

SUPPLEMENTAL MATERIAL

Table S1. Odds ratios with 95% CI for the levels of biomarkers of cardiovascular injury (hsCRP \geq vs. $<$ 2 mg/L) by smoking status, burden, years since quitting and intensity

	hsCRP \geq 2 mg/L		hsCRP $<$ 2 mg/L	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Smoking status	N=14,000		N=13,815	
Never	REF		REF	
Former	1.16 (1.07 – 1.25)	$<$ 0.001	1.03 (0.95 – 1.13)	0.44
Current	1.51 (1.36 – 1.68)	$<$ 0.001	1.70 (1.51 – 1.91)	$<$ 0.001
Pack-years of smoking (per 5 pack-years increase)	N=5,854/4,039/1,815		N=5,769/3,987/1,782	
Ever smokers	1.05 (1.04 – 1.07)	$<$ 0.001	1.04 (1.03 – 1.06)	$<$ 0.001
Former smokers	1.05 (1.03 – 1.07)	$<$ 0.001	1.03 (1.01 – 1.05)	0.007
Current smokers	1.04 (1.01 – 1.07)	0.005	1.05 (1.02 – 1.08)	0.001
Years since quitting smoking (5 years increase) among former smokers only	N=4,048		N=3,994	
	0.93 (0.90 – 0.96)	$<$ 0.001	0.95 (0.91 – 0.98)	$<$ 0.01
Smoking intensity (10 cigarettes/day) among current smokers	N=1,815		N=1,782	
	1.15 (1.04 – 1.28)	0.007	1.17 (1.04 – 1.30)	0.006

hsCRP indicates high-sensitivity C-reactive protein.

Bold items are statistically significant interaction terms ($P < 0.05$).

Table S2. Beta-coefficients/odds ratios and interaction P-values for age, sex, race and education in Model 2 by smoking status, burden, years since quitting and intensity

	Age (continuous)	Sex (binary) Females vs. males	Race (continuous ordinal) White, Brown, Black, Asian	Education (continuous ordinal) Less than elementary, elementary, high school, college
Ln hsCRP				
Former	0.0007, 0.76	-0.03, 0.44	0.042, 0.06	-0.013, 0.59
Current	0.013, <0.001	-0.30, <0.001	0.062, 0.03	-0.087, 0.004
Pack-years of smoking (ever smokers)	-0.001, 0.008	-0.015, 0.03	0.35	-0.008, 0.03
Time since quitting	0.75	0.60	0.57	0.59
Intensity of smoking	0.11	-0.105, 0.04	0.57	0.47
cIMT				
Former	0.001, 0.006	-0.014 (0.02)	0.003, 0.43	-0.007, 0.04
Current	0.002, 0.001	-0.024 (0.003)	0.010, 0.02	-0.009, 0.06
Pack-years of smoking (ever smokers)	0.11	-0.003, 0.03	0.91	-0.002, <0.001
Time since quitting	0.29	0.82	0.20	0.22
Intensity of smoking	0.14	0.65	0.27	0.44
ABI≤1.0				
Former	1.04, <0.001	0.56	0.32	0.22
Current	1.06, <0.001	0.90	0.09	0.10
Pack-years of smoking (ever smokers)	0.32	0.14	0.27	0.97
Time since quitting (former smokers)	0.09	0.96	0.16	0.97
Intensity of smoking	0.07	0.31	0.16	0.49

(current smokers)

CAC>0

Former	0.47	1.43, 0.05	0.82	0.91
Current	0.56	1.69, 0.02	0.19	0.30
Pack-years of smoking (ever smokers)	0.69	0.63	0.63	0.86
Time since quitting	0.80	0.84	0.56	0.06
Intensity of smoking	1.05, 0.01	0.83	1.48, 0.005	0.92

ABI indicates ankle-brachial index; CAC, coronary artery calcium; cIMT, carotid intima-media thickness; hsCRP, high-sensitivity C-reactive protein. Bold items are statistically significant interaction terms (P<0.05).

