**Supplemental table 1. 22 independent SNPs associated with the risk of pancreatic cancer in genome-wide association studies**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **CHR** | **Loci** | **SNP** | **Positiona** | **Reported gene** | **Minor/Major Allele** | **MAF**b | **MAFc** | **Reported** **OR (95% CI)** | **P-value** | **Risk allele**d | **Beta**e | **GWAS reference** |
| 1 | 1p36.33 | rs13303010 | 894,573 | *NOC2L* | G/A | 0.13 | 0.11 | 1.26 (1.19-1.35) | 8.4 x 10-14 | G | 0.2311 | Klein et al., 2018 |
| 1 | 1q32.1[1] | rs10919791 | 199,965,168 | *NR5A2* | A/G | 0.19 | 0.23 | 0.77 (0.71-0.84) | 6.4 x 10-10 | G | 0.2614 | Peterson et al., 2010  |
| 1 | 1q32.1[2] | rs2816938 | 199,985,368 | *NR5A2* | A/T | 0.26 | 0.23 | 1.21 (1.17-1.26) | 3.4 x 10-15 | A | 0.1906 | Zhang et al., 2016 |
| 2 | 2p14 | rs1486134 | 67,639,769 | *ETAA1* | G/T | 0.30 | 0.28 | 1.14 (1.09–1.19) | 3.4 x 10-9 | G | 0.1310 | Childs et al., 2015  |
| 3 | 3q28 | rs9854771 | 189,508,471 | *TP63* | A/G | 0.34 | 0.36 | 0.89 (0.85-0.93) | 2.4 x 10-8 | G | 0.1165 | Childs et al., 2015  |
| 5 | 5p15.33[1] | rs2736098 | 1,294,086 | *TERT* | T/C | 0.24 | 0.27 | 0.84 (0.79-0.88) | 6.9 x 10-15 | C | 0.1744 | Wolpin et al., 2014  |
| 5 | 5p15.33[2] | rs31490 | 1,344,458 | *CLPTM1L* | A/G | 0.49f | 0.45f | 1.20 (1.14-1.27) | 2.0 x 10-11 | A | 0.1823 | Wolpin et al., 2014  |
| 5 | 5p15.33[3] | rs35226131 | 1,295,373 | *TERT, CLPTM1L* | T/C | 0.02 | 0.03 | 0.67 (0.53-0.81) | 2.2 x 10-8 | C | 0.3425 | Peterson et al., 2010 |
| 7 | 7p12 | rs78417682 | 47,488,903 | *TNS3* | C/G | 0.10g | 0.12g | 0.85 (0.80-0.90) | 1.4 x 10-7 | G | 0.1863 | Klein et al., 2018 |
| 7 | 7p14.1 | rs17688601 | 40,866,663 | *SUGCT* | A/C | 0.25 | 0.27 | 0.88 (0.84-0.93) | 1.1 x 10-8 | C | 0.1278 | Childs et al., 2015  |
