SUPPLEMENTARY MATERIALS

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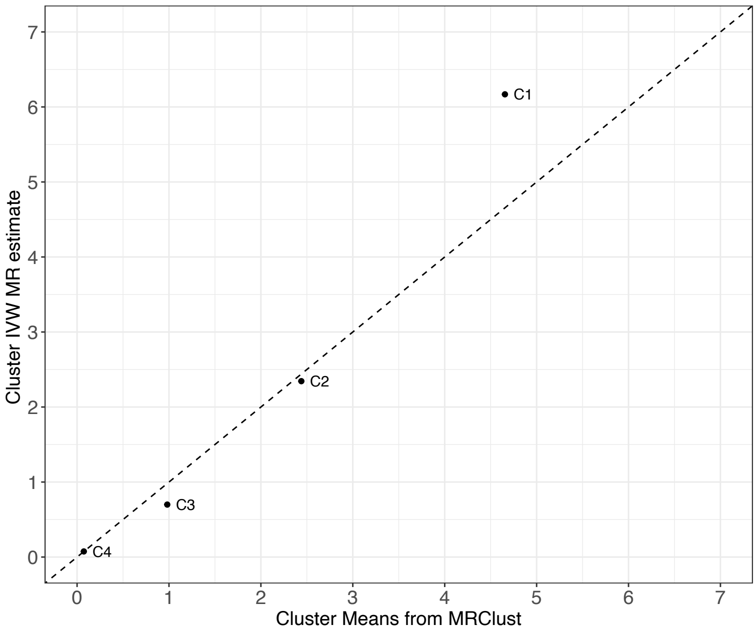
Supplementary Table 1. *UKB Participants' baseline characteristics*

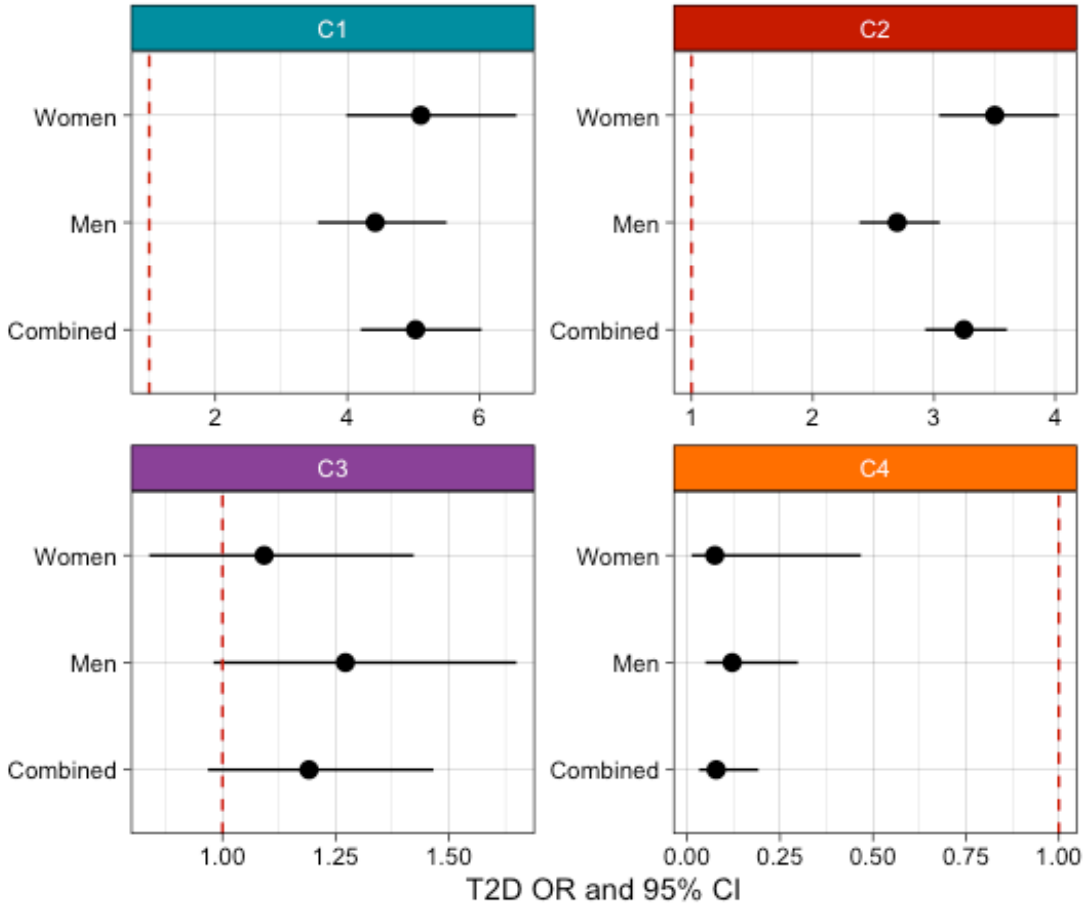
Attribute	***Females***	***Males***
N (%)	*194184 (53.8%)*	*166587*
BMI (mean, SD)	*27.04 (5.14)*	*27.85 (4.23)*
Age (mean, SD)	*56.68 (7.9)*	*57.13 (8.08)*
Alcohol: Never	*8368*	*2790*
Previous	*6927*	*5297*
Current	*178712*	*158360*
Smoking: Never	*115121*	*81400*
Previous	*61828*	*65014*
Current	*16587*	*19587*
T2D: No	*182033*	*148001*
Yes	*12151*	*18586*

