

## Supplementary Material

### The Atypical Antipsychotics and Sexual Dysfunction: A Pharmacovigilance-Pharmacodynamic Study

**Table S1 MedDRA Preferred Terms for Sexual Dysfunction manifestation.** We classify the PT terms with positive signals based on the manifestations of sexual dysfunction.

<b>Sexual Dysfunction manifestation</b>	<b>MedDRA preferred terms</b>
<b>Hypersexuality</b>	“compulsive sexual behavior,” “hypersexuality,” “excessive masturbation,” “libido increased.”
<b>Hyposexuality</b>	“sexual dysfunction,” “male sexual dysfunction,” “female sexual dysfunction,” “libido disorder,” “libido decreased,” “loss of libido,” “orgasm abnormal,” “male orgasmic disorder,” “female orgasmic disorder,” “disturbance in sexual arousal,” “anorgasmia.”
<b>Erectile Dysfunction</b>	“erectile dysfunction,” “priapism,” “painful erection,” “organic erectile dysfunction,” “spontaneous penile erection.”
<b>Ejaculatory Dysfunction</b>	“ejaculation disorder,” “ejaculation failure,” “ejaculation delayed,” “retrograde ejaculation,” “premature ejaculation.”
<b>Symptoms not specified</b>	“infertility,” “azoospermia,” “oligospermia,” “psychosexual disorder,” “paraphilia,” “exhibitionism,” “gender dysphoria,” “haematospermia.”



**Table S2 Continued**

HLGT	PT	Clozapine			Haloperidone			Lurasidone			Olanzapine		
		N	ROR (95%CI)	IC (95%CI)	N	ROR (95%CI)	IC (95%CI)	N	ROR (95%CI)	IC (95%CI)	N	ROR (95%CI)	IC (95%CI)
<b>Sexual function and fertility disorders</b>	Sexual dysfunction	105	2.63 (2.17-3.19)	1.38 (1.14-1.67)	10	20.53 (11-38.31)	4.34 (2.33-8.1)	37	5.12 (3.71-7.08)	2.35 (1.7-3.24)	159	8.16 (6.97-9.55)	2.99 (2.56-3.5)
	Priapism	30	2.15 (1.5-3.08)	1.09 (0.76-1.57)	19	113.98 (72.2-179.94)	6.79 (4.3-10.72)	-	-	-	87	12.97 (10.47-16.07)	3.64 (2.94-4.52)
	Retrograde ejaculation	10	3.79 (2.03-7.1)	1.9 (1.02-3.55)	25	832.09 (552.77-1252.56)	9.58 (6.36-14.42)	-	-	-	17	13.28 (8.18-21.56)	3.68 (2.27-5.98)
	Ejaculation failure	-	-	-	10	117.31 (62.73-219.4)	6.85 (3.66-12.8)	-	-	-	-	-	-
	Ejaculation disorder	-	-	-	8	64.87 (32.28-130.35)	6 (2.99-12.06)	-	-	-	15	2.98 (1.79-4.96)	1.57 (0.94-2.61)
	Erectile dysfunction	-	-	-	8	7.86 (3.92-15.78)	2.96 (1.48-5.95)	-	-	-	132	3.21 (2.7-3.81)	1.67 (1.4-1.98)
	Painful erection	-	-	-	-	-	-	-	-	-	20	14.98 (9.57-23.44)	3.85 (2.46-6.02)
	Infertility	-	-	-	-	-	-	-	-	-	12	4.61 (2.61-8.15)	2.19 (1.24-3.87)
	Haematospermia	-	-	-	-	-	-	-	-	-	6	5.28 (2.36-11.82)	2.38 (1.06-5.33)
<b>Sexual dysfunctions, disturbances and gender identity disorders</b>	Excessive masturbation	3	4.33 (1.38-13.61)	2.09 (0.66-6.56)	-	-	-	-	-	-	-	-	-
	Libido decreased	-	-	-	3	5.92 (1.91-18.4)	2.56 (0.82-7.96)	27	3.62 (2.48-5.29)	1.85 (1.27-2.7)	31	1.51 (1.06-2.15)	0.59 (0.42-0.84)
	Orgasm abnormal	-	-	-	3	83.63 (26.83-260.7)	6.37 (2.04-19.87)	-	-	-	5	3.44 (1.42-8.29)	1.77 (0.73-4.27)
	Hypersexuality	-	-	-	-	-	-	11	10.33 (5.7-18.71)	3.35 (1.85-6.08)	13	4.44 (2.57-7.67)	2.14 (1.24-3.69)
	Loss of libido	-	-	-	-	-	-	10	2.1 (1.13-3.9)	1.07 (0.57-1.99)	33	2.53 (1.8-3.56)	1.33 (0.95-1.88)
	Libido increased	-	-	-	-	-	-	6	4.87 (2.18-10.87)	2.28 (1.02-5.08)	-	-	-
	Disturbance in sexual arousal	-	-	-	-	-	-	3	5.31 (1.71-16.52)	2.4 (0.77-7.47)	-	-	-
	Female orgasmic disorder	-	-	-	-	-	-	3	14.72 (4.7-46.04)	3.86 (1.23-12.07)	-	-	-
	Hypersexuality	-	-	-	-	-	-	11	10.33 (5.7-18.71)	3.35 (1.85-6.08)	-	-	-
	Libido disorder	-	-	-	-	-	-	-	-	-	10	4.31 (2.31-8.04)	2.09 (1.12-3.91)
	Paraphilia	-	-	-	-	-	-	-	-	-	3	12.52 (3.95-39.61)	3.6 (1.14-11.39)
	Psychosexual disorder	-	-	-	-	-	-	-	-	-	3	5.29 (1.69-16.55)	2.39 (0.76-7.46)

