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Optimizing Treatment of Schizophrenia: Clinical and Economical Potential for Patient Switching to Long-Acting Injectables

Table S 1 References of clinical studies included in NMA

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Table S 2 - Details of the RCTs included in the meta-analysis

Study	Comparison	Relative efficacy (95% CI)
Alphs 2015	PAL 28 vs. FGA OAPs	0.681 (0.37 to 1.24)
Buckley 2014	RIS 14 vs. SGA OAPs	1.285 (0.88 to 1.88)
Carpenter 1999	FLU 42 vs. FLU 14	1.311 (0.59 to 2.93)
Csernansky 2002	ALO oral vs. RIS oral	1.93 (1.33 to 2.8)
Detke 2014	OLA 28 vs. OLA oral	1.086 (0.74 to 1.61)
Fleischhacker 2014	ARI 28 vs. ARI oral	0.985 (0.54 to 1.79)
Glick 2002	OLA oral vs. ALO oral	0.828 (0.62 to 1.11)
Hogarty 1979	FLU 14 vs. FLU oral	0.862 (0.42 to 1.78)
Ishigooka 2015	ARI 28 vs. ARI oral	0.92 (0.45 to 1.88)
Kane 2009	OLA oral vs. ARI oral	0.985 (0.46 to 2.12)
Kane 2010	OLA 14 vs. OLA oral	1.5 (0.82 to 2.76)
Kane 2010	OLA 28 vs. OLA oral	1.4 (0.78 to 2.52)
Kane 2010	OLA 28 vs. OLA 14	1 (0.58 to 1.73)
Keks 2007	RIS 14 vs. OLA oral	1.17 (0.68 to 2.02)
Kim 2008	RIS 14 vs. RIS oral	0.307 (0.12 to 0.81)
Lieberman 2005	OLA oral vs. RIS oral	0.575 (0.39 to 0.84)
Malla 2016	RIS 14 vs. SGA OAPs	1.894 (0.66 to 5.45)
McEvoy 2014	PAL 28 vs. ALO 28	1.294 (0.83 to 2.02)
Rosenheck 2011	RIS 14 vs. OAPs	0.87 (0.63 to 1.2)
Savitz 2016	PAL 84 vs. PAL 28	0.87 (0.56 to 1.35)
Schooler 1980	FLU 21 vs. FLU oral	0.668 (0.4 to 1.11)
Schooler 2005	RIS oral vs. ALO oral	0.864 (0.65 to 1.15)

ALO = haloperidol; ARI = aripiprazole; FLU = fluphenazine; OAP = oral antipsychotics; OLA = olanzapine; PAL = paliperidone; RIS = risperidone; SGA = second generation antipsychotics; ZUC = zuclopentixol