Supplementary Table 2. *Field codes of variables used*

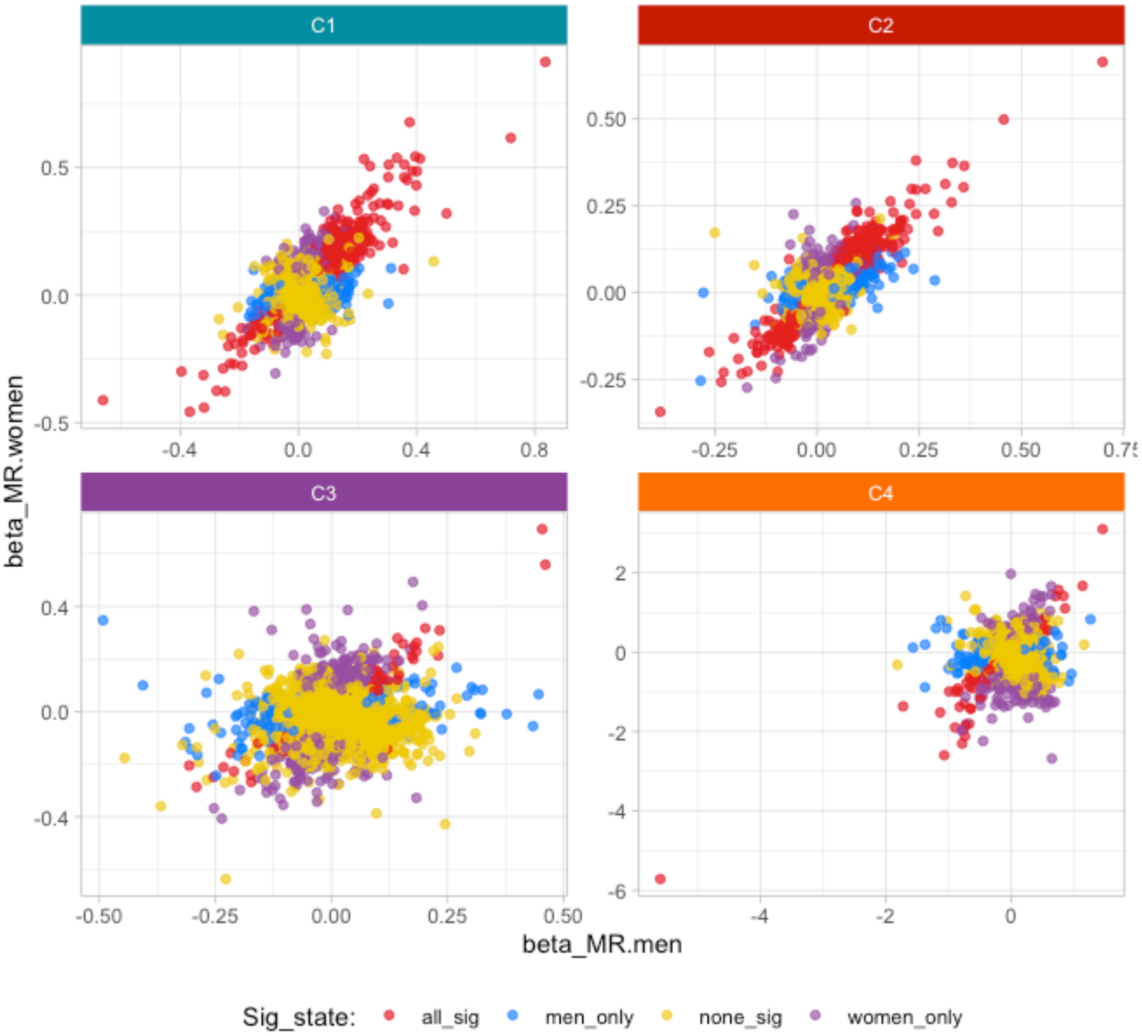
Phenotype/ Variable	***UKB Field code***
Age	*21022*
Sex	*30*
BMI	*23104*
Smoking status	*20116*
Alcohol consumption	*20117*
Genetic Batch	*22000*
UKB centre	*54*
Type-2 diabetes	*130708*
Height	*50*
Weight	*21002*
Genetic principal components	*22009*
Proteomic data	
Participation in the PPP cohort	*30903*
Time to processing for proteins	*Time to processing: Calculated as difference between olink processing start date and date of sample collection. Information provided in "resources" tab of Protein Biomarkers (https://biobank.ndph.ox.ac.uk/showcase/label.cgi?id=1839)*
Protein assay batch number	*30901*



