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Ashley W. Kranjac
Chapman University, kranjac@chapman.edu

Dinko Kranjac
University of La Verne, dinko@laverne.edu

Olivia Lounsbury
Chapman University

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Ashley W. Kranjac[1*], Dinko Kranjac[2], Olivia Lounsbury[3]

Author Affiliations:

[1]Department of Sociology, Wilkinson College, Chapman University, 1 University Drive, Orange, California

[2]Department of Psychology, College of Arts and Sciences, University of La Verne, 1950 Third Street, La Verne, California

[3]Department of Health Sciences, Crean College of Health and Behavioral Sciences, Chapman University, 1 University Drive, Orange, California

***Correspondence to**: kranjac@chapman.edu.

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Abstract

Objectives: Heightened inflammatory state, as measured by circulating C-reactive protein (CRP) levels, can promote inflammation-mediated disease risk. It is important to account for population fluctuation and sex variation in serum CRP concentrations on overall time trends. **Methods:** Using the National Health and Nutrition Examination Survey (NHANES) data, we specify linear and algebraic decomposition models separately by sex to identify the drivers of the changing trends in the distribution of CRP values in the population. **Results:** We found a nonsignificant overall increase in CRP, but a significant decrease among women and increase among men, over a 10-year period. We then used linear and algebraic decomposition techniques to identify the sources of change in CRP over time, separately for women and men. CRP increased among men mainly because lifestyle/health characteristics worsened over time, and because the size of socioeconomic/demographic groups with higher CRP increased and the size of groups with lower CRP decreased. The downward shift in CRP among women occurred because the typical woman across all cohorts had lower CRP levels. **Conclusions:** We identified two fundamentally different processes of change driving the decline and rise in CRP values among women and men, respectively.

Keywords: C-reactive protein; Inflammation; NHANES; Public Health; Statistics

INTRODUCTION

Systemic chronic inflammation (SCI) predicts all-cause mortality and plays a role in the etiology of cardiovascular and cerebrovascular disease, as well as major autoimmune, neurodegenerative, psychiatric, and cognitive disorders (Furman et al., 2019; Kaptoge et al., 2010; Kuo et al., 2005; Proctor et al., 2015). Medical professionals increasingly rely on circulating biomarkers to improve diagnostic and prognostic accuracy of heightened inflammatory activity (Furman et al., 2019; Kaptoge et al., 2010). C-reactive protein (CRP) is one of the SCI-related biomarkers, and modest increases in serum CRP levels are associated with a wide variety of physical and mental health problems such as heart disease, stroke, cancer, and diabetes mellitus (Furman et al., 2019; Kaptoge et al., 2010; Kuo et al., 2005). Given that CRP is a useful nonspecific prognostic marker of future disease and mortality (Furman et al., 2019; Kaptoge et al., 2010; Kuo et al., 2005; Proctor et al., 2015), we perused the relevant peer-reviewed literature and found that researchers seemingly neglect to examine CRP trends over time. We identified one notable exception, where authors used the National Health and Nutrition Examination Survey (NHANES) data to examine CRP trends from 1999–2010 (Ong et al., 2013). Ong et al. (2013) reported a significant decrease in CRP levels in a nationally representative population of U.S. adults. The authors of this single existing study on CRP trends did not take sex variation into account (Ong et al., 2013), even though researchers consistently report higher CRP levels in women, compared with those of men (McConnell et al., 2002; Woloshin & Schwartz, 2005). Using the same NHANES dataset (CDC, 2021), we performed separate analyses to compare the population distribution of CRP values by sex.

Here, we correctly specify models separately by sex and extend prior research (Ong et al., 2013) using the same 1999–2010 NHANES data (CDC, 2021) to identify the drivers of the

changing trends in the distribution of CRP values in the population. The putative mechanisms that impair normal immune function and influence the levels of circulating CRP are complex (Furman et al., 2019; Nazmi & Victora, 2007; Proctor et al., 2015; Slavich, 2015). Many of the SCI-promoting factors are related to a combination of non-heritable influences such as surrounding social and physical conditions, as well as lifestyle-related habits (Furman et al., 2019; Nazmi & Victora, 2007; Proctor et al., 2015; Slavich, 2015). Serum levels of CRP are associated with race/ethnicity (McConnell et al., 2002; Nazmi & Victora, 2007), education (Muscatell et al., 2018)), and demographic (e.g., sex (McConnell et al., 2002; Woloshin & Schwartz, 2005), socioeconomic (e.g., income (Nazmi & Victora, 2007)), and lifestyle-related (e.g., nutrition (Block et al., 2009; Smidowicz & Regula, 2015) factors, as well as with weight (Choi et al., 2013; Selvin et al., 2007), physical activity (Fedewaet al., 2017; Kasapis & Thompson, 2005; Plaisance & Grandjean, 2006), alcohol usage (Stewart et al., 2002), and tobacco smoking status (Gallus et al., 2018). Overlooked is the fact that fluctuating levels of CRP among individuals over time might be a result of two proximate sources: 1) individuals can change across sizable segments of society; and 2) the composition of a population can change. That is, levels of CRP can fluctuate due to changing public health habits *or* changing publics (Ryder, 1965; Firebaugh & Davis 1988; Firebaugh, 2008). To our knowledge, the effect of changing publics—changing population composition due to population turnover or cohort replacement—on CRP has yet to be explored. Here, we aim to explain the root causes of change in mean CRP levels over time, separately for women and men, by examining whether the observed shift in CRP values is attributable to broad sectors of individuals changing *or* populations changing.

METHODS

Data sources

We use the latest data where CRP measures are available to us, derived from six waves (1999/00, 2001/02, 2003/04, 2005/06, 2007/08, 2009/10) of the NHANES, a cross-sectional survey of the civilian, non-institutionalized US population (CDC, 2021). NHANES uses a complex multistage probability sampling design, with oversampling of smaller racial/ethnic subgroups (CDC, 2021). In all analyses, we used the NHANES sampling weights that adjust for non-response and unequal probabilities of selection (CDC, 2021).

