



# The role of smoking history in longitudinal changes in C-reactive protein between Black and White older adults in the US

Nancy C. Jao<sup>a,b</sup>, Aresha Martinez-Cardoso<sup>c</sup>, Moin Vahora<sup>c,d</sup>, Marcia M. Tan<sup>c,\*</sup>

<sup>a</sup> Department of Psychiatry and Human Behavior, Warren Alpert Medical School of Brown University, United States

<sup>b</sup> Center for Behavioral and Preventive Medicine, The Miriam Hospital, United States

<sup>c</sup> Department of Public Health Sciences, University of Chicago, United States

<sup>d</sup> College of Applied Health Sciences, University of Illinois – Urbana Champaign, United States

## ABSTRACT

Smoking cessation is associated with decreases in C-reactive protein (CRP), a biomarker of systemic inflammation and cancer risk; yet CRP levels remain higher long-term in individuals who quit vs. those who never smoked. While non-Hispanic, Black/African American (NHB) have higher levels of CRP vs. non-Hispanic, White/Caucasian (NHW) adults, the association between CRP and race has not been examined in individuals with smoking history. Utilizing longitudinal data from the Health and Retirement Study (HRS), the current study examined the effects of race and smoking history on CRP in older adults. NHB ( $n = 242$ ) and NHW ( $n = 1529$ ) participants completed HRS assessments in 2006, 2010, and 2014. Dried blood spots collected at each wave were assayed for CRP. Linear mixed models were used to examine the effect of race and smoking history on CRP across waves – controlling for sociodemographics, physical activity, body mass index (BMI), and current smoking. Overall, results showed no significant effects of race or current smoking on CRP; rather age, sex, education, BMI, physical activity, smoking history, and time  $\times$  race predicted CRP ( $ps < .04$ ). However, while age, sex, education, BMI, physical activity, and smoking history were also predictive of CRP in NHWs ( $ps < .04$ ) in race-stratified models, only BMI was a significant predictor of CRP in NHBs ( $p = .012$ ). BMI may be important in explaining inflammation-related disease risk in NHBs with a history of smoking. NHBs may not experience the same reductions in CRP with smoking cessation as NHWs – potentially contributing to tobacco-related health disparities.

## 1. Introduction

Cigarette smoking is the single leading cause of preventable death and disease in the US (U.S. Department of Health and Human Services, 2014). Cigarette smoking has been linked to increased risk for cancer, diabetes, cardiovascular disease, and respiratory disease – with individuals who smoke cigarettes 15 to 30 times more likely than those who do not smoke to develop lung cancer (U.S. Department of Health and Human Services, 2014). Despite successful efforts to reduce smoking rates among adults (e.g., from 24.7% in 1997 to 14.0% in 2017) (Jamal et al., 2018), individuals who identify as Black or African American still experience the highest rates of tobacco-related morbidity and mortality across all racial/ethnic groups (Fiore et al., 2008). Especially concerning, the health risks associated with smoking continue to persist for Black/African-Americans even after individuals have quit smoking (Berlin et al., 2012; Stahre et al., 2010; Webb Hooper, 2019). However, Black/African-American vs. White racial disparities in health outcomes associated with tobacco use and smoking cessation are not well understood, and it is unclear what behavioral, psychological, or molecular

mechanisms may drive these differences. In the current study, we sought to examine C-reactive protein (CRP), a biological mechanism associated with chronic disease risk that might potentially underlie these tobacco-related disparities.

Elevated systemic inflammation may be an important piece to the puzzle of disparities in tobacco-related health outcomes among Black Americans. A key pathway between tobacco smoke exposure and numerous health outcomes (Black et al., 2004; Elinav et al., 2013; Pepys & Hirschfield, 2003), chronic systemic inflammation may play an important role in disease development in adults with a history of smoking despite smoking cessation. In particular, CRP, an acute-phase protein and common marker of systemic inflammation, has been examined largely in tobacco research as a biomarker of chronic inflammation (Aldaham et al., 2015; Allin & Nordestgaard, 2011; Lagiou & Trichopoulos, 2011; Ohsawa et al., 2005; Pine et al., 2011; Tonstad & Cowan, 2009). As cigarette smoking has been associated with elevations of CRP levels (Tonstad & Cowan, 2009; Yanbaeva et al., 2007), smoking cessation has been associated with a decline in CRP levels over time (Hastie et al., 2008; King et al., 2017; Ohsawa et al., 2005) – with greater

*Abbreviations:* CRP, C-reactive protein; HRS, Health and Retirement Study; NHB, Non-Hispanic, Black/African American; NHW, Non-Hispanic, White.

\* Corresponding author at: 5841 S Maryland Ave, MC 2000, Chicago, IL 60637, United States.

*E-mail address:* [mmtan@uchicago.edu](mailto:mmtan@uchicago.edu) (M.M. Tan).

<https://doi.org/10.1016/j.pmedr.2022.101885>

Received 7 December 2021; Received in revised form 20 May 2022; Accepted 1 July 2022

Available online 5 July 2022

2211-3355/© 2022 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Table 1**  
Participant Characteristics (Overall and by Race).

	Overall (N = 1771)	NHW (N = 1529)	NHB (N = 242)	F or $\chi^2$	p
<i>Demographics at baseline</i>					
Age, mean (SD), years	64.3 (9.3)	64.6 (9.3)	62.4 (9.6)	11.26	0.001*
No. (%) female	867 (49.0%)	734 (48.0%)	133 (55.0%)	4.04	0.044*
Education, mean (SD), years	12.7 (2.9)	12.9 (2.8)	11.5 (3.3)	40.99	<0.001*
BMI, mean (SD), kg/m <sup>2</sup>	29.5 (5.4)	29.3 (5.4)	30.2 (5.6)	4.14	0.042*
No. (%) any physical activity	1492 (84.3%)	1295 (84.8%)	197 (81.4%)	1.77	0.184
<b>Baseline smoking history</b>				24.71	<0.001*
No. (%) Never	802 (45.3%)	710 (46.4%)	92 (38.0%)		
No. (%) Quit	511 (28.9%)	455 (29.8%)	56 (23.1%)		
No. (%) Smoking	458 (25.9%)	364 (23.8%)	94 (38.8%)		

