Table 1. Category 1: Randomized Controlled Studies Addressing Specific Switching Questions and Involving 2 or More Agents

Publication	Description of Trial	Switched From	Switched To	Duration	Outcomes Measured	Comments and Results
Lin et al. *J Clin Psychopharmacol*. **2013**;33(2):211–214. doi PubMed	Prospective, randomized, rater-blinded, inpatient, single site, Taiwan	Clozapine (N = 59 enrolled, 52 completed study)	Continue on clozapine or switch to zotepine	12 wk	BPRS, UKU, SAS, anticholinergic use, prolactin levels	Patients switched to zotepine showed significant increase in BPRS scores, more general adverse events and EPS, increased use of propranolol and anticholinergics, and increased prolactin levels. Switching from clozapine to zotepine should be done with caution
Buchanan et al. *J Clin Psychopharmacol*. **2012**;32(1):36–45. doi PubMed	2 randomized, double-blind studies, mainly outpatient, multicenter, multinational	949 patients with persistent negative symptoms being treated mostly with SGAs, but some with FGAs or depots	Asenapine (241 + 244 = 485) or olanzapine (240 + 224 = 464)	26 wk	Effect on negative symptoms	Negative symptoms improved with both agents; discontinuation rates higher and weight gain less with asenapine
Cazorla et al. *Neuropsychiatr Dis Treat*. **2012**;8:247–257. PubMed	Same studies as Buchanan et al, 2012 doi PubMed	See Buchanan et al	See Buchanan et al	26 wk	Safety and tolerability based on pooled results	Similar incidences of adverse effects in patients switching to asenapine or olanzapine
Chen et al. *J Psychopharmacol*. **2012**;26(9):1201–1210. doi PubMed	Randomized, prospective, open-label, outpatient, multicenter, North America	FGA or SGA other than aripiprazole or ziprasidone	Aripiprazole (n = 24) or ziprasidone (n = 28)	12 mo	Anthropometric and metabolic measures, psychopathology, QOL, motor adverse effects	Statistically significant improvements in weight, BMI, TG, HDL, and TG/HDL, which did not differ between treatments. Switching patients with metabolic side effects to aripiprazole or ziprasidone may be beneficial for some, but not all, metabolic measures, with minimal risk of worsening of psychopathology and possibly some benefit in that regard
Kim et al. *Int Clin Psychopharmacol*. **2012**;27(5):267–274. doi PubMed	Randomized, open-label, inpatient and outpatient, multicenter, Korea	Risperidone (N = 58)	Continue on risperidone (n = 28) or switch to paliperidone ER (n = 30)	12 wk	Cognitive function, PANSS, SOFAS	Some advantage for paliperidone in cognitive and social functioning after switch
Essock et al. *Am J Psychiatry*. **2011**;168(7):702–708. doi PubMed	Randomized, outpatient, multicenter, United States	AP polypharmacy (N = 127)	Switch to AP monotherapy (n = 65) or continue on polypharmacy (n = 62)	6 mo + 6 mo naturalistic follow-up	All-cause treatment discontinuation	Monotherapy associated with higher discontinuation rates (31% vs 14%), but weight loss compared to gain in polypharmacy group. Reasonable to try monotherapy with return to polypharmacy if needed
Stroup et al. CAMP study. *Am J Psychiatry*. **2011**;168(9):947–956. PubMed	Randomized, double-blind, outpatient, multicenter, United States	Patients who were overweight and had elevated non-HDL cholesterol and were treated with olanzapine, quetiapine, or risperidone	Switch to aripiprazole (n = 109) or stay on original AP (n = 106)	24 wk	Change in weight and other metabolic parameters (based on 89 who switched and 98 who stayed)	Switching to aripiprazole led to reductions in weight and improvement in other metabolic factors and was associated with higher rate of treatment discontinuation; rates of efficacy failure same in all groups
Kinon et al. *Neuropsychopharmacology*. **2010**;35(2):581–590. doi PubMed	Randomized, double-blind, outpatient, multicenter, 3 countries	628 screened and started on risperidone, 106 discontinued before 2 wk, 144 classified as early responders, and 378 as early nonresponders	Early nonresponders randomized to stay on risperidone (n = 192) or switch to olanzapine (n = 186)	12 wk	Switching vs staying after early (2-wk) nonresponse	Early response vs nonresponse appears to be a reliable marker of subsequent clinical outcomes
Kim et al. *Int Clin Psychopharmacol*. **2009**;24(4):181–188. doi PubMed	Open-label, randomized, outpatient, multicenter, Korea	292 patients switched from other APs	To aripiprazole (n = 245) or a non-aripiprazole AP (n = 47)	12 wk	Safety and efficacy outcomes	No between-group differences but positive outcomes with switching
Byerly et al. *Psychiatry Res*. **2008**;159(1–2):115–120. doi PubMed	Randomized, double-blind, outpatient, multicenter, United States	42 risperidone patients with sexual dysfunction	Continue on risperidone (n = 22) or switch to quetiapine (n = 20)	6 wk	Sexual dysfunction	No significant difference between groups, but slightly lower adjusted mean ASEX scores at wk 2 and 6 in quetiapine group
Cortese et al. *J Clin Psychopharmacol*. **2008**;28(1):69–73. doi PubMed	Randomized, outpatient, single site, Canada	22 patients with TD or parkinsonism whose previous AP was olanzapine (n = 7), risperidone (n = 7), or an FGA (n = 8)	Continue previous AP (n = 9) or switch to quetiapine (n = 13)	3 mo	Movement disorders	Significant reduction in parkinsonism, akathisia, and dyskinesia with quetiapine; subjects remaining on current treatment had increase in rigidity
Newcomer et al. *J Clin Psychiatry*. **2008**;69(7):1046–1056. doi PubMed	Randomized, double-blind, outpatient, multicenter, multinational	Olanzapine (N = 173)	Continue on olanzapine (n = 85) or switch to aripiprazole (n = 88)	16 wk	Changes in mean weight and fasting TG levels	Significant decrease in weight and TG levels with aripiprazole vs olanzapine; "limited evidence of negative psychiatric effects"
Suzuki et al. *Psychopharmacology (Berl)*. **2007**;195(2):285–295. doi PubMed	Randomized, open-label, outpatient, single site, Japan	Randomly assigned to olanzapine (n = 26), quetiapine (n = 26), risperidone (n = 26)	If failed to respond, assigned to trial of 1 of the other 2. If failed to respond to that 1, assigned to the 3rd agent	Up to three 8-wk trials	Effectiveness of sequential switches of APs	Switching is worthwhile after failure to respond to first agent. Somewhat lower response rates with quetiapine

