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Cost-effectiveness and cost-utility of selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, and tricyclic antidepressants in depression with comorbid cardiovascular disease

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ABSTRACT

Objective: There is a lack of clarity in the literature regarding the cost-effectiveness and cost-utility of antidepressants for treating real-world patients. The impact of comorbid cardiovascular disease (CVD) on the economic evaluations of antidepressants remains to be determined.
Method: Adult patients prescribed with antidepressants for depression were identified from the National Health Insurance Research Database in Taiwan. A cost-effectiveness and cost-utility analysis was conducted comparing selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants (TCAs), and by the presence of comorbid CVD.
Results: In terms of treatment success rates, SSRIs were the most cost-effective option compared to TCAs and SNRIs as revealed in the incremental cost-effectiveness ratios. The cost-effectiveness acceptability curves further showed differential findings in the cost-utility results by the presence of comorbid CVD.
Conclusion: To improve treatment success rates and quality-adjusted life years, SSRIs can be considered the most cost-effective option. Future research is needed to further clarify the impacts of physical comorbidities and other associated factors on the cost-effectiveness and cost-utility of pharmacological treatments in patients with depression.

1. Introduction

Although depression is among the top-ranking global causes of disability (Vos et al., 2012), cardiovascular disease (CVD) represents the leading cause of premature death (Lozano et al., 2012). The health and economic burden of depression and CVD individually is great, but can be considerably pronounced when the two conditions occur simultaneously. Major depressive disorder (MDD) per se is associated with excess premature mortality due to cardiovascular-related conditions (Angst et al., 2002). For patients with coronary heart disease, depressive symptoms are an independent risk factor for cardiac events (Barth et al., 2004; van Melle et al., 2004). Research has suggested the existence of a potentially shared pathophysiology as well as modifiable risk factors in depression and CVD (McNamara et al., 2013). Aside from these close interrelationships, the choice of pharmacotherapy may be influenced because individual antidepressants have a wide range of cardiovascular effects (Taylor, 2008). It is also noted that factors associated with CVD may impact remission outcomes of depression (Albus et al., 2011; Denollet et al., 2010). Therefore, the presence of CVD potentially could influence choice of pharmacotherapy, costs and effectiveness outcomes in patients with depression.

The measure of outcomes for economic evaluations should ideally allow the comparison of treatments across a range of diseases and conditions, which would be very difficult if every disease area uses a different outcome measure, e.g., the aforementioned

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remission outcome in patients with depression. This has led to the development of generic outcome measure such as the quality-adjusted life-year (QALY). The QALY approach provides a single index that combines information both on the length and quality of life for cost-utility analyses. Depression has been shown to influence the health-related quality of life of cardiac patients most dramatically, even more than do left ventricular ejection fraction and ischemia (Ruo et al., 2003). Conversely, it is less clear how the presence of CVD impacts quality of life in patients with depression. People suffering from both depression and CVD exhibited greater deficits in health-related quality of life than when suffering from either disease alone (O'Neil et al., 2013). Besides, treating one condition could affect the other pre-existing condition, resulting in lower quality of life than would be expected because of the pre-existing condition on its own. In light of this, it would be intriguing to examine the unexplored impacts of comorbid CVD on quality of life in cost-utility analyses for patients with depression.

There are certain issues regarding the existing evidence on the cost-effectiveness and cost-utility across pharmacological treatments of depression. According to a systematic review (Pan et al., 2012), only a very limited number of such studies have been conducted in real-world settings (Hosák et al., 2000; Peveler et al., 2005; Serrano-Blanco et al., 2006a, 2006b, 2009); the cost-effectiveness and cost-utility are rarely reported simultaneously. Among the available real-world data, the cost-utility results comparing tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) are conflicting (Kendrick et al., 2006; Serrano-Blanco et al., 2009). Additionally, the impact of major comorbidities such as CVD remains unknown. Although economic evaluations are highly context-specific, no existing data are from Asian countries. Whether individual categories of antidepressants differ in the cost-effectiveness and cost-utility in Asian populations is yet to be determined.