| 7 | 7q32.3 | rs6971499 | 130,680,521 | *LINC-PINT* | C/T | 0.13 | 0.15 | 0.81 (0.76-0.87) | 7.4 x 10-14 | T | 0.2107 | Wolpin et al., 2014  |
| 8 | 8q21.11 | rs2941471 | 76,470,404 | *HNF4G* | G/A | 0.41 | 0.43 | 0.89 (0.85-0.93) | 6.6 x 10-10 | A | 0.1165 | Klein et al., 2018 |
| 8 | 8q24.21[1] | rs10094872 | 128,719,884 | *MYC* | T/A | 0.39 | 0.36 | 1.14 (1.10-1.19) | 1.2 x 10-9 | T | 0.1310 | Zhang et al., 2016 |
| 8 | 8q24.21[2] | rs1561927 | 129,568,078 | *LINC00824, PVT1* | C/T | 0.25 | 0.27 | 0.89 (0.85-0.93) | 7.1 x 10-8 | T | 0.1165 | Wolpin et al., 2014 |
| 9 | 9q34.1 | rs687289 | 136,137,106 | *ABO* | T/C | 0.40h | 0.35h | 1.27 (1.20-1.35) | 1.6 x 10-16 | A | 0.2390 | Amundadottir et al., 2009  |
| 13 | 13q12.2 | rs9581943 | 28,493,997 | *PDX1* | A/G | 0.43 | 0.40 | 1.15 (1.12-1.19) | 5.1 x 10-14 | A | 0.1398 | Wolpin et al., 2014  |
| 13 | 13q22.1 | rs9543325 | 73,916,628 | *KLF5, KLF12* | C/T | 0.43 | 0.37 | 1.24 (1.19-1.28) | 1.2 x 10-22 | C | 0.2151 | Peterson et al., 2010 |
| 16 | 16q23.1 | rs7190458 | 75,263,661 | *BCAR1, CTRB1, CTRB2* | A/G | 0.06 | 0.04 | 1.36 (1.27-1.44) | 1.3 x 10-11 | A | 0.3075 | Wolpin et al., 2014  |
| 17 | 17q12 | rs4795218 | 36,078,510 | *HNF1B* | A/G | 0.21 | 0.23 | 0.88 (0.84-0.92) | 1.3 x 10-8 | G | 0.1278 | Klein et al., 2018 |
| 17 | 17q24.3 | rs11655237 | 70,400,166 | *LINC00673* | T/C | 0.14 | 0.12 | 1.26 (1.19–1.34) | 1.4 x 10-14 | T | 0.2311 | Childs et al., 2015  |
| 18 | 18q21.32 | rs1517037 | 56,878,274 | *GRP* | T/C | 0.17 | 0.19 | 0.86 (0.80-0.91) | 3.3 x 10-8 | C | 0.1508 | Klein et al., 2018 |
| 22 | 22q12.1 | rs16986825 | 29,300,306 | *ZNRF3* | T/C | 0.17 | 0.15 | 1.15 (1.10-1.20) | 1.2 x 10-8 | T | 0.1398 | Wolpin et al., 2014  |

