REVIEW ARTICLE

Antipsychotic switching in schizoaffective disorder: A systematic review

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Abstract

Objectives. To systematically review the evidence about the switching of antipsychotics in SZA in acute and maintenance treatment. Methods. A systematic review following the PRISMA statement identifying studies specifically conducted on, or including, SZA patients. Results. One analysis considered uniquely a SZA population, 13 more studies including an adequate SZA subsample were considered. Most of the studies were aimed at switching antipsychotic treatments to improve tolerability issues. Despite the absolute lack of trials specifically conducted on SZA populations, we found limited evidence on the use of aripiprazole, lurasidone, and, to a lesser extent, risperidone and ziprasidone as possible agents to substitute previous treatments whereas efficacy or, more frequently, tolerability issues arise. Evidence supports also the switch to risperidone long-acting injectable when the adherence to oral treatment may be a concern. Conclusions. Antipsychotic switching in SZA is a neglected topic that would need better profiling. Clinicians should keep in mind the receptor binding characteristics of drugs in order to optimize transitions. Evidence supports the switch to aripiprazole and lurasidone, less strongly to risperidone and ziprasidone. The switch to risperidone long-acting injectable is supported, especially in patients with limited treatment adherence to oral therapy.

Key words: schizoaffective disorder, switching strategy, antipsychotics, systematic review, PRISMA statement

Introduction

Schizoaffective disorder (SZA) consists of the concurrent presentation of symptoms of schizophrenia and affective disorders (APA 2013). It may account for up to one-quarter of admissions to acute units (Kent et al. 1995), thus representing a condition that needs a careful therapeutic strategy to control its pleomorphic presentations. Considerable advances in clinical, translational and therapeutic research on psychiatric disorders have been made, but SZA pays a documented delay in specifically aimed studies (Murru et al. 2012), with obvious therapeutic consequences.

Randomized controlled trials conducted on SZA samples are also scarce (Murru et al. 2011a), and most of the evidence consists of sub-analyses coming from schizophrenia trials (Cascade et al. 2009). Given the difficulty to establish a syndrome-based treatment plan, clinicians usually focus on symptoms, managing both psychotic and affective dimensions with complex therapies (Levinson et al. 1999) based on the combination of antipsychotics and mood stabilizers (Viesta 2010). Sometimes polypharmacy involves the use of different antipsychotics (Procyzhyn et al. 2010). This has been reported to bring forth the risk of useless prescriptions and
overtreatment in bipolar conditions (Murru et al. 2011b), but could also involve schizoaffective bipolar conditions.

Most clinical guidelines, both for schizophrenia (Hasan et al. 2013) and bipolar disorder (Grunze et al. 2013) suggest to wait and eventually optimize current treatment before considering the possibility of switching to a different antipsychotic. Nonetheless, achieving optimal treatment in chronic psychiatric disorders often implies switching between different medications, generally to manage either a lack of efficacy or a lack of tolerability (Buckley and Correll 2008). Drug selection, dosing and dose equivalence, management of inadequate response, adherence problems, and relapses are associated to the clinical need of a change in medication. Many strategies of switching antipsychotic medication have been proposed, but they can be resumed into four main strategies (McEvoy et al. 1999):

- **Abrupt switching**: discontinuing the previous antipsychotic immediately and initiating the new antipsychotic at full dosage (Figure 1a).
- **Tapering (overlapping and discontinuing)**: gradually initiating the new antipsychotic; once an effective dosage of the new antipsychotic is reached, previous antipsychotic is gradually discontinued (Figure 1b).
- **Cross-tapering**: gradual increase in dosage of the new antipsychotic while, at the same time, gradually discontinuing the previous antipsychotic (Figure 1c).
- **Plateau cross-tapering**: gradual increase in dosage of the new antipsychotic and discontinuing the previous antipsychotic after the new one has reached customary dosages (Figure 1d).

Consistent studies have been conducted on the switch of antipsychotic medication in schizophrenia (Correll 2010a; Bernardo et al. 2011), and in bipolar disorder (Grande et al. 2013), whilst research specifically conducted on SZA populations is lacking.

The need for treatment research on SZA may seem somewhat limited as most of the evidence is shared with schizophrenia. Nonetheless, three considerations should be made. First, DSM-5 (APA 2013) proposes stricter affective criteria, thus shifting SZA towards bipolar spectrum. Efficacy and tolerability profiles of the drugs may vary across these conditions with a need for different doses and for differentiated prophylaxis in preventing either psychotic/manic or depressive symptoms. This can be easily done in BD (Popovic et al. 2012), but there is need to understand where SZA patients exactly stand. Second, the lack of evidence on effective treatments in SZA is an actual risk for inappropriate prescription in this population, so that an impulse in research should be given, rather than silenced. Third, diagnosis of SZA benefits from a greatly improved reliability in DSM-5 (Freedman et al. 2013), and hopefully this may represent a first step to a better categorization, understanding and management of this clinical entity.

Figure 1. Strategies for switching antipsychotic medication.
The objective of the present review is to critically summarize the best evidence-based approaches to switching antipsychotic medications in studies aimed at SZA, compared to either placebo or active comparators. According to the results of the review, treatment strategies will be proposed.

Methods
The present review has been conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement (Moher et al. 2009).

Literature search
A systematic search was performed using MEDLINE/PubMed/Index Medicus, Cochrane Library, considering a time period ending on 31 July 2014. A cross-check between references obtained was done. A further search was performed in the site www.clinicaltrials.gov to check literature results and to get information on eventually started, ongoing, or concluded studies on SZA yet to be published.

The authors searched for randomized controlled trials, as well as open studies and systematic reviews on the topic, as follows.

MEDLINE/Pubmed/Index Medicus: to find studies with SZA patients included in the samples, potentially leading to published pooled analyses, authors used the keywords schizoaffective AND (switch OR switching OR change OR substitution OR shift) AND (antipsychotic* OR amisulpride OR aripiprazole OR asenapine OR chlorpromazine OR clozapine OR fluphenazine OR haloperidol OR lurasidone OR olanzapine OR paliperidone OR perphenazine ORquetiapine OR risperidone OR thioridazine OR ziprasidone).

To find standalone trials the specifier “[title]” was first used following the keywords “schizoaffective”, but as in many studies SZA patients have historically been included in wider populations, the search was repeated without the title specifier.

