OBJECTIVE: This meta-analysis aimed to compare the relative clinical benefit of olanzapine, a widely used first-line drug for the treatment of schizophrenia, with two new atypical antipsychotics, ziprasidone and aripiprazole, using an indirect common comparator approach.

METHODS: No comparative trials had been completed of olanzapine versus ziprasidone or aripiprazole at the time of the analysis, and so a common comparator approach via haloperidol, a benchmark typical antipsychotic, was employed. This method formally compares the absolute risk difference for the various atypicals compared with the common reference drug, haloperidol. All double-blind, randomised, controlled trials of olanzapine, ziprasidone or aripiprazole versus haloperidol were included in the meta-analysis. Random-effects and fixed-effects methods were employed and standard tests were used to determine heterogeneity. Studies were separated by duration into short-term trials (12 weeks or less) and medium- to long-term trials (>12 weeks).

RESULTS: The results of the medium- to longer-term comparison of olanzapine with ziprasidone showed that a significantly smaller proportion of patients treated with olanzapine required anticholinergic medication ($p = 0.019$) and fewer olanzapine-treated patients discontinued treatment due to any reason ($p = 0.034$), compared with those receiving ziprasidone. The short-term comparison of olanzapine with aripiprazole showed that significantly fewer olanzapine-treated patients required anticholinergic medication, compared with the aripiprazole-treated patients ($p = 0.006$). In the longer-term, a statistically significant difference in proportion of responders was revealed, favouring olanzapine ($p = 0.024$).

CONCLUSIONS: This analysis suggests that olanzapine is safer, as measured by less anticholinergic use, and is associated with fewer dropouts than ziprasidone in the medium- to longer-term. It is also suggested that olanzapine is safer, as measured by less anticholinergic use, than aripiprazole in the short-term and more efficacious in the longer-term. Despite a lack of head-to-head trials, the common comparator analysis allows indicative judgments to be made about the relative safety and efficacy of new therapies.