# Supplementary Figure S6. Forest plot: Subgroup analysis, factors related to patients' demographic and clinical characteristics

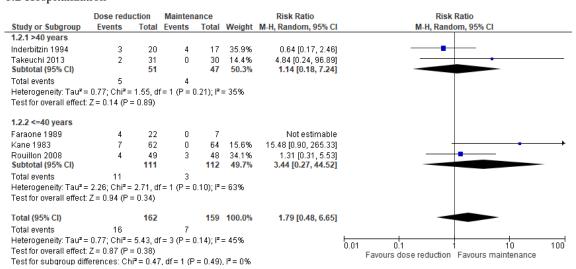
#### A. Mean age

#### 1. Relapse/Hospitalization

#### 1.1 Relapse (primary outcome)

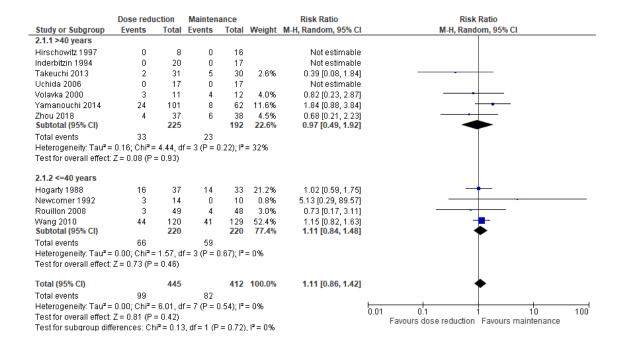
	Dose redu	iction	Mainten	Maintenance		Risk Ratio	Risk Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI			
1.1.1 >40 years										
Cookson 1987	3	9	1	9	4.6%	3.00 [0.38, 23.68]	<del>-   •</del>			
Inderbitzin 1994	5	20	4	17	11.5%	1.06 [0.34, 3.34]				
Takeuchi 2013	1	31	1	30	2.8%	0.97 [0.06, 14.78]				
Uchida 2006	0	17	0	17		Not estimable				
Volavka 2000	1	11	1	12	3.0%	1.09 [0.08, 15.41]	-			
Zhou 2018	4	37	6	38	11.0%	0.68 [0.21, 2.23]	<del></del>			
Subtotal (95% CI)		125		123	33.0%	1.02 [0.50, 2.07]	•			
Total events	14		13							
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup> =	1.49, dt	f = 4 (P = 0	).83); l²:	= 0%					
Test for overall effect:	Z = 0.06 (P = 0.06)	= 0.96)								
1.1.2 <=40 years										
Hogarty 1988	9	37	6	33	14.9%	1.34 [0.53, 3.36]	<del></del>			
Johnson 1987	9	28	3	31	10.8%	3.32 [1.00, 11.06]	-			
Kane 1983	26	62	3	64	11.5%	8.95 [2.85, 28.05]				
Newcomer 1992	3	14	0	10	2.6%	5.13 [0.29, 89.57]				
Rouillon 2008	4	49	3	48	8.3%	1.31 [0.31, 5.53]	<del></del>			
Wang 2010	19	120	10	129	18.9%	2.04 [0.99, 4.21]				
Subtotal (95% CI)		310		315	67.0%	2.56 [1.38, 4.75]	-			
Total events	70		25							
Heterogeneity: Tau <sup>2</sup> =	0.23; Chi <sup>2</sup> =	8.48, dt	f = 5 (P = 0)	).13); l²:	= 41%					
Test for overall effect:	Z = 2.98 (P :	= 0.003)								
Total (95% CI)		435		438	100.0%	1.90 [1.18, 3.07]	•			
Total events	84	.00	38			[, 0.07]	_			
Heterogeneity: Tau <sup>2</sup> =		14.22		- 0.16)	12 - 3004					
Test for overall effect:				- 0.10),	1 - 3070		0.01 0.1 1 10 100			
Test for subgroup diffe	,			- 0.06)	I2 - 72 7	٥٤.	Favours dose reduction Favours maintenance			
restror subdroub and	erences. Of	11 - 3.07	, ui = T (F	- 0.00)	11 - 72.7	70				

#### 1.2 Hospitalization

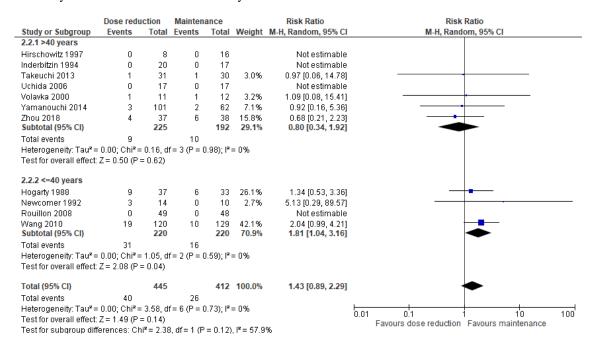


#### 2. Study discontinuation

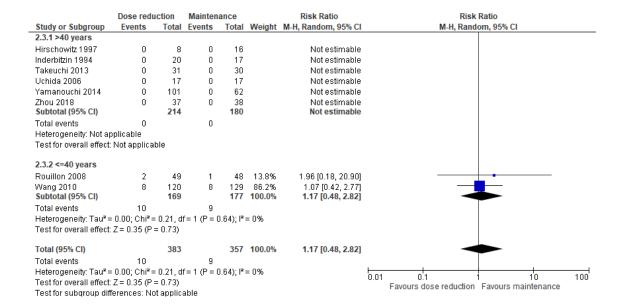
#### 2.1 Study discontinuation due to all causes