Cochrane Library and EMBASE: keywords were schizoaffective disorder AND (switch OR switching) AND (antipsychotic OR antipsychotics)

Crosscheck with CLINICALTRIALS. Keywords were schizoaffective disorder. Study indication specifiers: (schizoaffective disorder OR schizophrenia) AND (switch OR switching) AND (antipsychotic OR antipsychotics).

Study selection
The first step was to decide, on the basis of the abstract or full text, whether the article was a study on switching antipsychotic medication concerning a pure SZA sample or not. Data were classified into three groups: (1) data of interest, (2) duplicated data, and (3) data of no interest, according to the previously described criteria. After first exclusion, full studies were read and examined. Due to the paucity of studies specifically aimed at SZA samples, we decided to include for evaluation studies with mixed samples including schizoaffective patients. Number of included SZA patients should be clearly stated and of at least 30 individuals. Each citation was also reviewed to identify further possible studies of interest.

Data collection process and items
Studies should report details on design, sample description, inclusion/exclusion criteria, subset of SZA patients included, clear switching methods, clear outcome definitions and measures, and adverse events in order to be included in the present review.

Results

Systematic search results
The flow-chart of the studies considered and finally selected is presented in Figure 2.

The search first returned 1411 papers. A proportion of them were excluded because duplicated or not inherent results, so that 595 underwent title/abstract examination. Of them, 528 were excluded because representing opinions, case reports, and reviews.

A total of 67 studies were deemed eligible for complete evaluation. Among them, seven are still ongoing, one was suspended, four do not grant access to data, two do not specify inclusion diagnostic criteria, two do not specify switching criteria, 18 do not specify number of included SZA and 10 included a number of SZA patients inferior to 30.

The final selection for the present review includes 14 studies.

- Apart from one analysis (Mohl et al. 2005), no study was specifically aimed at switching antipsychotics in SZA populations.
- There were 13 studies including SZA populations, fulfilling inclusion criteria and included for review: Alptekin et al. 2009; Barak and Aizenberg 2010; Casey et al. 2003; Citrome et al. 2013; Gaebel et al.
switched with a specified cross-taper protocol depending on the frequency of injection. Total PANSS and all three subscales were significantly reduced from baseline to week 4 \((P < 0.001)\), with further improvements until endpoint. A total of 163 patients (66%) experienced a treatment-emergent adverse event (AE) during the 6-month treatment period; 43 patients (17%) experienced a treatment-emergent serious AE, mostly related to sexual function and hormones during the study.

The oldest study considered (Casey et al. 2003) is a randomized, parallel group 8-week open-label study assessing the effectiveness of a switch to a fixed dose of 30 mg/day of aripiprazole (ARP) from several first- and second-generation antipsychotics with abrupt, tapered and cross-tapered switching. No significant differences across the different switch strategies were observed. This is the only study in the present review that included separately unipolar \((n = 46)\) and bipolar \((n = 55)\) SZA out of 311 patients, although no separate results were presented. ARP proved good efficacy with the scales used (PANSS, CGI-I, CGI-S) and well tolerated (with scales SAS, BAS, AIMS), presenting a significant decrease in prolactin levels. Metabolic aspects are later discussed in Barak and Aizenberg’s meta-analysis (2010).

Content results

In all the included studies, DSM-IV criteria for SZA were used (APA 1994). Aside from one analysis purely conducted on a SZA sample of 249 patients (Mohl et al. 2005), a total of 690 SZA patients was assessed in wider, mixed schizophrenia samples (2938 total patients). No subsets of results for SZA patients were presented in any of the included studies.

An analysis (Mohl et al. 2005) of a non-randomized, single-arm, open-label trial, studied a sample of 249 SZA patients switched from different antipsychotics, either oral or depot, to a flexible regimen of risperidone long-acting injectable (RLAI) without an oral risperidone (RSP) run-in. Switching method from oral antipsychotic was abrupt, considering RLAI’s peculiar pharmacokinetics (i.e., abrupt interruption at day 21 from first injection), whilst depot treatments were

Included studies are presented in Table I.
Table I. Studies included and their designs.

<table>
<thead>
<tr>
<th>References</th>
<th>Study design details</th>
<th>Study characteristics</th>
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</thead>
<tbody>
<tr>
<td>1 Alptekin</td>
<td>Open-label, non-randomized, baseline-controlled, single treatment, flexible-dose</td>
<td>Study design: Duration 12 weeks SAD/TOT sample 45/287 Objective/Primary outcomes Effectiveness of switch to ZIP/Changes from BPRS Other efficacy outcomes Changes in CGI-S, CGI-I, PANSS, MADRS, GAF, DAI Other tolerability outcomes Changes in: m-SAS, BAS, AIMS, physical measures, ECG Inclusion criteria Age 18–65, Sch+ or SAD, CGI 1–4 for lack of efficacy, CGI 1–2 for side effects</td>
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<tr>
<td>2 Barak and Aizenberg</td>
<td>Metaanalysis of acute and maintenance trials on ARP Range: 8 to 56 weeks 140/786 Weight change/main change from baseline weight Other efficacy outcomes Other tolerability outcomes Inclusion criteria Trials with Sch+ or SAD patients treated with any antipsychotic and switched to aripiprazole monotherapy in acute-phase or maintenance treatment</td>
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<tr>
<td>3 Casey</td>
<td>Randomized, open-label, parallel-group</td>
<td>Study design: Duration 8 weeks SAD/TOT sample 55/311 Bipolar type 55/311 Unipolar type 46/311 Objective/Primary outcomes The relative efficacy, safety and tolerability of 3 strategies for switching stable outpatients from prior AP monotherapy to ARP/PANSS General and scubscales, CGI-I, CGI-S, SAS, BAS, AIMS; adverse effects registration Other efficacy outcomes Other tolerability outcomes Inclusion criteria 18–65 years, DSM-IV Sch+ or SAD, chronic and stable in terms of their disease condition, as defined by taking a stabilized dose of a single oral antipsychotic for at least 1 month prior to study entry. There must have been &quot;an adequate clinical reason for the patient to try a new medication&quot; other than current therapy. Not hospitalized for an acute episode for at least 2 months. Age &gt; 18, Sch+ or SAD, at least a partial response to, and were stable on, a first-line antipsychotic at a consistent dose. Clinically significant efficacy or tolerability concerns to justify switching, having taken part in the 6 weeks acute study (Continued)</td>
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<td>4 Citrome</td>
<td>Multicenter, open-label, flexible-dose, extension</td>
<td>Study design: Duration 6 months SAD/TOT sample 58/149 Objective/Primary outcomes To evaluate the long-term safety and tolerability of lurasidone/proportion of patients with adverse events (AEs), serious AEs (SAEs), or who discontinued due to AEs Other efficacy outcomes Mean change from both core and extension study baselines in the PANSS total scores, CGI-S scores, and CDSS scores Other tolerability outcomes Mean change from both core and extension study baselines in weight, lipids, and glycemic control, SAS, BARS, AIMS Inclusion criteria Age &gt; 18, Sch+ or SAD, at least a partial response to, and were stable on, a first-line antipsychotic at a consistent dose. Clinically significant efficacy or tolerability concerns to justify switching, having taken part in the 6 weeks acute study</td>
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<td>References</td>
<td>Study design</td>
<td>Duration</td>
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<tr>
<td>5 Gaebel (2010)</td>
<td>Multicenter, open-label, randomized, active-control, long-term treatment with RLAI vs oral quetiapine</td>
<td>2 years</td>
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<tr>
<td>6 Ganguli (2008)</td>
<td>Randomized, open-label, rater-blinded study</td>
<td>6 weeks</td>
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<tr>
<td>7 Karayal (2011)</td>
<td>Open-label, flexible-dose, multicenter study, with a 16-week follow-up</td>
<td>16 + 16 weeks</td>
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<tr>
<td>8 Kim (2009)</td>
<td>Prospective, randomized, open-label, multicenter trial</td>
<td>12 weeks</td>
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### Table I. (Continued)

