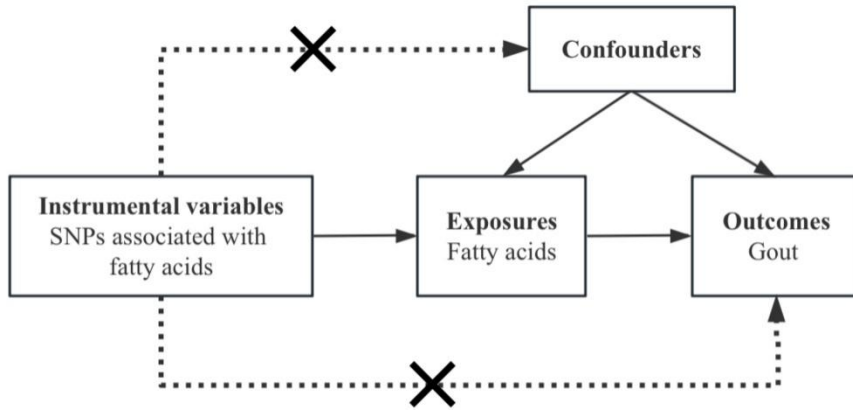
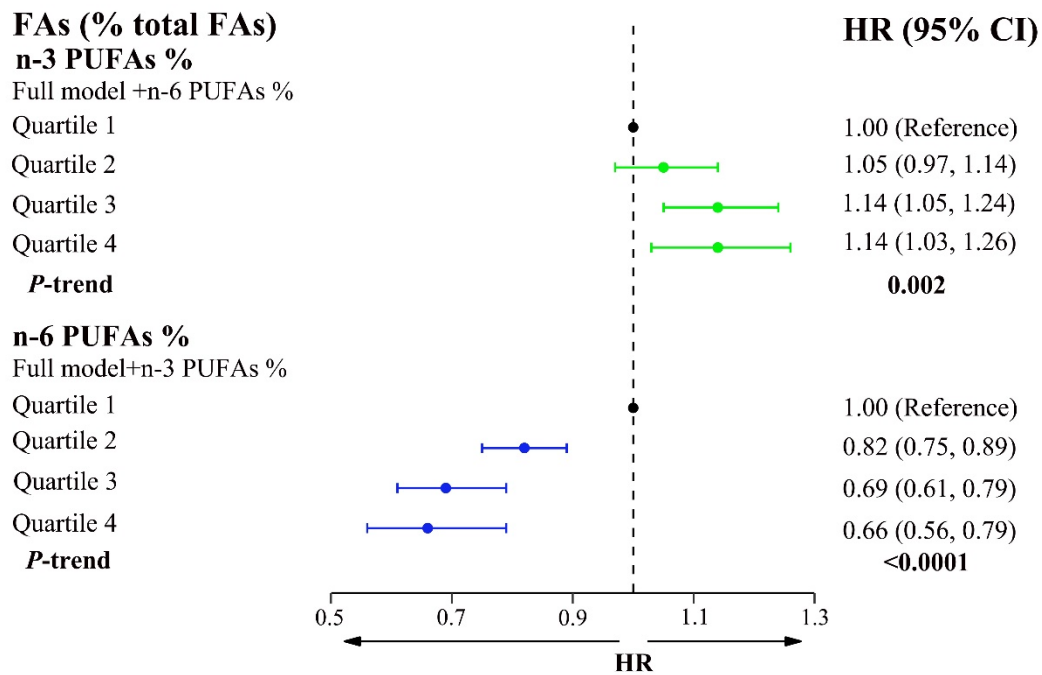


Supplementary Figure 1. Flowchart of the selection of participant selection from the UK Biobank study



Supplementary Figure 2. Conceptual framework for the Mendelian randomization analysis.

The core assumptions in an MR study, where genetic variants (i) should be robustly associated with the exposure, (ii) should be independent of any confounders of the exposure–outcome relationship, and (iii) should be associated with the outcome only via the exposure.



