Supplementary information tables 1: Moose checklist

Recommendation	Reported on (page no.
	of published paper)
Reporting of background should include	
Problem definition	1; Introduction
Hypothesis statement	1; Introduction
Description of study outcome(s)	2; Studies considered
	and search strategy
Type of exposure or intervention used	2; Studies considered
	and search strategy
Type of study designs used	2; Studies considered
	and search strategy
Study population	2; Studies considered
	and search strategy
Reporting of search strategy should include	
Qualifications of searchers (e.g., librarians and investigators)	2; Studies considered
	and search strategy
Search strategy, including time period included in the synthesis	2; Studies considered
and keywords	and search strategy
Effort to include all available studies, including contact with	2; Studies considered
authors	and search strategy
Databases and registries searched	2; Studies considered
	and search strategy
Search software used, name and version, including special features	NA
used (e.g., explosion)	
Use of hand searching (e.g., reference lists of obtained articles)	2; Studies considered
	and search strategy
List of citations located and those excluded, including justification	3; Figure 1
Method of addressing articles published in languages other than	NA
English	
Method of handling abstracts and unpublished studies	2; Studies considered
	and search strategy
Description of any contact with authors	2; Studies considered
	and search strategy
Reporting of methods should include	
Description of relevance or appropriateness of studies assembled	2; Studies considered
for assessing the hypothesis to be tested	and search strategy,
	study quality
Rationale for the selection and coding of data (e.g., sound clinical	NA
principles or convenience)	
Documentation of how data were classified and coded (e.g.,	2; Study quality
multiple raters, blinding, and interrater reliability)	
Assessment of confounding (e.g., comparability of cases and	2; Study quality
controls in studies where appropriate)	

Assessment of study quality, including blinding of quality	2; Study quality
assessors; stratification or regression on possible predictors of	
study results	
Assessment of heterogeneity	2; Statistical analyses
Description of statistical methods (e.g., complete description of	2; Statistical analyses
fixed or random effects models, justification of whether the	
chosen models account for predictors of study results, dose-	
response models, or cumulative meta-analysis) in sufficient detail	
to be replicated	
Provision of appropriate tables and graphics	3-11; Results
Reporting of results should include	
Graphic summarizing individual study estimates and overall	3-11; Results
estimate	
Table giving descriptive information for each study included	4-5; Table 1
Results of sensitivity testing (e.g., subgroup analysis)	19; Sensitivity
	analyses,
	supplementary table 5
Indication of statistical uncertainty of findings	Yes, presented as CIs
	in all results and
	figures
Reporting of discussion should include	
Quantitative assessment of bias (e.g., publication bias)	10-11; Discussion:
	Statistical analysis &
	Methodological issues
Justification for exclusion (e.g., exclusion of non–English-language	Not reported
citations)	
Assessment of quality of included studies	11-12; Discussion:
	Methodological issues
Reporting of conclusions should include	
Consideration of alternative explanations for observed results	11-12; Methodological
	issues & Causality
Generalization of the conclusions (i.e., appropriate for the data	13; Clinical
presented and within the domain of the literature review)	implications
Guidelines for future research	13; Clinical
	implications
Disclosure of funding source	14; Funding

From: Stroup DF, Berlin JA, Morton SC, et al. (2000) Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 283: 2008-2012.

<u>Supplementary information tables 2 – 6</u>

<u>Supplementary information table 2: Risk of pneumonia with individual antipsychotic drugs compared to no exposure</u>

Antipsychotic	No of studies	RR (95% Confidence	Weight (%)	l ² (%)
		Intervals)		
Amisulpride	1	1.14 (0.79 to 1.65)	5.6	NA
Chlorpromazine	1	1.10 (0.68 to 1.78)	4.8	NA
Clozapine	2	3.12 (2.59 to 3.74)	11	0
Haloperidol	2	2.75 (1.48 to 5.12)	10.7	78
Olanzapine	3	2.16 (1.51 to 3.09)	13.5	45.1
Pipamperone	1	1.55 (0.99 to 2.42)	5.07	NA
Quetiapine	2	1.79 (1.40 to 2.29)	12.3	33.2
Risperidone	3	1.86 (1.17 to 2.96)	16.6	81.3
Sulpiride	1	1.29 (0.94 to 1.77)	6	NA
Zotepine	2	1.50 (1.20 to 1.90)	11.5	0
Zuclopenthixol	1	2.25 (1.00 to 5.07)	2.9	NA
Overall	3	1.88 (1.57 to 2.25)	100	81.2

<u>Supplementary information table 3: Consensus Newcastle-Ottawa Scale (NOS) Case controlled studies</u>

		Selection		Comparability		Exposure						
Case controlled studies	Case definition	Represen- tativeness	Selection of controls	Definition of controls	Comparability (a)	Comparability (b)	Ascertainment	Method	Non-response rate			
Kuo et al (2013)	0	1	1	0	1	1	0	1	1			
Yang et al (2013)	0	1	1	0	1	1	0	1	1			
Gau et al (2010)	1	1	1	1	1	1	0	1	1			
Trifirò et al (2010)	1	1	1	1	1	1	0	1	1			

Knol et al (2008)	0	1	1	1	1	1	0	1	1
Wada et al (2001)	1	1	0	0	1	0	0	0	0
Liao et al 2013	0	1	1	1	1	1	0	1	1
Barnett et al (2006)	0	1	1	1	1	1	0	1	1
Pratt et al (2011))	0	1	1	1	1	1	0	1	1

NB: A study can be awarded a maximum of one star for each item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

Rating of 'cases' and 'comparability' for Case Control studies (Table 3)

