Predictors and moderators of hospitalisation and mortality in people with dementia using antipsychotics: A systematic review

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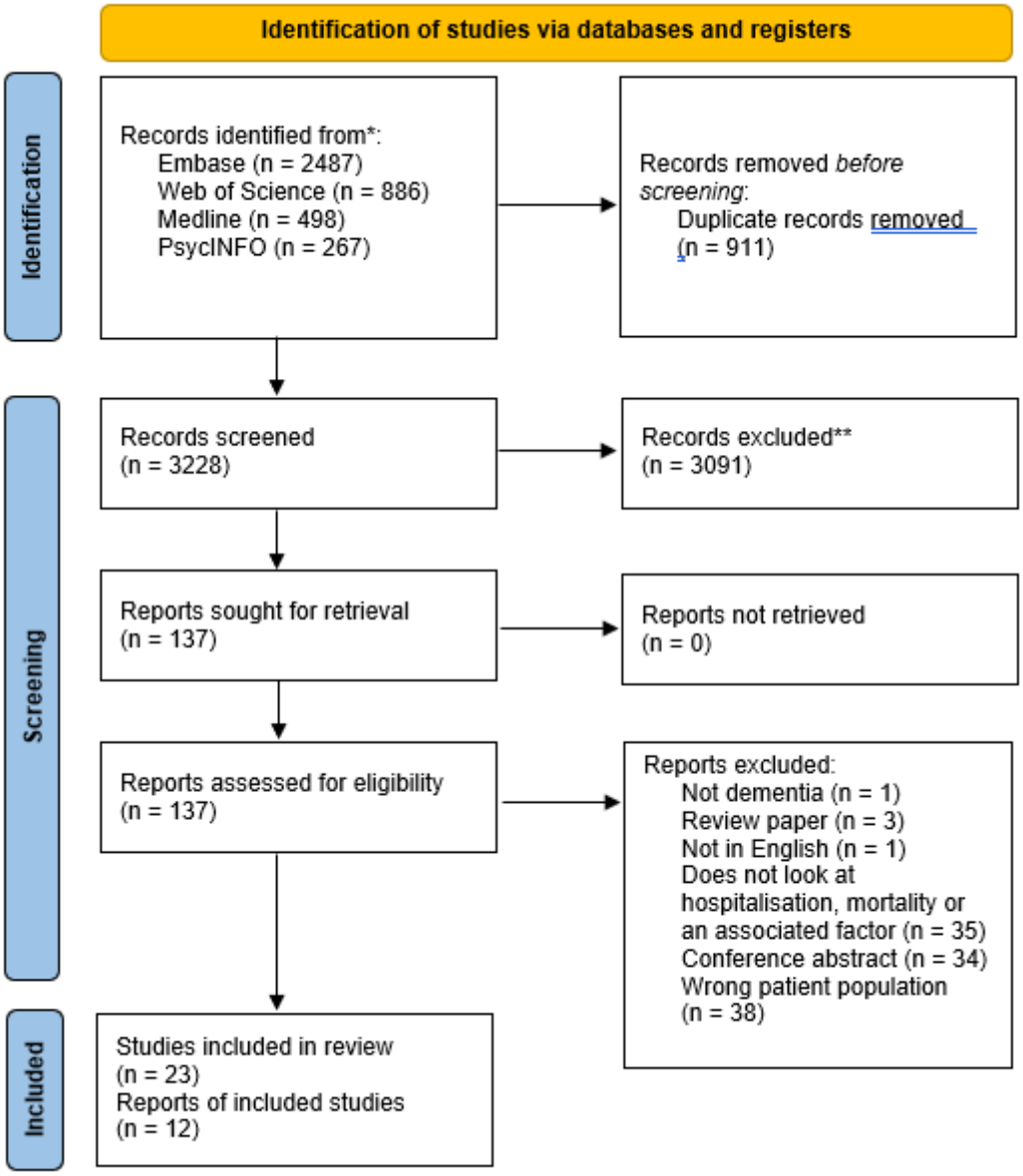

Supplementary Figure 1. PRISMA flow diagram. Figure adapted from https://www.prisma-statement.org/

Supplementary Table 1.

Search Strategy for Embase (Limits: Human, English language, Remove pre-print records, 2010-Current)

Concept	Other Words
Dementia	dement*.mp. OR vascular dement*.mp. OR Alzheimer*.mp. OR lewy bod*.mp. OR frontotemporal dement*.mp. OR (cogniti* adj3 impair*).mp. OR lbd.mp. OR multiinfarct dementia/ OR dementia/ OR frontotemporal dementia/ OR Alzheimer disease/ OR Lewy body/ OR cognitive defect/
Older adults	geriatric*.mp. OR elder*.mp. OR older.mp. OR advanced age.mp. OR aged.mp. OR aging.mp. OR geriatrics/ OR aged/ OR aging/
Antipsychotics	neuroleptic*.mp. OR antipsychotic*.mp. OR alphaFlupenthixol*.mp. OR Aminazine*.mp. OR Amisulpride*.mp. OR Amoxapine*.mp. OR Aripiprazole*.mp. OR Asenapine maleate*.mp. OR Benperidol*.mp. OR Brexpiprazole*.mp. OR Chlorazine*.mp. OR Chlordelazine*.mp. OR Chlorpiprazine*.mp. OR Chlorpromazin*.mp. OR Chormethiazole*.mp. OR cisFlupenthixol*.mp. OR Clomethiazole*.mp. OR Clopenthixol*.mp. OR Cloxazepine*.mp. OR Clozapine*.mp. OR Desmethylloxapine*.mp. OR Flufenazin*.mp. OR Flupenthixol decanoate*.mp. OR Flupentixol decanoate*.mp. OR Flupentixol*.mp. OR Fluphenazin*.mp. OR Fluphenazine decanoate*.mp. OR Fluphenazine Hydrochloride*.mp. OR Fumarate*.mp. OR Haloperidol*.mp. OR Iloperidone*.mp. OR Levomeprazin*.mp. OR Levomepromazin*.mp. OR Levopromazine*.mp. OR Loxapine Monohydrochloride*.mp. OR Loxapine*.mp. OR Loxapinsuccinate*.mp. OR Loxipine Maleate*.mp. OR Loxipine Succinate*.mp. OR Lurasidone*.mp. OR Melperone hydrochloride*.mp. OR Methotrimeprazine*.mp. OR Nalotenserin*.mp. OR Norquetiapine*.mp. OR Olanzapine embonate*.mp. OR Olanzapine*.mp. OR Oxilapine*.mp. OR Paliperidone*.mp. OR