Study population

Models were restricted to adults aged 20–74 years old with a completed body measurement component. Pregnant women were excluded. The total sample size across all waves is 26,278 participants.

Measures

Our primary outcome of interest is CRP (mg/L). We excluded individuals with CRP value below the detectable level of 0.20 mg/L (n = 893), and those with presumed acute inflammation (> 10.00 mg/L, n=2,867) (CDC, 2021; Pearson et al., 2003). We included covariates to represent demographic, socioeconomic, nutritional, and lifestyle/health factors known to associate with CRP. Sociodemographic characteristics include survey year, birth year, sex (1=male), race/ethnicity (1=non-Latino white), marital status (1=married), household income, and educational attainment (1=college graduate). Nutrition characteristics include total intake of energy (1 = ≤2,000 kcals), fat (1 = ≤78 grams), carbohydrates (1 = ≤100 grams), protein (1 = ≤56 grams), sodium (1 = ≤1,500 milligrams), and vitamin C (1 = >90 milligrams) during a 24-hour period. Physical activity was classified by rate of energy expenditure [1 = ≥3

and <6 metabolic equivalents (METS) defined as 3.5 ml O2·kg−1·min−1 or moderate expenditure], pursuant to a particular activity. Lifestyle/health characteristics include blood pressure (1 = ≤120/80 defined as mm/HG or a normal systolic/diastolic reading), current tobacco smoking status (1 = non-smoker), weekly alcohol usage (for women 2 = ≥1 and ≤7 drinks, 3 = >7 drinks; for men 2 = ≥1 and ≤14 drinks, 3 = >14 drinks), and body mass index (BMI; 1 = BMI ≥18.5 and <25.0 kg m-2 or "normal" weight).

Statistical analysis

To decompose aggregate change in CRP from 1999–2010, we used Firebaugh's linear decomposition technique (Firebaugh, 1989, 2008) to identify the sources of population-level change in CRP. Specifically, we assess whether the changing associations across society between demographic, socioeconomic, nutritional, and lifestyle/health factors and CRP is driving the linear change in CRP levels over time among women and men in the population, or whether changing population composition due to population turnover is what is driving the change in CRP. With this technique, cohort differences were estimated by regressing CRP on birth year and survey year. We estimated both an unconditional model that only included cohort (birth year) and period (survey year), as well as a series of conditional models that included the covariates to assess the impacts of demographic, socioeconomic, nutritional, and lifestyle/health factors on the estimated coefficients for cohort and period. This particular decomposition method assumes linearity (Firebaugh, 1989, 2008), but change in CRP may not be linear. Thus, we also collapsed birth year into cohort subgroups (Firebaugh, 1989, 2008) and used Kitagawa's (1955) algebraic decomposition method that does not assume linearity, wherein change in CRP is estimated between survey wave k+1 and k. Both techniques allowed us to partition total change in CRP into two components of aggregate change: intracohort change and cohort replacement.

Intracohort change is computed by multiplying the regression coefficient for the survey year variable by the length of the study period (i.e., last survey year - first survey year). Cohort replacement is generated by multiplying the regression coefficient for the birth year variable by the difference between the mean birth years for the final and initial survey years. Intracohort change indicates how much of the aggregated change in CRP is attributable to individuals across sizable segments of society changing (i.e., period changes), and cohort replacement indicates how much of the total change in CRP is attributable to population turnover (i.e., the death of old cohorts with higher/lower CRP and the birth of new cohorts with higher/lower CRP). We assigned the midpoint mean for each survey wave and used linear interpolation methods to account for the multi-year data collection design in the NHANES data (CDC, 2021).

RESULTS

The mean CRP levels increased, though not significantly, from 1999–2010 (2.51 mg/L and 2.55 mg/L, respectively), for adults aged 20–74 years (Table 1). Estimates among both women and men reveal significant CRP variation over this time period. CRP decreased significantly among women (1999: 2.67 mg/L vs. 2010: 2.62 mg/L, $P < 0.001$), and increased significantly among men (1999: 1.98 mg/L vs. 2010: 2.04, $P < 0.001$). We display trends in CRP overall, and separately for women and men (Figure 1). Overall, from 1999–2010, CRP was remarkably stable. In the early 2000s, CRP increased slightly before stabilizing, and then remained consistent until 2010. For both women and men, CRP varied substantially between 1999 and 2010. CRP is substantially higher in women compared to men over the entire study period, especially from the early 1990s to early 2000s. From 2003/04–2007/08, trends parallel one another.

<Figure 1>

To illustrate the potential trajectories of change in CRP values, we display cohort replacement and intracohort rate of change predictions for women and men. As shown in Figure 2, *if* intracohort change is central to the decline in CRP for women, then the decline would happen more quickly and be distributed more broadly among all birth cohorts and age groups. On the other hand, *if* cohort replacement is crucial to this decrease, then a gradual decrease in CRP would occur. With regard to men, *if* intracohort change is the principal driver of the increase in CRP, then age-specific CRP for all cohorts will increase after CRP began to increase in the early 2000s. These age-specific increases will be greater for more recent than earlier cohorts, leading to a faster rise. However, *if* cohort replacement is central to this increase, then CRP values for more recent cohorts will be higher than those of previous cohorts throughout adulthood, creating a more gradual rise since more time is needed for the cohort replacement mechanism to operate.

<Figure 2>

Before partitioning total change into its intracohort change and cohort replacement components, we present mean CRP values by age for the cohorts in our study with sufficient sample sizes (N ≥50) for the 10-year age group intervals, separately for women (Figure 3) and men (Figure 4). We do this as an initial step to determine the relative importance of intracohort change and cohort replacement on the CRP variation. In Figure 3, we see that both intracohort change and cohort replacement played significant roles in CRP decline among women from 1999–2010. Consistent with the cohort replacement explanation, more recent cohorts have lower CRP than do earlier cohorts over the course of adulthood. For example, 30–39-year-olds born between 1980 and 1989 have lower CRP than do 30–39-year-olds born between 1970 and 1979, and lower still than do cohorts born between 1960 and 1969. Consistent with the intracohort

change explanation, CRP decreased over the course of adulthood for multiple cohorts. The exception are two of the earliest cohorts (1930–1939 and 1940–1949), where CRP decreased as cohort members aged over time.

