | 56.6 ± 8.1 | 56.6 ± 8.1 | 56.7 ± 8.2 | **0.0040** |
| 40-49 y, % | 30,247 (23.5) | 6,112 (23.8) | 6,169 (24.0) | 6,024 (23.4) | 5,962 (23.2) | 5,980 (23.3) |  |
| 50-59 y, % | 41,848 (32.6) | 8,377 (32.6) | 8,399 (32.7) | 8,382 (32.6) | 8,380 (32.6) | 8,310 (32.3) |  |
| 60-70 y, % | 56,454 (43.9) | 11,220 (43.6) | 11,142 (43.3) | 11,306 (44.0) | 11,367 (44.2) | 11,419 (44.4) |  |
| Weight, kg | 86.2 ± 14.2 | 86.5 ± 14.4 | 86.4 ± 14.4 | 85.9 ± 14.1 | 86.2 ± 14.1 | 86.1 ± 14.1 | **0.0008** |
| Body mass index, kg/m2 | 27.8 ± 4.2 | 27.9 ± 4.3 | 27.9 ± 4.3 | 27.8 ± 4.2 | 27.8 ± 4.2 | 27.8 ± 4.2 | **0.0005** |
| Waist circumference, cm | 96.9 ± 11.3 | 96.9 ± 11.5 | 97.0 ± 11.4 | 96.8 ± 11.2 | 96.9 ± 11.2 | 96.9 ± 11.2 | 0.1797 |
| Waist-hip ratio | 0.934 ± 0.07 | 0.933 ± 0.07 | 0.935 ± 0.07 | 0.935 ± 0.06 | 0.935 ± 0.06 | 0.935 ± 0.07 | 0.1102 |
| Systolic blood pressure, mm Hg | 140.8 ± 17.4 | 140.9 ± 17.6 | 140.8 ± 17.4 | 140.8 ± 17.1 | 140.7 ± 17.4 | 140.9 ± 17.5 | 0.7467 |
| Diastolic blood pressure, mm Hg | 84.1 ± 10.0 | 83.8 ± 9.9 | 84.0 ± 10.0 | 84.1 ± 10.0 | 84.1 ± 10.0 | 84.4 ± 10.1 | **<0.0001** |
| Glucose, mmol/L | 5.17 ± 1.37 | 5.19 ± 1.45 | 5.19 ± 1.41 | 5.16 ± 1.37 | 5.16 ± 1.36 | 5.14 ± 1.26 | **<0.0001** |
| Glycated hemoglobin, mmol/mol | 36.2 ± 7.2 | 36.5 ± 7.3 | 36.5 ± 7.4 | 36.3 ± 7.3 | 36.1 ± 6.9 | 35.6 ± 6.7 | **<0.0001** |
| Triglycerides, mmol/L | 1.98 ± 1.14 | 1.94 ± 1.13 | 1.97 ± 1.14 | 1.98 ± 1.14 | 2.00 ± 1.16 | 1.98 ± 1.14 | **<0.0001** |
| Total cholesterol, mmol/L | 5.51 ± 1.12 | 5.49 ± 1.12 | 5.53 ± 1.12 | 5.54 ± 1.12 | 5.52 ± 1.12 | 5.48 ± 1.12 | 0.0741 |
| LDL-cholesterol, mmol/L | 3.50 ± 0.86 | 3.49 ± 0.86 | 3.51 ± 0.86 | 3.52 ± 0.86 | 3.50 ± 0.86 | 3.47 ± 0.86 | **0.0024** |
| HDL-cholesterol, mmol/L | 1.29 ± 0.31 | 1.28 ± 0.31 | 1.29 ± 0.31 | 1.29 ± 0.31 | 1.29 ± 0.31 | 1.28 ± 0.31 | 0.8549 |
| Uric acid, µmol/L | 354.3 ± 71.0 | 355.9 ± 72.0 | 353.2 ± 71.1 | 352.7 ± 70.1 | 353.9 ± 70.8 | 355.6 ± 70.8 | 0.9998 |
| Smoking status |  |  |  |  |  |  | 0.4764 |
| Never smoked | 63,363 (49.3) | 12,880 (50.1) | 12,666 (49.3) | 12,661 (49.3) | 12,581 (49.0) | 12,575 (48.9) |  |
| Stopped smoked | 49,356 (38.4) | 9,745 (37.9) | 9,889 (38.5) | 9,868 (38.4) | 9,883 (38.5) | 9,971 (38.8) |  |
| Occasionally smoking | 4,466 (3.5) | 871 (3.4) | 898 (3.5) | 910 (3.5) | 919 (3.6) | 868 (3.4) |  |
| Currently smoking | 11,313 (8.8) | 2,206 (8.6) | 2,247 (8.7) | 2,261 (8.8) | 2,317 (9.0) | 2,282 (8.9) |  |
| Alcohol drinking status |  |  |  |  |  |  | **0.0486** |
| Never drank | 2,232 (1.7) | 444 (1.7) | 435 (1.7) | 488 (1.9) | 462 (1.8) | 403 (1.6) |  |
| Stopped drinking | 4,156 (3.2) | 848 (3.3) | 790 (3.1) | 805 (3.1) | 819 (3.2) | 894 (3.5) |  |
| Occasionally drinking | 8,532 (6.6) | 1,636 (6.4) | 1,758 (6.8) | 1,714 (6.7) | 1,706 (6.6) | 1,718 (6.7) |  |
| Currently drinking | 113,533 (88.4) | 22,757 (88.6) | 22,711 (88.4) | 22,689 (88.3) | 22,706 (88.4) | 22,670 (88.3) |  |
| Physical activity |  |  |  |  |  |  | 0.3242 |
| Low | 20,601 (18.8) | 4,130 (18.9) | 4,149 (19.0) | 4,148 (19.0) | 4,083 (18.6) | 4,091 (18.7) |  |
| Moderate | 42,537 (38.9) | 8,604 (39.4) | 8,562 (39.1) | 8,520 (39.0) | 8,461 (38.6) | 8,390 (38.3) |  |
| High | 46,254 (42.3) | 9,097 (41.7) | 9,185 (42.0) | 9,170 (42.0) | 9,365 (42.7) | 9,437 (43.1) |  |
| **Females, *n*** | 142,817 | 28,566 | 28,560 | 28,566 | 28,564 | 28,561 |  |
| Hemoglobin, g/dL | 13.52 ± 0.93 | 13.39 ± 0.92 | 13.43 ± 0.92 | 13.49 ± 0.92 | 13.58 ± 0.92 | 13.71 ± 0.95 | **<0.0001** |
| Anemia (Hb <12.0 g/dL), % | 6,784 (4.8) | 1,637 (5.7) | 1,529 (5.4) | 1,386 (4.9) | 1,180 (4.1) | 1,052 (3.7) | **<0.0001** |
| Age, y | 56.1 ± 7.9 | 56.1 ± 7.9 | 56.1 ± 7.9 | 56.2 ± 7.9 | 56.1 ± 8.0 | 56.2 ± 7.9 | 0.2192 |
| 40-49 y, % | 34,432 (24.1) | 6,846 (24.0) | 7,021 (24.6) | 6,762 (23.7) | 6,969 (24.4) | 6,834 (23.9) |  |
| 50-59 y, % | 50,235 (35.2) | 10,152 (35.5) | 10,047 (35.2) | 10,119 (35.4) | 9,924 (34.7) | 9,993 (35.0) |  |
| 60-70 y, % | 58,150 (40.7) | 11,568 (40.5) | 11,492 (40.2) | 11,685 (40.9) | 11,671 (40.9) | 11,734 (41.1) |  |
| Had menopause, % | 85,641 (60.0) | 17,244 (60.4) | 16,988 (59.5) | 17,107 (59.9) | 17,139 (60.0) | 17,163 (60.1) | 0.3513 |
| Age at menopause, y | 46.6 ± 13.5 | 46.4 ± 13.5 | 46.5 ± 13.6 | 46.8 ± 13.2 | 46.5 ± 13.6 | 46.5 ± 13.5 | 0.4418 |
| Weight, kg | 71.3 ± 14.0 | 71.6 ± 14.3 | 71.3 ± 14.0 | 71.2 ± 13.8 | 71.2 ± 13.9 | 71.4 ± 13.9 | **0.0132** |
| Body mass index, kg/m2 | 26.9 ± 5.1 | 27.0 ± 5.2 | 26.9 ± 5.1 | 26.9 ± 5.1 | 26.9 ± 5.1 | 26.9 ± 5.1 | **0.0190** |
| Waist circumference, cm | 84.3 ± 12.5 | 84.4 ± 12.7 | 84.2 ± 12.5 | 84.3 ± 12.4 | 84.2 ± 12.5 | 84.4 ± 12.4 | 0.5857 |
| Waist-hip ratio | 0.815 ± 0.07 | 0.814 ± 0.07 | 0.814 ± 0.07 | 0.816 ± 0.07 | 0.815 ± 0.07 | 0.816 ± 0.07 | **0.0275** |
| Systolic blood pressure, mm Hg | 134.8 ± 19.1 | 134.8 ± 19.1 | 134.7 ± 19.1 | 134.8 ± 19.1 | 134.8 ± 19.1 | 135.0 ± 19.1 | 0.1680 |
| Diastolic blood pressure, mm Hg | 80.5 ± 9.9 | 80.2 ± 9.9 | 80.3 ± 9.9 | 80.5 ± 10.0 | 80.6 ± 10.0 | 80.9 ± 9.9 | **<0.0001** |
| Glucose, mmol/L | 5.05 ± 1.03 | 5.07 ± 1.08 | 5.05 ± 1.02 | 5.05 ± 1.02 | 5.04 ± 1.01 | 5.03 ± 1.00 | **<0.0001** |
| Glycated hemoglobin, mmol/mol | 35.5 ± 5.7 | 35.8 ± 5.8 | 35.7 ± 5.6 | 35.6 ± 5.6 | 35.4 ± 5.8 | 35.1 ± 5.5 | **<0.0001** |
| Triglycerides, mmol/L | 1.53 ± 0.84 | 1.51 ± 0.83 | 1.53 ± 0.84 | 1.54 ± 0.85 | 1.54 ± 0.84 | 1.56 ± 0.86 | **<0.0001** |
| Total cholesterol, mmol/L | 5.89 ± 1.12 | 5.88 ± 1.12 | 5.91 ± 1.12 | 5.90 ± 1.11 | 5.88 ± 1.12 | 5.86 ± 1.11 | **0.0010** |
| LDL-cholesterol, mmol/L | 3.63 ± 0.86 | 3.63 ± 0.86 | 3.65 ± 0.87 | 3.64 ± 0.86 | 3.62 ± 0.87 | 3.61 ± 0.86 | **<0.0001** |
| HDL-cholesterol, mmol/L | 1.61 ± 0.38 | 1.60 ± 0.38 | 1.61 ± 0.38 | 1.61 ± 0.38 | 1.61 ± 0.38 | 1.60 ± 0.37 | 0.1012 |
| Uric acid, µmol/L | 269.3 ± 65.4 | 270.4 ± 66.0 | 268.1 ± 64.9 | 268.4 ± 64.9 | 268.7 ± 65.1 | 270.7 ± 66.0 | 0.3715 |
| Smoking status |  |  |  |  |  |  | 0.2223 |
| Never smoked | 84,688 (59.3) | 17,161 (60.1) | 16,820 (58.9) | 16,814 (58.9) | 16,932 (59.3) | 16,961 (59.4) |  |
| Stopped smoked | 45,603 (32.0) | 8,909 (31.2) | 9,253 (32.4) | 9,247 (32.4) | 9,074 (31.8) | 9,120 (31.9) |  |
| Occasionally smoking | 3,012 (2.1) | 598 (2.1) | 601 (2.1) | 587 (2.1) | 643 (2.3) | 583 (2.0) |  |
| Currently smoking | 9,445 (6.6) | 1,890 (6.6) | 1,865 (6.5) | 1,902 (6.7) | 1,898 (6.7) | 1,890 (6.6) |  |
| Alcohol drinking status |  |  |  |  |  |  | 0.6109 |
| Never drank | 6,061 (4.3) | 1,204 (4.2) | 1,204 (4.2) | 1,199 (4.2) | 1,247 (4.4) | 1,207 (4.2) |  |
| Stopped drinking | 4,945 (3.5) | 971 (3.4) | 990 (3.5) | 1,006 (3.5) | 977 (3.4) | 1,001 (3.5) |  |
| Occasionally drinking | 19,783 (13.9) | 3,983 (14.0) | 3,928 (13.8) | 4,086 (14.3) | 3,867 (13.6) | 3,919 (13.7) |  |
| Currently drinking | 111,936 (78.4) | 22,389 (78.4) | 22,426 (78.6) | 22,252 (78.0) | 22,456 (78.7) | 22,413 (78.5) |  |
| Physical activity |  |  |  |  |  |  | 0.0756 |
| Low | 20,340 (18.1) | 4,196 (18.7) | 4,095 (18.2) | 3,913 (17.5) | 4,006 (17.8) | 4,130 (18.4) |  |
| Moderate | 48,402 (43.1) | 9,741 (43.4) | 9,658 (42.9) | 9,610 (43.0) | 9,724 (43.2) | 9,669 (43.1) |  |
| High | 43,547 (38.8) | 8,505 (37.9) | 8,786 (39.0) | 8,851 (39.6) | 8,758 (39.0) | 8,647 (38.5) |  |

Continuous variables are presented as mean ± s.d., whereas categorical characteristics are in *n* (%).

**Table S8:** Overall distributions of metabolic outcomes in Taiwan Biobank†

|  |  |  |  |
| --- | --- | --- | --- |
| **Metabolic Outcomes** | **All (*N*=61,352)** | **Males (*n*=19,012)** | **Females (*n*=42,340)** |
| **A. Metabolic syndrome‡** | **14,611 (23.8)** | **5,546 (29.2)** | **9,065 (21.4)** |
| **B. Central obesity§** | **27,400 (44.7)** | **7,169 (37.7)** | **20,231 (47.8)** |
| **C. Hypertension** | **14,636 (23.9)** | **6,523 (34.3)** | **8,113 (19.2)** |
| High blood pressure | 10,167 (16.6) | 4,690 (24.7) | 5,477 (12.9) |
| Self-reported hypertension | 7,926 (12.9) | 3,496 (18.4) | 4,430 (10.5) |
| **D. Diabetes mellitus** | **6,238 (10.2)** | **2,575 (13.6)** | **3,663 (8.7)** |
| Hyperglycemia | 5,597 (9.1) | 2,319 (12.2) | 3,278 (7.7) |
| Self-reported diabetes | 3,324 (5.4) | 1,411 (7.4) | 1,913 (4.5) |
| **E. Dyslipidemia** | **21,019 (34.3)** | **6,895 (36.6)** | **14,124 (33.4)** |
| Hypertriglyceridemia and/or low HDL-C levels | 18,245 (29.7) | 5,870 (30.9) | 12,375 (29.2) |
| Self-reported hyperlipidemia | 4,877 (8.0) | 1,893 (10.0) | 2,984 (7.1) |
| **F. Gout** | **12,382 (20.2)** | **6,294 (33.1)** | **6,088 (14.4)** |
| Hyperuricemia | 11,598 (18.9) | 5,613 (29.5) | 5,985 (14.1) |
| Self-reported gout | 2,127 (3.5) | 1,896 (10.0) | 231 (0.6) |

Data are presented as *n* (%). †In the TWB, outcomes are ascertained from elevated metabolic traits and self-reported metabolic conditions. ‡Following National Cholesterol Education Program Adult Treatment Panel III criteria. §Based on ethnic-specific cut-off for waist circumference. HDL-C, high-density lipoprotein cholesterol.

**Table S9:** Overall distributions of metabolic outcomes in UK Biobank†

|  |  |  |  |
| --- | --- | --- | --- |
| **Metabolic Outcomes** | **All (*N*=271,366)** | **Males (*n*=128,549)** | **Females (*n*=142,817)** |
| **A. Metabolic syndrome‡** | **109,437 (40.3)** | **62,252 (48.4)** | **51,880 (36.3)** |
| **B. Central obesity§** | **152,201 (56.1)** | **71,359 (55.5)** | **80,842 (56.6)** |
| **C. Hypertension** | **150,964 (55.6)** | **81,218 (63.2)** | **69,746 (48.8)** |
| High blood pressure | 114,935 (42.4) | 62,691 (48.8) | 52,244 (36.6) |
| Self-reported hypertension | 80,826 (29.8) | 44,071 (34.3) | 36,755 (25.7) |
| ICD diagnoses | 56,606 (20.9) | 31,659 (24.6) | 24,947 (17.5) |
| **D. Diabetes mellitus** | **19,027 (7.0)** | **11,815 (9.2)** | **7,212 (5.1)** |
| Hyperglycemia | 8,750 (3.2) | 5,659 (4.4) | 3,091 (2.2) |
| Self-reported diabetes | 12,915 (4.8) | 8,172 (6.4) | 4,743 (3.3) |
| ICD diagnoses | 14,680 (5.4) | 9,240 (7.2) | 5,440 (3.8) |
| **E. Dyslipidemia** | **169,152 (62.3)** | **89,276 (69.5)** | **79,876 (55.9)** |
| Hypertriglyceridemia and/or low HDL-C levels | 144,147 (53.1) | 75,732 (58.9) | 68,415 (47.9) |
| Self-reported dyslipidemia | 57,503 (21.2) | 33,383 (26.0) | 24,120 (16.9) |
| ICD diagnoses | 26,760 (9.9) | 16,652 (13.0) | 10,108 (7.1) |
| **F. Gout** | **38,273 (14.1)** | **25,112 (19.5)** | **13,161 (9.2)** |
| Hyperuricemia | 35,125 (12.9) | 22,255 (17.3) | 12,870 (9.0) |
| Self-reported gout | 4,195 (1.5) | 3,920 (3.1) | 275 (0.20) |
| ICD diagnoses | 2,757 (1.0) | 2,417 (1.9) | 340 (0.24) |

Data are presented as *n* (%). †In the UKB, outcomes are ascertained from elevated metabolic traits, self-reported metabolic conditions, and hospital in-patient records of subjects. ‡Following National Cholesterol Education Program Adult Treatment Panel III criteria. §Based on ethnic-specific cut-off for waist circumference. HDL-C, high-density lipoprotein cholesterol; ICD, International Classification of Diseases.