Abbreviations: CHR, chromosome; SNP, single nucleotide polymorphism; MAF, minor allele frequency; OR, odds ratio; CI, confidence interval; GWAS, genome-wide association study.

aSNP position and minor/major allele based on NCBI Human Genome Build 37

bAverage of minor allele frequency among cases in PanScanI/II, PanScanIII, and PanC4

cAverage of minor allele frequency among controls in PanScanI/II, PanScanIII, and PanC4

dRisk allele is the allele associated with increased risk of pancreatic cancer [if the risk allele is not our data, the complementary allele (e.g. A of rs687289) is reported.]

eCalculated beta coefficient per each risk allele using the reported OR in GWAS of PanScan, PanC4, or meta-analysis [if OR > 1 then beta = ln(OR); otherwise, beta = ln(1/OR)]

fUsing rs401681 on 5p15.33 (T/C) reported in Klein, et al. 2018.

gUsing rs73328514 on 7p12.3 (T/A) reported in Klein, et al. 2018

hUsing rs505922 on 9q34 (C/T) reported in Klein, et al. 2018

**Supplemental table 2. Missing data of 22 pancreatic cancer-associated SNPs by cohort**

|  |  |  |
| --- | --- | --- |
| **Loci** |  | **Missing percentage (%)** |
| **SNP** | **HPFS** |  | **NHS** |  | **PHS** |  | **WHI** |
| Case | Control |  | Case | Control |  | Case | Control |  | Case | Control |
| 1p36.33 | rs13303010 | 2.4 | 34.9 |  | 7.5 | 38.9 |  | 33.3 | 78.5 |  | 21.7 | 68.8 |
| 1q32.1[2] | rs2816938 | 2.4 | 34.9 |  | 7.5 | 38.9 |  | 33.3 | 78.5 |  | 21.7 | 68.8 |
| 2p14 | rs1486134 | 2.4 | 34.9 |  | 7.5 | 38.9 |  | 33.3 | 78.5 |  | 21.7 | 68.8 |
| 3q28 | rs9854771 | 2.4 | 34.9 |  | 7.5 | 38.9 |  | 33.3 | 78.5 |  | 21.7 | 68.8 |
| 5p15.33[3] | rs35226131 | 2.4 | 34.9 |  | 7.5 | 38.9 |  | 33.3 | 78.5 |  | 21.7 | 68.8 |
| 7p12 | rs78417682 | 2.4 | 34.9 |  | 7.5 | 38.9 |  | 33.3 | 78.5 |  | 21.7 | 68.8 |
| 7p14.1 | rs17688601 | 2.4 | 34.9 |  | 7.5 | 38.9 |  | 33.3 | 78.5 |  | 21.7 | 68.8 |
| 8q21.11 | rs2941471 | 2.4 | 34.9 |  | 7.5 | 38.9 |  | 33.3 | 78.5 |  | 21.7 | 68.8 |
| 8q24.21[1] | rs10094872 | 2.4 | 34.9 |  | 7.5 | 38.9 |  | 33.3 | 78.5 |  | 21.7 | 68.8 |
| 17q12 | rs4795218 | 2.4 | 34.9 |  | 7.5 | 38.9 |  | 33.3 | 78.5 |  | 21.7 | 68.8 |
| 17q24.3 | rs11655237 | 2.4 | 34.9 |  | 7.5 | 38.9 |  | 33.3 | 78.5 |  | 21.7 | 68.8 |
| 18q21.32 | rs1517037 | 2.4 | 34.9 |  | 7.5 | 38.9 |  | 33.3 | 78.5 |  | 21.7 | 68.8 |
| 1q32.1[1] | rs10919791 | 12.0 | 76.9 |  | 31.3 | 79.5 |  | 40.0 | 78.5 |  | 21.7 | 68.8 |
| 5p15.33[1] | rs2736098 | 12.0 | 76.9 |  | 31.3 | 79.5 |  | 40.0 | 78.5 |  | 21.7 | 68.8 |
| 5p15.33[2] | rs31490 | 12.0 | 76.9 |  | 31.3 | 79.5 |  | 40.0 | 78.5 |  | 21.7 | 68.8 |
| 7q32.3 | rs6971499 | 12.0 | 76.9 |  | 31.3 | 79.5 |  | 40.0 | 78.5 |  | 21.7 | 68.8 |
| 8q24.21[2] | rs1561927 | 12.0 | 76.9 |  | 31.3 | 79.5 |  | 40.0 | 78.5 |  | 21.7 | 68.8 |
| 9q34.1 | rs687289 | 12.0 | 76.9 |  | 31.3 | 79.5 |  | 40.0 | 78.5 |  | 21.7 | 68.8 |
| 13q12.2 | rs9581943 | 12.0 | 76.9 |  | 31.3 | 79.5 |  | 40.0 | 78.5 |  | 21.7 | 68.8 |
| 13q22.1 | rs9543325 | 12.0 | 76.9 |  | 31.3 | 79.5 |  | 40.0 | 78.5 |  | 21.7 | 68.8 |
| 16q23.1 | rs7190458 | 12.0 | 76.9 |  | 31.3 | 79.5 |  | 40.0 | 78.5 |  | 21.7 | 68.8 |
| 22q12.1 | rs16986825 | 12.0 | 76.9 |  | 31.3 | 79.5 |  | 40.0 | 78.5 |  | 21.7 | 68.8 |

Abbreviations: HPFS, Health Professionals Follow-up Study; NHS, Nurses’ Health Study; PHS, Physicans’ Health Study; WHI, Women’s Health Initiative; SNP, single nucleotide polymorphism; RAF, risk allelic frequency; uGRS, unweighted genetic risk score; wGRS, weighted genetic risk score.

**Supplemental table 3. Descriptive characteristics of study subjects in HPFS, NHS, PHS, and WHI cohorts (Total N = 1,591)**

