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Gender differences in the real-world effectiveness of smoking cessation medications: Findings from the 2010–2011 Tobacco Use Supplement to the Current Population Survey

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ABSTRACT

Background: Meta-analyses of clinical trial data have identified clinically relevant gender differences in the efficacy of smoking cessation pharmacotherapy. It is unclear whether these findings are generalizable to smokers quitting in real-world contexts.

Methods: Using Tobacco Use Supplement to the Current Population Survey (TUS-CPS) 2010–2011 cross-sectional data, we generated propensity score matched samples of smokers who quit either unassisted by medication, using only varenicline, or using only transdermal nicotine patch (TNP). We used generalized estimating equations to estimate gender differences in the comparative effectiveness of these cessation options for achieving 30-days of abstinence, adjusting for potential confounders.

Results: When stratified by gender, TNP was significantly more effective than unassisted quit attempts for men (OR = 1.37; 95%CI = 1.02,1.83; p = 0.03), but not for women (OR = 0.96; 95%CI = 0.71,1.31; p = 0.82). Varenicline was significantly more effective than unassisted quit attempts for women (OR = 1.63; 95%CI = 1.16, 2.31; p = 0.005), but not men (OR = 1.35; 95%CI = 0.94,1.96; p = 0.11). Varenicline was also more effective than TNP for women (OR = 1.51; 95%CI = 0.12,2.05; p = 0.007) but not men (OR = 0.92; 95%CI = 0.65,1.31; p = 0.64). A significant gender by medication interaction was found only for the comparison of varenicline to TNP (OR = 1.64; 95%CI = 1.04,2.61; p = 0.04).

Conclusions: Findings for varenicline vs. TNP were consistent with clinical trial data, showing greater differences in effectiveness for women compared to men. Results lend support to the generalizability of clinical trial findings, highlighting the importance of considering gender when offering treatment for smoking cessation.

1. Introduction

Cigarette smoking continues to affect a large portion of U.S. adults (Jamal, 2016), despite recent declines in smoking, and is therefore poised to adversely affect public health for the considerable future. However, declines in smoking suggest that more and more smokers are interested in quitting, and so it is important to continue exploring and improving upon the ability to aid smokers in their quit attempts. A large portion of those attempting to quit smoking use at least one of the medications approved by the U.S. Food and Drug Administration (nicotine replacement therapy (NRT), varenicline, or bupropion) as smoking cessation aids (Smith et al., 2015).

1.1. Sociopharmacology of tobacco addiction

Leventhal (2016) proposed the Sociopharmacological framework for the study of nicotine dependence and its treatment in the context of tobacco health disparities. In the model, psychopharmacological stimuli and resulting acute psychopharmacological effects are influenced by (and also influence) an individual's disparity group membership and related contextual factors, resulting in greater or lesser burden of tobacco use and tobacco-related morbidity and mortality. Study of the sociopharmacology of tobacco dependence and treatment holds great promise for reducing tobacco-related health disparities. Cross-cutting methodologies can be used to study the sociopharmacology of tobacco

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dependence by examining interactions between social/contextual factors and pharmacology-related variables using both observational and experimental study designs.

1.2. Gender disparities and tobacco use

Women have not traditionally been a focus of tobacco disparity research (Smith et al., 2014a; Smith et al., 2016a) perhaps in part because historically and throughout the world men have been more likely to smoke than women. Yet, in several countries smoking among men is on the decline while smoking among women is increasing, particularly among young women and among those with social and economic disadvantages (Amos et al., 2012). Further, across countries researchers have found that in any given quit attempt women are less likely to successfully quit smoking than men (Smith et al., 2016a). Factors underlying this difference may cover the full social-ecological spectrum of individual and contextual variables. For example, there are gender differences in the relationship between negative affect and tobacco use (Perkins and Karelitz, 2015), and women tend to be more strongly influenced by tobacco use cues than men (Carpenter et al., 2014). There are also important differences in hepatic metabolism for women compared to men (Ilic et al., 2013; Lamba et al., 2003), and these differences have been hypothesized to result in gender differences in smoking cessation medication response (Smith et al., 2016b). Women are much more likely than men to experience both sexual victimization and harassment (Breiding et al., 2014), both of which are associated with substance use (Kristman-Valente et al., 2013; Neville et al., 2014; Smith et al., 2014b). With regard to the U.S., there is a well-documented gender gap in income and poverty (DeNavas-Walt and Proctor, 2015; Institute for Women's Policy Research, 2015) and evidence suggests financial distress may be more strongly related to difficulty with quitting smoking among women compared to men (McKee et al., 2003).

