

Supplementary Table SI. Projected age-specific rates (per 100,000) and percentage changes for DALYs and Deaths of Rheumatoid Arthritis attributable to smoking in China, 2023–2035

Age Group	Sex	DALY Rate 2023	DALY Rate 2035 (95% CI)	Change (%)	Death Rate 2023	Death Rate 2035 (95% CI)	Change (%)
30-34	Both	2.56	2.56 (1.46–4.34)	0.03%	0.0018	0.0009 (0.00–0.00)	-50.0%
	Male	4.32	4.41 (3.02–5.79)	1.98%	0.0031	0.0016 (0.00–0.00)	-49.64%
	Female	0.36	0.33 (0.18–0.49)	-8.25%	0.0002	0.0001 (0.00–0.00)	-47.72%
35-39	Both	3.42	3.26 (2.69–3.84)	-2.31%	0.0030	0.0016 (0.00–0.00)	-46.7%
	Male	6.10	6.04 (4.79–7.29)	-0.97%	0.0055	0.0027 (0.00–0.00)	-51.41%
	Female	0.51	0.46 (0.31–0.61)	-9.34%	0.0004	0.0002 (0.00–0.00)	-50.53%
40-44	Both	4.88	4.64 (4.09–5.19)	2.23%	0.0069	0.0033 (0.00–0.00)	-52.2%
	Male	7.90	8.15 (6.99–9.30)	3.15%	0.0115	0.0055 (0.00–0.01)	-52.52%
	Female	1.04	0.96 (0.74–1.19)	-7.49%	0.0010	0.0005 (0.00–0.00)	-52.71%
45-49	Both	6.21	5.94 (5.32–6.56)	1.23%	0.0149	0.0071 (0.00–0.01)	-52.3%
	Male	10.32	10.42 (9.11–11.73)	0.96%	0.0235	0.0112 (0.01–0.02)	-52.40%
	Female	1.26	1.20 (0.97–1.43)	-4.87%	0.0023	0.0011 (0.00–0.00)	-53.75%
50-54	Both	7.94	7.72 (6.92–8.52)	-1.07%	0.0268	0.0134 (0.01–0.02)	-50.0%
	Male	13.59	13.12 (11.49–14.76)	-3.40%	0.0455	0.0228 (0.02–0.03)	-49.88%
	Female	1.88	2.02 (1.64–2.39)	7.07%	0.0055	0.0026 (0.00–0.00)	-53.20%
55-59	Both	9.42	9.15 (8.20–10.09)	-1.64%	0.0435	0.0242 (0.02–0.03)	-44.4%
	Male	15.74	15.31 (13.41–17.21)	-2.76%	0.0784	0.0435 (0.03–0.05)	-44.43%
	Female	2.88	2.75 (2.24–3.26)	-4.67%	0.0122	0.0061 (0.00–0.01)	-50.35%
60-64	Both	11.24	11.05 (9.91–12.18)	-1.49%	0.0848	0.0534 (0.04–0.07)	-37.0%
	Male	18.96	18.74 (16.41–21.06)	-1.17%	0.1480	0.0932 (0.07–0.11)	-37.01%
	Female	3.51	3.27 (2.67–3.87)	-6.78%	0.0242	0.0133 (0.01–0.02)	-45.08%
65-69	Both	12.87	12.73 (11.42–14.04)	-1.09%	0.1350	0.0855 (0.06–0.11)	-36.7%
	Male	21.74	21.83 (19.13–24.54)	0.45%	0.2398	0.1653 (0.13–0.20)	-31.08%
	Female	4.32	3.89 (3.17–4.60)	-10.07%	0.0432	0.0262 (0.02–0.03)	-39.41%
70-74	Both	12.87	12.62 (11.33–13.92)	-7.04%	0.1925	0.1319 (0.09–0.17)	-31.5%
	Male	23.97	22.05 (19.32–24.78)	-8.00%	0.3546	0.2430 (0.19–0.30)	-31.47%