<Figures 3 and 4>

In Figure 4, we see a different pattern of CRP change among men, wherein intracohort change appears to drive the relatively higher CRP. Indeed, if the cohort replacement explanation prevailed, we would expect more recent cohorts to have higher CRP than earlier cohorts, but CRP for more recent cohorts of men is consistently lower than that of previous cohorts throughout adulthood, aside from the higher CRP observed among the most recent cohort (1980–1989) of 20–29-year-olds. Consistent with the intracohort change explanation, CRP increased over the course of adulthood for nearly all cohorts of men.

Next, we turn to the compositional differences between cohorts for women (Figure 5) and men (Figure 6). We computed total change (total change = intracohort change + cohort replacement) for models that entered sociodemographic, nutritional, and lifestyle/health measures separately for women (Figure 5) and men (Figure 6) to estimate differences among cohorts and time periods. The top bars in Figures 5 and 6 illustrate the percentages of overall change in CRP attributable to intracohort change (dark gray) and cohort replacement (light gray), if compositional differences among the cohorts are ignored. We show estimates for unadjusted models (no control variables), and for conditional models that entered sociodemographic, nutritional, and lifestyle/health measures separately into the model. In Figure 5, we see that the 10-year decrease in CRP among women largely reflects intracohort change. The typical member of all cohorts of women presented with a lower CRP over time. In Figure 6, we see a different picture, compared with our presentation of CRP levels by age and cohorts (Figure 4). The higher

CRP among men from 1999–2010 is attributable comparatively more to between-cohort change (i.e., cohort replacement; Figure 6). The overall patterns of CRP among men (Figure 4) masked considerable variation based on the factors known to associate with CRP (Figure 6).

<Figures 5 and 6>

Accounting for changes in the population composition may influence the relative contributions of individual change (i.e., intracohort change) and population turnover (i.e., cohort replacement) to aggregate change. For example, if more recent cohorts of women had lower CRP than did previous cohorts because they were more active and had better diets, controlling for changes in physical activity and diet would attenuate or eliminate the influence of cohort replacement on total change. The 2nd through 5th bars in Figures 5 and 6 show how adjusting for these compositional differences influenced the relative contributions of intracohort change and cohort replacement. Our interest here is how much the bars shrink or expand when adding different sets of measures.

If we compare the top bar (i.e., no controls) with the bottom bar (i.e., all controls) in Figure 5, we see that, accounting for the sociodemographic, nutritional, and lifestyle/health differences among cohorts of women, the estimated contribution of cohort replacement to the decrease in CRP is greatly reduced. Adjusting for differences in the sociodemographic composition of the population among women from 1999–2010 had a minimal influence on estimates of intracohort change and cohort replacement for the CRP measure (2nd bar). Nevertheless, the changing sociodemographic composition of women *is* influencing the CRP decrease, as evidenced by the shrinking cohort replacement from 31% to 26%. More specifically, the size of groups known to have higher CRP levels among women (e.g., racial/ethnic minorities, the impoverished) decreased, and the more socioeconomically advantaged groups of women

increased. Hence, controlling for these changes attenuated the influence of cohort replacement. Women's nutritional changes over time had a negligible effect on CRP, as evidenced by the near identical unadjusted 1st bar and adjusted 3rd bar for nutrition. After adjusting for compositional differences among the cohorts, cohort replacement contributed minimally to the CRP decrease (11%; 4th bar in Figure 5). The modest influence of cohort replacement we observed for the unconditional model reflects between-cohort differences in lifestyle/health factors, evidenced by shrinking of the 4th bar when we control for changes in physical activity, blood pressure, alcohol usage, and smoking and weight status.

In Figure 6, we show the percentages of overall change in CRP among men. The increase in CRP is attributable to the large positive cohort replacement estimate. Negative intracohort change partially offset the sharp increase in CRP across cohorts. The partial offsetting of intracohort change over this period is evident in that cohort replacement accounted for nearly 60% of total change in CRP, while intracohort change offset 40% of this increase. Adjustment for between-cohort differences in sociodemographic composition among men substantially increased estimates of cohort replacement. This means that more recent cohorts of men have higher CRP levels than do earlier cohorts, in part, because they are more socioeconomically disadvantaged. Men's nutritional changes over time had a negligible effect on CRP. Changes in lifestyle/health played a more notable role in CRP increase. More specifically, changes in physical activity, blood pressure, alcohol usage, and smoking and weight status account for the overall shift and CRP increase. CRP increased, in part, because lifestyle/health characteristics worsened over time, and because the size of demographic and SES groups with higher CRP got bigger and the size of groups with lower CRP got smaller. We observed the substantial influence of cohort replacement for the unconditional model, which largely reflects between-cohort

lifestyle/health differences. Adjustments for all the compositional differences among the cohorts during the study period indicate that cohort replacement contributed moderately to CRP increase (32%; last bar in Figure 6). Results from the algebraic decomposition method, which does not assume linearity, reveal similar findings to estimates reported here for both women and men.