**Notes:** \* $p < .05$ . Baseline measurements were conducted in 2006. NHW = non-Hispanic, White; NHB = non-Hispanic, Black/African American. Any physical activity indicates individuals who self-reported at baseline engaging in moderate or vigorous levels of physical activity at least one to three times per month. Smoking history was categorized at baseline as 1) Never smoked cigarettes (i.e., denied any history of cigarette smoking), 2) Quit smoking by baseline (i.e., denied current cigarette smoking, but endorsed history of cigarette smoking), and 3) Smoking (i.e., endorsed current cigarette smoking). Significance values refer to between-group comparisons for NHWs vs. NHBs.

decreases in CRP levels the longer an individual has been smoke-free (Ohsawa et al., 2005). However, some studies have indicated that CRP levels in individuals who quit smoking still remain higher than those who never smoked cigarettes – despite long-term smoking cessation (e.g., 20 years) (Brenner et al., 2014; Hastie et al., 2008; King et al., 2017; McEvoy et al., 2015; Ohsawa et al., 2005). This elevated CRP has been linked to an increased risk of chronic disease (Brown et al., 2019; Pine et al., 2011; Shiels et al., 2013). For example, adults who have quit with higher levels of CRP had a two-fold increase in lung cancer compared to those with lower levels (Chaturvedi et al., 2010). The reason underlying sustained CRP levels post smoking cessation is unclear, but it has been hypothesized that it is related to the weight gain that occurs after quitting smoking (King et al., 2017).

There is a body of evidence indicating that Black/African-Americans adults have higher levels of CRP compared to White adults (Kelley-Hedgpepeth et al., 2008; Meaney et al., 2019; Morimoto et al., 2014; Paalani et al., 2011; Stepanikova et al., 2017). Previous research has shown that racial differences observed in CRP levels may be explained by adjusting for body mass index (BMI) (Kelley-Hedgpepeth et al., 2008; Stepanikova et al., 2017), although body weight did not fully explain the association (Kelley-Hedgpepeth et al., 2008). However, most of the studies examining racial disparities in CRP were cross-sectional. Of the little research conducted with longitudinal data, one study examining race effects on CRP found that Black adults had a greater increase in CRP over time (Zahodne et al., 2019). Still, no studies have examined longitudinal differences between Black and White adults in the context of smoking and cessation. Given the important links between levels of CRP, smoking exposure, and smoking cessation, racial differences in changes in CRP levels among individuals who quit smoking may partially explain disparities in tobacco-related health risks between Black/African-American and White adults.

Despite the wide body of work on Black/African-American vs. White racial disparities in tobacco- and smoking-related disease, post-cessation changes in systemic inflammation have not been studied as a potential

contributor to racial disparities in smoking-related morbidity and mortality. The current study aimed to characterize racial differences in longitudinal CRP change taking into account smoking status (i.e. current smoking behavior) and history (i.e., whether subjects have smoked in the past). Specifically, the current study utilized longitudinal smoking and inflammation data from the Health and Retirement Study (HRS) to examine the effects of smoking status and history on changes in CRP in Black/African-American and White older adults in the US.

## 2. Methods

### 2.1. Study design

The current study used de-identified data from the Health and Retirement Study (HRS) – an ongoing, nationally representative study of the economic, health, marital, and family status of older adults living in the US (Sonnega et al., 2014). The original HRS sample was recruited in 1992, and contained approximately 20,000 respondents born between 1924 and 1941. Additional waves of core data collection for the HRS have been conducted every two years since 1992. In 2006, the HRS initiated collection of anthropometric and blood-based biomarker data to create the HRS Biomarker Database. A random half-sample of HRS respondents was interviewed in 2006 and assessments have been repeated every four years. The current study utilized publicly available data from the 2006 (baseline), 2010, and 2014 waves of the HRS Core and Biomarker Databases. Study analyses were limited to the 1771 adult participants who identified as non-Hispanic, White/Caucasian (NHW) or non-Hispanic, Black/African American (NHB), denied ever having or developing cancer, and had complete CRP biomarker data available for all 2006, 2010, and 2014 HRS Waves.