**Table S10:** Distributions of different metabolic conditions among subjects in Taiwan Biobank (*N*=61,352) across quintiles of Hb-PRS

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Metabolic Conditions** | **All** | **Q1** | **Q2** | **Q3** | **Q4** | **Q5** | ***P*-trend** |
| **Males, *n*** | 19,012 | 3,802 | 3,803 | 3,802 | 3,803 | 3,802 |  |
| **Mean Hemoglobin, g/dL** | 15.04 | 14.79 | 14.98 | 15.04 | 15.11 | 15.28 |  |
| MetS-NCEP ATP III | 4,884 (25.7) | 920 (24.2) | 978 (25.7) | 944 (24.8) | 1,035 (27.2) | 1,007 (26.5) | **0.0066** |
| Obesity (BMI >27.0 kg/m2)† | 5,369 (28.3) | 1,067 (28.1) | 1,070 (28.1) | 1,063 (28.0) | 1,079 (28.4) | 1,090 (28.7) | 0.5267 |
| Overweight (BMI=24.0-26.9 kg/m2)† | 6,809 (35.8) | 1,317 (34.7) | 1,337 (35.2) | 1,386 (36.5) | 1,399 (36.8) | 1,370 (36.1) |  |
| Central Obesity (WC >90 cm in males, >80 cm in females) | 7,169 (37.7) | 1,398 (36.8) | 1,428 (37.6) | 1,427 (37.5) | 1,474 (38.8) | 1,442 (37.9) | 0.1696 |
| Hypertension (SBP/DBP >140/>90 mm Hg)‡ | 4,685 (24.7) | 913 (24.0) | 941 (24.7) | 914 (24.1) | 941 (24.8) | 976 (25.7) | 0.1322 |
| Prehypertension (SBP=120-139 mm Hg or DBP=80-89 mm Hg)‡ | 8,223 (43.3) | 1,651 (43.5) | 1,638 (43.1) | 1,669 (43.9) | 1,646 (43.3) | 1,619 (42.6) |  |
| Hyperglycemia based on FBG (>126 mg/dL) | 1,200 (6.3) | 232 (6.1) | 234 (6.2) | 245 (6.5) | 242 (6.4) | 247 (6.5) | 0.4213 |
| Impaired FBG (100-125 mg/dL) | 4,240 (22.3) | 780 (20.5) | 856 (22.5) | 874 (23.0) | 873 (23.0) | 857 (22.6) |  |
| Hyperglycemia based on HbA1c (>6.5%) | 2,221 (11.7) | 429 (11.3) | 428 (11.3) | 460 (12.1) | 455 (12.0) | 449 (11.8) | 0.2830 |
| Elevated HbA1c (5.7-6.4%) | 8,667 (45.6) | 1,846 (48.6) | 1,747 (45.9) | 1,759 (46.3) | 1,701 (44.8) | 1,614 (42.5) |  |
| Hypertriglyceridemia (TG >200 mg/dL) | 3,122 (16.4) | 598 (15.7) | 607 (16.0) | 593 (15.6) | 665 (17.5) | 659 (17.3) | **0.0125** |
| Elevated TG (150-199 mg/dL) | 2,635 (13.9) | 515 (13.6) | 518 (13.6) | 526 (13.8) | 524 (13.8) | 552 (14.5) |  |
| Hypercholesterolemia (TC >240 mg/dL) | 1,671 (8.8) | 335 (8.8) | 337 (8.9) | 324 (8.5) | 323 (8.5) | 352 (9.3) | 0.7148 |
| Elevated TC (200-239 mg/dL) | 5,624 (29.6) | 1,168 (30.7) | 1,125 (29.6) | 1,120 (29.5) | 1,122 (29.5) | 1,089 (28.7) |  |
| High LDL-C (>160 mg/dL) | 2,024 (10.7) | 408 (10.7) | 427 (11.2) | 386 (10.2) | 397 (10.4) | 406 (10.7) | 0.5742 |
| Elevated LDL-C (130-159 mg/dL) | 5,080 (26.7) | 1,092 (28.7) | 984 (25.9) | 1,015 (26.7) | 1,026 (27.0) | 963 (25.3) |  |
| Low HDL-C (<40 mg/dL in males, <50 mg/dL in females) | 4,384 (23.1) | 843 (22.2) | 903 (23.7) | 846 (22.3) | 902 (23.7) | 890 (23.4) | 0.2551 |
| Hyperuricemia (SUA >7.0 mg/dL in males, >6.0 mg/dL in females) | 5,611 (29.5) | 1,131 (29.8) | 1,090 (28.7) | 1,131 (29.8) | 1,122 (29.5) | 1,137 (29.9) | 0.6161 |
| **Females, *n*** | 42,340 | 8,468 | 8,466 | 8,470 | 8,468 | 8,468 |  |
| **Mean Hemoglobin, g/dL** | 13.01 | 12.78 | 12.93 | 13.04 | 13.11 | 13.21 |  |
| MetS-NCEP ATP III | 7,939 (18.8) | 1,573 (18.6) | 1,537 (18.2) | 1,554 (18.4) | 1,587 (18.8) | 1,688 (19.9) | **0.0134** |
| Obesity (BMI >27.0 kg/m2)† | 6,920 (16.4) | 1,364 (16.1) | 1,353 (16.0) | 1,361 (16.1) | 1,388 (16.4) | 1,454 (17.2) | 0.1508 |
| Overweight (BMI=24.0-26.9 kg/m2)† | 9,734 (23.0) | 1,958 (23.1) | 1,957 (23.1) | 1,931 (22.8) | 1,977 (23.4) | 1,911 (22.6) |  |
| Central Obesity (WC >90 cm in males, >80 cm in females) | 20,231 (47.8) | 4,119 (48.6) | 3,994 (47.2) | 4,021 (47.5) | 4,035 (47.7) | 4,062 (48.0) | 0.6222 |
| Hypertension (SBP/DBP >140/>90 mm Hg)‡ | 5,474 (12.9) | 1,053 (12.4) | 1,071 (12.7) | 1,098 (13.0) | 1,116 (13.2) | 1,136 (13.4) | **0.0302** |
| Prehypertension (SBP=120-139 mm Hg or DBP=80-89 mm Hg)‡ | 12,113 (28.6) | 2,423 (28.6) | 2,445 (28.9) | 2,431 (28.7) | 2,385 (28.2) | 2,429 (28.7) |  |
| Hyperglycemia based on FBG (>126 mg/dL) | 1,522 (3.6) | 301 (3.6) | 317 (3.7) | 310 (3.7) | 307 (3.6) | 287 (3.4) | 0.4851 |
| Impaired FBG (100-125 mg/dL) | 5,731 (13.5) | 1,147 (13.6) | 1,140 (13.5) | 1,122 (13.3) | 1,162 (13.7) | 1,160 (13.7) |  |
| Hyperglycemia based on HbA1c (>6.5%) | 3,151 (7.4) | 681 (8.0) | 648 (7.7) | 617 (7.3) | 612 (7.2) | 593 (7.0) | **0.0056** |
| Elevated HbA1c (5.7-6.4%) | 17,897 (42.3) | 3,738 (44.1) | 3,548 (41.9) | 3,556 (42.0) | 3,517 (41.5) | 3,538 (41.8) |  |
| Hypertriglyceridemia (TG >200 mg/dL) | 3,083 (7.3) | 607 (7.2) | 633 (7.5) | 615 (7.3) | 586 (6.9) | 642 (7.6) | 0.7573 |
| Elevated TG (150-199 mg/dL) | 3,869 (9.1) | 767 (9.1) | 719 (8.5) | 742 (8.8) | 807 (9.5) | 834 (9.9) |  |
| Hypercholesterolemia (TC >240 mg/dL) | 5,239 (12.4) | 1,112 (13.1) | 1,010 (11.9) | 1,088 (12.9) | 1,008 (11.9) | 1,021 (12.1) | 0.0557 |
| Elevated TC (200-239 mg/dL) | 14,306 (33.8) | 2,852 (33.7) | 2,886 (34.1) | 2,863 (33.8) | 2,903 (34.3) | 2,802 (33.1) |  |
| High LDL-C (>160 mg/dL) | 4,760 (11.3) | 978 (11.6) | 940 (11.1) | 950 (11.2) | 936 (11.1) | 956 (11.3) | 0.6058 |
| Elevated LDL-C (130-159 mg/dL) | 10,684 (25.2) | 2,140 (25.3) | 2,134 (25.2) | 2,141 (25.3) | 2,177 (25.7) | 2,092 (24.7) |  |
| Low HDL-C (<40 mg/dL in males, <50 mg/dL in females) | 11,601 (27.4) | 2,331 (27.5) | 2,310 (27.3) | 2,280 (26.9) | 2,287 (27.0) | 2,393 (28.3) | 0.4302 |
| Hyperuricemia (SUA >7.0 mg/dL in males, >6.0 mg/dL in females) | 5,977 (14.1) | 1,167 (13.8) | 1,206 (14.3) | 1,129 (13.3) | 1,237 (14.6) | 1,238 (14.6) | 0.0865 |

Data are presented as *n* (%). †Taiwan Ministry of Health classification for obesity and overweight. ‡Taiwan Society of Cardiology and Taiwan Hypertension Society classification. BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; HbA1c, glycosylated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MetS-NCEP ATP III, metabolic syndrome following National Cholesterol Education Program Adult Treatment Panel III criteria; SBP, systolic blood pressure; SUA, serum uric acid; TC, total cholesterol; TG, triglyceride; WC, waist circumference.

**Table S11:** Distributions of different metabolic conditions among subjects in UK Biobank (*N*=271,366) across quintiles of Hb-PRS

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Metabolic Conditions** | **All** | **Q1** | **Q2** | **Q3** | **Q4** | **Q5** | ***P*-trend** |
| **Males, *n*** | 128,549 | 25,709 | 25,710 | 25,712 | 25,709 | 25,709 |  |
| **Mean Hemoglobin, g/dL** | 15.03 | 14.91 | 14.94 | 15.00 | 15.08 | 15.21 |  |
| MetS-NCEP ATP III | 51,741 (40.3) | 10,243 (39.8) | 10,402 (40.5) | 10,358 (40.3) | 10,382 (40.4) | 10,356 (40.3) | 0.4065 |
| Obesity (BMI >30.0 kg/m2) | 32,225 (25.2) | 6,615 (25.7) | 6,596 (25.7) | 6,296 (24.5) | 6,432 (25.0) | 6,286 (24.5) | **0.0043** |
| Overweight (BMI=25.0-29.9 kg/m2) | 63,454 (49.5) | 12,512 (48.8) | 12,568 (49.0) | 12,809 (50.0) | 12,716 (49.6) | 12,849 (50.1) |  |
| Central Obesity (WC >94 cm in males, >80 cm in females) | 71,359 (55.5) | 14,222 (55.3) | 14,370 (55.9) | 14,162 (55.1) | 14,346 (55.8) | 14,259 (55.5) | 0.8410 |
| Hypertension (SBP/DBP >140/>90 mm Hg)† | 62,691 (52.1) | 12,431 (51.8) | 12,543 (52.0) | 12,616 (52.2) | 12,479 (51.8) | 12,622 (52.6) | 0.3450 |
| Prehypertension (SBP=130-139 mm Hg or DBP=85-89 mm Hg)† | 27,224 (22.6) | 5,468 (22.8) | 5,479 (22.7) | 5,524 (22.9) | 5,385 (22.4) | 5,368 (22.4) |  |
| Hyperglycemia based on GLU‡ (>11.1 mmol/L) | 1,237 (1.0) | 286 (1.11) | 266 (1.03) | 241 (0.94) | 242 (0.94) | 202 (0.79) | **0.0001** |
| Hyperglycemia based on HbA1c (>48 mmol/mol) | 5,528 (4.3) | 1,179 (4.6) | 1,140 (4.4) | 1,136 (4.4) | 1,070 (4.2) | 1,003 (3.9) | **<0.0001** |
| Hypertriglyceridemia (TG >2.30 mmol/L) | 35,393 (28.8) | 6,791 (27.6) | 7,058 (28.7) | 7,150 (29.0) | 7,227 (29.4) | 7,167 (29.1) | **<0.0001** |
| Elevated TG (1.70-2.29 mmol/L) | 25,840 (21.0) | 5,145 (20.9) | 5,232 (21.2) | 5,184 (21.0) | 5,120 (20.8) | 5,159 (20.9) |  |
| Hypercholesterolemia (TC >6.20 mmol/L) | 32,154 (25.0) | 6,263 (24.4) | 6,580 (25.6) | 6,556 (25.5) | 6,549 (25.5) | 6,206 (24.1) | 0.5098 |
| Elevated TC (5.20-6.29 mmol/L) | 42,170 (34.2) | 8,451 (34.3) | 8,342 (33.8) | 8,577 (34.7) | 8,443 (34.3) | 8,357 (33.9) |  |
| High LDL-C (>4.10 mmol/L) | 29,144 (22.7) | 5,802 (22.6) | 5,941 (23.1) | 5,969 (23.2) | 5,855 (22.8) | 5,577 (21.7) | **0.0116** |
| Elevated LDL-C (3.40-4.09 mmol/L) | 36,907 (30.0) | 7,393 (30.1) | 7,378 (30.0) | 7,454 (30.3) | 7,343 (29.9) | 7,339 (29.8) |  |
| Low HDL-C (<1.00 mmol/L in males, <1.30 mmol/L in females) | 33,613 (26.2) | 6,853 (26.7) | 6,704 (26.1) | 6,638 (25.8) | 6,718 (26.1) | 6,700 (26.1) | 0.1904 |
| Hyperuricemia (SUA >416.0 µmol/L in males, >357.0 µmol/L in females) | 22,255 (17.3) | 4,662 (18.1) | 4,334 (16.9) | 4,284 (16.7) | 4,389 (17.1) | 4,586 (17.8) | 0.6138 |
| **Females, *n*** | 142,817 | 28,566 | 28,560 | 28,566 | 28,564 | 28,561 |  |
| **Mean Hemoglobin, g/dL** | 13.52 | 13.39 | 13.43 | 13.49 | 13.58 | 13.71 |  |
| MetS-NCEP ATP III | 44,322 (31.0) | 8,768 (30.7) | 8,768 (30.7) | 8,859 (31.0) | 8,828 (30.9) | 9,099 (31.9) | **0.0034** |
| Obesity (BMI >30.0 kg/m2) | 32,140 (22.5) | 6,717 (23.5) | 6,377 (22.3) | 6,329 (22.2) | 6,306 (22.1) | 6,411 (22.5) | **0.0007** |
| Overweight (BMI=25.0-29.9 kg/m2) | 51,690 (36.3) | 10,090 (35.4) | 10,397 (36.5) | 10,509 (36.9) | 10,252 (36.0) | 10,442 (36.6) |  |
| Central Obesity (WC >94 cm in males, >80 cm in females) | 80,842 (56.6) | 16,196 (56.7) | 16,136 (56.5) | 16,207 (56.7) | 16,080 (56.3) | 16,223 (56.8) | 0.9958 |
| Hypertension (SBP/DBP >140/>90 mm Hg)† | 52,244 (39.2) | 10,411 (39.0) | 10,312 (38.6) | 10,475 (39.3) | 10,473 (39.2) | 10,573 (39.8) | 0.1858 |
| Prehypertension (SBP=130-139 mm Hg or DBP=85-89 mm Hg)† | 26,595 (19.9) | 5,284 (19.8) | 5,365 (20.1) | 5,305 (19.9) | 5,321 (19.9) | 5,320 (20.0) |  |
| Hyperglycemia based on GLU‡ (>11.1 mmol/L) | 591 (0.4) | 145 (0.51) | 125 (0.44) | 114 (0.40) | 109 (0.38) | 98 (0.34) | **0.0013** |
| Hyperglycemia based on HbA1c (>48 mmol/mol) | 3,046 (2.1) | 654 (2.3) | 613 (2.2) | 617 (2.2) | 615 (2.2) | 547 (1.9) | **0.0061** |
| Hypertriglyceridemia (TG >2.30 mmol/L) | 19,632 (14.3) | 3,768 (13.7) | 3,881 (14.2) | 3,943 (14.5) | 3,960 (14.5) | 4,080 (14.9) | **0.0001** |
| Elevated TG (1.70-2.20 mmol/L) | 22,937 (16.8) | 4,493 (16.4) | 4,499 (16.5) | 4,649 (17.0) | 4,565 (16.7) | 4,731 (17.3) |  |
| Hypercholesterolemia (TC >6.20 mmol/L) | 50,551 (35.4) | 10,080 (35.3) | 10,286 (36.0) | 10,259 (35.9) | 10,074 (35.3) | 9,852 (34.5) | **0.0092** |
| Elevated TC (5.20-6.20 mmol/L) | 48,027 (35.1) | 9,676 (35.3) | 9,607 (35.1) | 9,515 (34.8) | 9,630 (35.1) | 9,599 (35.1) |  |
| High LDL-C (>4.10 mmol/L) | 37,766 (26.4) | 7,602 (26.6) | 7,721 (27.0) | 7,648 (26.8) | 7,503 (26.3) | 7,292 (25.5) | **0.0004** |
| Elevated LDL-C (3.40-4.10 mmol/L) | 41,574 (30.4) | 8,437 (30.8) | 8,403 (30.8) | 8,163 (29.9) | 8,289 (30.3) | 8,282 (30.3) |  |
| Low HDL-C (<1.00 mmol/L in males, <1.30 mmol/L in females) | 44,996 (31.5) | 9,053 (31.7) | 8,909 (31.2) | 8,930 (31.3) | 8,998 (31.5) | 9,106 (31.9) | 0.4278 |
| Hyperuricemia (SUA >416.0 µmol/L in males, >357.0 µmol/L in females) | 12,870 (9.0) | 2,661 (9.3) | 2,517 (8.8) | 2,493 (8.7) | 2,542 (8.9) | 2,657 (9.3) | 0.9087 |

Data are presented as *n* (%). †European Society of Cardiology/National Institute for Health and Care Excellence classification. ‡Based on non-fasting/random blood biochemistry measured within 24 hours. BMI, body mass index; DBP, diastolic blood pressure; GLU, blood glucose; HbA1c, glycosylated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MS-NCEP ATP III, metabolic syndrome following National Cholesterol Education Program Adult Treatment Panel III criteria; SBP, systolic blood pressure; SUA, serum uric acid; TC, total cholesterol; TG, triglyceride; WC, waist circumference.

