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Supplementary Material S1 Search strategy

Schizophrenia: Schizophrenia OR Schizophrenias OR Schizophrenic Disorders OR Disorder, Schizophrenic OR Disorders, Schizophrenic OR Schizophrenic Disorder OR Dementia Praecox OR Psychotic Disorders OR Schizophrenia OR Schizophren OR Psychosis OR Psychot

Antipsychotics: Antipsychotics OR Anti-psychotics OR Neuroleptics OR Acepromazine OR Acetophenazine OR Amisulpride OR Aripiprazole OR Asenapine OR Benperidol OR Blonanserin OR Bromperidol OR Butaperazine OR Carpipramine OR Chlorproethazine OR Chlorpromazine OR Chlorprothixene OR Clocapramine OR Clopentixol OR Clothiapine OR Clotiapine OR Clozapine OR Cyamemazine OR Cyamepromazine OR Dixyrazine OR Droperidol OR Fluanisone OR Flupenthixol OR Flupentixol OR Fluphenazine OR Fluspirilen OR Fluspirilene OR Haloperidol OR Iloperidone OR Levomepromazine OR Levosulpiride OR Lithium OR Loxapine OR Lurasidone OR Melperone OR Mepazine OR Mesoridazine OR Methotrimeprazine OR Molindone OR Moperone OR Mosapramine OR Olanzapine OR Oxypertine OR Paliperidone OR Penfluridol OR Perazine OR Periciazine OR Pericyazine OR Perospirone OR Perphenazine OR Pimozide OR Pipamperone OR Pipothiazine OR Pipotiazine OR Prochlorperazine OR Promazine OR Promethazine OR Prothipendyl OR Quetiapine OR Remoxipiride OR Reserpine OR Risperdal OR Risperidone OR Seroquel OR Sertindole OR Stelazine OR Sulpiride OR Sultopride OR Thiopropazate OR Thioproperazine OR Thioridazine OR Tiospirone OR Thiothixene OR Tiapride OR Tiotixene OR Trifluoperazine OR Trifluperidol OR Trifluoperidol OR Triflupromazine OR Trifluperazine OR Veralipride OR Ziprasidone OR Zotepine OR Zuclopenthixol

Mortality: Mortality OR Death OR Years of Life Lost OR Suicide OR Survival OR Survival Analysis OR Kaplan-Meier Estimate OR Suicide OR Suicide, Assisted OR Heart Arrest OR Cardiac Arrest OR Heart Attack OR Heart Arrest OR Cardiovascular Stroke

Table S1 Basic characteristics of the included studies

Author (year)	Population diagnosis	Country and method of enrollment	Total sample size	Average follow-up time	Comparisons	Mean age (SD)	Male (%)
Randomized trials							
Alphs (2015)[1]	Schizophrenia (DSM)	USA	450	1.25	Paliperidone	37.7 (10.6)	193 (85.4)
	Outpatients	Recruitment		(2010-2013)	Other oral antipsychotics	38.6 (10.4)	190 (87.2)
Gaebel (2010)[2]	Schizophrenia 585	Multinational	711	2.00	Risperidone	40.6 (12.5)	195 (59.3)
Arce (2012)[3]	Schizoaffective 126 (DSM)	Recruitment		(2004-2007)	LAI		
	In- and outpatients				Quetiapine	42.6 (13.1)	191 (56.7)
					Aripiprazole	40.9 (12.9)	25 (55.6)
John (2020)[4]	Schizophrenia 234 (DSM)	USA	234	1.63	Aripiprazole	25.18 (4.3)	172 (73.5)
		Recruited from clinics		(2014-2019)	LAI		
					Clinician's choice	24.7 (4.1)	196 (76.9)
Matsumoto (2018)[5]	Schizophrenia 106 (DSM)	Japan	106	1.10	Aripiprazole	15.1 (1.4)	37 (54.4)
	Adolescents	NS		(2010-2014)			
	In- and outpatients						
Meltzer (2003)[6]	Schizophrenia 62	Multinational	980	2.00	Clozapine	37.1 (10.3)	301 (61.4)
	Schizoaffective 38 (DSM)	Recruitment		(1998-2001)	Olanzapine	37.0 (10.3)	301 (61.4)
	High risk suicide						
Ritchie (2010)[7]	Schizophrenia 66 (NS)	Australia	66	3.50	Olanzapine	69.9 (7.3)	10 (29.4)
	Old age	Recruited		(1997-2000)	Risperidone	69.7 (4.8)	9 (28.1)
		from psychiatric					
		treatment setting					
Savitz (2015)[8]	Schizophrenia 400 (DSM)	Multinational	400	2.00	Paliperidone	15.4 (1.6)	243 (61)
	Adolescent	NS		(2007-2012)			
Savitz (2016)[9]	Schizophrenia 1,429 (DSM)	Multinational	1,429	1.35	Paliperidone	38.4 (11.9)	782 (55)
		NS		(2012-2015)			