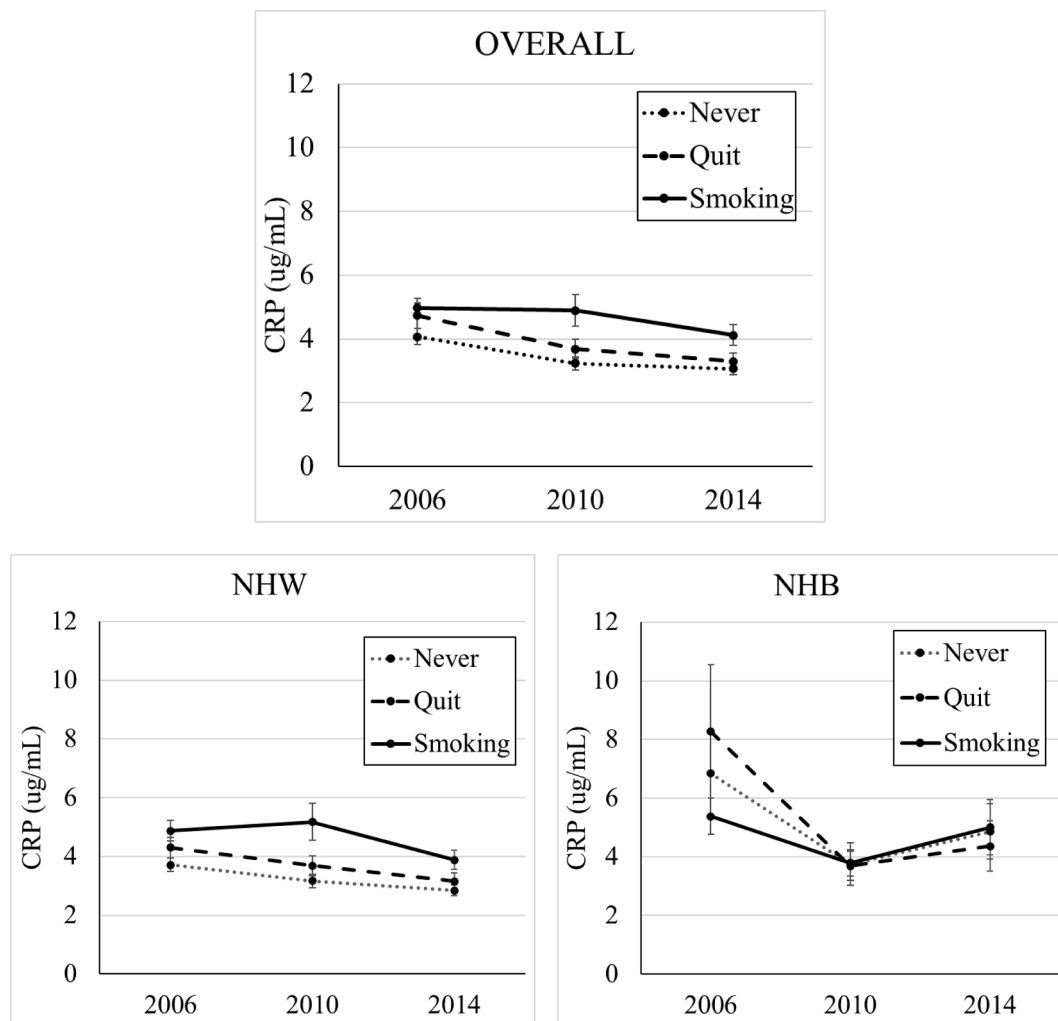
### 2.2. Measures

**Smoking variables.** Smoking is dynamic; therefore multiple measures were required to account for the multidimensional nature of smoking behavior in our analysis. At each wave of the HRS, participants self-reported whether they have ever smoked cigarettes (yes/no) and whether they were currently smoking cigarettes (yes/no). These items were used to create *smoking history* at baseline (smoking, quit, or never) and *current smoking status* longitudinally (yes or no) as indicators of past and current smoking behavior. Accounting for the potential effects of whether an individual ever smoked cigarettes (i.e., smoking history) vs. currently smoking cigarettes at a specific assessment (i.e., smoking status) is an important distinction (e.g., a person may smoke after having been quit for several years).

**Smoking history:** At baseline (2006) participants' smoking history was classified as: 1) Smoking (i.e., if they reported smoking cigarettes in the past and currently smoking cigarettes); 2) Quit (i.e., if they reported smoking cigarettes in the past, but denied currently smoking cigarettes); or 3) Never (i.e., if they denied smoking cigarettes in the past and denied currently smoking cigarettes) based on their response to an item that asked about whether they had ever smoked and their smoking behavior in 2006.

**Current smoking status:** At each follow-up wave (2010 & 2014), individuals reported whether they were currently smoking cigarettes (yes/no). Current smoking status was included in the analysis as a separate indicator of smoking behavior from smoking history as individuals who smoke may frequently transition from quitting and smoking over time.

**Inflammation.** We used CRP data from three assessment timepoints (2006, 2010, and 2014) in our analysis (Crimmins et al., 2013). In the original HRS study, participants were invited to participate in an enhanced-data-collection where dried blood spots from finger prick samples were obtained and assayed to generate CRP data [measured in units of micrograms per milliliter ( $\mu\text{g}/\text{mL}$ )]. Dried blood spot values were transformed by HRS to NHANES equivalent assay values for analytic use to align with more conventionally used whole blood assays



**Fig. 1. Notes:** Raw Mean ( $\pm$ SEM) CRP Levels based on Smoking History at Baseline. Smoking history was categorized at baseline as 1) Never smoked cigarettes (i.e., denied any history of cigarette smoking), 2) Quit smoking by baseline (i.e., denied current cigarette smoking, but endorsed history of cigarette smoking), and 3) Smoking (i.e., endorsed current cigarette smoking).

(Crimmins et al., 2013). Larger CRP values indicated a greater inflammatory response.

**Control variables.** Participants had verified sociodemographic data and provided physical health/measurements at each wave. Body mass index (BMI) was calculated from height and weight data in the HRS [(weight/(height)<sup>2</sup> x703)]; in the original study, weight was measured in pounds using a digital scale and height was measured to the nearest quarter inch. In the original study, participants also self-reported how often they engage in moderate and vigorous physical activity using a Likert scale: “Hardly ever or never”, “One to three times per month”, “At least once per week”, “More than one time per week”, or “Every day”. Participants who endorsed hardly ever or never engaging in either moderate or vigorous physical activity were categorized as self-reporting no level of physical activity at baseline. All participants reporting engaging in moderate or vigorous physical activity at least one to three times per month or more were categorized as reporting any physical activity at baseline. Additional control variables included sex (male vs female), age in years, and years of education. Other chronic diseases (e.g., heart disease, diabetes) that have been shown to have an effect on CRP levels were initially examined, but not included as controls in the final model as they were not associated with CRP in this sample.

### 2.3. Statistical analysis

All statistical analyses were conducted using IBM SPSS Statistics 27 for Windows with significance level set at  $p < .05$ . Differences in sociodemographic and sample characteristics were examined using chi-squares and one-way analysis of variances (ANOVAs) between NHW and NHB groups. To adjust for skewness, CRP values were log-transformed for analyses. Using linear mixed effect models, we examined whether race (NHW vs. NHB), smoking history at baseline (Smoking vs. Quit vs. Never), and time-varying smoking status at each wave (yes vs. no) would impact levels of CRP over time. Sex, age at baseline, education, self-reported level of physical activity at baseline, and time-varying BMI were also included in the model to account for potential effects on CRP levels. Time (Wave 2006 vs. 2010 vs. 2014) was also included in the model to account for any order effects. Mixed effect models included race (0 = NHW, 1 = NHB), sex (0 = male, 1 = female), mean-centered age at baseline in years, education in years, smoking history at baseline (0 = never, 1 = quit, 2 = smoking), physical activity at baseline (0 = none, 1 = any), and BMI, with time  $\times$  smoking history, time  $\times$  current smoking status, race  $\times$  time, race  $\times$  smoking history, and race  $\times$  current smoking status included as interactions. Models were then conducted separately by race to examine potential racial differences in model results to clarify the relationship between smoking history and race on CRP (Kaufman & Cooper, 2001; VanderWeele &

