Work Package 6 – D6.1: Meta-epidemiological comparison of effect sizes in matched studies

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In this deliverable, we report the methodology for a meta-epidemiological study comparing effect estimates obtained from randomized vs. non-randomized studies. We are currently finalizing analyses on this dataset and are preparing a manuscript for submission to a peer-reviewed journal. In the interest of preserving the novelty of this study, **we will share results of this study, along with the dataset, after 1 December 2022.**

Contents

Comparison of treatment effects in randomized and non-randomized studies of pharmacological interventions: a meta-epidemiological analysis of over 2,700 studies

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Introduction

Routine availability of new medicines to patients is determined by regulatory assessment of a positive benefit-risk ratio of the drug and a positive reimbursement decision by payers, often based on recommendations made by health technology assessment (HTA) bodies. Traditionally, evidence on the benefits and risks of new drugs is obtained from randomized controlled trials (RCTs), the gold standard study design for unbiased estimates of treatment effects.[1] While RCTs remain the mainstay of regulatory and reimbursement decisions for now, this paradigm is shifting and market access decisions are increasingly made on the basis of evidence obtained from non-randomized studies (NRS), including non-randomized clinical trials and observational studies. In the US, the proportion of market approvals for drugs based on single-arm studies (implicitly or explicitly comparing treatment effects against external controls) increased significantly from 4% in 1995-1997 to 17% in 2015-2017.[2] This shift is enabled by the increased use of various special regulatory pathways, which accounted for over 80% of all new drug approvals in the US in 2018.[3] Legislative changes in the US further promote the use of "real-world" (i.e., observational) data for regulatory decisions,[4] potentially including the use of observational data for initial market approval decisions as well as for extensions of existing approvals and confirmation of clinical benefit for conditionally approved products.[5] Similar uses of observational data have already been reported in Europe, Canada and Japan.[6,7]

Regulatory approval on the basis of NRS also impacts on reimbursement and coverage decisions. In England, the national HTA body relied solely on evidence from NRS in only 4% of technology appraisals from 2000 to 2016, but half of these were conducted in the last two years of the study.[8] This trend of increased reliance on NRS for market approval and coverage decisions is likely to

continue as both regulators and HTA bodies/payers move towards product life-cycle approaches that take into account additional evidence generated once the drug is on the market.[9–14] This evidence is likely to come from NRS, as manufacturers do not have an incentive to generate RCT evidence once their product is on the market. RCTs may also become unfeasible once a drug is widely available. Regulators, HTA bodies and payers therefore increasingly face situations where decisions about (continued) market access for a drug need to be made on the basis of data generated by NRS.

The prime challenge with relying on NRS as the basis for decisions about market access for new drugs lies in the limited internal validity of non-randomized study designs in comparison to the long-established gold standard for obtaining estimates of the treatment effect of an intervention, RCTs.[15,16] In particular, researchers and decision-makers are concerned about the risk of bias due to confounding in NRS, i.e. the risk of a systematic distortion of the true treatment effect due to an uneven distribution of participant characteristics between intervention and control group that impacts both the allocation of participants to intervention vs. control group as well as the outcome the study is measuring.[17] RCTs address this risk by design: if conducted properly, randomization of study participants into intervention and control groups will ensure that observable and unobservable (and therefore, measured and unmeasured) characteristics are, on average, similar.

Given the increasing number of drugs coming onto the market with evidence obtained from NRS only, and the policy changes further promoting their use, it is imperative to scrutinize the internal validity of NRS. Previous meta-epidemiological studies comparing treatment effects obtained from NRS to the long-established gold-standard study design, RCTs, were inconclusive.[18–40] However, the last comprehensive review covering a broad range of 45 clinical topics was published in 2001.[31] Since then, a large body of methodological literature has advanced NRS methods. Addressing the issue of risk of bias due to confounding in NRS, a range of relatively novel and more advanced analytical methods have been developed. These methods, including propensity score-based techniques, other matching methods, instrumental variables, and disease risk scores, among others,[41–43] aim to replicate the even distribution of confounding variables across intervention and control groups that randomization achieves in properly conducted RCTs. In theory, these methods increase internal validity by generating comparable groups of patients receiving experimental and control intervention. However, whether these techniques can reliably produce unbiased treatment effects remains unclear. Simulation models often lack generalizability beyond individual data sets,[44–47] and

empirical evaluations of the performance of some of these methods against the gold standard, RCT, are often limited to narrow therapeutic areas.[26,28,35]

In addition to the development of advanced analytical methods, there have been other efforts in recent years to improve the validity of NRS and promote their use for market access decisions, notably through the publication of good practice guidelines and standards for NRS for decision-making.[15,48–54]

Against the background of increased use of NRS for market access decisions of prescription drugs and potential higher quality evidence generated by modern NRS, it is important to assess whether treatment effect estimates generated by NRS are aligned with those of RCTs.

We conducted a meta-epidemiological study of matched sets of RCTs and NRS across a wide range of therapeutic areas to analyze how treatment effects for pharmacological interventions compare when obtained from randomized vs. non-randomized studies.

Methods

We conducted a meta-epidemiological study to answer the question: how do treatment effects obtained from randomized vs. non-randomized studies for the same pharmacological intervention in similar populations compare? A protocol for this study was registered on the PROSPERO database of systematic reviews (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=62204).

This deliverable reports descriptive findings of the dataset compiled. The methods for quantitative analysis of the comparability of treatment effects in RCTs and NRS will be described in detail when further findings are published.

Identification of clinical topics

We identified clinical topics with at least one RCT and one NRS being conducted to obtain estimates of the effectiveness of pharmacological treatments as defined in the participants, interventions, comparators, outcomes (PICO) framework. Topics were identified through three sources: (1) a review of existing meta-epidemiological studies comparing RCTs and NRS, (2) a database search in MEDLINE for meta-analyses including both RCTs and NRS, (3) a review of all systematic reviews indexed in the Cochrane Database of Systematic Reviews that included both RCTs and NRS. We only included clinical topics with meta-analyses published since 2009 to cover important clinical questions of the last 10 years and to include more recent NRS.

We only included topics where RCTs and NRS contributed to a single pooled estimate of the effectiveness of a pharmacological treatment, following the *"within meta-analyses"* approach for meta-epidemiological studies.[55] We therefore capitalized on the subject matter expertise of researchers and clinicians conducting meta-analysis in their area of interest, and who judged RCTs and NRS to be sufficiently similar to each with other with respect to study participants, intervention, comparator, and outcome, to be estimating the same underlying treatment effect. Systematic reviews where RCTs and NRS were pooled separately (e.g., due to concerns about heterogeneous patient populations in the two study designs) were excluded.

Records retrieved through database searches were screened at the title and abstract level independently by two reviewers (KD and MSK). Conflicting decisions were resolved by consensus. Full texts of remaining articles were screened by either MN or MSK, after double screening of a 10% sample of records showed almost perfect agreement (kappa score of 0.85).

For each included meta-analysis, we selected one clinical topic for data extraction. We extracted data for the primary outcome of the meta-analysis. In cases where the meta-analysis of the primary outcome did not include both RCTs and NRS, we extracted the next most prominently presented outcome with the highest number of contributing RCTs and NRS. We compared all identified clinical topics and individual studies on the basis of unique identifiers (preferably PubMed IDs, and in case not available ad hoc created IDs) to identify possible overlap.[56] Only unique individual studies were eligible to contribute to each clinical topic. The same individual study was eligible to contribute to several clinical topics.

Data extraction

Topic-level and study-level information was extracted from source meta-analyses using a pre-specified spreadsheet. Where possible, we used pre-specified categories for study design characteristics.

