

Appendix A – Search Strategies

MEDLINE via PubMed

Anticholinergics and Fractures

((("Cholinergic Antagonists"[MESH]) OR ("anticholinergic*" [TIAB]) OR ("anti-cholinergic" [TIAB])) AND (("fracture*" [TIAB]) OR ("Fractures, Bone"[MESH]))

Anticholinergics and osteoporosis and/or reduced bone mineral density

((("Cholinergic Antagonists"[MESH]) OR ("anticholinergic*" [TIAB]) OR ("anti-cholinergic" [TIAB])) AND (("Osteoporosis"[MESH]) OR ("Osteoporosis" [TIAB]) OR ("Bone Density"[MESH]) OR ("Bone loss" [TIAB]) OR ("Bone density loss" [TIAB]) OR ("Bone mineral density loss" [TIAB]) OR ("bone metabolism" [TIAB]) OR ("bone mass" [TIAB]) OR ("bone mass index" [TIAB]) OR ("bone strength" [TIAB]) OR ("dual-energy X-ray absorptiometry" [TIAB]) OR ("bone turnover marker*" [TIAB]))

EMBASE via Embase.com

Anticholinergics and Fractures

('cholinergic receptor blocking agent'/exp OR 'anticholinergic*':ti,ab OR 'anti-cholinergic*':ti;ab OR 'anti cholinergic*') AND ('fracture'/exp OR fracture*':ti,ab)

Anticholinergics and osteoporosis and/or reduced bone mineral density

('cholinergic receptor blocking agent'/exp OR 'anticholinergic*':ti,ab OR 'anti-cholinergic*':ti;ab OR 'anti cholinergic*') AND (('Osteoporosis'/exp OR 'Osteoporosis ti,ab OR 'Bone Density' ti,ab OR 'Bone loss' ti,ab OR 'Bone density loss' ti,ab OR 'Bone mineral density loss' ti,ab OR 'bone metabolism' ti,ab OR 'bone mass' ti, ab OR 'bone mass index' ti,ab OR 'bone strength' ti,ab OR 'dual-energy X-ray absorptiometry' ti,ab OR 'bone turnover marker*' ti,ab)

SCI via Web of Science

Anticholinergics and Fractures

((TS=("Cholinergic Antagonist*" OR "anticholinergic*" OR "anti-cholinergic*" OR "Antagonists, Cholinergic" OR "Antagonist, Cholinergic" OR "Cholinergic-Blocking Agents" OR "Agents, Cholinergic-Blocking" OR "Cholinergic Blocking Agents" OR "Cholinolytics" OR "Acetylcholine Antagonists" OR "Antagonists, Acetylcholine" OR "Cholinergic Receptor Antagonists" OR "Antagonists, Cholinergic Receptor" OR "Receptor Antagonists, Cholinergic" OR "Anticholinergic Agents" OR "Agents, Anticholinergic" OR "Anticholinergics" OR "Anti-Cholinergics" OR "Anti Cholinergics" OR "Muscarinic Antagonists" OR "Antagonists, Muscarinic" OR "Antimuscarinics" OR "Antimuscarinic Agents" OR "Agents, Antimuscarinic"

OR "Cholinergic Muscarinic Antagonists" OR "Antagonists, Cholinergic Muscarinic" OR "Muscarinic Antagonists, Cholinergic" OR "Nicotinic Antagonists" OR "Antagonists, Nicotinic") OR (TS=("anticholinergic burden" OR "anticholinergic load" OR "anticholinergic cognitive burden" OR "Drug Burden Index" OR "anticholinergic drug scale*" OR "Anticholinergic Risk Scale*" OR "anticholinergic activity" OR MARANTE OR "DBI-ACH" OR "Anticholinergic Loading Scale" OR "Summated Anticholinergic Medications Scale")) AND (TS=(fracture*))

