Long-term efficacy and safety of treatment with stimulants and atomoxetine in adult ADHD: A review of controlled and naturalistic studies.

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Attention-deficit/hyperactivity disorder (ADHD) is a common disorder of childhood that often persists into adulthood. Although stimulant medications are recommended as the first-line treatment for ADHD because of their documented short-term effects in children and adults, less is known about their effects on long-term outcome in adults. Here we review the long-term efficacy and safety of the stimulant drugs methylphenidate and amphetamine, as well as the related compound atomoxetine. We performed a systematic review to identify direct and indirect effects of stimulant therapy on long-term outcome in adults. Five randomized controlled trials (RCTs), and 10 open-label extension studies of initial short-term RCTs, with total follow-up of at least 24weeks, were identified. All these RCTs found that medication was significantly more efficacious than placebo in treating ADHD in adults, and the extension studies showed that this favorable effect of medication was maintained during the open-label follow-up period. However, since the maximum duration of these pharmacological trials was 4years, we also reviewed 18 defined naturalistic longitudinal and cross-sectional studies, to provide more information about longer term functional outcomes, side effects and complications. These observational studies also showed positive correlations between early recognition of the disorder, stimulant treatment during childhood and favorable long-term outcome in adult ADHD patients. In conclusion, stimulant therapy of ADHD has long-term beneficial effects and is well tolerated. However, more longitudinal studies of long duration should be performed. In addition, the ethical issues involved in performing double blind RCTs of many years duration should be further explored.