**Table S12:** Distributions of self-reported metabolic conditions among subjects in Taiwan Biobank (*N*=61,352) across quintiles of Hb-PRS

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Self-reported Metabolic Conditions** | **All** | **Q1** | **Q2** | **Q3** | **Q4** | **Q5** | ***P*-trend** |
| **Males, *n*** | 19,012 | 3,802 | 3,803 | 3,802 | 3,803 | 3,802 |  |
| **Mean Hemoglobin, g/dL** | 15.04 | 14.79 | 14.98 | 15.04 | 15.11 | 15.28 |  |
| Hypertension | 3,494 (18.4) | 663 (17.5) | 718 (18.9) | 707 (18.6) | 713 (18.8) | 693 (18.2) | 0.4634 |
| Diabetes mellitus | 1,409 (7.4) | 275 (7.2) | 274 (7.2) | 279 (7.3) | 294 (7.7) | 287 (7.6) | 0.3874 |
| Hyperlipidemia | 1,891 (10.0) | 408 (10.7) | 377 (9.9) | 344 (9.1) | 383 (10.1) | 379 (10.0) | 0.3747 |
| Gout | 1,896 (10.0) | 382 (10.1) | 367 (9.7) | 350 (9.2) | 420 (11.1) | 377 (9.9) | 0.4596 |
| **Females, *n*** | 42,340 | 8,468 | 8,466 | 8,470 | 8,468 | 8,468 |  |
| **Mean Hemoglobin, g/dL** | 13.01 | 12.78 | 12.93 | 13.04 | 13.11 | 13.21 |  |
| Hypertension | 4,427 (10.5) | 893 (10.6) | 859 (10.2) | 882 (10.4) | 903 (10.7) | 890 (10.5) | 0.6653 |
| Diabetes mellitus | 1,911 (4.5) | 394 (4.7) | 398 (4.7) | 396 (4.7) | 381 (4.5) | 342 (4.0) | **0.0456** |
| Hyperlipidemia | 2,981 (7.0) | 624 (7.4) | 586 (6.9) | 603 (7.1) | 575 (6.8) | 593 (7.0) | 0.3292 |
| Gout | 231 (0.55) | 47 (0.56) | 42 (0.50) | 46 (0.54) | 47 (0.56) | 49 (0.58) | 0.6737 |

Data are presented as *n* (%).

**Table S13:** Distributions of self-reported metabolic conditions among subjects in UK Biobank (*N*=271,366) across quintiles of Hb-PRS

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Self-reported Metabolic Conditions** | **All** | **Q1** | **Q2** | **Q3** | **Q4** | **Q5** | ***P*-trend** |
| **Men** | 128,549 | 25,709 | 25,710 | 25,712 | 25,709 | 25,709 |  |
| **Mean Hemoglobin, g/dL** | 15.03 | 14.91 | 14.94 | 15.00 | 15.08 | 15.21 |  |
| Hypertension | 44,071 (34.2) | 8,694 (33.8) | 8,759 (34.1) | 8,878 (34.5) | 8,798 (34.2) | 8,942 (34.8) | **0.0261** |
| Diagnosis by a doctor† | 32,612 (25.4) | 6,444 (25.1) | 6,487 (25.2) | 6,563 (25.5) | 6,523 (25.4) | 6,595 (25.7) |  |
| Use of medication‡ | 12,393 (9.6) | 2,390 (9.3) | 2,421 (9.4) | 2,478 (9.6) | 2,470 (9.6) | 2,634 (10.3) |  |
| Type of medication§ | 32,321 (25.1) | 6,345 (24.7) | 6,439 (25.0) | 6,477 (25.2) | 6,497 (25.3) | 6,563 (25.5) |  |
| Non-cancer illness†† | 37,806 (29.4) | 7,422 (28.9) | 7,527 (29.3) | 7,625 (29.7) | 7,588 (29.5) | 7,644 (29.7) |  |
| Diabetes mellitus | 8,172 (6.4) | 1,711 (6.7) | 1,709 (6.7) | 1,628 (6.3) | 1,595 (6.2) | 1,529 (6.0) | **0.0001** |
| Diagnosis by a doctor† | 8,039 (6.3) | 1,677 (6.5) | 1,684 (6.6) | 1,605 (6.2) | 1,570 (6.1) | 1,503 (5.9) |  |
| Use of medication‡ | 250 (0.19) | 59 (0.23) | 55 (0.21) | 51 (0.20) | 53 (0.21) | 32 (0.12) |  |
| Type of medication§ | 5,852 (4.6) | 1,246 (4.9) | 1,245 (4.8) | 1,164 (4.5) | 1,129 (4.4) | 1,068 (4.2) |  |
| Non-cancer illness†† | 7,867 (6.1) | 1,634 (6.4) | 1,635 (6.4) | 1,565 (6.1) | 1,546 (6.0) | 1,487 (5.8) |  |
| Hyperlipidemia | 33,383 (26.0) | 6,679 (26.0) | 6,665 (25.9) | 6,773 (26.3) | 6,707 (26.1) | 6,559 (25.5) | 0.3773 |
| Use of medication‡ | 28,197 (21.9) | 5,627 (21.9) | 5,631 (21.9) | 5,728 (22.3) | 5,675 (22.1) | 5,536 (21.5) |  |
| Type of medication§ | 30,447 (23.7) | 6,103 (23.7) | 6,073 (23.6) | 6,167 (24.0) | 6,091 (23.7) | 6,013 (23.4) |  |
| Non-cancer illness†† | 18,932 (14.7) | 3,799 (14.8) | 3,810 (14.8) | 3,816 (14.8) | 3,872 (15.1) | 3,635 (14.1) |  |
| Gout | 3,920 (3.1) | 853 (3.3) | 818 (3.2) | 730 (2.8) | 748 (2.9) | 771 (3.0) | **0.0073** |
| Type of medication§ | 2,837 (2.2) | 602 (2.3) | 580 (2.3) | 545 (2.1) | 560 (2.2) | 550 (2.1) |  |
| Non-cancer illness†† | 3,546 (2.8) | 788 (3.1) | 735 (2.9) | 650 (2.5) | 672 (2.6) | 701 (2.7) |  |
| **Women** | 142,817 | 28,566 | 28,560 | 28,566 | 28,564 | 28,561 |  |
| **Mean Hemoglobin, g/dL** | 13.52 | 13.39 | 13.43 | 13.49 | 13.58 | 13.71 |  |
| Hypertension | 36,755 (25.7) | 7,220 (25.3) | 7,216 (25.3) | 7,338 (25.7) | 7,412 (26.0) | 7,569 (26.5) | **0.0001** |
| Diagnosis by a doctor† | 30,595 (21.4) | 5,991 (21.0) | 5,987 (21.0) | 6,108 (21.4) | 6,214 (21.8) | 6,295 (21.0) |  |
| Use of medication‡ | 13,765 (9.6) | 2,693 (9.4) | 2,656 (9.3) | 2,758 (9.7) | 2,788 (9.8) | 2,870 (10.1) |  |
| Type of medication§ | 26,005 (18.2) | 5,087 (17.8) | 5,057 (17.7) | 5,249 (18.4) | 5,237 (18.3) | 5,375 (18.8) |  |
| Non-cancer illness†† | 31,663 (22.2) | 6,208 (21.7) | 6,190 (21.7) | 6,346 (22.2) | 6,384 (22.4) | 6,535 (22.9) |  |
| Diabetes mellitus | 4,743 (3.3) | 1,027 (3.6) | 934 (3.3) | 917 (3.2) | 927 (3.3) | 938 (3.3) | 0.0536 |
| Diagnosis by a doctor† | 4,632 (3.2) | 1,003 (3.5) | 920 (3.2) | 893 (3.1) | 907 (3.2) | 909 (3.2) |  |
| Use of medication‡ | 168 (0.12) | 45 (0.16) | 42 (0.15) | 36 (0.13) | 22 (0.08) | 23 (0.08) |  |
| Type of medication§ | 3,147 (2.2) | 716 (2.5) | 628 (2.2) | 601 (2.1) | 610 (2.1) | 592 (2.1) |  |
| Non-cancer illness†† | 4,103 (2.9) | 876 (3.1) | 806 (2.8) | 797 (2.8) | 812 (2.8) | 812 (2.8) |  |
| Hyperlipidemia | 24,120 (16.9) | 4,808 (16.8) | 4,779 (16.7) | 4,883 (17.1) | 4,804 (16.8) | 4,846 (17.0) | 0.3513 |
| Use of medication‡ | 16,977 (11.9) | 3,342 (11.7) | 3,325 (11.6) | 3,482 (12.2) | 3,425 (12.0) | 3,403 (11.9) |  |
| Type of medication§ | 21,850 (15.3) | 4,342 (15.2) | 4,330 (15.2) | 4,443 (15.6) | 4,327 (15.2) | 4,408 (15.4) |  |
| Non-cancer illness†† | 13,220 (9.3) | 2,535 (8.9) | 2,581 (9.0) | 2,724 (9.5) | 2,722 (9.5) | 2,658 (9.3) |  |
| Gout | 275 (0.19) | 48 (0.17) | 63 (0.22) | 57 (0.20) | 50 (0.18) | 57 (0.20) | 0.8306 |
| Type of medication§ | 190 (0.13) | 29 (0.10) | 49 (0.17) | 38 (0.13) | 33 (0.12) | 41 (0.14) |  |
| Non-cancer illness†† | 231 (0.16) | 39 (0.14) | 52 (0.18) | 43 (0.15) | 45 (0.16) | 52 (0.18) |  |

Data are presented as *n* (%). †UKB data fields 6150 and 2443 for self-reported diagnosis of high blood pressure and diabetes by a doctor. ‡Data fields 6177 and 6153 for self-reported use of medications. §Data field 20003 for type of prescription medications by verbal interview. ††Data field 20002 for self-reported non-cancer illnesses (hypertension, essential hypertension, diabetes, type 2 diabetes, high cholesterol, and gout).

**Table S14:** Cases of metabolic conditions identified from hospital in-patient records of UK Biobank subjects (*N*=271,366) across quintiles of Hb-PRS

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Diagnoses†** | **All** | **Q1** | **Q2** | **Q3** | **Q4** | **Q5** | ***P*-trend** |
| **Men** | 128,549 | 25,709 | 25,710 | 25,712 | 25,709 | 25,709 |  |
| **Mean Hemoglobin, g/dL** | 15.03 | 14.91 | 14.94 | 15.00 | 15.08 | 15.21 |  |
| Hypertension | 31,659 (24.6) | 6,224 (24.2) | 6,351 (24.7) | 6,389 (24.9) | 6,291 (24.5) | 6,404 (24.9) | 0.1693 |
| ICD9 diagnoses | 67 (0.05) | 13 (0.05) | 15 (0.06) | 13 (0.05) | 12 (0.05) | 14 (0.05) |  |
| ICD10 diagnoses | 31,632 (24.6) | 6,219 (24.2) | 6,347 (24.7) | 6,385 (24.8) | 6,286 (24.5) | 6,395 (24.9) |  |
| Diabetes Mellitus | 9,240 (7.2) | 1,949 (7.6) | 1,906 (7.4) | 1,847 (7.2) | 1,794 (7.0) | 1,744 (6.8) | **<0.0001** |
| ICD9 diagnoses | 49 (0.04) | 16 (0.06) | 8 (0.03) | 10 (0.04) | 7 (0.03) | 8 (0.03) |  |
| ICD10 diagnoses | 9,230 (7.2) | 1,942 (7.6) | 1,905 (7.4) | 1,845 (7.2) | 1,794 (7.0) | 1,744 (6.8) |  |
| Lipids Disorders | 16,652 (13.0) | 3,325 (12.9) | 3,339 (13.0) | 3,436 (13.4) | 3,386 (13.2) | 3,166 (12.3) | 0.1116 |
| ICD9 diagnoses | 22 (0.02) | 5 (0.02) | 4 (0.02) | 6 (0.02) | 3 (0.01) | 4 (0.02) |  |
| ICD10 diagnoses | 16,638 (12.9) | 3,324 (12.9) | 3,335 (13.0) | 3,431 (13.3) | 3,384 (13.2) | 3,164 (12.3) |  |
| Gout | 2,417 (1.9) | 509 (2.0) | 490 (1.9) | 444 (1.7) | 484 (1.9) | 490 (1.9) | 0.5231 |
| ICD9 diagnoses | 4 | 3 (0.01) | 0 | 0 | 1 | 0 |  |
| ICD10 diagnoses | 2,414 (1.9) | 507 (2.0) | 490 (1.9) | 444 (1.7) | 483 (1.9) | 490 (1.9) |  |
| **Women** | 142,817 | 28,566 | 28,560 | 28,566 | 28,564 | 28,561 |  |
| **Mean Hemoglobin, g/dL** | 13.52 | 13.39 | 13.43 | 13.49 | 13.58 | 13.71 |  |
| Hypertension | 24,947 (17.5) | 4,908 (17.2) | 4,930 (17.3) | 5,032 (17.6) | 4,996 (17.5) | 5,081 (17.8) | **0.0418** |
| ICD9 diagnoses | 49 (0.03) | 7 (0.02) | 15 (0.05) | 10 (0.04) | 4 (0.01) | 13 (0.05) |  |
| ICD10 diagnoses | 24,921 (17.5) | 4,902 (17.2) | 4,922 (17.2) | 5,029 (17.6) | 4,994 (17.5) | 5,074 (17.8) |  |
| Diabetes Mellitus | 5,440 (3.8) | 1,113 (3.9) | 1,066 (3.7) | 1,089 (3.8) | 1,107 (3.9) | 1,065 (3.7) | 0.5924 |
| ICD9 diagnoses | 30 (0.02) | 9 (0.03) | 8 (0.03) | 7 (0.02) | 5 (0.02) | 1 |  |
| ICD10 diagnoses | 5,429 (3.8) | 1,112 (3.9) | 1,064 (3.7) | 1,084 (3.8) | 1,104 (3.9) | 1,065 (3.7) |  |
| Lipids Disorders | 10,108 (7.1) | 1,989 (7.0) | 2,004 (7.0) | 2,088 (7.3) | 2,009 (7.0) | 2,018 (7.1) | 0.6435 |
| ICD9 diagnoses | 9 (0.01) | 1 | 4 (0.01) | 1 | 2 (0.01) | 1 |  |
| ICD10 diagnoses | 10,102 (7.1) | 1,988 (7.0) | 2,001 (7.0) | 2,088 (7.3) | 2,008 (7.0) | 2,017 (7.1) |  |
| Gout | 340 (0.24) | 63 (0.22) | 70 (0.25) | 62 (0.22) | 63 (0.22) | 82 (0.29) | 0.2337 |
| ICD9 diagnoses | 1 | 0 | 0 | 1 | 0 | 0 |  |
| ICD10 diagnoses | 339 (0.24) | 63 (0.22) | 70 (0.25) | 61 (0.21) | 63 (0.22) | 82 (0.29) |  |

Data are presented as *n* (%). †UKB data fields 41203 and 41205 provided diagnoses data from the hospital in-patient records of a subject, which were coded according to the International Classification of Diseases version-9 (ICD-9). Data fields 41202 and 41204 provided diagnoses data from the hospital in-patient records of a subject, which were coded according to the International Classification of Diseases version-10 (ICD-10).

**Table S15:** Odds ratios of metabolic syndrome across quintiles of Hb-PRS among Taiwanese Han Chinese and European Whites

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Metabolic Syndrome** | **Cases**  ***n* (%)** | **Crude**  **OR (95% CI)** | ***P*** | **Model 1**†  **OR (95% CI)** | ***P*** | **Model 2‡**  **OR (95% CI)** | ***P*** |
| Taiwanese Han Chinese (*N*=61,352) |  |  |  |  |  |  |  |
| *Males (n=19,012)* | 5,546 (29.2) |  |  |  |  |  |  |
| Q1 (14.79 g/dL) | 1,064 (28.0) | Reference | - | Reference | - | Reference | - |
| Q2 (14.98 g/dL) vs. Q1 | 1,102 (29.0) | 1.08 (0.98, 1.20) | 0.1293 | 1.08 (0.97, 1.20) | 0.1589 | 1.07 (0.96, 1.19) | 0.2088 |
| Q3 (15.04 g/dL) vs. Q1 | 1,095 (28.8) | 1.03 (0.93, 1.15) | 0.5265 | 1.04 (0.93, 1.15) | 0.5033 | 1.03 (0.93, 1.15) | 0.5710 |
| Q4 (15.11 g/dL) vs. Q1 | 1,150 (30.3) | **1.17 (1.06, 1.30)** | **0.0026** | **1.17 (1.06, 1.30)** | **0.0026** | **1.17 (1.05, 1.29)** | **0.0039** |
| Q5 (15.28 g/dL) vs. Q1 | 1,135 (29.9) | **1.13 (1.02, 1.25)** | **0.0218** | **1.13 (1.02, 1.26)** | **0.0202** | **1.13 (1.02, 1.26)** | **0.0183** |
| *Females (n=42,340)* | 9,065 (21.4) |  |  |  |  |  |  |
| Q1 (12.78 g/dL) | 1,795 (21.2) | Reference | - | Reference | - | Reference | - |
| Q2 (12.93 g/dL) vs. Q1 | 1,785 (21.1) | 0.99 (0.91, 1.08) | 0.8488 | 1.00 (0.92, 1.09) | 0.9512 | 1.00 (0.92, 1.09) | 0.9955 |
| Q3 (13.04 g/dL) vs. Q1 | 1,790 (21.1) | 1.02 (0.94, 1.11) | 0.6579 | 1.02 (0.94, 1.11) | 0.6301 | 1.02 (0.94, 1.11) | 0.6411 |
| Q4 (13.11 g/dL) vs. Q1 | 1,804 (21.3) | 1.01 (0.93, 1.09) | 0.8991 | 1.01 (0.93, 1.10) | 0.7537 | 1.01 (0.93, 1.10) | 0.7646 |
| Q5 (13.21 g/dL) vs. Q1 | 1,891 (22.3) | **1.12 (1.03, 1.22)** | **0.0062** | **1.13 (1.04, 1.22)** | **0.0055** | **1.13 (1.04, 1.22)** | **0.0048** |
| European Whites (*N*=271,366) |  |  |  |  |  |  |  |
| *Males (n=128,549)* | 62,252 (48.4) |  |  |  |  |  |  |
| Q1 (14.91 g/dL) | 12,364 (48.1) | Reference | - | Reference | - | Reference | - |
| Q2 (14.94 g/dL) vs. Q1 | 12,461 (48.5) | 1.02 (0.98, 1.05) | 0.3944 | 1.02 (0.98, 1.05) | 0.3234 | 1.02 (0.98, 1.05) | 0.4173 |
| Q3 (15.00 g/dL) vs. Q1 | 12,493 (48.6) | 1.02 (0.99, 1.06) | 0.2604 | 1.02 (0.98, 1.06) | 0.2881 | 1.02 (0.98, 1.05) | 0.3836 |
| Q4 (15.08 g/dL) vs. Q1 | 12,516 (48.7) | 1.02 (0.99, 1.06) | 0.1798 | 1.02 (0.99, 1.06) | 0.2758 | 1.02 (0.98, 1.05) | 0.3568 |
| Q5 (15.21 g/dL) vs. Q1 | 12,418 (48.3) | 1.01 (0.97, 1.04) | 0.6338 | 1.00 (0.97, 1.04) | 0.8688 | 1.00 (0.96, 1.04) | 0.9439 |
| *Females (n=142,817)* | 51,880 (36.3) |  |  |  |  |  |  |
| Q1 (13.39 g/dL) | 10,348 (36.2) | Reference | - | Reference | - | Reference | - |
| Q2 (13.43 g/dL) vs. Q1 | 10,267 (36.0) | 0.99 (0.96, 1.02) | 0.5571 | 1.00 (0.96, 1.03) | 0.8848 | 1.00 (0.96, 1.04) | 0.9776 |
| Q3 (13.49 g/dL) vs. Q1 | 10,325 (36.1) | 1.00 (0.97, 1.04) | 1.0000 | 1.00 (0.97, 1.04) | 0.9869 | 1.00 (0.96, 1.03) | 0.8881 |
| Q4 (13.58 g/dL) vs. Q1 | 10,345 (36.2) | 1.01 (0.97, 1.04) | 0.7673 | 1.01 (0.97, 1.05) | 0.6109 | 1.01 (0.98, 1.05) | 0.4677 |
| Q5 (13.71 g/dL) vs. Q1 | 10,595 (37.1) | **1.04 (1.01, 1.08)** | **0.0141** | **1.04 (1.01, 1.08)** | **0.0193** | **1.05 (1.01, 1.08)** | **0.0156** |

†Model 1 adjusted for age, age-squared and the first ten genetic principal components. ‡Model 2 further adjusted for smoking and alcohol consumption (and menopausal status in women).