|   | **HPFS**  |  | **NHS**  |  | **PHS** |  | **WHI** |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Cases**  | **Controls**  |  | **Cases** | **Controls** |  | **Cases** | **Controls** |  | **Cases** | **Controls** |
| **Variables** | N=83 | N=195 |  | N = 147 | N = 396 |  | N = 90 | N = 163 |  | N = 180 | N = 337 |
| ***Matching factors*** |  |  |  |  |  |  |  |  |  |  |  |
| **Age** |  |  |  |  |  |  |  |  |  |  |  |
| Age at diagnosis (year), mean (SD) | 73.1 (8.4) |  |  | 73.0 (7.4) |  |  | 73.2 (9.1) |  |  | 72.3 (7.5) |  |
| Age at blood draw (year), mean (SD) | 65.5 (7.9) | 65.4 (7.9) |  | 60.5 (6.0) | 60.6 (6.1) |  | 57.3 (8.8) | 55.0 (8.2) |  | 67.3 (7.2) | 67.2 (7.3) |
| **Smoking** |  |  |  |  |  |  |  |  |  |  |  |
| Current smoker, % | 9.6 | 11.8 |  | 18.5 | 16.7 |  | 17.8 | 17.2 |  | 7.3 | 5.4 |
| **Fasting status**  |  |  |  |  |  |  |  |  |  |  |  |
| Fasting < 8 hours, %  | 41.0 | 40.0 |  | 30.6 | 23.2 |  | 70.0 | 73.6 |  | 0.0 | 0.0 |
| Fasting >= 8 hours, % | 59.0 | 60.0 |  | 69.4 | 76.8 |  | 30.0 | 26.4 |  | 100.0 | 100.0 |
| ***Lifestyle and clinical factors*** |
| Body mass index (kg/m2), mean (SD) | 25.7 (3.3) | 25.7 (3.2) |  | 26.1 (5.4) | 25.3 (4.3) |  | 25.6 (2.9) | 24.7 (2.2) |  | 27.2 (6.1) | 26.8 (5.4) |
| Waist-to-hip ratio (inch/inch), mean (SD) | 0.9 (0.1) | 0.9 (0.1) |  | 0.8 (0.1) | 0.8 (0.1) |  | 1.0 (0.1) | 0.9 (0.1) |  | 0.8 (0.1) | 0.8 (0.1) |
|  Physical activity (MET-hr/wk), mean (SD) | 50.6 (65.1) | 41.0 (44.0) |  | 16.6 (19.1) | 16.8 (18.6) |  | 12.1 (11.1) | 14.4 (12.5) |  | 12.9 (12.8) | 15.6 (16.0) |
|  Diagnosed diabetes (yes), % | 4.8 | 3.6 |  | 6.1 | 3.5 |  | 4.4 | 1.2 |  | 6.7 | 3.0 |
| ***Biomarkers*** |
| Proinsulin (pM), mean (SD) | 21.8 (24.9) | 19.6 (34.0) |  | 15.4 (15.3) | 11.6 (16.4) |  | 24.3 (29.0) | 14.8 (11.4) |  | 11.6 (10.2) | 10.0 (9.2) |
| Adiponectin (ug/mL), mean (SD)  | 5.0 (2.3) | 6.1 (3.8) |  | 8.9 (6.1) | 8.5 (4.8) |  | 5.4 (3.1) | 5.8 (2.8) |  | 9.3 (5.7) | 10.0 (5.7) |
| Interleukin-6 (pg/mL), mean (SD) | 1.8 (2.9) | 1.6 (2.2) |  | 2.7 (5.1) | 1.6 (3.1) |  | 2.0 (3.8) | 2.3 (4.6) |  | 2.6 (4.2) | 2.4 (3.5) |
| Total BCAAs (μM), mean (SD) | 481.2 (85.9) | 387.9 (195.1) |  | 393.6 (201.6) | 279.5 (233.1) |  | 467.6 (234.4) | 413.6 (228.7) |  | 417.6 (115.9) | 409.5 (87.2) |
| Valine (μM), mean (SD) | 223.8 (35.0) | 219.6 (44.4) |  | 227.2 (46.5) | 220.8 (36.9) |  | 258.1 (45.8) | 238.5 (41.5) |  | 210.0 (45.8) | 203.8 (40.3) |
| Leucine (μM), mean (SD) | 167.2 (33.9) | 159.3 (37.5) |  | 161.1 (37.6) | 155.2 (28.2) |  | 195.4 (43.0) | 182.4 (40.6) |  | 139.9 (34.4) | 134.2 (29.7) |