**Table 2**  
Linear Mixed Model, Fixed Effects, Overall.

	Estimate	SE	df	t	p
<b>Intercept</b>	-0.16	0.08	1927.00	-1.99	0.047*
<b>Time (ref = 2006)</b>					
2010	-0.06	0.02	2562.47	-2.97	0.003*
2014	-0.19	0.03	2801.31	-7.60	<0.001*
<b>Age</b>	0.003	0.001	1519.55	2.06	0.039*
<b>Sex (ref = Male)</b>					
Female	0.08	0.02	1461.05	3.79	<0.001*
<b>Race (ref = NHW)</b>					
NHB	0.10	0.06	2263.13	1.68	0.093
<b>Education</b>	-0.02	0.004	1501.96	-4.64	<0.001*
<b>BMI</b>	0.02	0.002	1772.53	13.59	<0.001*
<b>Physical Activity (ref = None)</b>					
Any	-0.09	0.03	1488.35	-2.88	0.004*
<b>Smoking History (ref = Never)</b>					
Quit	0.05	0.03	2925.75	1.33	0.184
Smoking	0.18	0.04	2982.61	5.10	<0.001*
<b>Time × Smoking History</b>					
2010 × Quit	-0.001	0.03	2543.18	-0.03	0.973
2010 × Smoking	-0.05	0.05	2698.65	-1.10	0.270
2014 × Quit	-0.01	0.04	2740.10	-0.37	0.710
2014 × Smoking	-0.04	0.05	3010.36	-0.76	0.449
<b>Time × Smoking Status</b>					
2010 × Yes	0.07	0.04	2821.83	1.65	0.100
2014 × Yes	0.08	0.04	3776.59	1.71	0.088
<b>Time × Race</b>					
2010 × NHB	-0.15	0.04	2635.25	-3.41	0.001*
2014 × NHB	-0.06	0.05	3044.87	-1.17	0.242
<b>Race × Smoking History</b>					
NHB × Quit	0.06	0.08	1469.49	0.74	0.458
NHB × Smoking	0.02	0.10	3145.33	0.24	0.814
<b>Race × Smoking Status</b>					
NHB × Yes	-0.09	0.09	3960.52	-1.04	0.298

**Notes:** \* $p < .05$ ; NHW = non-Hispanic, White; NHB = non-Hispanic, Black/African American. Redundant estimates are not shown. Physical activity was categorized as any (i.e., self-reporting engaging in moderate or vigorous physical activity at least one to three times per month or more) vs. none (i.e., self-reporting hardly ever or never engaging in either moderate or vigorous physical activity). Smoking history was categorized at baseline as 1) Never smoked cigarettes (i.e., denied any history of cigarette smoking), 2) Quit smoking by baseline (i.e., denied current cigarette smoking, but endorsed history of cigarette smoking), and 3) Smoking (i.e., endorsed current cigarette smoking). Smoking status was categorized as currently smoking at time of assessment (yes) or abstinent at time of assessment (no).

Robinson, 2014). Post-hoc pairwise comparisons of least square means with Bonferroni adjustments were used to describe significant effects.

### 3. Results

The final analytic sample ( $N = 1,771$ ) included 1,529 (86.3%) adults who identified as NHW and 242 (13.7%) identified as NHB. Participants' characteristics by race are presented in Table 1. Compared to individuals who identify as NHW, individuals who identify as NHB were significantly more likely to identify as younger ( $p = .001$ ), female ( $p = .044$ ), have fewer years of education ( $p < .001$ ) and higher BMI ( $p = .042$ ), and

more likely to be currently smoking cigarettes at baseline ( $p < .001$ ). See Fig. 1 for a visual representation of the non-transformed mean scores of CRP over time by smoking history.

Table 2 presents the coefficients of the fixed effects model that tested the association between smoking on CRP across time. There were statistically significant main effects of time ( $F(2595,2) = 32.03, p < .001$ ), age ( $F(1520,1) = 4.26, p = .039$ ), sex ( $F(1461,1) = 14.34, p < .001$ ), education ( $F(1502,1) = 21.53, p < .001$ ), BMI ( $F(1773,1) = 184.67, p < .001$ ), physical activity ( $F(1488,1) = 8.28, p = .004$ ), and smoking history ( $F(2254,2) = 4.65, p = .010$ ) on the levels of CRP. There was also a statistically significant effect of time × race ( $F(2558,2) = 6.43, p = .002$ ), where, controlling for smoking history and status, NHWs showed a statistically significant decrease in CRP across all time points, while the NHB group had a significant decrease only from 2006 to 2010. The interactions between race and smoking history and race and smoking status were not significant, suggesting that smoking behavior did not contribute to racial differences in CRP.

However, model effects differed when analyzing NHW vs. NHB groups separately (Table 3). Results for the NHW group were similar to effects found in combined overall analyses, with time ( $F(2192,2) = 36.97, p < .001$ ), age ( $F(1315,1) = 4.28, p = .039$ ), sex ( $F(1269,1) = 12.16, p = .001$ ), education ( $F(1311,1) = 23.94, p < .001$ ), BMI ( $F(1492,1) = 189.53, p < .001$ ), physical activity ( $F(1288,1) = 9.94, p = .002$ ), and smoking history ( $F(1871,2) = 6.45, p = .002$ ) having statistically significant main effects on CRP levels. Yet, in the NHB group, only time ( $F(325,2) = 12.20, p < .001$ ) and BMI ( $F(436,1) = 6.35, p = .012$ ) had a statistically significant effect on CRP levels. There were no statistically significant interactive effects of time and smoking history or status for either group in the stratified analyses ( $ps > .05$ ).

### 4. Discussion

Smoking cessation is associated with decreases in levels of CRP, a biomarker of systemic inflammation that is implicated in cancer risk and cardiovascular disease. However, not all individuals who smoke cigarettes may experience the same benefits from quitting – particularly for NHB adults, who continue to have elevated rates of tobacco-related morbidity and mortality even after quitting. Using longitudinal smoking history and inflammation data on older adults in the HRS, this is the first study to our knowledge to examine whether the effects of smoking and cessation on CRP levels varies by race.