**Table S16:** Odds ratios of hypertension across quintiles of Hb-PRS among Taiwanese Han Chinese and European Whites

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Hypertension** | **Cases**  ***n* (%)** | **Crude**  **OR (95% CI)** | ***P*** | **Model 1**†  **OR (95% CI)** | ***P*** | **Model 2‡**  **OR (95% CI)** | ***P*** |
| Taiwanese Han Chinese (*N*=61,352) |  |  |  |  |  |  |  |
| *Males (n=19,012)* | 6,523 (34.3) |  |  |  |  |  |  |
| Q1 (14.79 g/dL) | 1,266 (33.3) | Reference | - | Reference | - | Reference | - |
| Q2 (14.98 g/dL) vs. Q1 | 1,315 (34.6) | 1.06 (0.96, 1.16) | 0.2438 | 1.05 (0.95, 1.15) | 0.3279 | 1.04 (0.95, 1.15) | 0.3991 |
| Q3 (15.04 g/dL) vs. Q1 | 1,298 (34.1) | 1.08 (0.99, 1.18) | 0.1031 | 1.09 (0.99, 1.19) | 0.0850 | 1.08 (0.98, 1.19) | 0.1048 |
| Q4 (15.11 g/dL) vs. Q1 | 1,320 (34.7) | 1.07 (0.98, 1.18) | 0.1241 | 1.08 (0.98, 1.19) | 0.1104 | 1.08 (0.98, 1.18) | 0.1242 |
| Q5 (15.28 g/dL) vs. Q1 | 1,324 (34.8) | 1.09 (0.99, 1.19) | 0.0642 | **1.10 (1.004, 1.21)** | **0.0417** | **1.10 (1.001, 1.21)** | **0.0473** |
| *Females (n=42,340)* | 8,113 (19.2) |  |  |  |  |  |  |
| Q1 (12.78 g/dL) | 1,583 (18.7) | Reference | - | Reference | - | Reference | - |
| Q2 (12.93 g/dL) vs. Q1 | 1,596 (18.9) | 1.01 (0.94, 1.09) | 0.7895 | 1.02 (0.94, 1.11) | 0.5630 | 1.02 (0.94, 1.11) | 0.5854 |
| Q3 (13.04 g/dL) vs. Q1 | 1,618 (19.1) | 1.03 (0.95, 1.11) | 0.4951 | 1.04 (0.95, 1.12) | 0.4124 | 1.04 (0.96, 1.12) | 0.3935 |
| Q4 (13.11 g/dL) vs. Q1 | 1,666 (19.7) | 1.06 (0.99, 1.15) | 0.1122 | **1.09 (1.01, 1.19)** | **0.0325** | **1.09 (1.01, 1.19)** | **0.0333** |
| Q5 (13.21 g/dL) vs. Q1 | 1,650 (19.5) | 1.05 (0.98, 1.14) | 0.1930 | 1.06 (0.98, 1.15) | 0.1576 | 1.06 (0.98, 1.15) | 0.1446 |
| European Whites (*N*=271,366) |  |  |  |  |  |  |  |
| *Males (n=128,549)* | 81,218 (63.2) |  |  |  |  |  |  |
| Q1 (14.91 g/dL) | 16,061 (62.5) | Reference | - | Reference | - | Reference | - |
| Q2 (14.94 g/dL) vs. Q1 | 16,205 (63.0) | 1.02 (0.99, 1.06) | 0.1888 | 1.03 (0.99, 1.07) | 0.0824 | 1.03 (0.99, 1.07) | 0.1026 |
| Q3 (15.00 g/dL) vs. Q1 | 16,368 (63.7) | **1.05 (1.02, 1.09)** | **0.0053** | **1.06 (1.02, 1.10)** | **0.0039** | **1.06 (1.02, 1.10)** | **0.0052** |
| Q4 (15.08 g/dL) vs. Q1 | 16,204 (63.0) | 1.02 (0.99, 1.06) | 0.1900 | 1.02 (0.98, 1.06) | 0.3526 | 1.02 (0.98, 1.06) | 0.3931 |
| Q5 (15.21 g/dL) vs. Q1 | 16,380 (63.7) | **1.06 (1.02, 1.09)** | **0.0035** | **1.05 (1.01, 1.09)** | **0.0130** | **1.05 (1.01, 1.09)** | **0.0194** |
| *Females (n=142,817)* | 69,746 (48.8) |  |  |  |  |  |  |
| Q1 (13.39 g/dL) | 13,827 (48.4) | Reference | - | Reference | - | Reference | - |
| Q2 (13.43 g/dL) vs. Q1 | 13,770 (48.2) | 1.00 (0.97, 1.04) | 0.9858 | 1.01 (0.97, 1.05) | 0.6235 | 1.01 (0.97, 1.05) | 0.5749 |
| Q3 (13.49 g/dL) vs. Q1 | 13,984 (49.0) | 1.02 (0.99, 1.06) | 0.1802 | 1.03 (0.99, 1.06) | 0.1884 | 1.03 (0.99, 1.07) | 0.1644 |
| Q4 (13.58 g/dL) vs. Q1 | 13,981 (49.0) | 1.03 (0.99, 1.06) | 0.1470 | 1.03 (1.00, 1.07) | 0.0732 | **1.04 (1.00, 1.08)** | **0.0495** |
| Q5 (13.71 g/dL) vs. Q1 | 14,184 (49.7) | **1.06 (1.02, 1.09)** | **0.0023** | **1.07 (1.03, 1.11)** | **0.0006** | **1.07 (1.03, 1.11)** | **0.0004** |

†Model 1 adjusted for age, age-squared and the first ten genetic principal components. ‡Model 2 further adjusted for smoking and alcohol consumption (and menopausal status in women).

**Table S17:** Odds ratios of dyslipidemia across quintiles of Hb-PRS among Taiwanese Han Chinese and European Whites

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Dyslipidemia** | **Cases**  ***n* (%)** | **Crude**  **OR (95% CI)** | ***P*** | **Model 1**†  **OR (95% CI)** | ***P*** | **Model 2‡**  **OR (95% CI)** | ***P*** |
| Taiwanese Han Chinese (*N*=61,352) |  |  |  |  |  |  |  |
| *Males (n=19,012)* | 6,895 (36.3) |  |  |  |  |  |  |
| Q1 (14.79 g/dL) | 1,364 (35.9) | Reference | - | Reference | - | Reference | - |
| Q2 (14.98 g/dL) vs. Q1 | 1,397 (36.7) | 1.07 (0.97, 1.18) | 0.1626 | 1.06 (0.96, 1.17) | 0.2423 | 1.07 (0.97, 1.17) | 0.2076 |
| Q3 (15.04 g/dL) vs. Q1 | 1,329 (35.0) | 0.99 (0.90, 1.10) | 0.8744 | 0.99 (0.89, 1.09) | 0.8114 | 0.99 (0.90, 1.09) | 0.8627 |
| Q4 (15.11 g/dL) vs. Q1 | 1,409 (37.1) | **1.11 (1.01, 1.22)** | **0.0401** | 1.10 (0.99, 1.21) | 0.0668 | **1.10 (1.001, 1.22)** | **0.0485** |
| Q5 (15.28 g/dL) vs. Q1 | 1,396 (36.7) | 1.08 (0.98, 1.20) | 0.1059 | 1.08 (0.98, 1.20) | 0.1114 | 1.08 (0.98, 1.19) | 0.1211 |
| *Females (n=42,340)* | 14,124 (33.4) |  |  |  |  |  |  |
| Q1 (12.78 g/dL) | 2,858 (33.8) | Reference | - | Reference | - | Reference | - |
| Q2 (12.93 g/dL) vs. Q1 | 2,801 (33.1) | 1.00 (0.93, 1.07) | 0.9445 | 1.00 (0.93, 1.07) | 0.9247 | 1.00 (0.94, 1.07) | 0.9894 |
| Q3 (13.04 g/dL) vs. Q1 | 2,807 (33.1) | 0.98 (0.91, 1.04) | 0.4579 | 0.97 (0.91, 1.04) | 0.4067 | 0.97 (0.91, 1.04) | 0.4047 |
| Q4 (13.11 g/dL) vs. Q1 | 2,761 (32.6) | 0.97 (0.91, 1.03) | 0.3306 | 0.97 (0.90, 1.03) | 0.2931 | 0.96 (0.90, 1.03) | 0.2871 |
| Q5 (13.21 g/dL) vs. Q1 | 2,897 (34.2) | 1.04 (0.98, 1.11) | 0.2080 | 1.04 (0.97, 1.11) | 0.2655 | 1.04 (0.97, 1.11) | 0.2539 |
| European Whites (*N*=271,366) |  |  |  |  |  |  |  |
| *Males (n=128,549)* | 89,276 (69.5) |  |  |  |  |  |  |
| Q1 (14.91 g/dL) | 17,684 (68.8) | Reference | - | Reference | - | Reference | - |
| Q2 (14.94 g/dL) vs. Q1 | 17,923 (69.7) | **1.05 (1.01, 1.09)** | **0.0223** | **1.05 (1.01, 1.09)** | **0.0217** | **1.04 (1.004, 1.08)** | **0.0305** |
| Q3 (15.00 g/dL) vs. Q1 | 17,963 (69.9) | **1.05 (1.01, 1.09)** | **0.0080** | **1.05 (1.01, 1.09)** | **0.0104** | **1.05 (1.01, 1.09)** | **0.0166** |
| Q4 (15.08 g/dL) vs. Q1 | 17,927 (69.7) | **1.05 (1.01, 1.09)** | **0.0198** | **1.04 (1.004, 1.08)** | **0.0307** | **1.04 (1.001, 1.08)** | **0.0468** |
| Q5 (15.21 g/dL) vs. Q1 | 17,779 (69.2) | 1.02 (0.98, 1.06) | 0.3610 | 1.01 (0.98, 1.05) | 0.5047 | 1.01 (0.97, 1.05) | 0.6437 |
| *Females (n=142,817)* | 79,876 (55.9) |  |  |  |  |  |  |
| Q1 (13.39 g/dL) | 16,007 (56.0) | Reference | - | Reference | - | Reference | - |
| Q2 (13.43 g/dL) vs. Q1 | 15,884 (55.6) | 0.99 (0.96, 1.02) | 0.5076 | 0.99 (0.96, 1.03) | 0.6058 | 0.99 (0.96, 1.03) | 0.6886 |
| Q3 (13.49 g/dL) vs. Q1 | 15,932 (55.8) | 1.01 (0.97, 1.04) | 0.7823 | 1.01 (0.97, 1.04) | 0.7605 | 1.00 (0.97, 1.04) | 0.8292 |
| Q4 (13.58 g/dL) vs. Q1 | 15,987 (56.0) | 1.01 (0.98, 1.04) | 0.6334 | 1.01 (0.98, 1.04) | 0.5810 | 1.01 (0.98, 1.05) | 0.4256 |
| Q5 (13.71 g/dL) vs. Q1 | 16,066 (56.3) | **1.04 (1.01, 1.08)** | **0.0188** | **1.04 (1.01, 1.07)** | **0.0236** | **1.04 (1.01, 1.08)** | **0.0220** |

†Model 1 adjusted for age, age-squared and the first ten genetic principal components. ‡Model 2 further adjusted for smoking and alcohol consumption (and menopausal status in women).

**Table S18:** Odds ratios of central obesity across quintiles of Hb-PRS among Taiwanese Han Chinese and European Whites

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Central Obesity** | **Cases**  ***n* (%)** | **Crude**  **OR (95% CI)** | ***P*** | **Model 1**†  **OR (95% CI)** | ***P*** | **Model 2‡**  **OR (95% CI)** | ***P*** |
| Taiwanese Han Chinese (*N*=61,352) |  |  |  |  |  |  |  |
| *Males (n=19,012)* | 7,169 (37.7) |  |  |  |  |  |  |
| Q1 (14.79 g/dL) | 1,398 (36.8) | Reference | - | Reference | - | Reference | - |
| Q2 (14.98 g/dL) vs. Q1 | 1,428 (37.6) | 1.03 (0.94, 1.13) | 0.4955 | 1.03 (0.94, 1.13) | 0.5030 | 1.03 (0.94, 1.13) | 0.5930 |
| Q3 (15.04 g/dL) vs. Q1 | 1,427 (37.5) | 1.03 (0.94, 1.13) | 0.5144 | 1.03 (0.94, 1.13) | 0.4937 | 1.03 (0.94, 1.13) | 0.5621 |
| Q4 (15.11 g/dL) vs. Q1 | 1,474 (38.8) | 1.09 (0.99, 1.19) | 0.0731 | 1.09 (0.99, 1.19) | 0.0843 | 1.08 (0.99, 1.19) | 0.0939 |
| Q5 (15.28 g/dL) vs. Q1 | 1,442 (37.9) | 1.05 (0.96, 1.15) | 0.3211 | 1.05 (0.96, 1.15) | 0.3263 | 1.05 (0.96, 1.15) | 0.3032 |
| *Females (n=42,340)* | 20,231 (47.8) |  |  |  |  |  |  |
| Q1 (12.78 g/dL) | 4,119 (48.6) | Reference | - | Reference | - | Reference | - |
| Q2 (12.93 g/dL) vs. Q1 | 3,994 (47.2) | 0.94 (0.89, 1.00) | 0.0573 | 0.95 (0.89, 1.01) | 0.0806 | 0.95 (0.89, 1.01) | 0.0813 |
| Q3 (13.04 g/dL) vs. Q1 | 4,021 (47.5) | 0.95 (0.90, 1.01) | 0.1199 | 0.96 (0.90, 1.02) | 0.1545 | 0.96 (0.90, 1.02) | 0.1566 |
| Q4 (13.11 g/dL) vs. Q1 | 4,035 (47.7) | 0.96 (0.91, 1.02) | 0.1960 | 0.97 (0.91, 1.03) | 0.3269 | 0.97 (0.91, 1.03) | 0.3083 |
| Q5 (13.21 g/dL) vs. Q1 | 4,062 (48.0) | 0.97 (0.92, 1.04) | 0.3926 | 0.98 (0.92, 1.04) | 0.5027 | 0.98 (0.92, 1.04) | 0.5205 |
| European Whites (*N*=271,366) |  |  |  |  |  |  |  |
| *Males (n=128,549)* | 71,359 (55.5) |  |  |  |  |  |  |
| Q1 (14.91 g/dL) | 14,222 (55.3) | Reference | - | Reference | - | Reference | - |
| Q2 (14.94 g/dL) vs. Q1 | 14,370 (55.9) | 1.02 (0.99, 1.06) | 0.1908 | 1.03 (0.99, 1.06) | 0.1259 | 1.03 (0.99, 1.06) | 0.1761 |
| Q3 (15.00 g/dL) vs. Q1 | 14,162 (55.1) | 0.99 (0.96, 1.03) | 0.5840 | 0.99 (0.96, 1.03) | 0.6392 | 0.99 (0.95, 1.02) | 0.5057 |
| Q4 (15.08 g/dL) vs. Q1 | 14,346 (55.8) | 1.02 (0.99, 1.06) | 0.2712 | 1.02 (0.98, 1.06) | 0.2975 | 1.02 (0.98, 1.05) | 0.3620 |
| Q5 (15.21 g/dL) vs. Q1 | 14,259 (55.5) | 1.01 (0.97, 1.04) | 0.7426 | 1.00 (0.97, 1.04) | 0.9092 | 1.00 (0.96, 1.03) | 0.9305 |
| *Females (n=142,817)* | 80,842 (56.6) |  |  |  |  |  |  |
| Q1 (13.39 g/dL) | 16,196 (56.7) | Reference | - | Reference | - | Reference | - |
| Q2 (13.43 g/dL) vs. Q1 | 16,136 (56.5) | 0.99 (0.96, 1.03) | 0.6328 | 1.00 (0.97, 1.04) | 0.9322 | 1.00 (0.97, 1.04) | 0.8702 |
| Q3 (13.49 g/dL) vs. Q1 | 16,207 (56.7) | 1.00 (0.97, 1.04) | 0.9260 | 1.01 (0.97, 1.04) | 0.6983 | 1.01 (0.97, 1.04) | 0.7774 |
| Q4 (13.58 g/dL) vs. Q1 | 16,080 (56.3) | 0.98 (0.95, 1.02) | 0.3321 | 0.99 (0.96, 1.02) | 0.5201 | 0.99 (0.96, 1.03) | 0.6337 |
| Q5 (13.71 g/dL) vs. Q1 | 16,223 (56.8) | 1.00 (0.97, 1.04) | 0.8012 | 1.00 (0.97, 1.04) | 0.9212 | 1.00 (0.97, 1.04) | 0.8919 |

†Model 1 adjusted for age, age-squared and the first ten genetic principal components. ‡Model 2 further adjusted for smoking and alcohol consumption (and menopausal status in women).

