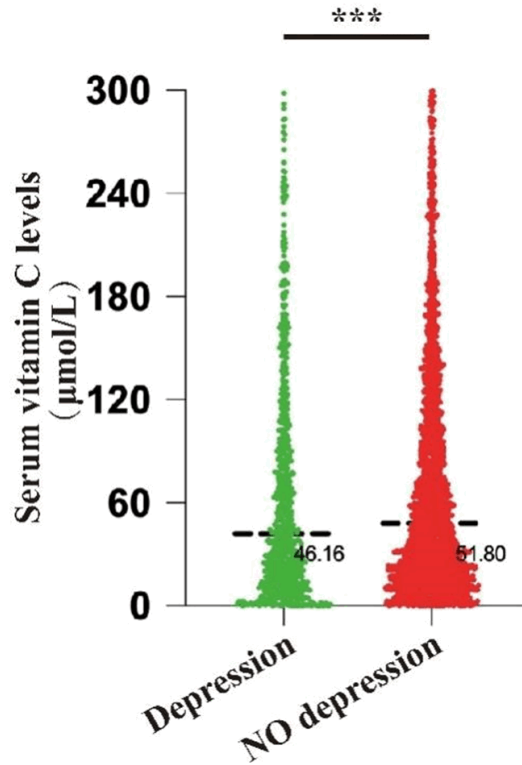


The association between vitamin C and depressive risk



**Supplementary Figure 1.** Comparison between serum vitamin C levels with depression and without depression. \*\*\*: Significance between the two groups  $P < 0.001$ .

**Supplementary Table 1.** Association between vitamin C intake and depressive risk

	Crude OR	Model 1	Model 2	Model 3	Model 4
Total	1.21 (1.03-1.41)	1.24 (1.06-1.45)	1.13 (0.96-1.33)	1.03 (0.88-1.22)	1.03 (0.87-1.21)

Figures are expressed as odds ratio (95% confidence interval). Model 1: Adjusted for gender, race and age. Model 2: Further adjusted for socioeconomic factors including education level, marital status and ratio of family income to poverty (PIR). Model 3: Further adjusted for drinking status, ever cigarette smoking and BMI. Model 4: Further adjusted for diabetes and hypertension.

## The association between vitamin C and depressive risk

**Supplementary Table 2.** Bidirectional causal association between vitamin C intake as supplement or medication and depressive risk estimated by MR

Exposure/Outcome	nSNP	IVW		MR Egger		Weighted median		Weighted mode		Simple mode		Heterogeneity p		Pleiotropy P
		OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	IVW	MR Egger	
Vitamin C supplements/Depression	23	2.42 (0.47-12.48)	0.292	3.39 (0.06-5.09)	0.558	1.57 (0.16-15.54)	0.702	1.71 (0.04-70.39)	0.781	1.71 (0.04-68.45)	0.779	0.898	0.866	0.858
Treatment vitamin C product/Depression	8	189.48 (0.13-284.22)	0.159	8596.92 (0.00-12895.38)	0.682	785.00 (0.05-1177.50)	0.175	4825.64 (0.00-7238.45)	0.301	2911.66 (0.00-4367.49)	0.356	0.385	0.286	0.86

Abbreviations: IVW, inverse-variance weighted; MR, Mendelian randomization; SNP, Single nucleotide polymorphisms.