Anticholinergics and osteoporosis and/or reduced bone mineral density

((TS=("Cholinergic Antagonist*" OR "anticholinergic*" OR "anti-cholinergic*" OR "Antagonists, Cholinergic" OR "Antagonist, Cholinergic" OR "Cholinergic-Blocking Agents" OR "Agents, Cholinergic-Blocking" OR "Cholinergic Blocking Agents" OR "Cholinolytics" OR "Acetylcholine Antagonists" OR "Antagonists, Acetylcholine" OR "Cholinergic Receptor Antagonists" OR "Antagonists, Cholinergic Receptor" OR "Receptor Antagonists, Cholinergic" OR "Anticholinergic Agents" OR "Agents, Anticholinergic" OR "Anticholinergics" OR "Anti-Cholinergics" OR "Anti Cholinergics" OR "Muscarinic Antagonists" OR "Antagonists, Muscarinic" OR "Antimuscarinics" OR "Antimuscarinic Agents" OR "Agents, Antimuscarinic" OR "Cholinergic Muscarinic Antagonists" OR "Antagonists, Cholinergic Muscarinic" OR "Muscarinic Antagonists, Cholinergic" OR "Nicotinic Antagonists" OR "Antagonists, Nicotinic")) OR (TS=("anticholinergic burden" OR "anticholinergic load" OR "anticholinergic cognitive burden" OR "Drug Burden Index" OR "anticholinergic drug scale*" OR "Anticholinergic Risk Scale*" OR "anticholinergic activity" OR MARANTE OR "DBI-ACH" OR "Anticholinergic Loading Scale" OR "Summated Anticholinergic Medications Scale")) AND (TS=("Osteoporosis" OR "Bone Density" OR "Bone loss" OR "Bone density loss" OR "Bone mineral density loss" OR "bone metabolism" OR "bone mass" OR "bone mass index" OR "bone strength" OR "dual-energy X-ray absorptiometry" OR "bone turnover marker*"))

Cochrane Controlled Register of Trials (CENTRAL)

Anticholinergics and Fractures

Anticholinergic* AND fracture*

Anticholinergics and osteoporosis and/or reduced bone mineral density

Anticholinergic* AND (Osteoporosis OR "Bone Density" OR "Bone loss" OR "Bone density loss" OR "Bone mineral density loss" OR "bone metabolism" OR "bone mass" OR "bone mass index" OR "bone strength" OR "dual-energy X-ray absorptiometry" OR "bone turnover marker*")

Open DOAR

Hand search in relevant repositories (Health and Medicine)

OSFPreprints

Anticholinergics and Fractures

anticholinergic* AND fracture*

Anticholinergics and osteoporosis and/or reduced bone mineral density

Anticholinergic* AND (Osteoporosis OR "Bone Density" OR "Bone loss" OR "Bone density loss" OR "Bone mineral density loss" OR "bone metabolism" OR "bone mass" OR "bone mass index" OR "bone strength" OR "dual-energy X-ray absorptiometry" OR "bone turnover marker**")

OpenGrey

Anticholinergics and Fractures

anticholinergic* AND fracture*

Anticholinergics and osteoporosis and/or reduced bone mineral density

Anticholinergic* AND (Osteoporosis OR "Bone Density" OR "Bone loss" OR "Bone density loss" OR "Bone mineral density loss" OR "bone metabolism" OR "bone mass" OR "bone mass index" OR "bone strength" OR "dual-energy X-ray absorptiometry" OR "bone turnover marker**")

GreyLit

Anticholinergics and Fractures

anticholinergic* AND fracture*

Anticholinergics and osteoporosis and/or reduced bone mineral density

Anticholinergic* AND (Osteoporosis OR "Bone Density" OR "Bone loss" OR "Bone density loss" OR "Bone mineral density loss" OR "bone metabolism" OR "bone mass" OR "bone mass index" OR "bone strength" OR "dual-energy X-ray absorptiometry" OR "bone turnover marker**")

Google Scholar

Anticholinergics and Fractures

anticholinergic*AND fracture* , First 500 results

Anticholinergics and osteoporosis and/or reduced bone mineral density

Anticholinergic* AND (Osteoporosis OR "Bone Density" OR "Bone loss" OR "Bone density loss" OR "Bone mineral density loss" OR "bone metabolism" OR "bone mass" OR "bone

mass index" OR "bone strength" OR "dual-energy X-ray absorptiometry" OR "bone turnover marker*"), First 500 results

Appendix B – Data Items

Variables	Data type	Coding
Search Process and management		
V_inclusion_to_full_text_review	Integer	
V_irrelevant	Integer	-1=Yes 0=No
V_inclusion_to_systematic_review	Integer	
V_Comments	Memo	
V_Publication	Attachment	
General		
V_First Author	Text	
V_Year of publication	Integer	
V_Country	Text	
V_Study title	Memo	
V_Abstract	Memo	
V_Journal	Text	
V_Doi	Text	

Methods		
V_Design	Integer	1=Case-Control Study 2=Nested Case-Control Study 3=Cohort Study 99=Other
V_design_other	Memo	
V_data source_setting	Integer	1=Claims data 2=Other administrative data 3=EMR 4=Primary data 99=Other
v_data_source_setting_other	Memo	
V_Inclusion criteria	Memo	
V_Exclusion criteria	Memo	
V_Study period_begin	Integer	
V_Study period_end	Integer	
V_Follow_up_type	Integer	1=Mean 2=Median 99=N.A.
V_Follow up duration	Integer	

