

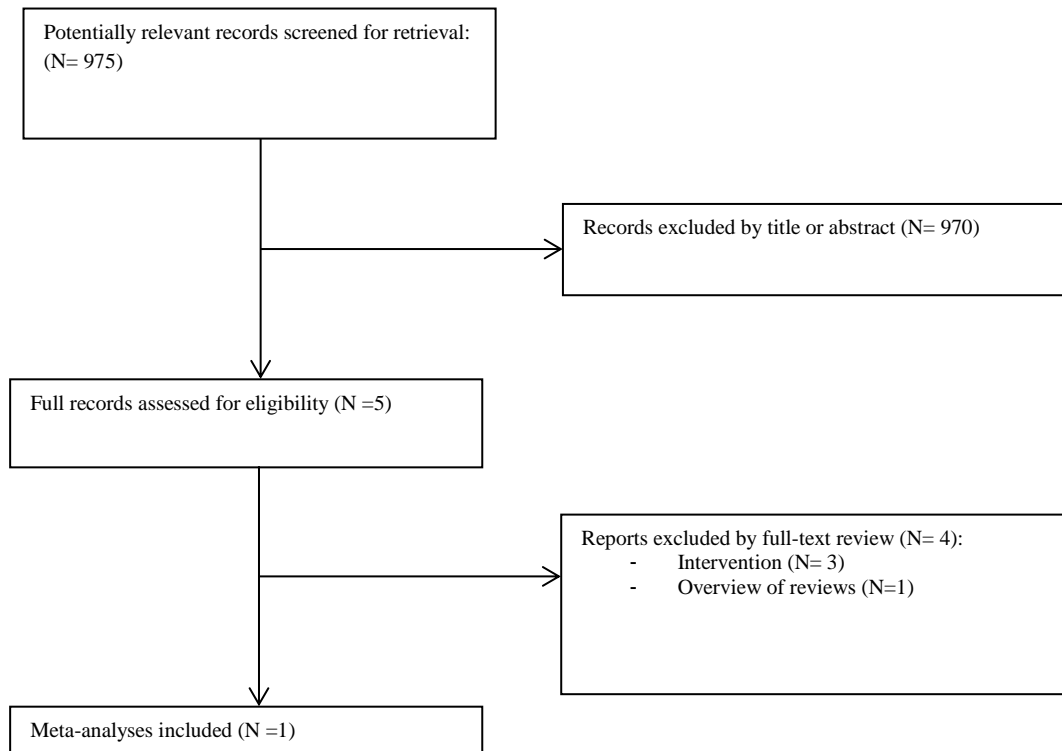
## Additional file 1

### Details and results of the search

PubMed search syntax, PRISMA diagrams for all therapy types and PICO questions for the included meta-analyses. The update search was conducted in August 2014.

#### [1] Hypertension (antihypertensive drugs)

(„Hypertension“[Mesh] AND "Meta-Analysis"[Publication Type])



#### Included study 1:

Law M. Morris JK. Jordan R. Wald N. Headaches and the treatment of blood pressure: results from a meta-analysis of 94 randomized placebo-controlled trials with 24.000 participants. *Circulation* 2005;112:2301-6.

#### PICO questions:

People: adults  
Intervention: 4 different classes of blood pressure–lowering drugs (thiazides, beta-blockers, ACE inhibitors, and angiotensin II receptor antagonists) in fixed doses  
Comparison: placebo  
Outcome: reductions in systolic and diastolic blood pressures, reduction in headaches

#### Included study 2 (selected post-hoc from the reports excluded by full-text review):

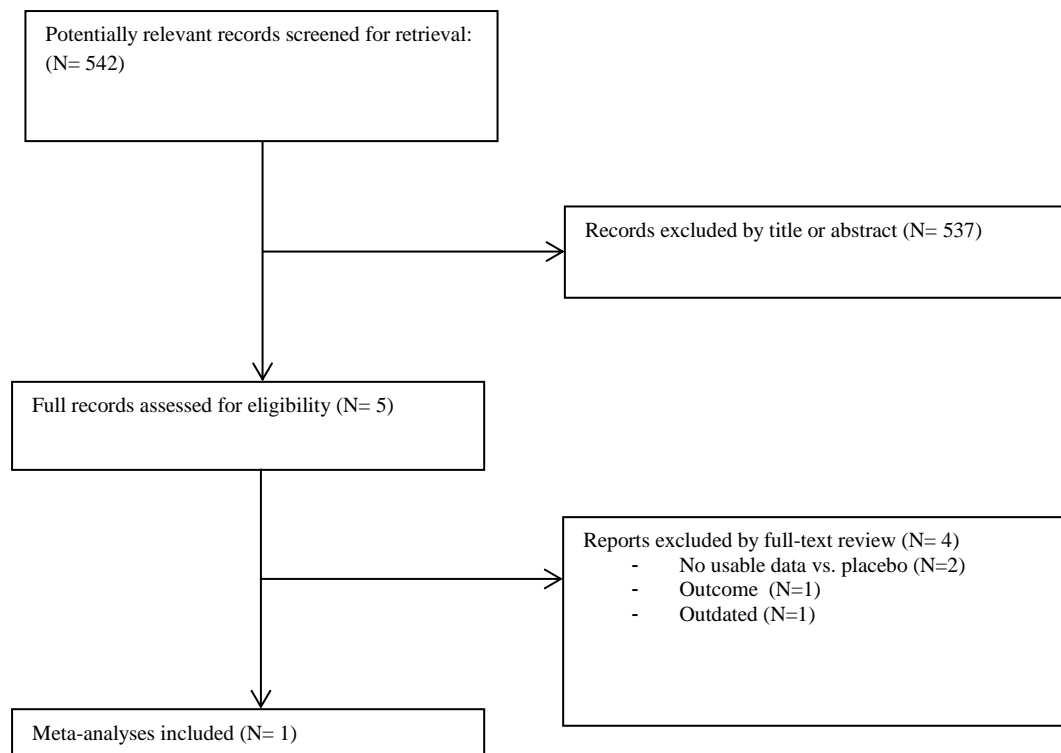
Turnbull, F. Blood Pressure Lowering Treatment Trialists, Collaboration. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomized trials. *Lancet* 2003;362:1527-35.

#### PICO questions:

People: adults  
Intervention: treatment strategies based on different drug classes (angiotensin-converting-enzyme inhibitors, calcium antagonists, angiotensin-receptor blockers, diuretics, beta blockers)  
Comparison: placebo  
Outcome: risks of total major cardiovascular events

## [2] Cholesterol (statins)

("lipid regulating agents"[MeSH Terms]) AND " Meta-Analysis "[Publication Type]



### Included study:

Baigent C. Keech A. Kearney PM. et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90.056 participants in 14 randomised trials of statins. *Lancet* 2005;366:1267-78.