| Isoleucine (μM), mean (SD) | 90.2 (21.3) | 85.2 (23.0) |  | 85.9 (22.3) | 83.3 (20.3) |  | 107.6 (28.8) | 97.7 (25.3) |  | 77.2 (21.3) | 72.7 (18.0) |
| ***Genetic risk factors*** |
| 22 SNPs (RAFa), % |  |  |  |  |  |  |  |  |  |  |  |
| 1p36.33 – rs13303010\_G  | 16.0 | 21.2 |  | 18.5 | 19.6 |  | 13.9 | 17.0 | 5 | 15.4 | 19.0 |
| 1q32.1 – rs10919791\_G  | 85.5 | 79.0 |  | 78.9 | 77.5 |  | 86.1 | 79.8 |  | 83.1 | 77.4 |
| 1q32.1 - rs2816938\_A | 24.7 | 24.4 |   | 17.4 | 24.7 |   | 21.7 | 24.4 |  | 26.9 | 19.2 |
| 2p14 - rs1486134\_G  | 29.5 | 26.9 |  | 27.2 | 29.4 |  | 27.8 | 29.4 |  | 29.4 | 28.8 |
| 3q28 - rs9854771\_G | 69.9 | 64.3 |  | 63.6 | 65.1 |  | 63.3 | 58.9 |  | 67.5 | 63.2 |
| 5p15.33[1] – rs2736098\_C | 77.9 | 72.7 |  | 79.4 | 73.9 |  | 79.8 | 72.6 |  | 77.1 | 74.2 |
| 5p15.33[2] – rs31490\_A  | 41.5 | 40.3 |  | 51.7 | 37.7 |  | 50.6 | 37.8 |  | 48.0 | 39.1 |
| 5p15.33[3] - rs35226131\_C | 99.1 | 98.1 |  | 97.1 | 97.3 |  | 97.2 | 96.4 |  | 97.2 | 96.6 |
| 7p12 - rs78417682\_G | 89.4 | 89.2 |  | 88.1 | 91.0 |  | 90.5 | 91.5 |  | 91.4 | 92.1 |
| 7p14.1 - rs17688601\_C | 77.7 | 72.1 |  | 74.4 | 72.8 |  | 76.7 | 76.2 |  | 78.9 | 73.8 |
| 7q32.3 – rs6971499\_T  | 86.7 | 87.2 |  | 86.4 | 83.7 |  | 83.5 | 87.2 |  | 83.3 | 83.8 |
| 8q21.11 – rs2941471\_A | 55.9 | 57.8 |  | 61.9 | 58.3 |  | 61.4 | 57.5 |  | 58.0 | 62.2 |
| 8q24.21[1] - rs10094872\_T  | 33.9 | 40.7 |   | 37.9 | 35.6 |   | 39.9 | 33.8 |  | 39.2 | 35.3 |
| 8q24.21[2] - rs1561927\_T | 75.3 | 72.6 |  | 74.8 | 72.6 |  | 74.4 | 73.3 |  | 68.9 | 75.2 |
| 9q34.1 – rs687289\_A | 40.2 | 34.1 |  | 36.6 | 36.5 |  | 36.3 | 29.0 |  | 38.9 | 33.4 |
| 13q12.2 – rs9581943\_A | 50.3 | 36.9 |  | 46.3 | 38.6 |  | 35.2 | 42.6 |  | 41.2 | 40.3 |
| 13q22.1 – rs9543325\_C  | 44.0 | 42.1 |  | 41.8 | 36.7 |  | 47.8 | 35.9 |  | 40.6 | 36.5 |
| 16q23.1 – rs7190458\_A | 2.9 | 4.3 |  | 7.7 | 4.0 |  | 5.9 | 5.4 |  | 3.9 | 2.8 |
| 17q12 - rs4795218\_G | 77.7 | 75.5 |  | 79.3 | 78.7 |  | 73.1 | 79.7 |  | 80.3 | 72.8 |
| 17q24.3 - rs11655237\_T  | 9.6 | 11.5 |  | 9.6 | 13.1 |  | 12.3 | 11.6 |  | 14.2 | 12.0 |
| 18q21.32 - rs1517037\_C  | 78.9 | 82.8 |  | 88.1 | 83.6 |  | 86.7 | 81.7 |  | 84.4 | 85.3 |
| 22q12.1 – rs16986825\_T | 16.3 | 15.9 |  | 15.3 | 14.7 |  | 14.4 | 15.6 |  | 16.6 | 15.5 |
| uGRS, mean (SD) | 23.7 (2.8) | 23.0 (2.6) |  | 23.6 (2.6) | 22.9 (2.6) |  | 23.6 (3.0) | 22.7 (2.6) |  | 23.7 (2.8) | 22.8 (2.7) |
| wGRSb, mean (SD) | 0.2 (1.0) | -0.1 (1.0) |  | 0.2 (1.0) | -0.1 (1.0) |  | 0.2 (1.0) | -0.1 (1.0) |  | 0.2 (1.0) | -0.1 (1.0) |