1.3. Gender and smoking cessation pharmacotherapy clinical efficacy

Given the existence of gender inequalities in the U.S. and elsewhere, accompanied by gender differences in smoking cessation, Leventhal's Sociopharmacological model provides a fitting framework for the study of gender differences in the effectiveness of smoking cessation pharmacotherapy. Previous research has built empirical support for this notion, finding important gender differences in the clinical efficacy of smoking cessation medications (McKee et al., 2015; Perkins and Scott, 2008; Scharf and Shiffman, 2004). In a recently published meta-analysis of over 30 clinical trials Smith et al. (2016a,b) demonstrated that the relative benefit of varenicline over transdermal nicotine patch (TNP) and bupropion was significantly greater among women compared to men. Although varenicline demonstrated equivalent efficacy for women and men, among women TNP and bupropion were substantially less efficacious than varenicline, while among men there was no significant difference in the clinical efficacy of the three medications.

1.4. Gender and smoking cessation pharmacotherapy real-world effectiveness

Clinical trial participants represent a relatively homogenous sample of cigarette smokers who are attempting to quit in highly regulated and unique contexts, making study of generalizability to real-world medication effectiveness critical. A number of investigations have documented the real-world effectiveness of smoking cessation medications (e.g., (Brose et al., 2013; Prado et al., 2011; Ucar et al., 2014)); however gender differences in real-world effectiveness are understudied. Walker et al. (2016) studied such differences using data from a national quit service in the United Kingdom, Quit-5. Their findings demonstrated that women were less likely than men to achieve 12-week abstinence, and that the relative advantage of varenicline over NRT was significantly greater for women compared to men. It is notable that this gender difference in effectiveness is consistent with efficacy results from clinical trial data (Smith et al., 2016b). Given that Walker et al. (2016) utilized data from health records, the authors were limited in their ability to adjust for potentially relevant confounders. There is a need to test hypotheses related to gender differences in smoking cessation medication effectiveness using data with availability of a range of potential confounders. Addressing this gap has the potential to help inform clinical decisions when considering smoking cessation pharmacotherapy options, improving personalized treatment of nicotine dependence and smoking cessation outcomes for both women and men.

1.5. Study aims and hypotheses

We conducted a comparative effectiveness investigation utilizing cross-sectional observational population data from the United States (U.S.), in order to compare the relative effectiveness of using TNP, varenicline only, or no medication during quit attempts for women versus men. In concordance with recommended practice, we utilized both propensity score matching and regression adjustment techniques to estimate medication effectiveness comparisons. We hypothesized that previous meta-analytic clinical trial findings would extend to real-world contexts, as supported by prior evidence (Walker et al., 2016), whereby the advantage of varenicline over TNP would be greater for women compared to men. Specifically, that women and men would demonstrate similar effectiveness for varenicline, but that TNP would be less effective for women as compared to men.

2. Material and methods

Data were analyzed from the 2010–2011 Tobacco Use Supplement of the Current Population Survey, collected by the U.S. Census Bureau and sponsored by the National Cancer Institute (U.S. Department of Commerce, 2012). We included in our sample those who were smoking 12 months prior to their interview and who made at least one quit attempt during since that time, regardless of the success of the outcome (n = 7906). We defined those who were smoking 12 months prior to the interview as persons who smoked at least 100 cigarettes in their lifetime and either a) were smoking 'all days' or 'some days' at the time of the interview (current smokers) and reported smoking for at least 1 year, or b) were not smoking at the time of the survey, but retrospectively reported they had been smoking 'all days' or 'some days' when asked, "Around this time 12 MONTHS AGO, were you smoking cigarettes every day, some days, or not at all?". Quit attempters were defined as meeting the criteria above for smoking 12 months ago and either a) among current smokers, reporting having made at least one attempt to quit smoking that lasted at least one day during the previous 12 months, or b) were former smokers at the time of the interview who had at least 30 days of abstinence. Former smokers who had achieved less than 30 days of abstinence were removed from analyses.

2.1. Measures

2.1.1. Smoking cessation outcome

Our smoking cessation outcome was having achieved at least 30-days of abstinence from smoking. When considering our smoking cessation outcome, we were constrained by the cross-sectional study design. For example, ideally, we would have considered a more extended time period of abstinence (e.g., 6 months); however, we had to take into account the inverse relationships between our time period for smoking abstinence and both statistical power and the potential for recall bias. We considered 30-day abstinence as providing adequate balance among these three factors; i.e., a balance between having achieved abstinence for a meaningful period of time, statistical power, and accuracy of recall.