### PICO questions:

People: all

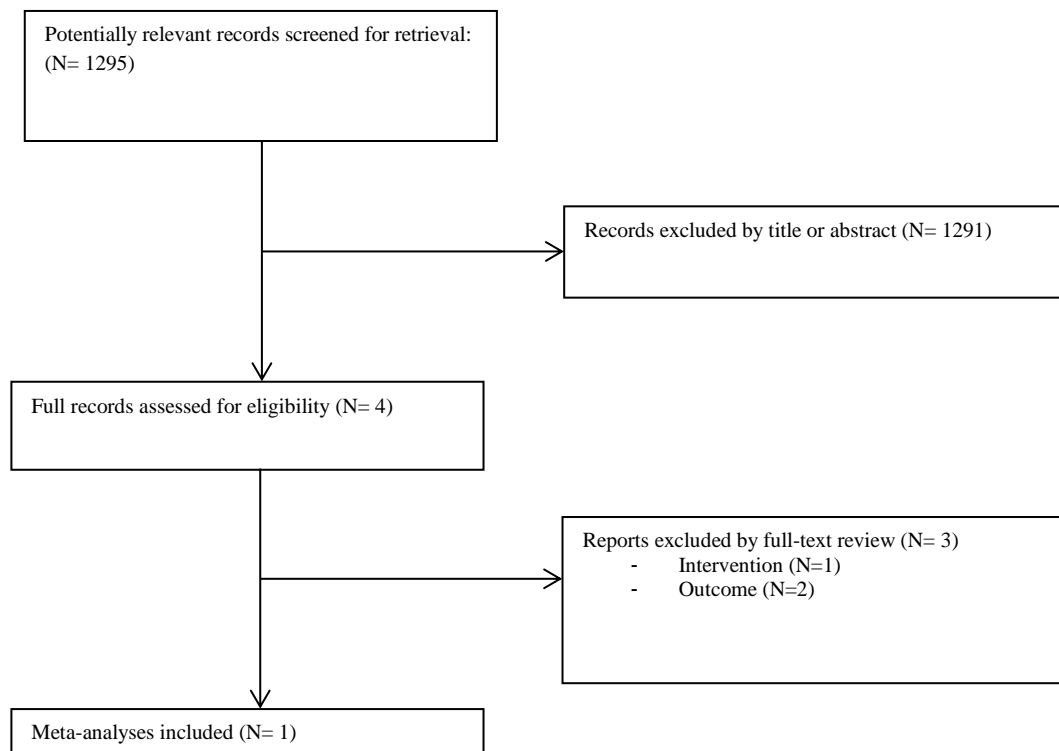
Intervention: statin therapy

Comparison: placebo, no treatment, usual care

Outcome: absolute LDL cholesterol difference, all-cause mortality, coronary heart disease mortality, and non- coronary heart disease mortality, major cardiovascular events

### [3] Antidepressants (major depressive disorder)

("depressive disorder"[MeSH Terms]) OR "antidepressive agents"[MeSH Terms]) AND "meta analysis"[Publication Type]



#### Included study:

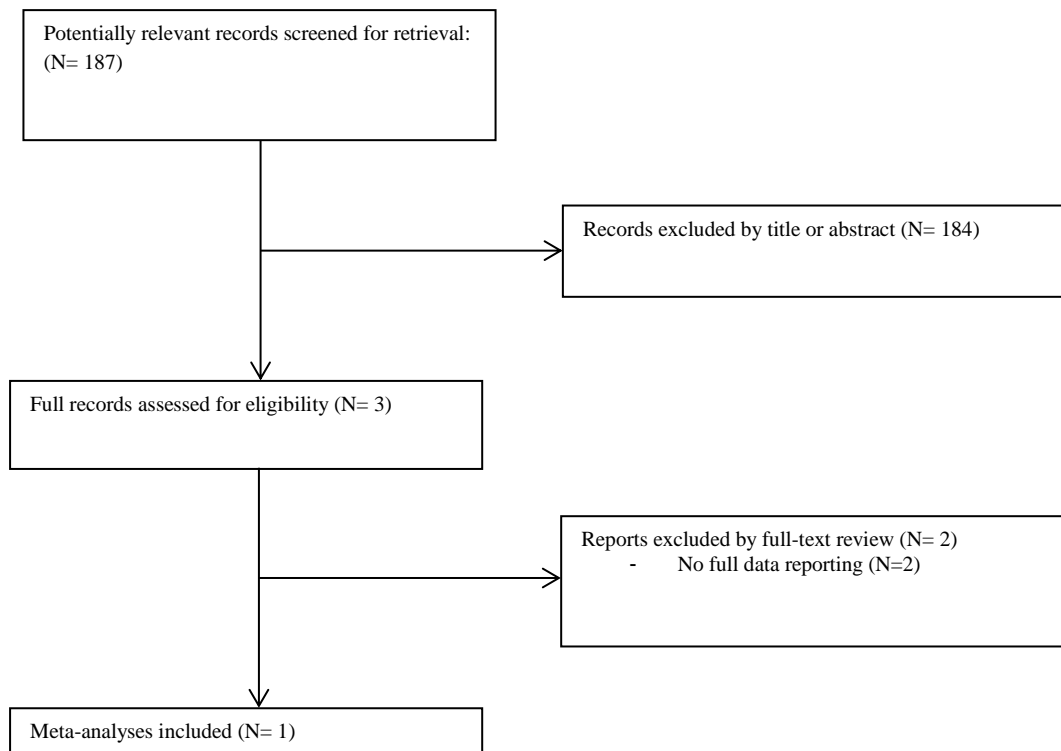
Undurraga J. Baldessarini RJ. Randomized, placebo-controlled trials of antidepressants for acute major depression: thirty-year meta-analytic review. *Neuropsychopharmacology*. 2012 Mar;37(4):851-64. doi: 10.1038/npp.2011.306. Epub 2011 Dec 14

#### PICO questions:

People: adults in an acute major depressive episode  
Intervention: antidepressants  
Comparison: placebo  
Outcome: reduction in initial depression rating-scale scores

#### [4] Anti-Ulcerants (proton pump inhibitors)

("proton pump inhibitors"[MeSH Terms]) AND "meta analysis"[Publication Type]



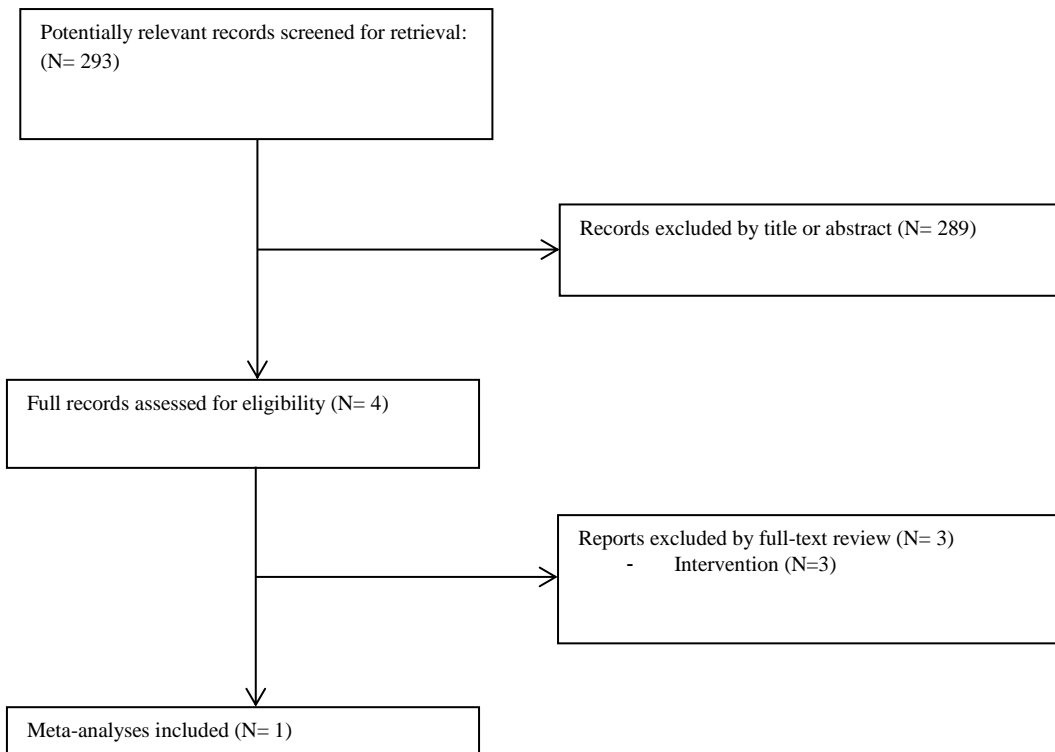
#### Included study:

Moayyedi P. Santana J. Khan M. Preston C. Donnellan C. Medical treatments in the short term management of reflux oesophagitis. Cochrane Database Syst Rev 2007:CD003244

#### PICO questions:

People: adults who had reflux oesophagitis diagnosed at endoscopy  
Intervention: proton pump inhibitors, H2 receptor antagonists, prokinetic therapy, sucralfate  
Comparison: against each other and placebo  
Outcome: proportion of patients who had reflux oesophagitis symptoms or oesophagitis persisting

**[5] Narcotics (analgesics for postoperative pain)**  
("narcotics"[MeSH Terms]) AND "meta analysis"[Publication Type]



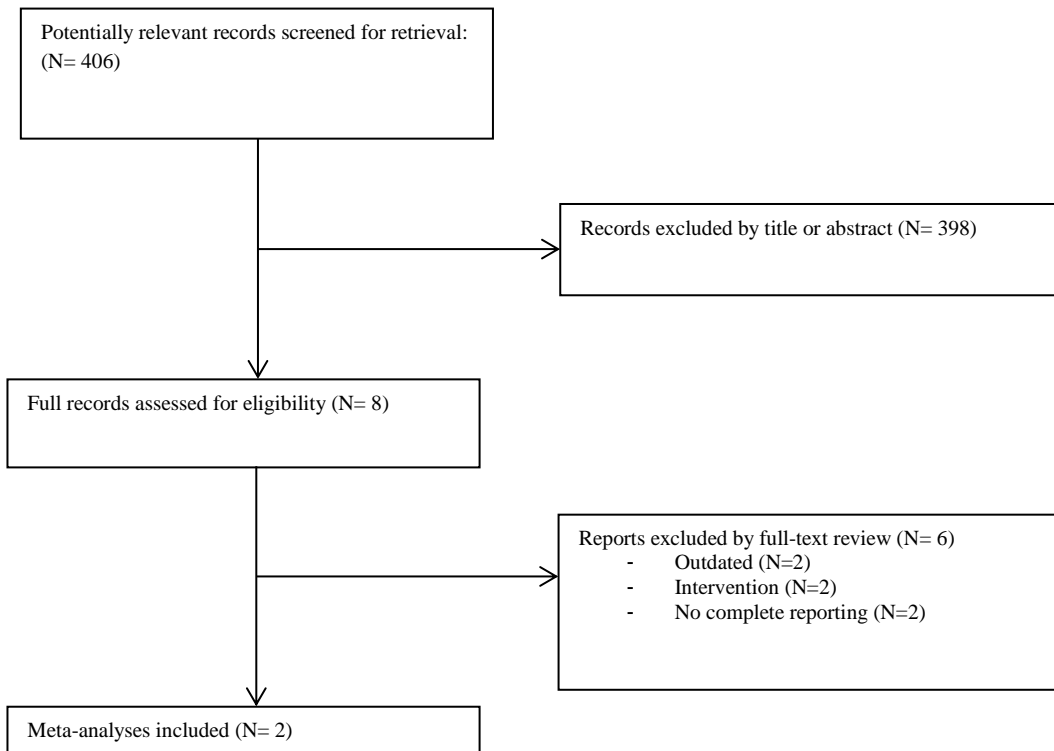
Included study:

Moore RA. Derry S. McQuay HJ. Wiffen PJ. Single dose oral analgesics for acute postoperative pain in adults. Cochrane Database Syst Rev 2011:CD008659.

PICO questions:

People: adults with acute postoperative pain  
Intervention: single dose oral analgesics  
Comparison: placebo  
Outcome: at least 50% maximum pain relief over four to six hours

**[6] Antidiabetes (metformin, GLP-1 analogues, DPP4-Inhibitors, SGLT2 inhibitors)**  
("hypoglycemic agents"[MeSH Terms]) AND "meta analysis"[Publication Type]



Included study 1:

Boussageon R. Supper I. Bejan-Angoulvant T. et al. Reappraisal of metformin efficacy in the treatment of type 2 diabetes: a meta-analysis of randomised controlled trials. PLoS medicine 2012;9:e1001204.

PICO questions:

People: people with type 2 diabetes  
Intervention: metformin  
Comparison: no treatment, placebo, diet  
Outcome: all-cause mortality and cardiovascular death

Included study 2:

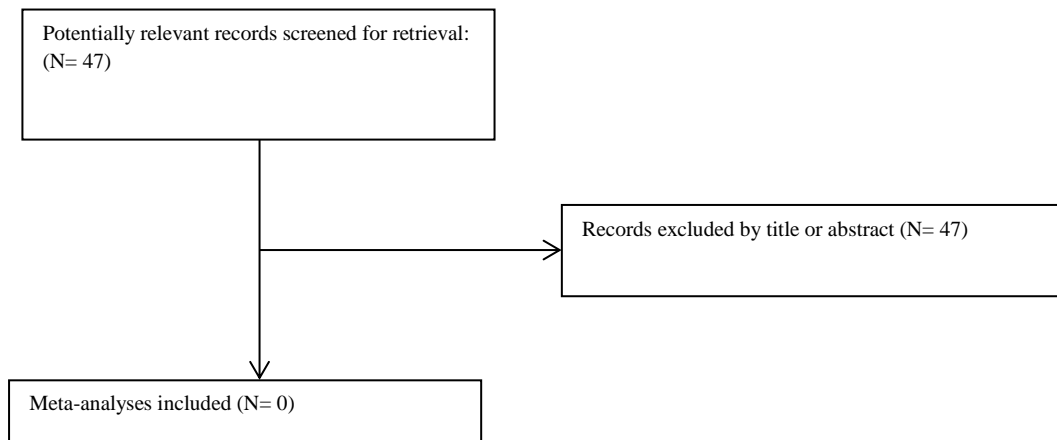
Saenz A. Fernandez-Esteban I. Mataix A. Ausejo M. Roque M. Moher D. Metformin monotherapy for type 2 diabetes mellitus. Cochrane Database Syst Rev 2005:CD002966

PICO questions:

People: people with type 2 diabetes  
Intervention: metformin  
Comparison: placebo, diet, or another pharmaceutical intervention  
Outcome: mortality, morbidity, quality of life, glycaemic control, body weight, lipid levels, blood pressure, insulinaemia, and albuminuria