#### 2.2 Study discontinuation due to inefficacy

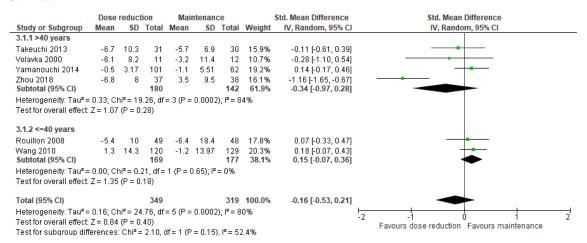


#### 2.3 Study discontinuation due to intolerability

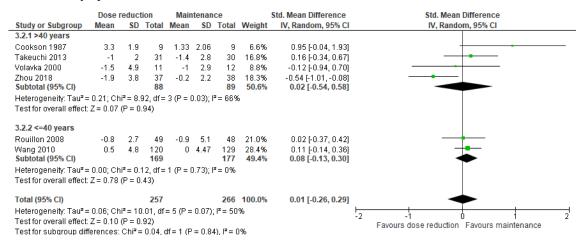


## 3. Psychopathology

#### 3.1 Total



#### 3.2 Positive symptoms



# 3.3 Negative symptoms

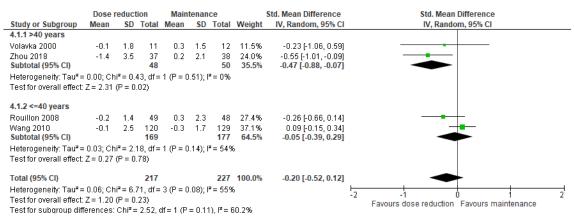
	Dose	Dose reduction Maintenance						Std. Mean Difference	Std. Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
3.3.1 >40 years											
Takeuchi 2013	-3	3.7	31	-1.3	2.8	30	19.6%	-0.51 [-1.02, 0.00]			
Volavka 2000	-1.1	2.9	11	0.1	1.9	12	13.4%	-0.48 [-1.31, 0.36]			
Zhou 2018	-2.4	7.4	37	3.7	6.6	38	20.3%	-0.86 [-1.34, -0.39]	<del></del>		
Subtotal (95% CI)			79			80	53.3%	-0.67 [-0.99, -0.35]	•		
Heterogeneity: Tau <sup>2</sup> :	= 0.00; Ch	$ii^2 = 1.3$	21, df=	2 (P = I	0.55);	$l^2 = 0\%$					
Test for overall effect	:: Z = 4.07	(P ≤ 0.	.0001)								
3.3.2 <=40 years											
Rouillon 2008	-2	3.6	49	-1.9	5.6	48	21.9%	-0.02 [-0.42, 0.38]	<del></del>		
Wang 2010	-0.5	3.9	120	-1.3	4.19	129	24.8%	0.20 [-0.05, 0.45]	<del>  </del>		
Subtotal (95% CI)			169			177	46.7%	0.14 [-0.08, 0.35]	<b>◆</b>		
Heterogeneity: Tau2:	= 0.00; Ch	$ii^2 = 0.8$	83, df=	1 (P = I	0.36);	$l^2 = 0\%$					
Test for overall effect	:: Z = 1.26	(P = 0.	.21)								
Total (95% CI)			248			257	100.0%	-0.29 [-0.72, 0.13]	-		
Heterogeneity: Tau <sup>2</sup> :	= 0.18; Ch	ıi² = 18	3.77, df	= 4 (P =	0.000		2 -1 1				
Test for overall effect	: Z = 1.35	(P = 0.	.18)			-2 -1 U 1 Favours dose reduction Favours maintenance					
Test for subgroup di	fferences:	Chi <sup>2</sup> =	: 16.73	. df = 1 (	i	i avours dose reduction. Favours maintenance					

#### 3.4 CGI-S

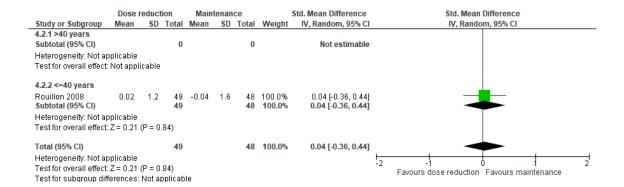
	Dose	reduct	tion	Maintenance Std. Mean Dif				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
3.4.1 >40 years									
Takeuchi 2013	-0.2	0.7	31	0	0.6	30	14.3%	-0.30 [-0.81, 0.20]	
Yamanouchi 2014	-0.1	0.55	101	0	1.06	62	34.0%	-0.13 [-0.44, 0.19]	<del></del>
Subtotal (95% CI)			132			92	48.3%	-0.18 [-0.44, 0.09]	•
Heterogeneity: Tau <sup>2</sup> =	= 0.00; CI	hi <b>=</b> 0.3	33, df=	1 (P = 0)	0.56); I	<sup>2</sup> = 0%			
Test for overall effect	Z = 1.29	(P = 0	.20)						
3.4.2 <=40 years									
Wang 2010	-0.1	1.1	120	-0.2	1.4	129	51.7%	0.08 [-0.17, 0.33]	<del>-</del>
Subtotal (95% CI)			120			129	51.7%	0.08 [-0.17, 0.33]	<b>*</b>
Heterogeneity: Not ap	pplicable								
Test for overall effect	Z = 0.62	(P = 0)	.53)						
Total (95% CI)			252			221	100.0%	-0.05 [-0.24, 0.15]	•
Heterogeneity: Tau <sup>2</sup> =	= 0.00; CI	hi <b>=</b> 2.3	21, df=	2(P = 0)	0.33); [	<sup>2</sup> = 9%			-2 -1 1 2
Test for overall effect: Z = 0.46 (P = 0.65)									Favours dose reduction Favours maintenance
Test for subgroup differences: Chi <sup>2</sup> = 1.87, df = 1 (P = 0.17), $I^2$ = 46.6%									1 avours dose reduction 1 avours maintenance