<table>
<thead>
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<th>References</th>
<th>Study design</th>
<th>Duration</th>
<th>SAD/TOT sample</th>
<th>Objective/Primary outcomes</th>
<th>Other efficacy outcomes</th>
<th>Other tolerability outcomes</th>
<th>Inclusion criteria</th>
</tr>
</thead>
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<tr>
<td>9 Lee (2010)</td>
<td>Randomized, open-label, multicenter study</td>
<td>14 weeks extension</td>
<td>42/166</td>
<td>To evaluate whether the previously published results of a 12-week study on the maintenance effectiveness and tolerability of ARP would be maintained up to 26 weeks/CGI-I</td>
<td>PANSS</td>
<td>UKU</td>
<td>1) Age: ≥ 18 years and ≤ 65 years; 2) Sch+ or SAD; 3) symptomatically stable on a constant dose of AP for at least 1 month; and 4) non-admission to a hospital for at least 3 months prior to the study</td>
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<td>10 McEvoy (2013)</td>
<td>Multicenter, randomized, open-label, parallel-group study</td>
<td>6 weeks</td>
<td>89/240</td>
<td>Effectiveness of switching to LUR/time to treatment failure (criteria given)</td>
<td>Time to discontinuation for any reason (all-cause discontinuation) Change in PANSS</td>
<td>Incidence of adverse events, change from baseline in weight, body mass index, waist circumference, fasting lipids, glucose, laboratory parameters, changes in AIMS, BAS, SAS, CGI-S, CDSS</td>
<td>Age ≥ 18 years, Sch+ and SAD, duration of illness ≥ 1 year, with insufficient efficacy and/or safety or tolerability concerns, “clinically stable” (nonacute phase of illness) for at least 8 weeks prior to baseline (CGI-S ≤ 4 at both screening and baseline), stable dose of previous AP (± 50%) for at least 28 days prior to screening, no exacerbation of Sch+ or SAD for at least 8 weeks prior to screening.</td>
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<td>11 Meyer (2005)</td>
<td>Post-hoc of Multicenter, Rater-Blinded, Open-Label Study</td>
<td>20 weeks</td>
<td>32/71</td>
<td>To examine the effects of switching from the OLZ to RSP on the prevalence of the metabolic syndrome in high-risk overweight or obese patients/difference from baseline in the prevalence of the metabolic syndrome (criteria given)</td>
<td>PANSS and CGI-S</td>
<td>–</td>
<td>Age 18 to 65, Sch+ or SAD, on a stable dose of OLZ for at least 30 days before. More at least 1 of the following: PANSS of 60 to 120; motivation to lose weight (assessed by direct inquiry); and/or the presence of DM-2 or laboratory abnormalities related to impaired glucose tolerance, including FPG &gt; 80 mg/dL or plasma glucose concentration &gt; 139 mg/dL on a 2-hour oral glucose tolerance test.</td>
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Table I. (Continued)

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<tr>
<th>References</th>
<th>Study design</th>
<th>Duration</th>
<th>SAD/TOT sample</th>
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<th>Other efficacy outcomes</th>
<th>Other tolerability outcomes</th>
<th>Inclusion criteria</th>
</tr>
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<tr>
<td>12 Mohl. 2005</td>
<td>Non-randomised, single-arm open label subanalysis</td>
<td>6 months</td>
<td>249/249</td>
<td>The maintained efficacy and tolerability of RLAI with direct change from prior therapy without oral-RSP run-in period/Reductions in PANSS, PANSS subscale or CGI</td>
<td>GAF, SF-36</td>
<td>ESRS</td>
<td>18 + years, SAD, need for a change in medication</td>
</tr>
<tr>
<td>13 Newcomer (2008)</td>
<td>Multicenter, randomized double-blind</td>
<td>16 weeks</td>
<td>40/173</td>
<td>Metabolic effects of ARP vs. OLZ in patients switched from OLZ/weight change from baseline</td>
<td>CGI-I, CGI-S</td>
<td>Percentage change from baseline in fasting triglycerides levels,</td>
<td>18–65 years, Sch+ or SAD, ther with OLZ 10–20mg/d 1 to 24 months prior, BMI &gt; 27 and CGI-S &lt; 4</td>
</tr>
<tr>
<td>14 Simpson (2008)</td>
<td>Pooled analysis of three open-label, flexible-dose, studies</td>
<td>1-year extension</td>
<td>46/185</td>
<td>To evaluate the long-term efficacy and tolerability of ZIP in patients switched from other AP and continuing on ZIP monotherapy for up to 1 year/PANSS scores</td>
<td>CGI-I</td>
<td>SARS AIMS BAS, treatment-emergent adverse effects</td>
<td>Adults with Sch+ or SAD</td>
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Sch+, Schizophrenia; SAD, Schizoaffective disorder; AP, Antipsychotic; ARP, Arpiprazole; OLZ, Olanzapine; LUR, Lurasidone; QTP, quetiapine; RLAI, Risperidone long-acting injectable; RSP, Risperidone; ZIP, Ziprasidone; TEAS, Treatment-emergent adverse events; AE, Adverse Events; Rating scales listed (see original articles for full references): AIMS, BARS, BAS, BPRS, CDSS, CGI-S, CGI-S, DAI, ESRS, GAF, IAQ; MADRS, m-SAS, PANSS, POM; SAS, SAES, SCoRS; SF-36, UKU.
In a post-hoc analysis of a multicentre, rater-blinded, open-label study (Meyer et al. 2005), 32 SZA patients out of 71 individuals were evaluated for 20 weeks after abrupt, 1-week cross-tapered and 2-week cross-tapered switch from olanzapine (OLZ) to RSP on a flexible regimen. The objective of the study was assessing possible changes in the prevalence of metabolic syndrome in high risk or obese patients. The prevalence of metabolic syndrome from baseline (53.5%) significantly reduced to 36.6% at the end of week 20 \( (P < 0.005) \).