	Perfenazine*.mp. OR Pericyazine*.mp. OR Perphenazine*.mp. OR Pimavanserin*.mp. OR Pimozide*.mp. OR Prochlorperazine*.mp. OR Promazine hydrochloride*.mp. OR Propaphenin*.mp. OR Prothipendyl*.mp. OR Quetiapine*.mp. OR Risperidone*.mp. OR Sertindole*.mp. OR Sulperide*.mp. OR Sulpiride*.mp. OR Thioridazine Hydrochloride*.mp. OR Thioridazine*.mp. OR Thiothixene*.mp. OR Tiaprid*.mp. OR Tiapridal*.mp. OR Trifluoperazine*.mp. OR Trifluoroperazine*.mp. OR Trifluperazine*.mp. OR Tripfluoperazine Hydrochloride*.mp. OR Ziprasidone*.mp. OR Zotemine*.mp. OR Zotepine*.mp. OR Zuclopenthixol*.mp. OR Zuclopenthixol*.mp. OR pimozide/ OR perphenazine/ OR loxapine/ OR levomepromazine/ OR haloperidol/ OR fluphenazine/ OR flupentixol/ OR chlorpromazine/ OR clomethiazole/ OR clopenthixol/ OR trifluoperazine/ OR thioridazine/ OR sulpiride/ OR risperidone/
Hospitalisation	hospitali?ation*.mp. OR medical admission*.mp. OR admission*.mp. OR hospital care*.mp. OR hospital readmission*.mp. OR patient admission*.mp. or patient readmission*.mp. OR hospitali?tion/
Mortality	mortality*.mp. OR death*.mp. OR fatal*.mp. OR survival*.mp. OR mortality/ OR death/ OR fatality/

Supplementary Table 2.

Search Strategy for Medline (Limits: Human, English language, Remove pre-print records, 2010-Current)

Concept	Other Words
Dementia	dement*.mp. OR vascular dement*.mp. OR Alzheimer*.mp. OR lewy bod*.mp. OR frontotemporal dement*.mp. OR (cogniti* adj3 impair*).mp. OR Dementia/ OR Frontotemporal Dementia/ OR Dementia, Vascular/ OR Dementia, Multi-Infarct/ OR Lewy Bodies/ OR Alzheimer Disease/ OR Cognition Disorders/ OR Cognitive Dysfunction/ OR lbd.mp.
Older adults	geriatric*.mp. OR elder*.mp. OR older.mp. OR advanced age.mp. OR aged.mp. OR aging.mp. OR Geriatrics/ OR Aged/ OR Aging/
Antipsychotics	neuroleptic*.mp. OR antipsychotic*.mp. OR alphaFlupenthixol*.mp. OR Aminazine*.mp. OR Amisulpride*.mp. OR Amoxapine*.mp. OR Aripiprazole*.mp. OR Asenapine maleate*.mp. OR Benperidol*.mp. OR Brexpiprazole*.mp. OR Chlorazine*.mp. OR Chlordelazine*.mp. OR Chlorpiprazine*.mp. OR Chlorpromazin*.mp. OR Chormethiazole*.mp. OR cisFlupenthixol*.mp. OR Clomethiazole*.mp. OR Clopenthixol*.mp. OR Cloxazepine*.mp. OR Clozapine*.mp. OR Desmethylloxapine*.mp. OR Flufenazin*.mp. OR Flupenthixol decanoate*.mp. OR Flupentixol decanoate*.mp. OR Flupentixol*.mp. OR Fluphenazin*.mp. OR Fluphenazine decanoate*.mp. OR Fluphenazine Hydrochloride*.mp. OR Fumarate*.mp. OR Haloperidol*.mp. OR Iloperidone*.mp. OR Levomeprazin*.mp. OR Levomepromazin*.mp. OR Levopromazine*.mp. OR Loxapine Monohydrochloride*.mp. OR Loxapine*.mp. OR Loxapinsuccinate*.mp. OR Loxipine Maleate*.mp. OR Loxipine Succinate*.mp. OR Lurasidone*.mp. OR Melperone hydrochloride*.mp. OR Methotrimeprazine*.mp. OR Nalotenserin*.mp. OR Norquetiapine*.mp. OR Olanzapine embonate*.mp. OR Olanzapine*.mp. OR Oxilapine*.mp. OR Paliperidone*.mp. OR