Table S3. Stratified analyses by age, sex, race and education for ln hsCRP where interaction P-values were < 0.05 by smoking status, burden, years since quitting and intensity

	Overall	P-value	Males	P-value	Females	P-value
Never	REF		REF		REF	
Former	0.01 (-0.02 – 0.05)	0.46	0.05 (-0.01 – 0.10)	0.13	-0.01 (-0.06 – 0.05)	0.82
Current	0.24 (0.19 – 0.29)	<0.001	0.39 (0.31 – 0.46)	<0.001	0.09 (0.01 – 0.16)	0.02
Pack-years of smoking	0.02 (0.01 – 0.03)	<0.001	0.03 (0.02 – 0.04)	<0.001	0.01 (-0.001 – 0.02)	0.07
Smoking intensity	0.10 (0.05 – 0.15)	<0.001	0.13 (0.06 – 0.20)	<0.001	0.05 (-0.03 – 0.13)	0.27
	Overall	P-value	Age<50	P-value	Age≥50	P-value
Never	REF		REF		REF	
Former	0.01 (-0.02 – 0.05)	0.46	-0.01 (-0.08 – 0.05)	0.69	0.03 (-0.02 – 0.08)	0.23
Current	0.24 (0.19 – 0.29)	<0.001	0.15 (0.06 – 0.23)	0.001	0.31 (0.24 – 0.37)	<0.001
Pack-years of smoking	0.02 (0.01 – 0.03)	<0.001	0.03 (0.02 – 0.05)	<0.001	0.02 (0.01 – 0.03)	<0.001
	Overall	P-value	High school or less	P-value	College	P-value
Never	REF		REF		REF	
Former	0.01 (-0.02 – 0.05)	0.46	0.01 (-0.05 – 0.07)	0.78	0.02 (-0.04 – 0.07)	0.50
Current	0.24 (0.19 – 0.29)	<0.001	0.27 (0.20 – 0.34)	<0.001	0.18 (0.09 – 0.26)	<0.001
Pack-years of smoking	0.02 (0.01 – 0.03)	<0.001	0.03 (0.02 – 0.04)	<0.001	0.01 (-0.00 – 0.02)	0.08
	Overall	P-value	Whites	P-value	Non-Whites	P-value
Never	REF		REF		REF	
Former	0.01 (-0.02 – 0.05)	0.46	-0.01 (-0.06 – 0.05)	0.80	0.04 (-0.02 – 0.10)	0.24

Current	0.24 (0.19 – 0.29)	<0.001	0.20 (0.13 – 0.28)	<0.001	0.28 (0.20 – 0.36)	<0.001
	Overall	P-value	Browns	P-value	Non-Browns	P-value
Never	REF		REF		REF	
Former	0.01 (-0.02 – 0.05)	0.46	0.02 (-0.06 – 0.09)	0.68	0.01 (-0.03 – 0.06)	0.58
Current	0.24 (0.19 – 0.29)	<0.001	0.25 (0.15 – 0.36)	<0.001	0.24 (0.17 – 0.30)	<0.001
	Overall	P-value	Blacks	P-value	Non-Blacks	P-value
Never	REF		REF		REF	
Former	0.01 (-0.02 – 0.05)	0.46	0.02 (-0.09 – 0.12)	0.78	0.01 (-0.03 – 0.06)	0.53
Current	0.24 (0.19 – 0.29)	<0.001	0.24 (0.10 – 0.37)	0.001	0.24 (0.18 – 0.30)	<0.001

HsCRP indicates high-sensitivity C-reactive protein.

Bold items are statistically significant interaction terms (P<0.05).

