



Lifestyle behavior patterns and mortality among adults in the NHANES 1988–1994 population: A latent profile analysis

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ABSTRACT

Evidence suggests interdependent associations of individual modifiable behaviors with health outcomes. However, such interrelations have not been accounted for in previous behavior-outcome associations. We conducted latent profile analysis (LPA) on self-reported levels of alcohol consumption, restaurant dining, vitamin/mineral supplement use, physical activity (PA) and smoke exposure (first- and second-hand smoke) separately for smokers (N = 4530) and non-smokers (N = 13,421) using data from the third National Health and Nutrition Examination Survey (NHANES III) to identify subgroups with similar levels within and across behaviors. Cox-proportional hazards models were used to compare mortality rates between subgroups from cancer, cardiovascular disease (CVD) and all-causes at an average of 16.4 (± 6.1) years follow-up. Five behavioral typologies were identified in non-smokers (“Moderates”, “Low Risk Factors”, “Restaurant Diners”, “Moderate Passive Smokers” and “Heavy Passive Smokers”), and four in smokers (“Moderates”, “Low Risk Factors”, “Heavy Smokers” and “Physically Active”). As a group, “Moderates” had levels of each behavior that were not significantly different from at least one other group. Compared to “Moderates”, in non-smokers “Restaurant Diners” had lower hazard from all-cause (hazard ratio (HR):0.84, 95% CI:0.74–0.97) and CVD (HR:0.59, 0.43–0.82) mortality, while “Low Risk Factors” had higher cancer mortality (HR:1.38, 1.03–1.84). In smokers, compared to “Moderates”, higher hazards for mortality were found for “Heavy Smokers” (all cause: HR:1.34, 1.12–1.60; CVD: HR:1.52, 1.04–2.23; cancer: HR:1.41 1.02–1.96) and “Low Risk Factors” (all-cause: HR:1.58, 1.14–2.17). Taken together, when restaurant dining, PA and smoking exposures are grouped together, novel predictions for mortality occur, suggesting data on multiple behaviors may be informative for risk stratification.

1. Introduction

Currently, seven in ten deaths are attributed to non-communicable diseases (NCDs), with CVD and cancer remaining the top two causes of death in the US (Kung et al., 2008). While NCDs have a complex etiology including genetic, metabolic, and psychosocial risk factors, most also include modifiable behaviors. According to the World Heart Federation and the American Cancer Society, the top modifiable behaviors contributing to both CVD and cancer, are low levels of physical activity (PA), high levels of inactivity, tobacco use/smoke exposure, dietary intake, and alcohol use (World Heart Federation, 2017). It is estimated that 55–65% of cancer-related deaths are linked to tobacco

and diet (Anand et al., 2008), and approximately 35% of CVD deaths and deaths from all-causes are associated with low levels of PA (Nocon et al., 2008). Less well understood is whether vitamin/mineral supplement use can reduce cancer and/or CVD risk associated with poor diet, or smoke exposure. Although theoretically vitamin/mineral supplement use should ameliorate risks posed by poor diet quality (by providing missing nutrients), or smoke exposure (by providing antioxidants to reduce smoke-related damage), findings across both epidemiological and experimental studies show little to no benefit (Fortmann et al., 2013).

Prior studies have shown that high risk behaviors such as smoking and alcohol use have shared correlates (e.g., socioeconomic status

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(Poortinga, 2007)) and tend to group together (Noble et al., 2015). For example, PA in adults is positively correlated with good dietary quality (Boutelle et al., 2000; de Vries et al., 2008), but also with alcohol use - a relationship which is stronger in women (Poortinga, 2007; Boutelle et al., 2000). Smokers may exercise less (Poortinga, 2007; Boutelle et al., 2000; Chioloro et al., 2006; French et al., 1996), though this may also be gender dependent (Sallis et al., 1989), have lower dietary quality (Poortinga, 2007; Chioloro et al., 2006; French et al., 1996; Ma et al., 2000), and consume more calories (French et al., 1996), and alcohol (Poortinga, 2007; de Vries et al., 2008; Chioloro et al., 2006; French et al., 1996; Patterson et al., 1994).

Understanding the inter-relations of health-related behaviors is important for understanding their relationship to health outcomes. Further, the distinct physiology of smokers and non-smokers (e.g. compared to non-smokers, smokers have greater imbalance between dietary antioxidant intake and metabolic demand for antioxidant protection, increasing susceptibility to oxidative damage (Kelly, 2002; Margetts and Jackson, 1993)) can, in turn, alter the relationship of health behaviors with health outcomes. Thus it is not surprising that the associations between health behaviors and health outcomes can vary between smokers and non-smokers (e.g., sodium intake (Sundstrom et al., 2015)). Similarly, the risks to cancer associated with fruit/vegetable intake and alcohol consumption, may be dependent on PA (Slattery and Potter, 2002) and smoking (Castellsague et al., 1999), respectively. Thus, studies have started to take a clustering approach to understand the relationships between dietary intake, smoke exposure and PA (Poortinga, 2007; Blair et al., 1985), finding population specific, distinct behavioral clusters. As yet, none have examined how such data-driven clustering associates with health outcomes to our knowledge. Doing so is important for improved risk stratification, but may also shed light on mixed findings in literature, such as multidirectional findings from vitamin/mineral supplement use. Further, each behavior may have a different magnitude of effect on mortality outcomes. For example, based on the World Health Organization, tobacco use was responsible for 1.5 million deaths compared to 0.6 million deaths attributed to physical inactivity in High-income countries (World Health Organization, 2009). These differences suggest the need for weighted approaches to health behavior analyses, but presently there is not enough evidence to support such weightings.