	Perfenazine*.mp. OR Pericyazine*.mp. OR Perphenazine*.mp. OR Pimavanserin*.mp. OR Pimozide*.mp. OR Prochlorperazine*.mp. OR Promazine hydrochloride*.mp. OR Propaphenin*.mp. OR Prothipendyl*.mp. OR Quetiapine*.mp. OR Risperidone*.mp. OR Sertindole*.mp. OR Sulperide*.mp. OR Sulpiride*.mp. OR Thioridazine Hydrochloride*.mp. OR Thioridazine*.mp. OR Thiothixene*.mp. OR Tiaprid*.mp. OR Tiapridal*.mp. OR Trifluoperazine*.mp. OR Trifluoroperazine*.mp. OR Trifluperazine*.mp. OR Tripfluoperazine Hydrochloride*.mp. OR Ziprasidone*.mp. OR Zotemine*.mp. OR Zotepine*.mp. OR Zuclopenthixol*.mp. OR Zuclopenthixol*.mp. OR pimozide/ OR perphenazine/ OR loxapine/ OR levomepromazine/ OR haloperidol/ OR fluphenazine/ OR flupentixol/ OR chlorpromazine/ OR clomethiazole/ OR clopenthixol/ OR trifluoperazine/ OR thioridazine/ OR sulpiride/ OR risperidone/
Hospitalisation	hospitali?ation*.mp. OR medical admission*.mp. OR admission*.mp. OR hospital care*.mp. OR hospital readmission*.mp. OR patient admission*.mp. or patient readmission*.mp. OR hospitali?ation/
Mortality	mortality*.mp. OR death*.mp. OR fatal*.mp. OR survival*.mp. OR mortality/ OR death/

Supplementary Table 3.

Search Strategy for PsycINFO (Limits: Human, English language, 2010-Current)

Concept	Other Words
Dementia	dement*.mp. OR vascular dement*.mp. OR Alzheimer*.mp. OR lewy bod*.mp. OR frontotemporal dement*.mp. OR (cogniti* adj3 impair*).mp. OR exp Vascular Dementia/ or exp Dementia/ or exp Dementia with Lewy Bodies/ OR exp Cognitive Impairment/ or exp Alzheimer's Disease/ OR exp Semantic Dementia/ OR lbd.mp.
Older adults	geriatric*.mp. OR elder*.mp. OR older.mp. OR advanced age.mp. OR aged.mp. OR aging.mp. OR exp Geriatrics/ OR exp Geriatric Patients/ or exp Aging/ or exp Older Adulthood/
Antipsychotics	neuroleptic*.mp. OR antipsychotic*.mp. OR alphaFlupenthixol*.mp. OR Aminazine*.mp. OR Amisulpride*.mp. OR Amoxapine*.mp. OR Aripiprazole*.mp. OR Asenapine maleate*.mp. OR Benperidol*.mp. OR Brexpiprazole*.mp. OR Chlorazine*.mp. OR Chlordelazine*.mp. OR Chlorpiprazine*.mp. OR Chlorpromazin*.mp. OR Chormethiazole*.mp. OR cisFlupenthixol*.mp. OR Clomethiazole*.mp. OR Clopenthixol*.mp. OR Cloxazepine*.mp. OR Clozapine*.mp. OR Desmethylloxapine*.mp. OR Flufenazin*.mp. OR Flupenthixol decanoate*.mp. OR Flupentixol decanoate*.mp. OR Flupentixol*.mp. OR Fluphenazin*.mp. OR Fluphenazine decanoate*.mp. OR Fluphenazine Hydrochloride*.mp. OR Fumarate*.mp. OR Haloperidol*.mp. OR Iloperidone*.mp. OR Levomeprazin*.mp. OR Levomepromazin*.mp. OR Levopromazine*.mp. OR Loxapine Monohydrochloride*.mp. OR Loxapine*.mp. OR Loxapinsuccinate*.mp. OR Loxipine Maleate*.mp. OR Loxipine Succinate*.mp. OR Lurasidone*.mp. OR Melperone hydrochloride*.mp. OR Methotrimeprazine*.mp. OR Nalotenserin*.mp. OR Norquetiapine*.mp. OR Olanzapine embonate*.mp. OR Olanzapine*.mp. OR Oxilapine*.mp. OR Paliperidone*.mp. OR Perfenazine*.mp. OR Pericyazine*.mp. OR Perphenazine*.mp. OR

	Pimavanserin*.mp. OR Pimozide*.mp. OR Prochlorperazine*.mp. OR Promazine hydrochloride*.mp. OR Propaphenin*.mp. OR Prothipendyl*.mp. OR Quetiapine*.mp. OR Risperidone*.mp. OR Sertindole*.mp. OR Sulperide*.mp. OR Sulpiride*.mp. OR Thioridazine Hydrochloride*.mp. OR Thioridazine*.mp. OR Thiothixene*.mp. OR Tiaprid*.mp. OR Tiapridal*.mp. OR Trifluoperazine*.mp. OR Trifluoroperazine*.mp. OR Trifluperazine*.mp. OR Tripfluoperazine Hydrochloride*.mp. OR Ziprasidone*.mp. OR Zotemine*.mp. OR Zotepine*.mp. OR Zuclopenthixol*.mp. OR Zuclopenthixol*.mp. OR exp pimozide/ OR exp perphenazine/ OR exp loxapine/ OR exp levomepromazine/ OR exp haloperidol/ OR exp fluphenazine/ OR exp flupentixol/ OR exp chlorpromazine/ OR exp clomethiazole/ OR exp clopenthixol/ OR exp trifluoperazine/ OR exp thioridazine/ OR exp sulpiride/ OR exp risperidone/
Hospitalisation	hospitali?ation*.mp. OR medical admission*.mp. OR admission*.mp. OR hospital care*.mp. OR hospital readmission*.mp. OR patient admission*.mp. or patient readmission*.mp. OR hospitalization/
Mortality	mortality*.mp. OR death*.mp. OR fatal*.mp. OR survival*.mp. OR exp mortality/ OR mortality rate/

Supplementary Table 4.