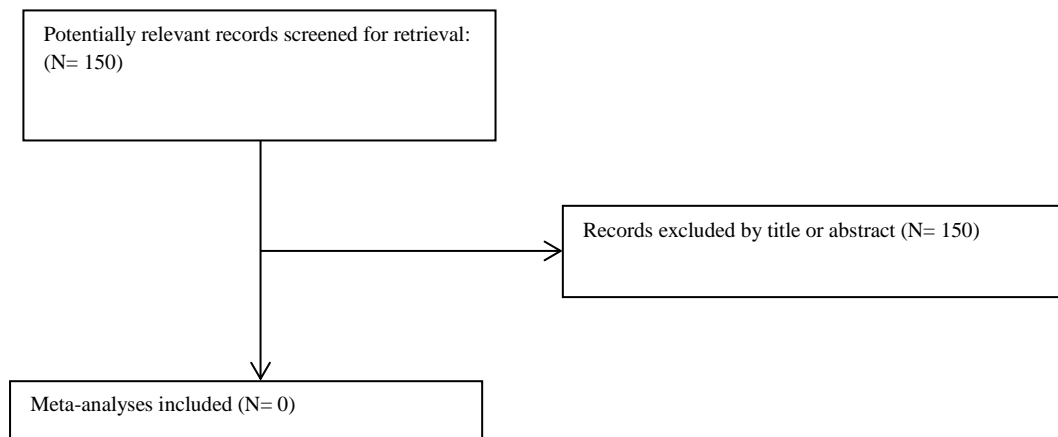
**[7] Thyroid (thyroid preparations for hypothyroidism)**

("hypothyroidism"[MeSH Terms]) AND "meta analysis"[Publication Type]



**[8] Anti-Epileptics (epileptic seizures)**

(("epilepsy"[MeSH Terms]) AND "anticonvulsants"[MeSH Terms]) AND "meta analysis"[Publication Type]

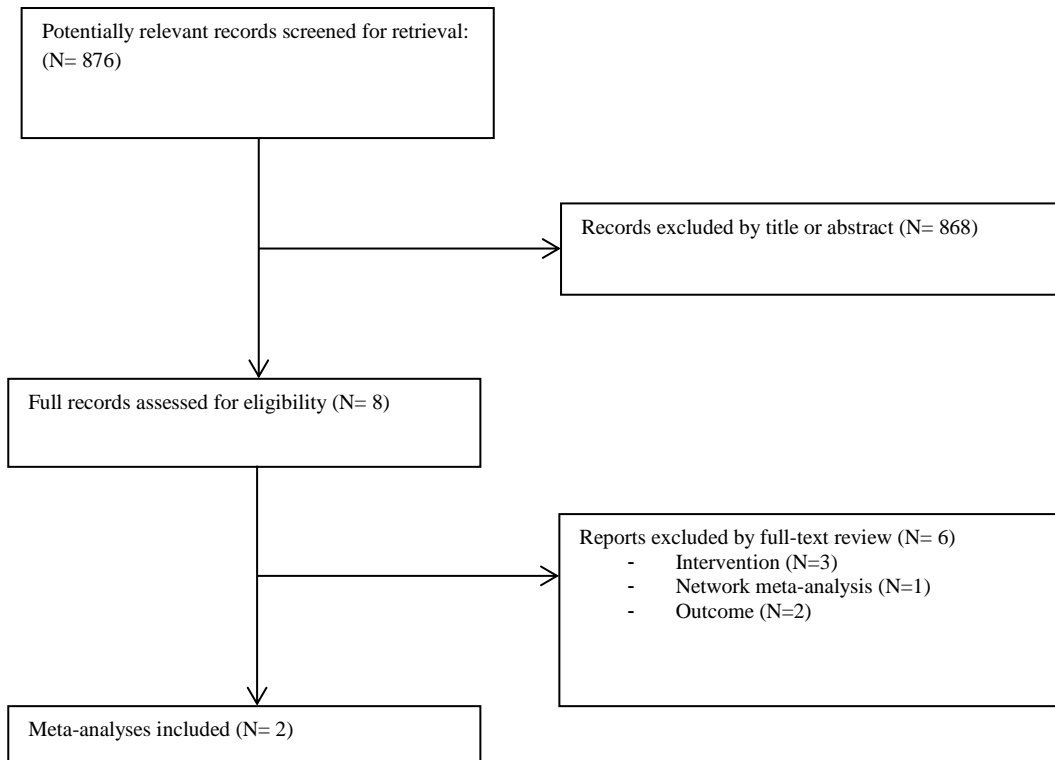


**[9] Contraceptives (hormonal contraceptives for birth control)**

Excluded: no "disease" as an indication

## [10] Respiratory (asthma, COPD)

("asthma"[MeSH Terms]) OR "pulmonary disease, chronic obstructive"[MeSH Terms]) AND "meta analysis"[Publication Type]



### Included study 1:

Barr RG. Bourbeau J. Camargo CA. Ram FS. Tiotropium for stable chronic obstructive pulmonary disease: A meta-analysis. *Thorax* 2006;61:854-62.

### PICO questions:

People: people with stable chronic obstructive pulmonary disease  
Intervention: tiotropium,  
Comparison: placebo, ipratropium bromide, or long acting Beta2 agonists  
Outcome: clinical events, symptom scales, pulmonary function, and adverse events

### Included study 2:

Sin DD. Man J. Sharpe H. Gan WQ. Man SF. Pharmacological management to reduce exacerbations in adults with asthma: a systematic review and meta-analysis. *JAMA* 2004;292:367-76

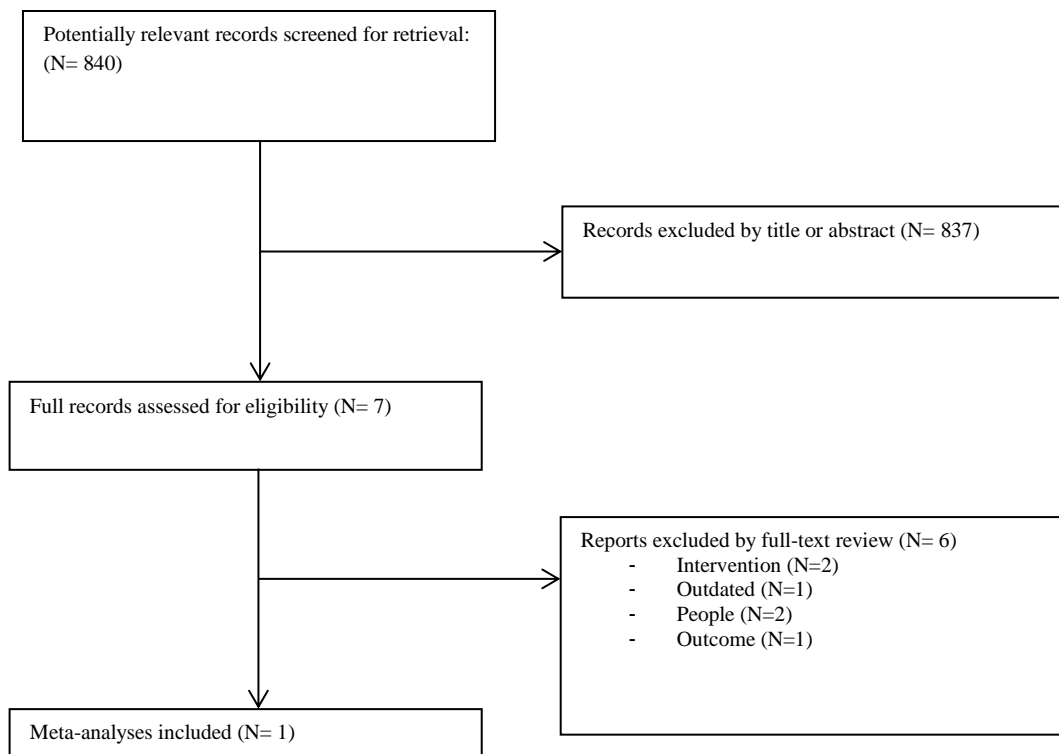
### PICO questions:

People: adults with chronic asthma  
Intervention: inhaled corticosteroids, long-acting beta2 agonists, leukotriene pathway modifiers/ receptor antagonists, and anti-IgE therapies  
Comparison: placebo, each other  
Outcome: exacerbations and/or forced expiratory volume in 1 second



**[11] Antiplatelets/anticoagulants (acetylsalicylic acid)**

((antiplatelet agents[MeSH Terms]) OR anticoagulant agents[MeSH Terms]) AND "meta analysis"[Publication Type]



Included study:

Baigent C. Blackwell L. Collins R. Emberson J. Godwin J. Peto R et al. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. Lancet 2009;373:1849-60.

PICO questions:

People: non-diabetic participants without occlusive disease at entry

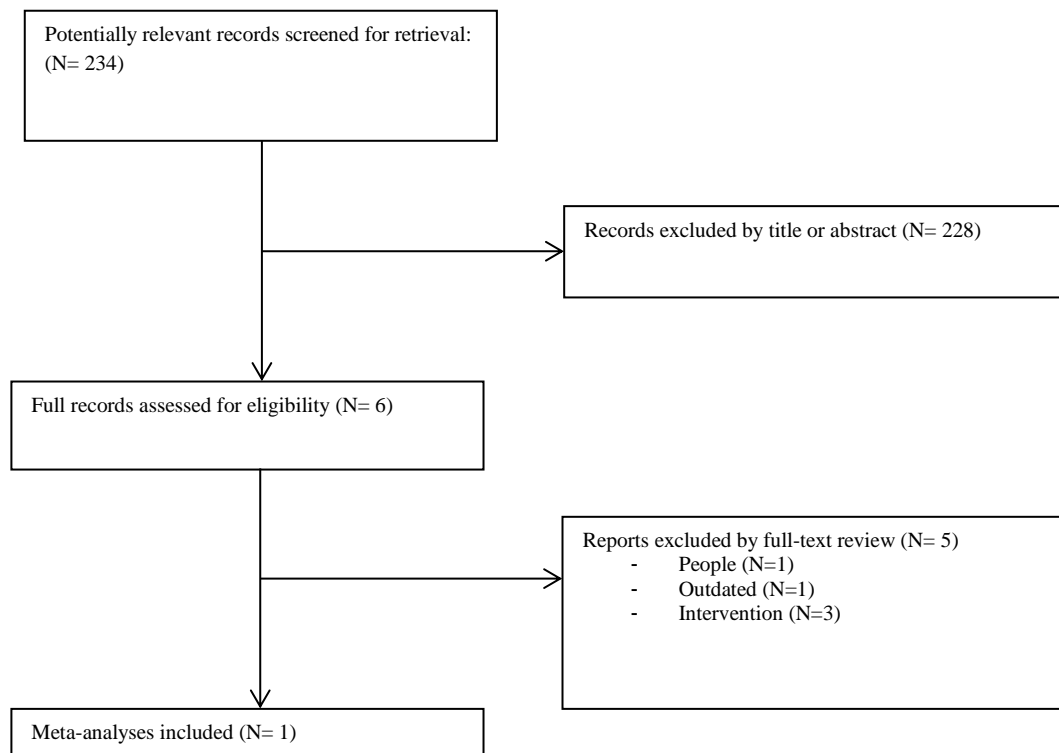
Intervention: long-term aspirin

Comparison: no aspirin (with no other antiplatelet drug in either group), including placebo

Outcome: serious vascular events (myocardial infarction, stroke, or vascular death) and major bleeds

**[12] ADHD (Amphetamines, Methylphenidates)**

("attention deficit disorder with hyperactivity"[MeSH Terms]) AND "meta analysis"[Publication Type]



Included study:

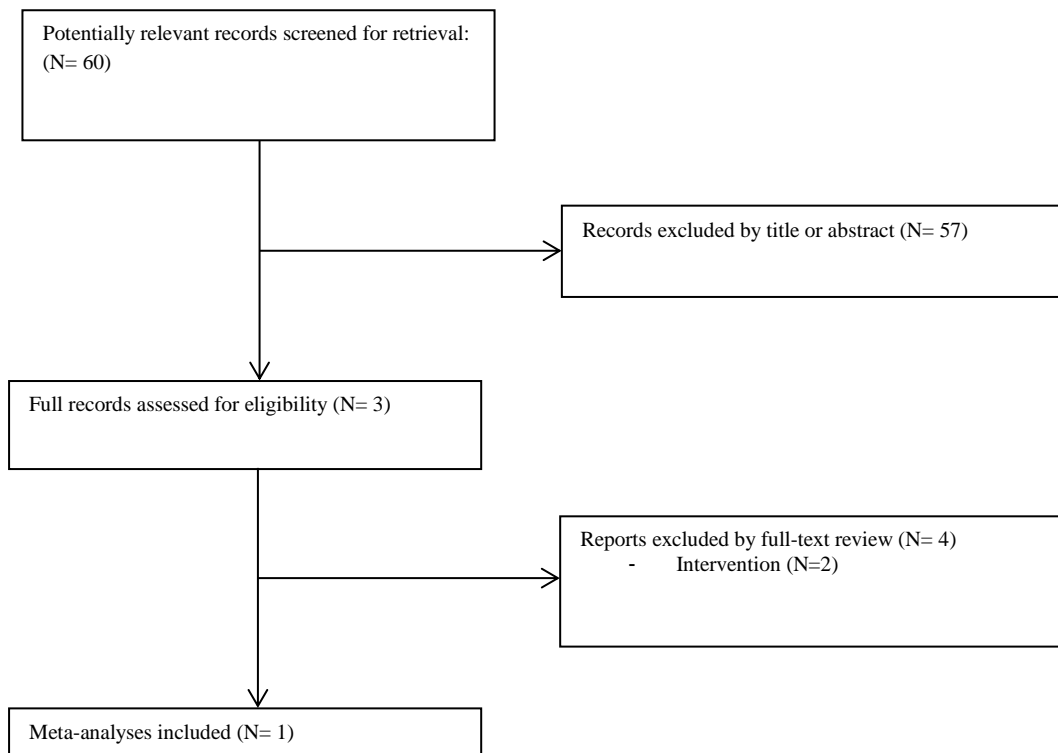
Faraone SV1, Buitelaar J. Comparing the efficacy of stimulants for ADHD in children and adolescents using meta-analysis. *Eur Child Adolesc Psychiatry*. 2010 Apr;19(4):353-64. doi: 10.1007/s00787-009-0054-3. Epub 2009 Sep 10

PICO questions:

People: children and adolescents with ADHD  
Intervention: amphetamine or methylphenidate  
Comparison: placebo  
Outcome: reduction in ADHD symptoms

### [13] Insomnia (Benzodiazepines)

(insomnia[MeSH Terms]) AND "meta analysis"[Publication Type]