Thomas (2010)[10]	Schizophrenia 9,809 (NS)	Europe	9,809	1.40	Sertindole	37.1†	2,710 (55.2)
		Asia		(2002-2008)	Risperidone	37.1	2,716 (55.3)
		Recruitment					
Zhang (2015)[11]	Schizophrenia 521 (DSM)	Asia-Pacific region	521	1.50	Paliperidone	28.7 (8.0)	341 (65.5)
		Recruitment		(2010-2013)			
Cohort studies							
Chang (2020)[12]	Schizophrenia (ICD)	Korea	80,581	7.00†	FGA only	35.2 (6.5)‡	40,789 (50.9)‡
	Newly diagnosed	Database		2004-2017	SGA only		
					Combined		
Cho (2019)[13]	Schizophrenia	UK	2,837	3.90	Clozapine	38.7 (11.4)‡	1,773 (62.5)‡
	Schizoaffective	Database		(2007-2016)	Non-clozapine		
	Bipolar disorder (ICD)						
	Treatment-resistant						
Christy (2018)[14]	schizophrenia	Hong Kong	178	10.00	Quetiapine	24.2 (6.4)	80 (45)
	Non-affective psychosis (DSM)	Medical records		(2003-2014)			
	first-episode						
Cullen (2013)[15]	Schizophrenia 2,132 (ICD)	USA	2,132	10.00	FGA	41.6 (10.1)	1,033 (51)
	Outpatients	Database		(1994-2004)	Others	41.6 (10.1)	1,097 (51.5)
Davis (2014)[16]	Schizophrenia	USA	320	NS	Clozapine	48 (0.6)	292 (91.3)
	Schizoaffective (DSM)	Database		(1993-2007)			
	In- and outpatients						
Deslandes (2015)[17]	Schizophrenia	UK	176	5.00	Risperidone	41.2 (12.9)	58 (69)
	Schizoaffective (NS)	Medical records		(2006-2013)	Aripiprazole	NS for total	NS for total
Dickson (1998)[18]	Schizophrenia 26 (DSM)	Canada	26	3.00	Continuers	31.8‡	24‡ (92.3)
	Treatment-resistant	Clinical records		(NS)	Discontinuers	(22-68)	
	In- and outpatients				Interrupted clozapine users		

Enger (2004)[19]	Schizophrenia 1,920 (ICD) In- and outpatients	United States Database	1,1520	1.76 (1995-1999)	Atypical only Typical only Both	38.2 (14)‡	4,766 (41.3)‡
Gaertner (2000)[20]	Schizophrenia 23 (ICD) Outpatients	Germany NS	23	3.80 (1993-NS)	Clozapine	40 (13)	18 (78.2)
Girgis (2011)[21]	Schizophrenia 122 Schizophreniform 38 (DSM) First episode In- and outpatients	China Medical records	160	9.00 (1995-2007)	Clozapine Chlopromazine	28.7 (6.9)‡	84 (52.2)‡
Hayes (2015)[22]	Schizophrenia 9,437 Schizoaffective 805 Bipolar affective disorder 4,512 (ICD) In- and outpatients	UK Medical records	14,754§	3.03 (2007-2011)	Clozapine Others Non-user	43.2 (16.1)§	7,985 (54.1)§
Hennessy (2002)[23]	Schizophrenia 124,718 (ICD) Outpatients	USA Database	12,4718	1.10 1993-1996	Clozapine Haloperidol Risperidone Thioridazine	NS	47,812 (50)
Joukamaa (2006)[24]	Schizophrenia (NS)	Finland Mini-Finland Health Survey	99	17.00 (1978-1994)	Polyphramacy Monotherapy No use	NS	46 (46.5)
Jihoon (2021)[25]	Schizophrenia 86,923 (ICD) In- and outpatients	Korea Database	86,923	5.86† (2003-2017)	Olanzapine Risperidone Aripiprazole Quetiapine Untreated	45 (32-60)†	42,353 (48.7)‡
Kadra (2018)[26]	Schizophrenia 5,896 Schizoaffective 639 Bipolar disorder 1,886 (ICD)	UK Records	10,945	4.48 2007-2014	Monotherapy Polypharmacy	42.2 38.1	4,684 (55.6) 1,470 (58.2)