#### 4. Adverse effects

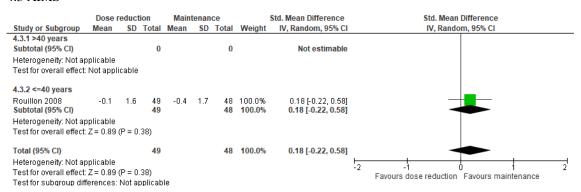
#### 4.1 SAS



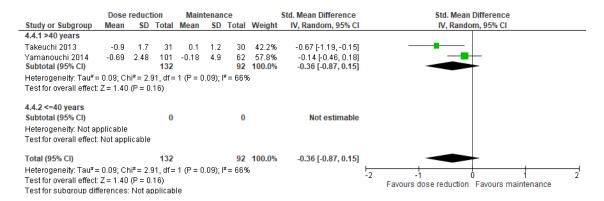
#### **4.2 BARS**



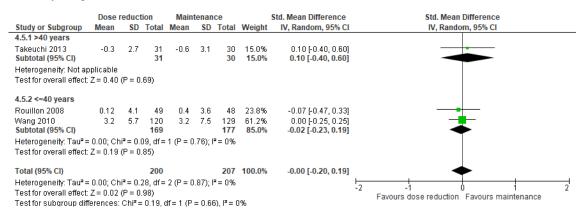
#### **4.3 AIMS**



#### 4.4 DIEPSS



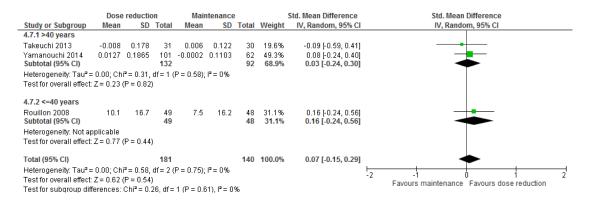
#### 4.5 Body weight



#### 4.6 Neurocognition

	Dose	reduct	ion	Mair	itenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.6.1 >40 years									
Takeuchi 2013	7	7.1	31	-0.1	8	30	45.4%	0.93 [0.40, 1.46]	
Zhou 2018	9.8	13.7	37	3.6	11.5	38	54.6%	0.49 [0.03, 0.95]	<del></del>
Subtotal (95% CI)			68			68	100.0%	0.69 [0.25, 1.12]	
Heterogeneity: Tau2:	= 0.03; Ch	$ni^2 = 1.5$	52, df=	1 (P = I	0.22); I	<sup>2</sup> = 349	6		
Test for overall effect	t: Z = 3.12	(P = 0	.002)						
4.6.2 <=40 years									
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not a	pplicable								
Test for overall effect	: Not app	licable							
Total (95% CI)			68			68	100.0%	0.69 [0.25, 1.12]	-
Heterogeneity: Tau <sup>2</sup> :	= 0.03; Ch	ni² = 1.5	52, df=	1 (P = I		-2 -1 0 1 2			
Test for overall effect	t: Z = 3.12	(P = 0)	.002)						-2 -1 U 1 2 Favours maintenance Favours dose reduction
Test for subgroup dit	fferences	: Not a	pplicab	ile					Favours maintenance Favours dose reduction

#### 4.7 QOL

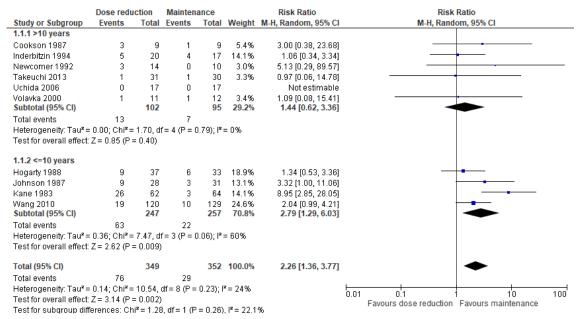


Abbreviations: AIMS, Abnormal Involuntary Movement Scale; BARS, Barnes Akathisia Rating Scale; CGI-S, Clinical Global Impressions – Severity scale; DIEPSS, Drug-Induced Extrapyramidal Symptoms Scale; QOL, quality of life; SAS, Simpson-Angus Scale