The goal of this study was to use latent profile analysis (LPA) on key health behaviors related to cancer and CVD risk, to define how these behaviors cluster together, and how all-cause, CVD- and cancer-specific mortality incidence differs between health behavior profiles during 23 years of follow-up. Since LPA is, by nature, population-specific, we used data from a large, nationally-representative study of US participants (NHANES). To provide the first association of behavior profiles with mortality outcomes, we used data from 1988 to 1994 at baseline (NHANES III) allowing sufficient follow-up to examine mortality as an outcome. We included measures of PA, alcohol use and smoking (both passive and direct), but as the NHANES diet data are from a single 24-hour recall and are not suitable for LPA (Freedman et al., 2008), we used frequency of meals consumed in restaurants as an indicator of overall dietary intake, since restaurant meals, tend to be higher in calories (Scourboutakos et al., 2013), overall fat (Lin et al., 1999), saturated fats (Scourboutakos et al., 2013; Lin et al., 1999), sodium and cholesterol (Scourboutakos et al., 2013), and lower in calcium, fiber and iron (Lin et al., 1999). In addition, we took the novel step of including self-reported vitamin/mineral supplement intake to start disentangling their mixed associations with health. Finally, due to different physiologies of smokers and non-smokers, and the robust associations of smoking status with other health behaviors (Poortinga, 2007; Kelly, 2002; Margetts and Jackson, 1993; Sundstrom et al., 2015; Slattery and Potter, 2002; Castellsague et al., 1999), we analyzed data separately among smokers and non-smokers at baseline.

2. Methods

This study was approved by the institutional review board at MD Anderson and declared not to be human subject's research.

2.1. Study population

Participants from NHANES III (1988–1994) were included if they were at least 20 years of age at the time of interview or exam, with evaluable data for smoking status ($n = 17,951$).

2.2. Measures

2.2.1. Alcohol consumption

Alcohol consumption was measured as the average number of drinks per day on a drinking day. Participants reporting fewer than 12 drinks lifetime or fewer than 12 drinks in the last year were coded as 0 drinks per day.

2.2.2. Restaurant habits

Restaurant habits were quantified using data from the Dietary Recall Index. Specifically, 'meal number' and 'meal place' were combined to estimate the number of weekly restaurant meals. Meals were considered 'restaurant meals' if they were consumed at a 'Fast Food/Take Out', 'Delicatessen', 'Restaurant', 'Cafeteria/Self-Serve Buffet', or 'Store'.

2.2.3. Active smoking

Smoking behavior was measured as the average number of cigarettes smoked per day as reported in the Tobacco Section of the Household Adult Data File (Centers for Disease Control and Prevention, 2018).

2.2.4. Passive smoking

Passive smoking was assessed from the Household Family Questionnaire portion of the Household Adult Data File. Total number of cigarettes passively smoked per day was calculated for smokers and non-smokers by summing the number of cigarettes smoked per day in the home by each smoking household member.

2.2.5. Physical activity

PA was measured from nine self-reported activity items, and open ended questions for up to four additional activities in the Exercise section of the Household Adult Data File. Metabolic Equivalent Task (MET) frequency was calculated by multiplying the MET value of each activity by the weekly frequency. Total leisure time MET frequency was defined as the sum of leisure time MET frequencies (excluding household and yard work activity), as previously reported (Dowda et al., 2003; Patek et al., 2012).

2.2.6. Vitamin/mineral supplement use

Vitamin/mineral supplement use was quantified as the number of vitamin/mineral supplements used in the last month, as reported in the Household Adult Questionnaire.

2.2.7. Demographic variables

Age in months was converted to years. Other demographic variables were gathered from the Interview Questionnaire and Physical Examination. Body mass index (BMI) and waist circumference were measured by trained study personnel. Poverty-to-Income Ratio (PIR, lower values indicating greater poverty) and education status were self-reported on the Household Family Questionnaire portion of the Household Adult Data file, and were categorized as follows: PIR – ≤ 1.3 , $> 1.3 < 3.5$, ≥ 3.5 , education – less than high school, high school graduate, some college or higher, as previously reported (Frazier-Wood et al., 2015).

2.2.8. Mortality outcomes

Outcomes were obtained using the National Death Index mortality files linked to NHANES III (1988–1994) with follow-up through December 31, 2011 (Centers for Disease Control and Prevention, 2016). All-Cause Mortality (ACM) included participants who died of any cause within the follow-up period. Deaths from CVD or cancer were determined using the Underlying Cause of Death Recode variable.

3. Statistical analyses

3.1. Latent profile analysis

LPA was chosen for its ability to identify unobservable profiles across multiple continuous indicators (Hagenaars and McCutcheon, 2002). Using M-plus 7 (Muthen and Muthen, 1998–2012), LPA was performed separately in smokers and non-smokers including the following health behaviors: alcohol consumption (average number of drinks/day on a drinking day), PA (total MET frequency/week), restaurant habits (number of meals eaten out/week), vitamin/mineral supplement use (number of supplements used), passive smoking (number of cigarettes smoked/day in the home by others), and among smokers only, individual smoking (number of cigarettes smoked/day).

The optimal number of classes was established based on a combination of fit criteria, conceptual and practical solutions. Fit criteria include the Akaike Information Criteria (AIC) (Akaike, 1987), the Bayesian Information Criterion (BIC) (Schwarz, 1978), the sample size adjusted BIC (aBIC) (Sclove, 1987), and statistical model comparison likelihood tests including Lo-Mendell-Rubin likelihood ratio test (LMR) (Lo et al., 2001) and the Bootstrap Likelihood Ratio Test (BLRT) (McLachlan and Peel, 2000). Classes were added one at a time until model fit, measured by decreasing AIC, BIC, LMR and BLRT, was no longer improved. Increasing values of entropy were also used to assess how well individuals were assigned to specific classes. Finally, class size and the theoretical meaning of the classes were considered. Specifically, we sought solutions that minimized very small class sizes and maintained clear differences between the identified classes.