The current study found that smoking history was associated with CRP levels among NHW adults, where individuals who had quit smoking had lower levels of CRP compared to individuals who were currently smoking cigarettes. However, smoking history only had a significant effect on CRP levels among NHW adults, but not for NHB adults. Racial differences in smoking behavior and history may influence CRP levels and contribute to these findings. Previous studies have suggested that NHB adults who smoke cigarettes may have poorer smoking cessation outcomes potentially due to other smoking-related cognitive, mood, and psychosocial factors (Bronars et al., 2015; Fu et al., 2008; Kulak et al., 2016). In our analysis, CRP levels might have remained elevated in NHB adults who had quit smoking due to lacking sufficient coping and support mechanisms to mitigate potential life stressors following smoking cessation. For instance, NHB adults who quit smoking have reported higher levels of psychological distress than those who continued smoking compared to NHW adults (Sachs-Ericsson et al., 2009). Therefore, NHB adults who quit smoking may benefit from supplemental longer term support while quitting smoking, such as evidence based cognitive behavioral therapy and other quit-aids.

While we controlled for sociodemographic variables, there may also be other factors that contribute to potential racial differences in CRP levels post smoking cessation. Previous research has also shown that NHB adults do not always experience the same levels of biological changes or health benefits from quitting smoking compared to NHW adults. For instance, data from the Multi-Ethnic Study of Atherosclerosis

**Table 3**  
Linear Mixed Model, Fixed Effects, By Race.

	NHW					NHB				
	Estimate	SE	df	t	p	Estimate	SE	df	t	p
<b>Intercept</b>	-0.18	0.09	1660.92	-2.04	0.041*	0.01	0.23	306.15	0.04	0.971
<b>Time (ref = 2006)</b>										
2010	-0.06	0.02	2256.75	-2.64	0.008*	-0.25	0.07	308.31	-3.80	<0.001*
2014	-0.19	0.03	2459.18	-7.21	<0.001*	-0.30	0.08	421.28	-3.58	<0.001*
<b>Age</b>	0.003	0.001	1314.53	2.07	0.039*	0.001	0.004	204.93	0.19	0.846
<b>Sex (ref = Male)</b>										
Female	0.08	0.02	1268.63	3.49	0.001*	0.13	0.08	195.30	1.68	0.094
<b>Education</b>	-0.02	0.00	1310.97	-4.89	<0.001*	-0.01	0.01	192.85	-0.45	0.657
<b>BMI</b>	0.02	0.00	1491.79	13.77	<0.001*	0.01	0.005	435.63	2.52	0.012*
<b>Physical Activity (ref = none)</b>										
Any	-0.10	0.03	1287.76	-3.15	0.002*	0.04	0.10	196.05	0.42	0.672
<b>Smoking History (ref = Never)</b>										
Quit	0.05	0.03	2732.00	1.43	0.154	0.06	0.11	350.57	0.53	0.593
Smoker	0.19	0.04	2826.81	5.28	<0.001*	0.04	0.10	355.37	0.35	0.724
<b>Time × Smoking History</b>										
2010 × Quit	-0.01	0.03	2227.23	-0.25	0.805	0.07	0.10	305.23	0.72	0.472
2010 × Smoking	-0.08	0.05	2330.12	-1.73	0.085	0.25	0.13	320.76	2.02	0.044*
2014 × Quit	-0.02	0.04	2376.03	-0.55	0.584	0.06	0.13	418.85	0.45	0.653
2014 × Smoking	-0.03	0.05	2586.23	-0.65	0.519	0.04	0.14	440.63	0.26	0.796
<b>Time × Smoking Status</b>										
2010 × Yes	0.10	0.05	2446.44	2.08	0.038*	-0.16	0.11	333.95	-1.43	0.152
2014 × Yes	0.05	0.05	3358.21	1.11	0.267	0.12	0.12	473.71	1.05	0.295

**Notes:** \* $p < .05$ ; NHW = non-Hispanic, White; NHB = non-Hispanic, Black/African American. Redundant estimates are not shown. Physical activity was categorized as any (i.e., self-reporting engaging in moderate or vigorous physical activity at least one to three times per month or more) vs. none (i.e., self-reporting hardly ever or never engaging in either moderate or vigorous physical activity). Smoking history was categorized at baseline as 1) Never smoked cigarettes (i.e., denied any history of cigarette smoking), 2) Quit smoking by baseline (i.e., denied current cigarette smoking, but endorsed history of cigarette smoking), and 3) Smoking (i.e., endorsed current cigarette smoking). Smoking status was categorized as currently smoking at time of assessment (yes) or abstinent at time of assessment (no).

(MESA) study showed that NHB adults who had quit smoking still had similar high-density lipoprotein (HDL) cholesterol levels as those who continued to smoke cigarettes (Berlin et al., 2012). NHB adults were also more likely to have lower awakening cortisol levels and blunted cortisol slopes one-month post-cessation compared to NHW adults (Stahre et al., 2010; Webb Hooper, 2019). In addition, the current study findings indicated that BMI has a significant effect on CRP levels in both NHW and NHB adults, even after accounting for smoking history and status and other sociodemographic variables. Notably, BMI was the only significant predictor of CRP for NHB adults in the stratified analysis. This is consistent with previous research that shows that adjusting for BMI may explain racial differences observed in CRP levels (Kelley-Hedgpeth et al., 2008; Stepanikova et al., 2017). Adiposity may have a particularly strong effect on change in CRP levels, especially in NHB adults (Asthana et al., 2010). Emerging evidence has suggested that NHB adults may experience more dramatic increases in adiposity post-cessation compared to NHW adults (Tan et al., 2021). Although NHB adults gain an average of four to ten pounds after quitting cigarette smoking within one year (Tan et al., 2018), longitudinal cohort studies have also shown disproportionate weight gain between NHW and NHB adults after quitting smoking over longer periods of time (e.g., 10–15 years), where NHB adults are twice as likely to gain weight and gain weight excessively after quitting (Klesges et al., 1998; Williamson et al., 1991). However, additional research, such as a hierarchical regression analysis, is needed to formally test potential explanations for the association between race, BMI, and CRP post-smoking cessation.