From the perspectives of healthcare provider, i.e., Bureau of National Health Insurance in Taiwan, a cost-effectiveness and cost-utility analysis was conducted between individual antidepressants in the current study based on the National Health Insurance Research Database (NHIRD) records of the entire national assemblage of patients with depression in Taiwan. The specific objective was to compare the cost-effectiveness and cost-utility between antidepressant categories and to test whether and how the presence of CVD affects the economic evaluations of pharmacological treatments of depression.

2. Materials and methods

2.1. Data

Data were extracted from the NHIRD in Taiwan. The NHIRD uses the International Classification of Diseases, 9th Revision, Clinical Modification diagnoses. Subjects were first identified according to inclusion criteria (see below) and the index date was defined as the date on which the subject was first prescribed an antidepressant for treatment of depressive disorders in 2003. A 2½-year dataset containing all NHI healthcare information on each subject spanning the index date (one year preceding and 1½ years following) was then established.

2.2. Participants

Participants aged 18 or older meeting the following criteria were included:

(1) They had been prescribed at least one antidepressant of interest (SSRIs, serotonin norepinephrine reuptake inhibitors (SNRIs), and TCAs) for treatment of MDD or other depression in 2003.
(2) Data on each participant for a minimum of 12 months before the index date and 18 months after the index date were available.
(3) They had been prescribed at least three antidepressants in the first three months after the index date (non-attrition) or at least four prescriptions during the 18-month observation period (returning-attrition) (Pan et al., 2013b).

2.3. Definition of treatment outcome status

A proxy definition for remission, i.e., antidepressant cessation for at least six months (Sicras-Mainar et al., 2010; Byford et al., 2011), was modified and adopted in the current study. This database definition of remission has previously been examined for its validity with that assigned by clinical criteria (Sicras-Mainar et al., 2010). However, to prevent confusion from actual remission defined by clinical rating scales, a more descriptive term 'treatment-free status' was used instead of 'remission'. We further defined 'sustained treatment-free status' as 'treatment success', which required no re-start of antidepressant treatments (late recontacts) through the 18-months follow-up period (Pan et al., 2013b). This treatment-success status has been shown to be associated with cost savings in the second and third years after commencing antidepressant treatments (Pan et al., 2013c). Study participants were grouped according to three treatment outcomes:

(1) Sustained treatment-free status, defined as patients who had undergone antidepressant cessation for at least six months and had not restarted antidepressant use by the end of the observation period.
(2) Continuous treatment, defined as patients who had not undergone an antidepressant cessation for at least six months.
(3) Late recontact, defined as patients who had undergone an antidepressant cessation for at least six months and had restarted antidepressant use after the cessation of antidepressant use.

2.4. Observation period for treatment outcome

For each individual, the observation period started on the index date and continued for 18 months after the index date. The additional six months after the first 12 months was included to ensure adequate time to assess whether a treatment-free status had been achieved. The treatment-free period, that is, the cessation of the antidepressant treatment could begin at any point during the 12 months after the index date, but a participant must have remained free of antidepressants for a minimum of six months to fulfil the criterion. Thus, an 18-months observation period to achieve the treatment outcome was required.

2.5. Utility weights

Health state valuations (utilities) are an essential component of cost-utility analyses. In economic evaluations 'utilities' are often used to measure outcomes and are anchored by 0 and 1, where 0 indicates death and 1 indicates full health. In the current study, the baseline utility values were from a naturalistic longitudinal observational study with 447 patients recruited at 56 Swedish primary care centres (Sobocki et al., 2007). The inclusion criteria of that study were similar to the current analyses (patients older than 18 years who initiated an antidepressant therapy in clinical settings because of depression). A generic instrument for obtaining utility values, the EuroQol five-dimensions (EQ-5D) questionnaire, was completed at each visit by the patient in that study. In the current study, the baseline utility value for patients with MDD was set at 0.42 assuming a heterogeneous group of MDD patients comprising