



- Title** Oral Naltrexone as a Treatment for Relapse Prevention in Formerly Opioid-Dependent Drug Users: A Systematic Review and Economic Evaluation
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Aim

To investigate the clinical and cost effectiveness of naltrexone for relapse prevention in detoxified, formerly opioid-dependent, individuals compared to any strategy that uses or does not use naltrexone, including treatment with placebo, other pharmacological treatments, psychosocial interventions, or no treatment.

Conclusions and results

Methodological quality was poor to moderate in the 26 randomized controlled trials (RCTs) that met the inclusion criteria. The results suggest that naltrexone as maintenance therapy may be better than placebo in treatment retention (not statistically significant). A meta-analysis of 7 RCTs gave the relative risk (RR) of loss of retention in treatment in the naltrexone arm as 0.94. The pooled hazard ratio (HR) reported in 5 of the RCTs for treatment retention data followed up to 35 weeks was calculated as 0.90 in favor of naltrexone (not statistically significant). The risk of drug abuse in naltrexone vs placebo, with or without psychological support in both arms, gave a pooled RR of 0.72 in favor of naltrexone (statistically significant). The pooled HR from 3 RCTs for opioid relapse-free rates was significantly different from placebo in favor of naltrexone 0.53, but fell off over time. The RR of reimprisonment while on naltrexone therapy showed results favoring naltrexone in the combined 2 studies of parolees or people on probation (small number of participants). Adverse events data showed no significant difference between naltrexone and placebo. The quality of the 9 RCTs of interventions designed to increase retention with naltrexone was poor to moderate, but all 3 modalities of enhanced care showed some evidence of effectiveness. All contingency management programs used incentive vouchers; mean duration of treatment retention was 7.4 weeks for the contingency management intervention vs 2.3 to 5.6 weeks for naltrexone treatment alone. Patients stayed on naltrexone 84 to 103 days (mean) with additional psychosocial therapy vs 43 to 64 days for the control group. In trials with added pharmacological agents,

the RRs of stopping treatment were 1.63 at 6 months and 1.31 at 12 months (favoring naltrexone plus fluoxetine) and was statistically significant at 6 months, but not at 12 months. A meta-analysis of the RR of stopping treatment at week 12 included 6 of the 9 studies. The pooled RR of stopping treatment was 0.81. The intervention groups had 19% fewer patients who stopped treatment compared with the control group (few studies of poor quality). No economic evaluations were identified. The point estimate for the cost effectiveness of naltrexone was GBP 42 500 per QALY. In a sensitivity analysis the incremental cost-effectiveness ratio varied between GBP 34 600 and GBP 42 500 per QALY gained.

Recommendations

Following successful withdrawal from opioids, naltrexone may be administered on a chronic basis to block future effects of opioids. Naltrexone appears to have limited benefit in helping formerly opioid-dependent individuals remain abstinent, but evidence quality is relatively poor and heterogeneous. Oral naltrexone is used infrequently in UK practice, which this review suggests is appropriate.

Methods

Major electronic databases were searched from inception to September 2005. Selected studies were screened and quality assessed. Meta-analyses were carried out as appropriate. A decision-analytic model using Monte Carlo simulation was developed that compared naltrexone as an adjunctive therapy to no naltrexone. It assumed compliance rates that were not enhanced by contingent management rewards. Utility values could not be identified from the literature, but were obtained from the Value of Health Panel.

Further research/reviews required

More information about the quality of life of people who use illicit opioids is needed to inform policy questions about the cost effectiveness of different programs and interventions.