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The Smoking Patterns of Women in their Forties: their relationship to later osteoporosis^{1, 2}

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Summary

Osteoporosis is prevalent among women 50 years of age and older and accounts for numerous fractures and the related deaths of many sufferers. In our study, 22.4% of the women reported having osteoporosis. Smoking contributes substantially to osteoporotic fractures. This study assessed how different trajectories of women's smoking, covering the ages 40 to 48, relate to osteoporosis at age 65. Trajectory analysis of tobacco use data permits smoking patterns to emerge which may have differing relationships to osteoporosis. Logistic regression analyses revealed the varying relationships of different smoking patterns to osteoporosis. As hypothesized, the chronic/heavy smokers were significantly more likely than the nonsmokers to report having osteoporosis [Adjusted Odds Ratio=2.23 (1.23–4.03)]. Quitters [*A.O.R.*=1.45 (0.68–3.08)] and moderate smokers [*A.O.R.*=1.90(0.72–5.00)] did not differ significantly from nonsmokers on the osteoporosis measure. Hence chronic/heavy smokers should not be the only focus of public health efforts to reduce smoking and the associated risks of osteoporosis. The findings also highlight the efficacy of women smokers quitting in their 40's in order to reduce their likelihood of contracting osteoporosis.

Osteoporosis has been defined as having bone mineral density at least 2.5 standard deviations below the normal young adult mean (Naidoo, Goff, & Klibanski, 2003; Riggs & Melton, 1995). Conservatively, osteoporosis has affected 13% to 18% (or 4–6 million) of women in the United States who are 50 years of age or older (Looker, *et al.*, 1997; Naidoo, *et al.*, 2003). Among women in the U.S. it has accounted for 1.5 million fractures annually. Almost a quarter of those experiencing fractures have died in less than a year (Mitchell, Kammerer, Schneider, Perez, & Bauer, 2003). Riggs & Melton (1995) reported that women 50 years old have had a lifetime risk for a spine, wrist, or hip fracture of almost 40%. A meta-analysis (Law & Hackshaw, 1997) has shown that, among females, 12% of all hip fractures have been attributable to smoking and cannot be explained by other factors. Moreover, current smokers, compared to nonsmokers, have not had an increased risk of hip fractures at age 50, but their risk has increased markedly at each decade of life thereafter; it was 71% greater at age 80 (see Law & Hackshaw, 1997).

While there has generally been a consensus among investigators that tobacco use is inversely related to bone mineral density, this has not always been the finding among young adult women and even among elderly women, and sometimes has been limited to heavy smokers as opposed to moderate or light smokers (Benson & Shulman, 2005; Daniel, Martin, & Drinkwater, 1992; Kiel, *et al.*, 1996; Law & Hackshaw, 1997; Slemenda, Hui, Longcope, & Johnston, 1989; Whiting, McCulloch, Bailey, & Houston, 1990). With a few

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exceptions (Benson & Shulman, 2005; Kiel, *et. al.*, 1996; Law & Hackshaw, 1997), these studies included relatively small samples. Lastly, while a few studies covered a two or three-year period (Elgán, Samsioe, & Dykes, 2003; Mazess & Barden, 1991; Slemenda *et. al.*, 1989), the remainder of the studies were cross-sectional. Our smoking measure builds on the more limited measures used by some investigators by incorporating amount, frequency, and duration of smoking across a significant time span. Following a developmental life course perspective, trajectory analysis can be used to examine differential smoking patterns. Rather than assuming that all smokers show the same smoking behavior over time, this method allows the data to determine the number and characteristics of different smoking patterns (i.e., one for chronic, heavy smokers, another for quitters, and one for moderate smokers). This method incorporates individual differences in the growth, stability, and decline in the frequency and quantity of smoking over time.

