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ADVERSE EVENTS ASSOCIATED WITH ANTIDEPRESSANTS: A SYSTEMATIC LITERATURE REVIEW AND NETWORK META-ANALYSIS.

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Abstract:

OBJECTIVES: Risks of adverse events can be a key factor influencing choice of antidepressant. The aim of this study was to identify the literature on key adverse events and synthesise this via network meta analyses (NMA).

METHODS: A systematic literature review was undertaken to identify randomised controlled trials of commonly prescribed antidepressants reporting on the adverse events of sexual dysfunction, weight change, insomnia, anxiety, and anhedonia. The antidepressants were: duloxetine, escitalopram, fluoxetine, paroxetine, sertraline, trazodone, venlafaxine, and vortioxetine. Inclusion was restricted to placebo-controlled trials in adults with major depressive disorder. Immediate release formulations were excluded. A random-effects NMA was used to estimate odds ratios (OR) for anxiety and insomnia.

RESULTS: A total of 610 articles were identified from searches and existing reviews, resulting in 47 included trials. The most common follow-up was eight weeks ($n = 30$), with durations ranging from six to 12 weeks. The most frequently reported adverse event was insomnia ($n = 36$); no studies reported data for anhedonia. From the NMA, anxiety was lowest with trazadone (OR 0.12, 95% credible interval 0.003 to 1.98), and highest with paroxetine (OR 2.53, 0.84 to 10.86). For insomnia, the only treatment with a lower risk than placebo was trazadone (OR 0.66, 0.31 to 1.37). There was variability in the reporting of weight changes and sexual dysfunction outcomes, so current results are not synthesised. Duloxetine typically had the largest weight decrease, whilst amongst studies reporting overall rates of sexual dysfunction the largest rates were generally observed for paroxetine and duloxetine.

CONCLUSION: Rates of key adverse events vary by antidepressant. Trazadone had the lowest rates for both anxiety and insomnia, whilst also demonstrating similar outcomes to placebo for weight change and sexual dysfunction. Some of the highest adverse events were observed for paroxetine and duloxetine. These results can inform treatment choices.