We based the categorization of study designs on typologies used in previous meta-epidemiological reviews.[32,57] We distinguished between RCT and NRS, where the former was defined by the use a random sequence to allocate study participants to intervention and control groups, and the latter by the absence of such a random sequence. We relied on the assessment made by the authors of the source meta-analyses whether a study should be categorized as RCT or NRS, except for studies included in Cochrane systematic reviews, where we used the detailed and consistently applied and

reported risk of bias assessment to distinguish studies using truly random vs. quasi-random sequences (e.g., date of birth, social insurance number) for participant allocation.

For NRS, we further distinguished between experimental and observational designs, a categorization applied by Schulz and Grimes,[1] Deeks et al.,[32] and more recently in the IMI GetReal project (https://rwe-navigator.eu/use-real-world-evidence/generate-real-world-evidence/), and also implicitly referred to in a checklist for quasi-experimental studies developed by Reeves and colleagues.[58] Experimental NRS are studies in which the investigator has some control over study conditions, including the allocation of participants into treatment and control groups. Examples include quasi-randomized trials (where the allocation mechanism falls short of true randomization, see above) and non-randomized clinical trials (where allocation is by patient or physician preference). Observational NRS lack the experimental intention of experimental NRS. They exploit natural variation in the use of interventions to study patient outcomes.

We extracted other study-level information as reported in the source meta-analyses, including analytical methods used, data sources of NRS, participant details, intervention details, risk of bias tool and score, number of participants in intervention and control arms, effect measure, and a measure of its variance.

Descriptive results

We will share detailed results of this study, along with the dataset, after 1 December 2022. This period will allow us to conduct additional analyses that emerged during the project lifetime and to publish these findings, preserving the novelty of the study. This deliverable therefore only reports descriptive results.

A total of 10,957 records were screened at the title and abstract level, and 830 were reviewed in full, resulting in a total of 336 included records (Figure 1). These 336 records contributed 346 unique clinical topics (2 records were meta-epidemiological studies contributing more than one topic), with 2,747 unique contributing studies (Median 3 RCTs (range 1-92) and 2 NRS (range 1-44) per topic).

Clinical topics ranged across a wide range of therapeutic areas, with anti-infectives system use (n=66, 19.1%) and blood and blood forming organs (n=64, 18.5%) the most common categories (Table 1). Roughly two thirds of topics had a placebo comparator (n=226). The narrowness of clinical topics was assessed as high for 32.1% (n=111) of topics, moderate for 48% (n=166), and low for 19.9% (n=69). The median publication year for individual studies was 2010 or later for 46.0% of topics.

The dataset has been published on Zenodo (10.5281/zenodo.4958221).

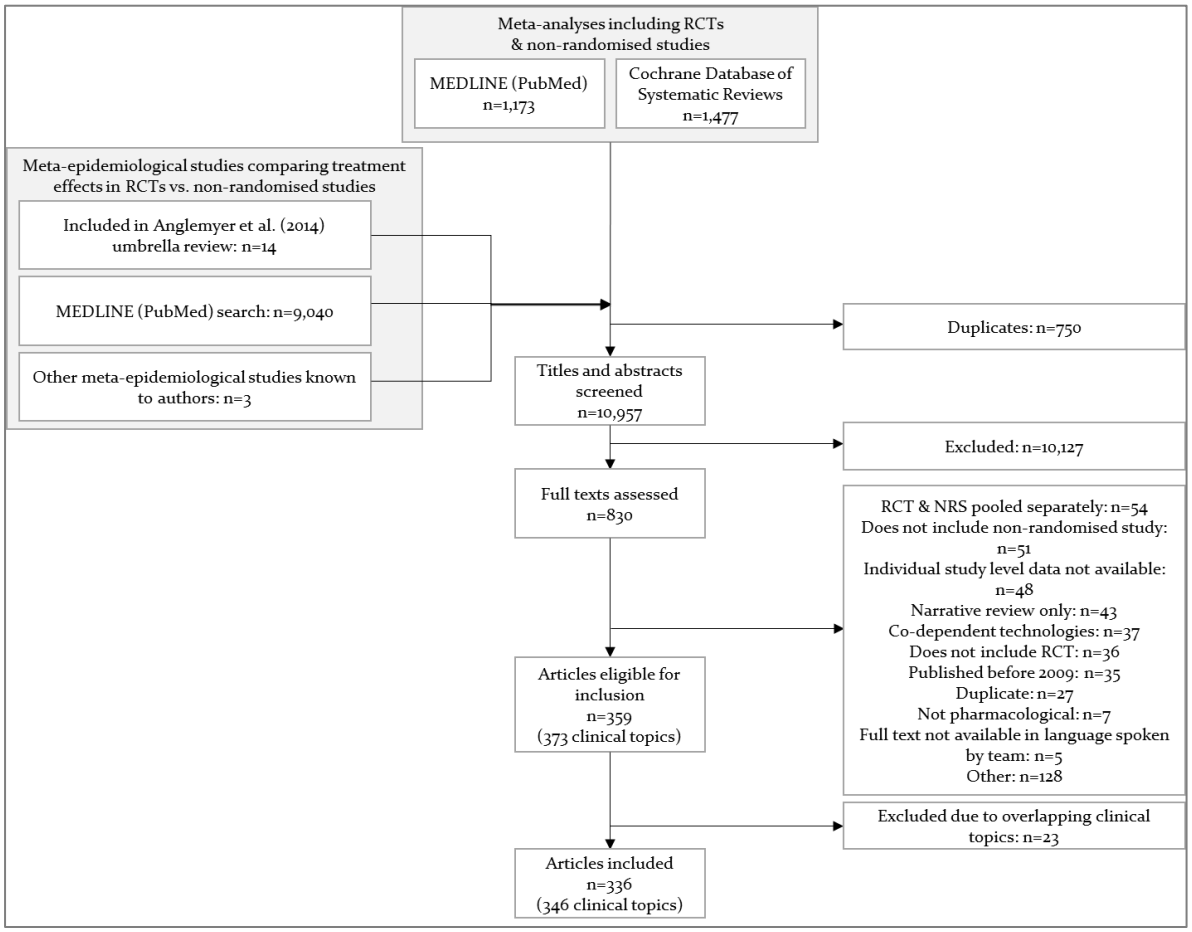

FIGURE 1: FLOW CHART OF SELECTION OF CLINICAL TOPICS FOR META-EPIDEMIOLOGICAL STUDY

TABLE 1: CHARACTERISTICS OF CLINICAL TOPICS WITH MATCHING NRS AND RCTS

Characteristic	Number of topics (%)
All topics	346 (100%)
Comparator	
Active	94 (27.2%)
Placebo/no treatment	226 (65.3%)
Includes both active and placebo-controlled studies	26 (7.5%)
Outcome type	
Mortality	59 (17.1%)
Other objective outcome	158 (45.7%)
Subjective outcome	126 (36.4%)
Includes studies with different types of outcomes	3 (0.9%)
Therapeutic area	
Alimentary tract & metabolism	23 (6.6%)
Blood & blood forming organs	64 (18.5%)
Cardiovascular system	45 (13%)
Dermatologicals	10 (2.9%)
Genito-urinary system & sex hormones	14 (4%)
Systemic hormonal preparations	19 (5.5%)
Antiinfectives systemic use	66 (19.1%)
Antineoplastic & immuno modulating agents	43 (12.4%)
Musculo-skeletal system	12 (3.5%)
Nervous system	27 (7.8%)
Antiparasitic products	9 (2.6%)
Respiratory system	7 (2%)
Sensory organs	4 (1.2%)
Various	3 (0.9%)
Risk of bias in NRS	
Low median risk of bias	97 (28%)
Moderate median risk of bias	61 (17.6%)
High median risk of bias	124 (35.8%)
No risk of bias information	64 (18.5%)
Time period	
Median publication year pre-2000	56 (16.2%)
Median publication year 2000-2009	131 (37.9%)
Median publication year 2010 and later	159 (46%)
Topic narrowness	
High (score of 10-12 out of 12)	111 (32.1%)
Moderate (score of 7-9 out of 12)	166 (48%)
DisLow (score of 4-6 out of 12)	69 (19.9%)

Conclusion

The dataset compiled for this study and for which descriptive findings are reported in this deliverable represents the largest dataset to answer questions about the comparability of treatment effects in randomized vs. non-randomized studies to date.