A question that remains in the literature is how the trajectories of smoking over the course of eight years in women in midlife relate to osteoporosis. The current study addressed this question and contributed to the literature in two major ways. First, this longitudinal study contributed by assessing, in the same, large group of women, the effect of smoking at multiple points in time from age 40 to 48. Chassin and her colleagues (2000) examined smoking trajectories over the period from early adolescence to the early thirties, but this method has not been used with samples in their forties. Second, these patterns might have differing relationships to osteoporosis. For example, the habitual smoking pattern might significantly differ from that of nonsmokers in the association with osteoporosis while the quitter and nonsmoker patterns might not differ significantly in this regard. These varying relationships might have different implications for intervention efforts.

Several investigators (Benson & Shulman, 2005; Kiel, *et. al.*, 1996; Misra, Papakostas, & Klibanski, 2004; Sampson, 2002; Snelling, Crespo, Schaeffer, Smith, & Walbourn, 2001) have indicated that demographic factors such as age, income, education level, and depressed mood may be related to bone mineral density. Hence, comparable variables were controlled in this study's analysis of the association of smoking patterns with osteoporosis.

In sum, this research focused on the relationship of trajectories or patterns of intraindividual changes in smoking over eight years to osteoporosis. Based on prior research, it was hypothesized that the trajectory analysis would yield four groups although larger samples might yield five groups (Brook, Balka, Ning, & Brook, 2007; Zhang, Pahl, & Brook, 2011; Riggs, Chou, Li, & Pentz, 2007). One would be characterized by chronic heavy cigarette smoking. Another trajectory would reflect non-use of cigarettes. The two intermediate groups would consist of quitters and moderate users. It was hypothesized that the chronic/heavy smoking trajectory group and the moderate users would be more likely to have osteoporosis than nonsmokers. The quitter trajectory group might not differ significantly from the nonsmokers in the association with osteoporosis.

Method

Participants and Procedure

Data in this study came from a larger community-based, random sample of children residing in two upstate New York counties at Time 1 (T1) in 1975 (N=976). In 1983 (Time 2, T2), we started to collect data on their mothers' smoking status and other psychosocial characteristics. The originally sampled families were selected to be representative of families in this area with regard to child sex, family intactness, family income, and education. The sample was 91.2% White and 8.8% African Americans and other minorities. There was a close match of the participants' family income, maternal education, and family structure with data reported by the 1980 Census conducted by the U.S. Census Bureau. For a

fuller description of the sample and a detailed sampling procedure, please see Cohen & Cohen (1996). The sample size of the women in 1983 at T2 was 772, in 1985–1986 at Time 3 (T3) was 717, in 1992 at Time 4 (T4) was 719, and in 2009 at Time 5 (T5) was 479. Of the mothers participating in the longitudinal study, by T5 104 were deceased, 27 refused to participate, and 143 were lost to follow-up.

Eighty-eight percent of the 479 T5 participants had complete data at T2–T5. Table 1 presents the participants' demographic characteristics. *T* test analyses compared the participants at T5 with the non-participants at T5 on the T2 measures. Compared with the non-participants at T5, the 479 participants showed a greater mean educational level ($t=6.5$, $p<0.001$), a greater family income ($t=5.3$, $p<0.001$), a lower mean depressive mood ($t=-2.6$, $p=0.01$), and a lower mean frequency of tobacco use ($t=-3.045$, $p=0.003$), all at T2. Thus, the sample in this study differs somewhat from the original sample.

Extensively trained and supervised lay interviewers administered private interviews at T1–T4. At T5, the participants completed self-administered questionnaires. Written informed consent was obtained from the participants at T1–T4; at T5, returning completed questionnaires was considered the equivalent of giving “consent.” The Institutional Review Boards of the Mount Sinai School of Medicine, New York Medical College, and New York University School of Medicine approved of the procedures used in this longitudinal study. Additional information regarding the study methodology is available in prior publications (Brook, Brook, Gordon, Whiteman, & Cohen, 1990; Cohen & Cohen, 1996).