Kasper (2010)[27]	Schizophrenia 2,321 (experience or clinical judgement) Not currently treated	Europe Recruitment	2,321	1.50 (1997-1998)	Sertindole Non-Sertindole	39† 42†	570 (54) 755 (60)
Kelly (2010)[28]	Schizophrenia 964 Schizoaffective 561 Disorder psychosis NOS 161 (DSM) In- and outpatients	USA Database	1,686	6-10 years (1994-2004)	Clozapine Risperidone	39 (9.8) 41.2 (11.7)	690 (64) 369 (61)
Khan (2017)[29]	Schizophrenia 503 Treatment-resistant (NS) Outpatients	Australia NS	503	9.00 (2009-2015)	Clozapine	44 (12)	397 (78.9)
Lee (2015)[30]	Schizophrenia 75 Schizoaffective 17 Bipolar disorder 1 (NS)	Canada Database	94	1.40 (2009-2010)	Clozapine	35.9	68 (72.3)
Lindstrom (1989)[31]	Schizophrenia 89 Schizoaffective 7 (ICD) In- and outpatients	Sweden Recruited from clinic	96	12.50 (1974-1986)	Clozapine	36.1	64 (66.7)
Modai (2000)[32]	Schizophrenia (ICD) Treatment resistant Inpatients	Israel Medical records	5,479	6.70 (1991-1997)	Clozapine Non-clozapine	67.4‡	NS
Montout (2002)[33]	Schizophrenia 3,325 (ICD) In- and outpatients	France Recruited from psychiatric sectors	3,325	4.00 (1993-1997)	Phenothiazines Butyrophenones Benzamides Thioxanthenes	39.3‡	2,127 (64)‡
Munro (1999)[34]	Schizophrenia (NS) Treatment-resistant	UK Ireland Database	12,720	8.00 (1990-1997)	Clozapine	36.8	8,533 (67)

Patrick (2020)[35]	Schizophrenia 646 Schizoaffective 400 Disorder psychosis NOS 153 (DSM) Inpatients	USA Patient records	1,199	20.00 (1994-2014)	Risperidone OR Clozapine	41 (11.4)	745 (62)
Pridan (2015)[36]	Schizophrenia 527 (DSM) (elderly) Inpatients	Israel Medical records	527	5.00 (2007-2012)	Clozapine Others	67.4 (7)‡	245 (46.5)‡
Ran (2015)[37]	Schizophrenia 510 (ICD)	China Epidemiological data	510	14.00 (1994-2008)	Treated Untreated	44.6‡	237 (43.9)‡
Rimon (1994)	Schizophrenia 96 Schizoaffective 7 (DSM) In- and outpatients	Finland Medical records	103	3.40 NS	Clozapine	36.9	59 (57.3)
Schulte (2016)[38]	Schizophrenia 81 Schizoaffective 13 NS In- and outpatients	Netherlands Database	94	12.30 (1989-2010)	Clozapine Never treated with clozapine	39 (11) 40 (11)	74 (78.8) 73 (77.7)
Srivastava (2002)[39]	Schizophrenia 25 (ICD) Treatment resistant	India NS	25	3.00 (1994-1997)	Clozapine	NS	15(60)
Taipale (2018)[40]	Schizophrenia Schizoaffective (ICD) Chronic patients First-episode In- and outpatients	Sweden Database	29,823	5.70 (2006-2014)	FGA SGA Non-user	44.9 (16-64)	16,999 (57)
Taipale (2020)[41]	Schizophrenia (ICD) Prevalent cohort 62,250 First-episode patients: 8,719 In- and outpatients	Finland Database	70,969	14.10† (1996-2015)	Antipsychotics Non-user	46.8 41.2	31,250 (50.2) 4,900 (56.2)

