
Marc Krause*, MA; Yikang Zhu*, Mmed; Maximilian Huhm1, MD; Johannes Schneider-Thoma1, MD; Irene Bighelli2, PhD; Anna Chaimani3, PhD; Stefan Leucht1, MD
1. Klinik und Poliklinik für Psychiatrie und Psychotherapie, Klinikum rechts der Isar, TU München, Ismaningerstr 22, 81675 München, Germany
2. Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, South Wan Ping Road 600, 200030 Shanghai, China
3. Institute of Social and Preventive Medicine (ISPM), Bern University

Objective
To integrate all the randomized evidence from the available antipsychotics used for schizophrenic children and adolescents by performing a network and pairwise meta-analysis.

Methods
DATA SOURCES: MEDLINE, EMBASE, PsycINFO, Cochrane Library, PubMed, Biosis, and ClinicalTrials.gov were searched up to Jul 31, 2017.

STUDY SELECTION: At least 2 independent reviewers selected published and unpublished single- and double-blind RCTs children and adolescents with schizophrenia (any study-defined criterion) that compared any antipsychotic (at any dose and in any oral form of administration) with another antipsychotic or placebo.

DATA EXTRACTION AND SYNTHESIS: At least two independent reviewers extracted all data and assessed the quality of all included trials with the Cochrane Collaboration’s risk-of-bias tool. Data were pooled in a frequentist setting.

STATISTICAL ANALYSIS: We performed a random effects pairwise meta-analyses and a NMA in a frequentist framework using Stata 14. For continuous outcomes, the effect sizes were calculated as hedges g standardized mean differences (SMDs). For binary outcomes, the effect sizes were calculated as log odds ratios (log ORs).

RESULTS
Twenty-eight unique open and blinded RCTs with 3003 unique participants (58% men; mean age 14.41 years), published from 1967 to March 2017 were identified through the literature search.

✓ Clozapine most efficacious drug, analysed
✓ Most drugs more efficacious vs placebo
✓ Insufficient efficacy for Hal, Triflu, Lox, Zip

LIMITATIONS:
✓ Gap of evidence for most side effects
✓ Just few studies for most comparisons
✓ Some NMA results based on indirect evidence

RESEARCH IN CONTEXT:
✓ Key findings similar to adult schizophrenics

Figure 1: Network plot of eligible comparisons for overall change in symptoms

Figure 2: Risk of bias summary

Figure 3: NMA results versus placebo expressed as SMD’s (hedges g)

A = overall symptoms, B = weight gain, C = prolactin increase
Ari = aripiprazole, Ase = asenapine, Cloz = clozapin, Fluph = fluphenazin, Hal = haloperidol, Lox = loxapine, Fluph = fluphenazine, Hal = haloperidol, Lox = loxapine, Mol = molindone, Ola = olanzapine, Pali = paliperidone, Quet =quetiapine, Ris = risperidone, Trifu = trifluperazine, Zip = ziprasidone
A negative value means a higher reduction of symptoms, higher weight gain or higher prolactin increase for the drug compared to placebo.