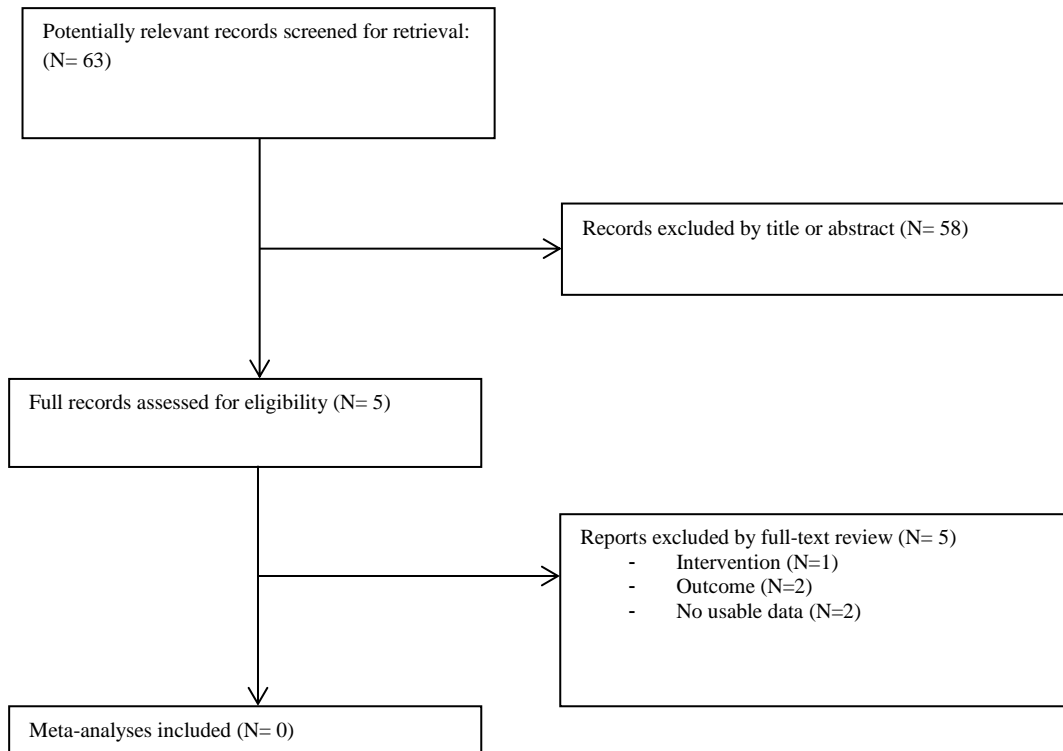
#### Included study:

Holbrook AM. Crowther R. Lotter A. Cheng C. King D. Meta-analysis of benzodiazepine use in the treatment of insomnia. Canadian Medical Association Journal. 2000;162(2):225-233

#### PICO questions:

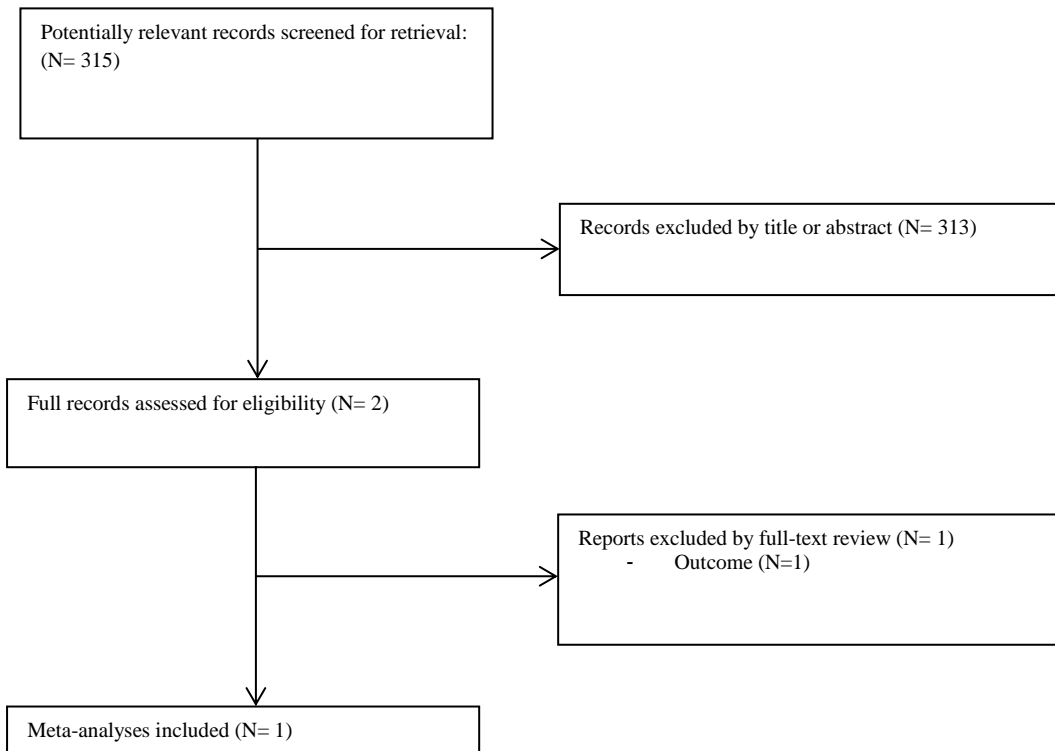
People: adults with insomnia  
Intervention: benzodiazepines  
Comparison: placebo or another active agent  
Outcome: sleep latency, total sleep time, adverse effects

**[14] Benign Prostate Hyperplasia (a-adrenergic blockers, 5-alpha-reductase inhibitors)**  
(("adrenergic alpha antagonists"[MeSH Terms]) OR "5 alpha reductase inhibitors"[MeSH Terms]) AND  
"meta analysis"[Publication Type]



### [15] Antipsychotics (schizophrenia)

("antipsychotic agents"[MeSH Terms]) AND "schizophrenia"[MeSH Terms] AND "meta analysis"[Publication Type]



#### Included study:

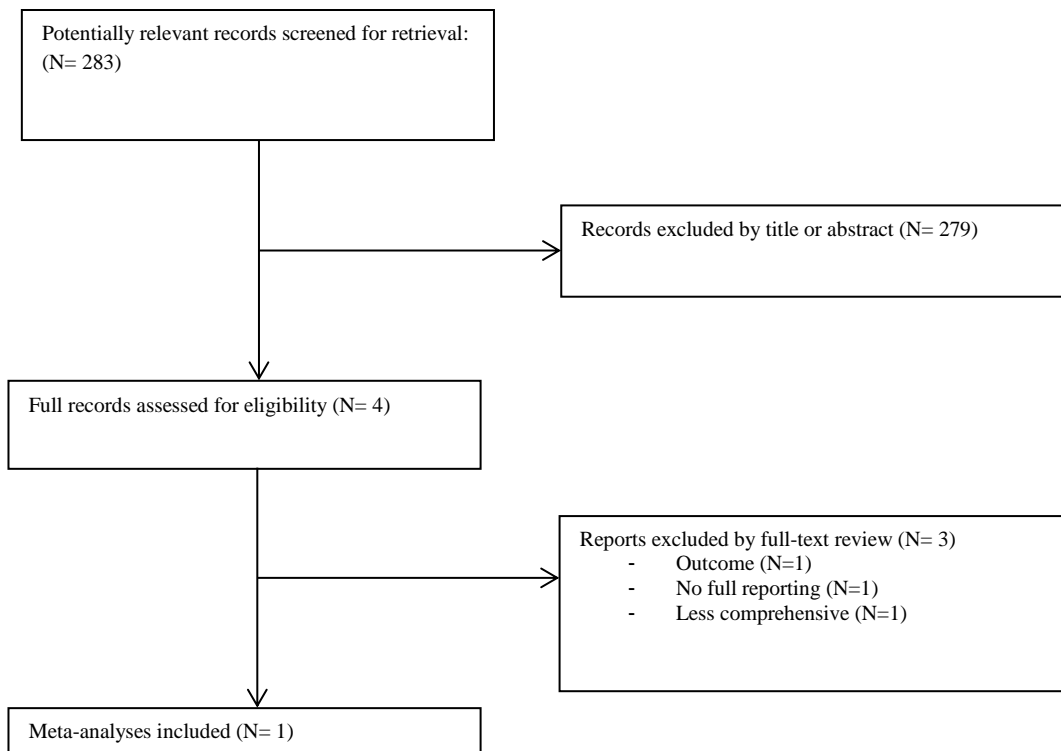
Leucht S. Arbter D. Engel RR. Kissling W. Davis JM. How effective are second generation antipsychotic drugs? A meta-analysis of placebo-controlled trials. *Molecular Psychiatry*. 2009;14(4):429-447.

