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Post-discharge smoking cessation in subgroups of hospitalized smokers: a latent class analysis.

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Abstract

Background: Hospitalization presents a window of opportunity to treat smoking, and hospital-initiated smoking treatment has demonstrated effectiveness. Despite effective interventions, not all smokers will discontinue use, highlighting the need to better understand which patients achieve cessation. Traditional regression methods may not capture the complexity of inpatient smoker subgroups.

Methods: We conducted latent class analysis (LCA) with data from 397 hospitalized adult cigarette smokers enrolled in a randomized trial. Six categorical indicator variables known to impact cessation were selected to estimate subgroups: health conditions (smoking-related disease (SRD), depressive symptoms, positive screen for alcohol problems) and smoking-related variables (time to first cigarette, cigarettes/day, smoking indoors). We estimated the probability of achieving biologically-verified seven-day tobacco cessation six months after discharge.

Results: A three-class model best fit the trial data: a *Light Smokers* subgroup had lower probability for most indicators; a *High Health Burden* subgroup had high smoking behavior probabilities and similar health problems to the *Light Smokers* subgroup; and a *Heavy Smoking Drinking Depressed* subgroup had high nicotine dependence, depressive symptoms, and alcohol

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The **University of Pittsburgh** Institutional Review Board reviewed and approved this secondary analysis study as exempt.

misuse probabilities. Probability of biologically-verified cessation conditional on class membership was significantly higher ($p < 0.001$) for the *High Health Burden* and the *Light Smokers* subgroups compared to the *Heavy Smoking Drinking Depressed* subgroup.

Conclusion: Results suggest that subgroups with lower probabilities of alcohol misuse and depression and higher probability of SRD had higher probability of successful cessation after hospital discharge. Hospitalized patients with nicotine dependence combined with behavioral and mental health problems have additional cessation barriers that may require intervention focus.

INTRODUCTION:

Hospitalization presents a window of opportunity to provide cessation interventions to smokers. Illness motivates smokers to quit, hospitals are smoke-free environments that encourage short-term abstinence, and treatment initiated in the hospital and continued after discharge increases long-term cessation.¹ While the evidence for hospital-initiated treatment is robust, not every smoker will achieve long-term cessation even with intensive treatment and follow-up, highlighting the need to understand which patient subgroups achieve cessation.

Previous research has demonstrated that successful smoking cessation is predicted by various factors including smoking-related characteristics and health conditions. Smoking behaviors, including the nicotine dependence markers of time to first cigarette after waking and the number of cigarettes consumed per day, can predict cessation.² Having a home indoor smoking ban has been shown to increase cessation;³ potentially important for patients returning home from hospital. Vulnerability to and diagnosis of smoking-related diseases (SRD) can increase successful cessation among medically ill smokers,^{4,5} while behavioral and mental health problems such as alcohol misuse and depression lower the likelihood of success.^{6,7} Complex intersections of multiple cessation predictors has not previously been tested among smokers receiving hospital-initiated interventions.

Complex patient subgroups, defined by patterns of predictors, are insufficiently identified using traditional multiple regression moderation analyses.⁸ Null hypothesis testing may inadequately capture the complex relationship between the outcome and predictors that influence each other compared with statistical models developed to best fit observed data.⁸ Additionally, testing predictors of clinical trial outcomes using null hypothesis tests for pre-specified groups is susceptible to Type I error and often involves conservative statistical corrections.⁹

Latent class analysis (LCA) is an informative method of predicting outcomes among patient subgroups¹⁰ and has been used to evaluate brief alcohol interventions for hospitalized patients¹¹ as well as cessation for tobacco interventions.^{12,13} LCA hypothesizes that a latent (i.e., unobserved) categorical variable predicted by multiple observed variables describes patient subgroups known as classes.¹⁴ LCA captures the variability of multiple patient characteristics by finding shared patterns of responses, then assigns each individual a class value based upon the probability that class best captures their unique characteristics.¹⁴

The objective of this study was to estimate the presence of latent patient subgroups among a sample of hospitalized smokers using multiple cessation predictors. A model of latent subgroups that best fit the observed cessation predictors could be used to understand which patterns predict achieving cessation.

METHOD:

Participants and Design

Data for this secondary analysis were collected in a randomized cessation intervention trial provided after hospital discharge. Participants were 397 adult daily smokers admitted to an academic teaching hospital who received cessation counseling during their stay, planned to quit post-discharge, and were willing to accept cessation medication. Study recruitment and intervention methods have been described in detail.¹⁵ Patients were randomized into either standard care (n=199; received inpatient counseling, given specific recommendation for post-discharge medication and counseling but post-discharge treatment not provided automatically), or a sustained care (n=198; standard care plus provided with up to three months free medication and interactive voice response telephonic counseling for medication use and support). Patients were contacted at one, three, and six months post-discharge to complete follow-up assessments. The primary outcome for the trial was biologically-verified past seven-day tobacco cessation at six months post-discharge. The sustained care intervention was superior to standard care for use of post-discharge smoking cessation treatment, and for cessation (relative risk=1.71, 95% CI: 1.14 – 2.56).¹⁶

Measures

Smoking cessation was defined in the parent study.^{15,16} Self-reported (yes/no) past seven-day smoking was assessed during follow-up surveys. Cessation at six months was verified by saliva cotinine, or expired air CO if still using nicotine replacement. Missing self-report outcomes and failure to complete the biological verification test were considered current smoking.