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Appendix

List of all included topics

Topic ID	Author and year	Topic
21	Agarwal 2018	Dual antiplatelet therapy and major adverse cardiac events (myocardial infarction, stroke, death) in patients following coronary artery bypass grafting
135	Chowdhury 2018	Lidocaine and survival to admission in patients after cardiac arrest, in- and out-of-hospital
151	Coussement 2018	Antimicrobial agents and incidence of urinary tract infection in kidney transplant patients
179	El Sayed 2018	Macrolide antibiotics and resolution of fever in people with a diagnosis of scrub typhus
183	Engelen 2018	Antifibrinolytic agents and post-operative bleeding in patients undergoing oral or dental procedures
189	Facciorusso 2018	Nonselective beta-blockers and survival in cirrhotic patients with ascites
226	Gonzalez 2018	Mefloquine and maternal peripheral parasitaemia at delivery in pregnant women
234	Graves 2018	Primaquine (or alternative 8-aminoquinoline drug) and potential infectiousness in patients with malaria
244	Hass 2018	Antiseptic solution and post-cesarean endometritis in pregnant women about to receive a cesarean delivery
307	Jian-Yu 2018	Metformin and overall survival in pancreatic cancer patients
387	Lewis 2018	Starches and all-cause mortality in participants who required fluid volume replacement
391	Li 2018	Actinomycin-d and complete response in patients with low-risk gestational trophoblastic neoplasia
437	Luni 2018	Adenosine and atrial fibrillation recurrence in patients with atrial fibrillation
517	Perez-Gaxiola 2018	Smectite and acute infectious diarrhoea duration in children

669	Tsai 2018	Gentamicin and infection rates in patients on peritoneal dialysis
673	Tunnicliffe 2018	Cyclophosphamide and renal relapse in people with biopsy-proven lupus nephritis
559	Qiu 2018	Ursodeoxycholic acid (UCDA) and glucorticoid (GC) and serum bilirubin in patients after Kasai procedure
570	Roberts 2018	Fosfomycin trometamol (FT) and overall infectious complications in patients undergoing transrectal ultrasound-guided prostate biopsies (TRUSPB)
571	Rodriguez-Zuniga 2018	Acyclovir and regression of lesions in patients with pityriasis rosea (PR)
664	Toews 2018	Antacids and clinically important upper gastrointestinal (GI) bleeding in patients admitted to intensive care unit
701	Wan 2018	Statins and arteriovenous fistula (AVF) failure in patients diagnosed with chronic renal failure using hemodialysis with AVF
711	Wang 2018	Anti-fibrinolytic agents and blood loss in patients after peri-acetabular osteotomy (PAO)
759	Yao 2016	Antiepileptic drug and occurrence of early seizure in patients with primary intracerebral hemorrhage (ICH)
5	Hernandez 2017	Pyrimethamine plus clindamycin and partial/complete clinical response in patients with HIV-associated cerebral toxoplasmosis
6	Kirkland 2017	Short-acting anticholinergic (SAAC) and short-acting beta-agonists (SABA) and peak expiratory flow in participants presenting to actue care setting with an uncomplicated exacerbation of asthma
585	Salata 2018	Renin-angiotensin system blockade (RASB) and abdominal aortic aneurysm (AAA) growth rate in patients in patients with AAA
20	Agarwal 2017	Dual antithrombic therapy (anticoagulant and single anti-platelet agent) and major bleeding in patients with an indication for long-term anticoagulation undergoing percutaneous coronary intervention with stenting
33	An 2017	Statins and overall risk fracture in patients
55	Barkat 2017	Dual antiplatelet therapy (aspirin and clopidogrel) and neck haematoma in patients of any age/gender diagnosed with symptomatic or asymptomatic carotid disease undergoing cartoid endarterectomy
80	Bonet 2017	Antibiotic prophylaxis and endometritis in women who had an uncomplicated vaginal birth

84	Bossard 2017	Heparin and prevention of radial artery occlusion in patients receiving transradial cardiac catheterization
89	Brito 2017	Antimony intralesional infiltration and clinical cure rate in patients with cutaneous leishmaniasis
100	Campbell 2017	Antifungal and fungal peritonitis in peritoneal dialysis patients
113	Chalhoub 2017	Combination therapy with immunomodulators and induction of remission in patients with Crohn's disease
115	Chao 2017	Preoperative hormonal stimulation and postoperative complication rates in patients after hypospadias repair surgery
124	Chen 2017	Bevacizumab and hypertension in patients older than 65 years with advanced colorectal cancer
162	David 2017	Intralesional, injected corticosteroids and heel pain at one month in adult participants with heel pain due to plantar fasciitis
168	Desiderio 2017	Hyperthermic intraperitoneal chemotherapy (HIPEC) with cytoreduction surgery (CRS) and overall survival in patients with evidence of gastric cancer peritoneal carcinomatosis
173	Dong 2017	Vonoprazan (VPZ) and Helicobacter pylori eradication in patients receiving H. pylori therapies
180	Elgendy 2017	Non-vitamin K antagonist oral anticoagulants (NOACs) and symptomatic thromboembolism in patients undergoing catheter ablation for atrial fibrillation
196	Filippini 2017	Disease modifying drugs and time to conversion to clinically definite multiple sclerosis in patients with first clinical attack suggestive of multiple sclerosis
205	Fukuta 2017	Beta-blockers and mortality in patients with heart failure with preserved ejection fraction (HFpEF)
215	Gausden 2017	Tranexamic acid (TXA) and rate of transfusion in patients undergoing orthopaedic trauma surgery
225	Gong 2017	Atropine and regression of refraction in patients younger than 18 years with myopia
231	Grabein 2017	Fosfomycin and clinical efficacy in patients needing antibiotics
240	Guerra 2017	Ranolazine and prevention of atrial fibrillation (AF) in patients in whom ranolazine is used to manage atrial fibrillation

241	Gunter 2017	Rofecoxib and myocardial infarction in patients who received non-steroidal anti-inflammatory drugs (NSAIDs)
250	Han 2017	Nucleoside analog entecavir (ETV) and normalised serum alanine aminotransferase levels (ALT norm) in patients with chronic hepatitis B (CHB) or Hepatits B virus (HBV) related liver cirrhosis
253	Harnoss 2017	Antibiotic treatment and treatment effectiveness in patients with uncomplicated acute appendicitis
262	Heal 2017	Topical antibiotics and risk of surgical site infection in patients after primary closure following surgery
282	Huang 2017	Antibiotic treatment and success rate of treatment in pediatric patients with acute uncomplicated appendicitis
283	Huang 2017	Atosiban and clinical pregnancy rate in women undergoing in vitro fertilization-embryo transfer
293	Hyun 2017	Tenofovir and Hepatitis B surface antigen (HBsAg) in infants of mother with chronic Hepatitis B virus infection
302	Ji 2017	Anti-vascular endothelial growth factor (anti-VEGF) and best-corrected visual acuity (BCVA) in patients with acute central serous chorioretinopathy (CSC)
308	Johnston 2017	Antibiotic treatment and mortality odds in patients presenting to emergency department (ED) and diagnosed with a sepsis illness
315	Kamal 2017	Rifaximin and spontaneous bacterial peritonitis (SBP) in patients above 18 years of age with cirrhosis
316	Kamal 2017	Statins and mortality in chronic liver disease patients
331	Khan 2017	Topical timolol and infantile hemangiomas (IH) resolution in infants with IH
332	Khan 2017	Angiotensin-converting enzyme inhibitors (ACE-Is) and angiotensin receptor blockers (ARBs) and all-cause mortality in patents with heart failure with preserved ejection fraction (HFpEF)
341	Kirsch 2017	Tranexamic acid (TXA) and change in hemoglobin in patients following primary shoulder arthroplasty
361	Kuang 2017	Liposomal bupivacaine periarticular injection (PAI) and pain in patients after total knee arthroplasty (TKA)
378	Lee 2017	Intravenous peramivir and time to alleviation of fever in patients with influenza