Supplementary Figure 3. Hazard ratios of incident gout associated with baseline plasma fatty acids (percentages in total fatty acids)

Results were adjusted for multivariable (model 1+MUFAs %+SFAs % in Table 2) and further adjusted for n-3 PUFAs % or n-6 PUFAs%

PUFAs, polyunsaturated fatty acids

Supplementary Table 1. The GWAS IDs of exposure and outcome

Exposure	GWAS IDs
Ratio of PUFA to TFA	ebi-a-GCST90092941
Ratio of MUFA to TFA	ebi-a-GCST90092929
Ratio of SFA to TFA	ebi-a-GCST90092981
Ratio of n-3 to TFA	ebi-a-GCST90092932
Ratio of n-6 to TFA	ebi-a-GCST90092935
Ratio of DHA to TFA	ebi-a-GCST90092817
Ratio of LA to TFA	ebi-a-GCST90092881
Ratio of n-6 to n-3	ebi-a-GCST90092934
Ratio of PUFA to MUFA	ebi-a-GCST90092940
Outcome	
Gout	finn-b-M13_GOUT

Never	2,646 (3.9)	2,622 (3.9)	2778 (4.1)	3734 (5.6)	2,717 (4.1)	2949 (4.4)	3164 (4.7)	2,950 (4.4)
Previous	2,687 (4.0)	2,357 (3.5)	2,090 (3.1)	2,433 (3.6)	1,763 (2.6)	2252 (3.4)	2486 (3.7)	3,066 (4.6)
Current	61,515 (91.8)	61,944 (92.4)	62,057 (92.6)	60,682 (90.5)	62,369 (93.1)	61699 (92.0)	61259 (91.4)	60,871 (90.8)
Lipid-lowering drugs, n (%)	16,236 (24.2)	11,803 (17.6)	9,260 (13.8)	8,937 (13.3)	7,470 (11.1)	9056 (13.5)	11847 (17.7)	17,863 (26.6)
Aspirin, n (%)	11,793 (17.6)	9,352 (13.9)	7,846 (11.7)	7,732 (11.5)	6,809 (10.2)	7853 (11.7)	9385 (14.0)	12,676 (18.9)
Diabetes, n (%)	7,439 (11.1)	3,763 (5.6)	2,610 (3.9)	2,486 (3.7)	1,893 (2.8)	2464 (3.7)	3956 (5.9)	7,985 (11.9)
CKD, n (%)	5,097 (7.6)	3,520 (5.2)	2,277 (3.4)	1,543 (2.3)	1,214 (1.8)	2087 (3.1)	3482 (5.2)	5,654 (8.4)

BMI, body mass index; CKD, chronic kidney disease;
Data are mean (SD) or number (%)

Supplementary Table 3. Associations of plasma fatty acids (percentages in total fatty acids) with risk of incident gout after excluding gout cases occurring in the first two years of follow-up (N=266, 204)

	Quartile for FAs %				<i>P</i> -trend
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
PUFAs %					
Events	2,100	1,113	720	492	
Model 1	1.00 (Ref.)	0.71 (0.66, 0.76)	0.58 (0.53, 0.63)	0.44 (0.40, 0.49)	<0.0001
Model 1+MUFAs % + SFAs %	1.00 (Ref.)	0.78 (0.71, 0.87)	0.70 (0.60, 0.82)	0.58 (0.47, 0.73)	<0.0001
MUFAs %					
Events	463	728	1,109	2,125	
Model 1	1.00 (Ref.)	1.23 (1.09, 1.39)	1.47 (1.32, 1.65)	2.06 (1.85, 2.30)	<0.0001
Model 1+PUFAs % + SFAs %	1.00 (Ref.)	1.08 (0.95, 1.23)	1.11 (0.96, 1.29)	1.33 (1.10, 1.59)	0.0006
SFAs %					
Events	857	907	1,021	1,640	
Model 1	1.00 (Ref.)	1.15 (1.04, 1.26)	1.22 (1.12, 1.34)	1.61 (1.48, 1.75)	<0.0001
Model 1+PUFAs % + MUFAs %	1.00 (Ref.)	1.01 (0.91, 1.12)	0.97 (0.86, 1.09)	1.11 (0.98, 1.26)	0.675
n-3 PUFAs %					
Events	1,088	1,166	1,169	1,002	
Model 1	1.00 (Ref.)	1.07 (0.99, 1.17)	1.13 (1.04, 1.23)	1.10 (1.00, 1.20)	<0.0001
Model 1+MUFAs % + SFAs %	1.00 (Ref.)	1.10 (1.01, 1.20)	1.20 (1.10, 1.31)	1.31 (1.19, 1.43)	<0.0001
DHAs %					
Events	1,546	1,164	929	786	
Model 1	1.00 (Ref.)	0.92 (0.86, 1.00)	0.85 (0.78, 0.92)	0.80 (0.73, 0.88)	0.0015
Model 1+MUFAs % + SFAs %	1.00 (Ref.)	1.12 (1.03, 1.21)	1.18 (1.08, 1.30)	1.34 (1.20, 1.49)	<0.0001
n-6 PUFAs %					
Events	2,099	1,115	699	512	
Model 1	1.00 (Ref.)	0.71 (0.66, 0.76)	0.55 (0.50, 0.60)	0.45 (0.41, 0.50)	<0.0001
Model 1+MUFAs % + SFAs %	1.00 (Ref.)	0.78 (0.71, 0.85)	0.65 (0.58, 0.74)	0.58 (0.49, 0.68)	<0.0001