V_Type_of_scale	Integer	1=ADS 2=ARS 3=ACB 4=DBI 5=ACL 6=SAMS 7=MARANTE 99=Other/Multiple
V_Assessment of exposure	Memo	
V_Assessment of Outcome	Memo	
V_Description of Controls	Memo	
V_Reference_Category	Memo	
V_Controls matched by/analysis adjusted for	Memo	
V_Limitations	Memo	
Results		
V_Number of included persons	Integer	
V_Number of cases	Integer	
V_Number of controls	Integer	
V_Risk estimate	Memo	

Risk of bias assessment (Newcastle-Ottawa Scale)		
V_NOSCC_S1	Integer	1= Yes, with independent validation 2= Yes, e.g. record linkage or based on self reports 3= No description
V_NOSCC_S2	Integer	1= Consecutive or obviously representative series of cases 2= Potential for selection biases or not stated
V_NOSCC_S3	Integer	1= Community controls (i.e. same community as cases) 2= Hospital controls 3= No description
V_NOSCC_S4	Integer	1= No history of disease (endpoint) 2= No description of source
V_NOSCC_C1	Integer	1= Adequate control for confounders 2= Inadequate control for confounders 3= No description of controlling
V_NOSCC_E1	Integer	1= Secure record (gold standard) 2= Structured interview where blind to case/control status 3= Interview not blinded to case/control status 4= Written self-report or medical record only 5= No description
V_NOSCC_E2	Integer	1=Yes

		2=No
V_NO SCC_E3	Integer	1= Same rate for both groups (incl. non-response not applicable) 2= Non respondents described 3= Rate different and no designation
V_NO SC S1	Integer	1= Very representative 2= Somewhat representative 3= Selected group of users e.g. nurses, volunteers 4= No description of the derivation of the cohort
V_NO SC S2	Integer	1= Drawn from the same community as the exposed cohort 2= Drawn from a different source 3= No description of the derivation of the non-exposed cohort
V_NO SC S3	Integer	1= Secure record (gold standard) 2= Structured interview 3= Self reported 4= No description
V_NO SC S4	Integer	1=Yes 2=No
V_NO SC C1	Integer	1= Adequate control for confounders 2= Inadequate control for confounders 3= No description of controlling
V_NO SC O1	Integer	1= Independent blind assessment

		2= Record linkage 3= Self report 4= No description
V_NOOSC_O2	Integer	1=Yes 2=No
V_NOOSC_O3	Integer	1= Complete follow up all subjects accounted for 2= Subjects lost to follow up unlikely to introduce bias 3= Subjects lost to follow up likely to introduce bias 4= No statement
Risk of bias assessment RTI Item Bank		
RTI_Q1	Integer	5=Prospective 6=Retrospective 7=Mixed
RTI_Q2	Integer	-1=Yes 2=Partially 0=No
RTI_Q3	Integer	-1=Yes 2=Partially 0=No 3=Cannot determine

RTI_Q4	Integer	-1=Yes 2=Partially 0=No 3=Cannot determine 4=Not applicable
RTI_Q5	Integer	-1=Yes 0=No 3=Cannot determine 4=Not applicable
RTI_Q6	Integer	-1=Yes 0=No
RTI_Q7	Integer	10=High 9=Medium 8=Low
RTI_Q8	Integer	-1=Yes 2=Partially 0=No 4=Not applicable
RTI_Q9	Integer	-1=Yes 0=No 3=Cannot determine

RTI_Q10	Integer	-1=Yes 0=No 3=Cannot determine 4=Not applicable
RTI_Q11	Integer	-1=Yes 2=Partially 0=No or do not know 4=Not applicable
RTI_Q12	Integer	-1=Yes 0=No 3=Cannot determine
RTI_Q13	Integer	-1=Yes 0=No 3=Cannot determine
RTI_Q14	Integer	-1=Yes 0=No or cannot determine 4=Not applicable
RTI_Q15	Integer	-1=Yes 2=Partially 0=No 3=Cannot determine

		4=Not applicable
RTI_Q16	Integer	-1=Yes 0=No 3=Cannot determine 4=Not applicable
RTI_Q17	Integer	-1=Yes 0=No 3=Cannot determine 4=Not applicable
RTI_Q18	Integer	-1=Yes 2=Partially 0=No 3=Cannot determine
RTI_Q19	Integer	-1=Yes 0=No 3=Cannot determine 4=Not applicable
RTI_Q20	Integer	-1=Yes 0=No 3=Cannot determine
RTI_Q21	Integer	-1=Yes

		2=Partially 0=No
RTI_Q22	Integer	-1=Yes 2=Partially 0=No 3=Cannot determine 4=Not applicable
RTI_Q23	Integer	-1=Yes 2=Partially 0=No
RTI_Q24	Integer	-1=Yes 0=No
RTI_Q25	Integer	-1=Yes 0=No 4=Not applicable
RTI_Q26	Integer	-1=Yes 0=No 3=Cannot determine
RTI_Q27	Integer	-1=Yes 0=No