#### 4.1. Strengths and limitations

Strengths of our study included our methodological approach, including longitudinal examination of change in inflammation and inclusion of a large, representative sample of NHB and NHW older adults. Specifically, our approach allowed for us to model individual change in CRP, which takes into account that each individual subject changes at a different rate across time, while also estimating group differences. We were also able to capture the dynamic nature of smoking behavior by incorporating both smoking status (within-subjects effects) and smoking history (between-subjects effects) in our analyses. Of note, we included in the initial analyses a measure of smoking intensity, as smoking intensity has been positively linked to mortality (Inoue-Choi et al., 2020). But smoking intensity was not found to be statistically significant, which is consistent with prior longitudinal research showing that smoking intensity is not associated with CRP (Asthana et al., 2010; King et al., 2017), and, therefore, was excluded from the final model.

Results should be considered in the context of study limitations. First, as NHB adults in the US experience some of the greatest disparities in smoking cessation and smoking-related health risks, our study analyses chose to focus only on participants who identified as NHB or NHW and excluded other racial/ethnic groups. Future work should examine sociodemographic and smoking history effects on levels of CRP to explore if similar trends are found for other ethnic and racial groups. Next, as there was limited evidence to suggest that prevalence of chronic diseases was especially pronounced in our sample, we did not control for occurrence of newly diagnosed chronic conditions (e.g., hypertension, diabetes) in the current analyses; nor did we control for metabolic syndrome. In the initial analyses, we included diagnoses of diabetes,

cardiovascular disease, and cancer; however, as these variables were excluded to create a more parsimonious model as they were not found to be statistically significantly associated with CRP in this sample. Finally, we were unable to include a robust measure of physical activity in the model, as it is strongly related to CRP (Lavie et al., 2011); our baseline measures of physical activity were self-report, dichotomous variables. However, future studies should also examine the effect of smoking history and race on levels of CRP in the context of other chronic conditions. Furthermore, although we accounted for the dynamicity of smoking, more work is needed to understand the nuanced relationships between changes in smoking behaviors and health across the life course.

## 5. Conclusions

While smoking cessation is undeniably beneficial for all individuals who smoke cigarettes, our findings showed that smoking cessation was associated with significantly lower CRP levels among NHW, but not NHB, older adults. Given the large tobacco-related health disparities experienced by NHB adults, including those who have quit smoking, more research is needed to understand why individuals who identified as NHB may not experience the same health benefits post-quitting as other ethnic/racial groups.

## 6. Disclosure of Funding and conflicts of interests

The content is solely the responsibility of the authors and does not necessarily represent the official views of NIH. NIH had no role in the study design, collection, analysis or interpretation of the data, writing the manuscript, or the decision to submit the paper for publication. Funding for this study and manuscript preparation was supported by the National Cancer Institute under grant number R21CA249357 to MMT. NCJ was supported by National Heart, Lung, and Blood Institute T32HL076134. All authors made significant contributions to the manuscript. No financial disclosures were reported by the authors of this paper.

## CRedit authorship contribution statement

**Nancy C. Jao:** Conceptualization, Data curation, Methodology, Software, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing – original draft. **Aresha Martinez-Cardoso:** Validation, Visualization, Writing – original draft. **Moin Vahora:** Investigation, Visualization, Writing – original draft. **Marcia M. Tan:** Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References

Aldaham, S., Foote, J.A., Chow, H.-H., Hakim, I.A., 2015. Smoking status effect on inflammatory markers in a randomized trial of current and former heavy smokers. *Int. J. Inflam.* 2015, 439396. <https://doi.org/10.1155/2015/439396>.

Allin, K.H., Nordestgaard, B.G., 2011. Elevated C-reactive protein in the diagnosis, prognosis, and cause of cancer. *Crit. Rev. Clin. Lab. Sci.* 48 (4), 155–170. <https://doi.org/10.3109/10408363.2011.599831>.

Asthana, A., Johnson, H.M., Piper, M.E., Fiore, M.C., Baker, T.B., Stein, J.H., 2010. Effects of smoking intensity and cessation on inflammatory markers in a large cohort of active smokers. *Am. Heart J.* 160 (3), 458–463. <https://doi.org/10.1016/j.ahj.2010.06.006>.

Berlin, I., Lin, S., Lima, J.A., Bertoni, A.G., 2012. Smoking status and metabolic syndrome in the multi-ethnic study of atherosclerosis. A cross-sectional study. *Tob. Induc. Dis.* 10 (1), 9. <https://doi.org/10.1186/1617-9625-10-9>.

Black, S., Kushner, I., Samols, D., 2004. C-reactive Protein. *J. Biol. Chem.* 279 (47), 48487–48490. <https://doi.org/10.1074/jbc.R400025200>.

Brenner, D.R., Scherer, D., Muir, K., Schildkraut, J., Boffetta, P., Spitz, M.R., Le Marchand, L., Chan, A.T., Goode, E.L., Ulrich, C.M., Hung, R.J., 2014. A review of the application of inflammatory biomarkers in epidemiologic cancer research. *Cancer Epidemiol., Biomarkers Prevent.* 23 (9), 1729–1751. <https://doi.org/10.1158/1055-9965.Epi-14-0064>.

Bronars, C.A., Faseru, B., Krebill, R., Mayo, M.S., Snow, T.M., Okuyemi, K.S., Ahluwalia, J.S., Cox, L.S., 2015. Examining smoking dependence motives among African American light smokers. *J. Smok Cessat* 10 (2), 154–161. <https://doi.org/10.1017/jsc.2014.7>.

Brown, D., Zingone, A., Yu, Y., Zhu, B., Candia, J., Cao, L., Ryan, B.M., 2019. Relationship between circulating inflammation proteins and lung cancer diagnosis in the national lung screening trial. *Cancer Epidemiol., Biomarkers Prevent.* 28 (1), 110–118. <https://doi.org/10.1158/1055-9965.Epi-18-0598>.

Chaturvedi, A.K., Caporaso, N.E., Katki, H.A., Wong, H.L., Chatterjee, N., Pine, S.R., Chanock, S.J., Goedert, J.J., Engels, E.A., 2010. C-reactive protein and risk of lung cancer. *J. Clin. Oncol.* 28 (16), 2719–2726. <https://doi.org/10.1200/jco.2009.27.0454>.

Crimmins, E., Faul, J., Kim, J.K., Guyer, H., Langa, K., Ofstedal, M.B., Sonnega, A., Wallace, R., Weir, D., 2013. Documentation of biomarkers in the 2006 and 2008 Health and Retirement Study. Survey Research Center University of Michigan, Ann Arbor, MI.