Table S 3 - Details of the observational studies included in the meta-analysis

Study	Comparison	Relative effectiveness (95% CI)
Aratò 1979	FGA LAIs 28 vs. FGA OAPs	0.106 (0.06 to 0.18)
Baser 2015	PAL 28 vs. SGA OAPs	0.623 (0.54 to 0.73)
Beauclair 2005	RIS 14 vs. RIS oral	0.103 (0.04 to 0.24)
Bitter I, 2013	RIS 14 vs. ARI oral	0.64 (0.54 to 0.76)
Bitter I, 2013	RIS 14 vs. OLA oral	0.767 (0.68 to 0.87)
Bitter I, 2013	RIS 14 vs. RIS oral	0.387 (0.34 to 0.44)
Bourin 1998	FGA LAIs 28 vs. FGA OAPs	1.333 (1.13 to 1.58)
Carswell 2010	RIS 14 vs. RIS oral	0.441 (0.38 to 0.51)
Chang 2012	RIS 14 vs. RIS oral	0.43 (0.32 to 0.58)
De Vito 1978	FLU 28 vs. FLU oral	0.355 (0.24 to 0.53)
Denham 1971	FLU 28 vs. FLU oral	0.262 (0.19 to 0.36)
Di Lorenzo 2017	PAL 28 vs. SGA OAPs	0.33 (0.12 to 0.9)
Grimaldi-Bensouda 2012	RIS 14 vs. FGA OAPs	0.49 (0.28 to 0.85)
Guo 2011	OLA oral vs. ARI oral	0.947 (0.53 to 1.7)
Joshi 2016	PAL 28 vs. RIS 14	0.798 (0.66 to 0.97)
Lafeuille 2015	PAL 28 vs. OAPs	0.75 (0.72 to 0.79)
Lindholm 1975	FLU 14 vs. FLU oral	0.447 (0.3 to 0.67)
Malm 1971	FGA LAIs 28 vs. FGA OAPs	0.294 (0.18 to 0.48)
Marcus 2015	FLU 28 vs. FGA OAPs	0.931 (0.63 to 1.39)
Marcus 2015	ALO 28 vs. FGA OAPs	0.91 (0.72 to 1.16)
Marcus 2015	RIS 14 vs. SGA OAPs	0.804 (0.57 to 1.14)
Marcus 2015	PAL 28 vs. SGA OAPs	0.695 (0.48 to 1)
Morrato EH, 2015	PAL 28 vs. SGA OAPs	0.904 (0.69 to 1.19)
Morritt 1974	FLU 28 vs. FLU oral	0.283 (0.17 to 0.49)
Peng 2011	SGA LAIs 21 vs. SGA OAPs	0.469 (0.33 to 0.67)
Polonowita 1976	FLU 28 vs. FLU oral	0.414 (0.27 to 0.64)
Ren 2011	RIS 14 vs. RIS oral	0.742 (0.68 to 0.81)
Schreiner A, 2014	RIS 14 vs. SGA OAPs	0.654 (0.46 to 0.92)
Taipale 2018	ZUC 14 vs. ZUC oral	0.92 (0.85 to 0.99)
Taipale 2018	RIS 14 vs. RIS oral	0.79 (0.75 to 0.84)
Taipale 2018	PER 14 vs. PER oral	0.81 (0.76 to 0.86)
Taipale 2018	OLA 14 vs. OLA oral	0.83 (0.7 to 0.98)
Taipale 2018	ALO 28 vs. ALO oral	0.83 (0.77 to 0.9)
Taipale 2018	FLU 14 vs. FLU oral	0.87 (0.63 to 1.21)
Taipale 2018	FLUP 21 vs. FLUP oral	1.01 (0.85 to 1.2)
Taipale 2018	ARI 28 vs. ARI oral	0.94 (0.75 to 1.18)
Taipale 2018	PAL 28 vs. OLA oral	0.82 (0.64 to 1.05)
Tan 1981	FLU 28 vs. FLU oral	0.8 (0.64 to 1)
Tiihonen 2006	OLA oral vs. ALO oral	0.54 (0.41 to 0.71)
Tiihonen 2006	RIS oral vs. ALO oral	0.89 (0.69 to 1.15)
Tiihonen 2011	RIS 14 vs. RIS oral	0.57 (0.3 to 1.08)
Tiihonen 2011	ZUC 14 vs. ZUC oral	0.49 (0.11 to 2.16)
Tiihonen 2011	ALO 28 vs. ALO oral	0.12 (0.01 to 1.28)

Study	Comparison	Relative effectiveness (95% CI)
Tiihonen 2017	RIS 14 vs. RIS oral	0.859 (0.7 to 1.05)
Tiihonen 2017	ZUC 14 vs. ZUC oral	0.791 (0.64 to 0.98)
Tiihonen 2017	OLA 14 vs. OLA oral	0.921 (0.65 to 1.31)
Tiihonen 2017	ALO 28 vs. ALO oral	0.79 (0.6 to 1.03)
Voss EA, 2015	PAL 28 vs. OAPs	0.54 (0.32 to 0.92)
Waldmann 1984	FLU 28 vs. FLU oral	0.201 (0.14 to 0.3)

ALO = haloperidol; ARI = aripiprazole; FLU = fluphenazine; FLUP: flupentixol; OAP = oral antipsychotics; OLA = olanzapine; PAL = paliperidone; RIS = risperidone; SGA = second generation antipsychotics; ZUC = zuclopentixol

Table S 4 – Results of metanalysis, not used in economical analysis

Frequency	Typical	Atypical
Daily (OAPs) - reference	1	0.89 (0.69 to 1.15)
Every 2 weeks	NA	0.61 (0.47 to 0.79)
Three-weekly	0.77 (0.72 to 0.82)	NA
Monthly	0.73 (0.66 to 0.81)	0.55 (0.43 to 0.71)
Quarterly	NA	0.36 (0.21 to 0.59)
Semi-annual	NA	0.21 (0.06 to 0.53)
Treatment effect	**RR (95% CI)**	**Credibility***
Typical LAIs vs. OAPs	0.81 (0.78 to 0.84)	100.0%
Atypical vs. Typical LAIs	0.85 (0.65 to 1.08)	91.4%
Inter-dose interval double-up	0.90 (0.81 to 0.99)	98.3%

Figure S 1 – Relative reduction in relapse rate of all the drugs evaluated in metanalysis vs oral haloperidol (reference)