Search Strategy for Web of Science (Limits: English language, 2010-Current)

Concept	Other Words
Dementia	dement* OR vascular dement* OR Alzheimer* OR lewy bod* OR frontotemporal dement* OR "cognit* impair*"
Older adults	geriatric* OR elder* OR older OR advanced age OR aged. OR aging
Antipsychotics	neuroleptic* OR antipsychotic* OR alphaFlupenthixol* OR Aminazine* OR Amisulpride* OR Amoxapine* OR Aripiprazole* OR Asenapine maleate* OR Benperidol* OR Brexpiprazole* OR Chlorazine* OR Chlordelazine* OR Chlorpiprazine* OR Chlorpromazin* OR Chormethiazole* OR cisFlupenthixol* OR Clomethiazole* OR Clopenthixol* OR Cloxazepine* OR Clozapine* OR Desmethylloxapine* OR Flufenazin* OR Flupenthixol decanoate* OR Flupentixol decanoate* OR Flupentixol* OR Fluphenazin* OR Fluphenazine decanoate* OR Fluphenazine Hydrochloride* OR Fumarate* OR Haloperidol* OR Iloperidone* OR Levomeprazin* OR Levomepromazin* OR Levopromazine* OR Loxapine Monohydrochloride* OR Loxapine* OR Loxapinsuccinate* OR Loxipine Maleate* OR Loxipine Succinate* OR Lurasidone* OR Melperone hydrochloride* OR Methotrimeprazine* OR Nalotenserin* OR Norquetiapine* OR Olanzapine embonate* OR Olanzapine* OR Oxilapine* OR Paliperidone* OR Perfenazine* OR Pericyazine* OR Perphenazine* OR Pimavanserin* OR Pimozide* OR Prochlorperazine* OR Promazine hydrochloride* OR Propaphenin* OR Prothipendyl* OR Quetiapine* OR Risperidone* OR Sertindole* OR Sulperide* OR Sulpiride* OR Thioridazine Hydrochloride* OR Thioridazine* OR Thiothixene* OR Tiaprid* OR Tiapridal* OR Trifluoperazine* OR Trifluoroperazine* OR Trifluperazine* OR Tripfluoperazine Hydrochloride* OR Ziprasidone* OR Zotemine* OR Zotepine* OR Zuclopenthixol* OR Zuclopenthixol*

Hospitalisation	hospitali?ation* OR medical admission* OR admission* OR hospital care* OR hospital readmission* OR patient admission* OR patient readmission*
Mortality	mortality* OR death* OR fatal* OR survival*

Supplementary Table 5. Predictors of mortality in people living with dementia using antipsychotics

Risk Factor	Risk Estimate	Reference group	Reference
Antipsychotic related characteristics			
All-cause mortality			
Duration of use			
31-60 days	aHR: 1.05 (0.77-1.43)	1-30 days	[34]
61-90 days	aHR: 0.90 (0.64-1.27)	1-30 days	[34]
91-184 days	aHR: 0.80 (0.61-1.05)	1-30 days	[34]
Antipsychotic type			
Typical	aHR: 0.95 (0.79-1.14)	Atypical antipsychotic	[25]
	aHR: 1.5 (1.1-2.1)	Atypical antipsychotic	[26]
Haloperidol	**aHR: 1.59 (1.36-1.85)*** **	Risperidone	[20]
	aHR: 1.52 (1.14-2.02)	Risperidone	[23]
Olanzapine	aHR: 1.06 (0.93-1.22)	Risperidone	[20]
	aHR: 1.02 (0.81-1.29)	Any other antipsychotic	[25]
Quetiapine	**aHR: 0.74 (0.65-0.83)*** **	Risperidone	[20]
	aHR: 0.84 (0.75-0.94)	Risperidone	[23]
	aHR: 0.95 (0.82-1.10)	Any other antipsychotic	[25]
Risperidone	aHR: 1.03 (0.86-1.22)	Any other antipsychotic	[25]
Anticholinergic properties	Caution Required: aHR: 0.97 (0.84-1.13)	No anticholinergic burden	[15]
	Review needed: aHR: 0.86 (0.72-1.02)	No anticholinergic burden	[15]
Dose			
Risperidone > 0.5mg	**aHR: 1.57 (1.36-1.81)**	Risperidone ≤ 0.5mg	[23]

Quetiapine ≤ 50mg	aHR: 1.18 (1.00-1.38)	Risperidone ≤ 0.5mg	[23]
Quetiapine > 50mg	aHR: 0.97 (0.78-1.21)	Risperidone ≤ 0.5mg	[23]
Haloperidol ≤ 1mg	**aHR: 1.66 (1.10-2.50)**	Risperidone ≤ 0.5mg	[23]
Haloperidol > 1mg	**HR: 2.55 (1.70-3.85)**	Risperidone ≤ 0.5mg	[23]
High dose typical antipsychotic (≥10mg equivalent olanzapine dose)	**aHR: 1.69 (1.53-1.88)*** **	Low dose typical antipsychotic (<10mg equivalent olanzapine dose)	[29]
Stroke related mortality			
Antipsychotic type			
Typical	aHR: 0.84 (0.49-1.44)	Atypical	[25]
Olanzapine	aHR: 1.27 (0.68-2.35)	Any other antipsychotic	[25]
Quetiapine	aHR: 0.92 (0.60-1.41)	Any other antipsychotic	[25]
Risperidone	aHR: 0.84 (0.49-1.44)	Any other antipsychotics	[25]
Patient characteristics			
All-cause mortality			
Increasing age	**aHR: 1.05 (1.01-1.08)*** **	One-year increments	[30]
Male	aHR: 1.37 (0.86-2.20)	Female	[30]
Dyslipidaemia	aHR: 0.30 (0.07-1.24)	No dyslipidaemia	[30]
BPSD profile			
Behavioural Symptom Improvement	HR: 0.93 (0.81-1.07)	Behavioural symptoms unimproved/worsened	[19]

