Numerous studies in different countries throughout the world have shown that 30-60% of schizophrenia patients, when treated with antipsychotic drugs, receive two or more antipsychotics simultaneously.

Reasons for antipsychotic polypharmacy are not often well described, they might be insufficient efficacy (was the maximal tolerable dosage given?), tolerability problems (severe or transient, treatable by other drugs?) or an “unfinished switching procedure”: Cross-tapering from antipsychotic A to antipsychotic B is stopped halfway at a reduced dosage of A and a sub-therapeutic dosage of B, because this combination seems to work. However, it is not known whether B alone would be better.

Most often, antipsychotics with different receptor binding and side effect profiles are combined, although scientific evidence supporting the common practice is rather limited. Most controlled studies did not reveal an advantage of the combination versus monotherapy. Particularly for clozapine, where anecdotal reports and open trials indicated the usefulness of a combination with amisulpride, aripiprazole or risperidone, double-blind trials were mostly negative. However, in individual patients, hard or impossible to define, well-reflected combinations might be justified.

The few controlled studies and the resulting suggestions for everyday practice are presented to answer the following questions: When (after how many weeks of monotherapy) is a combination justified? Are there any criteria to decide switching the antipsychotic versus combining antipsychotics? Which combination(s) of antipsychotics might be useful?