**Table S2 Continued**

HLGT	PT	Paliperidone			Quetiapine			Risperidone			Ziprasidone		
		N	ROR (95%CI)	IC (95%CI)	N	ROR (95%CI)	IC (95%CI)	N	ROR (95%CI)	IC (95%CI)	N	ROR (95%CI)	IC (95%CI)
<b>Sexual function and fertility disorders</b>	Erectile dysfunction	121	6.35 (5.31-7.6)	2.65 (2.21-3.17)	206	2.94 (2.56-3.37)	1.54 (1.34-1.77)	179	2.69 (2.32-3.11)	1.41 (1.22-1.64)	38	3.99 (2.9-5.49)	1.99 (1.45-2.74)
	Sexual dysfunction	80	8.75 (7.01-10.91)	3.11 (2.49-3.88)	143	4.27 (3.62-5.04)	2.07 (1.75-2.44)	153	4.83 (4.11-5.66)	2.24 (1.91-2.63)	26	5.69 (3.87-8.36)	2.5 (1.7-3.68)
	Priapism	29	9.08 (6.29-13.1)	3.17 (2.19-4.57)	203	18.66 (16.15-21.55)	4.1 (3.55-4.73)	159	15.09 (12.84-17.72)	3.82 (3.25-4.49)	52	33.37 (25.33-43.96)	5.02 (3.81-6.61)
	Ejaculation failure	23	14.33 (9.48-21.65)	3.81 (2.52-5.76)	-	-	-	22	3.91 (2.57-5.96)	1.95 (1.28-2.97)	3	3.71 (1.19-11.51)	1.89 (0.61-5.86)
	Retrograde ejaculation	16	26.89 (16.33-44.3)	4.7 (2.85-7.74)	10	4.5 (2.4-8.42)	2.14 (1.15-4.01)	13	6.2 (3.57-10.77)	2.6 (1.5-4.51)	-	-	-
	Ejaculation disorder	13	5.56 (3.22-9.6)	2.47 (1.43-4.26)	15	1.74 (1.05-2.9)	0.8 (0.48-1.32)	26	3.2 (2.18-4.72)	1.67 (1.13-2.45)	-	-	-
	Infertility	9	7.42 (3.85-14.32)	2.88 (1.49-5.55)	-	-	-	34	8.25 (5.86-11.63)	3 (2.13-4.22)	5	8.29 (3.44-19.98)	3.04 (1.26-7.33)
	Ejaculation delayed	6	13.37 (5.96-29.97)	3.72 (1.66-8.33)	-	-	-	-	-	-	-	-	-
	Azoospermia	4	11.21 (4.18-30.11)	3.47 (1.29-9.31)	-	-	-	-	-	-	-	-	-
	Male sexual dysfunction	4	8.48 (3.16-22.71)	3.07 (1.15-8.22)	7	4.06 (1.92-8.58)	2 (0.95-4.23)	-	-	-	-	-	-
	Painful erection	3	4.67 (1.5-14.52)	2.22 (0.71-6.89)	8	3.41 (1.7-6.87)	1.75 (0.87-3.53)	13	5.91 (3.4-10.25)	2.53 (1.46-4.39)	-	-	-
	Infertility female	-	-	-	17	4.94 (3.05-7.99)	2.28 (1.41-3.68)	-	-	-	-	-	-
