

## ADDITIONAL FILE 1

### **An empirical evaluation of the impact scenario of pooling bodies of evidence from randomized controlled trials and cohort studies in medical research**

Nils Bröckelmann<sup>1\*</sup>, Julia Stadelmaier<sup>1\*</sup>, Louisa Harms<sup>1</sup>, Charlotte Kubiak<sup>1</sup>, Jessica Beyerbach<sup>1</sup>, Martin Wolkewitz<sup>2</sup>, Jörg J Meerpohl<sup>1,3</sup>, Lukas Schwingshackl<sup>1</sup>

<sup>1</sup> Institute for Evidence in Medicine, Medical Center - University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany.

<sup>2</sup> Institute of Medical Biometry and Statistics, Faculty of Medicine and Medical Center - University of Freiburg, Freiburg, Germany.

<sup>3</sup> Cochrane Germany, Cochrane Germany Foundation, Freiburg, Germany.

\*contributed equally

Corresponding author:

Lukas Schwingshackl, PhD

Breisacher Straße 86, 79110 Freiburg, Germany

M: schwingshackl@ifem.uni-freiburg.de

P: +49 (0)761 203-96867

ORCID number: 0000-0003-3407-7594

Twitter: <https://twitter.com/LSchwingshackl>

**Content Supplement**

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### Appendix S1: Search strategy for systematic reviews in MEDLINE via PubMed

ID	Search
#1	"lancet london england"[Journal] OR "JAMA"[Journal] OR "bmj clinical research ed"[Journal] OR "jama internal medicine"[Journal] OR "Annals of internal medicine"[Journal] OR "PLoS medicine"[Journal] OR "BMC medicine"[Journal] OR "The Cochrane database of systematic reviews"[Journal] OR "Mayo Clinic proceedings"[Journal] OR "Canadian Medical Association journal"[Journal] OR "Nat Rev Dis Primers"[Journal] OR "J Cachexia Sarcopenia Muscle"[Journal] OR "N Engl J Med"[Journal]
#2	"systematic review"[Title/Abstract] OR "systematic literature review"[Title/Abstract] OR "systematic scoping review"[Title/Abstract] OR "systematic meta-review"[Title/Abstract] OR "systematic search"[Title/Abstract] OR "systematic review"[Publication Type] OR "meta analys*"[Title/Abstract] OR "meta analys*"[Publication Type] OR "cochrane database syst rev"[Journal]
#3	"random*"[Title/Abstract] OR "placebo"[Title/Abstract] OR "clinical trials as topic"[MeSH Terms:noexp] OR "trial"[Title]
#4	"epidemiolog*"[Title/Abstract] OR "cohort stud*"[Title/Abstract] OR "observation*"[Title/Abstract] OR "non rct*"[Title/Abstract] OR "non random*"[Title/Abstract]
#5	#1 AND #2 AND #3 AND #4
#6	#1 AND #2 AND #3 AND #4 Filters: from 2010/1/1 - 2019/12/31

**Table S1:** Explanation and definition for Population (P), Intervention/Exposure (I/E), Comparator (C), Outcome (O) similarity degree

Rating	Population	Intervention/Exposure	Comparator	Outcome
<b>1 = “more or less identical”</b>	Same health status and type of population	Same drug, invasive procedure, nutrition-intervention or vaccine	-Same drug or invasive procedure -Nutrition: Placebo vs. Nil or low intake; Low intake vs. Low intake	Same outcome
	e.g. -Both BoE with either healthy population, general population or diseased population -Same age category (both adults, both postmenopausal women)	e.g. - Both Enoxaparin - Both PCI - Both high dairy-intake	e.g. -Both no Enoxaparin -Both UKA -Placebo vs. No intervention or low intake	e.g. Mortality in both BoE
<b>2 = “similar but not identical”</b>	Populations with mixed health status in RCTs and/ or cohort studies	-Different drugs of the same class/ Any drug of the same class vs. Specific drug of the same class -Similar invasive procedure/ same invasive procedure with different co-interventions -Similar vaccines or identical vaccine with different route of administration -Supplementary or free food vs. Intake -Similar but not identical time frame of intervention	-Different drugs of the same class -Similar invasive procedures, drug, vaccine or diet -General dietary advice vs. High intake	-Similar outcome -Both with mixed similar outcomes