684	Vardakas 2018	Intravenous colistin combination antimicrobial treatment and mortality in adult patients with multi-drug resistant (MRD) or extensively-drug-resistant Gram-negative infections
805	Zhao 2018	Intravitreal injection of bevacizumab and best corrected visual acuity (BVCA) in patients with proliferative vitreoretinopathy (PVR)-related retinal detachment (RD) requiring surgical intervention
379	Lee 2017	Beta-lactam plus macrolide (BL-M) combination therapy and mortality in patients with severe community-acquired pneumonia (CAP) over 18 years of age
393	Li 2017	Nonsteroidal anti-inflammatory drugs (NSAIDs) and post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) in patients after ERCP
403	Liang 2017	Intravenous acetaminophen and pain control in patients undergoing total joint arthroplasty (TJA)
416	Liu 2017	Alternative antibiotics (ceftriaxone, doxycycline, tetracycline) and serological response rates at 12-month follow up in patients with primary, secondary, or early latent syphilis
467	Mesgarpour 2017	Erythropoiesis-stimulating agent (ESA) and any adverse event in critically-ill patients
492	Nairooz 2017	Pretreatment with clopidogrel and major adverse cardiac events in acute coronary syndrome (ACS) patients managed invasively
512	Ortize-Orendain 2017	Antipsychotic combinations and no clinically important response in patients with schizophrenia
562	Qiu 2017	Anti-tumor necrosis factor (TNF) combination therapy with immunomodulators and antidrug antibodies (ADAs) in patients with inflammatory bowel disease (IBD)
569	Rivero 2017	Anti-IgE agents (omalizumab) and nasal polyp score in patients with recalcitrant chronic rhinosinusitis with nasal polyps (CRSwNP)
582	Sahebkar 2017	Statins and vitamin D concentration in patients receiving statins
583	Sahebkar 2017	Tamoxifen and lipoprotein(a) [Lp(a)] in patients receiving tamoxifen
587	Salvi 2017	Antidepressant drugs and new-onset diabetes in patients at least 18 years receiving antidepressant drugs

609	Shi 2017	Intraventricular injections of recombinant tissue plasminogen activator (rt-PA) and good functional improvement in patients with a ruptured aneurysm causing subarachnoid hemorrahage (SAH)
619	Singh 2017	Platelet-rich plasma (PRP) injections and pain score at 3 months follow up in patients with plantar fasciopathy
620	Singh 2017	Liposomal bupivacaine and comparative length of hospital stay in adult patients undergoing primary total knee arthroplasty (TKA)
628	Sole-Lleonart 2017	Colistin or aminoglycosides and clinical resolution in mechanically ventilated patients with ventilator-associated pneumonia (VAP) caused by resistant pathogens
653	Tarantini 2017	Prasugrel or ticagrelor and composite of cardiovascular death, nonfatal myocardial infarction, nonfatal ischemic stroke in elderly patients with acute coronary syndrome (ACS)
658	Teng 2017	Epinephrine and postoperative hemoglobin loss in patients with unilateral primary total joint arthroplasty
676	Ukaigwe 2017	Apixaban and thromboembolic complications in patients diagnosed with atrial fibrillation undergoing catheter ablation
710	Wang 2017	Metformin and C-reactive protein (CRP) levels in women patients with polycystic ovary syndrome
713	Wang 2017	Hydroxychloroquine and erythrocyte sedimentation rate in patients with primary Sjogren's syndrome (pSS)
714	Wang 2017	Intra-articular injection of corticosteroid and range of abduction in patients undergoing primary adhesive capsulitis
718	Watti 2017	Prasugrel and mortality in adult patients who presented with all forms of acute coronary syndrome and underwent percutaneous coronary intervention
728	Wiysonge 2017	Corticosteroids and pericardiectomy in patients of all ages who required treatment for clinically diagnosed tuberculous pericarditis and HIV-negative
739	Xie 2017	Recombinant human granulocyte colony-stimulating factor (G-CSF) and endometrium thickness in patients with thin endometrium
758	Yang 2017	Erlotinib and progression-free survival in patients with non-small cell lung cancer (NSCLC)
763	Yong 2017	Heparin bridging therapy and major bleeding in patients taking oral anticoagulants and undergoing an elective operation

771	Zaiem 2017	Transdermal estrogen and body mass index (BMI) in patients with Turner Syndrome (TS)
774	Zeng 2017	Prothrombin complex concentrate (PCC) and mortality in neonate or infant patients with bleeding or risk of bleeding
779	Zhang 2017	Nedaplatin and overall response rate in patients pathologically diagnosed with metastatic/recurrent or advanced esophageal squamous-cell carcinoma (ESCC)
784	Zhang 2017	Hypertonic saline and rate of hospitalisation in infant patients diagnosed with acute bronchiolitis
785	Zhang 2017	Tranexamic acid (TXA) and hemoglobin drop in patients who received total knee arthroplasty for the first time
786	Zhang 2017	Tranexamic acid (TXA) and transfusion rate in patients who had undergone total knee arthroplasty (TKA) or total hip arthroplasty (THA) for the first time
789	Zhang 2017	Adjuvant steroid therapy and jaundice free rate in patients with biliary atresia (BA) following a Kasai portoenterostomy (KPE)
798	Zhang 2017	Thiazolidinediones (TZDs) and atrial fibrillation (AF) in diabetic patients
800	Zhao 2017	Iodised oil infusion chemotherapy without embolisation and survival rate in patients with hepatocellular carcinoma
807	Zhao 2017	New oral anticoagulants and thromboembolic complications in patients with nonvalvular atrial fibrillation undergoing catheter ablation
811	Zheng 2017	Statins and sustained virological response rate in chronic hepatitis C patients
814	Zhu 2017	Tacrolimus and overall remission in adult patients with primary membranous nephropathy (PMN)
32	Ampuero 2016	Sofosbuvir (SOF) + ribavirin (RBV) + pegylated interferon (PEG-IFN) and sustained virological response (SVR) in patients with hepatitis C virus
46	Ayoub 2016	Heparin and all-cause mortality in patients with atrial fibrillation requiring temporary interruption of warfarin
66	Benjo 2016	Vascular brachytherapy (VBT) and target lesion revascularization (TLR) in patients with in-stent restenosis (ISR)
723	Whiting 2017	Diuretics, ACE inhibitors, angiotensin receptor blockers (ARB), direct renin inhibitors, non-steroidal anti-inflammatories, metformin or sulfonylureas and acute kidney injury in patients experiencing intercurrent illnesses, radiological or surgical procedures