**Table S19:** Odds ratios of gout or hyperuricemia across quintiles of Hb-PRS among Taiwanese Han Chinese and European Whites

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Gout or Hyperuricemia** | **Cases**  ***n* (%)** | **Crude**  **OR (95% CI)** | ***P*** | **Model 1**†  **OR (95% CI)** | ***P*** | **Model 2‡**  **OR (95% CI)** | ***P*** |
| Taiwanese Han Chinese (*N*=61,352) |  |  |  |  |  |  |  |
| *Males (n=19,012)* | 6,294 (33.1) |  |  |  |  |  |  |
| Q1 (14.79 g/dL) | 1,274 (33.5) | Reference | - | Reference | - | Reference | - |
| Q2 (14.98 g/dL) vs. Q1 | 1,220 (32.1) | 0.93 (0.83, 1.05) | 0.2693 | 0.94 (0.83, 1.06) | 0.2885 | 0.93 (0.82, 1.05) | 0.2375 |
| Q3 (15.04 g/dL) vs. Q1 | 1,256 (33.0) | 0.98 (0.87, 1.10) | 0.6920 | 0.98 (0.87, 1.10) | 0.7006 | 0.97 (0.86, 1.10) | 0.6344 |
| Q4 (15.11 g/dL) vs. Q1 | 1,277 (33.6) | 1.01 (0.89, 1.13) | 0.9275 | 1.01 (0.89, 1.14) | 0.9044 | 1.00 (0.89, 1.13) | 0.9522 |
| Q5 (15.28 g/dL) vs. Q1 | 1,267 (33.3) | 1.02 (0.91, 1.15) | 0.6943 | 1.02 (0.91, 1.15) | 0.7017 | 1.02 (0.91, 1.15) | 0.7221 |
| *Females (n=42,340)* | 6,088 (14.4) |  |  |  |  |  |  |
| Q1 (12.78 g/dL) | 1,189 (14.0) | Reference | - | Reference | - | Reference | - |
| Q2 (12.93 g/dL) vs. Q1 | 1,226 (14.5) | 0.99 (0.88, 1.12) | 0.9087 | 1.00 (0.89, 1.12) | 0.9647 | 1.00 (0.89, 1.13) | 0.9972 |
| Q3 (13.04 g/dL) vs. Q1 | 1,158 (13.7) | 0.97 (0.86, 1.10) | 0.6549 | 0.97 (0.86, 1.09) | 0.6282 | 0.98 (0.87, 1.10) | 0.6849 |
| Q4 (13.11 g/dL) vs. Q1 | 1,256 (14.8) | 1.06 (0.95, 1.20) | 0.2954 | 1.07 (0.95, 1.20) | 0.2704 | 1.06 (0.95, 1.20) | 0.3021 |
| Q5 (13.21 g/dL) vs. Q1 | 1,259 (14.9) | **1.14 (1.02, 1.28)** | **0.0274** | **1.13 (1.01, 1.27)** | **0.0346** | **1.14 (1.01, 1.28)** | **0.0321** |
| European Whites (*N*=271,366) |  |  |  |  |  |  |  |
| *Males (n=128,549)* | 25,112 (19.5) |  |  |  |  |  |  |
| Q1 (14.91 g/dL) | 5,260 (20.5) | Reference | - | Reference | - | Reference | - |
| Q2 (14.94 g/dL) vs. Q1 | 4,903 (19.1) | **0.92 (0.88, 0.96)** | **<0.0001** | **0.92 (0.88, 0.96)** | **0.0002** | **0.92 (0.88, 0.96)** | **0.0002** |
| Q3 (15.00 g/dL) vs. Q1 | 4,834 (18.8) | **0.90 (0.86, 0.94)** | **<0.0001** | **0.90 (0.87, 0.95)** | **<0.0001** | **0.90 (0.87, 0.94)** | **<0.0001** |
| Q4 (15.08 g/dL) vs. Q1 | 4,952 (19.3) | **0.93 (0.89, 0.97)** | **0.0007** | **0.93 (0.89, 0.97)** | **0.0011** | **0.93 (0.89, 0.97)** | **0.0012** |
| Q5 (15.21 g/dL) vs. Q1 | 5,163 (20.1) | 0.98 (0.94, 1.02) | 0.2873 | 0.97 (0.93, 1.02) | 0.2236 | 0.97 (0.93, 1.02) | 0.1994 |
| *Females (n=142,817)* | 13,161 (9.2) |  |  |  |  |  |  |
| Q1 (13.39 g/dL) | 2,718 (9.5) | Reference | - | Reference | - | Reference | - |
| Q2 (13.43 g/dL) vs. Q1 | 2,581 (9.0) | **0.95 (0.89, 1.00)** | **0.0491** | 0.95 (0.90, 1.01) | 0.0885 | 0.95 (0.90, 1.01) | 0.1006 |
| Q3 (13.49 g/dL) vs. Q1 | 2,549 (8.9) | **0.93 (0.88, 0.99)** | **0.0145** | **0.93 (0.88, 0.99)** | **0.0142** | **0.93 (0.88, 0.98)** | **0.0122** |
| Q4 (13.58 g/dL) vs. Q1 | 2,594 (9.1) | 0.95 (0.90, 1.01) | 0.0745 | 0.95 (0.90, 1.01) | 0.0889 | 0.95 (0.90, 1.01) | 0.1049 |
| Q5 (13.71 g/dL) vs. Q1 | 2,719 (9.5) | 1.00 (0.95, 1.06) | 0.9832 | 0.99 (0.94, 1.05) | 0.8147 | 1.00 (0.94, 1.05) | 0.8559 |

†Model 1 adjusted for age, age-squared and the first ten genetic principal components. ‡Model 2 further adjusted for smoking and alcohol consumption (and menopausal status in women).

**Table S20:** Odds ratios of diabetes or hyperglycemia across quintiles of Hb-PRS among Taiwanese Han Chinese and European Whites

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Diabetes or Hyperglycemia** | **Cases**  ***n* (%)** | **Crude**  **OR (95% CI)** | ***P*** | **Model 1**†  **OR (95% CI)** | ***P*** | **Model 2‡**  **OR (95% CI)** | ***P*** |
| Taiwanese Han Chinese (*N*=61,352) |  |  |  |  |  |  |  |
| *Males (n=19,012)* | 11,727 (61.7) |  |  |  |  |  |  |
| Q1 (14.79 g/dL) | 2,422 (63.7) | Reference | - | Reference | - | Reference | - |
| Q2 (14.98 g/dL) vs. Q1 | 2,359 (62.1) | 0.93 (0.85, 1.02) | 0.1418 | 0.92 (0.83, 1.01) | 0.0721 | 0.91 (0.83, 1.01) | 0.0671 |
| Q3 (15.04 g/dL) vs. Q1 | 2,366 (62.3) | 0.94 (0.86, 1.03) | 0.1864 | 0.93 (0.85, 1.03) | 0.1658 | 0.93 (0.85, 1.03) | 0.1562 |
| Q4 (15.11 g/dL) vs. Q1 | 2,326 (61.2) | **0.90 (0.82, 0.99)** | **0.0235** | **0.89 (0.81, 0.98)** | **0.0165** | **0.89 (0.81, 0.98)** | **0.0166** |
| Q5 (15.28 g/dL) vs. Q1 | 2,254 (59.3) | **0.83 (0.76, 0.91)** | **<0.0001** | **0.82 (0.75, 0.91)** | **<0.0001** | **0.83 (0.75, 0.91)** | **<0.0001** |
| *Females (n=42,340)* | 21,936 (51.8) |  |  |  |  |  |  |
| Q1 (12.78 g/dL) | 4,582 (54.1) | Reference | - | Reference | - | Reference | - |
| Q2 (12.93 g/dL) vs. Q1 | 4,361 (51.5) | **0.90 (0.85, 0.96)** | **0.0007** | **0.89 (0.84, 0.95)** | **0.0006** | **0.89 (0.84, 0.95)** | **0.0007** |
| Q3 (13.04 g/dL) vs. Q1 | 4,353 (51.4) | **0.90 (0.85, 0.95)** | **0.0004** | **0.88 (0.83, 0.94)** | **0.0001** | **0.88 (0.83, 0.94)** | **0.0002** |
| Q4 (13.11 g/dL) vs. Q1 | 4,320 (51.0) | **0.88 (0.83, 0.94)** | **<0.0001** | **0.87 (0.82, 0.93)** | **<0.0001** | **0.87 (0.82, 0.93)** | **<0.0001** |
| Q5 (13.21 g/dL) vs. Q1 | 4,320 (51.0) | **0.88 (0.83, 0.94)** | **<0.0001** | **0.86 (0.81, 0.92)** | **<0.0001** | **0.86 (0.81, 0.92)** | **<0.0001** |
| European Whites (*N*=271,366) |  |  |  |  |  |  |  |
| *Males (n=128,549)* | 15,688 (12.2) |  |  |  |  |  |  |
| Q1 (14.91 g/dL) | 3,250 (12.6) | Reference | - | Reference | - | Reference | - |
| Q2 (14.94 g/dL) vs. Q1 | 3,290 (12.8) | 1.01 (0.96, 1.07) | 0.5977 | 1.01 (0.96, 1.06) | 0.7333 | 1.01 (0.95, 1.06) | 0.8665 |
| Q3 (15.00 g/dL) vs. Q1 | 3,122 (12.1) | 0.96 (0.91, 1.01) | 0.0858 | **0.95 (0.90, 0.99)** | **0.0402** | **0.94 (0.89, 0.99)** | **0.0181** |
| Q4 (15.08 g/dL) vs. Q1 | 3,068 (11.9) | **0.94 (0.89, 0.99)** | **0.0145** | **0.93 (0.88, 0.98)** | **0.0049** | **0.92 (0.87, 0.97)** | **0.0021** |
| Q5 (15.21 g/dL) vs. Q1 | 2,958 (11.5) | **0.90 (0.85, 0.95)** | **<0.0001** | **0.89 (0.84, 0.94)** | **<0.0001** | **0.88 (0.83, 0.93)** | **<0.0001** |
| *Females (n=142,817)* | 11,769 (8.2) |  |  |  |  |  |  |
| Q1 (13.39 g/dL) | 2,517 (8.8) | Reference | - | Reference | - | Reference | - |
| Q2 (13.43 g/dL) vs. Q1 | 2,330 (8.2) | **0.92 (0.87, 0.98)** | **0.0051** | **0.92 (0.87, 0.97)** | **0.0047** | **0.92 (0.87, 0.98)** | **0.0081** |
| Q3 (13.49 g/dL) vs. Q1 | 2,340 (8.2) | **0.92 (0.87, 0.98)** | **0.0079** | **0.92 (0.86, 0.97)** | **0.0035** | **0.91 (0.86, 0.97)** | **0.0031** |
| Q4 (13.58 g/dL) vs. Q1 | 2,346 (8.2) | **0.93 (0.87, 0.98)** | **0.0104** | **0.92 (0.87, 0.98)** | **0.0080** | **0.93 (0.87, 0.98)** | **0.0134** |
| Q5 (13.71 g/dL) vs. Q1 | 2,236 (7.8) | **0.88 (0.83, 0.93)** | **<0.0001** | **0.87 (0.82, 0.93)** | **<0.0001** | **0.87 (0.82, 0.93)** | **<0.0001** |

†Model 1 adjusted for age, age-squared and the first ten genetic principal components. ‡Model 2 further adjusted for smoking and alcohol consumption (and menopausal status in women).

**Table S21:** Odds ratios of type 2 diabetes across quintiles of Hb-PRS among Taiwanese Han Chinese and European Whites

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Type 2 Diabetes** | **Cases**  ***n* (%)** | **Crude**  **OR (95% CI)** | ***P*** | **Model 1**†  **OR (95% CI)** | ***P*** | **Model 2‡**  **OR (95% CI)** | ***P*** |
| Taiwanese Han Chinese (*N*=61,352) |  |  |  |  |  |  |  |
| *Males (n=19,012)* | 2,575 (13.6) |  |  |  |  |  |  |
| Q1 (14.79 g/dL) | 491 (12.9) | Reference | - | Reference | - | Reference | - |
| Q2 (14.98 g/dL) vs. Q1 | 509 (13.4) | 1.04 (0.91, 1.19) | 0.5414 | 1.04 (0.91, 1.19) | 0.5811 | 1.03 (0.90, 1.18) | 0.6471 |
| Q3 (15.04 g/dL) vs. Q1 | 524 (13.8) | 1.08 (0.94, 1.23) | 0.2659 | 1.09 (0.95, 1.24) | 0.2349 | 1.08 (0.94, 1.24) | 0.2576 |
| Q4 (15.11 g/dL) vs. Q1 | 531 (14.0) | 1.10 (0.96, 1.25) | 0.1788 | 1.11 (0.97, 1.27) | 0.1320 | 1.10 (0.96, 1.26) | 0.1677 |
| Q5 (15.28 g/dL) vs. Q1 | 520 (13.7) | 1.07 (0.94, 1.22) | 0.3274 | 1.09 (0.95, 1.24) | 0.2385 | 1.08 (0.94, 1.24) | 0.2565 |
| *Females (n=42,340)* | 3,663 (8.7) |  |  |  |  |  |  |
| Q1 (12.78 g/dL) | 785 (9.3) | Reference | - | Reference | - | Reference | - |
| Q2 (12.93 g/dL) vs. Q1 | 750 (8.9) | 0.95 (0.86, 1.06) | 0.3489 | 0.96 (0.86, 1.07) | 0.4404 | 0.96 (0.86, 1.07) | 0.4313 |
| Q3 (13.04 g/dL) vs. Q1 | 726 (8.6) | 0.92 (0.83, 1.02) | 0.1118 | 0.92 (0.82, 1.02) | 0.1204 | 0.92 (0.82, 1.02) | 0.1175 |
| Q4 (13.11 g/dL) vs. Q1 | 705 (8.3) | **0.89 (0.80, 0.99)** | **0.0301** | 0.90 (0.81, 1.00) | 0.0542 | **0.90 (0.80, 1.00)** | **0.0495** |
| Q5 (13.21 g/dL) vs. Q1 | 697 (8.2) | **0.88 (0.79, 0.98)** | **0.0168** | **0.88 (0.78, 0.98)** | **0.0162** | **0.88 (0.78, 0.98)** | **0.0165** |
| European Whites (*N*=271,366) |  |  |  |  |  |  |  |
| *Males (n=128,549)* | 11,815 (9.2) |  |  |  |  |  |  |
| Q1 (14.91 g/dL) | 2,248 (9.5) | Reference | - | Reference | - | Reference | - |
| Q2 (14.94 g/dL) vs. Q1 | 2,449 (9.5) | 0.96 (0.89, 1.05) | 0.3663 | 0.96 (0.88, 1.04) | 0.2920 | 0.95 (0.88, 1.03) | 0.2337 |
| Q3 (15.00 g/dL) vs. Q1 | 2,357 (9.2) | 0.96 (0.88, 1.04) | 0.2921 | 0.95 (0.87, 1.03) | 0.2013 | 0.94 (0.86, 1.02) | 0.1321 |
| Q4 (15.08 g/dL) vs. Q1 | 2,320 (9.0) | **0.90 (0.83, 0.98)** | **0.0112** | **0.89 (0.82, 0.97)** | **0.0059** | **0.88 (0.81, 0.96)** | **0.0036** |
| Q5 (15.21 g/dL) vs. Q1 | 2,241 (8.7) | **0.84 (0.77, 0.91)** | **<0.0001** | **0.83 (0.76, 0.91)** | **<0.0001** | **0.82 (0.76, 0.90)** | **<0.0001** |
| *Females (n=142,817)* | 7,212 (5.1) |  |  |  |  |  |  |
| Q1 (13.39 g/dL) | 1,478 (5.2) | Reference | - | Reference | - | Reference | - |
| Q2 (13.43 g/dL) vs. Q1 | 1,420 (5.0) | 0.93 (0.83, 1.04) | 0.1871 | 0.93 (0.83, 1.04) | 0.1798 | 0.93 (0.84, 1.04) | 0.2275 |
| Q3 (13.49 g/dL) vs. Q1 | 1,425 (5.0) | 0.94 (0.84, 1.05) | 0.2380 | 0.93 (0.83, 1.04) | 0.1868 | 0.92 (0.83, 1.03) | 0.1641 |
| Q4 (13.58 g/dL) vs. Q1 | 1,440 (5.0) | 0.93 (0.83, 1.03) | 0.1679 | 0.92 (0.83, 1.03) | 0.1561 | 0.93 (0.83, 1.04) | 0.2059 |
| Q5 (13.71 g/dL) vs. Q1 | 1,449 (5.1) | **0.82 (0.74, 0.92)** | **0.0008** | **0.82 (0.73, 0.92)** | **0.0006** | **0.82 (0.73, 0.92)** | **0.0009** |

†Model 1 adjusted for age, age-squared and the first ten genetic principal components. ‡Model 2 further adjusted for smoking and alcohol consumption (and menopausal status in women).