	<p>e.g.</p> <ul style="list-style-type: none"> <li>-Merged healthy and diseased population in one BoE vs. healthy population in the other BoE</li> <li>-Both BoE with merged healthy and diseased population</li> <li>-Population with cardiovascular risk factors (without manifest disease) vs. Healthy population</li> </ul>	<p>e.g.</p> <ul style="list-style-type: none"> <li>-Both different SGAs</li> <li>-Both similar regional anaesthetic nerve blocks</li> <li>-Various pneumococcal vaccines (2,3,12,14,17 and 23-valent) versus 23-valent only</li> <li>-One or two doses of measles containing vaccines versus unclear number of doses</li> <li>-Free non-caloric beverages vs. Low intake of SSBs</li> <li>-Early intervention with different time frame (first 14 vs. first 24 hours)</li> </ul>	<p>e.g.</p> <ul style="list-style-type: none"> <li>-Both different DDP-4 inhibitors</li> <li>-“Best medical treatment” with Aspirin and additionally with various other drugs</li> <li>-No vaccination or delayed vaccination versus no vaccination</li> <li>-Transfemoral vs. transapical TAVI</li> <li>-General dietary advice vs. High red meat intake</li> </ul>	<p>e.g.</p> <ul style="list-style-type: none"> <li>-Late stage only or all CRC vs. All CRC</li> <li>-Both with mixed sedation outcomes (e.g. Sleepiness, sedation)</li> </ul>
<b>3 = “broadly similar”</b>	<ul style="list-style-type: none"> <li>-Different health status of populations in RCTs and cohort studies</li> <li>-Other substantial differences (e.g. Age-category, type of population)</li> </ul>	<ul style="list-style-type: none"> <li>-Same drug for different indication</li> <li>-Enhanced treatment vs. Any treatment</li> <li>-Supplement vs. Status</li> <li>-Different time frame/ early treatment vs. Any treatment</li> </ul>	<ul style="list-style-type: none"> <li>-Active intervention (drug, invasive procedure, nutrient) vs. No intervention or placebo</li> <li>-Different time frame</li> </ul>	<p>-Broadly similar</p>
	<p>e.g.</p> <ul style="list-style-type: none"> <li>-Healthy population in one BoE vs. population with cardiovascular disease in the other BoE</li> <li>-Children/adolescents vs. Adults</li> <li>-Travellers vs. Pregnant women</li> </ul>	<p>e.g.</p> <ul style="list-style-type: none"> <li>-Digoxin for HF vs. digoxin post-myocardial infarction without HF</li> <li>-Dispatcher-assisted bystander CPR vs. unassisted bystander CPR</li> <li>-Enhanced training of birth attendants vs. Any support by birth attendant</li> <li>-Selenium supplements vs. High selenium status</li> <li>-Early ART vs. Any ART</li> </ul>	<p>e.g.</p> <ul style="list-style-type: none"> <li>-Restrictive transfusion vs. No transfusion</li> <li>-Placebo vs. Low selenium status</li> <li>-No vaccination of health care workers vs. Low share of vaccinated health care workers per facility</li> <li>-Pregnant women with untreated bacteriuria vs. Pregnant without screening for bacteriuria</li> <li>-Delayed ART vs. No ART</li> </ul>	<p>e.g.</p> <ul style="list-style-type: none"> <li>-Colorectal adenoma vs. Cancer</li> </ul>

ART: antiretroviral therapy; BoE: bodies of evidence; CRC: colorectal cancer; CPR: cardiopulmonary resuscitation; DDP-4: dipeptidyl peptidase 4; HF: heart failure; PCI: percutaneous coronary intervention; PI/ECO: population, intervention/ exposure, comparator, outcome; RCT: randomized controlled trial; SGA: second-generation antipsychotic; SSBs: sugar-sweetened beverages; TAVI: transcatheter aortic valve replacement; UKA: unicompartmental knee arthroplasty

**Table S2:** Ratings of Population (P), Intervention/Exposure (I/E), Comparator (C), Outcome (O) similarity degree for all identified body of evidence-pairs