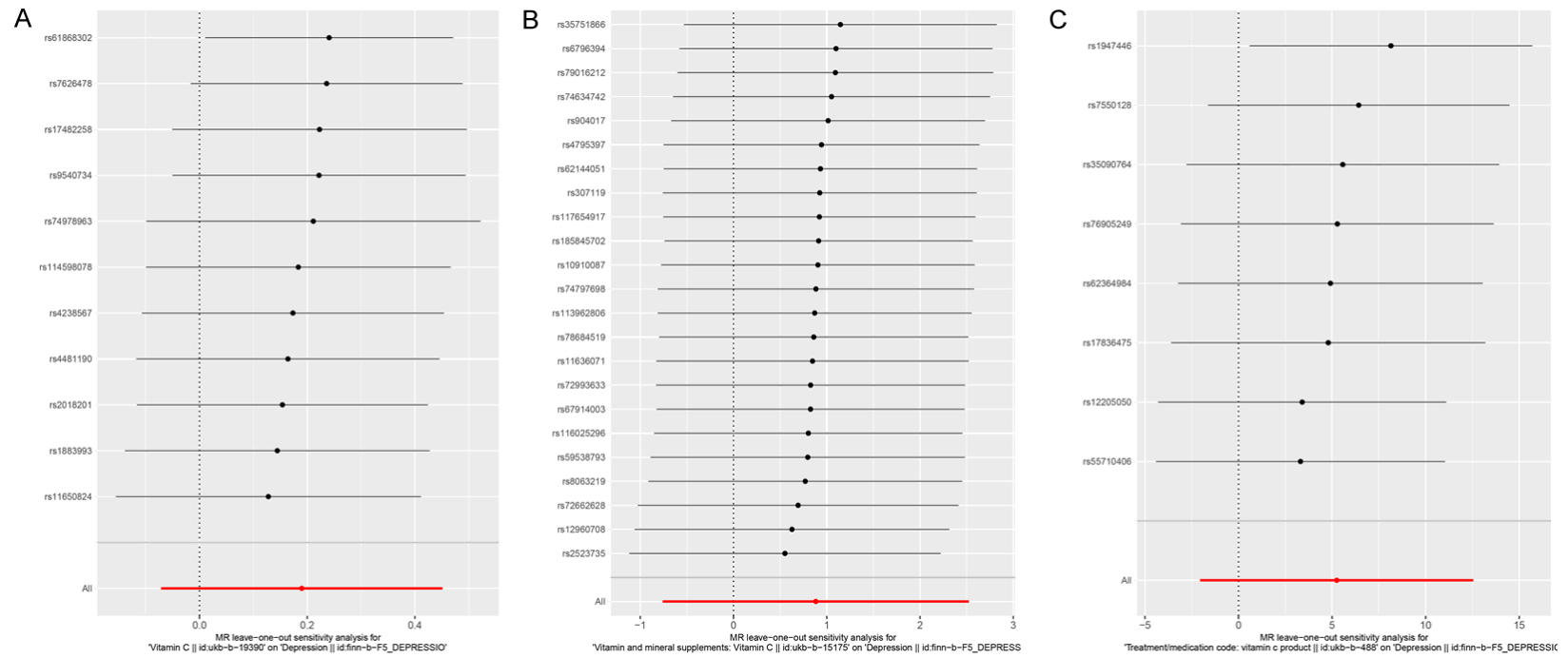
**Supplementary Table 3.** Detailed information of selected SNPs for MR analysis of the causal association between serum levels, intake as supplement or medication and depression