3.2. Class comparisons

After selecting the optimal number of classes for smokers and non-smokers, classes were compared to one another by behavior and demographic variables using the Kruskal-Wallis, followed by Dunn's test with an FDR-adjusted p value (q value) of 0.005 for non-smokers (pairwise comparisons across 5 groups) and 0.008 for smokers (pairwise comparisons across 4 groups) for means of continuous variables (Benjamini and Hochberg, 1995). Overall and pair-wise Chi-Square tests were conducted for categorical variables; p values for the overall Chi-Square tests and pairwise tests were adjusted using the FDR and Bonferroni methods, respectively.

3.3. Survival analyses

Mortality outcomes were compared across classes by constructing Cox Proportional Hazards Models in smokers and non-smokers with All-Cause, CVD or Cancer mortality as the outcomes. Full models included sex, race/ethnicity (limited to non-Hispanic (NH) White, NH African American, Mexican American and other – including other Hispanic), education, PIR category, health insurance, BMI, waist circumference and behavioral variables. The 'DIRECTADJ' option was used to generate adjusted survival curves by class from the Cox Proportional Hazards model. Statistical significance was assessed using the Log-Likelihood Ratio Test. Class comparisons and Survival analyses were conducted using SAS 9.4 (SAS Institute).

Table 1
Demographic characteristics of study populations from NHANES III (1988–1994).

	Never/former smokers	Current smokers	p value
Total number of participants	13,421	4530	
Age, years	52.77 (0.18)	44.16 (0.24)	< 0.0001
Sex			< 0.0001
Male	6114 (45.6)	2642 (58.3)	
Female	7307 (54.4)	1888 (41.7)	
Race/ethnicity			< 0.0001
NH White	6059 (45.2)	1758 (38.8)	
NH African American	3245 (24.2)	1581 (34.9)	
Mexican American	3573 (26.6)	1044 (23.1)	
Other race	205 (1.5)	58 (1.3)	
Other Hispanic	339 (2.5)	89 (1.9)	
BMI	27.44 (0.05)	26.07 (0.09)	< 0.0001
Waist circumference	94.10 (0.14)	91.17 (0.22)	< 0.0001
PIR			< 0.0001
≤ 1.3	3640 (30.4)	1604 (38.9)	
> 1.3 < 3.5	5394 (45.1)	1785 (43.3)	
≥ 3.5	2930 (24.5)	737 (17.8)	
Education			< 0.0001
Less than high school	5464 (41.1)	2039 (45.4)	
High school graduate	3784 (28.5)	1523 (33.9)	
Some college or higher	4038 (30.4)	929 (20.7)	
Health insurance status			< 0.0001
Insured	11,139 (85.9)	3326 (78.4)	
Un-insured	1822 (14.1)	918 (21.6)	

4. Availability of data and materials

The NHANES participant data (<https://wwwn.cdc.gov/nchs/nhanes/nhanes3/DataFiles.aspx>) and mortality follow-up data (<https://www.cdc.gov/nchs/data-linkage/mortality-public.htm>) are available from the Centers for Disease Control and Prevention.

5. Results

5.1. Population demographics

Compared to smokers, non-smokers were significantly older, had higher BMIs and waist circumferences, and included a higher percentage of women, individuals with higher income, college education, and health insurance (Table 1).

5.2. Behavior clustering

5.2.1. Non-smokers

For non-smokers, fit indices, statistical model comparisons, and practical considerations suggested a 5-class model (Supplementary Table S1). Of the five subgroups, one had values for each behavior which were not significantly different from another group (i.e. all behaviors were reported at the same level as at least one other subgroup). This subgroup was termed “the Moderates” and comprised the largest class (Table 2; Fig. 1A). A “Low Risk Factors” subgroup, notable for the highest vitamin/mineral supplement intakes (nearly 4) and PA levels (MET frequency of 23.26), and the lowest second-hand smoke exposure (< 0.5 cigarette/day) and alcohol use (< 1 drink/day) was identified, as was a subgroup termed “Restaurant Diners” who were distinguished from all other subgroups by their tendency to eat out frequently (11 meals/week; Table 2; Fig. 1A). The final two subgroups only differed from all other groups by their second-hand smoke exposure; “the Moderate Passive Smokers” were exposed to approximately one pack of second-hand cigarettes/day, while “the Heavy Passive Smokers” were exposed to nearly two and a half packs of cigarettes (48/day; Table 2; Fig. 1A).

Significant differences were found across subgroups by age, sex,

Table 2
Means of health behaviors and demographics by class – NHANES III (1988–1994) non-smokers.