#### PICO questions:

People: schizophrenic patients  
Intervention: second-generation antipsychotic drugs  
Comparison: placebo  
Outcome: reduction of schizophrenic symptoms

### [16] Osteoporosis (bisphosphonates)

((diphosphonates[MeSH Terms]) AND osteoporosis[MeSH Terms]) AND "meta analysis" [Publication Type]



#### Included study:

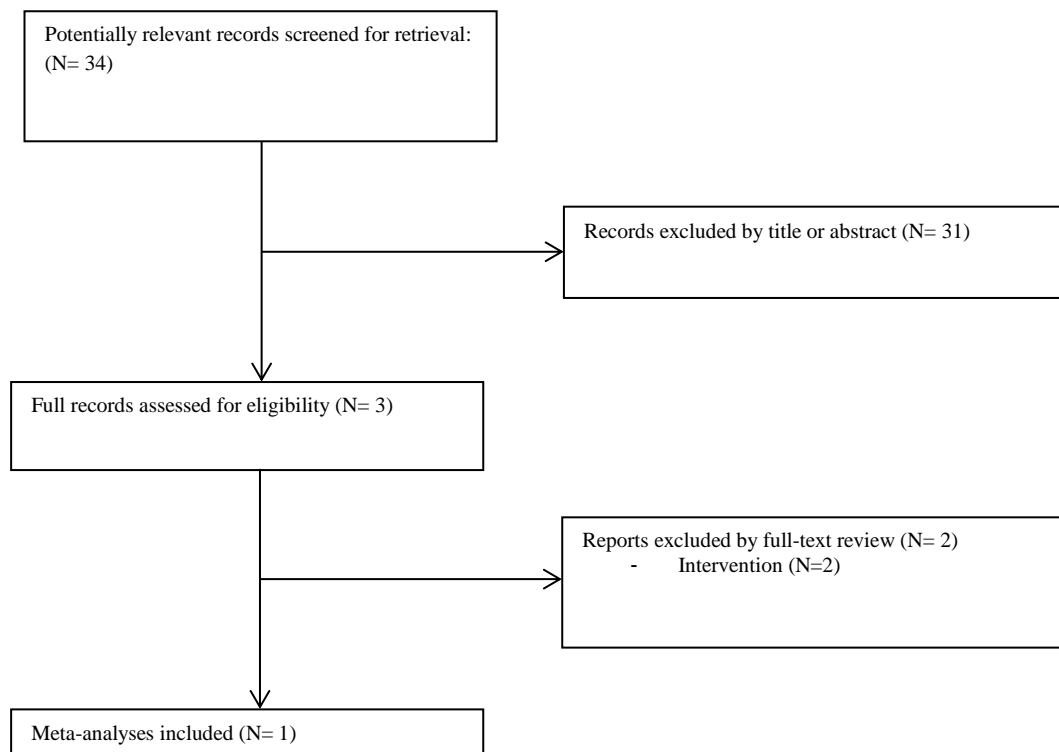
MacLean C. Newberry S. Maglione M. et al. Systematic review: comparative effectiveness of treatments to prevent fractures in men and women with low bone density or osteoporosis. *Ann Intern Med.* 2008 Feb 5;148(3):197-213. Epub 2007 Dec 17.

#### PICO questions:

People: people with low bone density or osteoporosis  
Intervention: various therapies (including bisphosphonates)  
Comparison: placebo, with each other  
Outcome: rate of or risk for fractures, adverse events

### [17] Overactive Bladder (anticholinergics)

("urinary bladder, overactive"[MeSH Terms]) AND "meta analysis"[Publication Type]



#### Included study:

Nabi G. Cody JD. Ellis G. Herbison P. Hay-Smith J. Anticholinergic drugs versus placebo for overactive bladder syndrome in adults. *Cochrane Database Syst Rev.* 2006 Oct 18;(4):CD003781.

#### PICO questions:

People: adults with overactive bladder syndrome

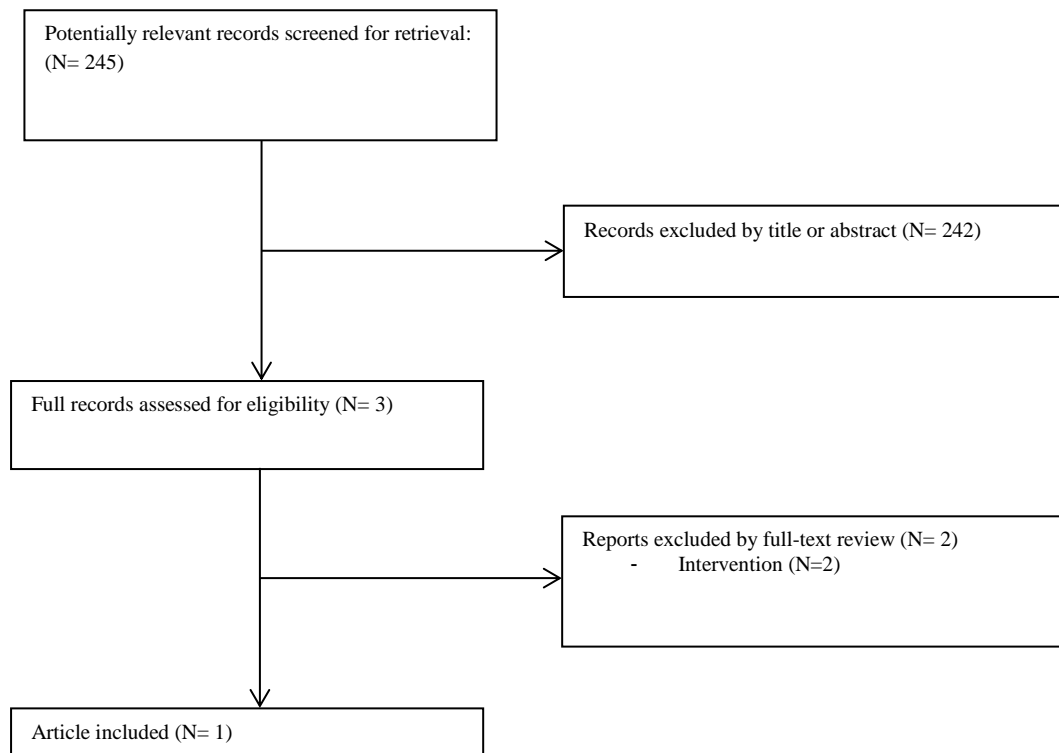
Intervention: anticholinergic drug

Comparison: no treatment, placebo

Outcome: various patient observations, number of leakage episodes, frequency and volume, quality of life, adverse events

### [18] Parkinson's (levodopa)

("parkinson disease"[MeSH Terms]) AND "meta analysis"[Publication Type]



#### Included study:

Fahn S. Oakes D. Shoulson I. Kieburtz K. Rudolph A. Lang A. et al. Levodopa and the progression of Parkinson's disease. N Engl J Med 2004; 351: 2498.