Table S4. Stratified analyses by age, sex, race and education for cIMT where interaction P-values were < 0.05) by smoking status and burden

	Overall	P-value	Males	P-value	Females	P-value
Never	REF		REF		REF	
Former	0.01 (0.01 – 0.02)	<0.001	0.02 (0.01 – 0.03)	<0.001	0.007 (-0.000 – 0.015)	0.06
Current	0.03 (0.02 – 0.04)	<0.001	0.04 (0.03 – 0.06)	<0.001	0.02 (0.01 – 0.03)	0.002
Pack-years of smoking	0.003 (0.002 – 0.004)	<0.001	0.004 (0.003 – 0.006)	<0.001	0.002 (0.000 – 0.003)	0.03
	Overall	P-value	Age<50	P-value	Age≥50	P-value
Never	REF		REF		REF	
Former	0.01 (0.01 – 0.02)	<0.001	0.02 (0.01 – 0.02)	<0.001	0.02 (0.01 – 0.03)	<0.001
Current	0.03 (0.02 – 0.04)	<0.001	0.03 (0.02 – 0.04)	<0.001	0.03 (0.01 – 0.04)	<0.001
	Overall	P-value	High school or less	P-value	College	P-value
Never	REF		REF		REF	
Former	0.01 (0.01 – 0.02)	<0.001	0.02 (0.01 – 0.03)	0.002	0.01 (0.00 – 0.02)	0.003
Current	0.03 (0.02 – 0.04)	<0.001	0.03 (0.02 – 0.05)	<0.001	0.02 (0.01 – 0.03)	<0.001
Pack-years of smoking	0.003 (0.002 – 0.004)	<0.001	0.005 (0.004 – 0.007)	<0.001	0.001 (-0.001 – 0.003)	0.27
	Overall	P-value	Whites	P-value	Non-Whites	P-value
Never	REF		REF		REF	
Former	0.01 (0.01 – 0.02)	<0.001	0.01 (0.00 – 0.02)	0.03	0.02 (0.01 – 0.03)	0.001
Current	0.03 (0.02 – 0.04)	<0.001	0.02 (0.01 – 0.03)	0.003	0.04 (0.03 – 0.05)	<0.001
	Overall	P-value	Browns	P-value	Non-Browns	P-value

Never	REF		REF		REF	
Former	0.01 (0.01 – 0.02)	<0.001	0.02 (0.01 – 0.03)	0.001	0.01 (0.00 – 0.02)	0.01
Current	0.03 (0.02 – 0.04)	<0.001	0.04 (0.02 – 0.06)	<0.001	0.02 (0.01 – 0.03)	<0.001
	Overall	P-value	Blacks	P-value	Non-Blacks	P-value
Never	REF		REF		REF	
Former	0.01 (0.01 – 0.02)	<0.001	0.01 (-0.01 – 0.03)	0.31	0.01 (0.01 – 0.02)	<0.001
Current	0.03 (0.02 – 0.04)	<0.001	0.04 (0.02 – 0.06)	0.001	0.02 (0.02 – 0.03)	<0.001

HsCRP indicates high-sensitivity C-reactive protein.
 Bold items are statistically significant interaction terms (P<0.05).

Table S5. Stratified analyses by hsCRP levels for CAC > 0 outcome (P-interaction > 0.05) by smoking status, burden, years since quitting and intensity

	Overall	P-value	hsCRP \geq 2	P-value CAC>0	hsCRP<2	P-value
Never	REF		REF		REF	
Former	1.12 (0.93 – 1.35)	0.22	1.35 (1.00 – 1.83)	<0.05	0.97 (0.76 – 1.23)	0.80
Current	1.83 (1.46 – 2.30)	<0.001	1.87 (1.31 – 2.67)	0.001	1.82 (1.34 – 2.47)	<0.001
Pack-years of smoking	1.11 (1.07 – 1.14)	<0.001	1.11 (1.06 – 1.16)	<0.001	1.10 (1.05 – 1.15)	<0.001
Years since quitting	0.87 (0.81 – 0.93)	<0.001	0.85 (0.76 – 0.95)	<0.01	0.86 (0.78 – 0.95)	0.003
Smoking intensity	1.26 (1.02 – 1.56)	0.033	1.45 (1.02 – 2.05)	0.04	1.21 (0.89 – 1.63)	0.22

CAC indicates coronary artery calcium; hsCRP, high-sensitivity C-reactive protein.
 Bold items are statistically significant interaction terms (P<0.05).