	Moderates N = 10,694	Low risk factors N = 670	Moderate passive smokers N = 665	Restaurant diners N = 1275	Heavy passive smokers N = 117	q value*
Physical activity (SEM)	16.56 ^a (0.26)	23.26 ^b (1.16)	17.76 ^a (1.18)	22.89 ^b (0.91)	14.61 ^a (2.38)	< 0.0001
Second-hand smoke	0.63 ^a (0.02)	0.37 ^b (0.07)	19.72 ^c (0.20)	0.77 ^a (0.07)	48.09 ^d (1.31)	< 0.0001
Alcohol use	1.18 ^a (0.02)	0.89 ^b (0.07)	1.37 ^{a,c} (0.10)	1.48 ^c (0.07)	1.83 ^{a,c} (0.36)	< 0.0001
Vitamin use	0.43 ^a (0.01)	3.98 ^b (0.05)	0.42 ^a (0.03)	0.53 ^c (0.02)	0.48 ^{a,c} (0.08)	< 0.0001
Restaurant meals	0.55 ^a (0.02)	1.27 ^b (0.12)	1.04 ^b (0.11)	11.04 ^c (0.12)	1.12 ^{a,b} (0.29)	< 0.0001
Demographics						
Age, mean (SEM)	53.22 ^a (0.20)	60.40 ^b (0.68)	49.68 ^c (0.78)	46.36 ^d (0.50)	55.85 ^{a,b} (1.92)	< 0.0001
Sex, N (%)	a	b	a,d	d	a,d	< 0.0001
Male	4852 (45.37)	222 (33.13)	316 (47.52)	663 (52.00)	61 (52.14)	
Female	5842 (54.63)	448 (66.87)	349 (52.48)	612 (48.00)	56 (47.86)	
BMI	27.49 ^a (0.06)	26.34 ^b (0.22)	28.14 ^c (0.26)	27.29 ^a (0.15)	27.29 ^{a,b,c} (0.57)	< 0.0001
Waist circumference	94.17 ^a (0.15)	92.04 ^b (0.57)	95.78 ^c (0.68)	93.65 ^b (0.41)	95.69 ^{a,c} (1.32)	0.0003
PIR	a	b	c	b	c	< 0.0001
≤ 1.3	3116 (32.93)	86 (13.89)	212 (35.39)	181 (15.26)	45 (45.92)	
> 1.3 < 3.5	4272 (45.15)	280 (45.23)	293 (48.91)	504 (42.50)	45 (45.95)	
≥ 3.5	2074 (21.92)	253 (40.87)	94 (15.69)	501 (42.24)	8 (8.16)	
Race/ethnicity	a	b	c	d	c	< 0.0001
NH White	4587 (42.89)	456 (68.06)	280 (42.11)	677 (53.10)	59 (50.43)	
NH African American	2659 (24.86)	88 (13.13)	237 (35.64)	220 (17.25)	41 (35.04)	
Mexican American	2994 (28.00)	99 (14.78)	124 (18.65)	342 (26.82)	14 (11.97)	
Other Hispanic	161 (1.51)	9 (1.34)	11 (1.65)	23 (1.80)	1 (0.85)	
Other	293 (2.74)	18 (2.69)	13 (1.95)	13 (1.02)	2 (1.71)	

Values with different superscript letters are statistically different from each other. For example, columns with ‘a’ are significantly different from columns with ‘b’, ‘c’, or ‘d’, but not different from other columns with ‘a’. The mean age of ‘Heavy-Passive Smokers’ is significantly different from the ‘Moderate Passive Smokers’ and the ‘Restaurant Diners’, but not different from the ‘Moderates’ or ‘Low Risk Factors’.

* Classes compared using Kruskal-Wallis test for continuous variables and Chi-Square for categorical variables, followed by pairwise comparisons.

race/ethnicity, BMI, waist circumference and PIR category. “Restaurant Diners” were the youngest, whereas “Low Risk Factors” were the oldest (alongside heavy passive smokers) and had the highest percentage of females and non-Hispanic Whites. “Moderate Passive Smokers” had the highest average BMI and waist circumferences, and more “Heavy Passive Smokers” were in the lowest PIR category than other classes. “The Moderates” had an average age range compared to the rest of non-smokers, with a slightly higher percentage of women (Table 2). When looking at health indicators, the “Low Risk Factors” group had the lowest BMIs (26.34), while the “Moderates” and the “Moderate Passive Smokers” had the highest BMIs (28.14 and 27.49, respectively) and, alongside the “Heavy-Passive Smokers”, had the highest waist circumference (95.78 and 95.69, respectively) (Table 2).

To test the potential influence former smoking status on class identity, we performed a sensitivity analysis, re-deriving the classes in the subset of non-smokers with no smoking history (never smokers, n = 8774), finding very similar class identities (Supplementary Table S2). We further compared the specific classification of individuals into similar subgroups when former smokers are excluded, finding all but the ‘Low Risk Factors’ group had very consistent class membership. Among never smokers, the class formerly identified by low-risk factors (increased levels of PA, vitamin/mineral supplement use and low alcohol consumption) was replaced by a group characterized by increased PA and increased alcohol consumption (Supplementary Table S3). Similarly, we performed additional sensitivity analyses to test the influence of sex on LPA class derivation and assignment, finding very similar class allocations in females (Restaurant Diners, Moderate Passive Smokers, Moderates, Low Risk Factors, and Heavy Passive Smokers) and males (Moderates, Restaurant Diners, Low Risk Factors, Heavy Passive Smokers and Physically Active) of all smoking statuses with very good agreement between original and new class membership (Supplementary Tables S4 and S5).

5.2.2. Smokers

For smokers, a 4-class model was selected based on the combination of fit indices and practical considerations (Supplementary Table S1). Despite the small size of one class, the unique lifestyle represented

made its inclusion practically important. Like non-smokers, a subgroup termed “The Moderates” was the largest, comprised of moderate levels of each behavior (Table 3, Fig. 1B). “The Heavy Smokers” had the greatest smoke exposure, both as active (1.5 packs/day) and passive (2 packs/day) exposure (Table 3, Fig. 1B). The subgroup with the overall healthiest lifestyle (“Low Risk Factors”) had similar values to “the Moderates”, but had higher PA, lower alcohol use (the lowest at 2.14 drinks/day; Table 3, Fig. 1B) and a higher vitamin/mineral supplement intake (the highest at 4.04; Table 3, Fig. 1B). The final subgroup, termed the “Physically Active”, were considerably more active than other groups (MET frequency of 103/week; Table 3, Fig. 1B), and smoked the fewest cigarettes (11.6/day Table 3, Fig. 1B) although they also had a moderate second-hand smoke exposure (13.65 cigarettes/day).

Comparing demographic characteristics revealed that the “Low Risk Factors” group, as in the non-smokers, was the oldest with a mean age of 49.28 years (though not different from the heavy smokers at 46.13), and had the highest percentage of females (61.31%), but unlike the non-smokers this subgroup had the most people in the highest PIR category (34.4% with PIR ≥ 3.5) and did not have the highest percentage of non-Hispanic Whites (60.58%). The latter of which was found in the “Heavy Smokers” (68.28% p < .001). The “Physically Active” subgroup were the youngest at 35.35 years old, with the highest percentage of males (67.21%). When turning to health indicators, as in non-smokers “The Moderates” had the highest BMI and high waist circumferences (26.27 and 91.67) and the “Low Risk Factors” subgroup had the lowest BMI (24.35) alongside the “Physically Active” (24.96).