**Table S22:** Sex-specific MR-Egger regressions of associations between iron status and risks of metabolic outcomes among Taiwanese Han Chinese and European Whites

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Metabolic Outcomes** | **Taiwanese Han Chinese** | | | | **European Whites** | | | |
|  | **Beta (95% CI)** | ***P*** | **Intercept (95% CI)** | ***P*** | **Beta (95% CI)** | ***P*** | **Intercept (95% CI)** | ***P*** |
| ***Males*** |  |  |  |  |  |  |  |  |
| Metabolic Syndrome | 0.22 (-0.03, 0.47) | 0.084 | -0.006 (-0.022, 0.010) | 0.483 | -0.01 (-0.04, 0.02) | 0.562 | 0.000 (0.000, 0.001) | 0.270 |
| Hypertension | 0.12 (-0.07, 0.31) | 0.214 | -0.006 (-0.020, 0.007) | 0.339 | **0.04 (0.01, 0.07)** | **0.027** | 0.000 (-0.001, 0.000) | 0.316 |
| Dyslipidemia | -0.06 (-0.24, 0.11) | 0.480 | 0.008 (-0.005, 0.021) | 0.227 | **0.05 (0.02, 0.08)** | **0.004** | -0.001 (-0.002, 0.000) | 0.055 |
| Central Obesity | -0.14 (-0.37, 0.08) | 0.207 | 0.012 (-0.003, 0.028) | 0.121 | -0.02 (-0.04, 0.01) | 0.204 | 0.000 (0.000, 0.001) | 0.149 |
| Gout or Hyperuricemia | 0.09 (-0.09, 0.27) | 0.326 | -0.004 (-0.016, 0.007) | 0.454 | -0.03 (-0.09, 0.03) | 0.404 | 0.000 (-0.002, 0.001) | 0.840 |
| Diabetes or Hyperglycemia | **-0.31 (-0.58, -0.05)** | **0.019** | 0.015 (0.000, 0.031) | 0.055 | **-0.16 (-0.24, -0.08)** | **<0.001** | **0.002 (0.000, 0.004)** | **0.042** |
| ***Females*** |  |  |  |  |  |  |  |  |
| Metabolic Syndrome | 0.16 (-0.07, 0.40) | 0.175 | -0.003 (-0.012, 0.006) | 0.540 | **0.03 (0.004, 0.05)** | **0.023** | 0.000 (-0.001, 0.000) | 0.593 |
| Hypertension | 0.13 (-0.05, 0.31) | 0.157 | -0.004 (-0.012, 0.004) | 0.332 | **0.05 (0.02, 0.09)** | **0.003** | -0.001 (-0.001, 0.000) | 0.072 |
| Dyslipidemia | -0.19 (-0.41, 0.03) | 0.083 | 0.009 (-0.002, 0.019) | 0.097 | 0.006 (-0.01, 0.02) | 0.553 | 0.000 (0.000, 0.001) | 0.709 |
| Central Obesity | 0.02 (-0.10, 0.14) | 0.715 | -0.001 (-0.007, 0.005) | 0.782 | -0.01 (-0.03, 0.01) | 0.413 | 0.000 (0.000, 0.001) | 0.457 |
| Gout or Hyperuricemia | 0.10 (-0.11, 0.32) | 0.342 | -0.001 (-0.011, 0.009) | 0.891 | 0.06 (-0.01, 0.14) | 0.104 | -0.001 (-0.003, 0.001) | 0.244 |
| Diabetes or Hyperglycemia | **-0.36 (-0.69, -0.04)** | **0.028** | 0.014 (-0.001, 0.028) | 0.060 | **-0.12 (-0.19, -0.05)** | **0.001** | 0.001 (-0.001, 0.003) | 0.359 |

**Figure S2:** Sex-specific MR-Egger plots of SNP-outcome estimates against SNP-exposure estimates for binary metabolic outcomes among Taiwanese Han Chinese

|  |  |
| --- | --- |
| **Males** | **Females** |
| A. Metabolic syndrome | |
|  |  |
| B. Central obesity | |
|  |  |
| C. Hypertension | |
|  |  |
| D. Dyslipidemia | |
|  | **\*** |

The blue line represents the MR-Egger model slope. Red asterisk indicates the SNP/s that may have possibly presented pleiotropic effects.

**Figure S2 (cont’d):** Sex-specific MR-Egger plots of SNP-outcome estimates against SNP-exposure estimates for binary metabolic outcomes among Taiwanese Han Chinese

|  |  |
| --- | --- |
| **Males** | **Females** |
| E. Gout or hyperuricemia | |
|  |  |
| F. Diabetes or hyperglycemia | |
| **\*** | **\*** |

The blue line represents the MR-Egger model slope. Red asterisk indicates the SNP/s that may have possibly presented pleiotropic effects.

**Figure S3:** Sex-specific MR-Egger plots of SNP-outcome estimates against SNP-exposure estimates for binary metabolic outcomes among European Whites

|  |  |
| --- | --- |
| **Males** | **Females** |
| A. Metabolic syndrome | |
|  |  |
| B. Central obesity | |
|  |  |
| C. Hypertension | |
|  | **\*** |
| D. Dyslipidemia | |
| **\*** |  |

The blue line represents the MR-Egger model slope. Red asterisk indicates the SNP/s that may have possibly presented pleiotropic effects.

**Figure S3 (cont’d):** Sex-specific MR-Egger plots of SNP-outcome estimates against SNP-exposure estimates for binary metabolic outcomes among European Whites

|  |  |
| --- | --- |
| **Males** | **Females** |
| E. Gout or hyperuricemia | |
|  |  |
| F. Diabetes or hyperglycemia | |
| **\*** |  |

The blue line represents the MR-Egger model slope. Red asterisk indicates the SNP/s that may have possibly presented pleiotropic effects.

**Table S23:** Sex-specific MR-Egger regressions of associations between iron status and metabolic traits among Taiwanese Han Chinese and European Whites

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Metabolic Traits** | **Taiwanese Han Chinese** | | | | **European Whites** | | | |
|  | **Beta (95% CI)** | ***P*** | **Intercept (95% CI)** | ***P*** | **Beta (95% CI)** | ***P*** | **Intercept (95% CI)** | ***P*** |
| ***Males*** |  |  |  |  |  |  |  |  |
| Waist circumference | 0.20 (-0.72, 1.13) | 0.669 | 0.003 (-0.052, 0.057) | 0.927 | -0.02 (-0.04, 0.01) | 0.204 | 0.000 (0.000, 0.001) | 0.149 |
| Systolic blood pressure | 0.40 (-0.74, 1.55) | 0.489 | -0.008 (-0.082, 0.066) | 0.832 | -0.01 (-0.19, 0.16) | 0.879 | 0.000 (-0.006, 0.006) | 1.000 |
| Diastolic blood pressure | **1.55 (0.21, 2.89)** | **0.024** | -0.058 (-0.136, 0.019) | 0.140 | **0.39 (0.19, 0.59)** | **<0.001** | -0.004 (-0.009, 0.001) | 0.109 |
| Fasting blood glucose | 1.34 (-0.93, 3.61) | 0.248 | -0.034 (-0.172, 0.104) | 0.625 | -0.004 (-0.02, 0.01) | 0.513 | 0.000 (-0.001, 0.000) | 0.072 |
| Triglycerides | 2.68 (-10.15, 15.52) | 0.682 | 0.119 (-0.730, 0.968) | 0.784 | **0.03 (0.01, 0.06)** | **0.009** | 0.000 (-0.001, 0.000) | 0.564 |
| HDL-cholesterol | -0.12 (-1.07, 0.82) | 0.797 | -0.009 (-0.071, 0.054) | 0.786 | 0.003 (-0.002, 0.01) | 0.224 | 0.000 (0.000, 0.000) | 0.234 |
| Uric acid | 0.005 (-0.10, 0.11) | 0.923 | 0.000 (-0.009, 0.008) | 0.924 | 0.04 (-1.51, 1.58) | 0.964 | -0.011 (-0.055, 0.033) | 0.621 |
| ***Females*** |  |  |  |  |  |  |  |  |
| Waist circumference | -0.11 (-0.68, 0.45) | 0.697 | 0.013 (-0.015, 0.041) | 0.363 | -0.04 (-0.16, 0.09) | 0.589 | 0.001 (-0.002, 0.004) | 0.568 |
| Systolic blood pressure | 0.56 (-0.64, 1.77) | 0.361 | -0.012 (-0.065, 0.041) | 0.667 | 0.11 (-0.19, 0.40) | 0.478 | -0.001 (-0.009, 0.008) | 0.877 |
| Diastolic blood pressure | 0.39 (-0.34, 1.13) | 0.295 | -0.005 (-0.034, 0.024) | 0.732 | **0.23 (0.03, 0.42)** | **0.021** | 0.000 (-0.005, 0.005) | 0.969 |
| Fasting blood glucose | -1.12 (-2.33, 0.09) | 0.069 | 0.041 (-0.004, 0.086) | 0.075 | -0.004 (-0.02, 0.01) | 0.524 | 0.000 (-0.001, 0.000) | 0.293 |
| Triglycerides | 0.22 (-6.19, 6.62) | 0.947 | 0.038 (-0.277, 0.353) | 0.812 | 0.01 (-0.004, 0.02) | 0.176 | 0.000 (0.000, 0.001) | 0.382 |
| HDL-cholesterol | 0.65 (-0.92, 2.22) | 0.416 | -0.033 (-0.105, 0.040) | 0.376 | -0.002 (-0.01, 0.01) | 0.695 | 0.000 (0.000, 0.000) | 0.776 |
| Uric acid | 0.05 (-0.05, 0.15) | 0.318 | 0.000 (-0.005, 0.004) | 0.831 | 0.89 (-0.80, 2.58) | 0.301 | -0.017 (-0.061, 0.026) | 0.434 |

**Figure S4:** Sex-specific MR-Egger plots of SNP-outcome estimates against SNP-exposure estimates for quantitative metabolic traits among Taiwanese Han Chinese

|  |  |
| --- | --- |
| **Males** | **Females** |
| A. Waist circumference | |
|  |  |
| B. Systolic blood pressure | |
|  |  |
| C. Diastolic blood pressure | |
|  |  |
| D. Fasting blood glucose | |
|  | **\*** |

The blue line represents the MR-Egger model slope. Red asterisk indicates the SNP/s that may have possibly presented pleiotropic effects.

**Figure S4 (cont’d):** Sex-specific MR-Egger plots of SNP-outcome estimates against SNP-exposure estimates for quantitative metabolic traits among Taiwanese Han Chinese

|  |  |
| --- | --- |
| **Males** | **Females** |
| E. Triglycerides | |
|  |  |
| F. HDL-cholesterol | |
|  |  |
| G. Uric acid | |
|  |  |

The blue line represents the MR-Egger model slope. Red asterisk indicates the SNP/s that may have possibly presented pleiotropic effects.

**Figure S5:** Sex-specific MR-Egger plots of SNP-outcome estimates against SNP-exposure estimates for quantitative metabolic traits among European Whites

|  |  |
| --- | --- |
| **Males** | **Females** |
| A. Waist circumference | |
|  |  |
| B. Systolic blood pressure | |
|  |  |
| C. Diastolic blood pressure | |
|  |  |
| D. Blood glucose | |
| **\*** |  |

The blue line represents the MR-Egger model slope. Red asterisk indicates the SNP/s that may have possibly presented pleiotropic effects.

**Figure S5 (cont’d):** Sex-specific MR-Egger plots of SNP-outcome estimates against SNP-exposure estimates for quantitative metabolic traits among European Whites

|  |  |
| --- | --- |
| **Males** | **Females** |
| E. Triglycerides | |
|  |  |
| F. HDL-cholesterol | |
|  |  |
| G. Uric acid | |
|  |  |

The blue line represents the MR-Egger model slope. Red asterisk indicates the SNP/s that may have possibly presented pleiotropic effects.

**Figure S6:** Comparison of OR plots between main MR and sensitivity analyses among Taiwanese Han Chinese, depicting causal roles of iron status on MetS and other metabolic outcomes

|  |  |
| --- | --- |
| **Main MR Analyses** | **Sensitivity Analyses** |
| **A. Metabolic Syndrome** | |
| **Males** |  |
|  |  |
| **Females** |  |
|  |  |
| **B. Hypertension** | |
| **Males** |  |
|  |  |
| **Females** |  |
|  |  |

ORs from the final models are presented for both main MR and sensitivity analyses, which fully adjusted for age, age-squared, first ten genetic principal components, smoking status, and alcohol consumption, as well as menopausal status in females.

**Figure S6 (cont’d):** Comparison of OR plots between main MR and sensitivity analyses among Taiwanese Han Chinese, depicting causal roles of iron status on MetS and other metabolic outcomes

|  |  |
| --- | --- |
| **Main MR Analyses** | **Sensitivity Analyses** |
| **C. Dyslipidemia** | |
| **Males** |  |
|  |  |
| **Females** |  |
|  |  |
| **D. Gout or Hyperuricemia** | |
| **Males** |  |
|  |  |
| **Females** |  |
|  |  |

ORs from the final models are presented for both main MR and sensitivity analyses, which fully adjusted for age, age-squared, first ten genetic principal components, smoking status, and alcohol consumption, as well as menopausal status in females.

**Figure S6 (cont’d):** Comparison of OR plots between main MR and sensitivity analyses among Taiwanese Han Chinese, depicting causal roles of iron status on MetS and other metabolic outcomes

|  |  |
| --- | --- |
| **Main MR Analyses** | **Sensitivity Analyses** |
| **E. Diabetes or Hyperglycemia** | |
| **Males** |  |
|  |  |
| **Females** |  |
|  |  |

ORs from the final models are presented for both main MR and sensitivity analyses, which fully adjusted for age, age-squared, first ten genetic principal components, smoking status, and alcohol consumption, as well as menopausal status in females.

**Figure S7:** Comparison of OR plots between main MR and sensitivity analyses among European Whites, depicting causal roles of iron status on MetS and other metabolic outcomes

|  |  |
| --- | --- |
| **Main MR Analyses** | **Sensitivity Analyses** |
| **A. Metabolic Syndrome** | |
| **Males** |  |
|  |  |
| **Females** |  |
|  |  |
| **B. Hypertension** | |
| **Males** |  |
|  |  |
| **Females** |  |
|  |  |

ORs from the final models are presented for both main MR and sensitivity analyses, which fully adjusted for age, age-squared, first ten genetic principal components, smoking status, and alcohol consumption, as well as menopausal status in females.

**Figure S7 (cont’d):** Comparison of OR plots between main MR and sensitivity analyses among European Whites, depicting causal roles of iron status on MetS and other metabolic outcomes

|  |  |
| --- | --- |
| **Main MR Analyses** | **Sensitivity Analyses** |
| **C. Dyslipidemia** | |
| **Males** |  |
|  |  |
| **Females** |  |
|  |  |
| **D. Gout or Hyperuricemia** | |
| **Males** |  |
|  |  |
| **Females** |  |
|  |  |

ORs from the final models are presented for both main MR and sensitivity analyses, which fully adjusted for age, age-squared, first ten genetic principal components, smoking status, and alcohol consumption, as well as menopausal status in females.

**Figure S7 (cont’d):** Comparison of OR plots between main MR and sensitivity analyses among European Whites, depicting causal roles of iron status on MetS and other metabolic outcomes

|  |  |
| --- | --- |
| **Main MR Analyses** | **Sensitivity Analyses** |
| **E. Diabetes or Hyperglycemia** | |
| **Males** |  |
|  |  |
| **Females** |  |
|  |  |

ORs from the final models are presented for both main MR and sensitivity analyses, which fully adjusted for age, age-squared, first ten genetic principal components, smoking status, and alcohol consumption, as well as menopausal status in females.

**Table S24:** Odds ratios from sensitivity analyses† of causal associations between metabolic syndrome and quintiles of Hb-PRS among Taiwanese Han Chinese and European Whites

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Metabolic Syndrome** | **Cases**  ***n* (%)** | **Crude**  **OR (95% CI)** | ***P*** | **Model 1‡**  **OR (95% CI)** | ***P*** | **Model 2§**  **OR (95% CI)** | ***P*** |
| Taiwanese Han Chinese (*N*=61,352) |  |  |  |  |  |  |  |
| *Males (n=19,012)* | 2,721 (19.5) |  |  |  |  |  |  |
| Q1 (14.83 g/dL) | 489 (17.5) | Reference | - | Reference | - | Reference | - |
| Q2 (15.00 g/dL) vs. Q1 | 546 (19.5) | **1.20 (1.04, 1.40)** | **0.0134** | **1.20 (1.04, 1.39)** | **0.0140** | **1.19 (1.03, 1.38)** | **0.0202** |
| Q3 (15.06 g/dL) vs. Q1 | 535 (19.1) | 1.12 (0.97, 1.30) | 0.1378 | 1.12 (0.97, 1.30) | 0.1327 | 1.11 (0.96, 1.29) | 0.1657 |
| Q4 (15.11 g/dL) vs. Q1 | 573 (20.5) | **1.22 (1.05, 1.41)** | **0.0090** | **1.21 (1.05, 1.40)** | **0.0108** | **1.20 (1.04, 1.39)** | **0.0156** |
| Q5 (15.31 g/dL) vs. Q1 | 578 (20.7) | **1.28 (1.10, 1.48)** | **0.0010** | **1.28 (1.10, 1.48)** | **0.0011** | **1.27 (1.10, 1.48)** | **0.0012** |
| *Females (n=42,340)* | 4,783 (13.6) |  |  |  |  |  |  |
| Q1 (12.72 g/dL) | 935 (13.3) | Reference | - | Reference | - | Reference | - |
| Q2 (12.87 g/dL) vs. Q1 | 935 (13.3) | 1.01 (0.91, 1.12) | 0.8741 | 1.01 (0.91, 1.12) | 0.8560 | 1.01 (0.91, 1.13) | 0.7984 |
| Q3 (12.97 g/dL) vs. Q1 | 943 (13.4) | 1.04 (0.94, 1.16) | 0.4541 | 1.05 (0.94, 1.16) | 0.4100 | 1.05 (0.94, 1.17) | 0.3849 |
| Q4 (13.04 g/dL) vs. Q1 | 949 (13.5) | 1.00 (0.90, 1.12) | 0.9356 | 1.01 (0.91, 1.12) | 0.8858 | 1.01 (0.91, 1.12) | 0.8807 |
| Q5 (13.15 g/dL) vs. Q1 | 1,021 (14.6) | **1.12 (1.01, 1.24)** | **0.0291** | **1.12 (1.01, 1.25)** | **0.0287** | **1.13 (1.01, 1.25)** | **0.0259** |
| European Whites (*N*=271,366) |  |  |  |  |  |  |  |
| *Males (n=128,549)* | 22,276 (30.8) |  |  |  |  |  |  |
| Q1 (14.92 g/dL) | 4,375 (30.3) | Reference | - | Reference | - | Reference | - |
| Q2 (14.96 g/dL) vs. Q1 | 4,483 (31.0) | 1.03 (0.99, 1.08) | 0.1739 | 1.03 (0.99, 1.08) | 0.1242 | 1.03 (0.99, 1.08) | 0.1845 |
| Q3 (15.00 g/dL) vs. Q1 | 4,462 (30.9) | 1.04 (0.99, 1.08) | 0.1063 | 1.04 (0.99, 1.08) | 0.0980 | 1.03 (0.99, 1.08) | 0.1364 |
| Q4 (15.09 g/dL) vs. Q1 | 4,511 (31.2) | 1.03 (0.99, 1.08) | 0.1549 | 1.03 (0.99, 1.08) | 0.1692 | 1.03 (0.98, 1.07) | 0.2237 |
| Q5 (15.20 g/dL) vs. Q1 | 4,445 (30.8) | 1.04 (1.00, 1.09) | 0.0776 | 1.04 (0.99, 1.08) | 0.0924 | 1.03 (0.99, 1.08) | 0.1386 |
| *Females (n=142,817)* | 21,440 (22.4) |  |  |  |  |  |  |
| Q1 (13.33 g/dL) | 4,324 (22.6) | Reference | - | Reference | - | Reference | - |
| Q2 (13.38 g/dL) vs. Q1 | 4,240 (22.1) | 0.98 (0.94, 1.02) | 0.4035 | 0.99 (0.95, 1.03) | 0.5722 | 0.99 (0.95, 1.03) | 0.5333 |
| Q3 (13.43 g/dL) vs. Q1 | 4,245 (22.2) | 0.99 (0.94, 1.03) | 0.4648 | 0.99 (0.95, 1.03) | 0.5212 | 0.98 (0.94, 1.03) | 0.4221 |
| Q4 (13.51 g/dL) vs. Q1 | 4,210 (22.0) | 0.99 (0.95, 1.03) | 0.5176 | 0.99 (0.95, 1.03) | 0.6723 | 0.99 (0.95, 1.04) | 0.7296 |
| Q5 (13.64 g/dL) vs. Q1 | 10,595 (37.1) | 1.03 (0.99, 1.08) | 0.1259 | 1.03 (0.99, 1.08) | 0.1259 | 1.04 (0.99, 1.08) | 0.1123 |

†Subjects ascertained from either self-reported data (i.e., physician-diagnosed health condition or intake of prescription medications) or hospital in-patient records were excluded from the sensitivity analyses. ‡Model 1 adjusted for age, age-squared and the first ten genetic principal components. §Model 2 further adjusted for smoking and alcohol consumption (and menopausal status in women).