Taub (2020)[42]	Schizophrenia 1,817 (ICD)	Israel	1,817	3.00	Clozapine	43.7 (13)	1,157 (63.7)
	In and out-patients	Database		(2012-2014)			
Tenback (2012)[43]	Schizophrenia 7,415 (DSM)	Netherland	10,5141	3.00	User	45.5 (13.9)	4,538 (61.2)
	In- and outpatients	Database		(2006-2008)	Non-user	39.9 (22.7)	45,931(47)
Tiihonen (2009)[44]	Schizophrenia 66,681 (ICD)	Finland	66,681	7.80	Antipsychotics	51‡	30,803 (46)‡
	Outpatients	Database		(1996-2006)	Non-user		
Ward (2006)[45]	Schizophrenia 45,045 (ICD)	Canada	45,045	3.10¶	Risperidone	NS	23,528 (52.2)‡
		Database		(1999-2003)	Olanzapine		
					Quetiapine		
Weitoft (2014)[46]	Schizophrenia	Sweden	26,046	6.00	Antipsychotics	48.4‡	14,397 (55.3)‡
	Schizoaffective (ICD)	Database		(2006-2011)	Non-user		
	In- and outpatients						
Wimberley (2017)[47]	Schizophrenia (ICD)	Denmark	2,370	6.80†	Clozapine	30.1†	1,284 (54.2)‡
	Treatment-resistant	Database		(1996-2013)	Others		
	In- and outpatients				Non-user		
Zalm (2020)[48]	Schizophrenia 23,627	Denmark	50,881	11.30	Clozapine	39.7 (16.5)†	28,290 (55.6)‡
	Schizoaffective 2,926	Database		(1995-2013)	Others		
	disorder psychosis NOS 9,081 (ICD)						
	Incidence-cohort						
	Prevalence-cohort						
	outpatients						
Case-control studies							
Chen (2015)[49]	Schizophrenia (ICD)	China	1,624	3.81	FGA	38.61 (12.3)	970 (59.7)
	Newly diagnosis	Taiwan		3.91	SGA	38.34 (12.7)	
		Database		(1997-2008)			

Mela (2016)[50]	Psychotic disorder	Canada	98	2.00	Clozapine	NS	94 (95.9)‡
	Related disorder	Medical records		(1984-2012)	Non-clozapine		
	Offenders						
	Inpatients						
Sernyak (2001)[51]	Schizophrenia 4,245 NS	USA	4,245	6.00	Clozapine ever	43.04 (9.3)	NS
	Inpatients	Database		(1992-1998)	Clozapine never	43.6 (11.1)	
Taylor (2009)[52]	Schizophrenia 250	UK	779	4.67	Clozapine	36.4 (11.6)	NS
	Schizoaffective 29	Database		2002-2006	Risperidone	38.6 (13.8)‖	
	Disorder psychosis NOS 43‖ NS						

LAI = long-acting injection; NOS = not otherwise specified; NS = nonspecific.

† Only provided the median age and follow-up time.

‡ No detailed data for each group, only for of the entire sample.

§ Only patients with schizophrenia were included in our analysis.

‖ Different follow-up times; we chose the longest.

¶ Diagnosis and mean age only specified for discontinuers.