5.3. Survival analyses between subgroups

5.3.1. Non-smokers

Using the “Moderates” as the referent class, among non-smokers, the “Low Risk Factors” group had significantly higher hazards for cancer mortality (HR: 1.38, 95% CI: 1.03, 1.84) (Table 4), whereas the “Restaurant Diners” had significantly lower hazards for mortality due to all-causes (HR: 0.84, 95% CI: 0.74, 0.97) and CVD (HR: 0.59, 95% CI: 0.43, 0.82). The two subgroups characterized by their high passive

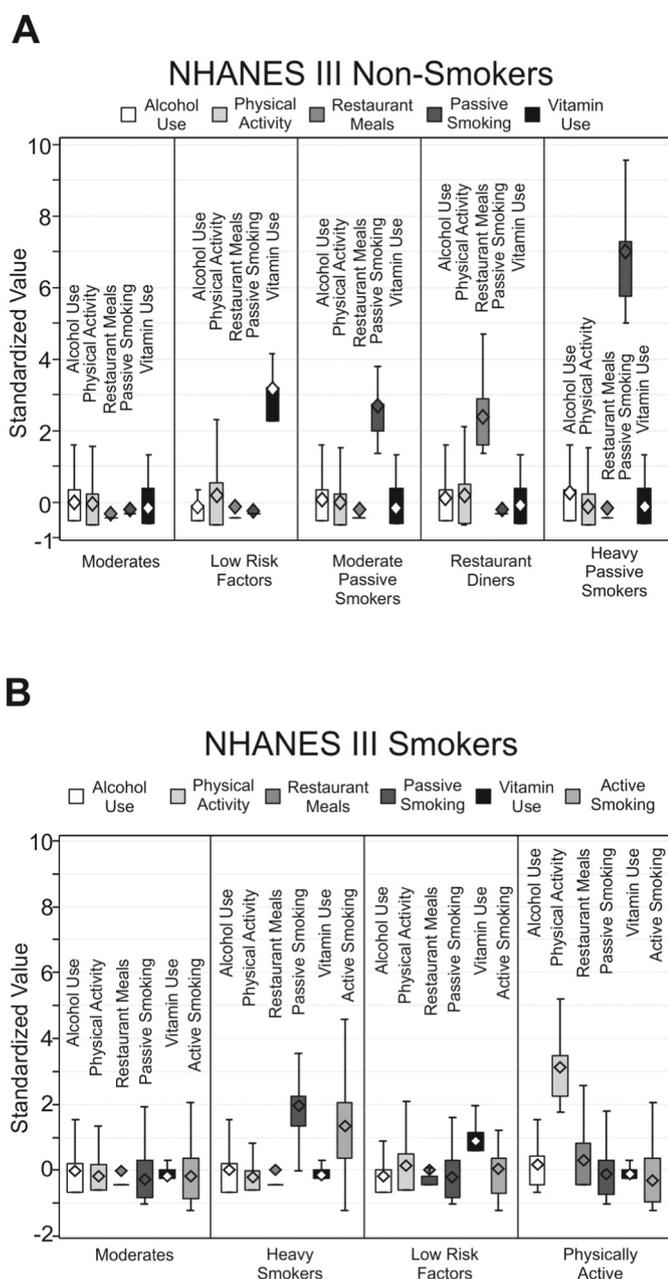


Fig. 1. Standardized behavior levels by class in non-smokers (A) and smokers (B).

smoke exposure (the “Moderate Passive Smokers” and the “Heavy Passive Smokers”) did not differ in their mortality hazards compared to the “Moderates”.

To evaluate the potential influence of former smokers on cancer mortality, we conducted a sensitivity analysis, repeating the cancer mortality Cox model excluding former smokers. Although the sample size was decreased (n = 6536, 300 events), the trends were the same, with the “Low Risk Factors” group having significantly increased hazards for cancer mortality (HR: 1.52, 95% CI: 1.01, 2.29, Supplementary Table S6).

5.3.2. Smokers

Using the “Moderates” as the referent class, among smokers the “Low Risk Factors” group had significantly increased hazards for all-cause mortality (HR: 1.58, 95% CI: 1.14, 2.17). Further, the subgroup characterized by the greatest smoke exposure: the “Heavy Smokers” had significantly higher hazards for all mortality causes: all-cause (HR:

1.34, 95% CI: 1.12, 1.60), CVD (HR: 1.52, 95% CI: 1.04, 2.23) and cancer (HR: 1.41, 95% CI: 1.02, 1.96). No other classes had significantly different mortality from the Moderates in this analysis (Table 5; Fig. 2).

6. Discussion

Prior studies have compared long-term mortality and other health outcomes by number of healthy behaviors, finding decreasing mortality with increasing healthy behaviors (Ford et al., 2012; Ford et al., 2011; Dam et al., 2008; Mamudu et al., 2017; Mamudu et al., 2018). However, individuals engage in differing patterns across health behaviors and such patterns may inform risk stratification. Prior studies indicate that dose matters for behaviors such as smoking (Doll and Peto, 1978) and PA (Warburton and Bredin, 2017), and that associations between a specific behavior and outcome are not independent from other, related behaviors (Ford et al., 2012; Ford et al., 2011; Dam et al., 2008). Thus, we conducted LPA across behaviors, including vitamin/mineral supplement use for the first time, quantifying the associations of these behavior patterns with demographics and assessing their long-term effects on mortality outcomes, providing unique insight into the links between lifestyle and mortality.