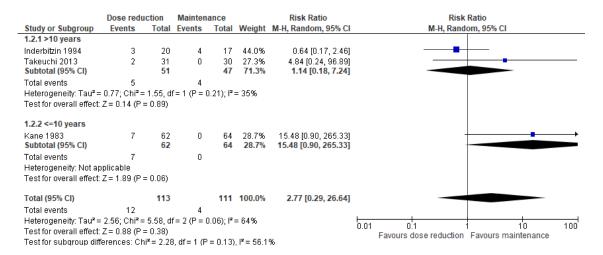
#### B. Mean illness duration

#### 1. Relapse/Hospitalization

#### 1.1 Relapse (primary outcome)

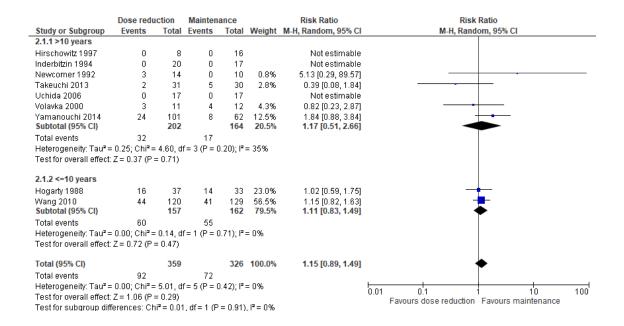


#### 1.2 Hospitalization

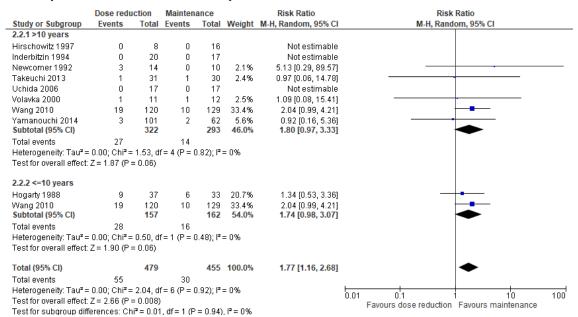


#### 2. Study discontinuation

#### 2.1 Study discontinuation due to all causes



#### 2.2 Study discontinuation due to inefficacy

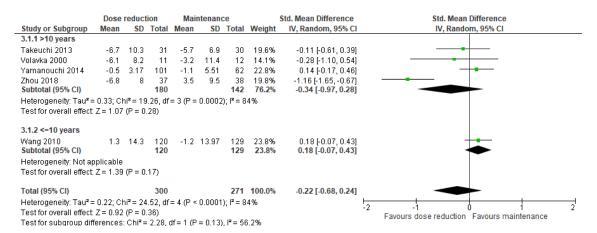


## 2.3 Study discontinuation due to intolerability

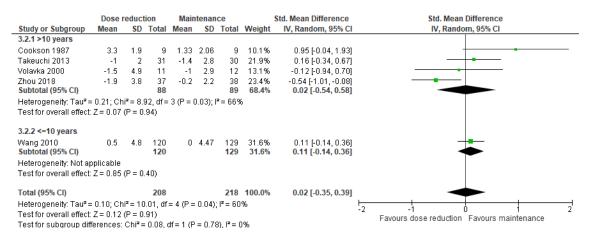
Risk Ratio		
100		
_		

# 3. Psychopathology

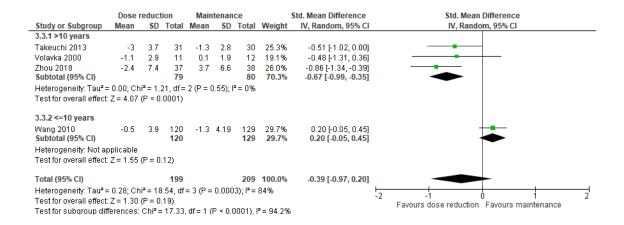
#### 3.1 Total



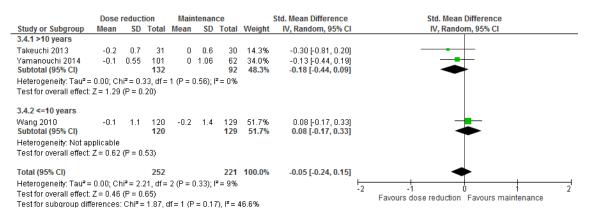
#### 3.2 Positive symptoms



#### 3.3 Negative symptoms

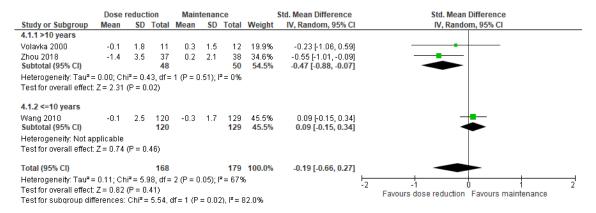


#### 3.4 CGI-S



#### 4. Adverse effects

#### 4.1 SAS



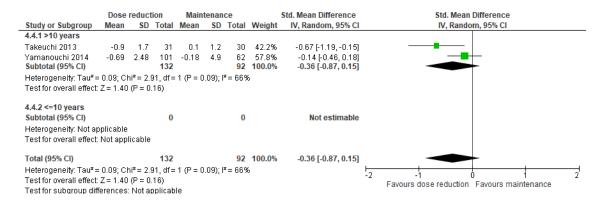
#### **4.2 BARS**

	Dose re	eductio	on	Main	tenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD 7	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.2.1 >10 years									
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not ap	plicable								
Test for overall effect:	Not applic	able							
4.2.2 <=10 years									
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not ap	plicable								
Test for overall effect:	Not applic	able							
Total (95% CI)			0			0		Not estimable	
Heterogeneity: Not ap	plicable								<u> </u>
Test for overall effect:	Not applic	able							-2 -1 0 1 2  Favours dose reduction Favours maintenance
Test for subaroun diffe	roncoe: N	dot ann	nlicahl	lo .					ravours dose reduction Favours maintenance

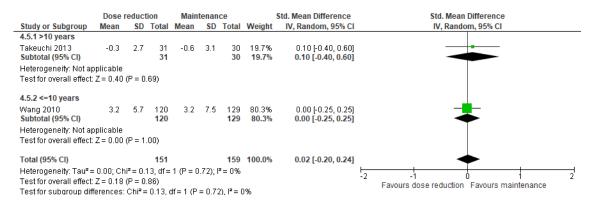
#### **4.3 AIMS**

Study on Sub	Dose r				tenan			Std. Mean Difference				Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI			iv, Rando	om, 95% CI		
4.3.1 >10 years														
Subtotal (95% CI)			0			0		Not estimable						
Heterogeneity: Not ap	plicable													
Test for overall effect:	Not appli	cable												
4.3.2 <=10 years														
Subtotal (95% CI)			0			0		Not estimable						
Heterogeneity: Not ap	plicable													
Test for overall effect:	Not appli	cable												
Total (95% CI)			0			0		Not estimable						
Heterogeneity: Not ap	plicable								-2	+		<del>!</del>	<del>                                     </del>	
Test for overall effect:	Not appli	cable							-2	Favours dos	e reduction	Eavoure m	aintenance	2
Test for subgroup diff	erences:	Not a	pplicab	le						i avouis uos	e readcitori	i avouis iii	annendice	

# 4.4 DIEPSS



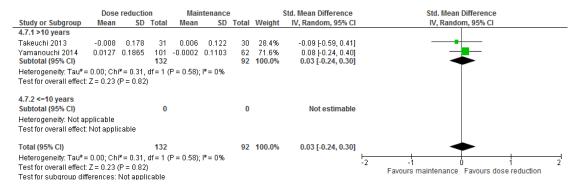
# 4.5 Body weight



#### 4.6 Neurocognition

	Dose reduction Maintenance				ce		Std. Mean Difference	Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	I IV, Random, 95% CI
4.6.1 >10 years									
Takeuchi 2013	7	7.1	31	-0.1	8	30	45.4%	0.93 [0.40, 1.46]	
Zhou 2018	9.8	13.7	37	3.6	11.5	38	54.6%	0.49 [0.03, 0.95]	<del>   </del>
Subtotal (95% CI)			68			68	100.0%	0.69 [0.25, 1.12]	
Heterogeneity: Tau2:	= 0.03; CI	$hi^2 = 1.9$	52, df=	1 (P = I	0.22); [	$^{2} = 349$	6		
Test for overall effect	t: Z = 3.12	(P = 0	.002)						
4.6.2 <=10 years									
Subtotal (95% CI)			0			0		Not estimable	•
Heterogeneity: Not a	pplicable								
Test for overall effect	: Not app	licable							
Total (95% CI)			68			68	100.0%	0.69 [0.25, 1.12]	
Heterogeneity: Tau2:	= 0.03; CI	hi² = 1.	52, df=	1 (P = I	0.22); [	<sup>2</sup> = 349	6		
Test for overall effect	t: Z = 3.12	(P = 0	.002)	•	- ''				-2 -1 0 1 Favours maintenance Favours dose reduction
Test for subgroup dit	fferences	· Not a	nnlicah	ile					Favours maintenance Favours dose reduction

#### 4.7 QOL

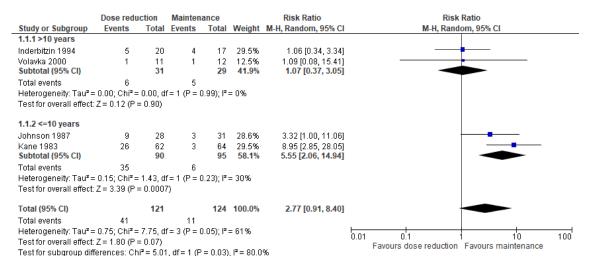


Abbreviations: AIMS, Abnormal Involuntary Movement Scale; BARS, Barnes Akathisia Rating Scale; CGI-S, Clinical Global Impressions – Severity scale; DIEPSS, Drug-Induced Extrapyramidal Symptoms Scale; QOL, quality of life; SAS, Simpson-Angus Scale