86	Branger 2016	Second-line disease modifying drugs (SLDMD) and percentage brain volume change (PBVC) in patients with relapsing-remitting multiple sclerosis (RRMS)
92	Brustia 2016	Topical haemostatic agents (THA) and blood transfusion in adult patients undergoing major or minor, open or laparscopic liver surgery or (split) transplantation
98	Caldwell 2016	Tricyclic drug and lack of 14 consecutive dry nights in children patients with nocturnal enuresis
111	Chai-Adisaksopha 2016	Fresh frozen plasma and all-cause mortality in adult patients who presented with warfarin associated major bleeding or required urgent warfarin reversal for surgery or an invasive procedure
194	Ferrer 2016	Macrolides and acute liver injury in patients receiving macrolides
238	Gray 2016	Statins and overall mortality in colorectal cancer patients
249	Han 2016	Heparin and cathether-related infections in patients receiving hemodialysis with central venous catheters
251	Hannah 2016	Tacrolimus and complete remission in patients with systemic lupus erythematosus (SLE) complicated by lupus nephritis
252	Hao 2016	Vancomycin and mortality in adult patients with a bacterial infection
267	Henssler 2016	Combinations of antidepressants and standardised mean difference in adult patients suffering from acute depression
264	Hemkens 2016	Lipid lowering treatment and mortality in patients receiving major non-cardiac surgery
264	Hemkens 2016	Clopidogrel treatment and mortality in patients with drug eluting stents
264	Hemkens 2016	Clopidogrel and mortality in patients after coronary artery bypass graft
273	Horbach 2016	Bleomycin and size reduction in patients with vascular malformations
275	Horita 2016	Beta lactam plus macrolide and all-cause mortality in patients with community-acquired pneumonia
278	Hu 2016	Sorafenib and time to progression in patients with hepatocellular carcinoma (HCC) receiving transarterial chemoembolization (TACE)
285	Huang 2016	Therapeutic anticoagulation and thrombosis progression in patients with isolated calf muscle vein thrombosis (ICMVT)
289	Hughes 2016	Corticosteroids and change in disability grade in patients with Guillain-Barre syndrome (GBS)

299	Jain 2016	Intranasal midazolam and seizure cessation in patients (>1 month of age) with acute convulsive seizures
305	Jiang 2016	Tranexamic acid (TXA) and postoperative hemoglobin concentration in patients with knee osteoarthritis undergoing simultaneous bilateral total knee arthroplasty (TKA)
320	Kaplan 2016	Hydroxychloroquine and stillbirth rates in pregnant patients
333	Khan 2016	Levetiracetam and early post-traumatic brain injury seizure (PTS) in adult patients with severe traumatic brain injury (TBI)
337	Kim 2016	Mupirocin and residual staphylococcal colonization in patients with sinusitis
353	Kovacs 2016	Artemisins and stillbirth in patients of child bearing age or pregnant patients of any gestational age
354	Kowalewski 2016	Oral anticoagulation and major adverse cardiovascular or cerebrovascular and thromboemoblic events (MACCE) in patients undergoing coronary angiography with or without percutaneous coronary intervention and on long term vitamin K antagonists anticoagulation
385	Leone 2016	Antiepileptic treatment and seizure recurrence within 1 year in patients of any age with a first unprovoked seizure
390	Li 2016	Non-vitamin K antagonist oral anticoagulants (NOACs) and stroke or systemic embolism in adult patients with non-valvular atrial fibrillation
418	Liu 2016	Topical steroids and clinical efficacy in pre-adolescent patients with phimosis
459	Meduri 2016	Aripiprazole and change in Young Mania Rating Scale (YMRS) in patients of both sexes and all genders with a diagnosis of bipolar of schizoaffective disorder
466	Mesfin 2016	Protease inhibitors and preterm birth in pregnant patients infected with HIV receiving antiretroviral therapy during pregnancy
484	Munnee 2016	Insulin and mortality in patients with Type 2 diabetes mellitus
487	Murphy 2016	Antibiotic prophylaxis and infection rate in patients requiring surgical treatment for a simple hand wound
489	Muzii 2016	Oral contraceptives and endometrioma recurrence in patients after surgery for endometrioma
498	Neufeld 2016	Antipsychotic and delirium prevention in postoperative adult patients

501	Nie 2016	Rituximab and 2-year overall survival in patients with Burkitt's lymphoma (BL)
514	Ortiz-Salas 2016	Intravenous immunoglobulin (IVIG) and efficacy in patients with Myasthenia Gravis (MG)
521	Pan 2016	Dexmedetomidine and heart rate in pediatric patients undergoing congenital heart disease surgery
527	Paul 2016	Antibiotic therapy and all-cause mortality in adult patients with pneumonia, bacteraemia, and severe sepsis/septic shock with microbiologically documented infections
529	Paul 2016	Antiviral prophylaxis and hepatitis B virus (HBV) reactivation in patients with chronic HBV infection
551	Puig 2016	Proton-pump inhibitor, amoxicillin and metronidazole (PAM) and intention to treat eradication rate in patients with Helicobacter pylori (H. pylori)
607	Shen 2016	Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II type 1 receptor blockers (ARBs) and incidence of cancer in patients receiving ACEIs and ARBs
666	Tran-Duy 2016	Proton pump inhibitors (PPIs) and gastric polyps in patients receiving PPIs
670	Tsaousi 2016	Dexmedetomidine (DEX) and hypotension in adult neurocritical care (NCC) patients
672	Tully 2016	Diuretic drugs and incident dementia in older adult patients without dementia
709	Wang 2016	Botulinum toxin A (BTX-A) injections and pelvic pain in patients diagnosed with bladder pain syndrome (BPS)/interstitial cystitis (IC)
741	Xing 2016	Dopamine and urine output in heart failure (HF) adult patients
745	Xu 2016	Micafungin and invasive fungal infections in patients undergoing hematopoetic stem cell transplantation (HSCT)
749	Yang 2016	Prophylactic entecavir and hepatitis B virus (HBV) reactivation in patients who were HBV surface antigen (HBsAg)-positive or with resolved HBV infection and received chemotherapy
753	Yang 2016	Oral anticoagulation therapy (OAT) and postoperative bleeding in patients who were receiving OAT and required dental extraction
755	Yang 2016	Antiviral therapy and complete remission in patients with hepatitis B virus-associated membranous nephropathy (HBV-MN)

762	Yin 2016	Rituximab and complete remission rate in patients with refractory nephrotic syndrome (NS)
776	Zeng 2016	Metformin and early pregnancy loss in pregnant patients with polycystic ovary syndrome (PCOS)
777	Zhai 2016	Gabapentin and visual analogue scale (VAS) pain in patients who underwent a primary total knee arthroplasty (TKA)
715	Wang 2016	Nucleotide/nucleoside analog (NA) monotherapy and complete remission of proteinuria in patients with hepatitis B virus-associated glomerulonephritis (HBG-GN)
788	Zhang 2016	Dehydroepiandrosterone (DHEA) and clinical pregnancy rate in patients with poor ovarian response (POR) undergoing in vitro fertilization or intracytoplasmic sperm injection (IVF/ICSI)
804	Zhao 2016	Pioglitazone and in-stent restenosis in patients with type 2 diabetes mellitus (T2DM) and underwent percutaneous coronary intervention (PCI)
806	Zhao 2016	Statins and peak aortic valve velocity after 24 months in patients with aortic stenosis
810	Zheng 2016	Erlotinib/gefitinib and response rate in patients with brain metastases (BM) and non-small-cell lung cancer (NSCLC)
815	Zhu 2016	Statins and incidence of vasospasm in patients with aneurysmal subarachnoid haemorrhage (SAH)
818	Zhuang 2016	Renin-angiotensin system blockade (RASB) and incidence of Alzheimer's disease in hypertensive patients without neurological disorders
3	Gandhi 2015	Dual-antiplatelet therapy (DAPT) and 30-day major stroke in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation (TAVI) who were not eligible for surgical aortic valve replacement
8	Muanda 2015	Antimalarials and low birth weight in pregnant patients
38	Araujo 2015	Chemotherapy and overall survival in patients with potentially resectable colorectal liver metastases (CRLM)
45	Austin 2015	Oral/topical non-absorbed antifungal prophylaxis and incidence of fungal infection in very low birth weight infant patients
47	Bai 2015	Lidocaine and postoperative pain score in adult patients
49	Bakhshehian 2015	Vancomycin powder and deep surgical-site infections in patients receiving spine surgery