Finding several, discreet groups definable by their health behaviors and distinguished by demographic characteristics is well supported in literature (Busch et al., 2013; Leech et al., 2014; Ottevaere et al., 2011). In both smokers and non-smokers, the largest group was characterized by moderate levels of each behavior. Comparing with prior studies including alcohol, PA and smoking, our moderate clusters approximate groups with one or two health risk factors in non-smokers or smokers, respectively (Kvaavik et al., 2010; Shankar et al., 2010). Consistent with prior studies, we identified classes of heavily smoke exposed participants, which experienced worse all-cause, CVD and cancer mortality (Doll and Peto, 1978; Lv et al., 2015). Also consistent with prior studies, we found lower incidences of CVD- and cancer-specific mortality among smokers who were very physically active (average MET frequency of 103), though this was not statistically significant when compared to Moderates (O'Donovan et al., 2017; Lallukka et al., 2016; Borrell, 2014).

Our finding of lower HR for the class characterized by restaurant dining is surprising as previous literature consistently finds eating outside the home to be associated with increased total fat, total energy intake (Lachat et al., 2012; Adams et al., 2015) and poorer diet quality (Nguyen and Powell, 2014). In our study, behaviors were reported from 1988 to 1994; recent data indicate increases in the frequency of meals consumed outside the home, along with changes in the quality of food consumed outside the home (Guthrie et al., 2002; Kant and Graubard, 2004), including increases in the proportion of fast food meals (Cohen, 2016), and increases in serving size (Young and Nestle, 2003) and sodium content (Rudelt et al., 2014). Thus, even when the same demographic eat outside the home now, their meals are higher in dietary factors associated with CVD, cancer and mortality compared to when our data were collected, suggesting that Restaurant Diners in our data may still have been eating healthier than more recent populations. This seems to be supported by the fact that this group did not have the highest BMI (Moderate Passive Smokers) or waist circumference (Moderate Passive Smokers and Heavy Passive Smokers) among non-smokers, whereas current studies indicate that eating outside the home is associated with obesity risk (Seguin et al., 2016). Inclusion of data from food frequency questionnaires would permit a direct dietary quality assessment in future studies.

Our observation of increased cancer mortality in non-smokers and increased all-cause mortality in smokers for the classes characterized by low risk factors is unexpected, and may be influenced by the reasons for adopting this lifestyle. Specifically, these groups were both characterized by high vitamin/mineral supplement use. Prior studies have found that a majority of people use such supplementation for health improvement (Bailey et al., 2013), raising the possibility of unreported/

Table 3
Means of health behaviors and demographics by class – NHANES III (1988–1994) smokers.

	Moderates N = 3591	Heavy smokers N = 558	Low risk factors N = 137	Physically active N = 244	q value*
Physical activity (SEM)	11.93 ^a (0.27)	10.89 ^a (0.72)	21.24 ^b (2.24)	103.07 ^c (0.46)	< 0.0001
Second-hand smoke	11.05 ^a (0.15)	45.50 ^b (0.67)	12.31 ^{a,c} (0.98)	13.65 ^c (0.88)	< 0.0001
Cigarettes/day	13.21 ^a (0.16)	31.23 ^b (0.60)	15.99 ^c (1.05)	11.6 ^d (0.61)	< 0.0001
Alcohol use	2.95 ^a (0.08)	3.00 ^{a,c} (0.21)	2.14 ^b (0.27)	3.76 ^c (0.37)	0.0003
Vitamin use	0.31 ^a (0.01)	0.37 ^{a,c} (0.03)	4.07 ^b (0.13)	0.48 ^c (0.05)	< 0.0001
Restaurant meals	1.62 ^a (0.06)	1.77 ^a (0.18)	1.81 ^{a,b} (0.34)	3.00 ^b (0.50)	0.0055
Demographics					
Age, mean (SEM)	44.26 ^a (0.28)	46.13 ^{a,b} (0.66)	49.28 ^b (1.39)	35.25 ^c (0.83)	< 0.0001
Sex, N (%)	a	a	b	c	< 0.0001
Male	2110 (58.76)	315 (56.45)	53 (38.69)	164 (67.21)	
Female	1481 (41.24)	243 (43.55)	84 (61.31)	80 (32.79)	
BMI	26.27 ^a (0.10)	25.66 ^b (0.27)	24.35 ^c (0.41)	24.96 ^{b,c} (0.31)	< 0.0001
Waist circumference	91.67 ^a (0.25)	91.37 ^a (0.67)	86.51 ^b (1.17)	85.95 ^b (0.85)	< 0.0001
PIR	a	a	b	a	< 0.0001
≤ 1.3	1287 (39.61)	201 (38.65)	19 (15.20)	97 (41.81)	
> 1.3 < 3.5	1398 (43.03)	234 (45.00)	63 (50.40)	90 (38.79)	
≥ 3.5	564 (17.36)	85 (16.35)	43 (34.40)	45 (19.40)	
Race/ethnicity	a	b	c	d	< 0.0001
NH White	1231 (34.28)	381 (68.28)	83 (60.58)	63 (25.82)	
NH African American	1300 (36.20)	133 (23.84)	30 (21.90)	118 (48.36)	
Mexican American	944 (26.29)	34 (6.09)	17 (12.41)	49 (20.08)	
Other Hispanic	47 (1.31)	5 (0.90)	0 (0.00)	6 (2.46)	
Other	69 (1.92)	5 (0.90)	7 (5.11)	8 (3.28)	

Values with different superscript letters are statistically different from each other. For example, columns with ‘a’ are significantly different from columns with ‘b’, ‘c’, or ‘d’, but not different from other columns with ‘a’. Sex distribution in the ‘Moderates’ and ‘Heavy Smokers’ classes are significantly different from ‘Low Risk Factors’ and ‘Physically Active’, but not different from each other.

* Classes compared using Kruskal-Wallis test for continuous variables and Chi-Square for categorical variables, followed by pairwise comparisons.

undiagnosed medical problems for which participants sought improvement through use of higher levels of vitamin/mineral supplements. Among non-smokers, the increased hazard remained after exclusion of former smokers, suggesting that this effect is not due to late-

effects of previous smoking exposures. Alternatively, these findings may result from our approach to evaluate the overall effects of behaviors and demographics of the group simultaneously. Specifically, these groups were reasonably active with an average MET frequency of 23 for non-

Table 4
Cox proportional hazards models – NHANES III (1988–1994) non-smokers.