DISCUSSION

Our analysis is motivated by discoveries over the past two decades that implicate systemic chronic inflammation in the etiology of a wide variety of physical and mental health problems (Furman et al., 2019; Slavich, 2015). Heightened inflammatory state, as measured by circulating C-reactive protein (CRP) levels, is associated with inflammation-mediated disease risk for cardiometabolic, cerebrovascular, autoimmune, neurodegenerative, and psychiatric illness (Furman et al., 2019; Kaptoge et al., 2010; Kuo et al., 2005; Proctor et al., 2015; Slavich, 2015). We identified only one published study where researchers sought to characterize serum CRP trends among U.S. adults (Ong et al., 2013). Ong et al. (2013) reported an overall significant decreasing trend in mean CRP levels from 1999–2010. We used the same NHANES data (CDC, 2021) and, conversely, found a nonsignificant increase in mean CRP levels from 1999–2010 (Table 1). Similar to Ong et al. (2013), we included six waves of data to analyze the 10-year trend. But we reported mean CRP value change from 1999/00–2009/10 (Figure 1), whereas Ong et al. (2013) combined the 1999/00 and 2001/02, and 2007/08 and 2009/10, waves of data, and reported mean CRP value change from 1999/02–2007/10 (Ong et al., 2013). Furthermore, Ong et al. (2013) did report that the study participants with heightened levels of CRP tended to be women, but did not perform CRP trend analyses separately for women and men (Ong et al., 2013). Our results are in line with previously published findings (McConnell et al., 2002; Woloshin & Schwartz, 2005) and indicate that CRP levels among women, compared

with those of men, were substantially higher across the entire study period. Importantly, we show that the sharp increase in CRP levels for women between the 1999/00 and 2001/02 waves drives the *overall* (i.e., data for women and men combined) downward CRP trend reported by Ong et al. (2013). Thus, Ong et al. (2013) observed the decreasing trend because they combined the 1999/00 and 2001/02 waves of data.

Here, we expand upon previous research on CRP trends over time (Ong et al., 2013), and show that CRP levels *decreased* significantly among women and *increased* significantly among men between 1999 and 2010. Then, we use Firebaugh's linear (Firebaugh, 1989, 2008) and Kitagawa's (1955) algebraic decomposition techniques to identify the *sources* of the changing trends in the distribution of CRP values in the adult U.S. population from 1999–2010. More specifically, we partition total change in CRP into two components of aggregate change: intracohort change (i.e., individuals across sizable segments of society changing) and cohort replacement (i.e., the population changing). We show that the observed contrasting patterns of intracohort change and cohort replacement imply different social experiences for women and men. For women, *less* pronounced cohort replacement and *more* pronounced intracohort change estimates indicate that the decrease in CRP levels was distributed more broadly across women born to different cohorts. This means that the changing environment is influencing all women, across all ages, in terms of health/lifestyle gains, and that is why we see a population-level decrease in CRP levels. For men, on the other hand, *more* pronounced cohort replacement and *less* pronounced intracohort change estimates indicate that the increase in CRP is driven by higher CRP levels among younger cohorts. In other words, CRP increased, in part, because the size of demographic and socioeconomic groups with higher CRP got bigger and the size of

groups with lower CRP got smaller, and because lifestyle/health characteristics worsened over time.

Limitations

Our estimates may—at least in part—reflect the time points available with CRP measure in the NHANES (CDC, 2021). Thus, we acknowledge that our estimates may shift after the NHANES dataset is updated with additional CRP data. Still, we use the latest data available to us. Related, the cross-sectional nature of our data limits our ability to make causal inferences. Similarly, the sometimes-crude nature of measures available in the NHANES for several key concepts (e.g., lack of information on childhood adversity and trauma; Alvarez et al., 2018; Fagundes et al., 2013; Lin et al., 2016) may influence estimates presented here. Also, changes in CRP for both women and men in our sample remain within the 1 mg/L to <3 mg/L throughout the majority of the study period. This is important to note given that levels of CRP at <1 mg/L, 1 mg/L to <3 mg/L, and =>3 mg/L are used to distinguish between individuals with low, moderate, and high risk of future adverse cardiovascular events, respectively (e.g., myocardial infarction, ischemic stroke; Kaptoge et al., 2010). This means that the observed change in CRP over time reported here may not lead to increased/decreased cardiovascular risk based on standard guidelines (Kaptoge et al., 2010). Moreover, we did not link individual- and family-level data to neighborhood measures despite a growing body of evidence that hints at a connection between neighborhood characteristics and inflammation (King, 2013; Heredia et al., 2021). Finally, we dichotomized nutritional intake measures to normal/high ranges due to a lack of variation among men, likely masking more nuanced patterns.

Conclusions

In line with our findings, published data indicate that SES influences health-related behaviors such as diet, exercise, and tobacco and alcohol use (Berger et al., 2019; Pampel et al., 2010). This is noteworthy given that increased basal inflammation is associated with higher socioeconomic disadvantage (Muscatell et al., 2018; Nazmi & Victoria, 2007; Pampel et al., 2010), belonging to racial/ethnic minority population (McConnell et al., 2002; Muscatell et al., 2018), sedentary lifestyle (Fedawa et al., 2017; Kasapis & Thompson, 2005; Plaisance & Grandjean, 2006), poor dietary habits (Block et al., 2009; Smidowicz & Regula, 2015), and obesity (Choi et al., 2013; Selvin et al., 2007; Visser et al., 1999). Here we show that individuals across sizable segments of the population (i.e., intracohort change) drove the decreasing CRP levels among women. Thus, policy initiatives have the potential to further drive these downward trends. Our results indicate that interventions should target all age groups and birth cohorts of women given that decreases in CRP have been widely distributed across all ages and generations. On the other hand, for men, increases in CRP largely reflect population turnover. As such, CRP trends rose gradually over time as new birth cohorts with higher CRP replaced older cohorts with lower CRP. Since the rising rates among men are largely a result of population turnover, policy efforts should focus on younger males given that changes are happening more between, rather than within, cohorts. Overall, our findings draw attention to two underlying mechanisms that shape sex-specific shifts in CRP.