**Table S25:** Odds ratios from sensitivity analyses† of causal associations between hypertension and quintiles of Hb-PRS among Taiwanese Han Chinese and European Whites

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Hypertension** | **Cases**  ***n* (%)** | **Crude**  **OR (95% CI)** | ***P*** | **Model 1‡**  **OR (95% CI)** | ***P*** | **Model 2§**  **OR (95% CI)** | ***P*** |
| Taiwanese Han Chinese (*N*=61,352) |  |  |  |  |  |  |  |
| *Males (n=19,012)* | 3,023 (19.5) |  |  |  |  |  |  |
| Q1 (14.82 g/dL) | 599 (19.3) | Reference | - | Reference | - | Reference | - |
| Q2 (14.99 g/dL) vs. Q1 | 595 (19.2) | 0.99 (0.87, 1.13) | 0.8975 | 0.99 (0.87, 1.13) | 0.8657 | 0.98 (0.86, 1.12) | 0.7976 |
| Q3 (15.06 g/dL) vs. Q1 | 592 (19.1) | 0.99 (0.87, 1.12) | 0.8215 | 0.99 (0.87, 1.13) | 0.9053 | 0.99 (0.87, 1.12) | 0.8173 |
| Q4 (15.11 g/dL) vs. Q1 | 609 (19.6) | 1.02 (0.90, 1.16) | 0.7532 | 1.03 (0.91, 1.17) | 0.6292 | 1.03 (0.90, 1.17) | 0.6690 |
| Q5 (15.30 g/dL) vs. Q1 | 628 (20.3) | 1.06 (0.94, 1.20) | 0.3553 | 1.08 (0.95, 1.22) | 0.2603 | 1.07 (0.94, 1.22) | 0.2803 |
| *Females (n=42,340)* | 3,683 (9.7) |  |  |  |  |  |  |
| Q1 (12.74 g/dL) | 691 (9.1) | Reference | - | Reference | - | Reference | - |
| Q2 (12.90 g/dL) vs. Q1 | 734 (9.7) | 1.07 (0.96, 1.19) | 0.2315 | 1.07 (0.96, 1.20) | 0.2181 | 1.07 (0.96, 1.20) | 0.2120 |
| Q3 (13.00 g/dL) vs. Q1 | 735 (9.7) | 1.07 (0.96, 1.19) | 0.2200 | 1.08 (0.97, 1.21) | 0.1754 | 1.08 (0.97, 1.21) | 0.1568 |
| Q4 (13.07 g/dL) vs. Q1 | 761 (10.0) | 1.11 (0.99, 1.24) | 0.0535 | **1.13 (1.01, 1.26)** | **0.0296** | **1.14 (1.02, 1.27)** | **0.0255** |
| Q5 (13.17 g/dL) vs. Q1 | 762 (10.1) | **1.11 (1.00, 1.24)** | **0.0499** | 1.11 (0.99, 1.25) | 0.0567 | **1.12 (1.00, 1.25)** | **0.0499** |
| European Whites (*N*=271,366) |  |  |  |  |  |  |  |
| *Males (n=128,549)* | 53,655 (69.3) |  |  |  |  |  |  |
| Q1 (14.92 g/dL) | 10,581 (68.4) | Reference | - | Reference | - | Reference | - |
| Q2 (14.95 g/dL) vs. Q1 | 10,720 (69.2) | 1.04 (0.99, 1.09) | 0.0914 | 1.05 (0.99, 1.10) | 0.0643 | 1.05 (0.99, 1.10) | 0.0705 |
| Q3 (15.00 g/dL) vs. Q1 | 10,842 (70.0) | **1.08 (1.03, 1.14)** | **0.0013** | **1.08 (1.03, 1.14)** | **0.0014** | **1.08 (1.03, 1.14)** | **0.0017** |
| Q4 (15.09 g/dL) vs. Q1 | 10,738 (69.4) | 1.05 (0.99, 1.10) | 0.0562 | 1.04 (0.99, 1.10) | 0.0843 | 1.04 (0.99, 1.10) | 0.0849 |
| Q5 (15.21 g/dL) vs. Q1 | 10,774 (69.6) | **1.06 (1.01, 1.11)** | **0.0182** | **1.06 (1.01, 1.12)** | **0.0143** | **1.06 (1.01, 1.11)** | **0.0172** |
| *Females (n=142,817)* | 53,592 (53.5) |  |  |  |  |  |  |
| Q1 (13.34 g/dL) | 10,651 (53.1) | Reference | - | Reference | - | Reference | - |
| Q2 (13.39 g/dL) vs. Q1 | 10,641 (53.1) | 1.00 (0.96, 1.04) | 0.9160 | 1.00 (0.96, 1.04) | 0.9058 | 1.00 (0.96, 1.05) | 0.8574 |
| Q3 (13.44 g/dL) vs. Q1 | 10,742 (53.6) | 1.02 (0.98, 1.06) | 0.3679 | 1.02 (0.98, 1.06) | 0.3844 | 1.02 (0.98, 1.06) | 0.3385 |
| Q4 (13.52 g/dL) vs. Q1 | 10,720 (53.5) | 1.01 (0.98, 1.05) | 0.4930 | 1.02 (0.98, 1.06) | 0.3274 | 1.02 (0.98, 1.06) | 0.2900 |
| Q5 (13.65 g/dL) vs. Q1 | 14,184 (49.7) | 1.04 (0.99, 1.08) | 0.0620 | **1.05 (1.01, 1.10)** | **0.0143** | **1.05 (1.01, 1.10)** | **0.0123** |

†Subjects ascertained from either self-reported data (i.e., physician-diagnosed health condition or intake of prescription medications) or hospital in-patient records were excluded from the sensitivity analyses. ‡Model 1 adjusted for age, age-squared and the first ten genetic principal components. §Model 2 further adjusted for smoking and alcohol consumption (and menopausal status in women).

**Table S26:** Odds ratios from sensitivity analyses† of causal associations between dyslipidemia and quintiles of Hb-PRS among Taiwanese Han Chinese and European Whites

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Dyslipidemia** | **Cases**  ***n* (%)** | **Crude**  **OR (95% CI)** | ***P*** | **Model 1‡**  **OR (95% CI)** | ***P*** | **Model 2§**  **OR (95% CI)** | ***P*** |
| Taiwanese Han Chinese (*N*=61,352) |  |  |  |  |  |  |  |
| *Males (n=19,012)* | 4,998 (29.2) |  |  |  |  |  |  |
| Q1 (14.80 g/dL) | 965 (28.2) | Reference | - | Reference | - | Reference | - |
| Q2 (14.98 g/dL) vs. Q1 | 1,015 (29.7) | 1.07 (0.97, 1.19) | 0.1852 | 1.07 (0.96, 1.19) | 0.2116 | 1.06 (0.95, 1.18) | 0.2853 |
| Q3 (15.04 g/dL) vs. Q1 | 975 (28.5) | 1.01 (0.91, 1.13) | 0.7944 | 1.02 (0.92, 1.13) | 0.7572 | 1.01 (0.91, 1.12) | 0.8693 |
| Q4 (15.10 g/dL) vs. Q1 | 1,027 (30.0) | 1.09 (0.98, 1.21) | 0.1006 | 1.09 (0.98, 1.21) | 0.1144 | 1.08 (0.97, 1.19) | 0.1816 |
| Q5 (15.29 g/dL) vs. Q1 | 1,016 (29.7) | 1.08 (0.97, 1.19) | 0.1765 | 1.07 (0.97, 1.19) | 0.1924 | 1.07 (0.96, 1.19) | 0.2010 |
| *Females (n=42,340)* | 11,135 (28.3) |  |  |  |  |  |  |
| Q1 (12.76 g/dL) | 2,242 (28.5) | Reference | - | Reference | - | Reference | - |
| Q2 (12.90 g/dL) vs. Q1 | 2,212 (28.1) | 0.98 (0.92, 1.05) | 0.5920 | 0.98 (0.91, 1.05) | 0.5576 | 0.98 (0.92, 1.05) | 0.6116 |
| Q3 (13.01 g/dL) vs. Q1 | 2,199 (27.9) | 0.97 (0.91, 1.04) | 0.4433 | 0.97 (0.91, 1.04) | 0.3906 | 0.97 (0.91, 1.04) | 0.3969 |
| Q4 (13.08 g/dL) vs. Q1 | 2,182 (27.7) | 0.96 (0.90, 1.03) | 0.2851 | 0.96 (0.90, 1.03) | 0.2404 | 0.96 (0.89, 1.03) | 0.2357 |
| Q5 (13.19 g/dL) vs. Q1 | 2,300 (29.2) | 1.04 (0.97, 1.11) | 0.3076 | 1.03 (0.96, 1.10) | 0.3905 | 1.03 (0.96, 1.11) | 0.3758 |
| European Whites (*N*=271,366) |  |  |  |  |  |  |  |
| *Males (n=128,549)* | 52,479 (56.5) |  |  |  |  |  |  |
| Q1 (14.96 g/dL) | 10,324 (55.6) | Reference | - | Reference | - | Reference | - |
| Q2 (14.99 g/dL) vs. Q1 | 10,562 (56.8) | **1.05 (1.01, 1.10)** | **0.0131** | **1.06 (1.01, 1.10)** | **0.0113** | **1.05 (1.01, 1.10)** | **0.0126** |
| Q3 (15.04 g/dL) vs. Q1 | 10,557 (56.8) | **1.05 (1.01, 1.10)** | **0.0152** | **1.05 (1.01, 1.10)** | **0.0119** | **1.05 (1.01, 1.10)** | **0.0150** |
| Q4 (15.12 g/dL) vs. Q1 | 10,562 (56.8) | **1.05 (1.01, 1.10)** | **0.0131** | **1.06 (1.01, 1.10)** | **0.0099** | **1.05 (1.01, 1.10)** | **0.0148** |
| Q5 (15.25 g/dL) vs. Q1 | 10,474 (56.4) | 1.03 (0.99, 1.08) | 0.1147 | 1.04 (0.99, 1.08) | 0.0872 | 1.03 (0.99, 1.08) | 0.1102 |
| *Females (n=142,817)* | 54,223 (45.2) |  |  |  |  |  |  |
| Q1 (13.38 g/dL) | 10,884 (45.3) | Reference | - | Reference | - | Reference | - |
| Q2 (13.42 g/dL) vs. Q1 | 10,783 (44.9) | 0.98 (0.94, 1.02) | 0.2421 | 0.98 (0.95, 1.02) | 0.3024 | 0.98 (0.95, 1.02) | 0.2995 |
| Q3 (13.48 g/dL) vs. Q1 | 10,759 (44.8) | 0.97 (0.94, 1.01) | 0.1424 | 0.98 (0.94, 1.01) | 0.1624 | 0.97 (0.94, 1.01) | 0.1218 |
| Q4 (13.56 g/dL) vs. Q1 | 10,843 (45.2) | 0.99 (0.95, 1.02) | 0.4562 | 0.99 (0.95, 1.03) | 0.5406 | 0.99 (0.96, 1.03) | 0.6751 |
| Q5 (13.69 g/dL) vs. Q1 | 10,954 (45.6) | 1.01 (0.97, 1.04) | 0.7283 | 1.01 (0.97, 1.04) | 0.7736 | 1.01 (0.97, 1.04) | 0.7744 |

†Subjects ascertained from either self-reported data (i.e., physician-diagnosed health condition or intake of prescription medications) or hospital in-patient records were excluded from the sensitivity analyses. ‡Model 1 adjusted for age, age-squared and the first ten genetic principal components. §Model 2 further adjusted for smoking and alcohol consumption (and menopausal status in women).

**Table S27:** Odds ratios from sensitivity analyses† of causal associations between gout or hyperuricemia and quintiles of Hb-PRS among Taiwanese Han Chinese and European Whites

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Gout or Hyperuricemia** | **Cases**  ***n* (%)** | **Crude**  **OR (95% CI)** | ***P*** | **Model 1‡**  **OR (95% CI)** | ***P*** | **Model 2§**  **OR (95% CI)** | ***P*** |
| Taiwanese Han Chinese (*N*=61,352) |  |  |  |  |  |  |  |
| *Males (n=19,012)* | 4,396 (25.7) |  |  |  |  |  |  |
| Q1 (14.80 g/dL) | 891 (26.0) | Reference | - | Reference | - | Reference | - |
| Q2 (14.97 g/dL) vs. Q1 | 848 (24.8) | 0.93 (0.81, 1.07) | 0.3153 | 0.94 (0.81, 1.08) | 0.3624 | 0.93 (0.81, 1.07) | 0.2956 |
| Q3 (15.04 g/dL) vs. Q1 | 903 (26.4) | 0.99 (0.87, 1.14) | 0.9361 | 1.00 (0.87, 1.15) | 0.9666 | 0.99 (0.86, 1.14) | 0.8932 |
| Q4 (15.11 g/dL) vs. Q1 | 864 (25.3) | 0.98 (0.86, 1.13) | 0.8045 | 0.99 (0.86, 1.13) | 0.8264 | 0.98 (0.85, 1.13) | 0.7712 |
| Q5 (15.28 g/dL) vs. Q1 | 890 (26.0) | 1.04 (0.91, 1.20) | 0.5554 | 1.04 (0.91, 1.19) | 0.5729 | 1.04 (0.91, 1.19) | 0.5878 |
| *Females (n=42,340)* | 5,850 (13.9) |  |  |  |  |  |  |
| Q1 (12.78 g/dL) | 1,142 (13.6) | Reference | - | Reference | - | Reference | - |
| Q2 (12.93 g/dL) vs. Q1 | 1,181 (14.0) | 0.99 (0.88, 1.11) | 0.8095 | 0.99 (0.88, 1.11) | 0.8681 | 0.99 (0.88, 1.12) | 0.8912 |
| Q3 (13.04 g/dL) vs. Q1 | 1,110 (13.2) | 0.94 (0.83, 1.05) | 0.2817 | 0.94 (0.83, 1.05) | 0.2664 | 0.94 (0.83, 1.06) | 0.2920 |
| Q4 (13.11 g/dL) vs. Q1 | 1,206 (14.3) | 1.07 (0.96, 1.20) | 0.2232 | 1.08 (0.96, 1.21) | 0.1939 | 1.07 (0.96, 1.20) | 0.2309 |
| Q5 (13.21 g/dL) vs. Q1 | 1,211 (14.4) | 1.12 (1.00, 1.25) | 0.0540 | 1.11 (0.99, 1.25) | 0.0654 | 1.11 (0.99, 1.25) | 0.0650 |
| European Whites (*N*=271,366) |  |  |  |  |  |  |  |
| *Males (n=128,549)* | 20,045 (16.2) |  |  |  |  |  |  |
| Q1 (14.92 g/dL) | 4,181 (16.9) | Reference | - | Reference | - | Reference | - |
| Q2 (14.95 g/dL) vs. Q1 | 3,872 (15.7) | **0.91 (0.87, 0.96)** | **0.0002** | **0.92 (0.87, 0.96)** | **0.0004** | **0.92 (0.87, 0.96)** | **0.0003** |
| Q3 (15.01 g/dL) vs. Q1 | 3,880 (15.7) | **0.92 (0.87, 0.96)** | **0.0002** | **0.92 (0.88, 0.96)** | **0.0006** | **0.92 (0.88, 0.96)** | **0.0005** |
| Q4 (15.09 g/dL) vs. Q1 | 3,956 (16.0) | **0.94 (0.89, 0.98)** | **0.0064** | **0.94 (0.90, 0.99)** | **0.0103** | **0.94 (0.90, 0.99)** | **0.0115** |
| Q5 (15.21 g/dL) vs. Q1 | 4,156 (16.8) | 0.99 (0.95, 1.04) | 0.7624 | 0.99 (0.95, 1.04) | 0.7034 | 0.99 (0.94, 1.04) | 0.6568 |
| *Females (n=142,817)* | 12,631 (8.9) |  |  |  |  |  |  |
| Q1 (13.39 g/dL) | 2,618 (9.2) | Reference | - | Reference | - | Reference | - |
| Q2 (13.44 g/dL) vs. Q1 | 2,469 (8.7) | **0.94 (0.88, 0.99)** | **0.0222** | **0.94 (0.89, 0.99)** | **0.0421** | **0.94 (0.89, 0.99)** | **0.0493** |
| Q3 (13.49 g/dL) vs. Q1 | 2,446 (8.6) | **0.92 (0.87, 0.98)** | **0.0074** | **0.92 (0.87, 0.98)** | **0.0072** | **0.92 (0.87, 0.98)** | **0.0059** |
| Q4 (13.58 g/dL) vs. Q1 | 2,499 (8.8) | 0.95 (0.90, 1.00) | 0.0677 | 0.95 (0.90, 1.01) | 0.0804 | 0.95 (0.90, 1.01) | 0.0962 |
| Q5 (13.71 g/dL) vs. Q1 | 2,599 (9.1) | 0.99 (0.94, 1.05) | 0.7506 | 0.98 (0.93, 1.04) | 0.5896 | 0.99 (0.93, 1.04) | 0.6336 |

†Subjects ascertained from either self-reported data (i.e., physician-diagnosed health condition or intake of prescription medications) or hospital in-patient records were excluded from the sensitivity analyses. ‡Model 1 adjusted for age, age-squared and the first ten genetic principal components. §Model 2 further adjusted for smoking and alcohol consumption (and menopausal status in women).