Total N = 9947	All-cause mortality	CVD mortality	Cancer mortality
	N events = 3171	N events = 817	N events = 639
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Class			
Moderates (ref)	1.00	1.00	1.00
Low risk factors	1.08 (0.94, 1.24)	0.90 (0.68, 1.21)	1.38 (1.03, 1.84)
Moderate passive smokers	1.03 (0.87, 1.22)	1.17 (0.85, 1.62)	1.03 (0.71, 1.50)
Restaurant diners	0.84 (0.74, 0.97)	0.59 (0.43, 0.82)	0.92 (0.69, 1.23)
Heavy passive smokers	1.18 (0.82, 1.71)	0.75 (0.31, 1.82)	1.21 (0.54, 2.72)
Age, years	1.10 (1.096, 1.103)	1.11 (1.106, 1.12)	1.08 (1.07, 1.09)
Sex			
Male (ref)	1.00	1.00	1.00
Female	0.66 (0.61, 0.72)	0.53 (0.43, 0.63)	0.57 (0.47, 0.68)
Race/ethnicity			
NH White (ref)	1.00	1.00	1.00
NH African American	1.06 (0.96, 1.16)	0.82 (0.67, 1.01)	1.33 (1.08, 1.64)
Mexican American	0.83 (0.74, 0.92)	0.78 (0.63, 0.97)	0.92 (0.72, 1.16)
Other	0.61 (0.48, 0.77)	0.59 (0.37, 0.96)	0.73 (0.44, 1.21)
BMI	1.00 (0.99, 1.01)	1.02 (0.99, 1.05)	0.99 (0.95, 1.02)
Waist circumference	1.00 (1.00, 1.01)	1.00 (0.99, 1.01)	1.01 (1.00, 1.03)
PIR			
≤ 1.3 (ref)	1.00	1.00	1.00
> 1.3 < 3.5	0.88 (0.81, 0.96)	0.79 (0.67, 0.94)	1.04 (0.85, 1.27)
≥ 3.5	0.72 (0.64, 0.81)	0.68 (0.54, 0.85)	0.85 (0.65, 1.10)
Education			
Less than high school (ref)	1.00	1.00	1.00
High school graduate	0.91 (0.83, 1.00)	0.93 (0.78, 1.12)	1.06 (0.87, 1.30)
Some college or higher	0.83 (0.75, 0.92)	0.87 (0.71, 1.07)	0.95 (0.76, 1.19)
Health insurance status			
Insured (ref)	1.00	1.00	1.00
Un-insured	1.02 (0.86, 1.22)	0.71 (0.46, 1.10)	1.04 (0.73, 1.49)

Table 5
Cox proportional hazards models – NHANES III (1988–1994) smokers.

Total N = 3398	All-cause mortality	CVD mortality	Cancer mortality
	N events = 995	N events = 199	N events = 282
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Class			
Moderates (ref)	1.00	1.00	1.00
Heavy smokers	1.34 (1.12, 1.60)	1.52 (1.04, 2.23)	1.41 (1.02, 1.96)
Low risk factors	1.58 (1.14, 2.17)	1.30 (0.60, 2.82)	1.52 (0.84, 2.75)
Physically active	1.10 (0.77, 1.57)	0.36 (0.09, 1.48)	0.89 (0.44, 1.83)
Age, years	1.08 (1.08, 1.09)	1.09 (1.08, 1.11)	1.08 (1.07, 1.09)
Sex			
Male (ref)	1.00	1.00	1.00
Female	0.78 (0.68, 0.90)	0.64 (0.46, 0.88)	0.93 (0.72, 1.21)
Race/ethnicity			
NH White (ref)	1.00	1.00	1.00
NH African American	1.18 (1.01, 1.38)	1.10 (0.77, 1.57)	1.39 (1.05, 1.85)
Mexican American	0.76 (0.62, 0.93)	0.84 (0.54, 1.32)	0.54 (0.35, 0.83)
Other	0.69 (0.45, 1.06)	1.34 (0.65, 2.80)	0.43 (0.16, 1.17)
BMI	0.97 (0.95, 1.00)	1.00 (0.95, 1.06)	0.96 (0.91, 1.01)
Waist circumference	1.02 (1.01, 1.03)	1.02 (1.0, 1.04)	1.01 (0.99, 1.03)
PIR			
≤ 1.3 (ref)	1.00	1.00	1.00
> 1.3 < 3.5	0.77 (0.66, 0.89)	0.78 (0.56, 1.09)	0.74 (0.56, 0.98)
≥ 3.5	0.56 (0.45, 0.69)	0.66 (0.41, 1.06)	0.81 (0.55, 1.20)
Education			
Less than high school (ref)	1.00	1.00	1.00
High school graduate	0.97 (0.83, 1.13)	1.01 (0.71, 1.44)	0.88 (0.65, 1.17)
Some college or higher	0.95 (0.78, 1.15)	1.03 (0.67, 1.58)	0.77 (0.53, 1.12)
Health insurance status			
Insured (ref)	1.00	1.00	1.00
Un-insured	0.92 (0.75, 1.13)	0.79 (0.48, 1.29)	1.25 (0.87, 1.79)

smokers and 21 for smokers, but tended to be older (60.4 and 49.3 years old for smokers and non-smokers, respectively) than individuals in the other groups, putting them at inherently increased risk for cancer development and mortality. Controlling for the mean effect of age on mortality in the model should minimize the effect of age on outcome, but is not able to alter the effect of age on class membership, which may be a moderating factor. Finally, since these analyses were based on a single measurement of health behavior, we are not able to assess behavior stability. Additional, longitudinal study of this behavioral class may provide critical insights into the long-term effects and sustainability of a ‘Low Risk Factors’ lifestyle to understand its relationship with mortality outcomes.