Measures

Cigarette smoking from T2 through T4—Participants reported their current smoking at each time point, T2–T4. The frequency and amount were rated as none (0), less than half pack a day (1), half pack to one pack a day (2), and more than one pack a day (3).

Osteoporosis—At T5, the participants were asked “In the last 15 years, have you had osteoporosis?” Those who reported having osteoporosis were coded 1 and those who did not were coded 0.

Controls—The control variables for the logistic regression analyses consisted of the mothers' age at T5, educational level at T2, family income at T2, and depressive mood at T2. Depressive mood was a 5 item scale ($\alpha=0.80$) adapted from Derogatis, Lipman, Richels, Uhlenhuth, & Covi (1974). This self-report measure has been found to have predictive validity in our studies of other samples (Brook, Ning, & Brook, 2006; Brook, *et al.*, 2008). The items were as follows: “Within the past few years, how much were you bothered by: (1) feeling hopeless about the future; (2) feeling no interest in things; (3) feeling low in energy or slowed down; (4) feeling lonely; and (5) feeling blue.” The answer options for this scale ranged from (1) “Not at all” to (5) “Extremely.”

Analysis

Using the Mplus software (Muthén & Muthén, 2007), Growth Mixture Modeling (GMM) analyses were conducted to identify the developmental trajectories of tobacco use. The dependent variable (tobacco use at each time point) was treated as a censored normal variable. The full information maximum likelihood (FIML) approach, as implemented in Mplus, was applied for missing data (Schafer & Graham, 2002). Each of the trajectory polynomials was set to be quadratic. The minimum Bayesian Information Criterion (BIC) was used to determine the number of trajectory groups (*G*). Groups with less than 5% of the sample were not considered because of concern about overextraction of latent classes. After extracting latent classes, each participant was assigned to the trajectory group with the

largest Bayesian posterior probability (*BPP*). For each of the trajectory groups, an indicator variable was created, which had a value of 1 if the participant had the largest *BPP* for that group and 0 otherwise. The observed trajectory for a group was the average of tobacco use at each time point for participants assigned to the group (see Figure 1).

Logistic regression analyses were conducted using SAS Business Analytics Software (SAS Institute INC, Cary, NC, USA) to assess the associations between the trajectories of tobacco use and osteoporosis. The *BPPs* of the trajectories of tobacco use (one of them was chosen as the reference) and the control variables (i.e., age at T5, educational level at T2, family income at T2, and depressive mood at T2) were included as the independent variables. The indicator variable of reported osteoporosis was used as the dependent variable. We fit two multivariate logistic regression models to test the contribution of the trajectory groups. First, we entered the control variables in the analysis. Second, we added the three *BPPs* of the trajectory group memberships. We conducted a likelihood ratio test to examine the contribution of the trajectory group memberships to predicting osteoporosis.

Results

Trajectories of Tobacco Use

The solutions for the three-group trajectory ($BIC = 3748.04$), the four-group trajectory ($BIC = 3689.36$), and the five-group trajectory ($BIC = 3657.67$) were calculated. Although the *BIC* for the 5-group trajectory was lower than that for the 4-group trajectory, the five-group solution was not considered because there was one trajectory group with only 2.1% of the sample. Participants were then assigned to the tobacco trajectory group that best depicted their tobacco use over time. The average classification probabilities for group membership ranged from 0.855 to 0.995, and the entropy was 0.933, both of which indicated a satisfactory classification (Nagin, 1999).

Figure 1 presents the four observed tobacco use trajectories. The trajectory groups were: a) chronic/heavy smokers (25.4%; mean *BPP*=92.9%, min *BPP*=53.7%, max *BPP*=100%); b) quitters (10.2%; mean *BPP*=95.5%, min *BPP*=46.1%, max *BPP*=99.9%); c) moderate smokers (6.7%; mean *BPP*=85.5%, min *BPP*=37.8%, max *BPP*=100%); and d) nonusers (57.7%; mean *BPP*=99.5%, min *BPP*=83.7%, max *BPP*=100%). As noted in Figure 1, the chronic/heavy smokers smoked about 20 cigarettes per day from age 40 to their late-forties. Quitters used about ten cigarettes per day at age 40 and quit completely by age 48. Moderate users smoked less than ten cigarettes per day from age 40 to their late-forties.

