Aripiprazole for schizophrenia: a Cochrane review

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BACKGROUND
Aripiprazole is an atypical antipsychotic that is reported to be effective in the treatment of all phases of schizophrenia and to have cognitive-enhancing effects.

AIMS
We report a systematic review of randomised controlled trials of aripiprazole for people with schizophrenia and schizophrenia-like psychoses.

METHODS
• A search was conducted in August 2004\textsuperscript{1}.
• Data were collected by electronic database and manual searches and by direct contact.
• We reliably selected randomised clinical trials comparing aripiprazole at any dose with any other antipsychotics or placebo.
• We analyzed data using RevMan software and calculated random effects relative risk (RR) and its 95% confidence interval (CI) by intention-to-treat.

RESULTS
We identified ten relevant randomised studies.

Most only reported data up to 12 weeks and were undertaken in North America or Europe. Despite 4125 people participating in ten randomised studies, we were unable to extract any usable data on death, service outcomes, general functioning, behaviour, engagement with services, satisfaction with treatment; economic outcomes or cognitive functioning. Study attrition was very large and, overall, data reporting poor.

Two studies reported \textbf{8 deaths} but did not supply data by group of allocation.\textsuperscript{2} Causes of these deaths include suicide. People randomised in these two trials were suffering an acute relapse of schizophrenia. Despite possible mitigating factors this finding has not been widely disseminated.

\textit{Even if the mortality of people with schizophrenia is two to three times that of the general population the age-standardised death rate in the two randomised studies we can be sure about exceeds even that pessimistic estimate by 400-500\%}.\textsuperscript{3}

Also, in the FDA site,\textsuperscript{2} an additional 53 deaths are reported in those known to be allocated to aripiprazole in various trials. However, we cannot be sure these deaths occurred in trials relevant to this review.

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\textbf{Compared with placebo} aripiprazole significantly decreased relapse in both the short and medium term (n=300, 1 RCT, RR 0.66 CI 0.53 to 0.81, NNT 5 CI 4 to 8). It also produced better compliance with study protocol (n=1348, 5 RCTs, RR 0.66 CI 0.49 to 0.88, NNT 15 CI 10 to 41). Aripiprazole may decrease prolactin levels below that expected from placebo (n=305, 1 RCT, RR 0.32 CI 0.13 to 0.81, NNT 14 CI 11 to 50).

\textbf{Compared with typical antipsychotics} there were no significant benefits for aripiprazole with regards to global state (see Figure), mental state, quality of life or leaving the study early. Both groups reported similar rates of adverse effects, but akathisia (n=956, 3 RCTs, RR 0.31 CI 0.17 to 0.57, NNT 3 CI 2 to 5) and also the need for antiparkinson drugs, at least compared with 10-20mg/day haloperidol, (n=1854, 4 RCTs, RR 0.45 CI 0.33 to 0.60, NNT 4 CI 3 to 5) were reduced. Aripiprazole did however cause more insomnia than perphenazine (n=300, 1 RCT, RR 2.23 CI 1.57 to 3.18, NNH 4 CI 3 to 9).

\textbf{Compared with atypical antipsychotics} aripiprazole was no better or worse on outcomes of global state and leaving the study early. The rates of adverse effects were also similar, with the exception of less elevation of prolactin (n=301, 1 RCT, RR 0.04 CI 0.02 to 0.08, NNT 2) and less prolongation of the average QTc (30mg/day) (n=200, 1 RCT, WMD -10.0, CI -16.99 to -3.01) compared with risperidone.

CONCLUSIONS
Clinicians and consumers should be better informed of both the positive and negative effects of this drug.

Aripiprazole’s real effects are unclear, because of the needs of both the regulatory authorities and industry.

Large, long, well designed, conducted and reported pragmatic randomised controlled trials should be part of the regulatory authority’s requirements.

REFERENCES
\textsuperscript{3}. Carson et al = 97/201, Carson