

SUPPLEMENTARY MATERIAL

Associations of light smoking with serum carcinoembryonic antigen and relative leukocyte telomere length in men with asthma

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Supplementary Table 1. Expanded full-cohort models for the associations of light smoking with serum CEA and relative leukocyte telomere length

Outcome	Term or model contrast	N	β (95% CI)	Adjusted ratio (95% CI)	p value
CEA	Alcohol use	150	0.009 (−0.090 to 0.108)	1.021 (0.813 to 1.281)	0.859
CEA	Metabolic syndrome	150	−0.030 (−0.108 to 0.049)	0.934 (0.780 to 1.119)	0.457
CEA	Asthma×smoking interaction	150	0.024 (−0.059 to 0.107)	1.057 (0.873 to 1.279)	0.566
CEA	Smoking association among healthy participants	150	0.047 (−0.005 to 0.098)	1.113 (0.989 to 1.254)	0.075
CEA	Smoking association among participants with asthma	150	0.071 (0.005 to 0.137)	1.177 (1.011 to 1.370)	0.035
RTL	Alcohol use	148	−0.110 (−0.400 to 0.180)	0.776 (0.398 to 1.515)	0.458
RTL	Metabolic syndrome	148	0.072 (−0.452 to 0.595)	1.179 (0.353 to 3.935)	0.789
RTL	Asthma×smoking interaction	148	−0.267 (−0.969 to 0.435)	0.540 (0.107 to 2.723)	0.456
RTL	Smoking association among healthy participants	148	−0.083 (−0.750 to 0.585)	0.827 (0.178 to 3.843)	0.808
RTL	Smoking association among participants with asthma	148	−0.350 (−0.591 to −0.109)	0.447 (0.256 to 0.779)	0.004

Note. Expanded full-cohort models included age, asthma status, light-smoking status, the asthma×smoking interaction, alcohol use, and derived metabolic syndrome. Healthy nonsmokers were the reference group. CEA was analysed after $\log_{10}$ transformation using ordinary least-squares regression with HC3 robust standard errors. RTL was analysed using median regression with 2,000 bootstrap replicates stratified by asthma–smoking group. Adjusted ratios were calculated as 10^{β} and represent geometric-mean ratios for CEA and conditional-median ratios for RTL. The asthma-specific smoking contrast combines the smoking and asthma×smoking coefficients. Confidence intervals are 95%, and all p values are two-sided.

Abbreviations: β , regression coefficient; CEA, carcinoembryonic antigen; CI, confidence interval; HC3, heteroscedasticity-consistent covariance estimator type 3; RTL, relative leukocyte telomere length.

Supplementary Table 2. Complete-data unadjusted comparisons of serum CEA and relative leukocyte telomere length across study groups

Outcome	Analysis	N	Omnibus comparison	Omnibus p value	Key pairwise comparison	Adjusted pairwise p value
CEA	Complete-data sensitivity	156	Kruskal–Wallis $H(3)=13.740$	0.003	Asthmatic light smokers vs healthy nonsmokers	0.001
RTL	Complete-data sensitivity	155	Welch ANOVA $F(3,70.258)=0.962$	0.416	—	—
RTL	Additional rank-based complete-data analysis	155	Kruskal–Wallis $H(3)=7.852$	0.049	Asthmatic light smokers vs asthmatic nonsmokers	0.048

Note. Complete-data analyses included all available observations without Tukey outlier exclusion. CEA pairwise comparisons and the additional rank-based RTL pairwise comparisons used Dunn tests with Bonferroni adjustment. The Welch ANOVA result did not support post hoc pairwise testing. All p values are two-sided.

Abbreviations: ANOVA, analysis of variance; CEA, carcinoembryonic antigen; RTL, relative leukocyte telomere length.

Supplementary Table 3. Complete-data multivariable sensitivity analyses

Supplementary Table S3A. Complete-data full-cohort base models

Outcome	Term or model contrast	N	β (95% CI)	Adjusted ratio (95% CI)	p value
CEA	Age, centered	156	0.002 (−0.000 to 0.005)	1.005 (0.999 to 1.011)	0.089
CEA	Asthma status	156	0.023 (−0.041 to 0.088)	1.055 (0.909 to 1.224)	0.481
CEA	Smoking association among healthy participants	156	0.075 (0.015 to 0.134)	1.187 (1.036 to 1.361)	0.014
CEA	Asthma×smoking interaction	156	0.029 (−0.066 to 0.125)	1.070 (0.858 to 1.334)	0.546
CEA	Smoking association among participants with asthma	156	0.104 (0.029 to 0.179)	1.271 (1.069 to 1.509)	0.007
RTL	Age, per year	155	0.002 (−0.005 to 0.010)	1.005 (0.988 to 1.022)	0.579
RTL	Asthma status	155	0.160 (−0.499 to 0.818)	1.444 (0.317 to 6.584)	0.635
RTL	Smoking association among healthy participants	155	−0.102 (−0.752 to 0.548)	0.791 (0.177 to 3.533)	0.759
RTL	Asthma×smoking interaction	155	−0.271 (−0.969 to 0.427)	0.536 (0.107 to 2.674)	0.447
RTL	Smoking association among participants with asthma	155	−0.373 (−0.620 to −0.126)	0.424 (0.240 to 0.749)	0.003