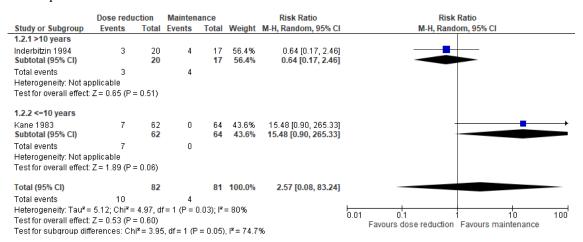
#### C. Mean treatment duration

## 1. Relapse/Hospitalization

#### 1.1 Relapse (primary outcome)



#### 1.2 Hospitalization



# 2. Study discontinuation

## 2.1 Study discontinuation due to all causes

	Dose redu	Dose reduction Maintena		ance		Risk Ratio	Risk Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI			
2.1.1 >10 years										
Hirschowitz 1997	0	8	0	16		Not estimable				
Inderbitzin 1994	0	20	0	17		Not estimable				
Volavka 2000 Subtotal (95% CI)	3	11 <b>39</b>	4	12 <b>45</b>	100.0% <b>100.0%</b>	0.82 [0.23, 2.87] <b>0.82 [0.23, 2.87]</b>				
Total events	3		4							
Heterogeneity: Not as	pplicable									
Test for overall effect	Z= 0.31 (P	= 0.75)								
2.1.2 <=10 years										
Subtotal (95% CI)		0		0		Not estimable				
Total events	0		0							
Heterogeneity: Not ap	pplicable									
Test for overall effect	: Not applica	ble								
Total (95% CI)		39		45	100.0%	0.82 [0.23, 2.87]				
Total events	3		4							
Heterogeneity: Not as	pplicable									
Test for overall effect	: Z = 0.31 (P :	= 0.75)					0.01 0.1 1 10 100 Favours dose reduction Favours maintenance			
Test for subaroup dif	ferences: No	t applic	able				ravours dose reduction Favours maintenance			

# 2.2 Study discontinuation due to inefficacy

D	ose reduc	ction	Mainten	ance		Risk Ratio	Risk Ratio
Study or Subgroup E	vents	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
2.2.1 >10 years							
Hirschowitz 1997	0	8	0	16		Not estimable	
Inderbitzin 1994	0	20	0	17		Not estimable	$\perp$
Volavka 2000	1	11	1	12	100.0%	1.09 [0.08, 15.41]	
Subtotal (95% CI)		39		45	100.0%	1.09 [0.08, 15.41]	
Total events	1		1				
Heterogeneity: Not applic	able						
Test for overall effect: Z=	0.06 (P =	0.95)					
2.2.2 <=10 years							
Subtotal (95% CI)		0		0		Not estimable	
Total events	0		0				
Heterogeneity: Not applic	able						
Test for overall effect: No	t applicabl	le					
Total (95% CI)		39		45	100.0%	1.09 [0.08, 15.41]	
Total events	1		1				
Heterogeneity: Not applic	able						
Test for overall effect: Z =		0.95)					0.01 0.1 1 10 100
Test for subaroup differe			able				Favours dose reduction Favours maintenance

# 2.3 Study discontinuation due to intolerability

	Dose reduction		Maintenance			Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Rand	om, 95% CI	
2.3.1 >10 years										
Hirschowitz 1997	0	8	0	16		Not estimable				
Inderbitzin 1994	0	20	0	17		Not estimable				
Subtotal (95% CI)		28		33		Not estimable				
Total events	0		0							
Heterogeneity: Not ap	plicable									
Test for overall effect:	Not applicab	le								
2.3.2 <=10 years										
Subtotal (95% CI)		0		0		Not estimable				
Total events	0		0							
Heterogeneity: Not ap	plicable									
Test for overall effect:	Not applicat	le								
Total (95% CI)		28		33		Not estimable				
Total events	0		0							
Heterogeneity: Not ap	plicable						-		<u> </u>	100
Test for overall effect:		ile					0.01	0.1 Favours dose reduction	1 10	100
Test for subgroup diff			able					ravours dose reduction	ravours maintenam	Le

# 3. Psychopathology

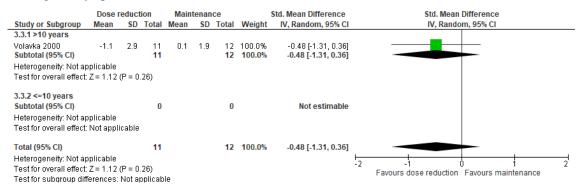
# 3.1 Total

	Dose reduction Maintenance					ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
3.1.1 >10 years									
Volavka 2000	-6.1	8.2	11	-3.2	11.4	12		-0.28 [-1.10, 0.54]	
Subtotal (95% CI)			11			12	100.0%	-0.28 [-1.10, 0.54]	
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 0.67	(P = 0.	51)						
3.1.2 <=10 years									
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not ap	plicable								
Test for overall effect:	Not appli	icable							
Total (95% CI)			11			12	100.0%	-0.28 [-1.10, 0.54]	
Heterogeneity: Not ap	plicable								-2 -1 1 2
Test for overall effect:	Z = 0.67	(P = 0.	51)						Favours dose reduction Favours maintenance
Test for subgroup diff	ferences:	Not a	oplicab	le					. around add readons. I around maintenance

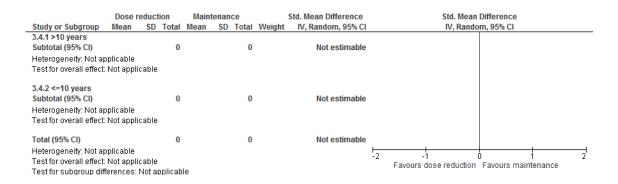
# 3.2 Positive symptoms

	Dose r	educt	ion	Main	tenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
3.2.1 >10 years									
Volavka 2000 Subtotal (95% CI)	-1.5	4.9	11 <b>11</b>	-1	2.9	12 <b>12</b>	100.0% <b>100.0</b> %	-0.12 [-0.94, 0.70] - <b>0.12 [-0.94, 0.70]</b>	
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 0.29 (	(P = 0.	.77)						
3.2.2 <=10 years Subtotal (95% CI) Heterogeneity: Not ap Test for overall effect:		icable	0			0		Not estimable	
restroi overali ellect.	140t appii	cabic							
Total (95% CI) Heterogeneity: Not ap Test for overall effect: Test for subgroup diff	Z = 0.29 (			le		12	100.0%	-0.12 [-0.94, 0.70]	-2 -1 0 1 2 Favours dose reduction Favours maintenance

