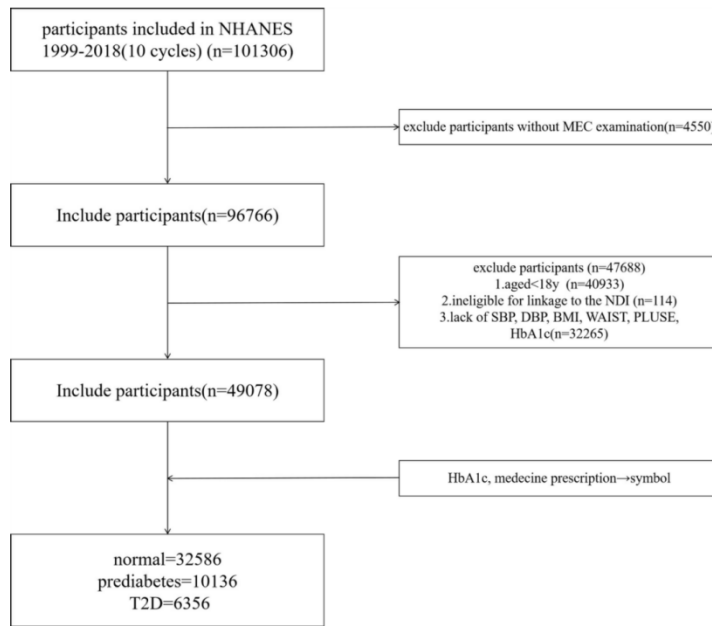
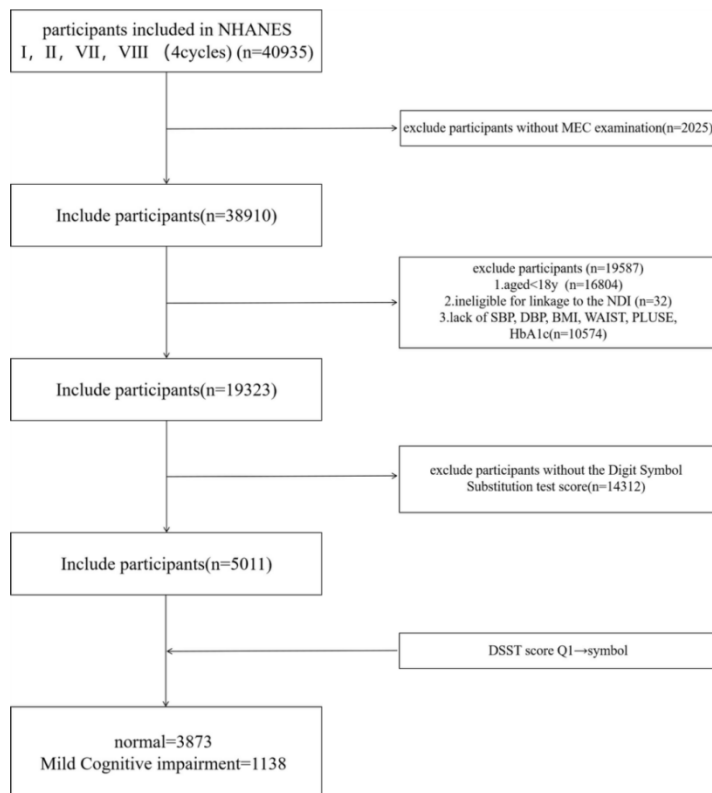
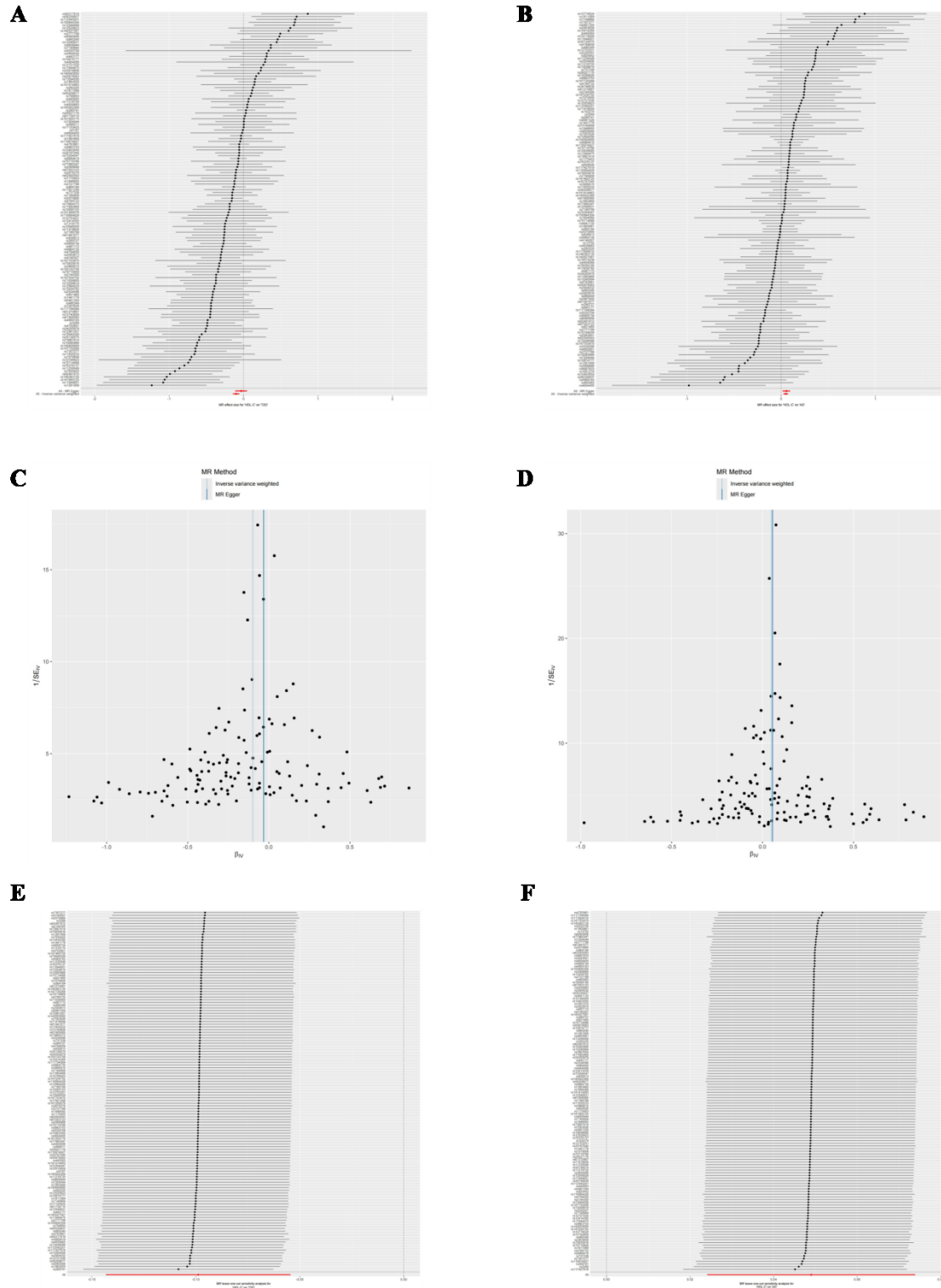