Table S2 Quality assessment of included studies with cohort and case-control studies

Study	Selection (out of 4 stars)	Comparability (out of 2 stars)	Outcome (out of 3 stars)	Total score (maximum 9)
Cohort studies				
Chang (2020)	****	**	**	8
Cho J (2019)	***	**	**	7
Christy (2018)	***	**	**	7
Cullen (2013)	****		***	7
Davis (2014)	**		**	4
Deslandes (2015)	***		**	5
Dickson (1998)	***		***	6
Enger (2004)	****	**	***	9
Gaertner (2000)	***		*	4
Girgis (2011)	****	**	**	8
Hayes (2015)	****	**	**	8
Hennessy (2002)	****	**	***	9
Jihoon (2021)	****	**	**	8
Joukamaa (2006)	****	**	**	8
Kadra G (2018)	****	**	***	9
Kasper (2010)	***		**	5
Kelly (2010)	***	**	**	7
Khan (2017)	***		***	6
Lee (2015)	***		**	5
Lindstro (1989)	**		***	5
Modai (2000)	****		**	6
Montout (2002)	****		*	5
Munro (1999)	***		**	5
Patrick (2020)	***		**	5
Pridan (2014)	***		***	6
Pridan (2015)	***		***	6
Ran (2015)	****		**	6
Rimon (1994)	***		**	5
Schulte (2016)	****	**	**	8
Srivastava (2002)	**		**	4
Taipale (2018)	****	**	***	9
Taipale (2020)	****	**	***	9
Taub (2020)	***	**	***	8
Tenback (2012)	****	**	**	8
Tiihonen (2009)	****	**	***	9
Ward (2006)	**		**	4
Weitoft (2014)	****	**	**	8
Wimberley (2017)	****	**	**	8

Zalm (2020)	****	**	***	9
Case-control studies				
Chen (2015)	****	**	**	8
Mela (2016)	***		*	4
Sernyak (2001)	****	**	**	8
Taylor (2009)	**	*	*	4

Table S3 Meta-regression of the mortality of schizophrenia patients using antipsychotics

Variable	**β**	**Se**	**95%CI**		**p-value**
			Lower limit	**Upper limit**	
Follow-up time	0.0008	0.0011	-0.0014	0.0030	0.4534
Mean age	0.0018	0.0006	0.0007	0.0029	0.0010
Male (%)	-0.0001	0.0005	-0.0011	0.0009	0.8111
Sample size	0.0000	0.0000	-0.0000	0.0000	0.0609

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Figure S1 Quality assessment of included studies with randomized design