# 3.3 Negative symptoms



# 3.4 CGI-S



# 4. Adverse effects

# 4.1 SAS

	Dose r	reduct	tion	Main	tenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.1.1 >10 years									
Volavka 2000 Subtotal (95% CI)	-0.1	1.8	11 <b>11</b>	0.3	1.5	12 <b>12</b>	100.0% <b>100.0%</b>	-0.23 [-1.06, 0.59] - <b>0.23 [-1.06, 0.59]</b>	
Heterogeneity: Not app	olicable								
Test for overall effect: 2	Z = 0.56	(P = 0	.58)						
4.1.2 <=10 years									
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not app	licable								
Test for overall effect: N	Vot appli	icable							
Total (95% CI)			11			12	100.0%	-0.23 [-1.06, 0.59]	
Heterogeneity: Not app	licable								
Test for overall effect: Z	Z= 0.56	(P = 0)	.58)						-2 -1 0 1 2 Favours dose reduction Favours maintenance
Test for subgroup diffe	rences:	Not a	pplicab	le					Favours dose reduction Favours maintenance

# 4.2 BARS

I	Dose red	uction	Main	tenan	ce		Std. Mean Difference		Std. Mean Diff	ference
Study or Subgroup N	lean 9	SD Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random,	95% CI
4.2.1 >10 years										
Subtotal (95% CI)		0			0		Not estimable			
Heterogeneity: Not appli	cable									
Test for overall effect: No	t applicat	ole								
4.2.2 <=10 years										
Subtotal (95% CI)		0			0		Not estimable			
Heterogeneity: Not applie	cable									
Test for overall effect: No	t applicat	ole								
Total (95% CI)		0			0		Not estimable			
Heterogeneity: Not applic	cable							<u>-2</u>	<u> </u>	<u> </u>
Test for overall effect: No	t applicat	ole						-2	-1 U Favours dose reduction Fa	1 2
Test for subgroup differe	nces: No	t annlicah	ile						ravours dose reduction Fa	avours mannerlance

# 4.3 AIMS

	Dose reduct	tion	Maint	tenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup 1	Mean SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	CI IV, Random, 95% CI
4.3.1 > 10 years Subtotal (95% CI) Heterogeneity: Not appl	licable	0			0		Not estimable	е
Test for overall effect: N  4.3.2 <=10 years Subtotal (95% CI) Heterogeneity: Not appl Test for overall effect: N	icable	0			0		Not estimable	е
Total (95% CI) Heterogeneity: Not appl Test for overall effect: N Test for subgroup differ	ot applicable		le		0		Not estimable	e

# 4.4 DIEPSS

	Dose red	duction	Mair	itenance		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD To	al Mean	SD Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.4.1 >10 years							
Subtotal (95% CI)			0	0		Not estimable	
Heterogeneity: Not appl	licable						
Test for overall effect: N	ot applica	able					
4.4.2 <=10 years							
Subtotal (95% CI)			0	0		Not estimable	
Heterogeneity: Not appl	licable						
Test for overall effect: N	ot applica	able					
Total (95% CI)			0	0		Not estimable	
Heterogeneity: Not appl	licable						
Test for overall effect: N	ot applica	able					-2 -1 0 1 2  Favours dose reduction Favours maintenance
Tast for subarous differ	ences N	lot annlic	ahle				ravours dose reduction Favours maintenance

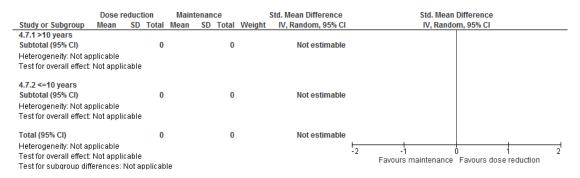
# 4.5 Body weight

	Dose reduc	tion	Main	tenan	ce		Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI
4.5.1 > 10 years Subtotal (95% CI) Heterogeneity: Not ap Test for overall effect:	•	0			0		Not estimable		
4.5.2 <=10 years Subtotal (95% CI) Heterogeneity: Not ap Test for overall effect:	•	0			0		Not estimable		
Total (95% CI) Heterogeneity: Not ap Test for overall effect: Test for subgroup diffe	Not applicable		ile		0		Not estimable	-2	-1 0 1 2 Favours dose reduction Favours maintenance

#### 4.6 Neurocognition

	Dose r	educt	ion	Main	tenan	се		Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI
4.6.1 >10 years										
Subtotal (95% CI)			0			0		Not estimable		
Heterogeneity: Not ap	plicable									
Test for overall effect:	Not appli	icable								
4.6.2 <=10 years										
Subtotal (95% CI)			0			0		Not estimable		
Heterogeneity: Not ap	plicable									
Test for overall effect:	Not appli	icable								
Total (95% CI)			0			0		Not estimable		
Heterogeneity: Not ap	plicable								<u> </u>	<del></del>
Test for overall effect:	Not appli	icable							-2	-1 U 1 2 Favours maintenance Favours dose reduction
Teet for eubaroun diff				lo.						ravours maintenance ravours dose reduction

# 4.7 QOL

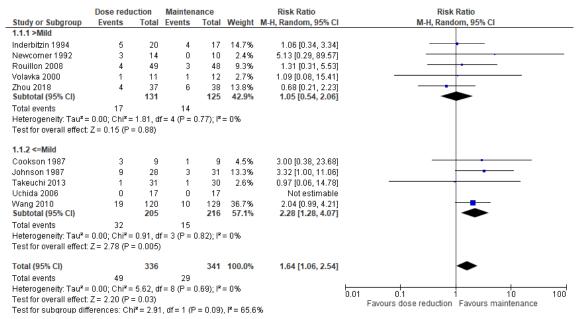


Abbreviations: AIMS, Abnormal Involuntary Movement Scale; BARS, Barnes Akathisia Rating Scale; CGI-S, Clinical Global Impressions – Severity scale; DIEPSS, Drug-Induced Extrapyramidal Symptoms Scale; QOL, quality of life; SAS, Simpson-Angus Scale