Age Group	Sex	DALY Rate 2023	DALY Rate 2035 (95% CI)	Change (%)	Death Rate 2023	Death Rate 2035 (95% CI)	Change (%)
75-79	Female	4.13	3.80 (3.10–4.49)	-8.10%	0.0664	0.0428 (0.03–0.05)	-35.53%
	Both	13.79	12.29 (11.02–13.55)	-12.18%	0.3059	0.2173 (0.15–0.28)	-28.9%
	Male	25.51	22.87 (20.04–25.71)	-10.33%	0.5515	0.3601 (0.28–0.44)	-34.70%
80-84	Female	3.98	3.21 (2.62–3.80)	-19.36%	0.0955	0.0616 (0.05–0.07)	-35.52%
	Both	13.01	11.04 (9.90–12.18)	-18.62%	0.4316	0.2772 (0.20–0.35)	-35.8%
	Male	24.73	21.50 (18.83–24.17)	-13.07%	0.7702	0.4911 (0.39–0.60)	-36.24%
85-89	Female	4.61	3.21 (2.62–3.80)	-30.41%	0.1509	0.0937 (0.08–0.11)	-37.94%
	Both	12.06	11.18 (10.03–12.34)	-19.02%	0.5950	0.4652 (0.34–0.59)	-21.8%
	Male	28.07	24.66 (21.58–27.74)	-12.16%	1.3167	0.8317 (0.65–1.01)	-36.83%
90-94	Female	4.38	3.18 (2.59–3.78)	-27.32%	0.2275	0.1411 (0.12–0.17)	-37.96%
	Both	7.82	9.00 (8.04–9.95)	0.97%	0.4919	0.4919 (0.20–0.84)	0.00%
	Male	23.35	20.81 (18.14–23.49)	-10.88%	1.5257	0.9671 (0.74–1.20)	-36.61%
95+	Female	4.52	3.40 (2.76–4.05)	-24.68%	0.3297	0.2170 (0.17–0.26)	-34.19%
	Both	3.65	6.99 (6.11–7.87)	-14.04%	0.3136	0.2078 (0.11–0.31)	-33.7%
	Male	16.59	14.08 (11.69–16.47)	-15.11%	1.5706	1.0411 (0.66–1.42)	-33.71%
	Female	5.00	4.00 (3.16–4.84)	-19.95%	0.4608	0.3332 (0.24–0.43)	-27.69%

Supplementary Table SII. Summary of MR results for the analysis (Smoking on RA)

Method	No. of SNPs	OR (95% CI)	Pval
MR Egger	117	1.77 (0.48-6.51)	0.390
Weighted median	117	1.65 (1.07-2.54)	0.021
Inverse variance weighted	117	1.63 (1.20-2.21)	0.002
Simple mode	117	2.75 (0.91-8.30)	0.075
Weighted mode	117	1.45 (0.59-3.55)	0.419

CI, confidence interval; MR, Mendelian randomization; OR, odds ratio; SNP, single-nucleotide polymorphism. The analysis assessed the causal effect of genetic liability to rheumatoid arthritis (exposure) on smoking status (outcome). The Inverse Variance Weighted (IVW) method serves as the primary analysis.

Supplementary Table SIII. Summary of MR results for the reverse analysis (RA on Smoking), including sensitivity analyses

Method	No. of SNPs	OR (95% CI)	P-value
Inverse Variance Weighted	20	1.00 (0.99–1.01)	0.414
MR Egger	20	0.99 (0.98–1.00)	0.110
Weighted Median	20	1.00 (0.99–1.00)	0.266
Simple Mode	20	1.00 (0.98–1.02)	0.886
Weighted Mode	20	1.00 (0.99–1.00)	0.375

CI, confidence interval; MR, Mendelian randomization; OR, odds ratio; SNP, single-nucleotide polymorphism. The analysis assessed the causal effect of genetic liability to rheumatoid arthritis (exposure) on smoking status (outcome). The Inverse Variance Weighted (IVW) method serves as the primary analysis.

Supplementary Table SIV. Binding energies of Riboflavine with core targets associated with smoking and rheumatoid arthritis.

Target	UniProt ID	Binding Energy (kcal/mol)	Binding Energy (kJ/mol)	Ki (Dissociation Constant, μ M)
MTHFR	P42898	-7.9	-33.07	1.6
TP53	P04637	-7.5	-31.39	3.14
IL1B	P01584	-6.5	-27.21	16.99
TNF	P01375	-6.3	-26.37	23.82
IL6	P05231	-6.1	-25.53	33.4
CXCL8	P10145	-5.5	-23.02	92.04