**A****B**

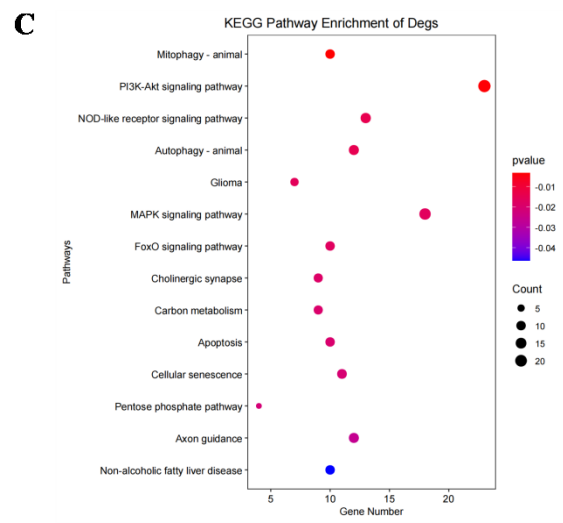
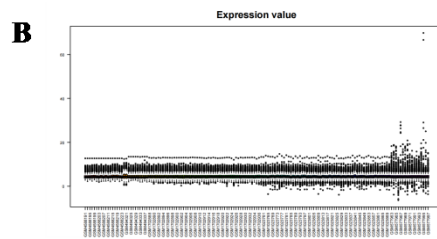
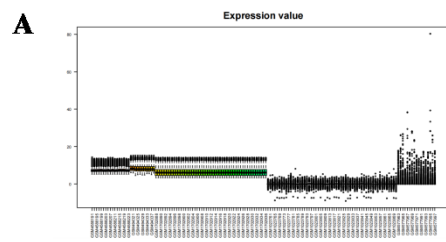
**Supplementary Figure S1.** Flow chart .The selection of eligible participants in the NHANES.