Six indicators were selected from the available baseline trial data and considered important to cessation based upon prior research demonstrating an association between the cessation predictor (indicator) and cessation (outcome), as reviewed above. These indicators represented three smoking-related variables and three health conditions that altogether were linked as cessation predictors to form patient subgroups in this clinical trial.

The smoking variables included two markers of nicotine dependence:² cigarettes per day (≤ 10 vs. >10) and time to first cigarette (≤ 30 vs. > 30 minutes), as well as presence of a home smoking ban (“Does anyone smoke in your home?” yes/no). The three health status binary (yes/no) indicators included any discharge diagnosis of SRD, positive screen for alcohol use problems, and positive screen for depressive symptoms. SRD was defined using *ICD-9-CM* codes corresponding to the 2014 U.S. Surgeon General’s Report for cancer, cardiovascular disease, pulmonary disease, and perinatal conditions.¹⁷ A positive screen for alcohol use problems was defined by scores ≥ 4 for males or ≥ 3 for females on the 3-item Alcohol Use Disorders Identification Test (AUDIT-C, range: 0–12).¹⁸ A positive screen for depressive

symptoms was defined by a score ≥ 7 on the 8-item Center for Epidemiological Studies Depression scale (CESD-8, range: 0–24).¹⁹

Analysis

LCA to identify subgroups of participants was conducted with the six indicator variables using Mplus 7.4 (Mplus, Los Angeles, CA) with a distal categorical outcome.²⁰ The optimal number of subgroups was identified using an iterative process of increasing the number of subgroups until best fit was achieved using the Akaike Information Criterion (AIC), sample-size adjusted Bayesian Information Criterion (aBIC), and the bootstrapped likelihood ratio test (BLRT).²¹ The highest posterior probability for each patient determined subgroup assignment, and the average probability in each subgroup provided a measure of assignment accuracy. Posterior probability values closer to 1 indicate better agreement between observed patient data and the subgroup response pattern. The biologically-verified smoking cessation primary outcome and secondary self-report cessation outcomes were added using Lanza's approach²² to test whether the probability of cessation varied by subgroup. Equality of outcome distributions across subgroups was tested using Wald's chi-square test. Differences in patient characteristics were compared across assigned subgroups using ANOVA for continuous variables and chi-square tests for categorical variables. A three-step approach accounting for LCA measurement error using multinomial logistic regression²⁰ confirmed these differences (Supplemental Table 1). The xxx Institutional Review Board reviewed and approved this secondary analysis as exempt.

RESULTS:

A latent variable with three subgroups was found using model fit criteria (Supplemental Table 2) with entropy of 0.623 (BLRT $p=0.013$). Subgroup labels describe the pattern of affirmative responses (Figure 1). Baseline demographics are displayed in Table 1. The *Light Smokers* subgroup ($n=140$, 35.3%) was characterized by lower probabilities of smoking dependence, depressive symptoms, and alcohol use problems. *Light Smokers* had class assignment accuracy of 0.816 on average. Patients were on average age 52.5 years, 79% were White, 49% reported more than high school education, and 46% randomized to sustained care.

The *High Health Burden* subgroup was the largest ($n=230$, 57.9%) characterized by high probability of smoking risks and SRD but slightly lower probability of depressive symptoms and alcohol use problems. Class assignment accuracy was 0.861 on average. These patients were slightly, though not significantly, older than the *Light Smokers* subgroup; 48% were female; significantly more were White (91%), 49% had more than high school education, and 53% randomized to sustained care.

Finally, the *Heavy Smoking Drinking Depressed* subgroup ($n=27$, 6.8%) characterized individuals with high levels of smoking dependence, symptoms of depression and alcohol use problems, but lower probability of smoking inside their home and having SRD. Class assignment accuracy was 0.755 on average. Patients in this subgroup were significantly younger (41 years) than the other subgroups; 41% were female, 74% were White; 44% had more than high school education, and 48% randomized to sustained care.

The conditional probability of biologically-verified cessation was significantly different (Wald $\chi^2(df=2)=18.3$, $p<.0001$) across subgroups. The probability of verified cessation at six-month follow-up was 0.435 ($SE=0.14$) in the *Light Smokers* subgroup, 0.206 ($SE=0.05$) in the *High Health Burden* subgroup, and 0.003 ($SE=0.043$) in the *Heavy Smoking Drinking Depressed* subgroup. In pairwise comparisons, *Light Smokers* had the highest probability of smoking cessation, but not significantly different from the *High Health Burden* subgroup. The *Heavy Smoking Drinking Depressed* subgroup had a significantly lower probability of smoking cessation compared to both the *Light Smokers* and *High Health Burden* subgroups. For the self-reported smoking cessation outcomes, there were significant differences at one month between the *Light Smokers* and *Heavy Smoking Drinking Depressed* subgroups, and at six months between the *Heavy Smoking Drinking Depressed* and both the *Light Smokers* and *High Health Burden* subgroups (Table 1).