54	Bang 2015	Intragastric botulinum toxin A and weight loss in patients with obesity
83	Bosanquet 2015	Anaesthetic and postoperative opioid use in patients undergoing lower limb amputation
107	Carneiro 2015	Androgen deprivation therapy and cardiovascular mortality in patients with prostate cancer
118	Chen 2015	Triple therapy and major adverse cardiovascular events (MACE) and stroke in patients with an indication for oral anticoagulant therapy (OAC) who underwent percutaneous coronary intervention (PCI)
128	Chen 2015	Moxifloxacin and rate of negative culture conversion in patients with pulmonary tuberculosis or acid-fast bacilli
130	Cheng 2015	Dexamethasone and postoperative voice quality at 48h in patients undergoing thyroidectomy
146	Coppola 2015	Antifibrinolytic agents and postoperative replacement treatment administration in patients with haemophilia or other congenital bleeding disorders undergoing surgery
159	Dahal 2015	Aldosterone antagonists and systolic blood pressure (SBP) in adult patients with resistant hypertension (RH)
164	de Frutos 2015	Coenzyme Q10 and intropic drug use after cardiac surgery requiring cardiopulmonary bypass (GPB)
170	Di 2015	Vancomycin and initial clinical cure rate in patients with clostridium difficile infection (CDI)
557	Qin 2016	Concurrent chemotherapy (CCRT) and overall survival in patients who were postoperative for cervical cancer
186	Estcourt 2015	Prophylactic granulocytes and all-cause mortality within 30 days in patients with neutropenia or neutrophil dysfunction
193	Feng 2015	Metformin and gestational diabetes mellitus (GDM) in pregnant patients with polycystic ovary syndrome (PCOS) receiving metformin to get conception
208	Fung 2015	Empirical antifungal strategies and invasive fungal disease (IFD) in patients with hematologic malignancy or hematopoietic stem-cell transplantation (HSCT) with high-risk febrile neutropenia (FN)
243	Haas 2015	Ethanol and perinatal mortality in patients with threatened preterm labor
260	He 2015	Calcium channel blockers (CCBs) and gastrointestinal bleeding (GIB) in patients receiving CCBs

277	Hu 2015	Acetylcysteine (NAC) and overall survival in patients with non-acetaminophen induced acute liver failure (NAI-ALF)
304	Jiang 2015	Sildenafil and oxygen consumption at peak exercise in patients with pulmonary hypertension (PH) and left heart disease (LHD)
328	Kessel 2015	Intracameral antibiotic and endophthalmitis in patients with age-related cataract undergoing phacoemulsification
356	Krajewski	Low-chloride resuscitation fluids and mortality in acutely ill patients in the intensive care unit (ICU) or surgical patients in the perioperative period
358	Kroon 2015	Indomethacin and number of any adverse events in patients with axial spondyloarthritis
343	Kitsios 2015	Activated protein C and short term in-hospital mortality in patients with severe sepsis or septic shock
343	Kitsios 2015	Artificial hyperoncotic colloid IV fluids and short term ICU mortality in patients with shock
343	Kitsios 2015	Hyperoncotic IV albumin and short term mortality ICU in patients with hemodynamic instability
343	Kitsios 2015	Diuretics (loop) and short term in-hospital mortality in patients with acute kidney injury
343	Kitsios 2015	Statins and short term ICU mortality in patients with severe sepsis
343	Kitsios 2015	Statins and short term in-hospital mortality in patients with acute respiratory distress syndrome (ARDS)
343	Kitsios 2015	Hydrocortisone IV and short term ICU mortality in patients with septic shock
343	Kitsios 2015	Liberal packed red blood cell transfusion and short term in-hospital mortality in patients with anemia
343	Kitsios 2015	Liberal packed red blood cell transfusion and short term ICU mortality in patients with anemia
388	Li 2015	Gemcitabine-combined S1 therapy (GS) and objective response rate in patients with pancreatic cancer, no prior treatment, an Eastern Cooperative Oncology Group status between 0 and 2, and adequate organ function
398	Li 2015	Topical anti-glaucoma medication vs. selective laser trabeculoplasty and intraocular pressure reduction in patients with open-angle glaucoma
404	Liet 2015	Heliox inhalation and change in CO2 in the 1st hour after starting treatment in infant patients hospitalised with acute bronchiolitis

406	Lim 2015	Antibiotic prophylaxis and incidence of infected pancreatic necrosis in patients with acute necrotizing pancreatitis (ANP)
408	Lim 2015	Levosimendan and intensive care unit stay in patients undergoing cardiac surgery
409	Lin 2015	Adjuvant chemotherapy and overall survival in patients with hepatocellular carcinoma who underwent liver transplantation
426	Liu 2015	Anticoagulation and new pulmonary embolisms, progression of deep vein thrombosis (DVT) and deaths in patients with acute DVT
428	Loomba 2015	Epinephrine and out-of-hospital return of spontaneous circulation (ROSC) in patients with out-of-hospital cardiac arrest (OHCA)
443	Ma 2015	Intra-arterial thrombolysis (IAT) and favorable outcome in patients with ischemic stroke
450	Mao 2015	Corticosteroid therapy and platelet count in patients with hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome
485	Muranushi 2015	Aspirin and non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDS) and squamous cell carcinoma (SCC) in patients receiving aspirin and non-aspirin NSAIDs for cutaneous SCC
486	Muranushi 2015	Aspirin and non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDS) and basal cell carcinoma (BCC) in patients receiving aspirin and non-aspirin NSAIDs for BCC prevention
500	Niafar 2015	Metformin and Vitamin B12 (VB12) serum concentrations in patients with type 2 diabetes
504	Ogunlesi 2015	Adjunctive parenteral corticosteroid and all-cause death until hospital discharge in newborn patients (from birth to 28 days) with bacterial meningitis or suspect meningitis
507	Ohlsson 2015	Intravenous immunoglobulin and mortality from any cause during initial hospitalisation in newborn patients (<28 days) with serious infection
520	Pammi 2015	Pentoxyifylline and all cause mortality during hospital stay in newborn patients (<28 days) with confirmed/suspected sepsis or necrotizing enterocolitis
522	Pan 2015	Oral antiplatelet agent and good functional outcome in patients receiving intravenous thrombolysis with recombinant tissue plasminogen activator (rtPA)
548	Prins 2015	Beta blockers and short term mortality in patients receiving beta blockers

549	Proietti 2015	Warfarin and pocket hematoma in patients undergoing permanent pacemaker (PM) or implantable cardioverter defibrillator (ICD) implantation
632	Sotiriadis 2015	Antenatal corticosteroids and cerebral palsy in children patients whose mothers were administered a single course of antenatal corticosteroids for the acceleration of fetal lung maturation
642	Suthar 2015	Co-trimoxazole and death in adult patients with CD4 counts >350 cells per uL and off antiretroviral therapy (ART)
647	Talukdar 2015	Methionine and pain in patients with chronic pancreatitis
654	Taylor 2015	Antibiotic lock and rates of confirmed catheter-related infection in newborn infants of any postmenstrual age who required central venous catheters (CVCs)
675	Turgeon 2015	Dual antiplatelet therapy (DAPT) and all-cause mortality in adult patients following transcatheter aortic valve implantation (TAVI)
687	Vecchio 2015	Steroids and end-stage kidney disease in adult and children patients with IgA nephropathy (IgAN)
698	Vyas 2015	Clopidogrel and major adverse cardiovascular events (MACE) in patients with ST-elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI)
707	Wang 2015	Recombinant human erythropoietin (rhEPO) and MDI score in preterm infant patients
724	Widmer 2015	Antimicrobial and maternal cure rate in patients identified as having asymptomatic bacteriuria during pregnancy
726	Wilhelmus 2015	Idoxuridine and healing at 7 days in patients with epithelial keratitis
732	Wu 2015	Thiazolidinediones and cancer incidence in patients receiving anti-diabetic medications (ADMs)
579	Rys 2018	Continuous subcutaneous insulin infusion (CSII) and HbA1c levels in the first trimester in pregnant patients with pregestational type 1 diabetes mellitus (T1DM)
613	Shin 2015	5-fluorouracil (5-FU) and keloid recurrence rate in patients with keloids excised
630	Song 2017	Angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) and disease-free survival (DFS) in patients diagnosed with cancer