Abbreviations: HPFS, Health Professionals Follow-up Study; NHS, Nurses’ Health Study; PHS, Physicans’ Health Study; WHI, Women’s Health Initiative; MET, metabolic equivalent of task; BCAAs, branched-chain amino acids; SNP, single nucleotide polymorphism; RAF, risk allelic frequency; uGRS, unweighted genetic risk score; wGRS, weighted genetic risk score; SD, standard deviation.

aEstimated risk allelic frequency based on raw genotype dosage data [RAF = (average of allelic dosage)/2]

bStandardized variables with mean = 0 and SD= 1 within each cohort

cComplete missing Variables

**Supplemental table 4. Univariable odds ratios and 95% CIs with pancreatic cancer risk by cohort**a

|   | **Pooled data** | **HPFS** | **NHS** | **PHS** | **WHI** |
| --- | --- | --- | --- | --- | --- |
|  | **(N = 1,591)** | **(N = 278)** | **(N = 543)** | **(N = 253)** | **(N = 517)** |
| **Variables** | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| ***Lifestyle and clinical factors*** |  |  |  |  |  |
| Body mass indexb | 1.15 (1.03, 1.27) | 0.99 (0.76, 1.28) | 1.17 (0.98, 1.40) | 1.51 (1.13, 2.00) | 1.07 (0.90, 1.29) |
| Waist-to-hip ratiob | 1.19 (1.06, 1.33) | 1.17 (0.87, 1.57) | 1.25 (0.98, 1.60) | 1.34 (0.95, 1.88) | 1.13 (0.94, 1.35) |
| Physical activityb | 0.94 (0.85, 1.05) | 1.19 (0.93, 1.51) | 1.01 (0.84, 1.21) | 0.84 (0.65, 1.08) | 0.82 (0.67, 1.00) |
|  Diagnosed diabetes (yes) | 2.36 (1.32, 4.21) | 1.34 (0.38, 4.78) | 2.68 (0.82, 8.75) | 3.61 (0.66, 19.74) | 2.60 (1.05, 6.41) |
|  |  |  |  |  |  |
| ***Circulating biomarkers*** |  |  |  |  |  |
| Proinsulinb | 1.24 (1.10, 1.40) | 1.06 (0.81, 1.39) | 1.33 (1.01, 1.74) | 2.39 (1.22, 4.69) | 1.19 (1.00, 1.42) |
| Adiponectin (≥ 4.4 ug/ml) | 0.57 (0.43, 0.76) | 0.52 (0.29, 0.92) | 0.64 (0.35, 1.14) | 0.54 (0.29, 1.01) | 0.58 (0.34, 0.99) |
| Interleukin-6b | 1.10 (0.98, 1.22) | 1.03 (0.80, 1.33) | 1.30 (1.01, 1.66) | 0.93 (0.66, 1.29) | 1.07 (0.90, 1.27) |
|  Total BCAAsb | 1.37 (1.14, 1.64) | 1.38 (0.86, 2.23) | 1.74 (0.92, 3.29) | 2.59 (1.29, 5.21) | 1.24 (1.00, 1.53) |
|  |  |  |  |  |  |
| ***Genetic risk score*** |  |  |  |  |  |
|  wGRSb | 1.37 (1.23, 1.53) | 1.29 (0.97, 1.70) | 1.32 (1.08, 1.61) | 1.42 (1.08, 1.87) | 1.43 (1.19, 1.72) |

Abbreviations: HPFS, Health Professionals Follow-up Study; NHS, Nurses’ Health Study; PHS, Physicans’ Health Study; WHI, Women’s Health Initiative; OR, odds ratio; CI, confidence interval; BCAAs, branched-chain amino acids; wGRS, weighted genetic risk score.

aEstimated based on raw data only

bStandardized variables within each cohort with mean = 0 and SD= 1 within each cohort