(continued)

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Ciudad et al. *Prog Neuropsychopharmacol Biol Psychiatry*. **2006**;30(8):1515–1522. doi PubMed	Randomized, open-label, outpatient, multicenter, Spain	FGAs (N = 235)	Olanzapine (n = 120) or risperidone (n = 115)	1 y	Social functioning in patients with prominent negative symptoms	Olanzapine associated with greater improvement than risperidone in social functioning
Kinon et al. *Psychoneuroendocrinology*. **2006**;31(5):577–588. doi PubMed	Randomized, open-label, inpatient and outpatient, multicenter, United States	Patients with hyperprolactinemia: FGA (n = 25) and risperidone (n = 29)	Continue on current AP (9 FGA and 18 risperidone) or switch to olanzapine (n = 27)	4 mo	Prolactin levels	Prolactin levels reduced and sexual functioning improved with olanzapine
Mori et al. *Prog Neuropsychopharmacol Biol Psychiatry*. **2004**;28(4):659–665. doi PubMed	Randomized, inpatient, single site, Japan	FGAs; patients switched over 4 wk and then anticholinergics discontinued over 4 wk (N = 77)	Olanzapine (n = 20), perospirone (n = 18), quetiapine (n = 20), risperidone (n = 19)	8 wk	Immediate memory, verbal working memory	Significant improvement in immediate memory with olanzapine and risperidone
Yamashita et al. *J Clin Psychiatry*. **2004**;65(11):1525–1530. doi PubMed	Randomized, inpatient, single site, Japan	FGA (N = 92)	Olanzapine (n = 20), perospirone (n = 24), quetiapine (n = 28), risperidone (n = 20)	8 wk	Subjective sleep quality	Improved subjective quality of sleep
Bai et al. *J Clin Psychiatry*. **2003**;64(11):1342–1348. doi PubMed	Randomized, double-blind, placebo-controlled	49 patients on FGAs with schizophrenia and severe TD	Risperidone (n = 22) or placebo (n = 20)	12 wk	Scores on AIMS and ESRS as well as BPRS	Risperidone, 6 mg/d, produced more improvement in severe TD than discontinuing APs
Godleski et al. *J Clin Psychiatry*. **2003**;64(2):119–122. doi PubMed	Randomized, open-label, outpatient, single site, United States	Depot FGAs (N = 26)	Continue on depot (n = 13) or switch to oral olanzapine (n = 13)	3 mo	Efficacy and safety parameters	Significant clinical improvement in olanzapine group; no difference in side effects between groups except for weight
Ritchie et al. *Int J Geriatr Psychiatry*. **2003**;18(5):432–440. doi PubMed	Randomized, multicenter, outpatient, Australia	FGAs (N = 66)	Olanzapine (n = 34) or risperidone (n = 32); 12 did not complete crossover for final N = 54	4-wk crossover period	Motor EPS, efficacy, safety, and QOL in elderly patients with schizophrenia	Improvement in core symptoms and motor side effects; olanzapine patients more likely to complete switching process and had better improvement in QOL

Abbreviations: AIMS = Abnormal Involuntary Movement Scale, AP = antipsychotic, ASEX = Arizona Sexual Experiences Scale, BMI = body mass index, BPRS = Brief Psychiatric Rating Scale, CAMP = Comparison of Antipsychotics for Metabolic Problems study, EPS = extrapyramidal side effects, ER = extended release, ESRS = Extrapyramidal Symptom Rating Scale, FGA = first-generation antipsychotic, HDL cholesterol = high density lipoprotein cholesterol, PANSS = Positive and Negative Syndrome Scale, QOL = quality of life, SAS = Simpson Angus Scale, SGA = second-generation antipsychotic, SOFAS = Social and Occupational Functioning Assessment Scale, TD = tardive dyskinesia, TG = triglycerides, UKU = Udvalg for Kliniske Undersogelser Rating Scale.