A 6-week, randomized, open-label, rater-blinded study (Ganguli et al. 2008) assessed the efficacy and safety of three different switching strategies from OLZ to RSP, with PANSS change as primary outcome. SZA population represented more than one-third of the total patients (52 patients out of 123). The switching methods were abrupt, gradual cross-tapered (in 1 week) and slower cross-tapered (in 2 weeks). Improvements in PANSS scores were seen in each of the three groups of patients, and plateau cross-tapering showed to be more successful due to a lower rate of dropouts for adverse effects. No significant changes from baseline to week 6 or endpoint were observed in vital signs, body weight, or anthropometric measures.

The only multicentre, randomized double-blind study (Newcomer et al. 2008) included was a 16-week assessment of the metabolic effects in 173 patients (40 SZA), switched from OLZ to ARP with a cross-tapered modality. The primary objective of the study was to assess weight change after switching to ARP: as the study was included in Barak and Aizenberg’s meta-analysis, results concerning weight change are therein presented. Secondary objectives were to compare the percentage change in fasting triglyceride levels whilst tertiary objectives were to assess efficacy and safety measures. Switchers to ARP, compared to people stayed with OLZ, showed significant decrease in triglyceride levels starting from week 16 \( (P = 0.002) \) and following timepoints. Efficacy measures (CGI-I) were significantly better in the OLZ group from week 6 to endpoint \( (P < 0.05) \). Significant improvements from baseline in fasting total cholesterol and HDL-C were observed with ARP vs. OLZ at week 16 and following timepoints \( (higest P < 0.028) \).

A pooled analysis (Simpson et al. 2008) was conducted on three open-label, flexible-dose, studies presenting a 1-year extension evaluating the long-term efficacy and tolerability of ziprasidone (ZIP) in 46 SZA out of 185 patients switched to ZIP from: typical antipsychotics, OLZ and RSP. Switching modality consisted of three ways: (1) abrupt switch; (2) cross-tapered in 2 weeks; and (3) cross-tapered in 2 weeks with delayed reduction of the previous treatment. Significant improvements were observed at 1 year according to the outcome efficacy and tolerability measures used.

An open-label, non-randomized, single-treatment, flexible-dose study (Altepkin et al. 2009) was aimed at evaluating during 12 weeks the effectiveness of a switch to ZIP through: (1) abrupt switch, (2) tapered in 7 days with previous treatment at 50% dosage, and (3) tapered in 7 days at with previous treatment at 100% dosage. Pre-switch treatments consisted of haloperidol (Hal), OLZ and RSP. Primary outcome was measured as change in BPRS and showed non-inferiority of ZIP over all three medications, with largest effect magnitude at week 12. As for tolerability profile, significant mean weight loss was observed in the OLZ pre-switch. Switching to ZIP had a neutral effect on metabolic parameters and prolactin.

A prospective, randomized, open-label, multicentre trial (Kim et al. 2009) of 12 weeks assessed the switch to ARP with only a 2-week cross-tapered strategy. Pre-switch treatments included amisulpride (AMP), OLZ, QTP and RSP. ARP showed efficacy not superior to the standard care group. It resulted in improvement from baseline on all efficacy outcome measures. In addition, the remission rate was increased from 43.9% at baseline to 51.7% at 12 weeks after ARP treatment. Weight change aspects are included in the following meta-analysis.

Weight change after a switch to acute and maintenance ARP treatment was evaluated in a meta-analysis (Barak and Aizenberg 2010). Three of the studies included (Casey et al. 2003; Newcomer et al. 2008; Kim et al. 2009) are also included in the present review, whilst two other studies with SZA samples (Spurling et al. 2007; Schorr et al. 2008) are not because of lacking to meet inclusion criteria. A total of 140 SZA patients out of sample of 786 psychotic patients were evaluated after switching from different antipsychotic treatments: AMP (3%), clozapine (CLZ, 1%), OLZ 352 (46%), QTP (1%), RSP (30% and typical antipsychotic (22%). In all studies, a reduction in weight was reported. The major significant findings of the meta-analysis were (1) the significant \( (P < 0.001) \) mean weight reduction following the switch to ARP; (2) this reduction was statistically greater for patients diagnosed with schizophrenia when compared to that of patients diagnosed with SZA; and (3) the most significant mean weight reduction was noted in patients with OLZ as a pre-switch treatment.

A multicentre, open-label, randomized, comparative study (Gaebel et al. 2010) was conducted on a population switched from stable treatment with RSP, OLZ, or typical antipsychotics to RLAI vs. oral QTP. A total of 118 SZA patients were included in the study, 56 on RLAI and 62 on QTP. The primary
outcome was time-to-relapse. Safety evaluations included AEs), clinical laboratory tests, and vital signs.

A randomized, open-label, multicentre continuation study (Lee et al. 2010) of another study (Kim et al. 2009) assessed effectiveness during the 14 following weeks. A sample of 42 SZA patients out of 166 was enrolled in the study. Previous antipsychotic treatments were mainly RSP and first-generation drugs. They were maintained in 31 patients and cross-tapered during 2 weeks to ARP, used in 10–30 mg/day doses in the remaining 135 patients. Most clinically stable outpatients maintained their remission states after being switched to ARP, without serious symptom aggravation and AEs over a course of the total 26 weeks.

An open-label, 16-week, flexible-dose, multicentre study (Karayal et al. 2011) looked at the effects of switching from QTP to ZIP primarily on weight, other safety parameters and effectiveness. Out of a total sample of 241 patients, 86 SZA patients were included. ZIP was introduced and QTP tapered off, resulting in a statistically significant decrease in weight. By endpoint, small mean decreases were observed in levels of total cholesterol, LDL, and triglycerides at week 16, but no change in fasting glucose or HbA1c was detected. At week 16, there were also significant changes indicating improvement in the secondary clinical assessments, including the PANSS scores, CGI-S, CDSS, SCORS and GAF. There was no change in the AIMS.