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Table 1: Weighted Means and Standard Errors for Independent and Dependent Variables for Adults Aged 20-74, 1999-2010 NHANES; N = 26,278

	1999-2010		1999		2010		Δ2010-1999
Dependent Variable	Mean	Std.Err.	Mean	Std.Err.	Mean	Std.Err.	
CRP (mg/dL)							
Overall	2.38	0.03	2.51	0.07	2.55	0.08	0.04
Women	2.60	0.03	2.67	0.06	2.62	0.06	-0.05***
Men	2.00	0.02	1.98	0.04	2.04	0.05	0.06***
Independent Variables							
Demographic							
Age	43.52	0.17	43.24	0.42	45.56	0.50	-2.32***
Birth Year	1961	0.17	1956	0.42	1964	0.50	-8.44***
Sex							
Women	0.59	0.01	0.62	0.02	0.54	0.02	-0.08***
Men*	0.41	0.01	0.38	0.02	0.46	0.02	0.08***
Race							
Non-Latino white*	0.79	0.00	0.78	0.01	0.69	0.01	-0.09*
Non-Latino black	0.08	0.00	0.07	0.01	0.12	0.01	0.05***
Latino	0.04	0.00	0.08	0.01	0.04	0.01	-0.04
Other Race	0.09	0.01	0.07	0.01	0.15	0.01	0.08
Marital Status							
Married*	0.64	0.01	0.63	0.01	0.58	0.02	-0.05
Widowed/Divorced/Separated	0.18	0.00	0.20	0.01	0.24	0.01	0.04**
Not married	0.18	0.01	0.17	0.01	0.18	0.01	0.01**
Socioeconomic Status							
Household Income	58.59	0.41	54.10	0.98	43.61	0.84	-10.49***
Education							
Less than High School	0.17	0.01	0.18	0.02	0.28	0.02	0.10**
High school Graduate	0.27	0.01	0.29	0.01	0.30	0.02	0.01
Some College	0.34	0.01	0.31	0.01	0.29	0.02	-0.02***
College Graduate*	0.22	0.01	0.22	0.01	0.13	0.02	-0.09
Nutrition							
Energy (kcal)							
≤2,000*	0.41	0.01	0.42	0.00	0.51	0.01	0.09
>2,000	0.59	0.01	0.58	0.00	0.49	0.01	-0.09
Fat (gm)							
≤78*	0.45	0.01	0.47	0.00	0.51	0.01	0.04
>78	0.55	0.01	0.53	0.00	0.49	0.01	-0.04
Carbohydrates (gm)							
≤100*	0.95	0.00	0.95	0.00	0.96	0.01	0.01***
>100	0.05	0.00	0.05	0.00	0.04	0.01	-0.01***

Protein (gm)							
≤56*	0.78	0.00	0.76	0.00	0.76	0.01	-0.00
>56	0.22	0.00	0.24	0.00	0.24	0.01	0.00
Sodium (mg)							
≤1,500*	0.07	0.00	0.91	0.00	0.93	0.01	0.02***
>1,500	0.93	0.00	0.09	0.00	0.07	0.01	-0.02***
Vitamin C (mg)							
≤89	0.67	0.01	0.61	0.00	0.69	0.01	0.08
>90*	0.33	0.01	0.39	0.00	0.31	0.01	-0.08
Lifestyle & Health							
Activity							
<3 METS	0.28	0.01	0.25	0.01	0.55	0.01	0.30***
≥3 and <6 METS*	0.40	0.01	0.40	0.01	0.27	0.01	-0.13***
≥6 METS	0.32	0.01	0.35	0.01	0.18	0.01	-0.17***
Blood Pressure (systolic/ diastolic)							
≤120/80*	0.74	0.00	0.76	0.00	0.71	0.01	-0.05***
>120/80	0.26	0.00	0.24	0.00	0.29	0.01	0.05***
Current Smoking Status							
Non-Smoker*	0.81	0.00	0.78	0.01	0.82	0.01	0.04
Smoker	0.19	0.00	0.22	0.01	0.18	0.01	-0.04
Weekly Alcohol Usage							
Women							
0 drinks*	0.15	0.00	0.13	0.01	0.17	0.01	0.04***
≥1 and ≤7 drinks	0.72	0.00	0.74	0.01	0.68	0.01	-0.06***
>7 drinks	0.13	0.00	0.14	0.01	0.15	0.01	0.01
Men							
0 drinks*	0.13	0.00	0.13	0.01	0.14	0.01	0.01
≥1 and ≤14 drinks	0.71	0.00	0.73	0.01	0.67	0.01	-0.06***
>14 drinks	0.16	0.00	0.14	0.01	0.18	0.01	0.04**
Body Mass Index (kg)/height $(m)^2$							
<18.5	0.02	0.00	0.01	0.00	0.03	0.01	0.02
≥18.5 & <25.0*	0.33	0.01	0.31	0.01	0.28	0.01	-0.03***
≥25.0	0.37	0.01	0.39	0.01	0.36	0.01	-0.03
≥30.0	0.25	0.01	0.25	0.01	0.28	0.01	0.03***
≥40	0.03	0.00	0.03	0.01	0.05	0.01	0.02***

Source: NHANES 1999-2010

*Note: * Indicates Reference Group*

Note: Asterisks indicate significant change evaluated using two-tailed independent means t-test