1. Is the case definition adequate?

- a) yes, with independent validation (i.e. using more than 1 database to verify cases) *
- b) yes, e.g. record linkage or based on self-reports
- c) no description

2. Comparability of cases and controls on the basis of the design or analysis

- a) study controls for 'Age' (selected by authors as the most important factor) *
- b) study controls for any additional factor: Smoking, gender, chronic respiratory diseases (asthma and/or COPD), or psychiatric diagnosis. *

NB: Two *s if propensity score matching or adjustment for multiple variables

<u>Supplementary information table 4: Consensus Newcastle-Ottawa Scale (NOS) for Cohort studies</u>

			Selection		Compa	Comparability		Outcome		
Cohort studies	Represen- tativeness	Selection of unexposed	Ascertainment of exposure	Outcome not present at start	Comparability (a)	Comparability (b)	Assessment	Length of follow-up	Adequacy of follow-up	
Aparasu et al (2013)	1	1	0	0	1	1	1	1	0	
Huybrechts et al (2012)	1	1	0	0	1	1	1	1	1	
Wang et al (2007)	1	1	0	0	1	1	1	1	0	
Huybrechts et al (2011)	1	1	0	0	1	1	1	1	0	
Dharmarajan et al (2011)	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Star et al (2010)	NA	NA	NA	NA	NA	NA	NA	NA	NA	

Ī	Jackson et al (2015)	1	1	0	0	1	1	1	1	0
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Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

Supplementary information table 5: Sensitivity analyses

A: Sensitivity analysis on variations of the primary analysis

Comparison	No of	RR	95% Confidence	I ² (%)			
	studies		Interval				
DerSimonian & Laird	d CIs in stud	ies of pr	neumonia				
SGA vs no SGA	6	1.93	1.65 to 2.26	44.7			
FGA vs no FGA	5	1.70	1.44 to 2.00	45.8			
FGA vs SGA	7	1.07	0.90 to 1.28	50.2			
Antipsychotic exposure vs no	2	2.02	1.08 to 3.77	63.2			
exposures							
Individual antipsychotic	11*	1.88	1.57 to 2.25	81.2			
Excluding se	lf-control co	ase serie	?S				
SGA vs no SGA excluding SCCS	5	2.11	1.54 to 2.88	46.5			
DerSimonian & Laird CIs in studies of mortality							
Antipsychotic exposure vs no	4 ^{\$}	1.50	1.05 to 2.14	51.0			
exposure							

^{*}Number of Individual antipsychotic from 3 studies; \$ Number of comparisons from 2 studies

B: Sensitivity analysis removing each study in turn in SGA vs no SGA analysis

Study omitted	Estimate	95% Confidence interval		
Kuo et al (2013)	2.10	1.69	2.63	
Yang et al (2013)	1.92	1.60	2.31	
Gau et al (2010)	1.92	1.63	2.28	
Trifiro et al (2010)	1.88	1.61	2.20	
Knol et al (2008)	1.79	1.61	1.98	
Pratt et al (2011)	2.11	1.69	2.62	
Combined	1.93	1.65	2.26	

C: Sensitivity analysis removing each study in turn in FGA vs no FGA analysis

Study omitted	Estimate	95% Confid	95% Confidence interval		
Kuo et al (2013)	1.75	1.45	2.09		
Yang et al (2013)	1.57	1.39	1.78		
Trifiro et al (2010)	1.68	1.38	2.06		
Knol et al (2008)	1.76	1.43	2.16		
Pratt et al (2011)	1.72	1.36	2.19		
Combined	1.69	1.44	2.00		

D: Sensitivity analysis removing each study in turn in FGA vs SGA analysis

Study omitted	Estimate	95% Confidence inter	val
Aparasu et al (2013)	1.04	0.85	1.28
Huybrechts et al (2012)	1.05	0.86	1.27
Wang et al (2007)	1.14	0.96	1.36
Trifiro et al (2010)	1.11	0.93	1.32
Huybrechts et al (2011)	1.08	0.88	1.32
Dharmarajan et al (2011)	1.08	0.86	1.37
Jackson et al (2015)	1.02	0.87	1.20
Combined	1.07	0.90	1.28

Supplementary information table 6: Database searches

Database:	Embase	<1974 to	2016	Week	18>
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Search Strategy:

- 1 *pneumonia/ (43195)
- 2 *neuroleptic agent/ (28232)
- 3 1 and 2 (28)
- 4 exp pneumonia/ (229474)
- 5 2 and 4 (105)
- 6 from 5 keep 1,3-6,8,11-13,16,19-20,22,24-25,27-29,33,38,40-41,43,45,47,50,54,57-58,61,67,69 (32)

Database: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to April 2016>

Search Strategy:

- 1 *Antipsychotic Agents/ (33153)
- 2 exp Pneumonia/ (80258)
- 3 1 and 2 (43)
- 4 from 3 keep 1,4-7,9-14,17-23,26-28,31,41 (23)

Database: PubMed, Inception to April 2016

Search	Query	Items found
#1	("Antipsychotic Agents"[Mesh]) AND	13
	"Pneumonia, Aspiration"[Mesh]	
#2	("Pneumonia, Bacterial"[Mesh]) AND	5
	"Antipsychotic Agents"[Mesh]	
#3	(#1 or #2)	18
#4	Antipsychotic and pneumonia Filters:	0
	Observational Study	
#5	Antipsychotic and pneumonia Schema: all filters:	0
	Observational Study	
#6	Antipsychotic and pneumonia	199
#7	(#3 or #6)	199
#8	From #7 Select 19 document(s)	19