Elinav, E., Nowarski, R., Thaiss, C.A., Hu, B., Jin, C., Flavell, R.A., 2013. Inflammation-induced cancer: crosstalk between tumours, immune cells and microorganisms. *Nat. Rev. Cancer* 13 (11), 759–771. <https://doi.org/10.1038/nrc3611>.

Fiore, M.C., Jaen, C.R., Baker, T.B., Bailey, W.C., Benowitz, N.L., Curry, S.J., Dorfman, S.F., Froelicher, E.S., Goldstein, M.G., Healtor, C.G., Henderson, P.N., Heyman, R.B., Koh, H.K., Kottke, T.E., Lando, H.A., Mecklenburg, R.E., Mermelstein, R.J., Mullen, P.D., Orleans, C.T., Robinson, L., Stitzer, M.L., Tommasello, A.C., Villejo, L., Wewers, M.E., Murray, E.W., Bennett, G., Heishman, S., Husten, C., Morgan, G., Williams, C., Christiansen, B.A., Piper, M.E., Hasselblad, V., Fraser, D., Theobald, W., Connell, M., Leitzke, C., Panel, P.G.U., Liaisons, P.G.U., & Staff, P.G.U., 2008. Treating tobacco use and dependence: 2008 update US Public Health Service Clinical Practice Guideline executive summary. *Respiratory Care*, 53(9), 1217-1222. <Go to ISI>://WOS:000259153500011.

Fu, S.S., Kodl, M.M., Joseph, A.M., Hatsukami, D.K., Johnson, E.O., Breslau, N., Wu, B., Bierut, L., 2008. Racial/Ethnic disparities in the use of nicotine replacement therapy and quit ratios in lifetime smokers ages 25 to 44 years. *Cancer Epidemiol., Biomarkers Prevent.* 17 (7), 1640–1647. <https://doi.org/10.1158/1055-9965.EPI-07-2726>.

Hastie, C.E., Haw, S., Pell, J.P., 2008. Impact of smoking cessation and lifetime exposure on C-reactive protein. *Nicotine Tob. Res.* 10 (4), 637–642. <https://doi.org/10.1080/14622200801978722>.

Inoue-Choi, M., Christensen, C.H., Rostron, B.L., Cosgrove, C.M., Reyes-Guzman, C., Apelberg, B., Freedman, N.D., 2020. Dose-response association of low-intensity and nondaily smoking with mortality in the United States. *JAMA Netw. Open* 3 (6), e206436. <https://doi.org/10.1001/jamanetworkopen.2020.6436>.

Jamal, A., Phillips, E., Gentzke, A.S., Homa, D.M., Babb, S.D., King, B.A., Neff, L.J., 2018. Current Cigarette Smoking Among Adults — United States, 2016. *MMWR Morb. Mortal. Wkly Rep.* 67 (2), 53–59. <Go to ISI>://WOS:0004422763400001. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5772802/pdf/mm6702a1.pdf>.

Kaufman, J.S., Cooper, R.S., 2001. Commentary: considerations for use of racial/ethnic classification in etiologic research. *Am. J. Epidemiol.* 154 (4), 291–298. <https://doi.org/10.1093/aje/154.4.291>.

Kelley-Hedgpeeth, A., Lloyd-Jones, D.M., Colvin, A., Matthews, K.A., Johnston, J., Sowers, M.R., Sternfeld, B., Pasternak, R.C., Chae, C.U., 2008. Ethnic differences in C-reactive protein concentrations. *Clin. Chem.* 54 (6), 1027–1037. <https://doi.org/10.1373/clinchem.2007.098996>.

King, C.C., Piper, M.E., Gepner, A.D., Fiore, M.C., Baker, T.B., Stein, J.H., 2017. Longitudinal Impact of Smoking and Smoking Cessation on Inflammatory Markers of Cardiovascular Disease Risk. *Arterioscler. Thromb. Vasc. Biol.* 37 (2), 374–379. <https://doi.org/10.1161/atvbaha.116.308728>.

Klesges, R.C., Ward, K.D., Ray, J.W., Cutter, G., Jacobs Jr., D.R., Wagenknecht, L.E., 1998. The prospective relationships between smoking and weight in a young, biracial cohort: the Coronary Artery Risk Development in Young Adults Study. *J. Consult. Clin. Psychol.* 66 (6), 987–993.

Kulak, J.A., Cornelius, M.E., Fong, G.T., Giovino, G.A., 2016. Differences in Quit Attempts and Cigarette Smoking Abstinence Between Whites and African Americans in the United States: Literature Review and Results From the International Tobacco Control US Survey. *Nicotine Tob. Res.* 18 (Suppl 1), S79–S87. <https://doi.org/10.1093/ntr/ntv228>.

Lagiou, P., Trichopoulos, D., 2011. Inflammatory biomarkers and risk of lung cancer. *J. Natl Cancer Inst.* 103 (14), 1073–1075. <https://doi.org/10.1093/jnci/djr220>.

Lavie, C.J., Church, T.S., Milani, R.V., Earnest, C.P., 2011. Impact of physical activity, cardiorespiratory fitness, and exercise training on markers of inflammation. *J. Cardiopulm. Rehabil. Prev.* 31 (3), 137–145. <https://doi.org/10.1097/HCR.0b013e3182122827>.

McEvoy, J.W., Nasir, K., DeFilippis, A.P., Lima, J.A., Bluemke, D.A., Hundley, W.G., Barr, R.G., Budoff, M.J., Szklo, M., Navas-Acien, A., Polak, J.F., Blumenthal, R.S., Post, W.S., Blaha, M.J., 2015. Relationship of cigarette smoking with inflammation and subclinical vascular disease: the Multi-Ethnic Study of Atherosclerosis. *Arterioscler. Thromb. Vasc. Biol.* 35 (4), 1002–1010. <https://doi.org/10.1161/ATVBAHA.114.304960>.