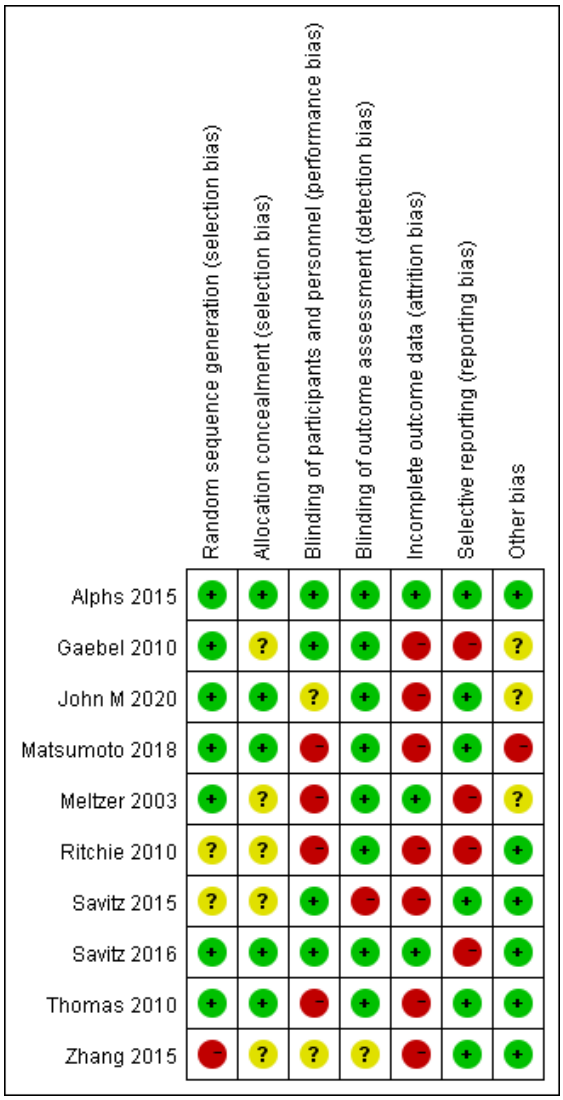

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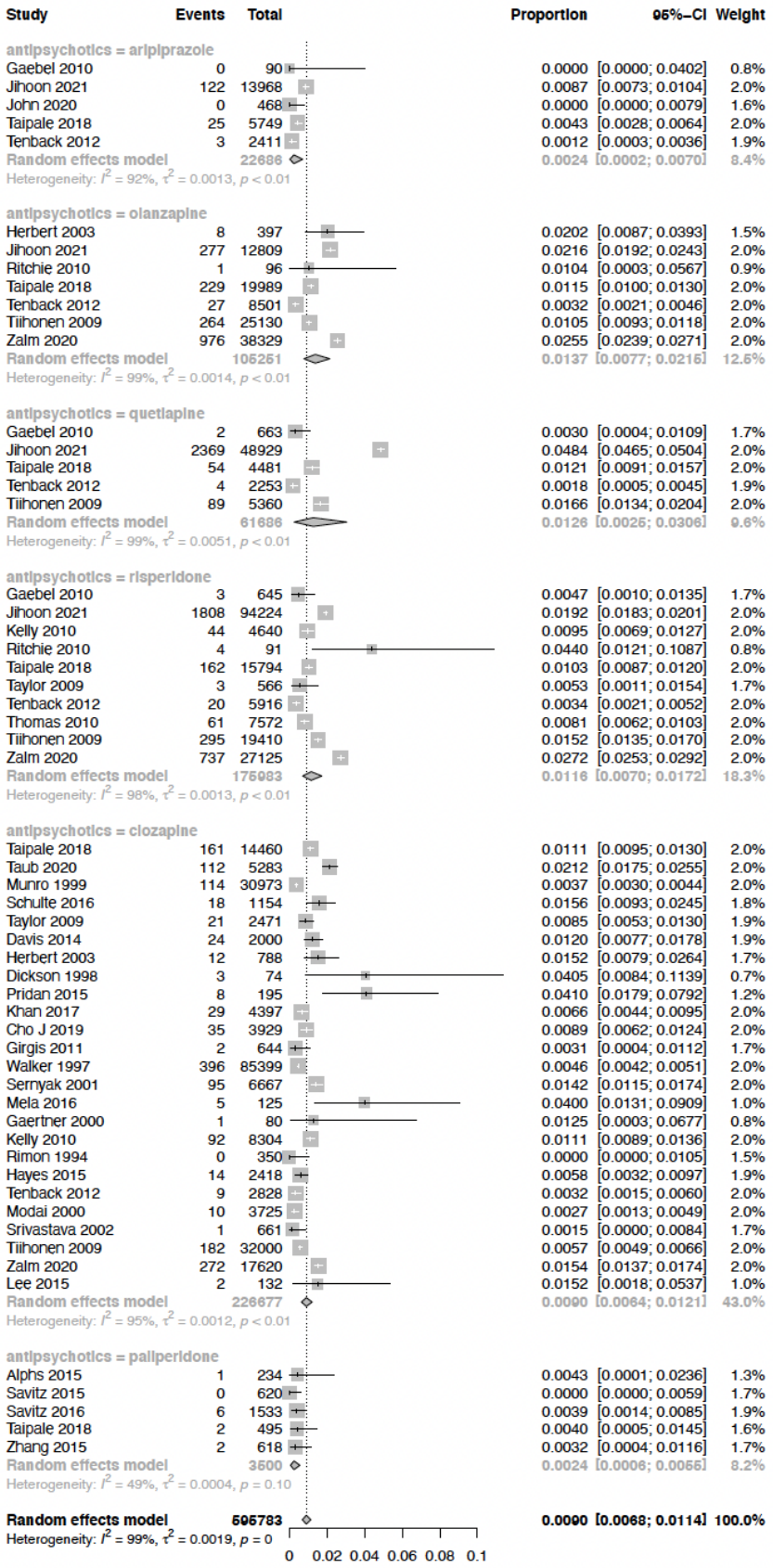
Figure S2 Comparison of long-term death of schizophrenia using different antipsychotics



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