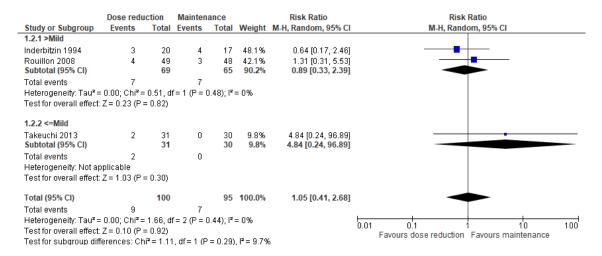
#### D. Mean symptom severity

#### 1. Relapse/Hospitalization

#### 1.1 Relapse (primary outcome)

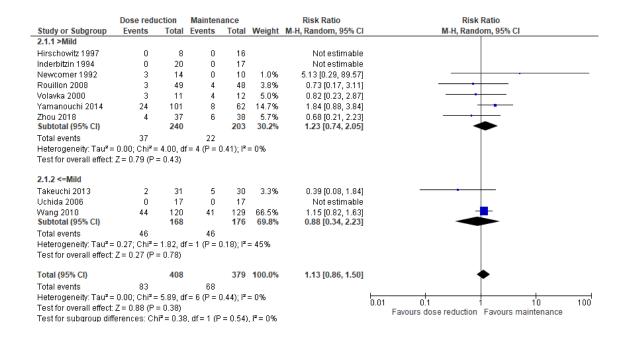


#### 1.2 Hospitalization

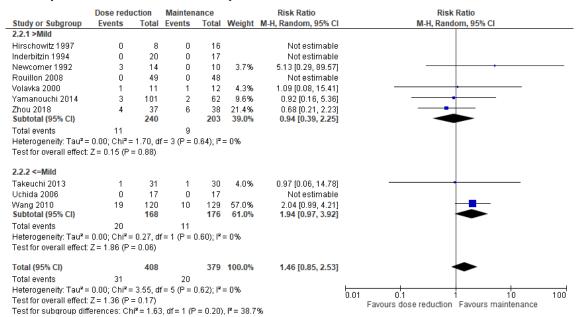


# 2. Study discontinuation

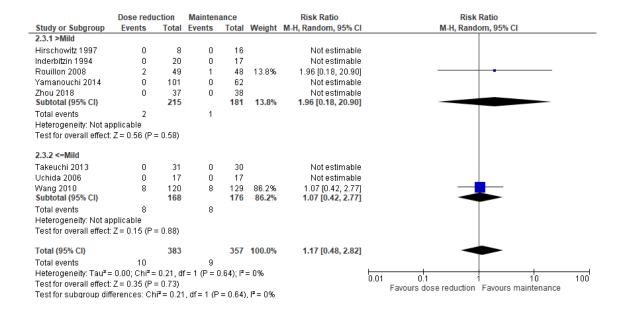
# 2.1 Study discontinuation due to all causes



#### 2.2 Study discontinuation due to inefficacy

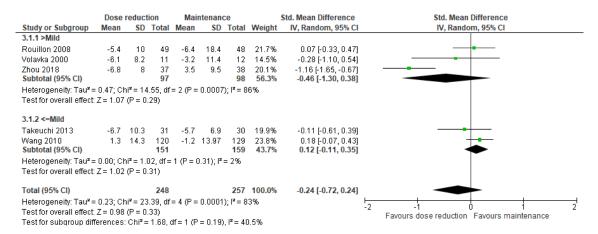


## 2.3 Study discontinuation due to intolerability

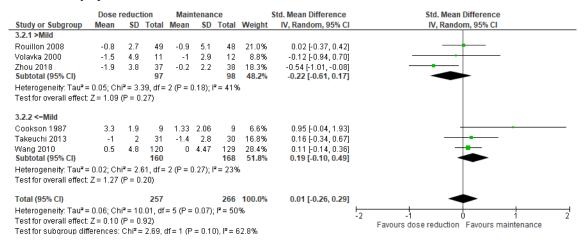


## 3. Psychopathology

#### 3.1 Total



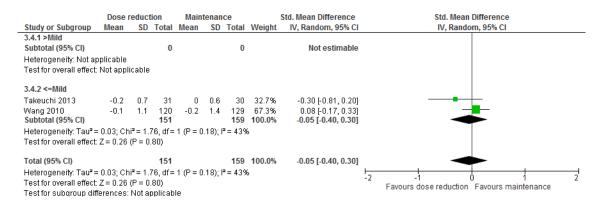
#### 3.2 Positive symptoms



#### 3.3 Negative symptoms

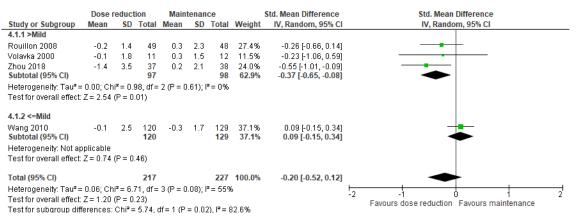
	Dose	reduct	tion	Main	itenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
3.3.1 >Mild									
Rouillon 2008	-2	3.6	49	-1.9	5.6	48	21.9%	-0.02 [-0.42, 0.38]	
Volavka 2000	-1.1	2.9	11	0.1	1.9	12	13.4%	-0.48 [-1.31, 0.36]	<del></del>
Zhou 2018	-2.4	7.4	37	3.7	6.6	38	20.3%	-0.86 [-1.34, -0.39]	
Subtotal (95% CI)			97			98	55.7%	-0.44 [-1.02, 0.15]	
Heterogeneity: Tau2:	= 0.19; Ch	ni <b>=</b> 7.1	14, df=	2 (P = 0	0.03);	P = 729	6		
Test for overall effect	Z = 1.47	(P = 0	.14)						
3.3.2 <=Mild									
Takeuchi 2013	-3	3.7	31	-1.3	2.8	30	19.6%	-0.51 [-1.02, 0.00]	
Wang 2010	-0.5	3.9	120	-1.3	4.19	129	24.8%	0.20 [-0.05, 0.45]	_+-
Subtotal (95% CI)			151			159	44.3%	-0.12 [-0.81, 0.57]	
Heterogeneity: Tau2:	= 0.21; Ch	ni² = 5.9	95, df=	1 (P = 0)	0.01);	r= 839	6		
Test for overall effect	Z = 0.34	(P = 0	.73)						
Total (95% CI)			248			257	100.0%	-0.29 [-0.72, 0.13]	
Heterogeneity: Tau <sup>2</sup> :	= 0.18; Ch	ni² = 18	3.77, df	= 4 (P =	0.000	9); l²=	79%	H	2 -1 0
Test for overall effect	: Z = 1.35	(P = 0)	.18)					•	-2 -1 U 1 Favours dose reduction Favours maintenance
Test for subgroup dit	ferences:	Chi <sup>2</sup> =	0.47.	df = 1 (P	= 0.4	9), $I^2 = 0$	0%		i avours dose reduction. Edvours maintenance