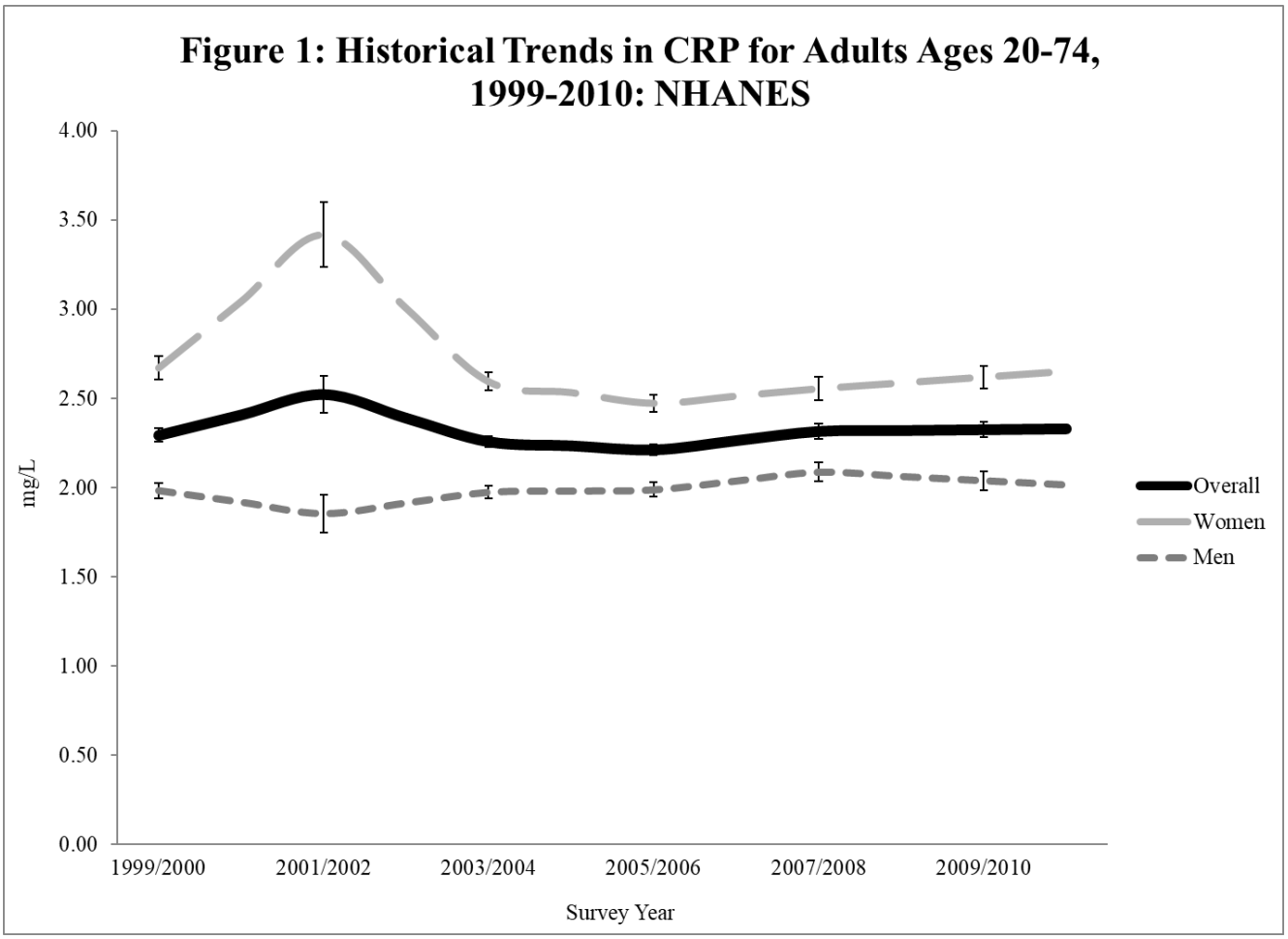
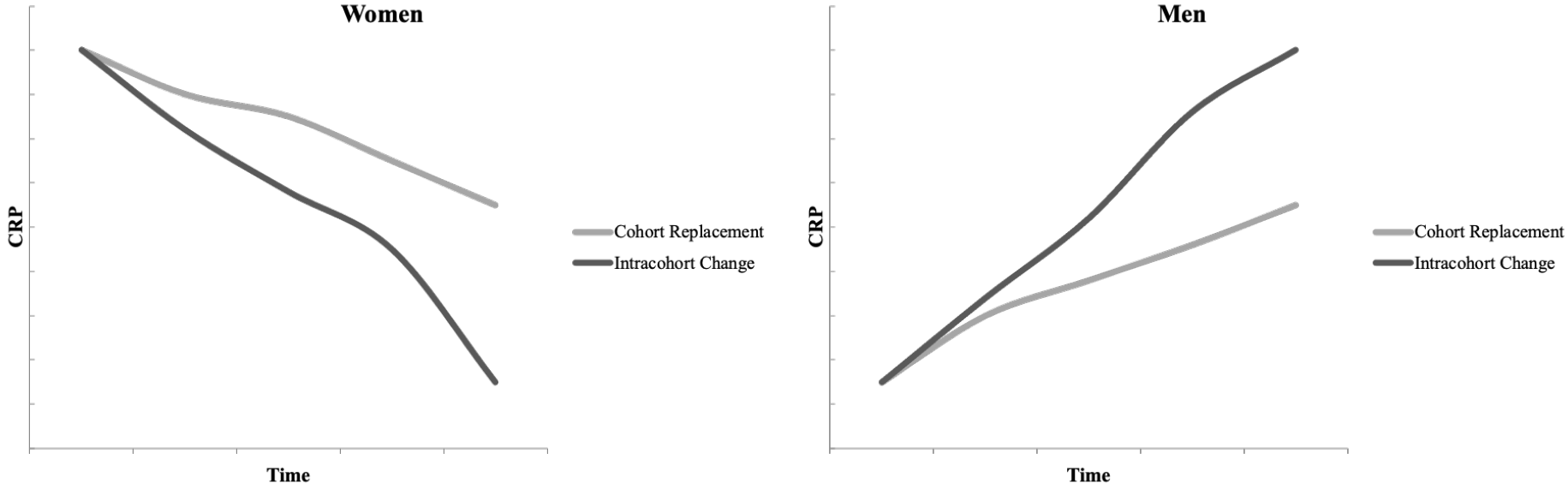


Figure 1: Historical Trends in CRP for Adults Ages 20-74, 1999-2010: NHANES
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
mg/L
1999/2000
2001/2002
2003/2004
2005/2006
2007/2008
2009/2010
Survey Year
Overall
Women
Men