Correlation analyses indicated that younger age ($r=-0.21$, $p<0.001$), lower educational level ($r=-0.15$, $p=0.0015$), lower family income ($r=-0.20$, $p<0.001$), and greater depression ($r=0.17$, $p<0.001$) were significantly associated with a higher probability of belonging to the chronic/heavy smoker group.

Group Membership as a Predictor of Osteoporosis

Logistic analyses of the *BPPs* of tobacco group membership as predictors of osteoporosis ($N=479$) were conducted. Among the T5 participants, 22.4% reported having osteoporosis. The prevalence of osteoporosis among nonusers, quitters, moderate smokers, and chronic/heavy smokers was 18.6%, 26.5%, 25.0%, and 29.4%, respectively.

The Likelihood Ratio test indicated that the *BPPs* of the trajectories of tobacco use significantly predicted osteoporosis (Likelihood Ratio $\chi^2(3)=7.96$, $p=0.047$) over and above the control variables (i.e., age at T5, educational level at T2, family income at T2, and depressive mood at T2). Table 2, shows the results of the multivariate logistic regression analyses using the controls listed above. As compared with the probability of belonging to

the nonsmoker group, the probability of belonging to the chronic/heavy smoker group was significantly associated with having developed osteoporosis when they were between the mean ages of 50 and 65 years ($A.O.R.=2.23$; $p<0.05$). The probabilities of belonging to the quitters ($A.O.R.=1.45$; $p>0.05$) and the moderate smokers ($A.O.R.=1.90$; $p>0.05$), as compared with the probability of belonging to the nonuser groups, were not significantly associated with having osteoporosis. Of the controls, only age was significantly related to having osteoporosis after adjusting for other factors (other control variables and the *BPPs* of the smoking trajectories) in the analyses. Additional analyses indicated that the *A.O.R.* of the *BPP* of belonging to the chronic/heavy smokers did not differ significantly from the *A.O.R.* of the *BPP* of belonging to the quitters ($A.O.R.=1.54$; $p>0.05$) or the *BPP* of belonging to the moderate smokers ($A.O.R.=1.18$; $p>0.05$) in the likelihood of having osteoporosis.

Discussion

As noted in the Analysis Section, operating within a life span, developmental framework, the present study, which covers a 25-year period, investigated the relationship of smoking at multiple points in time to osteoporosis. This approach was used to identify distinct groups or trajectories of smoking behavior. Trajectory analysis enabled the study to examine differential patterns which incorporated individual differences in the growth, stability, and decline in smoking over time. In addition to providing information on the development of smoking, the findings make another distinct contribution. The findings enable us to identify ways in which different trajectories of smoking are related to osteoporosis in women in late mid-life.

This investigation of the development of smoking identified women following trajectories of no-use, moderate use, quitting, and chronic/heavy use. The majority of women were nonusers. Among the smokers, most were in the chronic/heavy group, probably due to the addictive nature of nicotine, followed by quitters, and moderate smokers. Overall, these findings are in agreement with some of the previous studies investigating the patterns of smoking over time despite these studies use of younger samples (Chassin, Presson, Potts, & Sherman, 2000; Riggs, *et. al.*, 2007; White, Nagin, Replogle, & Stouthamer-Loeber, 2004). However, studies using far larger samples have found a greater number of trajectory groups (Chassin *et. al.*, 2008; Orlando, Tucker, Ellickson, & Klein, 2004).