Reference	Intervention/ Exposure (as defined by the authors)	Intervention / Exposure type	Outcome (as defined by the authors)	Outcome-category	Rating of PI/ECO-similarity degree					Included in the pooling scenario (Yes/No)
				(e.g., cancer outcomes, cardiovascular disease, all-cause mortality)	Patients/ Population	Intervention/ Exposure	Comparator	Outcome	Overall	
Abou-Setta 2011 (1)	Nerve block	Invasive	Delirium	Neurological	2	2	2	1	2	No
Abou-Setta 2011 (1)	Spinal anaesthesia	Invasive	All-cause mortality	All-cause mortality	2	1	1	1	2	No
Aburto 2013 (2)	Low sodium	Nutrition	All-cause mortality	All-cause mortality	2	2	2	1	2	Yes
Aburto 2013 (2)	Low sodium	Nutrition	Cardiovascular disease	Cardiovascular disease	2	2	2	2	2	Yes
Ahmad 2015 (3)	Intra-aortic balloon pump	Invasive	All-cause mortality	All-cause mortality	1	1	1	1	1	Yes
Alexander 2017 (4)	High DHA and EPA	Nutrition	Coronary heart disease	Cardiovascular disease	2	2	2	1	2	No
Alexander 2017 (4)	High DHA and EPA	Nutrition	Coronary heart disease mortality	Cardiovascular disease	2	2	2	1	2	No
Alexander 2017 (4)	High DHA and EPA	Nutrition	Coronary heart disease incidence	Cardiovascular disease	2	2	2	1	2	No
Alipanah 2018 (5)	Self-administered therapy	Drug	Treatment success	Infectiological	3	2	1	1	3	Yes
Alipanah 2018 (5)	Self-administered therapy	Drug	Treatment completion	Drug safety	3	2	1	1	3	Yes
Alipanah 2018 (5)	Self-administered therapy	Drug	All-cause mortality	All-cause mortality	3	2	1	1	3	Yes
Anglemyer 2013 (6)	Antiretroviral therapy	Drug	HIV infection	Infectiological	2	2	3	1	3	Yes
Azad 2017 (7)	Nonnutritive sweeteners	Nutrition	Body Mass Index	Metabolic	2	2	1	1	2	Yes

Barnard 2015 (8)	Surgical abortion by mid-level providers	Invasive	Failure or incomplete abortion	Obstetrical	2	2	1	1	2	Yes
Barnard 2015 (8)	Surgical abortion by mid-level providers	Invasive	Complications	Obstetrical	2	2	1	1	2	Yes
Barnard 2015 (8)	Surgical abortion by mid-level providers	Invasive	Abortion failure and complications	Obstetrical	2	2	1	1	2	Yes
Bellemain-Appaix 2012 (9)	Clopidogrel pretreatment for percutaneous coronary intervention	Drug	All-cause mortality	All-cause mortality	2	2	2	1	2	Yes
Bellemain-Appaix 2012 (9)	Clopidogrel pretreatment for percutaneous coronary intervention	Drug	Major bleeding	Drug safety	2	2	2	1	2	Yes
Bellemain-Appaix 2012 (9)	Clopidogrel pretreatment for percutaneous coronary intervention	Drug	Coronary heart disease	Cardiovascular disease	2	2	2	1	2	Yes
Bellemain-Appaix 2014 (10)	P2Y12 inhibitor pretreatment in non-ST elevation acute coronary syndrome	Drug	All-cause mortality	All-cause mortality	2	2	2	1	2	Yes
Bellemain-Appaix 2014 (10)	P2Y12 inhibitor pretreatment in non-ST elevation acute coronary syndrome	Drug	Major bleeding	Drug safety	2	2	2	1	2	Yes
Bellemain-Appaix 2014 (10)	P2Y12 inhibitor pretreatment in non-ST elevation acute coronary syndrome	Drug	Main composite ischemic endpoint	Cardiovascular disease	2	2	2	1	2	Yes
Bloomfield 2016 (11)	Mediterranean diet	Nutrition	Breast cancer	Oncological	2	2	2	1	2	Yes