#### 3.4 CGI-S



#### 4. Adverse effects

#### 4.1 SAS



#### **4.2 BARS**

	Dose r	educt	ion	Main	tenan	ce		Std. Mean Difference		Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	
4.2.1 >Mild										<u>L</u>	
Rouillon 2008 Subtotal (95% CI)	0.02	1.2	49 <b>49</b>	-0.04	1.6	48 <b>48</b>	100.0% <b>100.0%</b>	0.04 [-0.36, 0.44] <b>0.04 [-0.36, 0.44]</b>		-	
Heterogeneity: Not a	pplicable										
Test for overall effect	Z = 0.21 (	(P = 0.	.84)								
4.2.2 <=Mild											
Subtotal (95% CI)			0			0		Not estimable			
Heterogeneity: Not a	oplicable										
Test for overall effect	Not appli	cable									
Total (95% CI)			49			48	100.0%	0.04 [-0.36, 0.44]			
Heterogeneity: Not ap Test for overall effect Test for subgroup dif	Z= 0.21 (	•		le					-2	-1 0 1 Favours dose reduction Favours maintenance	<u></u>

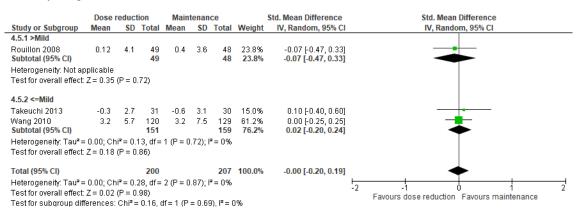
#### **4.3 AIMS**

	Dose re	educt	ion	Main	tenan	ce		Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI
4.3.1 >Mild										
Rouillon 2008 Subtotal (95% CI)	-0.1	1.6	49 <b>49</b>	-0.4	1.7	48 <b>48</b>	100.0% <b>100.0%</b>	0.18 [-0.22, 0.58] <b>0.18 [-0.22, 0.58]</b>		-
Heterogeneity: Not ap	oplicable									
Test for overall effect:	Z = 0.89 (	P = 0	38)							
4.3.2 <=Mild										
Subtotal (95% CI)			0			0		Not estimable		
Heterogeneity: Not ap	plicable									
Test for overall effect:	Not appli	cable								
Total (95% CI)			49			48	100.0%	0.18 [-0.22, 0.58]		-
Heterogeneity: Not ap Test for overall effect: Test for subgroup diff	Z=0.89 (			le					-2	Favours dose reduction Favours maintenance

# 4.4 DIEPSS

	Dose	reduct	tion	Main	tenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	CI IV, Random, 95% CI
4.4.1 >Mild									
Subtotal (95% CI)			0			0		Not estimable	le
Heterogeneity: Not ap	plicable								
Test for overall effect:	Not appl	icable							
4.4.2 <=Mild									_
Takeuchi 2013	-0.9	1.7	31	0.1	1.2	30	100.0%	-0.67 [-1.19, -0.15]	
Subtotal (95% CI)			31			30	100.0%	-0.67 [-1.19, -0.15]	5]
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 2.54	(P = 0)	.01)						
Total (95% CI)			31			30	100.0%	-0.67 [-1.19, -0.15]	5]
Heterogeneity: Not ap	plicable								-2 -1 0 1 2
Test for overall effect:	Z = 2.54	(P = 0)	.01)						Favours dose reduction Favours maintenance
Test for subgroup diff	ferences:	Not a	pplicab	le					i avouis uose reduction. Favouis ilidiliteridiice

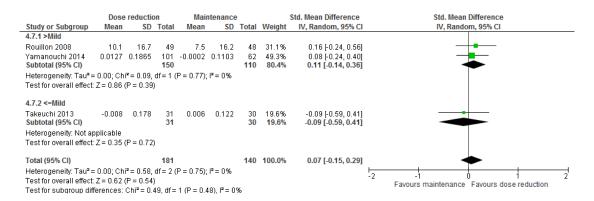
# 4.5 Body weight



# 4.6 Neurocognition

	Dose	reduct	ion	Main	itenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	CI IV, Random, 95% CI
4.6.1 >Mild									
Zhou 2018	9.8	13.7	37 <b>37</b>	3.6	11.5	38 <b>38</b>	54.6%	0.49 [0.03, 0.95]	
Subtotal (95% CI)			31			36	54.6%	0.49 [0.03, 0.95]	
Heterogeneity: Not ap									
Test for overall effect	Z = 2.07	(P = 0.	.04)						
4.6.2 <=Mild									
Takeuchi 2013	7	7.1	31	-0.1	8	30	45.4%	0.93 [0.40, 1.46]	6)
Subtotal (95% CI)			31			30	45.4%	0.93 [0.40, 1.46]	
Heterogeneity: Not ap	pplicable								
Test for overall effect	Z = 3.43	(P = 0.	0006)						
Total (95% CI)			68			68	100.0%	0.69 [0.25, 1.12]	
Heterogeneity: Tau* =	= 0.03; CH	$ni^2 = 1.5$	52, df=	1 (P = 0	0.22); f	<sup>2</sup> = 349	5		1 1
Test for overall effect	Z=3.12	(P = 0.	002)						-2 -1 0 1 Favours maintenance Favours dose reduction
Test for subgroup dif		•		df=1 (P	= 0.22	2), <b>I²</b> = 3	34.4%		ravours maintenance Favours dose reduction

## 4.7 QOL



Abbreviations: AIMS, Abnormal Involuntary Movement Scale; BARS, Barnes Akathisia Rating Scale; CGI-S, Clinical Global Impressions – Severity scale; DIEPSS, Drug-Induced Extrapyramidal Symptoms Scale; QOL, quality of life; SAS, Simpson-Angus Scale