LAs %					
Events	2,166	1,112	689	458	
Model 1	1.00 (Ref.)	0.72 (0.66, 0.77)	0.55 (0.50, 0.60)	0.43 (0.39, 0.48)	<0.0001
Model 1+MUFAs %+SFAs %	1.00 (Ref.)	0.79 (0.73, 0.86)	0.65 (0.58, 0.72)	0.55 (0.48, 0.62)	<0.0001
PUFAs/MUFAs ratio					
Events	2,148	1,109	703	465	
Model 1	1.00 (Ref.)	0.70 (0.65, 0.75)	0.56 (0.52, 0.62)	0.46 (0.41, 0.51)	<0.0001
n-6/n-3 PUFAs ratio					
Events	1,323	1,175	1,041	886	
Model 1	1.00 (Ref.)	0.86 (0.80, 0.93)	0.78 (0.72, 0.84)	0.69 (0.64, 0.76)	<0.0001

DHAs, docosahexaenoic acids; LAs, linoleic acids; MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated fatty acids; SFAs, saturated fatty acids.

Model 1 was adjusted for age (years), sex (male, female), race/ethnicity (White, Asian or Asian British, Black or Black British, Mixed), social deprivation score (in quintiles), BMI (kg/m²), smoking status (never, former, current), alcohol consumption (never, former, current), use of lipid-lowering medication (yes, no) and aspirin (yes, no), and history of diabetes (yes, no) and chronic kidney disease (yes, no) at baseline.

Supplementary Table 4. Associations of plasma fatty acids (percentages in total fatty acids) with risk of incident gout after excluding participants with extreme BMI (<18.5 or >40 kg/m²) (N=261,792)

	Quartile for FAs %				<i>P</i> -trend
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
PUFAs %					
Events	2,323	1,225	781	541	
Model 1	1.00 (Ref.)	0.71 (0.66, 0.76)	0.57 (0.53, 0.62)	0.44 (0.40, 0.49)	<0.0001
Model 1+MUFAs %+SFAs %	1.00 (Ref.)	0.79 (0.72, 0.87)	0.71 (0.61, 0.82)	0.61 (0.49, 0.75)	<0.0001
MUFAs %					

Events	498	795	1,229	2,348	
Model 1	1.00 (Ref.)	1.24 (1.11, 1.39)	1.49 (1.34, 1.66)	2.09 (1.88, 2.31)	<0.0001
Model 1+PUFAs % + SFAs %	1.00 (Ref.)	1.10 (0.97, 1.24)	1.15 (0.99, 1.33)	1.38 (1.16, 1.64)	<0.0001
SFAs %					
Events	958	985	1,084	1,843	
Model 1	1.00 (Ref.)	1.12 (1.02, 1.22)	1.16 (1.06, 1.26)	1.59 (1.46, 1.72)	<0.0001
Model 1+PUFAs % + MUFAs %	1.00 (Ref.)	0.99 (0.90, 1.09)	0.92 (0.82, 1.03)	1.10 (0.98, 1.24)	0.054
n-3 PUFAs %					
Events	1,196	1,273	1,302	1,099	
Model 1	1.00 (Ref.)	1.06 (0.98, 1.14)	1.14 (1.05, 1.23)	1.09 (1.00, 1.19)	0.013
Model 1+MUFAs % + SFAs %	1.00 (Ref.)	1.08 (1.00, 1.17)	1.21 (1.12, 1.31)	1.30 (1.19, 1.42)	<0.0001
DHAs %					
Events	1,726	1,245	1,039	860	
Model 1	1.00 (Ref.)	0.89 (0.82, 0.96)	0.86 (0.79, 0.93)	0.79 (0.73, 0.86)	<0.0001
Model 1+MUFAs % + SFAs %	1.00 (Ref.)	1.07 (0.99, 1.15)	1.19 (1.09, 1.30)	1.32 (1.20, 1.47)	<0.0001
n-6 PUFAs %					
Events	2,327	1,227	745	571	
Model 1	1.00 (Ref.)	0.71 (0.66, 0.76)	0.53 (0.49, 0.58)	0.46 (0.42, 0.51)	<0.0001
Model 1+MUFAs % + SFAs %	1.00 (Ref.)	0.78 (0.72, 0.85)	0.63 (0.56, 0.71)	0.59 (0.51, 0.69)	<0.0001
LAs %					
Events	2,386	1,222	750	512	
Model 1	1.00 (Ref.)	0.71 (0.66, 0.77)	0.54 (0.50, 0.59)	0.44 (0.40, 0.49)	<0.0001
Model 1+MUFAs % + SFAs %	1.00 (Ref.)	0.79 (0.73, 0.85)	0.64 (0.58, 0.70)	0.55 (0.49, 0.63)	<0.0001
PUFAs/MUFAs ratio					
Events	2,371	1,228	767	504	
Model 1	1.00 (Ref.)	0.70 (0.65, 0.75)	0.56 (0.52, 0.61)	0.46 (0.41, 0.51)	<0.0001
n-6/n-3 PUFAs ratio					
Events	1,446	1,328	1,138	958	
Model 1	1.00 (Ref.)	0.89 (0.83, 0.96)	0.78 (0.72, 0.84)	0.69 (0.64, 0.75)	<0.0001