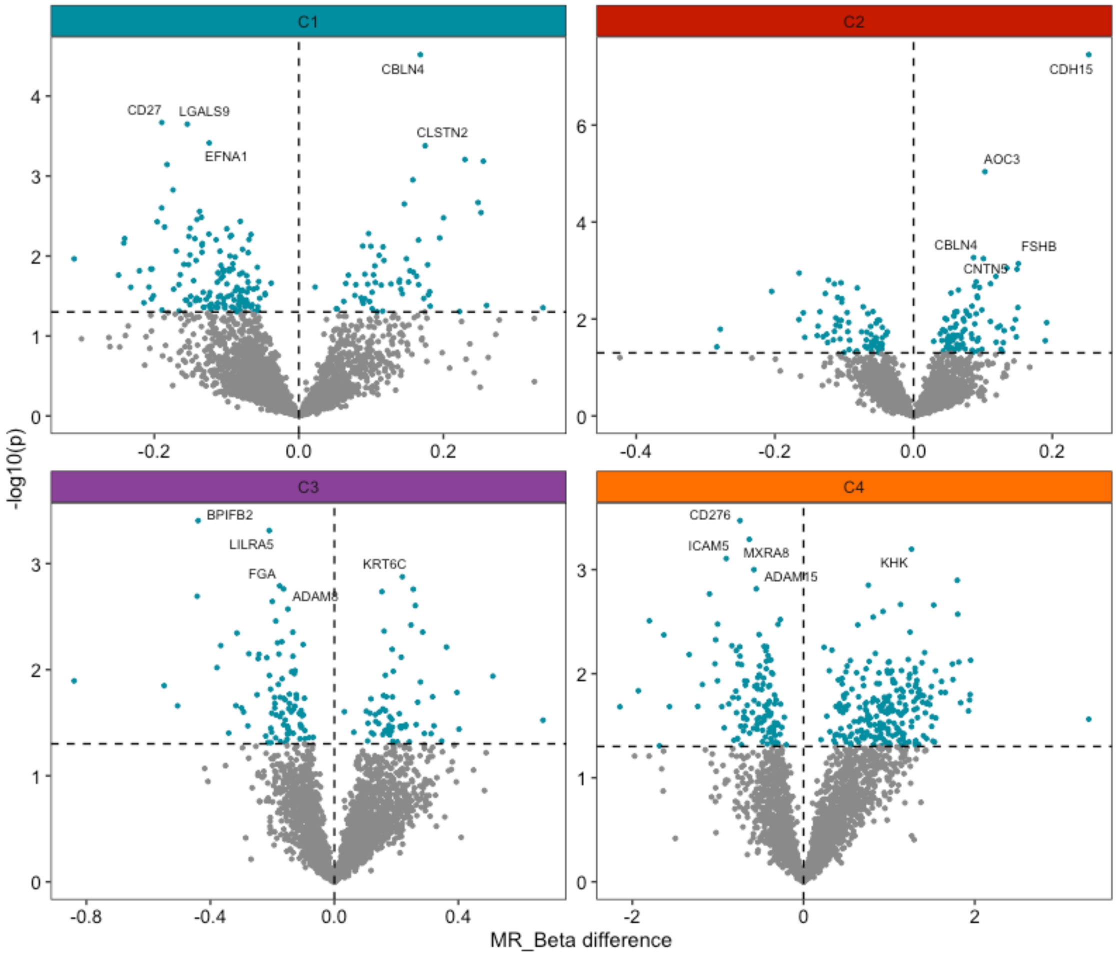
Supplementary Figure 1*. A comparison of cluster means from MR-clust and the inverse-variance weighted (IVW) Mendelian randomization (MR) estimates. Values in the figure are presented as exponentiated cluster means (on X) and odds ratios (OR) for IVW MR estimates (on Y).*



Supplementary Figure 2. *Cluster-specific MR estimates for effect of BMI on T2D, from UKB in sex-combined and sex-stratified analyses.*



Supplementary Figure 3. *Cluster-specific MR estimates for effect of BMI on protein levels, sex-combined and sex-stratified analyses. Abbreviations: Sig_state = indicates whether a protein is significantly associated with BMI in males (men_only), females (women_only), both (all_sig), or neither (none_sig), with a significance threshold of* $p < 0.05$.



Supplementary Figure 4. *Difference between males and females in cluster-specific MR estimates for effect of BMI on protein levels. Blue points represent proteins with a significant (p <0.05) difference between males and females, and grey points represent proteins with no significant difference.*