Table S6. Baseline mean absolute difference (95% CI) in levels of biomarkers of cardiovascular injury (hsCRP) and cIMT, and odds ratios (OR) for measures of subclinical atherosclerosis (ABI<1.0 and CAC>0) by second-hand smoking status

Exposure	Ln hsCRP (mg/L)		cIMT (mm)		ABI < 1.0		CAC (Agatston)* > 0	
	β -coeff (95% CI)	P-trend	β -coeff (95% CI)	P-trend	OR (95% CI)	P-trend	OR (95% CI)	P-trend
Model 2								
0	REF	<0.001	REF	<0.01	REF	0.51	REF	0.09
1	0.05 (0.01 – 0.09)		0.01 (-0.00 – 0.02)		1.13 (0.94 – 1.36)		0.95 (0.78 – 1.16)	
2	0.10 (0.03 – 0.17)		0.01 (0.00 – 0.03)		1.15 (0.85 – 1.55)		1.37 (1.03 – 1.84)	
3	0.15 (-0.01 – 0.30)		0.02 (-0.01 – 0.05)		0.56 (0.23 – 1.38)		0.96 (0.52 – 1.77)	
Model 3								
0	REF	0.03	REF	0.09	REF	0.44	REF	0.925
1	0.04 (-0.00 – 0.08)		0.01 (-0.00 – 0.01)		1.06 (0.88 – 1.28)		0.92 (0.75 – 1.12)	
2	0.05 (-0.02 – 0.13)		0.01 (-0.01 – 0.02)		0.95 (0.71 – 1.30)		1.22 (0.91 – 1.64)	
3	0.07 (-0.09 – 0.23)		0.01 (-0.02 – 0.04)		0.42 (0.17 – 1.03)		0.76 (0.41 – 1.41)	

Model 1 is adjusted for age, sex, race, education (results are not shown)

Model 2 is adjusted for Model 1 plus study site, family history of MI, body mass index, systolic blood pressure, LDL cholesterol, HDL cholesterol, triglycerides, hypertension status, diabetes mellitus, statin use.

Model 3 is adjusted for Model 2 plus self-reported smoking status (never, former, current).

Second-hand smoke and smoking status for Ln hsCRP

P-interaction (former*shs) =0.54

P-interaction (current*shs) =0.82

Table S7. Baseline relative risk ratios (RRR) with 95% confidence intervals (CI) for categories of coronary artery calcium (CAC) using multinomial logistic regression models among 4,278 participants in ELSA-Brasil

Exposure	CAC (Agatston) = 0	CAC (Agatston) >0 and ≤100	CAC (Agatston) >100 and ≤400	CAC (Agatston) >400
	OR (95% CI)	RRR (95% CI)	P-value	RRR (95% CI)
Smoking burden (pack-years of smoking per 5-unit increase)				
Ever smokers*	REF	1.09 (1.05-1.12)	<0.001	1.13 (1.08-1.18)
Former smokers	REF	1.08 (1.04-1.31)	<0.001	1.12 (1.05-1.18)
Current smokers	REF	1.06 (1.00-1.13)	0.062	1.13 (1.03-1.23)
Years since quitting smoking among former smokers				
Per 5-year increase	REF	0.86 (0.80-0.93)	<0.001	0.92 (0.81-1.03)
Smoking intensity among current smokers†				
Per 10 cigarettes/day increase	REF	1.15 (0.91-1.46)	0.236	1.60 (1.15-2.21)

This was a complete case analysis. Models were adjusted for age, sex, race, education, study site, alcohol use, family history of myocardial infarction, body mass index, systolic blood pressure, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, hypertension status, diabetes mellitus, statin use.

*Includes both former and current smokers

†Also adjusted for duration of smoking in year