DHAs, docosahexaenoic acids; LAs, linoleic acids; MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated fatty acids; SFAs, saturated fatty acids.

Model 1 was adjusted for age (years), sex (male, female), race/ethnicity (White, Asian or Asian British, Black or Black British, Mixed), social deprivation score (in quintiles), BMI (kg/m²), smoking status (never, former, current), alcohol consumption (never, former, current), use of lipid-lowering medication (yes, no) and aspirin (yes, no), and history of diabetes (yes, no) and chronic kidney disease (yes, no) at baseline.

Supplementary Table 5. Associations of plasma fatty acids (percentages in total fatty acids) with risk of incident gout when further adjusted for physical activity, history of cardiovascular disease and diet score

	Quartile for FAs %				<i>P</i> -trend
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
PUFAs %					
Events	2,425	1,300	818	563	
Model 1+MUFAs %+SFAs %	1.00 (Ref.)	0.81 (0.74, 0.89)	0.72 (0.63, 0.84)	0.62 (0.51, 0.76)	<0.0001
MUFAs %					
Events	519	832	1,291	2,464	
Model 1+PUFAs %+SFAs %	1.00 (Ref.)	1.11 (0.99, 1.26)	1.19 (1.03, 1.37)	1.43 (1.21, 1.70)	<0.0001
SFAs %					
Events	993	1,045	1,157	1,911	
Model 1+PUFAs %+MUFAs %	1.00 (Ref.)	1.01 (0.92, 1.11)	0.96 (0.86, 1.07)	1.13 (1.01, 1.27)	0.020
n-3 PUFAs %					
Events	1,254	1,338	1,368	1,146	
Model 1+MUFAs %+SFAs %	1.00 (Ref.)	1.10 (1.02, 1.19)	1.24 (1.15, 1.34)	1.34 (1.23, 1.47)	<0.0001
DHAs %					
Events	1,806	1,322	1,085	893	
Model 1+MUFAs %+SFAs %	1.00 (Ref.)	1.10 (1.02, 1.18)	1.21 (1.11, 1.32)	1.36 (1.23, 1.51)	<0.0001
n-6 PUFAs %					

Events	2,436	1,294	785	591	
Model 1+MUFAs %+SFAs %	1.00 (Ref.)	0.77 (0.71, 0.84)	0.62 (0.56, 0.70)	0.57 (0.49, 0.66)	<0.0001
LAs %					
Events	2,509	1,283	786	528	
Model 1+MUFAs %+SFAs %	1.00 (Ref.)	0.79 (0.73, 0.85)	0.64 (0.58, 0.70)	0.54 (0.48, 0.62)	<0.0001
PUFAs/MUFAs ratio					
Events	2,482	1,301	800	523	
Model 1	1.00 (Ref.)	0.70 (0.66, 0.75)	0.55 (0.51, 0.60)	0.44 (0.40, 0.49)	<0.0001
n-6/n-3 PUFAs ratio					
Events	1,515	1,393	1,194	1,004	
Model 1	1.00 (Ref.)	0.87 (0.81, 0.93)	0.75 (0.69, 0.81)	0.65 (0.60, 0.71)	<0.0001

Model 1 was adjusted for age (years), sex (male, female), race/ethnicity (White, Asian or Asian British, Black or Black British, Mixed), social deprivation score (in quintiles), BMI (kg/m²), diet quality score, physical activity (in quartiles), smoking status (never, former, current), alcohol consumption (never, former, current), use of lipid-lowering medication (yes, no) and aspirin (yes, no), and history of diabetes (yes, no), cardiovascular disease (yes, no) and chronic kidney disease (yes, no) at baseline.