Exposure	Outcome	GWAS ID of exposure	GWAS ID of outcome	Sample size	SNP	$\beta$	se	P
Vitamin C	Depression	ukb-b-19390	finn-b-F5_DEPRESSIO	64979	rs9540734	-0.0259285	0.00548469	2.30E-06
Vitamin C	Depression	ukb-b-19390	finn-b-F5_DEPRESSIO	64979	rs7626478	0.0279796	0.00610134	4.50E-06
Vitamin C	Depression	ukb-b-19390	finn-b-F5_DEPRESSIO	64979	rs74978963	0.150814	0.0310213	1.20E-06
Vitamin C	Depression	ukb-b-19390	finn-b-F5_DEPRESSIO	64979	rs61868302	-0.0571013	0.0118391	1.40E-06
Vitamin C	Depression	ukb-b-19390	finn-b-F5_DEPRESSIO	64979	rs4481190	-0.0306375	0.00574377	9.60E-08
Vitamin C	Depression	ukb-b-19390	finn-b-F5_DEPRESSIO	64979	rs4238567	0.0253068	0.00550812	4.30E-06
Vitamin C	Depression	ukb-b-19390	finn-b-F5_DEPRESSIO	64979	rs2018201	-0.0808079	0.0171646	2.50E-06
Vitamin C	Depression	ukb-b-19390	finn-b-F5_DEPRESSIO	64979	rs1883993	0.044959	0.00935324	1.50E-06
Vitamin C	Depression	ukb-b-19390	finn-b-F5_DEPRESSIO	64979	rs17482258	0.042829	0.00926045	3.70E-06
Vitamin C	Depression	ukb-b-19390	finn-b-F5_DEPRESSIO	64979	rs11650824	0.0794787	0.0158822	5.60E-07
Vitamin C	Depression	ukb-b-19390	finn-b-F5_DEPRESSIO	64979	rs114598078	0.0655782	0.0137636	1.90E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs904017	0.0032693	0.00064653	4.30E-07
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs8063219	-0.0029635	0.00060466	9.50E-07
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs79016212	0.0101431	0.00217178	3.00E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs78684519	-0.0076822	0.00167051	4.30E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs74797698	0.00800637	0.00171495	3.00E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs74634742	0.00642704	0.00138683	3.60E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs72993633	0.00661841	0.0013443	8.50E-07
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs72662628	0.0112041	0.00244331	4.50E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs6796394	0.00329826	0.00071574	4.10E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs67914003	-0.0065778	0.00135111	1.10E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs62144051	-0.0047476	0.00102246	3.40E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs59538793	0.0030913	0.0006426	1.50E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs4795397	-0.0032106	0.00058687	4.50E-08

## The association between vitamin C and depressive risk

Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs35751866	0.00320121	0.00068285	2.80E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs307119	-0.0028932	0.00060273	1.60E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs2523735	-0.004176	0.00082378	4.00E-07
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs185845702	-0.0140867	0.00302992	3.30E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs12960708	-0.0034192	0.00068912	7.00E-07
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs12535840	-0.002778	0.00059741	3.30E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs117654917	0.0118145	0.00255892	3.90E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs11636071	0.00303318	0.00065744	4.00E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs116025296	0.0117469	0.00249333	2.50E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs113962806	0.00701094	0.00151217	3.50E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs10910087	0.00299287	0.00065161	4.40E-06
Vitamin and mineral supplements: Vitamin C	Depression	ukb-b-15175	finn-b-F5_DEPRESSIO	460351	rs10000324	-0.0028352	0.00059545	1.90E-06
Treatment/medication code: vitamin c product	Depression	ukb-b-488	finn-b-F5_DEPRESSIO	462933	rs76905249	0.00219608	0.00043622	4.80E-07
Treatment/medication code: vitamin c product	Depression	ukb-b-488	finn-b-F5_DEPRESSIO	462933	rs7550128	0.00181212	0.00035462	3.20E-07
Treatment/medication code: vitamin c product	Depression	ukb-b-488	finn-b-F5_DEPRESSIO	462933	rs62364984	0.00153669	0.00032936	3.10E-06
Treatment/medication code: vitamin c product	Depression	ukb-b-488	finn-b-F5_DEPRESSIO	462933	rs55710406	0.00120477	0.0002377	4.00E-07
Treatment/medication code: vitamin c product	Depression	ukb-b-488	finn-b-F5_DEPRESSIO	462933	rs35090764	0.00114641	0.00023581	1.20E-06
Treatment/medication code: vitamin c product	Depression	ukb-b-488	finn-b-F5_DEPRESSIO	462933	rs1947446	0.00120413	0.00026136	4.10E-06
Treatment/medication code: vitamin c product	Depression	ukb-b-488	finn-b-F5_DEPRESSIO	462933	rs17836475	-0.0013695	0.00028479	1.50E-06
Treatment/medication code: vitamin c product	Depression	ukb-b-488	finn-b-F5_DEPRESSIO	462933	rs12205050	0.00155101	0.00031525	8.70E-07

## The association between vitamin C and depressive risk



**Supplementary Figure 2.** Leave-one-out sensitivity analysis of individual genetic variation in these all examinations. A: Serum vitamin C levels on depressive risk; B: Supplement vitamin C on depressive risk; C: Medication vitamin C on depressive risk.