Figure 2. Predictions of Change in C-reactive Protein (CRP) Values



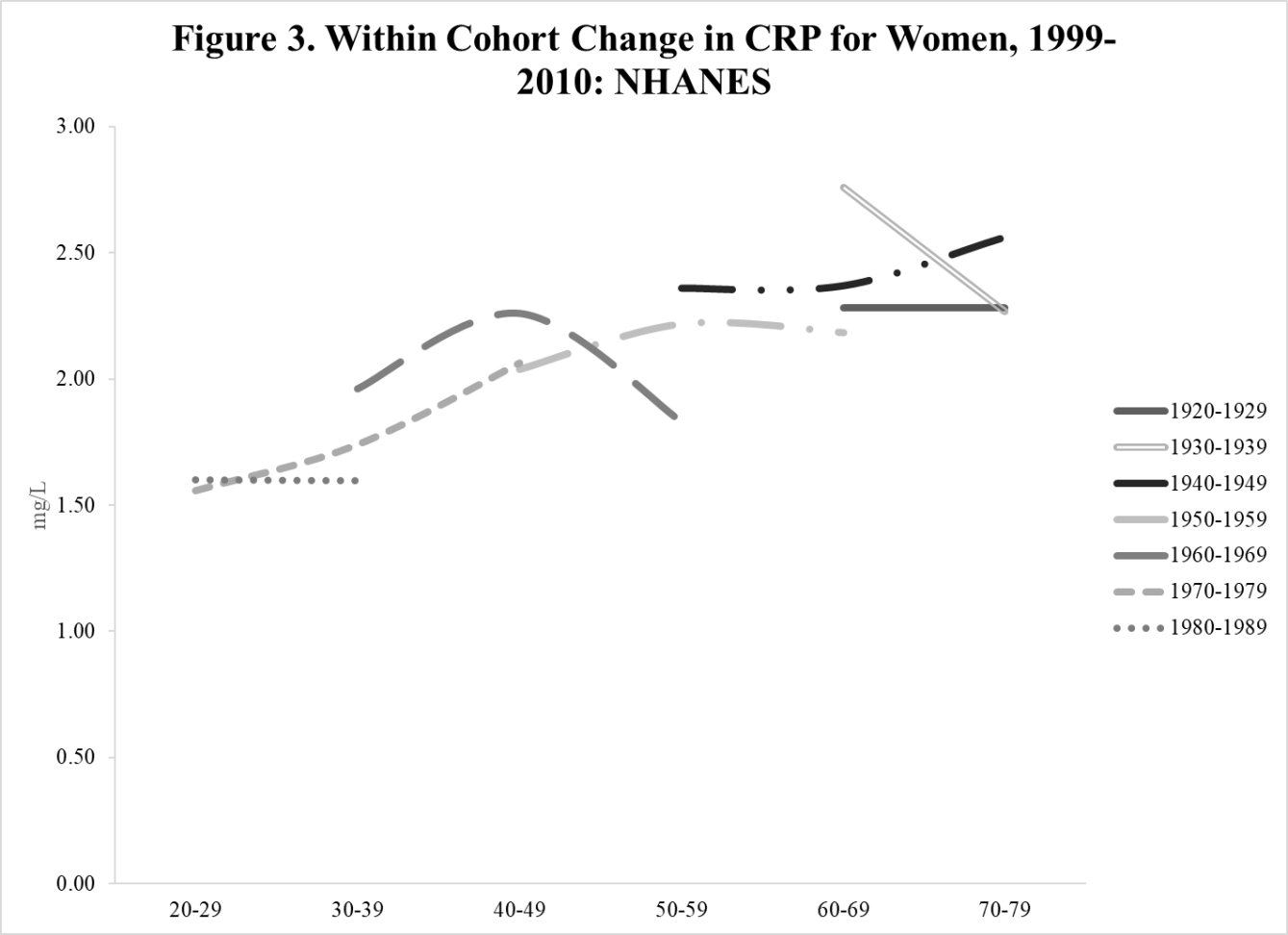


Figure 3. Within Cohort Change in CRP for Women, 1999-2010: NHANES
3.00
2.50
2.00
1.50
1.00
0.50
0.00
mg/L
20-29
30-39
40-49
50-59
60-69
70-79
1920-1929
1930-1939
1940-1949
1950-1959
1960-1969
1970-1979
1980-1989