Another multicentre, randomized, open-label, parallel-group 6-week study (McEvoy et al. 2013) assessed the switch to lurasidone (LUR). The primary outcome was time to treatment failure measured as discontinuation for any cause, whilst AEs and other tolerability measures were secondary outcomes. Schizoaffective patients were 89 out of 240. LUR was introduced with three different cross-tapered methods. No statistically significant or clinically relevant differences in time to treatment failure were observed among the three randomized treatment groups. Time to all-cause discontinuation differed significantly ($P = 0.0368$) for those receiving a sedating AP (OLZ, QTP) compared to non-sedating AP (all others, see Table II).

The last study included (Citrome et al. 2013), represents a 6-month, open-label, extension of the previous LUR one. There were 58 out of 149 SZA patients maintained in this continuation study. A total of 98 patients (65.8%) completed the 6-month study. The objective was to evaluate LUR long-term safety and tolerability, measured as proportion of patients with AEs, serious AEs, or who discontinued due to AEs. A total of 66.2% had at least one AE. Only mild or moderate AEs were experienced by most patients.

Insomnia was the most common event, followed by nausea, akathisia, and anxiety. Severe events were reported by 10 patients, dysphoria being the most frequent. No clinically relevant metabolic changes were observed (see Table III).

Discussion

The objective of the present study was to systematically review the evidence on the switch of antipsychotic treatments in studies specifically aimed at or including SZA populations. According to the results of the review, a secondary objective was to propose treatment strategies for managing SZA patients.

The first striking result is the overall lack of evidence on the topic, despite its clinical relevance. The analysis from Mohl et al. (2005) is the only study specifically directed at SZA patients, whilst none of the other studies present separate results for the schizoaffective sub-population. In this sense, this systematic review clearly outlines the lack of informative trials on the topic of switching antipsychotic treatments in SZA patients, despite their frequent occurrence in clinical practice. All studies considered switching to oral antipsychotics, apart from two (Mohl et al. 2005; Gaebel et al. 2010) that assessed RLAI.

The switching strategies adopted varied across the studies, and seem to have an overall similar validity.

Special attention must be paid during the transition from previous to actual treatment, as new side effects may be transient whilst withdrawal symptoms may occur (Bauer et al. 2010). Thus, both the physician and the family/caregiver should actively support the patient encouraging adherence and persistence of treatment. More gradual discontinuation of the first antipsychotic may thus minimize problems in the switching, as reported in patients with schizophrenia (Newcomer et al. 2013) and bipolar disorder (Grande et al. 2014).

Managing antipsychotic switching in acute treatment

In acute treatment, different studies assessed switching to four different drugs: two to ARP, one to LUR, one to RSP and one to ZIP.

ARP is the only drug in which the most used switching strategies have been experimentally tested and proved not to influence the effectiveness of the treatment (Casey et al. 2003). Most clinically stable outpatients maintain their remission states after being switched to ARP (Kim et al. 2009).

LUR was evaluated on three different cross-tapered switching strategies, showing no inferiority
Table II. Switching details across studies.

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<tr>
<th>References</th>
<th>Pre-switch drug with # of patients or dose</th>
<th>Switching method</th>
<th>Post-switch drug (dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Alptekin (2009)</td>
<td>Hal, OLZ; RSP</td>
<td>3 groups: 1. abrupt switch, 2. cross-taper in 7 days at 50% dosage, 3. cross-taper in 7 days at 100% dosage</td>
<td>ZIP 80–160mg/d, mean 118mg/d</td>
</tr>
<tr>
<td>2 Barak and Aizenberg (2010)</td>
<td>Amisul 17 (3%), CLZ 11 (1%), OLZ 352 (46%), QTP 10 (1%), RSP 226 (30%), TAP 168 (22%)</td>
<td>Cross-taper in 2 weeks</td>
<td>ARP 1 to 5mg/d, Mean 2.3mg/d</td>
</tr>
<tr>
<td>3 Casey (2003)</td>
<td>Hal 15, Thioridazine 7, Other TAP 2, OLZ 173, RSP 112</td>
<td>3 groups: 1. Abrupt switch from QTP/RSP to ARP 30 mg, 2. immediate initiation of ARP 30 mg tapering OLZ/RSP, 3. Cross-tapering QTP/RSP to ARP over 14 days.</td>
<td>ARP 30mg/d</td>
</tr>
<tr>
<td>4 Citrome (2013)</td>
<td>Aripiprazole 32 (21.6%), Quetiapine 31 (20.9%), Risperidone 29 (19.6%), Ziprasidone 18 (12.2%), Olanzapine 13 (8.8%), Paliperidone 7 (4.7%), Iloperidone 2 (1.4%), Asenapine 2 (1.4%), TAP 14 (9.5%)</td>
<td>Continuation study from McEvoy 2013: cross-tapered to 1 of 3 open-label LUR arms: 1. LUR 40 mg/d for 14 days, then adjusted, 2. LUR 40 mg/d for 7 days, then 80 mg/d, then adjusted, 3. LUR 80 mg/d then adjusted</td>
<td>LUR 40, 80, and 120mg were the modal daily doses for 19 (42.9%), 65 (34.4%), and 64 (43.9%) of patients, respectively. Overall mean (SD) daily LUR dose was 102.0 (77.1) mg, RLAIs were the modal daily doses for 19 (42.9%), 65 (34.4%), and 64 (43.9%) of patients, respectively. Overall mean (SD) daily LUR dose was 102.0 (77.1) mg,</td>
</tr>
<tr>
<td>5 Gaebel (2010)</td>
<td>RSP (40%), OLZ (30%), TAP (30%)</td>
<td>RLAI and after 3 weeks tapering of oral drug or QTP cross-switched in 2 weeks</td>
<td>RLAIs with mode doses 33.6 ± 10.1 mg/2 weeks or QTP mode dose 413.4 ± 159.2 mg/d</td>
</tr>
<tr>
<td>6 Ganguli (2008)</td>
<td>OLZ Mean 14.4 ± 5.4 mg/d, 15.5 ± 6.3 mg/d, 16.4 ± 7.9 mg/d</td>
<td>3 groups 1. abrupt, 2. gradual cross-taper (1 week), 3. slower cross-taper (2 weeks) tapering off QTP</td>
<td>RSP 4.2±1.4 mg/d, 4.6 ± 1.4 mg/d, 4.1 ± 1.4 mg/d</td>
</tr>
<tr>
<td>7 Karayal (2011)</td>
<td>QTP Minimum 300mg/d</td>
<td>Cross-tapering over 14 days</td>
<td>ZIP 133.0 ± 27.4 mg/d</td>
</tr>
<tr>
<td>8 Kim (2009)</td>
<td>Amisul, OLZ, QTP, RSP</td>
<td>Cross-taper in 2 weeks</td>
<td>ARP 10–30 mg/d</td>
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<tr>
<th>References</th>
<th>Pre-switch drug with # of patients or dose</th>
<th>Switching method</th>
<th>Post-switch drug (dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9 Lee (2010)</td>
<td>RSP (76), Hal (72), trifluoper (56), fluphen (48), perphen (44).</td>
<td>Cross-taper in 2 weeks</td>
<td>ARP 10–30 mg/d</td>
</tr>
<tr>
<td>10 McEvoy (2013)</td>
<td>ARP (44%), ASE (2%), ILO (4%), OLZ (24%), PAL (9%), QTP (62%), RSP (51%), TAP (17%), ZIP (27%)</td>
<td>Cross-tapered to 1 of 3 open-label LUR arms: 1. LUR 40 mg/d for 14 days, then adjusted, 2. LUR 40 mg/d for 7 days, then 80 mg/d, then adjusted, 3. LUR 80 mg/d then adjusted</td>
<td>LUR 40, 80, 120 mg/d fixed dose</td>
</tr>
<tr>
<td>11 Meyer (2005)</td>
<td>OLZ Mean. 15.5 mg/d (no SD)</td>
<td>OLZ discontinued in 3 ways: 1. abrupt discontinuation of OLZ; 2. cross-tapered in 1 week; 3. cross-tapered in 2 weeks.</td>
<td>RSP Mean 4.3 mg/d (no SD)</td>
</tr>
<tr>
<td>12 Mohl. (2005)</td>
<td>AAP (57%), depot TAP (40%), oral TAP (12%) 80% on AP monotherapy</td>
<td>Oral AP: Directly (abrupt) after 21st days injection or tapered in 3 days. Depot TAP: cross-switched</td>
<td>RLAI 49% with 25 mg/d, 24% with 37.5 mg/d, 27% with 50 mg/d 1 (0.4%) 75 mg/d 13 Newcomer (2008)</td>
</tr>
<tr>
<td>14 Simpson (2008)</td>
<td>TAP = 71; OLZ = 71; RSP = 43</td>
<td>1 of 3 ways: 1. abrupt switch; 2. cross-tapered in 2 weeks 3. cross-tapered in 2 weeks with delayed reduction of previous AP</td>
<td>ZIP Median 120 mg/d</td>
</tr>
</tbody>
</table>

