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Comparison of Suicide Attempts/Behaviors Following Smoking Cessation Treatments Among Schizophrenic Smokers

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A B S T R A C T

Background: Smoking cessation may lead to depression in some smokers and result in increased risk of suicide.
Objective: To compare the risk of suicide attempts/behaviors associated with different smoking cessation medications among schizophrenic patients.
Methods: A retrospective cohort study was conducted using General Electric (GE) medical record database (1995–2011). The first day of being prescribed a smoking cessation medication defined as index date. Patients were followed up to one year from index date. Patients' suicide behaviors or attempts were identified through ICD-9 codes and E-codes. Cox proportional hazards model was applied to examine the association between smoking cessation medication and suicidal/self-injurious behaviors.
Results: Our cohort consisted of 3925 patients with diagnosis of schizophrenia or schizoaffective disorder who initiated cessation medication. Among them, 104 (2.65%) had suicide attempts or behavior within one-year follow up. However, statistically significant difference in the risk of suicide attempts/behaviors was not detected across cessation regimens in the Cox proportional hazard analysis. Only comorbidity index was found to be associated with suicide, which showed that higher Charlson comorbidity index was associated with higher risks of suicide behaviors within one year (HR = 1.15, 95% CI = 1.04–1.27).
Conclusion: There were no significant differences in suicide attempts/behaviors with different cessation medications.

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Tobacco use causes approximately 443,000 premature deaths annually in the United States (US) (CDC, 2008; Fletcher & Frith, 2008) and 5.4 million worldwide (Leung, Leung, Hon, & Kong, 2009). As compared to the general population, schizophrenic patients have much higher smoking rates, higher nicotine dependence level, and lower smoking cessation rates (Dipasquale et al., 2013; George et al., 2008; Lo et al., 2011). Although individuals with schizophrenia constitute approximately less than 1% of the general population, the medical and economic burden of cigarette smoking is enormous in this population (Dickerson et al., 2013; George et al., 2008). Thus, there is great public health significance in developing safe and effective tobacco cessation pharmacotherapies for this population.

Smoking cessation is highly recommended by public health department of various organizations and several smoking cessation interventions strategies are available for smokers. The available cessation pharmacotherapies include nicotine replacement therapy (NRT), Bupropion SR, and the most recently approved Varenicline (Jimenez-Ruiz, Berlin, & Hering, 2009; Pierce & Gilpin, 2002). Bupropion was originally approved by the FDA for treating depression under brand name Wellbutrin® in 1996 (Fava et al., 2005). In the following year, FDA approved the same ingredients but under trade name Zyban® for smoking cessation (George et al., 2008). The FDA suggested dosage regimen for cessation pharmacotherapy is usually for 12 weeks.

Suicide is the leading cause of premature death among patients with schizophrenia with a 50% lifetime risk for suicide attempts and 9–13% for completed suicide (Meltzer et al., 2003; Shibre et al., 2014). In comparison, the lifetime risk for suicide in the general population of U.S. is approximately 1% (Meltzer et al., 2003). Many of the important risk factors for suicide in schizophrenia included being young, male, with a high level of education, mood disorder, previous suicide attempts, drug misuse, unemployment, previous poor adherence to treatment and recent loss (Chang, Stuckler, Yip, & Gunnell, 2013; Hawton, Sutton, Haw, Sinclair, & Deeks, 2005; Hor & Taylor, 2010).

Trying to quit smoking may (1) lead to major depression in some smokers and (2) result in a withdrawal syndrome that includes worsened mood and other behaviors that would increase the risk of suicide. Many studies have found that negative effect symptoms are the most common symptoms of tobacco withdrawal. Some epidemiological studies reported that the increased risk is due to cessation medications and is independent of quitting (Moore, Furberg, Glenmullen, Maltsberger, & Singh, 2011). The U.S. FDA has required black box warnings regarding

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serious suicidal/self injurious side effects for Varenicline and Bupropion (Moore et al., 2011).

To date, no studies have been conducted among this minority population examining which cessation medication could lead to lower risks of suicide attempts or behaviors. This information is critical for healthcare professionals as they may need to monitor their patients more closely during the process of quitting.

1. METHODS

1.1. Data Source

The data used for this study were extracted from the General Electric Centricity Electronic Medical Record (GE EMR) database. The Centricity EMR database is used by more than 20,000 clinicians and contains longitudinal ambulatory electronic health data for more than 7.4 million patients, including demographics, vital signs, laboratory results, medication list entries, prescriptions, and diagnoses. GE EMR data was determined appropriate for the analysis due to the availability of some forms of NRTs which were OTCs and could not be captured in claims data. We have developed a protocol for linking the different files as reflected in Fig. 1.