Note. Base models included age, asthma status, light-smoking status, and the asthma×smoking interaction. Healthy nonsmokers were the reference group. CEA was analysed using log₁₀-transformed ordinary least-squares regression with HC3 robust standard errors. RTL was analysed using median regression with 1,000 bootstrap replicates stratified by asthma–smoking group. The smoking coefficient equals the smoking contrast among healthy participants and is therefore shown once. Adjusted ratios were calculated as 10^β. Confidence intervals are 95%, and all p values are two-sided.

Supplementary Table S3B. Complete-data expanded full-cohort models

Outcome	Term or model contrast	N	β (95% CI)	Adjusted ratio (95% CI)	p value
CEA	Alcohol use	156	−0.014 (−0.122 to 0.094)	0.968 (0.755 to 1.242)	0.796
CEA	Metabolic syndrome	156	−0.050 (−0.136 to 0.036)	0.890 (0.731 to 1.085)	0.248
CEA	Asthma×smoking interaction	156	0.032 (−0.065 to 0.130)	1.077 (0.861 to 1.348)	0.511
CEA	Smoking association among healthy participants	156	0.075 (0.015 to 0.135)	1.188 (1.035 to 1.363)	0.015
CEA	Smoking association among participants with asthma	156	0.107 (0.030 to 0.184)	1.280 (1.072 to 1.527)	0.007
RTL	Alcohol use	155	−0.067 (−0.347 to 0.213)	0.857 (0.450 to 1.635)	0.640
RTL	Metabolic syndrome	155	0.064 (−0.487 to 0.616)	1.160 (0.326 to 4.130)	0.819
RTL	Asthma×smoking interaction	155	−0.254 (−0.960 to 0.451)	0.557 (0.110 to 2.826)	0.480
RTL	Smoking association among healthy participants	155	−0.085 (−0.766 to 0.595)	0.821 (0.171 to 3.940)	0.806
RTL	Smoking association among participants with asthma	155	−0.340 (−0.586 to −0.094)	0.457 (0.259 to 0.806)	0.007

Note. Expanded models included age, asthma status, light-smoking status, the asthma×smoking interaction, alcohol use, and derived metabolic syndrome. Healthy nonsmokers were the reference group. CEA was analysed using log₁₀-transformed ordinary least-squares regression with HC3 robust standard errors. RTL was analysed using median regression with 1,000 bootstrap replicates stratified by asthma–smoking group. Adjusted ratios were calculated as 10^β. Confidence intervals are 95%, and all p values are two-sided.

Supplementary Table S3C. Complete-data asthma-only models

Outcome	Adjustment model	N	Smoking β (95% CI)	Adjusted ratio (95% CI)	p value
CEA	Age + asthma severity	73	0.100 (0.022 to 0.178)	1.259 (1.053 to 1.506)	0.012
CEA	Age + severity + alcohol + waist circumference + blood pressure	73	0.097 (0.010 to 0.184)	1.250 (1.022 to 1.529)	0.030
RTL	Age + asthma severity	73	−0.250 (−0.534 to 0.034)	0.562 (0.292 to 1.082)	0.085
RTL	Age + severity + alcohol + waist circumference + blood pressure	73	−0.382 (−0.708 to −0.056)	0.415 (0.196 to 0.879)	0.022

Note. Analyses were restricted to participants with asthma and included all available outcome observations. The expanded model additionally included alcohol use, waist circumference ≥ 102 cm, and elevated blood pressure. CEA was analysed using $\log_{10}$ -transformed ordinary least-squares regression with HC3 robust standard errors. RTL was analysed using median regression with 1,000 bootstrap replicates stratified by smoking status. Ratios compare light smokers with nonsmokers. Confidence intervals are 95%, and all p values are two-sided.

Abbreviations for Supplementary Table S3: β , regression coefficient; CEA, carcinoembryonic antigen; CI, confidence interval; HC3, heteroscedasticity-consistent covariance estimator type 3; RTL, relative leukocyte telomere length.

