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Editorial

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Treatment and Risk of Death for Antidepressant Medication

Mahmoud M. Alseoudy*

Comprehensive assessments of potential mortality risks related to antidepressant medication (ADM) use are relatively rare, and to the extent that they exist, they typically specialize in suicide or self-harm, or single causes of mortality, like cardiac death. Most research on the efficacy of depression treatment employs randomized controlled trials (RCTs), which frequently include highly selected populations (typically excluding sick and older adults) receiving state-of-the-art care with close clinical follow-up over short time horizons. Although RCTs could also be the gold standard of depression treatment trials, they are doing not inform policy or practice on how world treatment influences depression or mortality outcomes at the population level. Large longitudinal studies that carefully address treatment selection biases can complement RCTs by providing useful and infrequently available information on how depression treatment may or might not affect longer-term outcomes like mortality.

The present study extends upon prior work on depression and mortality to assess the association between ADM use among patients with depression and risk of all-cause mortality compared to closely comparable patients not receiving ADMs during a large health system, employing several methods to deal with potential treatment selection biases also as controlling for multiple clinical and demographic factors. We hypothesized that in analyses that didn't fully address potential treatment selection biases, it's going to appear that ADMs are related to an increased risk of mortality (e.g., sicker patients take ADMs and also are more likely to die). However, we also hypothesized that in analyses that addressed potential selection biases, ADMs could also be related to a decreased risk of mortality, or no increased risk of mortality. Finally, although older ADMs are known to possess more side effects than newer ADMs or selective serotonin reuptake inhibitors (SSRIs), supported prior research we hypothesized that older ADMs would be related to lower mortality risks than newer ADMs or SSRIs.

Patient cohort

All Veterans older than 18 years with a depression diagnosis (International Classification of Diseases Ninth Revision codes: 293.83, 296.2, 296.3, 296.90, 296.99, 298.0, 300.4, 301.12, 309.0, 309.1, 311) recorded during financial year (FY) 2006 who received treatment during a VHA facility a minimum of once therein same year were included during this study. After identifying the earliest VA facility visit in FY2006 with a depression diagnosis (index date), patient clinical administrative data (including inpatient and outpatient diagnoses and health services utilization) were obtained for one year preceding and one year following the index date.

Dependent variable

The primary outcome, all-cause mortality, was assessed using National Death Index (NDI) data up to at least one year post-index date.

Key experimental variable

The analyses considered exposure in two ways: as time-fixed and binary (any ADM used versus not) or as time-varying exposure over the follow-up time. The first exposure variable was exposure to any ADM within the first 90 days following the index date in FY2006. To work out exposure during this 90-day period, every day was considered as either exposed to an ADM or not supported days of supply and date of fill. ADM fills that occurred during the 90 days before the index date were also included when assessing medication exposure during this period; for instance , if a patient received a 30-day fill fortnight before the index date, then the 16 days following the index date (i.e., 30 days dispensed minus 14 pre-index days) were considered as exposed. Thus a patient is often considered as exposed to ADM supported a prescription filled before index date if the availability remained beyond the index date. When accounting for exposure days as time-varying, we considered seven days or less of a niche between two consecutive fills as endless exposure, which is smaller gap than the 14-day gap previous researchers have wont to predict discontinuation.

Patient characteristics

We controlled for baseline socio-demographic, clinical, and utilization characteristics that would be related to patient mortality. Demographic characteristics included: age at index date (18–29, 30–39, 40–49, 50–59, 60–69, 70–79, ≥ 80), sex (female, male), and race (White, African American, other). Prior psychotherapy was defined supported having any psychotherapy (Current Procedural Terminology codes 90804–90815, 90845, 90847, 90853, 90857) in 90 days before the index date. Baseline utilization characteristics were defined supported administrative data during the 90 days before the index date and included: psychotherapy visits (0, ≥ 1), the numbers of outpatient visits excluding psychotherapy visits (0, 1, or ≥ 2), psychiatric hospitalizations (0, ≥ 1), non-psychiatric hospitalizations (0, ≥ 1).

For models requiring time-dependent covariates (e.g., MSMs), all exposure, clinical and utilization variables were updated for each 90-day interval during the year after the index date supported data during the year before , and including that 90-day interval (i.e., four quarters of data).

Data analyses

The primary analytic goal was to assess the relative hazard of death related to ADM use during a 1 year follow-up period after depression diagnosis (i.e., index date), and therefore the secondary goal was to match the mortality risks across the three different classes of ADMs. We first examined the distributions of all baseline variables and their relationships with ADM exposure, also like one-year mortality. Because the analyses are supported observational data,

***Corresponding author:** Mahmoud M. Alseoudy, Department of Anesthesia and Surgical Intensive Care, Mansoura University, Mansoura, Egypt, E-mail: drs31odymansora@mans.edu.eg

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ADM exposure isn't independent of baseline factors. Hence, for both the first and secondary objectives, we used three analytic approaches to deal with potential confounding and treatment indication biases: conventional Cox regression (Cox), propensity-based Cox regression (PS), and marginal structural models (MSM). Each approach has its own assumptions, and therefore the goal was to draw a careful conclusion across the various approaches.

Mortality comparison across three ADM classes

We first fit a Cox model using the complete cohort data and indicators for exposure to every of the three ADM classes during the primary 90 days, using no ADM use because the reference group, where an individual are often exposed to quite one class of ADMs. We also examined the distribution of patterns of exposure to different classes of ADMs during the primary 90 days, and supported these examinations, repeated the Cox model restricting the info to those patients exposed to one ADM class during the primary 90 days. Within the analysis of ADM class comparison supported single class exposed patients, the first exposure variables were two indicators, one for newer non-SSRI agents and one for older non-SSRI agents, with exposure to SSRIs because the reference group. For the comparison of three ADM classes during a PS model, a multinomial model for exposure within the first 90 days to 3 classes of ADMs was fit inconsiderately for parsimony. We then used a Cox regression model, inversely weighted by the estimated propensities, to estimate one-year hazard ratios related to older and with newer ADMs using SSRIs because the reference group. Additionally to propensity weighing, the Cox model was adjusted for a limited set of baseline covariates to regulate for his or her effects on mortality risk.

Author Affiliation

Department of Anesthesia and Surgical Intensive Care, Mansoura University, Mansoura, Egypt