	Organic erectile dysfunction	-	-	-	15	19 (11.19-32.26)	4.12 (2.43-7)	-	-	-	-	-	-
	Spontaneous penile erection	-	-	-	6	3.02 (1.35-6.77)	1.58 (0.71-3.54)	5	2.65 (1.1-6.4)	1.39 (0.58-3.37)	-	-	-
	Female sexual dysfunction	-	-	-	4	6.02 (2.23-16.27)	2.55 (0.94-6.9)	-	-	-	-	-	-
<b>Sexual dysfunctions, disturbances and gender identity disorders</b>	Loss of libido	44	7.3 (5.42-9.82)	2.85 (2.12-3.84)	36	1.61 (1.16-2.24)	0.69 (0.49-0.95)	52	2.47 (1.88-3.24)	1.29 (0.98-1.7)	-	-	-
	Libido decreased	40	4.21 (3.08-5.75)	2.07 (1.51-2.82)	69	1.98 (1.56-2.51)	0.98 (0.77-1.24)	84	2.54 (2.05-3.15)	1.33 (1.08-1.65)	-	-	-
	Anorgasmia	16	7.51 (4.59-12.3)	2.9 (1.77-4.74)	-	-	-	-	-	-	-	-	-
	Psychosexual disorder	13	52.12 (29.69-91.5)	5.61 (3.19-9.84)	7	7.37 (3.47-15.67)	2.84 (1.33-6.03)	19	22.51 (14.03-36.13)	4.35 (2.71-6.99)	-	-	-
	Hypersexuality	6	4.39 (1.97-9.79)	2.13 (0.95-4.74)	22	4.43 (2.91-6.77)	2.12 (1.39-3.24)	25	5.33 (3.58-7.92)	2.38 (1.6-3.55)	-	-	-
	Orgasm abnormal	5	7.4 (3.07-17.87)	2.88 (1.19-6.94)	-	-	-	7	2.98 (1.41-6.27)	1.56 (0.74-3.29)	-	-	-
	Libido disorder	4	3.69 (1.38-9.85)	1.88 (0.7-5.01)	-	-	-	-	-	-	-	-	-
	Premature ejaculation	3	5.2 (1.67-16.2)	2.37 (0.76-7.38)	-	-	-	-	-	-	-	-	-
	Libido increased	-	-	-	26	4.56 (3.09-6.73)	2.17 (1.47-3.19)	17	3.12 (1.93-5.04)	1.63 (1.01-2.63)	8	10.29 (5.13-20.64)	3.35 (1.67-6.72)
	Excessive masturbation	-	-	-	15	28.59 (16.64-49.11)	4.65 (2.71-7.99)	7	13.06 (6.09-28.02)	3.63 (1.69-7.78)	-	-	-
	Disturbance in sexual arousal	-	-	-	7	2.65 (1.26-5.59)	1.4 (0.66-2.94)	-	-	-	-	-	-
	Orgasmic sensation decreased	-	-	-	4	3.89 (1.44-10.45)	1.94 (0.72-5.21)	-	-	-	-	-	-
	Compulsive sexual behaviour	-	-	-	-	-	-	13	6.17 (3.56-10.72)	2.59 (1.49-4.5)	-	-	-
	Exhibitionism	-	-	-	-	-	-	5	31.94 (12.47-81.83)	4.8 (1.87-12.3)	-	-	-