651	Tang 2016	Statins and plaque volumes in patients with acute coronary syndrome (ACS), myocardial infarction (MI), or unstable angina
736	Wu 2015	Angiotensin converting enzyme inhibitors (ACEIs) and angiotension receptor blockers (ARBs) and contrast-induced nephropathy (CIN) in patients undergoing coronary angiography (CAG)
737	Xia 2015	Nucleotide/nucleoside analog (NA) antiviral therapy and 3-year survival in patients with hepatitis B virus (HBV)-related hepatocellular carcinoma (HCC) after curative treatment
738	Xia 2015	Mesenchymal stem cells (MSCs) injection and pain on a visual analogue scale (VAS) in patients knee osteoarthritis (OA)
760	Ye 2015	Renin-angiotensin system (RAS)-targeting antihypertensive drugs and changes in cognitive function in patients with Alzheimer's disease (AD)
764	Yong 2015	Anti-vascular endothelial growth factor (VEGF) and complete polyp regression in patients with polypoidal choroidal vasculopathy (PCV) who are treatment-naïve
801	Zhao 2015	Bisphosphonate and lumbar bone mineral density (BMD) in adult patients after cardiac transplantation
803	Zhao 2015	Hormone replacement therapy (HRT) and femoral neck bone mineral density (BMD) in healthy postmenopausal women who had not regularly exercised prior to enrollment (<2 h/week)
823	Zuo 2015	Tenofovir and virological response rate at 24 weeks in patients with chronic heptatitis B virus (HBV) infection
35	Andia 2014	Platelet-rich plasma (PRP) and pain as visual analogue score (VAS) at 6 months in patients with tedinography
37	Antoniou 2014	Statins and all-cause mortality in patients with peripheral arterial disease affecting the lower limbs
41	Arnaud 2014	Aspirin and first thrombosis in patients with antiphospholipid antibodies (aPL)
51	Ballinger 2014	Oral antibiotics and primary treatment failure in patients with peritoneal dialysis (PD) and developed PD-associated peritonitis
63	Bellemain-Appaix	P2Y12 Inhibitors and all-cause mortality in patients with non-ST elevation acute coronary syndrome (ACS)
71	Bhangu 2014	Non-steroidal anti-inflammatory drugs (NSAIDs) and anastomotic leak rates in patients following colonic or small bowel resection
91	Brogly 2014	Buprenorphine maintenance therapy (BMT) and neonatal abstinence syndrome (NAS) in patients who were pregnant while receiving BMT

93	Budden 2014	High-dose oxytocin and caesarean section in pregnant patients for induction of labour
136	Chrcanovic 2014	Antibiotic use and implant failure in patients receiving a dental implant
143	Clifton 2014	Dipeptidyl peptidase IV (DPP-IV) inhibitors and heart failure in patients receiving DPP-IV inhibitors
819	Ziff 2015	Digoxin and heart failure related hospitalisations in patients who experienced atrial fibrillation or heart failure
149	Costi 2014	Sevoflurane anaesthetic and emergence agitation in patients younger than 18 years of age presenting for general anaesthesia with or without surgical intervention
154	Critchley 2014	Steroid therapy and all-cause mortality in patients with pulmonary tuberculosis
157	Cui 2014	Aspirin and pancreatic cancer risk in patients receiving aspirin
210	Furtado 2014	Iodine131 lipiodol and disease free survival (DFS) at 1 year in adult patients with resected hepatocellular carcinoma (HCC)
254	Haroon 2014	TNF-alpha inhibitors and spine bone mineral density (BMD) in patients with ankylosing spondylitis (AS)
272	Hong 2014	Anakinra and remission rate in patients with adult-onset Still disease (AoSD)
276	Hu 2014	Nonsteroidal anti-inflammatory drugs (NSAIDs) and risk of melanoma in patients receiving NSAIDs
318	Kanbay 2014	Allopurinol and flow-mediated dilatation in patients receiving allopurinol
345	Klimo 2014	Preoperative antibiotic and shunt infection in children patients undergoing shunt surgery
380	Leibovici-Weissman 2014	Antimicrobial and clinical failure in patients with diarrhoea
382	Lemos 2014	Tumor necrosis factor inhibitors (anti-TNF) and improvements of 20% in the American College of Rheumatology (ACR20) in adult patients with psoriatic arthritis (PsA)
402	Liang 2014	Chemoradiotherapy and local recurrence of gastric cancer in patients following resection of gastric cancer with D2 lymphadenectomy
420	Liu 2014	Polymyxins monotherapy and clinical response in patients with Acinetobacter baumannii (A. baumannii)

432	Lu 2014	Telbivudine and HBsAg seropositivity in infant patients who received active-passive immunoprophylaxis postpartum born to mothers who received telbivudine during pregnancy
439	Lussana 2014	Acetylsalicylic acid (ASA) and arterial thrombosis in patients undergoing total hip replacement (THR) or total knee replacement (TKR)
455	Mbeye 2014	Cotrimoxazole prophylactic treatment (CPT) and malaria incidence in HIV positive and HIV-exposed uninfected (HEU) children in sub-Saharan Africa
465	Merlotti 2014	Lipid-affecting drugs and type 2 diabetes mellitus (T2DM) incidence in patients receiving lipid-affecting drugs
478	Moraes 2014	Platelet-rich therapy (PRT) and function in patients with musculoskeletal soft tissue injuries
503	O'Brien 2014	Postmenopausal hormone therapy and Alzheimer's disease risk in patients using postmenopausal hormone therapy
509	Okoli 2014	Oseltamivir and community transmission of influenza in patients with influenza, influenze-like illness (ILI), or who had close contact with any of the above persons
523	Pani 2014	Anticonvulsants and alcohol use in patients with alcohol dependence
528	Paul 2014	Beta lactam antibiotic monotherapy and all-cause mortality in hospitalized patients with sepsis
537	Peters 2014	Calcium channel blockers and Alzheimer's disease incidence in very elderly patients free of cognitive decline or dementia at baseline
543	Prasad 2014	Lorazepam IV and non-cessation of seizures in patients with status epilepticus
546	Prijic 2014	Carvedilol and mortality/heart transplantation in pediatric patients with impaired systemic ventricle systolic function
563	Radeva-Petrova 2014	Preventive antimalarials and severe anaemia (mother) in patients living in malaria-endemic areas
572	Rojas-Villarraga 2014	Hormone replacement therapy (HRT) and thrombosis in patients with systemic lupus erythematosus (SLE)
573	Rokkas 2014	Metformin and colon neoplasia in patients with type 2 diabetes
592	Sant'anna 2014	Vitamin K antagonist continuation and postoperative bleeding in patients receiving cardiovascular implantable electronic devices (CIED)