Women who reported being chronic/heavy smokers over an eight-year period from the mean age of 40 to a mean age of 48, were significantly more likely than nonsmokers at age 65 to report that they had developed osteoporosis. The moderate smokers and quitters were not more likely than the nonsmokers to report having developed osteoporosis. It is possible that the moderate smoking group was too small and thus there was insufficient power to find a significant difference between that group and the nonsmokers in the association with osteoporosis. Moreover, these relationships showed the role of smoking patterns in osteoporosis beyond the effect of demographic factors and depressive mood. The study's results are consistent with those of investigators who found that age (Snelling, *et. al.*, 2001) was related to having osteoporosis and with those who found that years of education (Benson & Shulman, 2005; Snelling, *et. al.*, 2001) were not associated with osteoporosis. The current findings contrasted with those of Misra, *et. al.* (2004) who, in a review article, reported evidence that depression heightened the risk of osteoporosis. Misra, *et. al.* cited research that was cross-sectional or produced over a period of just a few years while the present study examined the relationship over an eight year period. It is more difficult to obtain relationships between variables measured many years apart than when only a few years separate the measurements. The difference in time frames is a likely a contributor to the difference in results.

This study's findings were generally consistent with research that has found that heavier smokers were more at risk for having lower bone density than were nonsmokers (Law & Hackshaw, 1997) and those investigators who found that all smokers, regardless of the level of smoking, differed from nonsmokers (Mazess & Barden, 1991). However, these investigators defined the smoking categories *a priori* rather than estimating them from the results of trajectory analysis which examines intraindividual differences over extended time periods. Furthermore, some studies (Daniel, *et al.*, 1992; Elgán, *et al.*; Mazess & Barden, 1991) had samples younger than this study's and one study (Kiel *et al.*, 1996) included women who were older than the current participants. This study's results are consistent with the conclusion in Law & Hackshaw's (1997) paper that quitters appear similar to nonsmokers in their reduced risk for low bone mineral density in comparison with smokers. Despite the consistency of this study's results with those of these other investigators, the advantage of this study is that trajectory analysis permits us to assess the variable relationships of the different smoking patterns to osteoporosis.

This study's findings contrasted with those of Kiel and his colleagues (1996), who tested for differences between both heavy and moderate smoking females up to age 35 and comparable nonsmokers in their risk for low bone mineral density as seniors. They found no consistent relationship between smoking and bone mineral density, perhaps because their study participants were younger than those in this study. Other studies (Daniel, *et al.*, 1992; Slemenda, *et al.*, 1989; Whiting, *et al.*, 1990) found differences between heavy smokers and nonsmokers in their risk for low bone mineral density. In accord with this study's results, they found no differences between moderate smokers and nonsmokers in their risk.

Previous investigators have suggested that both physical and psychological mechanisms may explain the link between smoking and osteoporosis. As regards physical mechanisms, smoking may have a direct effect on bone density by lowering bone metabolism (Elgán, *et al.*, 2003; Law & Hackshaw, 1997) or smoking may lower estrogen levels which, in turn, decrease bone mineral density (Elgán, *et al.*, 2003; Mazess & Barden, 1991; Sampson, 2002). Lastly, smokers' reduced calcium absorption and retention may contribute to their lower bone mineral density (Benson & Shulman, 2005; Kiel, *et al.*, 1996; Law & Hackshaw, 1997). With respect to psychological mechanisms, nonsmokers, quitters, and moderate smokers as compared with chronic/heavy smokers, may be more health conscious. Related to this, nonsmokers are more likely to exercise (Kaczynski, Manske, Mannell, & Grewal, 2008; Vainionpää, Korpelainen, Vihriälä, Rinta-Paavola, Leppäluoto, & Jämsä, 2006; VanKim, Laska, Ehlinger, Lust, & Story, 2010). Physical exercise is a protective factor that may reduce the likelihood of osteoporosis. Nonsmokers are less likely to drink alcohol to excess (Sampson, 2002) and more likely to have better diets (Wilson, *et al.*, 2005). Smokers who have health insurance may be more likely to enter cessation programs than those who do not (Troyer, Ferketich, Murray, Paskett, & Wewers, 2011). These may all be protective factors that will lessen the likelihood of osteoporosis.

