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COMPARATIVE EFFICACY, EFFECTIVENESS AND HARMS OF SECOND-GENERATION ANTIDEPRESSANTS IN THE PHARMACOLOGIC TREATMENT OF ADULT DEPRESSION

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**Introduction:** Second-generation antidepressants dominate the medical management of major depressive disorder (MDD). Two published comparative effectiveness reviews (CER) provide conflicting evidence about the comparative efficacy and safety of second-generation antidepressants for treating MDD.

**Objectives:** To compare the benefits and harms of bupropion, citalopram, desvenlafaxine, duloxetine, escitalopram, fluoxetine, fluvoxamine, mirtazapine, nefazodone, paroxetine, sertraline, trazodone, and venlafaxine for the treatment of MDD in adults.

**Methods:** We updated a CER published in 2007 by the Agency for Healthcare Research and Quality searching MEDLINE, Embase, The Cochrane Library, and the International Pharmaceutical Abstracts up to May 2010. Two persons independently reviewed the literature, abstracted data, and rated the risk of bias. If data were sufficient, we conducted meta-analyses of head-to-head trials of the relative benefit of response to treatment. In addition, we conducted mixed treatment comparisons to derive indirect estimates of the comparative efficacy among all second-generation antidepressants.

**Results:** Overall, no substantial differences in efficacy could be detected among second-generation antidepressants. Statistically significant differences in response rates between some compared drugs are small and likely not clinically relevant. Differences exist in the incidence of specific adverse events and the onset of action. Venlafaxine leads to higher rates of nausea and vomiting, sertraline to higher rates of diarrhea, and mirtazapine to higher rates of weight gain than comparator drugs. Bupropion caused lower rates of sexual dysfunction than other antidepressants.

**Conclusions:** Our findings indicate that the existing evidence does not warrant the choice of one second-generation antidepressant over another based on greater efficacy and effectiveness.