Hallucination	**aHR: 0.39 (0.24-0.64)*** **	No hallucination	[30]
Delirium	aHR: 0.67 (0.41-1.10)	No delirium	[30]
Concomitant drug use			
Benzodiazepines	**aHR: 2.19 (1.83-2.63)*** **	Antipsychotic Use Only	[27]
Antidepressants	**aHR: 0.61 (0.50-0.74)*** **	Antipsychotic Use Only	[27]
Benzodiazepines & Antidepressants	**aHR: 1.41 (1.14-1.73)*** **	Antipsychotic Use Only	[27]
Medication review			
Dose change (at least once)	**aHR: 0.42 (0.22-0.79)****	No dose change	[30]
Treatment change (at least once)	aHR: 0.32 (0.10-1.04)	No treatment change	[30]
COVID-19			
Any antipsychotic COVID-19	**aOR: 1.93 (1.71-2.17)**	No COVID-19	[18]
Quetiapine COVID-19	**aOR: 2.18 (1.78-2.66)**	No COVID-19	[18]
Haloperidol COVID-19	**aOR: 1.39 (1.20-1.62)**	No COVID-19	[18]
Olanzapine COVID-19	**aOR: 1.32 (1.03-1.68)**	No COVID-19	[18]
Risperidone COVID-19	**aOR: 2.57 (1.71-3.86**	No COVID-19	[18]

aHR – adjusted hazards ratio, BPSD – behavioural and psychological symptoms of dementia

*** $p<0.001$

** $p<0.01$

Suppementary Table 6. Moderators of the association between antipsychtoic use and mortality in people living with dementia

Risk Factor	Risk Estimate	Reference group	Interaction term significance	Reference
All-cause mortality				
Gender				
Total population	aHR: 0.91 (0.73-1.14)	Non-user		[16]
Male	aHR: 0.79 (0.51-1.24)	Non-user	p = 0.962	[16]
Female	aHR: 0.90 (0.70-1.15)	Non-user		[16]
Co-existing conditions				
Total population	**aHR: 1.35 (1.27-1.43)**	Non-user		[28]
Cerebrovascular disease	**aHR: 1.17 (1.05-1.32)**	Non-user	p = 0.001	[28]
No cerebrovascular disease	**aHR: 1.41 (1.31-1.50)**	Non-user		[28]
Heart disease	aHR: 1.19 (1.08-1.30)	Non-user	p = 0.2433	[28]
No heart disease	aHR: 1.26 (1.17-1.36)	Non-user		[28]
Diabetes	aHR: 1.15 (1.01-1.32)	Non-user	p = 0.4913	[28]
No diabetes	aHR: 1.25 (1.18-1.34)	Non-user		[28]
Dementia subtype				
Total population	aHR: 1.06 (0.99-1.13)	Non-user		[17]
Alzheimer's disease	aHR: 1.06 (0.99-1.14)	Non-user	N/A	[17]
Total population	**aHR: 1.14 (1.05-1.24)**	Non-user		[25]
Alzheimer's disease	**aHR: 1.22 (1.05-1.42)**	Non-user	p = 0.571	[25]
No Alzheimer’s disease	**aHR: 1.15 (1.04-1.28)**	Non-user		[25]
Vascular dementia	**aHR: 1.29 (1.11-1.51)**	Non-user	p = 0.090	[25]
No vascular dementia	**aHR: 1.11 (1.01-1.23)**	Non-user		[25]
Mixed-type Dementia	aHR: 0.90 (0.74-1.09)	Non-user	p = 0.001	[25]
No mixed type dementia	**aHR: 1.25 (1.13-1.37)**	Non-user		

Unspecified or other dementia	aHR: 1.09 (0.90-1.32)	Non-user	p = 0.435	[25]
No unspecified or other dementia	**aHR: 1.17 (1.07-1.29)**	Non-user		[25]
Total population	**aHR: 1.4 (1.2-1.5)**	Non-user	N/A	[33]
Alzheimer's disease	**aHR: 1.35 (1.19-1.54)**	Non-user		[33]
Vascular dementia	**aHR: 1.33 (1.17-1.51)**	Non-user		[33]
Other dementia	**Mixed-type Dementia: aHR: 1.32 (1.16-1.50)**	Non-user		[33]
	Unspecified Dementia: aHR: 1.33 (1.17-1.50)	Non-user		[33]
	Other Dementia: aHR: 1.21 (0.78-1.85)	Non-user		[33]
	Frontotemporal Dementia: aHR: 1.15 (0.69-1.94)	Non-user		[33]
	Lewy Body Dementia: aHR: 1.07 (0.89-1.30)	Non-user		[33]
BPSD profile				
Total population	**aHR: 1.14 (1.05-1.24)**	Non-user		[25]
Agitation & Psychosis	aHR: 1.00 (0.78-1.27)	Non-user	p = 0.076	[25]
Above symptom not present	**aHR: 1.21 (1.11-1.32)**	Non-user		[25]
Psychosis & No Agitation	aHR: 1.26 (1.00-1.60)	Non-user	p = 0.443	[25]
Above symptom not present	**aHR: 1.13 (1.04-1.24)**	Non-user		[25]
Agitation & No Psychosis	aHR: 1.16 (0.99-1.36)	Non-user	p = 0.994	[25]
Above symptom not present	**aHR: 1.14 (1.04-1.25)**	Non-user		[25]
No Agitation & Psychosis	aHR: 1.13 (1.00-1.28)	Non-user	p = 0.495	[25]
Above symptom not present	aHR: 1.10 (0.99-1.23)	Non-user		[25]