593	Sardar 2014	Dabigatran and risk of thromboembolic complications in patients with atrial fibrillation (AF) undergoing catheter ablation
599	Serpa Neto 2014	Hydroxyethyl starches (HES) and development of acute kidney injury (AKI) in patients with sepsis
600	Seth 2014	Allopurinol and acute gout attacks in patients diagnosed with chronic gout
606	Sharma 2014	Bisphosphonate therapy and atrial fibrillation (AF) in patients requiring bisphosphonate therapy for any indication
610	Shi 2014	Statins and risk of liver cancer in patients using statins
611	Shim 2014	Hormone replacement therapy and endometrial cancer (EC) in patients receiving surgical treatment for EC
623	Smaill 2014	Antibiotic and maternal febrile morbidity/fever in patients undergoing cesarean section
637	Stern 2014	Trimethoprim/sulfamethoxazole (TMP/SMX) and any adverse event in non-HIV immunocompromised patients
640	Strohmeier 2014	IV therapy and persistent bacteruria after treatment in children patients with acute pyelonephritis
681	van Herwaarden 2014	Anti-tumor necrosis factor (TNF) and Proportion persistent low disease activity in patients with rheumatoid arthritis (RA) and low disease activity
708	Wang 2014	Carvedilol and incidence of postoperative atrial fibrillation in adult patients undergoing cardiac surgery
742	Xiong 2014	Anti-vascular endothelial growth factor (VEGF) and percentage of intraocular pressure reduction (IOPR%) in glaucoma patients who underwent Trab or phacotrabeculectomy
770	Yuan 2014	Non-enzyme-inducing antiepileptic (AEDs) and post-surgery seizure in patients who had undergone glioma resection surgery
780	Zhang 2014	Chemotherapy and 5-year event-free survival rate in patients with newly diagnosed, primary, well-differentiated osteosarcoma, and without prior treatment, aged <50 years, without signs of pulmonary metastasis
783	Zhang 2014	Astragalus and conventional treatment and proteinuria at end of treatment in patients with chronic kidney disease of all ages
795	Zhang 2014	Traditional Chinese medicine (TCM) plus conventional drug and Hamilton rating scale for depression in patients with Parkinson's Disease (PD)
813	Zhou 2014	Radiotherapy and overall mortality rate in patients with rectal cancer

119	Chen 2013	Short-course highly active antiretroviral treatment (HAART) and CD4 count ≤12 months in patients during primary HIV infection
190	Falagas 2013	Amphotericin B deoxycholate and nephrotoxicity in patients with fungal infections
212	Galappaththy 2013	Primaquine and Plasmodium vivax detection > 30 days after starting primaquine in patients with P. vivax malaria
809	Zheng 2014	Aloe vera v 33% MgSO4 and total incidence of phlebitis in patients
218	Gharaibeh 2013	Tranexamic acid and short-term visual acuity from 20/20 to 20/40 in patients with traumatic hyphema following closed globe trauma
259	He 2013	S-1 and overall response rate (ORR) in patients with advanced gastric adenocarcinoma
269	Hodson 2013	Antiviral prophylaxis and cytomegalovirus (CMV(disease and CMV infection in patients who have undergone at least one solid organ transplant
286	Huang 2013	Amiodarone and survival to hospital discharge in adult patients with cardiac arrest
312	Kabra 2013	Antibiotic and development of pneumonia in child patients with measles
326	Kenyon 2013	Oxytocin and caesarean section in patients in labour
334	Khoshbin 2013	Platelet-rich plasma and the Western Ontario and McMaster Universities Arthritis Index (WOMAC) in patients with knee osteoarthritis (OA)
365	Kwok 2013	Omeprazole and major adverse cardiac events (MACE) in patients receiving clopidogrel
424	Liu 2013	Nonsteroidal anti-inflammatory drugs (NSAIDs) and risk of brain tumour in patients using NSAIDs
550	Prutsky 2013	Antibiotic and cat scratch disease incidence in patients receiving treatment for Bartonella
624	Smit 2013	Phenobarbital and all intraventricular haemorrhage in preterm infants
722	Westhoff 2013	Oxytocin and postpartum haemorrhage (PPH) in pregnant patients anticipating a vaginal delivery
12	Abolhassani 2013	Immunoglobulin and IgG trough levels in adult and child patients with primary antibody deficiencies (PAD)
19	Afolabi 2012	Epidural anaesthesia and mean umbilical arterial pH in patients having elective or emergency caesarean section for any indication

50	Baldinger 2012	L-threonine 2 g/d and muscle cramp in patients with amyotrophic lateral sclerosis (ALS)
77	Bloom 2012	Glucocorticoid injection and overall pain in patients with rotator cuff disease or adhesive capsulitis
85	Boyle 2012	Immunotherapy and large local reaction to field or challenge sting in patients with previous systemic reactions or large local reactions to insect sting or venom
87	Brennan 2012	Topical preparations with active ingredients and presence of stretch marks in pregnant patients prior to 20 weeks gestation
178	Edmonds 2012	Inhaled corticosteroids (ICS) and admission to hospital in patients with acute asthma
545	Price 2012	Testosterone and subjective improvement in symptoms of intermittent claudication in patients with lower limb atherosclerosis
445	Mackeen 2011	Tocolytic and perinatal mortality in pregnant patient with singleton pregnancies and a gestational age between 23 and 36 weeks and six days who are diagnosed with preterm premature rupture of membranes (PPROM)
518	Paciaroni 2011	Anticoagulants and all deep venous thrombosis (DVT) in patients with hemorrhagic stroke
605	Shang 2011	Bacillus Calmette-Guerin (BCG) and frequency of tumour recurrence (relapse) in adult patients with Ta and T1 bladder cancer treated with transurethral resection
30	Allen 2010	Probiotic and mean duration of diarrhoea in adult and child patients with acute diarrhoea caused by infectious agent
184	Engelman 2010	Methylprednisolone and any organ dysfunction or complication in patients undergoing surgery for esophageal cancer
221	Gillespie 2010	Antibiotic agent and deep surgical site infection in patient undergoing surgery for internal fixation or replacement arthroplasty
236	Graves 2010	Injected cholera vaccine and cholera cases (year 2 follow up) in patients older than 5 years and well irrespective of immune status or special risk category
265	Henderson-Smart 2010	Methylxanthine and failed apnoea reduction after 2-7 days in preterm infant patients with recurrent apnoea
291	Hunt 2010	Ethamsylate and neonatal mortality (to 28 days postnatal age) in infant patients <35 completed weeks or < 2000 grams

472	Miyake 2010	Interferon (IFN) treatment and hepatocellular carcinoma development in patients receiving IFN treatment
515	Osborn 2010	Opiate and treatment failure in newborn infant patients with neonatal abstinence syndrome (NAS) in the neonatal period born to mothers with an opiate dependence
516	Osborn 2010	Phenobarbitone and treatment failure in newborn infant patients with neonatal abstinence syndrome (NAS) in the neonatal period born to mothers with an opiate dependence
615	Sim 2010	Estrogen preparations and lumbar bone mineral density in premenopausal patients ranging in age from 12 to 45 with anorexia nervosa
634	Squizzato 2010	Statins and venous thromboembolism (VTE) in adult patients receiving statins
26	Alfirevic 2009	Oxytocin and caesarean section in pregnant patients due for third trimester induction of labour
314	Kalil 2009	Valganciclovir and cytomegalovirus (CMV) in patients after solid organ transplant
648	Tang 2009	Corticosteroid and hospital mortality in patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS)
454	Matthews 2016	Deflazacort and weight gain in patients with Duchenne muscular dystrophy (DMD)
750	Yang 2016	Piperacillin/taxobactam and mortality in patients receiving piperacillin/tazobactam
617	Sinclair 2011	Whole cell vaccines and cases of cholera at 1 year follow up in adult and children patients without cholera symptoms