Bolland 2015 (12)	High calcium	Nutrition	All fractures	Orthopaedic	1	2	1	1	2	Yes
Bolland 2015 (12)	High calcium	Nutrition	Vertebral fracture	Orthopaedic	1	2	1	1	2	Yes
Bolland 2015 (12)	High calcium	Nutrition	Hip fracture	Orthopaedic	1	2	1	1	2	Yes
Brenner 2014 (13)	Sigmoidoscopy	Invasive	Colorectal cancer mortality	Oncological	1	1	1	1	1	Yes
Brenner 2014 (13)	Sigmoidoscopy	Invasive	Colorectal cancer incidence	Oncological	1	1	1	2	2	Yes
Chowdhury 2012 (14)	High omega-3	Nutrition	Cerebrovascular disease	Cardiovascular disease	2	2	1	1	2	Yes
Chowdhury 2014a (15)	High $\alpha$ -linolenic acid	Nutrition	Coronary heart disease	Cardiovascular disease	3	2	2	1	3	Yes
Chowdhury 2014a (15)	High omega-3	Nutrition	Coronary heart disease	Cardiovascular disease	3	2	2	1	3	Yes
Chowdhury 2014a (15)	High omega-6	Nutrition	Coronary heart disease	Cardiovascular disease	3	2	2	1	3	Yes
Chowdhury 2014b (16)	High vitamin D	Nutrition	All-cause mortality	All-cause mortality	2	3	3	1	3	No
Chung 2011 (17)	High vitamin D	Nutrition	Colorectal cancer	Oncological	2	3	3	1	3	No
Chung 2011 (17)	High vitamin D	Nutrition	Breast cancer	Oncological	2	3	3	1	3	No
Chung 2016 (18)	High calcium	Nutrition	Cardiovascular mortality	Cardiovascular disease	2	2	1	1	2	Yes
Ding 2017 (19)	High dairy	Nutrition	Systolic blood pressure	Cardiovascular disease	2	1	1	1	2	Yes
Fenton 2018 (20)	Radiation therapy	Invasive	Erectile dysfunction	Urological	1	1	2	1	2	Yes
Fenton 2018 (20)	Radical Prostatectomy	Invasive	Urinary incontinence	Urological	1	1	2	1	2	Yes
Fenton 2018 (20)	Radical Prostatectomy	Invasive	Erectile dysfunction	Urological	1	1	2	1	2	Yes
Filippini 2017 (21)	Disease-modifying drugs	Drug	Conversion to clinically definite multiple sclerosis	Neurological	1	2	1	1	2	Yes



Fluri 2010 (22)	Extracranial-intracranial arterial bypass	Invasive	All-cause mortality	All-cause mortality	2	1	2	1	2	Yes
Fluri 2010 (22)	Extracranial-intracranial arterial bypass	Invasive	Stroke	Cardiovascular disease	2	1	2	1	2	Yes
Fluri 2010 (22)	Extracranial-intracranial arterial bypass	Invasive	Stroke mortality or dependency	Cardiovascular disease	1	1	2	1	2	Yes
Gargiulo 2016 (23)	Transcatheter aortic valve implantation	Invasive	Early all-cause mortality	All-cause mortality	2	2	1	1	2	Yes
Gargiulo 2016 (23)	Transcatheter aortic valve implantation	Invasive	Mid-term all-cause mortality	All-cause mortality	2	2	1	1	2	Yes
Gargiulo 2016 (23)	Transcatheter aortic valve implantation	Invasive	Long-term all-cause mortality	All-cause mortality	2	1	1	1	2	Yes
Hartling 2013 (24)	Treating gestational diabetes mellitus	Nutrition	High birth weight	Obstetrical	2	1	1	1	2	Yes
Hartling 2013 (24)	Treating gestational diabetes mellitus	Nutrition	Large-for-gestational age neonate	Obstetrical	2	1	1	1	2	Yes
Hartling 2013 (24)	Treating gestational diabetes mellitus	Nutrition	Shoulder dystocia	Obstetrical	2	1	1	1	2	Yes
Henderson 2019 (25)	Treating asymptomatic bacteriuria	Drug	Pyelonephritis	Infectiological	2	2	3	1	3	Yes
Higgins 2016 (26)	Bacillus Calmette-Guérin vaccination	Vaccine	All-cause mortality	All-cause mortality	3	1	2	1	3	Yes
Higgins 2016 (26)	Measles containing vaccines	Vaccine	All-cause mortality	All-cause mortality	3	2	2	1	3	Yes
Hopley 2010 (27)	Total hip arthroplasty	Invasive	Reoperation	Orthopaedic	2	1	1	1	2	Yes
Hopley 2010 (27)	Total hip arthroplasty	Invasive	Dislocation	Orthopaedic	2	1	1	1	2	Yes
Hopley 2010 (27)	Total hip arthroplasty	Invasive	Deep infection	Infectiological	2	2	1	1	2	Yes
Hüpfel 2010 (28)	Chest-compression-only cardiopulmonary	Cardiopulmonary	Survival	All-cause mortality	1	3	3	1	3	Yes