As with other studies, ours had weaknesses that limit its interpretation. While the number of individuals available for our analysis was large, lifestyle information was collected at a single time point, before- and after which behaviors may have changed in important ways. Whether behavior changes contributed to increased or decreased mortality risk is unknown. Further, all of the variables included in the LPA were self-reported, potentially leading to significant over-estimations of behaviors such as PA and under-estimation of cigarette and alcohol use. Also, to reduce the influence of simulated or imputed data, we used NHANES data without applying the population weights that allow analyses to be representative of the US population at the time of the survey, limiting the overall generalizability of the results. Additionally, such a data-driven approach may lead to results that are overly specific to the population studied, limiting general relevance. Further, the omission of PA duration, which was not collected by NHANES, may lead to an over-estimation of PA reported by participants. Finally, the inclusion of former smokers in the non-smoker group may confound the mortality outcomes (US Department of Health and Human Services, 2014), though a sensitivity analysis restricted to never smokers showed very similar results.

7. Conclusions

Health behaviors cluster into distinct lifestyle patterns, which predict mortality during long-term follow-up among non-smokers and smokers. This suggests that mortality outcomes may be best improved through targeting a combination of behaviors, and/or ensuring that altering one behavior does not have undesired effects on other related behaviors. While future research is needed to assess the long-term stability of individual behaviors and behavior patterns, this study highlights the importance of assessing health behavior clustering to the prevention of mortality from all causes, CVD and cancer.

Conflict of interest

All authors declare that no conflict of interest exists.

Study presentation

An early version of this work was presented in poster form at the 2015 annual meeting of the American Society for Preventive Oncology, March 15–17, Birmingham, AB.

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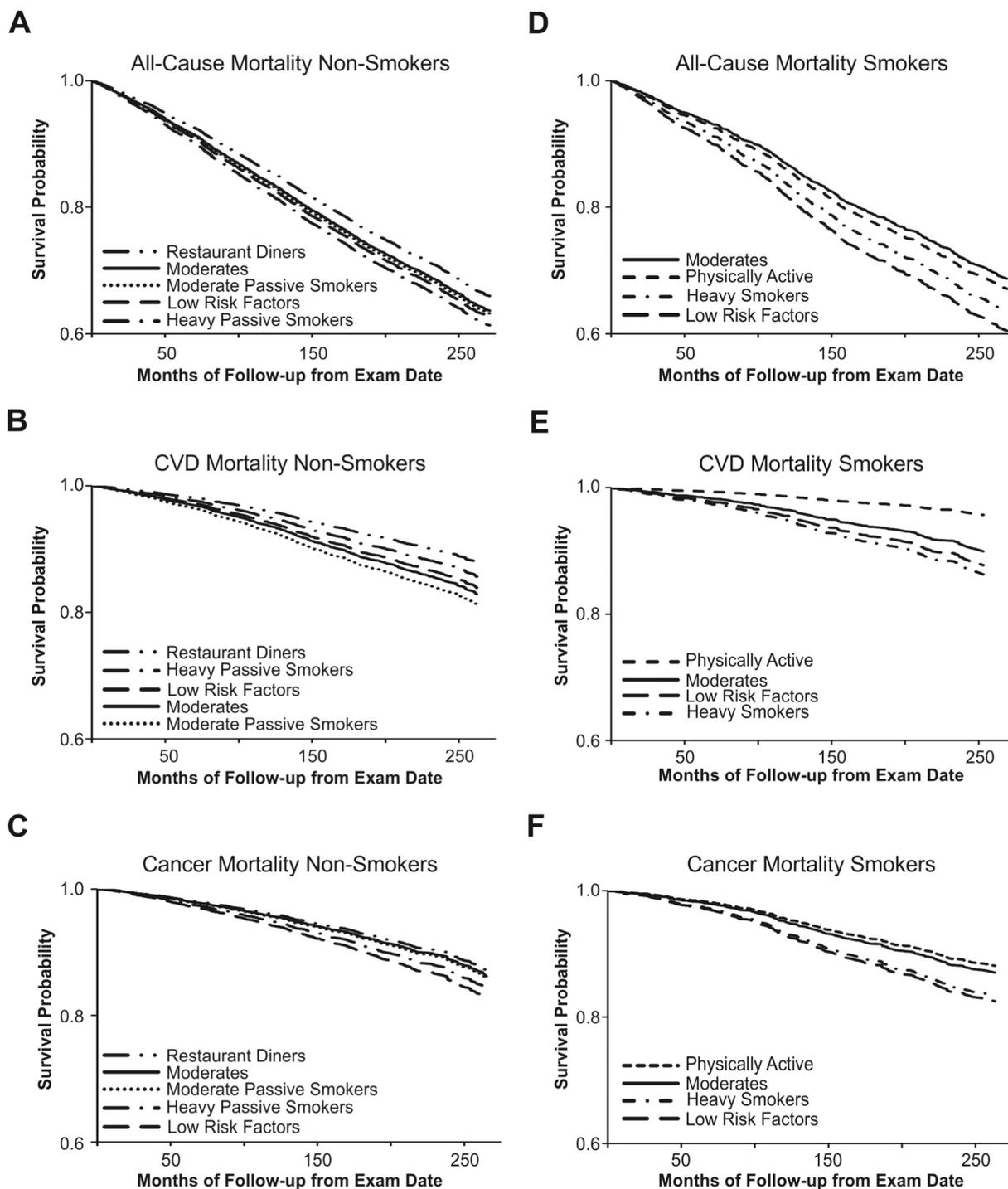


Fig. 2. Adjusted survival curves by behavior class in Non-Smokers (A–C) and Smokers (D–F). All-Cause mortality (A, D), Cardiovascular Disease mortality (B, E) and Cancer mortality (C, F) are shown. Legend order reflects relative curve order. Please note the scale shown is from 0.6 to 1.0.

government.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jypmed.2019.01.012>.

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