Amisul, amisulpride; AAP, Atypical antipsychotics; AP, antipsychotic; ARP, aripiprazole; ASE, Asenapine; CLZ, clozapine; fluphen, Fluphenazine; ILO, iloperidone; Hal, haloperidol; LUR, Lurasidone; OLZ, olanzapine; PAL, paliperidone; Perphen, Perphenazine; QTP, quetiapine; RLAI, risperidone long-acting injectable; RSP, risperidone; TAP, typical antipsychotic; Trifluoperazine; ZIP, ziprasidone.
Table III. Efficacy and tolerability outcomes.

<table>
<thead>
<tr>
<th>References</th>
<th>Outcomes</th>
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</thead>
<tbody>
<tr>
<td>1 Alptekin (2009)</td>
<td>Noninferiority of ZIP, largest magnitude at week 12.</td>
</tr>
<tr>
<td>2 Barak and Aizenberg (2010)</td>
<td>Mean weight significant reduction after switch to ARP (p = 0.001). Mean weight reduction greater for Sch+ (-2.67 kgs) than SAD (-2.18 kgs), P &lt; 0.022. 3. Most significant change vs. OLZ, -2.74 Kg (P &lt; 0.001)</td>
</tr>
<tr>
<td>3 Casey (2003)</td>
<td>Efficacy with ARP in all three groups. Adverse Effects was broadly comparable across all groups, and AEs were generally mild to moderate in severity and time-limited. The reduction in body weight and plasma prolactin levels following switch to ARP were comparable across the three groups. Any of the 3 strategies evaluated can be used safely for switching patients to ARP from AP monotherapy</td>
</tr>
<tr>
<td>4 Citrome (2013)</td>
<td>Most commonly reported AEs were insomnia (13 patients [8.8%]), nausea (13 patients [8.8%]), akathisia (12 patients [8.1%]), and anxiety (9 patients [6.1%]). Most patients had only mild or moderate AEs. Severe AEs were uncommon; these events were reported by 10 patients (6.8%): 2 patients (1.4%) had severe dysphoria, and no other severe AE was reported by more than 1 subject. No signal for clinically relevant adverse changes in body weight, lipids, glucose, insulin, or prolactin. Patients were able to maintain clinical improvement (as assessed by PANSS, CGI-S, and CDSS) over 6 months of follow up.</td>
</tr>
<tr>
<td>5 Gaebel (2010)</td>
<td>Difference in time-to-relapse for patients treated with RLAI vs quetiapine (P = 0.0001). The relative risk for relapse was less than half with RLAI compared with QTP. No difference in time-to-relapse for presence or absence of oral RSP run-in. Total PANSS improved significantly compared with baseline for both groups at each (P = 0.001). RLAI and QTP were both safe and well tolerated. No significant between group differences in weight gain. ESRs total scores decreased similarly after randomization to either RLAI or quetiapine.</td>
</tr>
<tr>
<td>6 Ganguli (2008)</td>
<td>Improvements in PANSS scores were seen in each of the three groups of patients. A tapering switching method may be more successful than abrupt withdrawal strategies. No significant changes from baseline to week 6 or endpoint were seen in vital signs, body weight, or anthropometric measures</td>
</tr>
</tbody>
</table>
### Table III. (Continued)