Figure 4. Within Cohort Change in CRP for Men, 1999-2010: NHANES

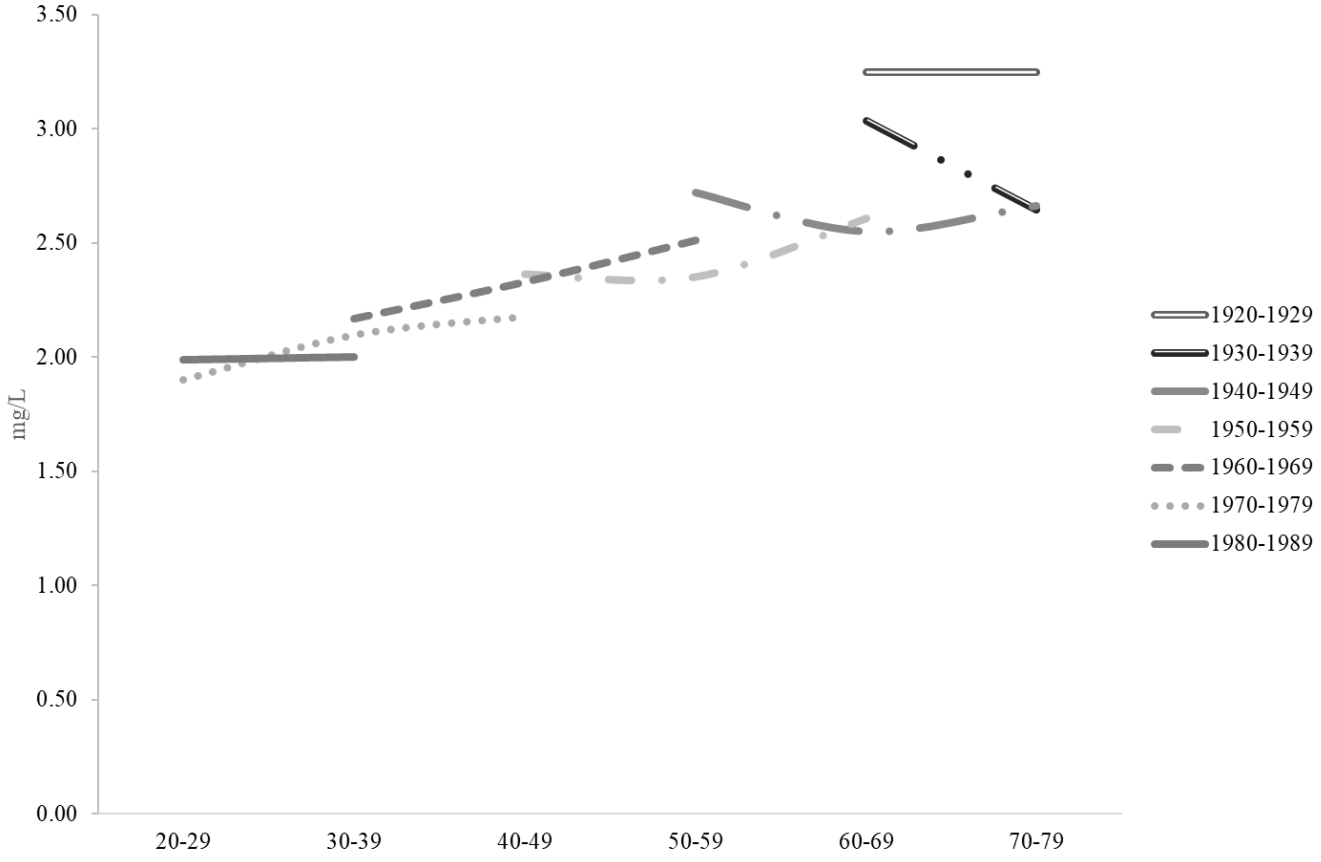


Figure 5. Intracohort Change and Cohort Replacement for Women, Unadjusted and Adjusted Compositional Effects, 1999-2010: NHANES

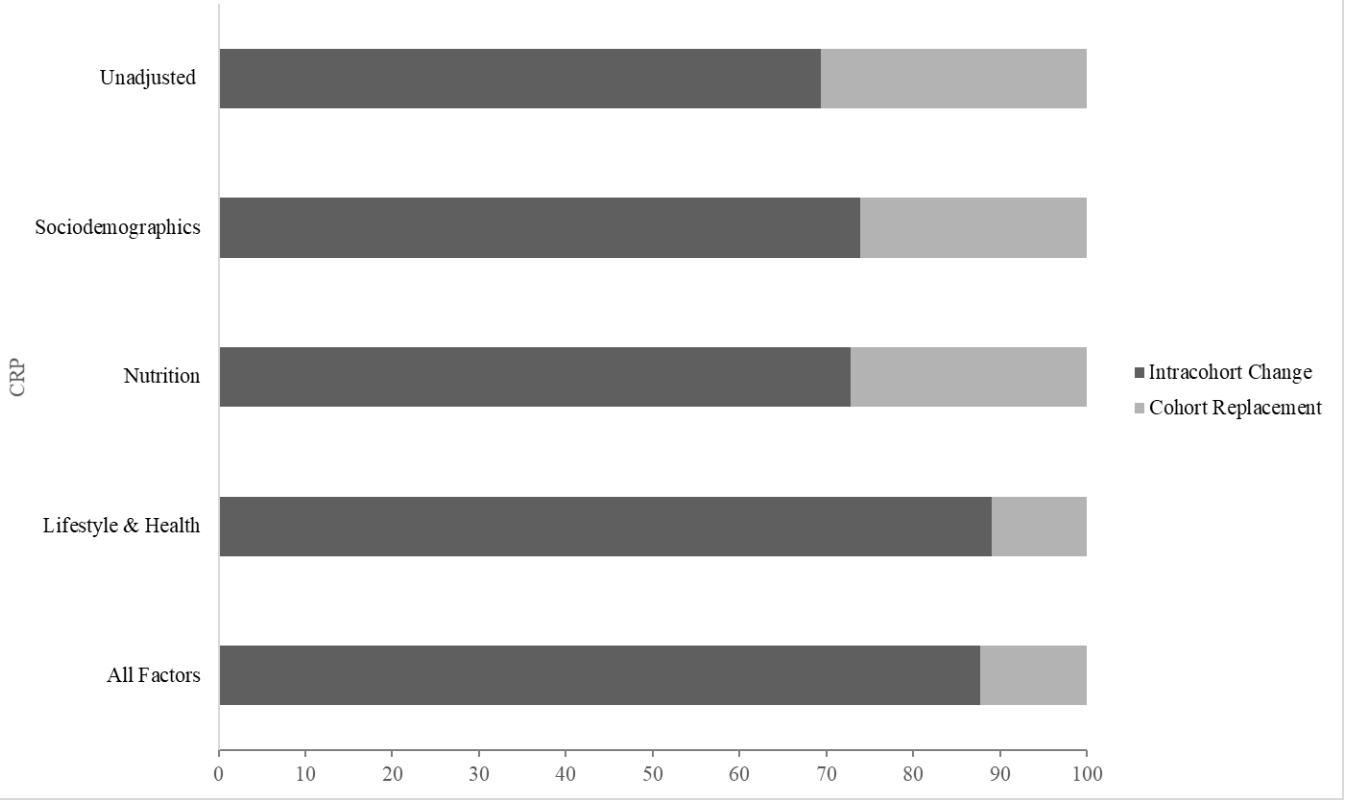


Figure 6. Intracohort Change and Cohort Replacement for Men, Unadjusted and Adjusted Compositional Effects, 1999-2010: NHANES