Genetic instruments
221 SNPs associated with predicted VAT using UK Biobank data
\( (N = 325,153) \)

Outcomes
Type 2 diabetes
Discovery \( (N = 159,208) \)
Replication \( (N = 70,127) \)

Glucose-related traits
HbA1c \( (N = 200,622) \)
FG \( (N = 200,622) \)
2hGlu \( (N = 200,622) \)
FI \( (N = 200,622) \)

SNP-VAT
SNP-T2D
and glucose-related traits

Data sources

MR analyses
Univariable MR
Inverse-variance weighted
Weighted median
MR-Egger regression
MR-RAPS
CAUSE
Bi-directional MR
GSMR

Outlier detection
MR-PRESSO
GSMR

Sensitivity analyses

Multivariable MR
Adjusted for BMI, WC, WHR and smoking

Associations
Type 2 diabetes

**Outcome**
- BMI
- WC
- WHR
- Smoking

**Variables**

**OR (95% CI)**
- 2.60 (1.91, 3.54)
- 1.23 (0.91, 1.67)
- 2.08 (1.59, 2.72)
- 1.87 (1.39, 2.52)
- 2.49 (2.09, 2.97)
- 2.55 (2.15, 3.03)
- 2.70 (2.32, 3.14)
- 2.65 (2.28, 3.08)
- 1.74 (1.19, 2.55)
- 1.33 (0.94, 1.88)
- 1.18 (0.85, 1.64)
- 1.31 (0.96, 1.80)
- 1.39 (1.10, 1.74)
- 1.44 (1.16, 1.79)
- 1.56 (1.30, 1.88)
- 1.55 (1.30, 1.86)

**p value**
- 1.44×10^{-09}
- 1.78×10^{-01}
- 1.11×10^{-07}
- 5.48×10^{-06}
- 3.93×10^{-24}
- 4.69×10^{-21}
- 1.87×10^{-37}
- 4.21×10^{-28}
- 4.57×10^{-03}
- 1.07×10^{-01}
- 3.15×10^{-01}
- 9.45×10^{-02}
- 4.92×10^{-03}
- 1.26×10^{-03}
- 2.89×10^{-05}
- 3.43×10^{-06}

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**Fig. 2**

Colour
Study population of the Maastricht Study (N=8005)

Missing data for corneal nerve images (n=3850)

Insufficient quality of corneal nerve images (n=532)

Study population with corneal nerve images of sufficient quality (n=3623)

Missing data for confounders (n=152)

Study population with complete data on confounders (n=3471)

Study population with complete data on glucose metabolism status (n=3471): normal glucose metabolism (n=2225), prediabetes (n=509), type 2 diabetes (n=729) and other type of diabetes (n=8)

Study population with complete data on measures of glycaemia: fasting plasma glucose (n=3470), 2 h post-load glucose (n=3328), HbA1c (n=3468), skin autofluorescence (n=3254) and duration of diabetes (n=574)
Prediabetes versus NGM status

Type 2 diabetes versus NGM status

Measures of glycemia

Fasting plasma glucose, per SD

2-Hour post-load glucose, per SD

HbA1c, per SD

Skin autofluorescence, per SD

Duration of diabetes, per SD

Composite Z-score of corneal nerve fiber measures

Indicates that a greater measure of the determinant is associated with a lower composite Z-score corneal nerve fiber measures

Indicates that a greater measure of the determinant is associated with a greater composite Z-score corneal nerve fiber measures