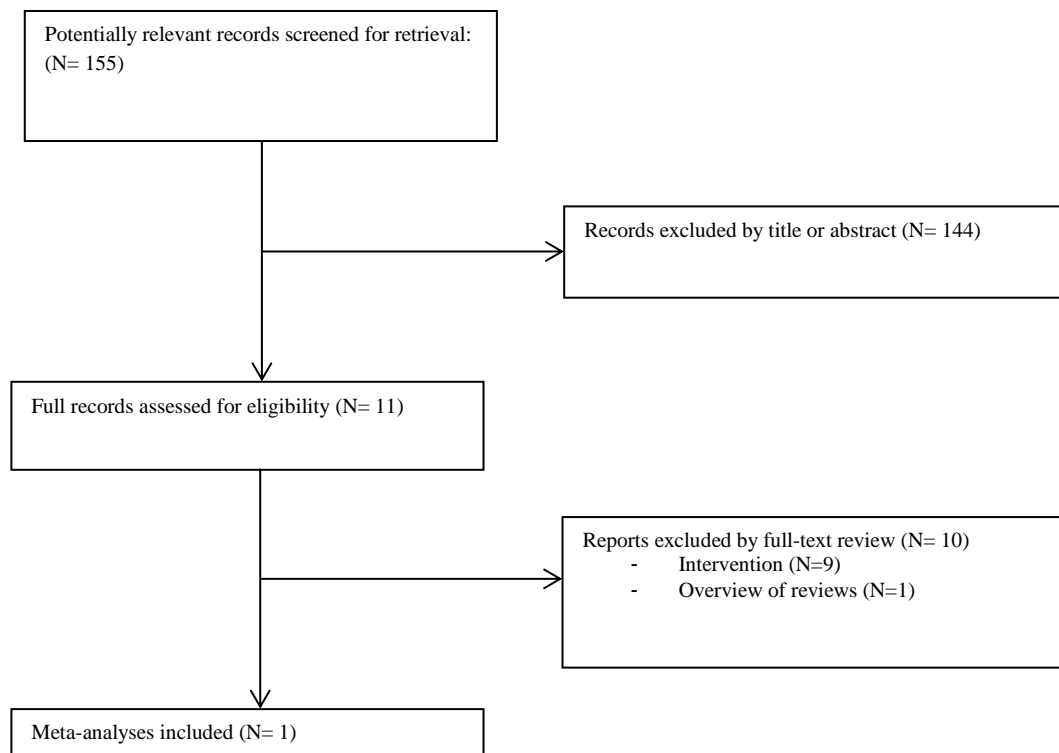
#### PICO questions:

People: patients with early Parkinson's disease  
Intervention: carbidopa-levodopa  
Comparison: placebo  
Outcome: reduction of symptoms



### [19] Migraine (analgesics)

("migraine disorders"[MeSH Terms]) AND "meta analysis"[Publication Type]



#### Included study:

Derry CJ. Derry S. Moore RA. Sumatriptan (oral route of administration) for acute migraine attacks in adults. Cochrane Database of Systematic Reviews 2012. Issue 2.

#### PICO questions:

People: adults with migraine

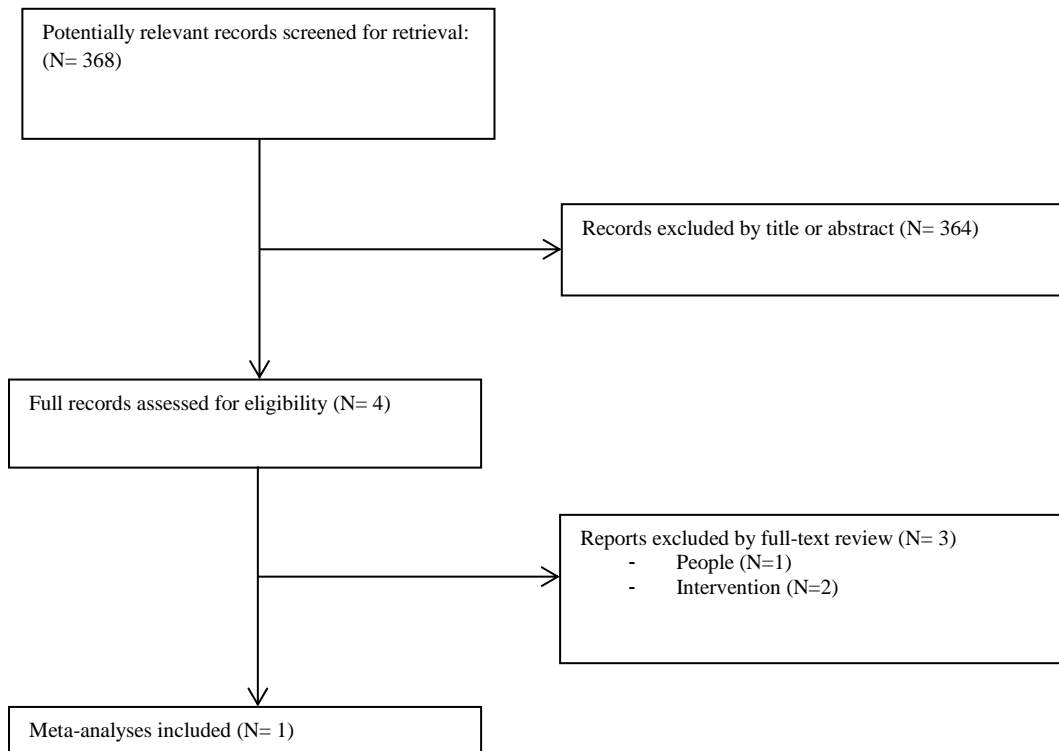
Intervention: oral sumatriptan

Comparison: placebo or other active intervention

Outcome: pain-free at two hours, headache relief, sustained pain-free during the 24 hours postdose, sustained headache relief during the 24 hours postdose, pain intensity and pain relief

## [20] Alzheimer's (cholinesterase inhibitors)

("alzheimer disease"[MeSH Terms]) AND "meta analysis"[Publication Type]



### Included study:

Birks J. Cholinesterase inhibitors for Alzheimer's disease. Cochrane Database Syst 571 Rev. 2006(1):CD005593.

### PICO questions:

People: people with mild, moderate or severe dementia due to Alzheimer's disease  
Intervention: cholinesterase inhibitors (donepezil, galantamine and rivastigmine)  
Comparison: placebo, with each other  
Outcome: reduction of symptoms