This study has several limitations. As some participants may have underreported their smoking, this study's findings would be strengthened by having smoking data at intervals before age 40, by having biochemical verification of smoking levels, by incorporating additional controls such as genetic background and nutrition and exercise (Benson & Shulman, 2005; Misra *et al.*, 2004; Naidoo *et al.*, 2003; Sampson, 2002), by having an objective measure for the diagnosis of osteoporosis (e.g., medical test), more detailed measurement of ethnicity (e.g., the southern Europeans versus northern Europeans), and a clinical diagnosis of depression (DSM-IVR). It would also have been preferable to control for early body mass index, but we did not have this data at T2-T4. A somewhat larger proportion of our sample (22%) reported having osteoporosis than did so in national samples (13%-18%) (Looker, *et al.*, 1997; Naidoo, *et al.*, 2003). However, our sample consisted

primarily of white women who are more likely to have osteoporosis than women from other ethnic groups. The group-based approach we used is subject to methodological limitations (Nagin & Tremblay, 2005). Particularly, the number of trajectory groups depends on the nature of the analyses and data even with a larger sample. Lastly, we lost some participants due to attrition. Had we been able to include these non-participants in our T5 data, we would have had greater variability, which might have strengthened our results.

Despite these caveats, it is noteworthy that this longitudinal analysis that incorporated individual smoking patterns over time indicated that chronic/heavy smokers were at risk for developing osteoporosis relatively early, between the mean ages of 50 and 65. These results suggested that public health efforts to reduce smoking and the associated risks of osteoporosis will be most effective if they target those who smoke a pack a day or more. In addition, the results infer that women smokers who quit in their 40s will reduce their risk of developing osteoporosis.

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Figure 1. Women's Tobacco Use Trajectories From the Mean Ages of 40 to 48

Note: Smoking score: None=0; Less than half pack a day=1; Half pack to one pack a day=2; More than one pack a day=3.

TABLE 1

Demographic Characteristics (*N*=479)

Demographic Characteristics	%
Race/Ethnicity	
White	91.2
Non-White	8.8
Age at T5	
50–60	19.6
61–70	60.2
>70	20.2
Marital Status at T5	
Married	67.2
Single	0.4
Divorced	15.3
Widowed	17.1
Employment Status at T5	
Employed (Full Time and Part Time)	40.7
Retired	42.4
Other (e.g., Homemaker, Unemployed)	17.9
Educational Level by T5	
Less than high school	8
High school	53
Some college or higher	39
Annual Personal Income at T5	
\$0–10,000	19.3
\$10,001–35,000	47.7
\$35,001–75,000	28.3
>\$75,000	4.7

TABLE 2

Logistic Regression of Trajectories of Cigarette Smoking with Nonsmokers as the Reference Group on Osteoporosis at T5($\bar{X}$ age=65 years) ($N=479$).

Smoking Trajectories	Osteoporosis A.O.R. (95% C.I.)
<i>BPP</i> of Belonging to the Chronic/Heavy Smoker Group	2.23 (1.23 – 4.03) **
<i>BPP</i> of Belonging to the Quitter Group	1.45 (0.68 – 3.08)
<i>BPP</i> of Belonging to the Moderate Smoker Group	1.90 (0.72 – 5.00)
T2 Age	1.09 (1.05–1.13) ***
T2 Educational Level	1.01 (0.90–1.14)
T2 Family Income Level	0.92 (0.83–1.02)
T2 Depressive mood	1.05 (0.97–1.13)

Note: A.O.R. = Adjusted Odds Ratio; C.I. = confidence interval;

**
 $p < 0.01$;

 $p < 0.001$.

BPP = Bayesian posterior probability