<table>
<thead>
<tr>
<th>References</th>
<th>Outcomes</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Results</strong></td>
<td>Drug vs comparator (P-value)</td>
<td>Secondary Results</td>
</tr>
<tr>
<td>7 Karayal (2011)</td>
<td>Statistically significant decrease in weight, with a mean change from baseline of −0.73 kg.</td>
<td>Small mean decreases in levels of total cholesterol, LDL, and triglycerides at week 16, but no change in fasting glucose or HbA1c. At week 16, there were also significant changes indicating improvement in the secondary clinical assessments, including the PANSS scores, CGI-S, CDSS, SCoRS and GAF. There was no change in the AIMS</td>
</tr>
<tr>
<td>8 Kim (2009)</td>
<td>Mean CGI-Improvement score at 12 weeks was 3.56 ± 1.29 (95% confidence interval: 3.39–3.73) in the ARP group, indicating that ARP was effective</td>
<td>–</td>
</tr>
<tr>
<td>9 Lee (2010)</td>
<td>Mean CGI-I did not significantly differ between groups. Most clinically stable outpatients maintain their remission states after being switched to ARP, without serious symptom aggravation and adverse events over a course of 26 weeks.</td>
<td>–</td>
</tr>
<tr>
<td>10 McEwry (2013)</td>
<td>No statistically significant or clinically relevant differences in time to treatment failure were observed among the 3 randomized treatment groups (log-rank P = 0.0861).</td>
<td>Time to all-cause discontinuation differed significantly (log-rank P = 0.0368) for those receiving a sedating AP compared to those receiving a nonsedating AP.</td>
</tr>
<tr>
<td>11 Meyer (2005)</td>
<td>Switching from OLZ to RSP was associated with a significant reduction in the prevalence of metabolic syndrome</td>
<td>–</td>
</tr>
<tr>
<td>12 Mohl. (2005)</td>
<td>Mean scores for the total PANSS and all three subscales were significantly reduced from baseline to week 4 (p = 0.001), with further improvements until treatment endpoint. Significant improvements from baseline to endpoint were seen in the mood symptom domains of anxiety/depression and uncontrolled hostility/excitement. Mean GAF score improved significantly from baseline to endpoint.</td>
<td>–</td>
</tr>
<tr>
<td>13 Newcomer (2008)</td>
<td>Weight decreased significantly with ARP vs. OLZ. Significant differences in percentage change in triglyceride levels were observed with ARP (decrease) vs. OLZ (increase). More subjects with ARP had clinically relevant (&gt;7% weight loss) vs. OLZ and a lower percentage of subject receiving ARP had clinically relevant weight gain.</td>
<td>CGI-I were statistically significantly better with OLZ vs. ARP and more subjects discontinued ARP than OLZ.</td>
</tr>
</tbody>
</table>

AE, Adverse Effects; AP, Antipsychotic drug; SAD, Schizoaffective Disorder; ARP, Aripiprazole; Hal, Haloperidol; OLZ, Olanzapine; QTP, Quetiapine; RLAI, Risperidone Long-acting Injectable; RSP, Risperidone; ZIP, Ziprasidone; BMI, Body Mass Index; Scales used: AIMS, BAIMS, BAS, BPRS, CDSS, CGI-I, CGI-S, GAF, MADRS, PANSS, SARS, SCoRS.
to previous treatments (McEvoy et al. 2013). Depending on whether LUR is switched from a sedating antipsychotic (OLZ, QTP) or not, special care must be paid respectively to the insurmountable of insomnia, fatigue, anxiety, or vomiting, somnolence, sedation and akathisia.

Switching to RSP from OLZ resulted in a 31.5% reduction in the diagnosis of the metabolic syndrome in the pooled sample of patients (Ganguli et al. 2008). Although the notion than switching from OLZ generally improves metabolic syndrome may be well assumed, a meta-analysis (Moteshafi et al. 2012) concluded that adverse effects expressed differently according to phenotype, as a higher weight gain in schizophrenia patients than in bipolar disorder patients was observed. In addition, increases in blood glucose, total cholesterol and triglyceride levels were numerically higher in the schizophrenia group compared with the bipolar disorder group, albeit not statistically significant. The question whether SZA patients may be more similar to either phenotype remains open.

ZIP was evaluated in an open-label flexible-dose study (Alteptkin et al. 2009), showing general improvement. An abrupt switch strategy to a ZIP drug regimen was preferred. A selection bias consisted in the exclusion of patients with contraindication for treatment with ZIP.

Managing antipsychotic switching in maintenance treatment

A total of seven studies assessed the switch to different antipsychotics in maintenance treatment, considering that the meta-analysis (Barak and Aizenberg 2010) encompasses one acute and eight maintenance studies (ranging from 16 weeks to 2 years of duration). These studies share the objectives of assessing tolerability and improved metabolic profile of patients switched to four different drugs: ARP, LUR, RSP and ZIP. Patients with mental illness are at increased risk for cardiovascular disease; mortality statistics indicate that there is a 1.2- to 4.9-fold increase in mortality in patients with schizophrenia and bipolar disorder compared to general population (Colton and Manderscheid 2006). Understandably, longer-term studies on switching antipsychotic treatment have the objective of improving the tolerability of the treatment, especially weight gain and metabolic issues.

ARP was assessed in three studies: the effectiveness of ARP was assessed in a 14-week extension continuation study (Lee et al. 2010), while metabolic improvement after switching from OLZ treatment was the objective of the 16-week study (Newcomer et al. 2008) and the meta-analysis (Barak and Aizenberg 2010). The metabolic improvement in patients switched to ARP suggests that switching might be considered for any antipsychotic-treated patients who had gained weight, especially with pre-existing risk factors.

LUR was assessed in a continuation study (Citrome et al. 2013), showing good efficacy and tolerability. This represents a relevant topic for the treatment of unipolar and bipolar depressed SZA patients, given the consistent evidence for this drug in the treatment of depressive symptoms in schizophrenia (Nasrallah et al. 2014) and in bipolar depression (Loebel et al. 2014). An old study (Meyer et al. 2005) studied the switch to RSP in patients treated with OLZ, plus the possible integration of a behavioural therapy aimed at reducing weight gain. The metabolic syndrome was highly prevalent at baseline, and the switch to RSP was significantly associated with a reduction in this prevalence.

The last studies included tested the effectiveness of switching to ZIP treatment: patients were switched from QTP (Karayal et al. 2011), or from a number of typical antipsychotic, OLZ and RSP (Simpson et al. 2008). ZIP seemed generally effective and well tolerated, showing improvement in extrapyramidal and metabolic side effects.