A. T2D; B.MCI

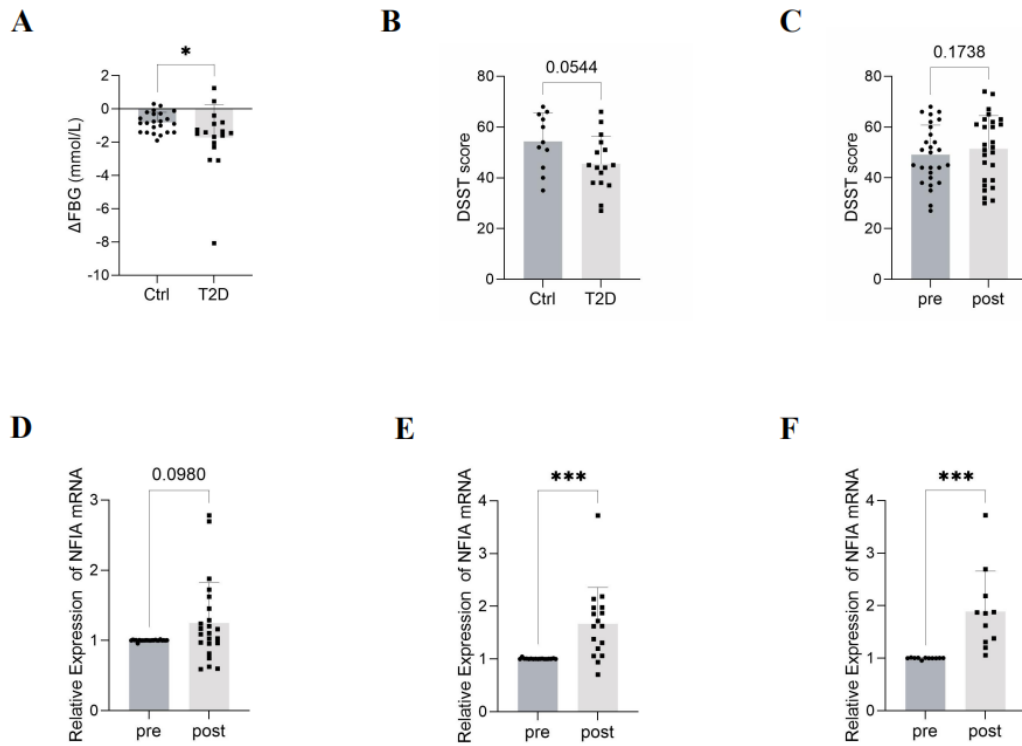


**Supplementary Figure S2.** A-B. Forest plots for MR analyses; C-D. Funnel plots for MR analyses; E-F. Plots of “leave-one-out” analyses for MR analyses.

Across all figures, Exposure: HDL-C. Outcomes: T2D in Fig. A, C, E; MCI in Fig. B, D, F.