1.2. Study Population

We included patients who were enrolled between 12/13/1995 to 10/31/2011. From the GE database, we identified patients with a diagnosis of schizophrenia or schizoaffective disorder (ICD-9 code 295.00–295.99) (Zammit et al., 2004). Patients below 18 years of age or those who received Wellbutrin® (Bupropion SR) for depression 6 months prior to index date were excluded. Those who were prescribed more than one medication the same day as their index medication were also excluded from this study.

After identifying the population, we constructed a series of new-user cohort of patients who had newly initiated using cessation medications. Only the first exposure to each of the smoking cessation medication was examined so we could be sure that the suicide event was not affected by the previous cessation product they took. The first day of being prescribed smoking cessation medication was defined as the index date.

1.3. Definitions of Suicidal/Self Injurious Behaviors

We identified patients' suicidal behaviors or attempts through ICD9 codes and E-codes. Comprehensive codes for suicide were extracted from the literature search, some examples were poisoning by solid or liquid (E950); hanging, strangulation, or suffocation (E953); drowning (E954), or jumping from a high place (E957) (Levi et al., 2003; Walkup, Townsend, Crystal, & Olfson, 2012).

1.4. Analysis Plan

Observation began on the day (index day) a patient received his or her first smoking cessation medication and continued until one year after the treatment exposure. Patients would either have the behavior or be censored at the end of follow up. They were censored if they satisfied any of the three conditions below: (1) the last day of index medication being prescribed, (2) switching over to (or adding on) another smoking cessation medication, and (3) did not have records for suicide attempts or behaviors when they reached the one year follow up. We first carried out descriptive statistics and chi-sq. analyses to examine the associations between patients' characteristics and the outcome. We then used the Cox proportional hazards model to study the factors associated with suicidal/self injurious behaviors developed over the course of follow-up.

The primary outcome of interest in this Cox regression model was the cessation medication they received. Other potential confounders were included in Cox regression model as well, which included: age, race, gender, region (midwest, northeast, south, west), BMI (normal, over-weight, or obese), payment type (government or non government insurance), specialty group (primary care, specialty care), had previous

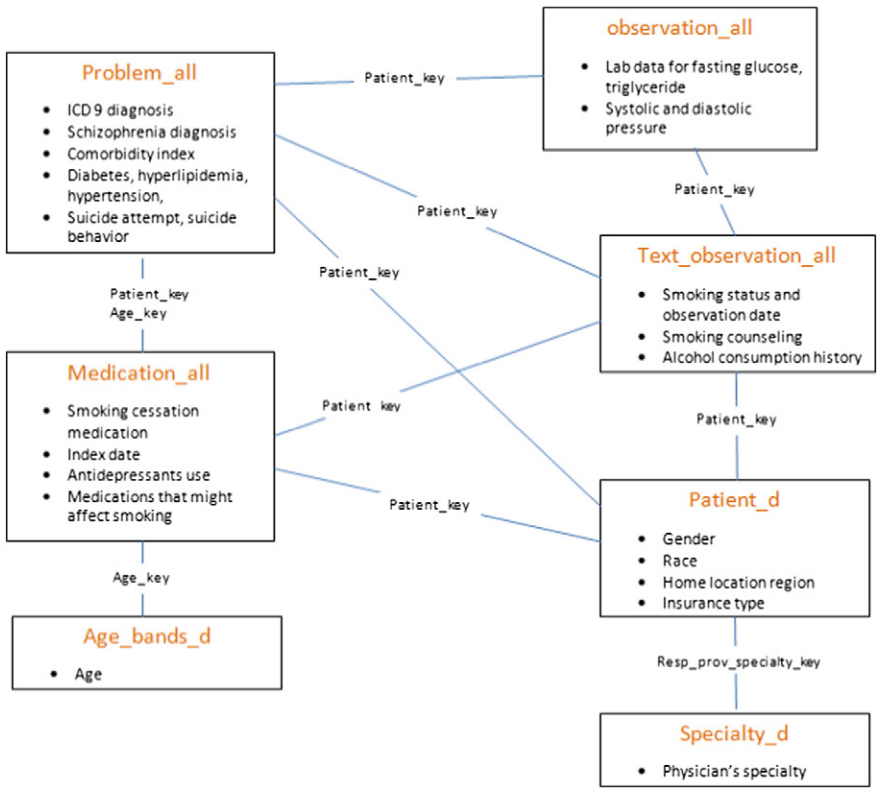

Fig. 1. Linkage between GE data files.

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