Managing switching to long-acting or depot treatment

RLAI was assessed in two studies. Despite the poor overall quality of the methods used in both studies, the first (Mohl et al. 2005) is aimed exclusively at SZA population. Tapering off previous oral medication is the switching modality adopted in both studies. The presence of a QTP arm in the other study (Gaebel et al. 2010) allowed for an active comparison, showing that relative risk for relapse was less than half with RLAI compared with QTP. Notably, this study provides more insight into the differences between two treatment approaches rather than a direct comparison of two pharmacological agents, because of non-blinded treatment with oral vs. injectable therapy used in this study and the ability to more completely ensure adherence to injectable therapy, an issue which is clinically relevant and frequent in SZA (Murruru et al. 2012b), it is not easily predictable (Murruru et al. 2013), and may have a significant negative impact on treatment response in schizophrenic, schizoaffective (Lindentmayer et al. 2009) and bipolar (Sajatovic et al. 2009) patients. For this reason clinicians should assess carefully adherence issues in order to determine whether the scarce symptom control may be due to inappropriate assumption of the treatment or not.

Contrarily, results from the ETOS study (Roussidis et al. 2013) showed that in schizophrenia switching
from an ineffective treatment to another agent may be efficacious, well tolerated, even resulting in an increased adherence to treatment. So, successfully switching to another oral compound may improve attitude towards medication due to the perceived benefits and better tolerability. Also in SZA populations a careful choice of a new treatment could regain some of the formerly poor adherent patients.

**Unmet practical issues in switching antipsychotic treatment**

Atypical antipsychotics bind to a variety of receptors (Scherk et al. 2007) and different efficacy and tolerability profiles have to be taken into account (Buckley et al. 2007). Whatever switching strategy is adopted, (side) effects may be predicted by keeping in mind the pharmacodynamic of the chosen drug: whenever the affinity to a receptor is lower for a receptor system than for the dopaminergic receptor a side effect associated with the blockade of this receptor is likely to occur as part of antipsychotic treatment (Correll 2010b). On the other hand, it is possible that withdrawing the former antipsychotic results in exacerbation of some symptoms, such is the case of switching from drugs with greater propensity to cause sedation that may be temporarily dealt with adjunctive.

As has been pointed out throughout, the major limitation of the management of antipsychotic medications in SZA is the overall lack of trials specifically conducted on this population. This could be wrongly seen as a lack of need for clinical research on effective treatments in SZA. Even if second-generation antipsychotics have generally proven effectiveness in both schizophrenia and bipolar disorder, we know from clinical practice that these compounds may not be equally efficient in treating or preventing psychotic and affective episodes, as the same drug may be differently effective in preventing relapses into a manic polarity or into a depressive one, and that consequently doses used may vary. In bipolar disorder, Predominant Polarity is a clinical concept with demonstrated ground (Colom et al. 2006; Rosa et al. 2008; Popovic et al. 2014) and based on the observation that a proportion of bipolar patients (roughly 50%) shows a tendency to relapse either into mania or depression. In SZA, the presence of pure psychotic episodes sums up, bringing to the impossibility of adopting the concept of Predominant Polarity without an adaptation to these clinical features. Anyway, SZA patients do show a tendency to relapse to depression, mania or pure psychotic episodes (Murr et al. 2012b), with yet-to-demonstrate implications on the course of illness. Clinicians should choose accordingly the type of antipsychotic to switch to, a view that is also reinforced in the dimensional assessment of psychotic disorders in DSM-5 (APA 2013). Whilst, in bipolar disorder, the concept of Polarity Index of a treatment (Popovic et al. 2012) may drive the clinicians to a choice that best tailors on the single patient and his/her history and course of illness, in SZA population this is impossible for lack of placebo-controlled trials (Murr et al. 2011a) that allow to calculate specific Numbers Needed to Treat's. Such limitations are consequently reflected in this review, which cannot benefit from specific relapse-type recommendations.

**Combination therapies**

Differently from schizophrenia and similarly to bipolar disorder, clinical management of SZA often relies on combination treatments with classical mood stabilizers (i.e., lithium, valproate, lamotrigine) in the prevention of affective relapses. The extent to which lithium may be effective in the treatment of SZA has not been investigated, and despite a grounded practice in bipolar disorder (Nivoli et al. 2009) the role of this drug in schizophrenia seems negative (Leucht et al. 2007), maybe less strongly in augmentation (Leucht et al. 2004). Classical mood stabilizers could have a role as adjunctive treatment to ongoing antipsychotics, thus increasing efficacy and reducing the need for switching antipsychotic.

The use and type of combined treatments should be decided on the base of their efficacy and tolerability profile and their receptor affinity profile, to avoid cumulative prescription of redundant agents (Murr et al. 2011b). In bipolar disorder, most patients receive combinations of antipsychotics and mood-stabilizers and sometimes antidepressants (Vieta et al. 2013), similarly to what schizoaffective patients are usually treated with (Vieta 2010). From a pharmacodynamic standpoint, the affinity of the different antipsychotics for D2 dopaminergic, muscarinic cholinergic, histaminergic, and adrenergic receptors (Richelson et al. 2010) may have implications for the switch in terms of both discontinuing the previous antipsychotic and introducing the new one (Ereshesky and Dugan 2000), either if the withdrawal is abrupt or the introduction involves tapering (Bernardo et al. 2011).

This systematic review presents two major limitations. First, data are scarce and most evidence does not derive directly from studies conducted on pure SZA patients. Second, primary outcomes of the included studies were heterogeneous, covering
efficacy and/or tolerability issues, thus complicating comparison between the compounds in our study.

Conclusions
Despite being a relevant clinical issue, the topic of antipsychotic switching in SZA populations grounds on scant scientific evidence composed, in general, of low-quality data.

Keeping in mind receptor binding characteristics of each antipsychotic may help to rule out the best strategy in the switching, in order to optimize doses without exposing the patient to a risk of relapse or increased side effects.

This systematic review identified limited evidence on effective switching. Specifically, scientific ground is present for switching to aripiprazole, lurasidone and, to a lesser extent, risperidone and ziprasidone. Switching seems appropriate when tolerability issues, specifically metabolic and weight gain, are compromising the course of illness and wellbeing of schizoaffective patients. Evidence is present also for RLAI, making it a viable option, whereas adherence to oral treatment seems questionable. Plateau cross-switching should be considered as the ideal, safer strategy to adopt in terms of costs-benefits for stabilized patients. More abrupt strategy may be adequate in specific, urgent cases, but clinicians have to consider that it may bear an increased risk for relapses that the limited evidence available has not extensively investigated. In the future, specific trials should be conducted on schizoaffective populations, or, at least, results for schizoaffective sub-populations should be provided in trials which enrol mixed samples.

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References


Antipsychotic switching in schizoaffective disorder