Frailty Score				
Total population	**aHR: 1.24 (1.02-1.51)**	Non-user		[24]
Robust	**aHR: 1.83 (1.18-2.83)**	Non-user	P = 0.2697 (robust vs prefrail), P = 0.0301 (robust vs frail), and P = 0.2214 (prefrail vs frail)	[24]
Pre-frail	**aHR: 1.34 (0.97-1.87)**	Non-user		[24]
Frail	aHR: 1.02 (0.75-1.38)	Non-user		[24]
Stroke-related mortality				
Dementia subtype				
Total population	**aHR: 1.28 (1.01-1.63)**	Non-user		[25]
Alzheimer's disease	aHR: 1.03 (0.57-1.83)	Non-user	p = 0.194	[25]
No Alzheimer's disease	**aHR: 1.41 (1.08-1.84)**	Non-user		[25]
Vascular dementia	aHR: 1.34 (0.94-1.91)	Non-user	p = 0.614	[25]
No vascular dementia	aHR: 1.23 (0.89-1.71)	Non-user		[25]
Mixed-type dementia	aHR: 1.42 (0.85-2.39)	Non-user	p = 0.867	[25]
No mixed-type dementia	**aHR: 1.34 (1.02-1.76)**	Non-user		[25]
Unspecified or other dementia	aHR: 1.22 (0.64-2.34)	Non-user	p = 0.506	[25]
No unspecified or other dementia	**aHR: 1.39 (1.07-1.80)**	Non-user		[25]
BPSD profile				
Total population	**aHR: 1.28 (1.01-1.63)**	Non-user		[25]
Agitation & Psychosis	aHR: 0.73 (0.33-1.61)	Non-user	p = 0.288	[25]
Above symptom not present	**aHR: 1.34 (1.05-1.71)**	Non-user		[25]
Psychosis & No Agitation	aHR: 1.61 (0.82-3.13)	Non-user	p = 0.481	[25]
Above symptom not present	aHR: 1.18 (0.92-1.52)	Non-user		[25]
Agitation & No Psychosis	aHR: 1.53 (0.97-2.43)	Non-user	p = 0.367	[25]
Above symptom not present	aHR: 1.16 (0.89-1.52)	Non-user		[25]
No Agitation nor Psychosis	aHR: 1.20 (0.84-1.71)	Non-user	p = 0.910	[25]

Above symptom not present	aHR: 1.27 (0.92-1.77)	Non-user		[25]

aHR – adjusted hazards ratio, BPSD – behavioural and psychological symptoms of dementia, N/A – not available

Supplementary Table 7. Predictors of hospitalisation in people living with dementia using antipsychotics

Risk Factor	Risk Estimate	Reference group	Reference
Antipsychotic-related characteristics			
All-cause hospitalisation			
Antipsychotic type			
Quetiapine	**aIRR: 0.92 (0.87-0.98**)	Risperidone	[21]
Emergency department visit			
Antipsychotic type			
Risperidone	aHR: 1.00 (0.84-1.18)	Any other antipsychotic	[25]
Olanzapine	aHR: 0.81 (0.65-1.00)	Any other antipsychotic	[25]
Quetiapine	aHR: 1.12 (0.97-1.30)	Any other antipsychotic	[25]
Typical	aHR: 0.89 (0.74-1.07)	Atypical	[25]
Anticholinergic burden			
Caution Required	aHR: 1.03 (0.85-1.24)	No Anticholinergic Burden	[15]
Review Needed	aHR: 0.95 (0.86-1.06)	No Anticholinergic Burden	[15]
Stroke-related hospitalisation			
Duration of use			
Quetiapine 1-60 days	aHR: 1.17 (0.84-1.87)	Risperidone	[22]
Quetiapine 61-120 days	aHR: 1.66 (0.95-2.91)	Risperidone	[22]
Quetiapine 121-180 days	aHR: 0.92 (0.51-1.66)	Risperidone	[22]
Quetiapine 181-365 days	aHR: 1.03 (0.65-1.63)	Risperidone	[22]
Quetiapine >365 days	aHR: 1.04 (0.73-1.49)	Risperidone	[22]
Antipsychotic type			

Risperidone	aHR: 0.82 (0.46-1.44)	Any other antipsychotic	[25]
Olanzapine	aHR: 0.77 (0.36-1.61)	Any other antipsychotic	[25]
Quetiapine	aHR: 1.12 (0.91-1.37)	Risperidone	[22]
	aHR: 1.38 (0.88-2.16)	Any other antipsychotic	[25]
Typical	aHR: 0.86 (0.48-1.57)	Atypical	[25]
Injury related hospitalisations			
Cumulative antipsychotic DDD			
26-225	**Hip fracture: aOR: 1.10 (1.01-1.21)**	0-25 Cumulative Exposure	[38]
226-1135	Hip fracture: aOR: 1.05 (0.96-1.15)	0-25 Cumulative Exposure	[38]
>1135	**Hip fracture: aOR: 1.12 (1.02-1.22)**	0-25 Cumulative Exposure	[38]
Duration of use			
16-65 days	Hip fracture: aOR: 0.94 (0.85-1.03)	Exposure duration 0-15	[38]
65-215 days	Hip fracture: aOR: 0.93 (0.85-1.02)	Exposure duration 0-15	[38]
>215 days	Hip fracture: aOR: 1.07 (0.97-1.17)	Exposure duration 0-15	[38]
Average daily dose (DDD/day)			
0.5-1	Hip fracture: aOR: 1.05 (0.92-1.20)	Average Daily Dose ≤0.5	[38]
1-2	Hip fracture: aOR: 1.10 (0.98-1.24)	Average Daily Dose ≤0.5	[38]