Supplementary Table 4. Sensitivity analyses restricted to participants aged 35–50 years**Supplementary Table S4A. Age-restricted full-cohort models**

Outcome	Term or model contrast	N	β (95% CI)	Adjusted ratio (95% CI)	p value
CEA	Age, centered	113	0.002 (−0.004 to 0.007)	1.004 (0.992 to 1.016)	0.556
CEA	Asthma status	113	0.049 (−0.029 to 0.127)	1.119 (0.936 to 1.339)	0.215
CEA	Smoking association among healthy participants	113	0.047 (−0.005 to 0.098)	1.114 (0.990 to 1.253)	0.074
CEA	Asthmaxsmoking interaction	113	0.017 (−0.080 to 0.114)	1.040 (0.832 to 1.299)	0.731
CEA	Smoking association among participants with asthma	113	0.064 (−0.019 to 0.146)	1.158 (0.958 to 1.399)	0.129
RTL	Age, per year	111	−0.014 (−0.048 to 0.020)	0.969 (0.896 to 1.048)	0.430
RTL	Asthma status	111	0.097 (−0.562 to 0.756)	1.250 (0.274 to 5.698)	0.773
RTL	Smoking association among healthy participants	111	−0.021 (−0.644 to 0.602)	0.953 (0.227 to 4.002)	0.947
RTL	Asthmaxsmoking interaction	111	−0.169 (−0.924 to 0.586)	0.678 (0.119 to 3.854)	0.661
RTL	Smoking association among participants with asthma	111	−0.190 (−0.605 to 0.226)	0.646 (0.248 to 1.682)	0.371

Note. Models were restricted to participants aged 35–50 years and included age, asthma status, light-smoking status, and the asthmaxsmoking interaction. Healthy nonsmokers were the reference group. CEA was analysed using $\log_{10}$ -transformed ordinary least-squares regression with HC3 robust standard errors. RTL was analysed using median regression with 1,000 bootstrap replicates stratified by asthma–smoking group. The smoking coefficient equals the smoking contrast among healthy participants and is therefore shown once. Adjusted ratios were calculated as 10^{β} . Confidence intervals are 95%, and all p values are two-sided.

Supplementary Table S4B. Age-restricted asthma-only models

Outcome	Adjustment model	N	Smoking β (95% CI)	Adjusted ratio (95% CI)	p value	Model status
CEA	Age + asthma severity	33	0.062 (−0.034 to 0.158)	1.153 (0.925 to 1.437)	0.195	Estimated
RTL	Age + asthma severity	30	Not estimable	Not estimable	—	Not reliably estimable because of sparse data
RTL	Smoking + age (exploratory simplified model)	30	−0.218 (−0.569 to 0.133)	0.606 (0.270 to 1.360)	0.224	Exploratory

Note. Analyses were restricted to participants with asthma aged 35–50 years. The severity-adjusted RTL median-regression model was not reliably estimable because of sparse data; therefore, a simplified smoking-plus-age model is presented as exploratory. CEA was analysed using log₁₀-transformed ordinary least-squares regression with HC3 robust standard errors. The estimated RTL model used 1,000 bootstrap replicates stratified by smoking status. Ratios compare light smokers with nonsmokers. Confidence intervals are 95%, and all p values are two-sided.

Abbreviations for Supplementary Table S4: β , regression coefficient; CEA, carcinoembryonic antigen; CI, confidence interval; HC3, heteroscedasticity-consistent covariance estimator type 3; RTL, relative leukocyte telomere length.

Supplementary Table 5. Model diagnostics

Outcome	Model	N	Shapiro–Wilk W	Shapiro–Wilk p	Breusch–Pagan statistic	Breusch–Pagan p	Maximum Cook’s distance	N with Cook’s D >4/N	Maximum VIF	Condition number	Bootstrap replicates
CEA	Primary full-cohort	150	0.987	0.167	5.057	0.281	0.083	8	3.125	81.16	—
CEA	Expanded full-cohort	150	0.987	0.166	7.233	0.300	0.114	12	3.256	70.91	—
CEA	Expanded asthma-only	70	0.989	0.791	10.028	0.263	0.123	8	3.220	129.19	—
RTL	Primary full-cohort	148	—	—	—	—	—	—	3.209	80.15	2,000
RTL	Expanded full-cohort	148	—	—	—	—	—	—	3.345	70.17	2,000
RTL	Expanded asthma-only	67	—	—	—	—	—	—	3.085	119.57	2,000

Note. Shapiro–Wilk, Breusch–Pagan, and Cook’s-distance diagnostics apply to the CEA ordinary least-squares models and are not directly applicable to RTL median-regression models. Variance inflation factors and condition numbers were assessed for both outcomes. The relatively large condition numbers indicate potential numerical sensitivity related to model coding and scale; however, maximum variance inflation factors remained below 3.4. Diagnostic findings were considered when interpreting model stability.

Abbreviations: CEA, carcinoembryonic antigen; Cook’s D, Cook’s distance; RTL, relative leukocyte telomere length; VIF, variance inflation factor.