DISCUSSION:

Three subgroups of hospitalized smokers were found using LCA with six cessation predictors observed in a clinical trial. While randomization into study arm did not differ significantly, subgroups had significantly different probabilities of achieving verified smoking cessation at six-month follow-up. Comparing these subgroups, for hospitalized patients a lower probability of depressive symptoms and alcohol use problems, and higher probability of SRD was associated with greater success of achieving cessation. While each of these indicators independently predicts cessation in the general population, the combined pattern strongly predicted cessation outcomes for hospitalized smokers. The two largest subgroups (*High Health Burden* vs. *Light Smokers*) differed in the probability of smoking behavior but had similar patterns of health conditions including depressive symptoms, alcohol use problems, and SRD (Figure 1). These patterns did not generate significant differences in cessation, whereas differences in cessation were predicted by differences in health conditions (*High Health Burden* and *Light Smokers* vs. *Heavy Smoking Drinking Depressed* subgroup).

The demographic subgroup analyses conducted for the parent study found a significant study interaction for non-White participants achieving cessation with sustained care.¹⁶ This current analysis found proportionally more racial minorities in subgroups with both the highest and the lowest probabilities of cessation. This suggests that differences in cessation after discharge may be more complex than demographics and based in part on patterns of cessation predictors.

Hospitalized smokers have complex needs and barriers to smoking cessation.⁵ Cessation predictors including markers of nicotine dependence,² smoking inside the home,³ as well as comorbid physical, behavioral, and mental health concerns^{6,7} likely influence one another. Interest in personalized medical care using the right treatment for the right patient²³ has generated biological risk prediction discoveries;²⁴ however, personalized care and intervention tailoring require further knowledge about the differential treatment impact, particularly to address tobacco-related health disparities among patient subgroups.²⁵ Using LCA, patient subgroups that represent patterns of predictors could be used to increase tobacco treatment effectiveness. For example, providers could input clinical data into a latent

class algorithm that identifies the most effective treatment for a patient profile and provide a personalized care plan. As more patient data are accumulated, additional classes and treatment modalities could be evaluated creating a robust menu of interventions.

There are limitations to this study. This analysis was conducted post hoc from clinical trial data not collected to explore latent subgroups. In addition, latent subgroups are probabilistic with possible misclassification associated with attempts to categorize individuals. We did not control for significant differences in demographics in assessing the conditional outcome probabilities. Although covariates can be included in a single-step approach, this could change item response and class membership probabilities for the latent class variable.²² Alternatively, a classify-analyze approach using pseudoclass draws based on posterior probabilities²⁶ or a three-step approach that accounts for class assignment error could control for covariates.²⁷ In these models, class membership is assigned and outcomes added to the model with covariate controls; however, each approach has limitations related to assigning membership, compared to Lanza's approach that estimates the conditional probability of the outcome based on the probability of class membership.^{20,22}

In summary, hospitalization presents a window of opportunity to initiate smoking treatment and for individuals to make a cessation attempt.¹ The complex relationship between smoking behaviors and comorbid health conditions predicted post-discharge cessation among subgroups of patients identified using latent class analysis (LCA). These findings offer unique insight into how cessation predictors intersect to create a patient profile and has potential to inform personalized care and intervention tailoring. While treatment guidelines for smoking recommend multiple modalities for the best cessation outcomes,²⁸ LCA could be a useful tool in developing a profile-based approach to optimize cessation impact.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Latent class conditional item affirmative response probabilities.

Table 1.

Baseline Characteristics and Smoking Cessation Outcome by Subgroups

	Total Sample	Light Smokers	High Health Burden	Heavy Smoking Drinking Depressed	p
N (%)	399	140 (35.3)	230 (57.9)	27 (6.8)	
Age, mean (<i>SD</i>)	52.5 (12.1)	52.5 (12.4)	53.9 (10.9)	41.4 (14.1)	<0.001
Gender, % Female	48.6	58.6	48.3	40.7	0.081
Race, % White	81.1	79.3	90.8	74.1	0.002
Education, % High school or less	51.5	50.7	51.5	55.6	0.899
Intervention study arm, %	49.9	45.7	52.6	48.2	0.43
>10 cigarettes smoked per day, %	67.8				
Smoke within 30 minutes, %	77.6				
Home smoking ban, %	38.7				
Smoking related diagnosis, %	45.2				
Alcohol use problems, %	36.6				
Depressive symptoms, %	65.5				
Conditional probability (<i>SE</i>) of cessation outcome					
1 month self-report		0.686 (0.09)	0.451 (0.07)	0.248 (0.1)	0.006
3 month self-report		0.541 (0.18)	0.414 (0.04)	0.27 (0.12)	0.555
6 month self-report		0.804 (0.27)	0.353 (0.06)	0.132 (0.08)	0.013
6 month biologically confirmed		0.435 (0.14)	0.206 (0.05)	0.003 (0.04)	<0.001

SD=standard deviation, SE=standard error.

^a Items scaled from 1–10; 1 = lowest score, 10 = highest score.