>2	**Hip fracture: aOR: 1.19 (1.08-1.31)**	Average Daily Dose ≤0.5	[38]
Antipsychotic type			
Atypical	**Hip fracture: aOR: 1.17 (1.08-1.27)**	Typical	[38]
Quetiapine	Head Injury: aHR: 1.27 (0.99-1.62)	Risperidone	[35]
	Traumatic Brain Injury: aHR: 1.59 (1.14-2.21)	Risperidone	[35]
Pneumonia hospitalisation			
Duration of use			
1-3 months	**aHR: 0.61 (0.49-0.74)**	<1 month	[36]
4-6 months	**aHR: 0.39 (0.32-0.48)**	<1 month	[36]
7-12 months	**aHR: 0.26 (0.22-0.32)**	<1 month	[36]
>12 months	**aHR: 0.10 (0.08-0.12)**	<1 month	[36]
Antipsychotic type			
Quetiapine	**aHR: 0.87 (0.78-0.96)**	Risperidone	[36]
Haloperidol	aHR: 1.21 (0.93-1.55)	Risperidone	[36]
Patient related characteristics			
All-cause hospitalisations			
Concomitant drug use			
Benzodiazepines	**aHR: 1.55 (1.29-1.86)*** **	Antipsychotics only	[37]
Antidepressants	aHR: 1.14 (0.98-1.33)	Antipsychotics only	[37]
Benzodiazepines & Antidepressants	**aHR: 1.26 (1.04-1.54)** **	Antipsychotics only	[37]
Hip fracture hospitalisations			

Exposure status			
Current user (0-30 days)	**aOR: 3.07 (2.84-3.32)**	Past User (>180 days)	[38]
Recent user (31-80 days)	**aOR: 1.56 (1.41-1.73)**	Past User (>180 days)	[38]
Drug interaction			
Benzodiazepines	Hip fracture: aHR: 1.50 (0.99-2.26)	Antipsychotics only	[37]
Antidepressants	Hip fracture: aHR: 0.83 (0.57-1.21)	Antipsychotics only	[37]
Benzodiazepines & Antidepressants	Hip fracture: aHR: 0.93 (0.58-1.49)	Antipsychotics only	[37]
Stroke-related hospitalisations			
COVID-19			
Any antipsychotic COVID-19	**aOR: 1.36 (1.21-1.52)**	No COVID-19	[18]
Quetiapine COVID-19	**aOR: 1.42 (1.18-1.70)**	No COVID-19	[18]
Haloperidol COVID-19	**aOR: 1.23 (1.02-1.48)**	No COVID-19	[18]
Olanzapine COVID-19	aOR: 0.94 (0.74-1.20)	No COVID-19	[18]
Risperidone COVID-19	**aOR: 1.60 (1.09-2.34)**	No COVID-19	[18]

aHR – adjsuted hazard ratio, aIRR – adjusted incidence rate ratio, DDD – daily defined doses

*** $p<0.001$

** $p<0.01$

Supplementary Table 8. Moderators of the association between antipsychotic use and hospitalisation in people living with dementia

Risk Factor	Risk Estimate	Reference group	Interaction term significance	Reference
Emergency Department visit				
BPSD symptoms				
Total population	aHR: 1.07 (0.99-1.15)	Non-user		[25]
Agitation & Psychosis	aHR: 0.89 (0.71-1.13)	Non-user	p = 0.327	[25]
Above symptom not present	aHR: 1.02 (0.94-1.11)	Non-user		[25]
Psychosis & No Agitation	aHR: 1.20 (0.97-1.48)	Non-user	p = 0.042	[25]
Above symptom not present	aHR: 0.96 (0.88-1.04)	Non-user		[25]
Agitation & No Psychosis	aHR: 0.95 (0.80-1.11)	Non-user	p = 0.392	[25]
Above symptom not present	aHR: 1.02 (0.93-1.11)	Non-user		[25]
No Agitation & Psychosis	aHR: 0.97 (0.86-1.09)	Non-user	p = 0.774	[25]
Above symptom not present	aHR: 1.01 (0.90-1.12)	Non-user		[25]
Dementia Subtype				
Total population	aHR: 1.07 (0.99-1.15)	Non-user		[25]
Alzheimer's disease	aHR: 1.04 (0.91-1.20)	Non-user	p = 0.370	[25]
No Alzheimer’s disease	aHR: 0.98 (0.89-1.08)	Non-user		[25]
Vascular dementia	aHR: 0.97 (0.83-1.13)	Non-user	p = 0.706	[25]
No vascular dementia	aHR: 1.01 (0.92-1.11)	Non-user		[25]
Mixed-type dementia	aHR: 0.96 (0.81-1.14)	Non-user	p = 0.201	[25]
No mixed-type dementia	aHR: 1.01 (0.92-1.11)	Non-user		[25]
Unspecified or other dementia	aHR: 0.92 (0.76-1.12)	Non-user	p = 0.762	[25]
No unspecified or other dementia	aHR: 1.01 (0.93-1.11)			[25]