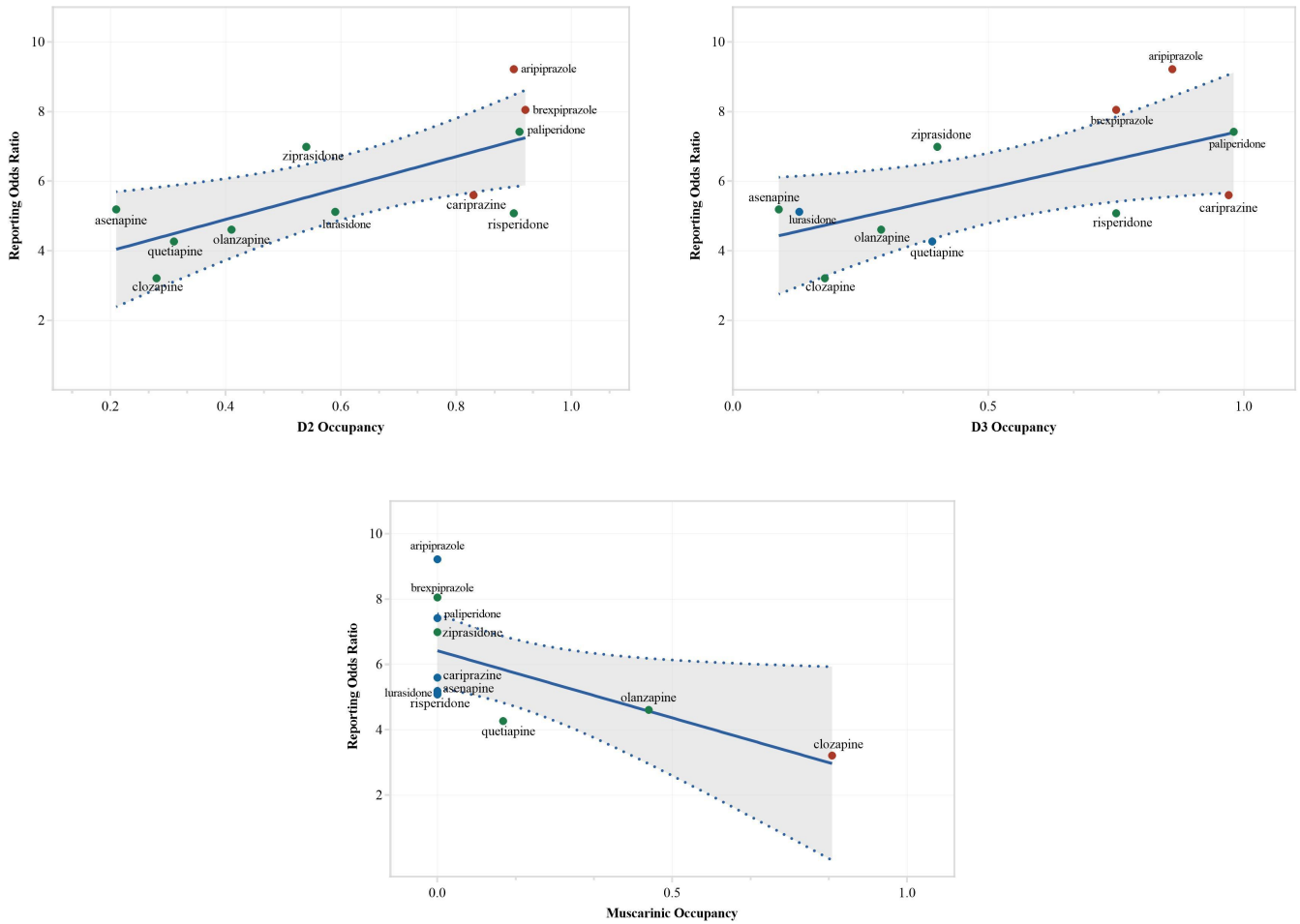


Figure S1. Association between activity on D2, D3 and Muscarinic receptor and reporting of sexual dysfunction with atypical antipsychotics – Main Analysis. Drugs were color-coded to show their activity: red indicates agonists (including partial agonists), green indicates antagonists, and blue indicates unavailable activity.