**Serious Psychological Distress and Risk of Mortality among US Adults: Potential Mediation**

**Introduction**

Many studies have reported reductions of excess mortality associated with mental illness or nonspecific serious psychological distress (SPD) by statistical adjustment of their findings to reflect the impact of other factors. These factors include unhealthy lifestyle factors (e.g., cigarette smoking, drinking alcoholic beverages), physical illness, and socioeconomic disadvantage that are known to be disproportionately more prevalent in this vulnerable subgroup and also cited as the major determinants of morbidity and mortality overall.

The increased morbidity and mortality among individuals with severe mental illness may be primarily due to a higher prevalence of modifiable risk factors. Mental depression leads to self-medication with increased cigarette smoking, and the adverse effect on long-term health can outweigh the apparent short-term relief from that illness. One study has estimated that and 60 percent of the excess mortality in this vulnerable population in the clinical setting is due to physical illness. Thus smoking and physical illness could be potential mediators in the relationship between mental illness and the risk of mortality. However, systematic analyses estimating the magnitude of reduction in the risk of mortality associated with mental illness due to adjustment of each of these factors by age group in the context of U.S. general population have been rare.

Women are more likely than men to be diagnosed with serious psychological distress or major depression. Previous studies have reported mixed results on gender differences in depression-related mortality: higher risks for men than women; and significant elevated mortality in men associated with past-year major depression but not women, only suggesting that men with major depression were more likely to die while women with major depression were more likely to be disabled. But, little is known about the cause-structure of death for possible gender differences in severe psychological distress or major depression-related mortality.

Understanding how current smokers and those who never smoked in their life time in different age-gender subgroups compare with respect to the excess risk attributable to mental illness is necessary to formulate effective policies and interventions to lessen some of the burden of premature death among U.S. adults. Accordingly, we examined the risk of all-cause death and cause-specific death, particularly external causes of injury (i.e., accidents, homicide, and suicide) and deaths attributable to smoking among smokers, over the follow-up period, in relation to past-month severe psychological distress or major depression by potential mediators including cigarette smoking and other co-occurring conditions in men and women aged 35 years or older, based upon sample adults’ self-reports in the National Health Interview Survey (NHIS).

**Data and Methods**

Data were used from the 1997-2010 NHIS Linked Mortality Files (LMF) [The public use versions of these files are expected to be released around March, 2014 – this sentence will be deleted]. We chose to use these particular years of data because to date the 1997-2010 NHIS are the only survey cohorts for which the Kessler-6 data are available to measure sample adults’ psychological distress levels and the mortality follow-up data are also linked. Of them, the 1999 NHIS is the only cohort for which the Composite Diagnostic Interview Short Form (CIDI-SF) data are available to measure major depression.

The study excluded respondents younger than age 35 at the time of interview to conform to previous analyses that examined the excess mortality caused from cigarette smoking. The key exposure variable was a Kessler-6 based psychological distress measure (score range: 0-24). An individual with a total score of ≥13 was considered having serious psychological distress (SPD). SPD has been shown to be associated with anxiety disorders and depression but does not identify a specific mental illness. Another key exposure variable was a CIDI-SF-based measure with questions used in the 1999 NHIS only (score range: 0-7). An individual was classified as having major depression if he/she endorsed questions with positives responses to three or more symptoms questions. Individuals who provided positive responses to fewer than three questions were defined as not having major depression. The potential mediator variables will include cigarette smoking status, presence/absence of chronic diseases, body mass index (BMI), and functional disability, which are already included in the data files. Several socio-demographic factors that have been shown in previous studies to influence the relationship between mental illness and mortality were considered for inclusion in this study. These factors included the following: age at interview in years (35 to 44, 45 to 64, 65 to 74, 75 or older); gender (male vs. female); education (less than high school, high school graduate/GED [general equivalency diploma]/some college, college graduate); race/ethnicity (white, not Hispanic or Latino; black or African American, not Hispanic or Latino; Hispanic or Latino; and other, which included non-Hispanic Asians, Pacific Islanders, and Native Americans); and marital status (currently married, separated or divorced, widowed, never married).

Because the public use files included the year and quarter instead of the exact dates of birth, interview and death (if died), survival times were measured by subtracting the year and quarter of death or censoring time from the year and quarter of interview. For a small number of cases, the survival time of 0 (if interview and death or censoring took place in the same quarter of the year) was coerced to 1. Using the *expand* command in Stata 11, we created a person-quarter-year analytic file to which each NHIS participant contributed as many discrete quarter-year (range: 1-39) as he/she had been followed-up. The attained age was initially constructed by setting its value the same as age at interview for the first person-quarter-year of follow-up and then cumulating it by quarter-year up to the last person-quarter-year of follow-up for each study participant. All person-level predictors were assigned to the respective person-quarter-year of follow-up. The age at death and the underlying cause-of-death category (if the person had died over the follow-up period), if relevant, were added to the very last person-year of observation. The 113-category underlying cause-of-death variable (based on ICD-10 codes) included in the NHIS-LMF was collapsed into leading/ cause of death categories.

All data preparation work was performed in SAS 9.3 and statistical analyses using Stata 13. An appropriate analysis weight was used to account for differential probabilities of selection, nonresponse, and noncoverage. The survey design variables were used to adjust for clustering and stratification in order to produce the correct standard errors or 95% confidence intervals (CIs) of the estimates. For all statistical tests, a p-value of <.05 was considered significant. We used the svy: -cloglog- in Stata to perform proportional hazards analyses of grouped survival data. To assess the impact of the adjustment for potential mediators, we compared the appropriate models, calculating the percentage reduction in the relative risk of mortality associated with SPD.