Stroke-related hospitalisation				
BPSD profile				
Total population	aHR: 1.02 (0.80-1.29)	Non-user		[25]
Agitation & Psychosis	aHR: 0.97 (0.42-2.21)	Non-user	p = 0.774	[25]
Above symptom not present	aHR: 1.07 (0.82-1.38)	Non-user		[25]
Psychosis & No Agitation	**aHR: 2.16 (1.09-4.25)**	Non-user	p = 0.064	[25]
Above symptom not present	aHR: 0.93 (0.71-1.22)	Non-user		[25]
Agitation & No Psychosis	aHR: 1.10 (0.64-1.88)	Non-user	p = 0.813	[25]
Above symptom not present	aHR: 1.03 (0.78-1.35)	Non-user		[25]
No Agitation & Psychosis	aHR: 0.97 (0.67-1.40)	Non-user	p = 0.437	[25]
Above symptom not present	aHR: 1.19 (0.83-1.70)	Non-user		[25]
Dementia Subtype				
Total population	aHR: 1.02 (0.80-1.29)	Non-user		[25]
Alzheimer's disease	aHR: 0.91 (0.52-1.58)	Non-user	p = 0.509	[25]
No Alzheimer’s disease	aHR: 1.15 (0.87-1.53)	Non-user		[25]
Vascular dementia	aHR: 0.93 (0.59-1.48)	Non-user	p = 0.250	[25]
No vascular dementia	aHR: 1.19 (0.88-1.61)	Non-user		[25]
Mixed-type dementia	**aHR: 1.65 (1.07-2.56)**	Non-user	p = 0.130	[25]
No mixed-type dementia	aHR: 0.95 (0.69-1.29)	Non-user		[25]
Unspecified or other dementia	aHR: 0.77 (0.40-1.50)	Non-user	p = 0.741	[25]
No unspecified or other dementia	aHR: 1.18 (0.90-1.55)	Non-user		[25]
Hip fracture hospitalisations				
Total population	aOR: 1.38 (1.32-1.45)	Non-user		[38]
Age				
50-65	**aOR: 1.40 (1.17-1.67)**	Non-user	N/A	[38]

65-80	**aOR: 1.41 (1.32-1.50)**	Non-user		[38]
≥80	**aOR: 1.33 (1.23-1.43)**	Non-user		[38]
Sex				
Women	**aOR: 1.42 (1.33-1.51)**	Non-user	N/A	[38]
Men	**aOR: 1.33 (1.24-1.43)**	Non-user		[38]

aHR – adjusted hazard ratio, aOR – adjusted odds ratio, BPSD – behavioural and psychological symptoms of dementia, N/A – not available

Supplementary Table 9. Predictors of hospitalisation AND mortality in people living with dementia using antipsychotics

Risk Factor	Risk Estimate	Reference group	Reference
Antipsychotic characteristics			
Antipsychotic dose			
Medium dose	**Women: aOR: 1.40 (1.22-1.61)**	Low dose	[31]
	Men: aOR: 1.32 (1.13-1.54)	Low dose	[31]
High dose	**Women: aOR: 2.13 (1.62-2.80)**	Low dose	[31]
	Men: aOR: 2.34 (1.75-3.14)	Low dose	[31]
Patient characteristics			
Gender			
Men	**aOR: 1.47 (1.33-1.62)**	Women	[31]
Setting of care			
Long-term care	**Women: aOR: 0.71 (0.62-0.81)**	Community care	[31]
	Men: aOR: 0.82 (0.71-0.96)	Community care	[31]
Age			
≥85	Women: aOR: 1.20 (0.97-1.49)	Age 66-84	[31]
	Men: aOR: 1.01 (0.79-1.28)	Age 66-84	[31]
CCI score			
1	Women: aOR: 1.21 (1.00-1.46)	CCI Score: 0	[31]
	Men: aOR: 1.18 (0.94-1.49)	CCI Score: 0	[31]
≥2	**Women: aOR: 1.53 (1.27-1.84)**	CCI Score: 0	[31]
	Men: aOR: 1.53 (1.23-1.90)	CCI Score: 0	[31]

aOR – adjusted odds ratio, CCI – charlson comorbidity index

Supplementary Table 10. Quality Assessment for case-control studies

Author (Year), Country	**Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?**	**Were cases and controls matched appropriately?**	**Were the same criteria used for identification of cases and controls?**	**Was exposure measured in a standard, valid and reliable way?**	**Was exposure measured in the same way for cases and controls?**	**Were confounding factors identified?**	**Were strategies to deal with confounding factors stated?**	**Were outcomes assessed in a standard, valid and reliable way for cases and controls?**	**Was the exposure period of interest long enough to be meaningful?**	**Was appropriate statistical analysis used?**
Tang et al (2021), Taiwan [38]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Supplementary Table 11. Quality Assessment for cohort studies

Author (Year), Country	Were the two groups similar and recruited from the same population?	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	Was the exposure measured in a valid and reliable way?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	Were the outcomes measured in a valid and reliable way?	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	Were strategies to address incomplete follow up utilized?	Was appropriate statistical analysis used?
Brannstrom et al (2017), Sweden [16]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Bishara et al (2021), United Kingdom [15]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Dennis et al (2017), United Kingdom [17]	Yes	Yes	Yes	Yes	yes	Yes	Yes	Yes	Yes	Yes	Yes
Harrison et al (2021), United States [18]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Huang et al (2015), United States [19]	Yes	Yes	Yes	Yes	Not clear	Yes	Yes	Yes	Yes	Yes	Yes
Kales et al (2012), United States [20]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Koponen et al (2019), Finland [21]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Koponen et al (2022),	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Finland [22]											
Koponen et al (2017), Finland [23]	Yes	Yes	yes	Yes	Yes	Yes	yes	Yes	Yes	Yes	Yes
Maxwell et al (2018), Canada [24]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	yes	Yes
Musicco et al (2011), Italy [26]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Mueller et al (2020), United Kingdom [25]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Norgaard et al (2020), Denmark [27]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Norgaard et al (2022),	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Denmark [28]											
Perreault et al (2024), Canada [29]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Rafaniello et al (2014), Italy [30]	Yes	Yes	Yes	Yes	Not clear	Yes	Yes	Yes	YEs	Yes	Yes
Rochon et al (2013), Canada [31]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Rossom et al (2010), United States [32]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Schwertner et al (2019), Sweden [33]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Simoni-Wastila et al (2016),	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

United States [34]											
Tapiainen et al (2020), Finland [35]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Zakarias et al (2021), Denmark [37]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Tolppanen et al (2016), Finland [36]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes