|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Training population**  **(D.E.S.I.R participants)** | | |  | | **Validation population** | | | |
| Risk factor | *n* with  lower risk  / *n* with higher risk | AROC  Low → High risk stratum  (*p*-value) | iAROC  Low → High  risk stratum  (*p*-value) |  | *n* with  lower risk  / *n* with higher risk | | AROC  Low → High  risk stratum  (*p*-value) | iAROC  Low → High  risk stratum  (*p*-value) |
| Men | 499 / 545 | 0.91 → 0.86  (*p* = 0.10) | 0.83 → 0.83  (*p* = 0.81) |  | (76 / 52) | | 0.75 → 0.69  (*p* = 0.48) | 0.68 → 0.71  (*p* = 0.79) |
| Age ≥45 years | 399 / 645 | 0.89 → 0.87  (*p* = 0.59) | **0.86 → 0.73**  **(*p* = 1.26×10-6)** |  | (46 / 82) | | 0.72 → 0.72  (*p* = 0.98) | 0.74 → 0.56  (*p* = 0.11) |
| BMI ≥ 25 kg.m-2 | 573 / 471 | 0.88 → 0.86  (*p* = 0.55) | 0.82 → 0.82  (*p* = 0.85) |  | (25 / 103) | | 0.83 → 0.70  (*p* = 0.21) | 0.57 → 0.59  (*p* = 0.29) |
| Fasting glucose ≥ 5.6 mmol.L-1 | 701 / 343 | 0.80 → 0.86  (*p* = 0.09) | **0.74 → 0.82**  **(*p* = 0.01)** |  | (53 / 75) | | 0.71 → 0.73  (*p* = 0.84) | 0.63 → 0.68  (*p* = 0.61) |
| Elevated blood pressure\* | 398 / 646 | 0.86 → 0.88  (*p* = 0.61) | 0.82 → 0.84  (*p* = 0.43) |  | (20 / 108) | | 0.61 → 0.75  (*p* = 0.35) | 0.48 → 0.69  (*p* = 0.07) |
| Triglycerides ≥ 1.7 mmol.L-1 | 781 / 263 | 0.87 → 0.87  (*p* = 0.95) | 0.83 → 0.83  (*p* = 0.89) |  | (38 / 90) | | 0.74 → 0.71  (*p* = 0.82) | 0.63 → 0.70  (*p* = 0.42) |
| Reduced HDL cholesterol‡ | 851 / 193 | 0.88 → 0.88  (*p* = 0.86) | 0.85 → 0.82  (*p* = 0.45) |  | ( 38 / 90) | | 0.71 → 0.73  (*p* = 0.79) | 0.72 → 0.67  (*p* = 0.69) |
| Current smoker | 811 / 233 | 0.88 → 0.89  (*p* = 0.65) | 0.85 → 0.85  (*p* = 0.81) |  | (101 / 27) | | 0.70 → 0.81  (*p* = 0.27) | 0.66 → 0.77  (*p* = 0.41) |
| Waist circumference:  ≥94 cm men, ≥80 cm women | 672 / 372 | 0.89 → 0.84  (*p* = 0.09) | 0.83 → 0.82  (*p* = 0.68) |  | (33 / 95) | | 0.81 → 0.71  (*p* = 0.42) | 0.59 → 0.68  (*p* = 0.39) |

**Supplementary Table 2.** Discriminative performances of metabolomic risk scores (AROC for MRS1 and integrated AROC or iAROC for MRS2) when study participants were stratified as being at lower or higher risk to develop type 2 diabetes according to 9 classical risk factors. \*Elevated blood pressure (BP) is defined as diagnosed hypertension or systolic BP≥130 mm Hg or diastolic BP≥85 mm Hg; and ‡reduced HDL cholesterol by: ≤1.03 mmol/L in men, ≤1.29 mmol/L in women.