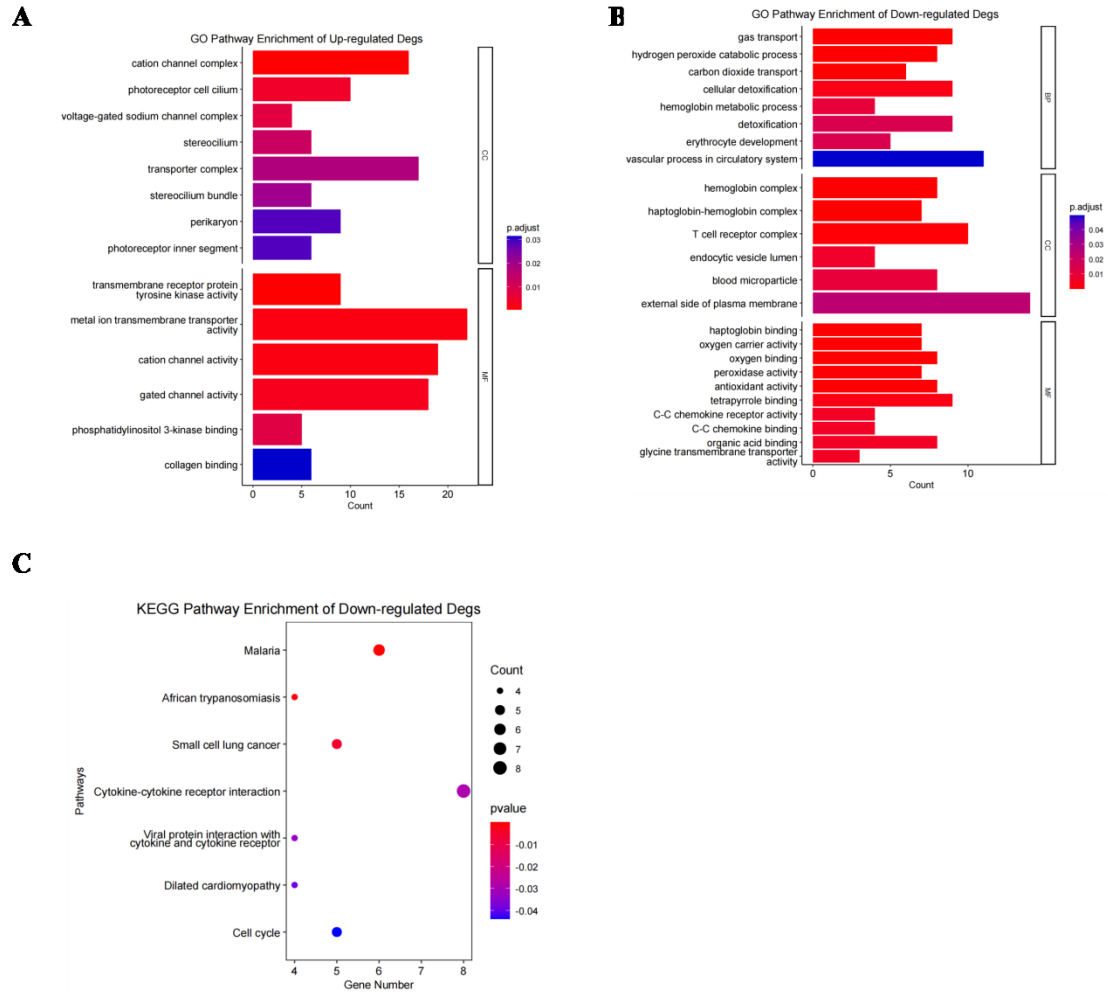


**Supplementary Figure S3.** A-B. Removal of batch effects in different datasets; C.KEGG enrichment of Degrading Genes;

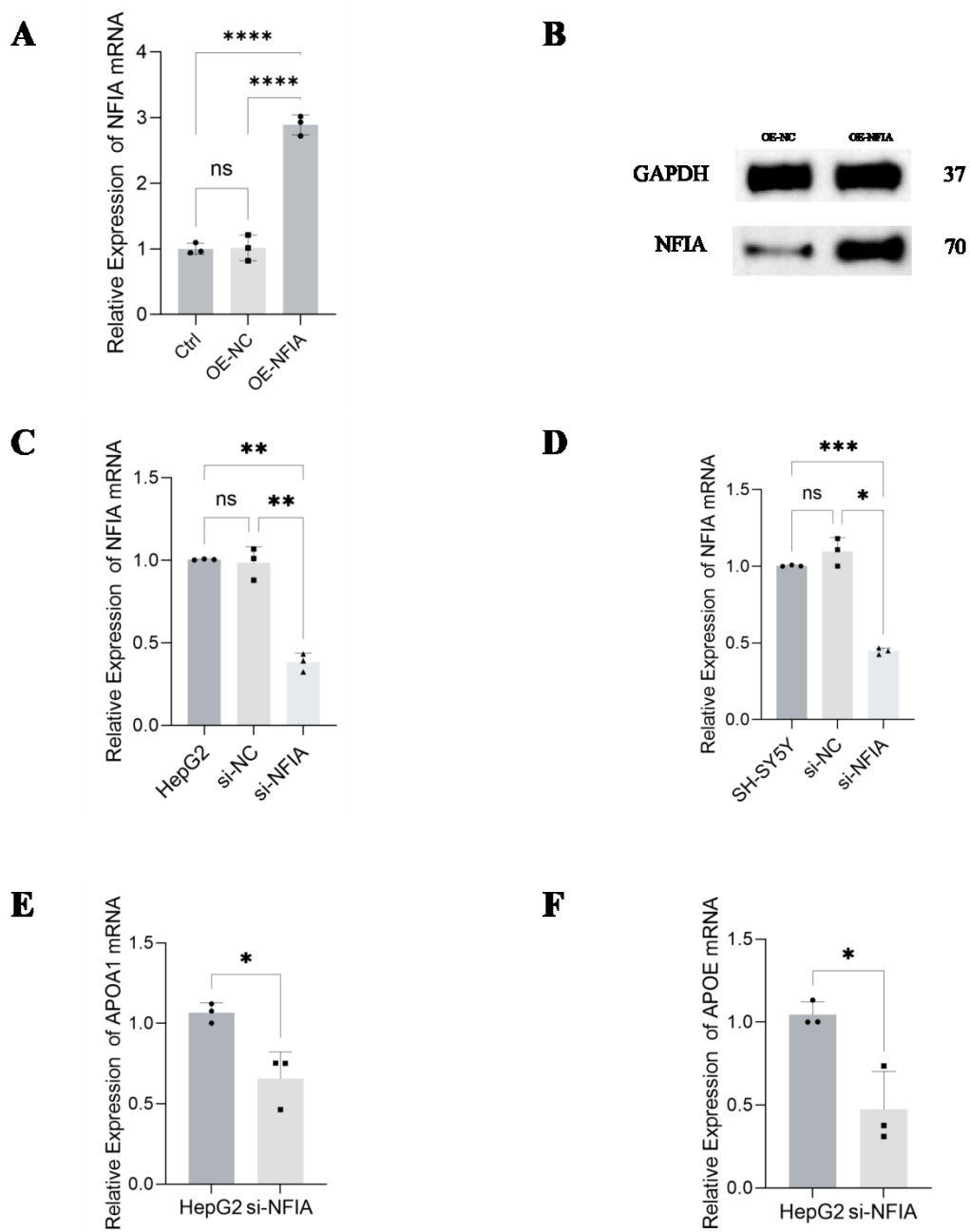


**Supplementary Figure S4.** Analysis of relevant indicators before and after Modified Fasting Therapy. A. Changes in FBG after Modified Fasting Therapy. Ctrl: n=23 , T2D: n=17 ; B. DSST scores for T2D and Ctrl groups at baseline, Ctrl: n=11, T2D: n=16; C. DSST score before and after Modified Fasting Therapy, n=27; D-F. Expression of NFIA in peripheral blood among different groups, D. Ctrl: n=23, E. T2D: n=17, F. MCI: n=11

All plots are shown as Mean  $\pm$  SD. \*p<0.05, \*\*p<0.01, \*\*\*p<0.001, \*\*\*\*p<0.0001



**Supplementary Figure S5.** A-B. GO analysis of the up / downregulated DEGs involved in MFT samples regarding biological process, cellular component, and molecular function; C. KEGG analysis of the downregulated DEGs involved in MFT samples



**Supplementary Figure S6.** A-B. q-PCR and western blot of NFIA overexpression efficiency in HepG2; C-D. q-PCR of NFIA interfering efficiency; E. q-PCR of APOA1 in HepG2; F. q-PCR of APOE in HepG2