**Table S28:** Odds ratios from sensitivity analyses† of causal associations between diabetes or hyperglycemia and quintiles of Hb-PRS among Taiwanese Han Chinese and European Whites

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Diabetes or Hyperglycemia** | **Cases**  ***n* (%)** | **Crude**  **OR (95% CI)** | ***P*** | **Model 1‡**  **OR (95% CI)** | ***P*** | **Model 2§**  **OR (95% CI)** | ***P*** |
| Taiwanese Han Chinese (*N*=61,352) |  |  |  |  |  |  |  |
| *Males (n=19,012)* | 10,318 (58.6) |  |  |  |  |  |  |
| Q1 (14.80 g/dL) | 2,141 (60.8) | Reference | - | Reference | - | Reference | - |
| Q2 (15.00 g/dL) vs. Q1 | 2,080 (59.1) | 0.93 (0.85, 1.02) | 0.1378 | 0.91 (0.83, 1.01) | 0.0698 | 0.91 (0.83, 1.01) | 0.0668 |
| Q3 (15.06 g/dL) vs. Q1 | 2,087 (59.3) | 0.94 (0.85, 1.03) | 0.1839 | 0.94 (0.85, 1.03) | 0.1793 | 0.93 (0.85, 1.03) | 0.1686 |
| Q4 (15.14 g/dL) vs. Q1 | 2,040 (58.0) | **0.89 (0.81, 0.98)** | **0.0142** | **0.88 (0.80, 0.97)** | **0.0104** | **0.88 (0.80, 0.97)** | **0.0109** |
| Q5 (15.30 g/dL) vs. Q1 | 1,970 (56.0) | **0.82 (0.74, 0.90)** | **<0.0001** | **0.81 (0.74, 0.90)** | **<0.0001** | **0.82 (0.74, 0.90)** | **<0.0001** |
| *Females (n=42,340)* | 20,025 (49.5) |  |  |  |  |  |  |
| Q1 (12.77 g/dL) | 4,193 (51.9) | Reference | - | Reference | - | Reference | - |
| Q2 (12.93 g/dL) vs. Q1 | 3,971 (49.1) | **0.90 (0.84, 0.95)** | **0.0005** | **0.89 (0.83, 0.95)** | **0.0004** | **0.89 (0.83, 0.95)** | **0.0005** |
| Q3 (13.03 g/dL) vs. Q1 | 3,963 (49.0) | **0.89 (0.84, 0.95)** | **0.0003** | **0.88 (0.82, 0.94)** | **0.0001** | **0.88 (0.82, 0.94)** | **0.0001** |
| Q4 (13.10 g/dL) vs. Q1 | 3,939 (48.7) | **0.88 (0.83, 0.94)** | **<0.0001** | **0.87 (0.82, 0.93)** | **<0.0001** | **0.87 (0.81, 0.93)** | **<0.0001** |
| Q5 (13.21 g/dL) vs. Q1 | 3,959 (49.0) | **0.89 (0.84, 0.95)** | **0.0002** | **0.87 (0.82, 0.93)** | **<0.0001** | **0.87 (0.81, 0.93)** | **<0.0001** |
| European Whites (*N*=271,366) |  |  |  |  |  |  |  |
| *Males (n=128,549)* | 4,409 (3.8) |  |  |  |  |  |  |
| Q1 (14.93 g/dL) | 912 (3.9) | Reference | - | Reference | - | Reference | - |
| Q2 (14.96 g/dL) vs. Q1 | 956 (4.1) | 1.05 (0.96, 1.15) | 0.2980 | 1.05 (0.95, 1.15) | 0.3353 | 1.05 (0.95, 1.15) | 0.3540 |
| Q3 (15.02 g/dL) vs. Q1 | 854 (3.6) | 0.93 (0.85, 1.03) | 0.1593 | 0.93 (0.84, 1.02) | 0.1155 | 0.92 (0.84, 1.01) | 0.0823 |
| Q4 (15.10 g/dL) vs. Q1 | 879 (3.8) | 0.96 (0.88, 1.06) | 0.4287 | 0.95 (0.87, 1.05) | 0.3231 | 0.95 (0.86, 1.04) | 0.2392 |
| Q5 (15.22 g/dL) vs. Q1 | 808 (3.4) | **0.88 (0.80, 0.97)** | **0.0107** | **0.87 (0.79, 0.96)** | **0.0061** | **0.87 (0.79, 0.95)** | **0.0037** |
| *Females (n=142,817)* | 4,847 (3.6) |  |  |  |  |  |  |
| Q1 (13.39 g/dL) | 1,102 (4.1) | Reference | - | Reference | - | Reference | - |
| Q2 (13.43 g/dL) vs. Q1 | 964 (3.6) | **0.87 (0.80, 0.95)** | **0.0020** | **0.87 (0.80, 0.95)** | **0.0023** | **0.88 (0.80, 0.96)** | **0.0033** |
| Q3 (13.49 g/dL) vs. Q1 | 976 (3.6) | **0.88 (0.81, 0.96)** | **0.0048** | **0.88 (0.80, 0.96)** | **0.0031** | **0.87 (0.80, 0.95)** | **0.0028** |
| Q4 (13.58 g/dL) vs. Q1 | 961 (3.5) | **0.87 (0.79, 0.95)** | **0.0016** | **0.87 (0.79, 0.95)** | **0.0014** | **0.87 (0.79, 0.95)** | **0.0018** |
| Q5 (13.71 g/dL) vs. Q1 | 844 (3.1) | **0.76 (0.69, 0.83)** | **<0.0001** | **0.75 (0.69, 0.83)** | **<0.0001** | **0.75 (0.69, 0.83)** | **<0.0001** |

†Subjects ascertained from either self-reported data (i.e., physician-diagnosed health condition or intake of prescription medications) or hospital in-patient records were excluded from the sensitivity analyses. ‡Model 1 adjusted for age, age-squared and the first ten genetic principal components. §Model 2 further adjusted for smoking and alcohol consumption (and menopausal status in women).

**Table S29:** Causal estimates from sensitivity analyses† of associations between genetically instrumented hemoglobin concentration and metabolic traits among Taiwanese Han Chinese

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Metabolic Trait** | ***N*** | **Model 1‡** | | | **Model 2§** | | |
|  |  | **Beta** | **SE** | ***P*-value** | **Beta** | **SE** | ***P*-value** |
| Males (*n*=19,005) |  |  |  |  |  |  |  |
| SBP, mm Hg | 15,511 | 38.76 | 25.60 | 0.1299 | 37.54 | 25.51 | 0.1411 |
| DBP, mm Hg | 15,511 | **47.69** | **17.19** | **0.0055** | **46.36** | **17.12** | **0.0068** |
| FBG, mg/dL | 17,596 | 42.77 | 26.80 | 0.1105 | 42.91 | 26.76 | 0.0702 |
| TG, mg/dL | 17,114 | **660.00** | **175.96** | **0.0002** | **658.98** | **173.81** | **0.0002** |
| HDL-C, mg/dL | 17,114 | -21.32 | 18.14 | 0.2399 | -21.17 | 17.91 | 0.2371 |
| UA, mg/dL | 17,109 | 1.94 | 2.03 | 0.3391 | 2.20 | 2.02 | 0.2759 |
| HbA1c, % | 17,596 | -1.65 | 1.11 | 0.1369 | -1.68 | 1.11 | 0.1308 |
| TC, mg/dL | 17,114 | -91.26 | 55.29 | 0.0988 | -89.35 | 55.29 | 0.1061 |
| LDL-C, mg/dL | 17,114 | **-134.40** | **49.62** | **0.0068** | **-132.41** | **49.57** | **0.0076** |
| Females (*n*=42,330) |  |  |  |  |  |  |  |
| SBP, mm Hg | 37,903 | 43.20 | 30.82 | 0.1611 | 45.68 | 30.80 | 0.1380 |
| DBP, mm Hg | 37,903 | **69.20** | **19.50** | **0.0004** | **70.18** | **19.49** | **0.0003** |
| FBG, mg/dL | 40,419 | -26.73 | 27.35 | 0.3284 | -27.77 | 27.34 | 0.1213 |
| TG, mg/dL | 39,348 | 165.71 | 135.06 | 0.2199 | 163.43 | 134.89 | 0.2257 |
| HDL-C, mg/dL | 39,348 | 4.87 | 26.24 | 0.8529 | 4.04 | 26.17 | 0.8774 |
| UA, mg/dL | 42,099 | **4.89** | **2.12** | **0.0207** | **4.74** | **2.11** | **0.0247** |
| HbA1c, % | 40,419 | **-4.58** | **1.09** | **<0.0001** | **-4.62** | **1.09** | **<0.0001** |
| TC, mg/dL | 39,348 | **-152.38** | **66.96** | **0.0229** | **-154.58** | **66.67** | **0.0204** |
| LDL-C, mg/dL | 39,348 | -87.50 | 60.26 | 0.1465 | -88.35 | 60.08 | 0.1414 |

†Subjects ascertained from either self-reported data (i.e., physician-diagnosed health condition or intake of prescription medications) or hospital in-patient records were excluded from the sensitivity analyses. ‡Model 1 adjusted for age, age-squared and the first ten genetic principal components. §Model 2 further adjusted for smoking and alcohol consumption (and menopausal status in women).

**Table S30:** Causal estimates from sensitivity analyses† of associations between genetically instrumented hemoglobin concentration and metabolic traits among European Whites

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Metabolic Trait** | ***N*** | **Model 1‡** | | | **Model 2§** | | |
|  |  | **Beta** | **SE** | ***P*-value** | **Beta** | **SE** | ***P*-value** |
| Males (*n*=128,549) |  |  |  |  |  |  |  |
| SBP, mm Hg | 77,410 | -30.57 | 32.94 | 0.3534 | -30.14 | 32.92 | 0.3598 |
| DBP, mm Hg | 77,410 | **95.08** | **20.14** | **<0.0001** | **95.15** | **20.13** | **<0.0001** |
| GLU, mmol/L | 117,271 | **-2.15** | **1.38** | **0.0374** | **-2.16** | **1.38** | **0.0382** |
| TG, mmol/L | 90,356 | **9.38** | **2.25** | **<0.0001** | **8.99** | **2.25** | **<0.0001** |
| HDL-C, mmol/L | 90,356 | 0.36 | 0.65 | 0.5798 | 0.47 | 0.64 | 0.4647 |
| UA, μmol/L | 123,482 | -15.72 | 118.52 | 0.8945 | -18.70 | 117.67 | 0.8737 |
| HbA1c, mmol/mol | 117,271 | **-125.87** | **7.28** | **<0.0001** | **-127.97** | **7.21** | **<0.0001** |
| TC, mmol/L | 90,356 | -1.94 | 1.99 | 0.3308 | -1.93 | 1.98 | 0.3308 |
| LDL-C, mmol/L | 90,356 | **-3.68** | **1.53** | **0.0160** | **-3.68** | **1.53** | **0.0158** |
| Females (*n*=142,817) |  |  |  |  |  |  |  |
| SBP, mm Hg | 100,255 | 35.93 | 43.45 | 0.4083 | 35.93 | 43.41 | 0.4079 |
| DBP, mm Hg | 100,255 | **174.95** | **24.92** | **<0.0001** | **176.44** | **24.91** | **<0.0001** |
| GLU, mmol/L | 135,898 | **-7.75** | **1.64** | **<0.0001** | **-7.81** | **1.64** | **<0.0001** |
| TG, mmol/L | 115,003 | **9.43** | **1.96** | **<0.0001** | **9.68** | **1.94** | **<0.0001** |
| HDL-C, mmol/L | 115,003 | 0.62 | 0.98 | 0.5246 | 0.49 | 0.96 | 0.6079 |
| UA, μmol/L | 142,287 | -32.58 | 143.64 | 0.8206 | -17.62 | 143.26 | 0.9021 |
| HbA1c, mmol/mol | 135,898 | **-190.44** | **8.30** | **<0.0001** | **-188.51** | **8.22** | **<0.0001** |
| TC, mmol/L | 115,003 | **-7.23** | **2.47** | **0.0035** | **-7.08** | **2.46** | **0.0041** |
| LDL-C, mmol/L | 115,003 | **-9.35** | **1.95** | **<0.0001** | **-9.14** | **1.94** | **<0.0001** |

†Subjects ascertained from either self-reported data (i.e., physician-diagnosed health condition or intake of prescription medications) or hospital in-patient records were excluded from the sensitivity analyses. ‡Model 1 adjusted for age, age-squared and the first ten genetic principal components. §Model 2 further adjusted for smoking and alcohol consumption (and menopausal status in women).

**Table S31:** Odds ratios of anemia across quintiles of Hb-PRS among Taiwanese Han Chinese and European Whites

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Anemia** | **Cases**  ***n* (%)** | **Crude**  **OR (95% CI)** | ***P*** | **Model 1**†  **OR (95% CI)** | ***P*** | **Model 2‡**  **OR (95% CI)** | ***P*** |
| Taiwanese Han Chinese (*N*=61,352) |  |  |  |  |  |  |  |
| *Males (n=19,012)* | 917 (4.8) |  |  |  |  |  |  |
| Q1 (14.79 g/dL) | 264 (6.9) | Reference | - | Reference | - | Reference | - |
| Q2 (14.98 g/dL) vs. Q1 | 202 (5.3) | **0.75 (0.62, 0.91)** | **0.0030** | **0.74 (0.61, 0.90)** | **0.0021** | **0.74 (0.62, 0.90)** | **0.0023** |
| Q3 (15.04 g/dL) vs. Q1 | 161 (4.2) | **0.59 (0.48, 0.73)** | **<0.0001** | **0.59 (0.48, 0.72)** | **<0.0001** | **0.59 (0.48, 0.72)** | **<0.0001** |
| Q4 (15.11 g/dL) vs. Q1 | 168 (4.4) | **0.62 (0.51, 0.76)** | **<0.0001** | **0.62 (0.51, 0.76)** | **<0.0001** | **0.62 (0.51, 0.76)** | **<0.0001** |
| Q5 (15.28 g/dL) vs. Q1 | 122 (3.2) | **0.44 (0.36, 0.55)** | **<0.0001** | **0.44 (0.36, 0.55)** | **<0.0001** | **0.44 (0.36, 0.55)** | **<0.0001** |
| *Females (n=42,340)* | 6,503 (15.4) |  |  |  |  |  |  |
| Q1 (12.78 g/dL) | 1,706 (20.2) | Reference | - | Reference | - | Reference | - |
| Q2 (12.93 g/dL) vs. Q1 | 1,415 (16.7) | **0.80 (0.74, 0.86)** | **<0.0001** | **0.78 (0.72, 0.85)** | **<0.0001** | **0.78 (0.72, 0.84)** | **<0.0001** |
| Q3 (13.04 g/dL) vs. Q1 | 1,240 (14.6) | **0.68 (0.63, 0.74)** | **<0.0001** | **0.67 (0.61, 0.72)** | **<0.0001** | **0.66 (0.61, 0.72)** | **<0.0001** |
| Q4 (13.11 g/dL) vs. Q1 | 1,129 (13.3) | **0.61 (0.56, 0.66)** | **<0.0001** | **0.59 (0.55, 0.64)** | **<0.0001** | **0.59 (0.54, 0.64)** | **<0.0001** |
| Q5 (13.21 g/dL) vs. Q1 | 1,013 (12.0) | **0.54 (0.50, 0.59)** | **<0.0001** | **0.52 (0.48, 0.57)** | **<0.0001** | **0.52 (0.48, 0.57)** | **<0.0001** |
| European Whites (*N*=271,366) |  |  |  |  |  |  |  |
| *Males (n=128,549)* | 2,841 (2.2) |  |  |  |  |  |  |
| Q1 (14.91 g/dL) | 732 (2.9) | Reference | - | Reference | - | Reference | - |
| Q2 (14.94 g/dL) vs. Q1 | 644 (2.5) | **0.88 (0.79, 0.98)** | **0.0162** | **0.87 (0.78, 0.97)** | **0.0143** | **0.87 (0.78, 0.97)** | **0.0143** |
| Q3 (15.00 g/dL) vs. Q1 | 554 (2.2) | **0.75 (0.67, 0.84)** | **<0.0001** | **0.75 (0.67, 0.84)** | **<0.0001** | **0.74 (0.66, 0.83)** | **<0.0001** |
| Q4 (15.08 g/dL) vs. Q1 | 498 (1.9) | **0.67 (0.60, 0.76)** | **<0.0001** | **0.67 (0.60, 0.75)** | **<0.0001** | **0.67 (0.60, 0.75)** | **<0.0001** |
| Q5 (15.21 g/dL) vs. Q1 | 413 (1.6) | **0.56 (0.49, 0.63)** | **<0.0001** | **0.55 (0.49, 0.62)** | **<0.0001** | **0.54 (0.48, 0.61)** | **<0.0001** |
| *Females (n=142,817)* | 6,784 (4.8) |  |  |  |  |  |  |
| Q1 (13.39 g/dL) | 1,637 (5.7) | Reference | - | Reference | - | Reference | - |
| Q2 (13.43 g/dL) vs. Q1 | 1,529 (5.4) | **0.93 (0.87, 1.00)** | **0.0486** | **0.92 (0.85, 0.99)** | **0.0208** | **0.91 (0.85, 0.98)** | **0.0110** |
| Q3 (13.49 g/dL) vs. Q1 | 1,386 (4.9) | **0.84 (0.78, 0.90)** | **<0.0001** | **0.83 (0.77, 0.90)** | **<0.0001** | **0.83 (0.77, 0.89)** | **<0.0001** |
| Q4 (13.58 g/dL) vs. Q1 | 1,180 (4.1) | **0.71 (0.66, 0.77)** | **<0.0001** | **0.70 (0.65, 0.76)** | **<0.0001** | **0.70 (0.65, 0.75)** | **<0.0001** |
| Q5 (13.71 g/dL) vs. Q1 | 1,052 (3.7) | **0.63 (0.58, 0.68)** | **<0.0001** | **0.63 (0.58, 0.68)** | **<0.0001** | **0.62 (0.57, 0.67)** | **<0.0001** |

†Model 1 adjusted for age, age-squared and the first ten genetic principal components. ‡Model 2 further adjusted for smoking and alcohol consumption (and menopausal status in women).