**Supplemental table 5. Estimated ORs and 95% CIs from multivariablea risk models for pancreatic cancer including clinical/biomarker model**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Clinical** **model** | **Clinical/****genetic****model** | **Clinical/****biomarker****model** | **Clinical/****genetic/****biomarker model** |
| **Full follow-up period** |  |  |  |  |
| Model comparison (*P*-value**b**) |  | 3.24e-08 | 2.10e-05 | 6.03e-05 |
| Model AUC | 0.61 | 0.65 | 0.64 | 0.67 |
|  | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) |
|  |  |  |  |  |
| Body mass indexc | 1.08 (0.97, 1.21) | 1.07 (0.95, 1.20) | 0.99 (0.88, 1.11) | 0.98 (0.86, 1.10) |
| Waist-to-hip ratioc | 1.13 (1.01, 1.26) | 1.12 (1.00, 1.26) | 1.08 (0.96, 1.22) | 1.08 (0.96, 1.21) |
| Physical activityc | 0.96 (0.86, 1.06) | 0.95 (0.85, 1.06) | 0.97 (0.87, 1.08) | 0.97 (0.86, 1.08) |
| Diagnosed diabetes (yes) | 2.10 (1.16, 3.79) | 2.19 (1.19, 4.02) | 1.63 (0.89, 3.01) | 1.70 (0.91, 3.19) |
| wGRSc |  | 1.37 (1.22, 1.53) |  | 1.36 (1.21, 1.52) |
| Proinsulinc |  |  | 1.16 (1.02, 1.30) | 1.16 (1.03, 1.31) |
| Adiponectin (≥ 4.4 ug/ml) |  |  | 0.73 (0.56, 0.95) | 0.76 (0.58, 0.99) |
| Interleukin-6c |  |  | 1.09 (0.99, 1.21) | 1.10 (0.99, 1.23) |
| Total BCAAsc |  |  | 1.27 (1.05, 1.53) | 1.25 (1.04, 1.51) |
| **0-10 years follow-up period** |  |  |  |  |
| Model comparison (*P*-value**b**) |  | 2.91e-07 | 1.05e-03 | 2.92e-03 |
| Model AUC  | 0.61 | 0.67 | 0.65 | 0.69 |
|  | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) |
|  |  |  |  |  |
| Body mass indexc | 1.05 (0.91, 1.22) | 1.04 (0.90, 1.21) | 0.97 (0.83, 1.13) | 0.96 (0.82, 1.12) |
| Waist-to-hip ratioc | 1.08 (0.93, 1.25) | 1.06 (0.91, 1.23) | 1.02 (0.88, 1.19) | 1.00 (0.86, 1.17)  |
| Physical activityc | 0.86 (0.74, 1.00) | 0.86 (0.74, 1.01) | 0.87 (0.74, 1.02) | 0.88 (0.75, 1.03) |
| Diagnosed diabetes (yes) | 2.22 (1.09, 4.54) | 2.14 (1.02, 4.50) | 1.71 (0.81, 3.59) | 1.65 (0.77, 3.56) |
| wGRSc |  | 1.44 (1.25, 1.67) |  | 1.43 (1.23, 1.65) |
| Proinsulinc |  |  | 1.08 (0.94, 1.25) | 1.10 (0.94, 1.27) |
| Adiponectin (≥ 4.4 ug/ml) |  |  | 0.67 (0.47, 0.97) | 0.70 (0.48, 1.02) |
| Interleukin-6c |  |  | 1.12 (0.98, 1.28) | 1.13 (0.98, 1.30) |
| Total BCAAsc |  |  | 1.28 (1.04, 1.58) | 1.24 (1.00, 1.54) |

Abbreviations: AUC, Area under the ROC curve; OR, odds ratio; CI, confidence interval; BCAAs, branched-chain amino acids; wGRS, weighted genetic risk score.

aAdjusted for matching factors, age, cohort (also gender), race/ethnicity, smoking status, fasting status, and month/year of blood collection.

**b***P*-value was estimated from the likelihood ratio test comparing the clinical/genetic model to the clinical model, clinical/biomarker model to the clinical model, and the clinical/genetic/biomarker model to the clinical/genetic model.

cStandardized variables with mean = 0 and SD= 1 within each cohort

**Supplemental figure 1. Flow diagram of study participants and missing data**

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