Meaney, C.L., Mitchell, K.A., Zingone, A., Brown, D., Bowman, E., Yu, Y., Wenzlaff, A.S., Neslund-Dudas, C., Pine, S.R., Cao, L., Schwartz, A.G., Ryan, B.M., 2019. Circulating

- Inflammation Proteins Associated With Lung Cancer in African Americans. *J. Thoracic Oncol.* 14 (7), 1192–1203. <https://doi.org/10.1016/j.jtho.2019.03.014>.
- Morimoto, Y., Conroy, S.M., Ollberding, N.J., Kim, Y., Lim, U., Cooney, R.V., Franke, A. A., Wilkens, L.R., Hernandez, B.Y., Goodman, M.T., Henderson, B.E., Kolonel, L.N., Le Marchand, L., Maskarinec, G., 2014. Ethnic differences in serum adipokine and C-reactive protein levels: the multiethnic cohort. *Int. J. Obesity* 38 (11), 1416–1422. <https://doi.org/10.1038/ijo.2014.25>.
- Ohsawa, M., Okayama, A., Nakamura, M., Onoda, T., Kato, K., Itai, K., Yoshida, Y., Ogawa, A., Kawamura, K., Hiramori, K., 2005. CRP levels are elevated in smokers but unrelated to the number of cigarettes and are decreased by long-term smoking cessation in male smokers. *Prev. Med.* 41 (2), 651–656. <https://doi.org/10.1016/j.ypmed.2005.02.002>.
- Paalani, M., Lee, J.W., Haddad, E., Tonstad, S., 2011. Determinants of inflammatory markers in a bi-ethnic population. *Ethn. Dis.* 21 (2), 142–149.
- Pepys, M.B., Hirschfield, G.M., 2003. C-reactive protein: a critical update. *J. Clin. Invest.* 111 (12), 1805–1812. <https://doi.org/10.1172/jci18921>.
- Pine, S.R., Mechanic, L.E., Enewold, L., Chaturvedi, A.K., Katki, H.A., Zheng, Y.L., Bowman, E.D., Engels, E.A., Caporaso, N.E., Harris, C.C., 2011. Increased levels of circulating interleukin 6, interleukin 8, C-reactive protein, and risk of lung cancer. *J. Natl Cancer Inst.* 103 (14), 1112–1122. <https://doi.org/10.1093/jnci/djr216>.
- Sachs-Ericsson, N., Schmidt, N.B., Zvolensky, M.J., Mitchell, M., Collins, N., Blazer, D.G., 2009. Smoking cessation behavior in older adults by race and gender: the role of health problems and psychological distress. *Nicotine Tob. Res.* 11 (4), 433–443. <https://doi.org/10.1093/ntr/ntp002>.
- Shiels, M.S., Pfeiffer, R.M., Hildesheim, A., Engels, E.A., Kemp, T.J., Park, J.H., Katki, H. A., Koshiol, J., Shelton, G., Caporaso, N.E., Pinto, L.A., Chaturvedi, A.K., 2013. Circulating inflammation markers and prospective risk for lung cancer. *J. Natl Cancer Inst.* 105 (24), 1871–1880. <https://doi.org/10.1093/jnci/djt309>.
- Sonnega, A., Faul, J.D., Ofstedal, M.B., Langa, K.M., Phillips, J.W., Weir, D.R., 2014. Cohort Profile: the Health and Retirement Study (HRS). *Int. J. Epidemiol.* 43 (2), 576–585. <https://doi.org/10.1093/ije/dyu067>.
- Stahre, M., Okuyemi, K.S., Joseph, A.M., Fu, S.S., 2010. Racial/ethnic differences in menthol cigarette smoking, population quit ratios and utilization of evidence-based tobacco cessation treatments. *Addiction* 105 (Suppl 1), 75–83. <https://doi.org/10.1111/j.1360-0443.2010.03200.x>.
- Stepanikova, I., Bateman, L.B., Oates, G.R., 2017. Systemic inflammation in midlife: race, socioeconomic status, and perceived discrimination. *Am. J. Prev. Med.* 52 (1s1), S63–S76. <https://doi.org/10.1016/j.amepre.2016.09.026>.
- Tan, M.M., Okuyemi, K.S., Resnicow, K., Dietz, N.A., Antoni, M.H., Webb Hooper, M., 2018. Association between smoking cessation and weight gain in treatment-seeking African Americans. *Addict. Behav.* 81, 84–90. <https://doi.org/10.1016/j.addbeh.2018.02.002>.
- Tan, M.M., Bush, T., Lovejoy, J.C., Javitz, H., Torres, A.J., Wassum, K., Spring, B., 2021. Race differences in predictors of weight gain among a community sample of smokers enrolled in a randomized controlled trial of a multiple behavior change intervention. *Prev. Med. Rep.* 21, 101303. <https://doi.org/10.1016/j.pmedr.2020.101303>.
- Tonstad, S., Cowan, J.L., 2009. C-reactive protein as a predictor of disease in smokers and former smokers: a review. *Int. J. Clin. Pract.* 63 (11), 1634–1641. <https://doi.org/10.1111/j.1742-1241.2009.02179.x>.
- U.S. Department of Health and Human Services, 2014. The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General; U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
- VanderWeele, T.J., Robinson, W.R., 2014. On the causal interpretation of race in regressions adjusting for confounding and mediating variables. *Epidemiology* 25 (4), 473–484. <https://doi.org/10.1097/ede.000000000000105>.
- Webb Hooper, M., 2019. Racial/ethnic differences in physiological stress and relapse among treatment seeking tobacco smokers. *Int. J. Environ. Res. Public Health* 16 (17). <https://doi.org/10.3390/ijerph16173090>.
- Williamson, D.F., Madans, J., Anda, R.F., Kleinman, J.C., Giovino, G.A., Byers, T., 1991. Smoking cessation and severity of weight gain in a national cohort. *N. Engl. J. Med.* 324 (11), 739–745. <https://doi.org/10.1056/NEJM199103143241106>.
- Yanbaeva, D.G., Dentener, M.A., Creutzberg, E.C., Wesseling, G., Wouters, E.F., 2007. Systemic effects of smoking. *Chest* 131 (5), 1557–1566. <https://doi.org/10.1378/chest.06-2179>.
- Zahodne, L.B., Kraal, A.Z., Zaheed, A., Farris, P., Sol, K., 2019. Longitudinal effects of race, ethnicity, and psychosocial disadvantage on systemic inflammation. *SSM – Popul. Health* 7. <https://doi.org/10.1016/j.ssmph.2019.100391>, 100391–100391.