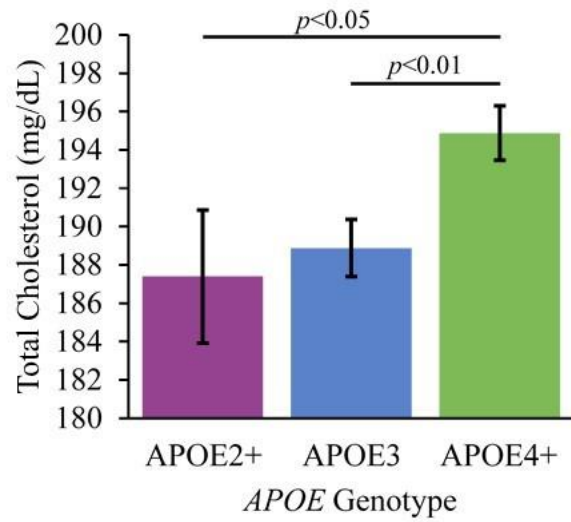


SUPPLEMENTARY MATERIAL

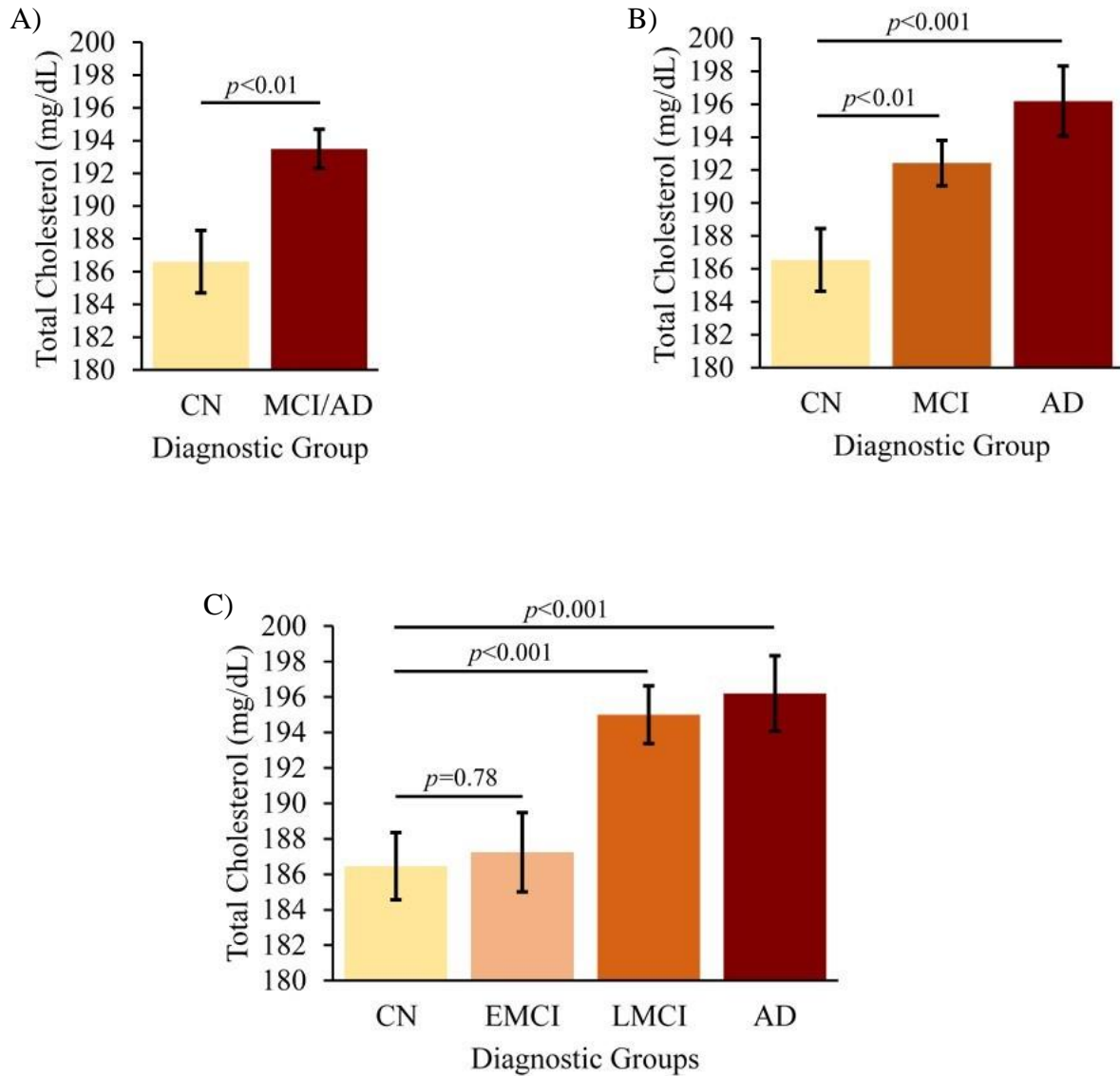
**Supplementary Table 1. Assessing possible confounding between APOE genotype and available risk factors.**

<b>Characteristic</b>	<b>APOE Genotype</b>			<b>p-value</b>
	<b>APOE2+</b>	<b>APOE3</b>	<b>APOE4+</b>	
Age (years) (M)	74.35	75.3	73.87	0.08
Female (%)	55.56	46.47	54.13	0.27
Education (M)	16.26	16.39	16.13	0.70
Body Mass Index (M)	26.94	27.37	26.07	0.04
Hypertension (%)	44.44	49.38	40.37	0.28
History of Smoking (%)	40.74	37.76	37.61	0.91

Differences in dementia risk factors between genotype groups were examined among controls (N = 404) to assess for possible confounding for MR [43]. Body Mass Index was unevenly distributed across APOE groups ( $p < 0.05$ ), indicating the potential for confounding. This variable was therefore included as a covariate in mendelian randomization analysis. M, mean.



**Supplementary Figure 1. Comparison of Total Cholesterol Levels Between APOE Genotypes.** APOE4+ carriers had significantly higher total cholesterol compared to APOE2+ and APOE3 carriers.



**Supplementary Figure 2. Comparison of Total Cholesterol Levels Between Diagnostic Groups.** A) Those with MCI or AD had significantly higher total cholesterol than the CN group. B) When treated as separate groups, AD and MCI both had significantly higher total cholesterol compared to the CN group. C) AD and late MCI, but not early MCI, groups had significantly higher total cholesterol than the CN group. CN, cognitively normal (controls); MCI, mild cognitive impairment; AD, Alzheimer’s disease; EMCI, early mild cognitive impairment; LMCI, late mild cognitive impairment.