	nary resuscitation	resuscitation								
Jamal 2013 (29)	Non-calcium-based phosphate binders	Drug	All-cause mortality	All-cause mortality	2	2	1	1	2	Yes
Jefferson 2010 (30)	Parenteral influenza vaccine	Vaccine	Influenza-like illness	Infectiological	2	2	3	1	3	Yes
Jefferson 2010 (30)	Parenteral influenza vaccine	Vaccine	Influenza	Infectiological	2	2	1	1	2	Yes
Jefferson 2012 (31)	Inactivated influenza vaccines	Vaccine	Influenza	Infectiological	1	2	1	1	2	Yes
Jefferson 2012 (31)	Inactivated influenza vaccines	Vaccine	Influenza-like illness	Infectiological	1	2	1	1	2	Yes
Jin 2012 (32)	High total flavonoids	Nutrition	Colorectal neoplasms	Oncological	3	2	2	3	3	Yes
Johnston 2019 (33)	Red meat	Nutrition	All-cause mortality	All-cause mortality	2	2	2	1	2	No
Johnston 2019 (33)	Red meat	Nutrition	Cardiovascular mortality	Cardiovascular disease	2	2	2	1	2	No
Johnston 2019 (33)	Red meat	Nutrition	Cardiovascular disease	Cardiovascular disease	2	2	2	1	2	No
Kansagara 2013 (34)	Transfusion	Transfusion	All-cause mortality	All-cause mortality	2	3	3	2	3	Yes
Keag 2018 (35)	Caesarean section	Invasive	Urinary incontinence	Obstetrical	3	2	2	1	3	Yes
Keag 2018 (35)	Caesarean section	Invasive	Fecal incontinence	Obstetrical	3	2	2	1	3	Yes
Kredo 2014 (36)	Antiretroviral therapy by nurses	Drug	All-cause mortality	All-cause mortality	2	3	1	1	3	Yes
Kredo 2014 (36)	Antiretroviral therapy by nurses	Drug	Attrition	Drug safety	2	3	1	1	3	Yes
Kredo 2014 (36)	Nurses for maintenance of antiretroviral therapy	Drug	All-cause mortality	All-cause mortality	2	3	2	1	3	Yes
Li 2014 (37)	Exenatide	Drug	Acute pancreatitis	Drug safety	2	1	2	2	2	Yes
Li 2016 (38)	DDP-4 inhibitors	Drug	Heart failure	Drug safety	2	2	2	1	2	Yes

Li 2016 (38)	DDP-4 inhibitors	Drug	Hospital admission for heart failure	Drug safety	2	2	2	1	2	Yes
Matthews 2018 (39)	Tamoxifen	Drug	Heart failure	Drug safety	2	3	1	1	3	Yes
Menne 2019 (40)	SGLT-2 inhibitors	Drug	Acute kidney injury	Drug safety	2	2	2	1	2	Yes
Mesgarpour 2017 (41)	Erythropoiesis stimulating agents	Drug	Venous thrombo-embolism	Drug safety	2	2	2	1	2	Yes
Mesgarpour 2017 (41)	Erythropoiesis stimulating agents	Drug	All-cause mortality	All-cause mortality	2	2	2	1	2	Yes
Moberley 2013 (42)	Pneumococcal polysaccharide vaccines	Vaccine	Invasive pneumococcal disease	Infectiological	2	2	1	1	2	Yes
Molnar 2015 (43)	Neoral (Cyclosporin)	Drug	Acute rejection of kidney transplant	Drug safety	2	1	2	1	2	Yes
Navarese 2013 (44)	Early intervention for NSTEMI-ACS	Invasive	All-cause mortality	All-cause mortality	2	2	1	1	2	Yes
Navarese 2013 (44)	Early intervention for NSTEMI-ACS	Invasive	Myocardial infarction	Cardiovascular disease	2	2	1	1	2	Yes
Navarese 2013 (44)	Early intervention for NSTEMI-ACS	Invasive	Major bleeding	Drug safety	2	2	1	1	2	Yes
Nelson 2010 (45)	Caesarean section	Invasive	Anal incontinence, feces	Obstetrical	3	2	2	1	3	Yes
Nelson 2010 (45)	Caesarean section	Invasive	Anal incontinence, flatus	Obstetrical	3	2	2	1	3	Yes
Nieuwenhuijse 2014 (46)	Ceramic-on-ceramic bearings for total hip arthroplasty	Invasive	Harris Hip Score	Orthopaedic	2	1	1	1	2	Yes
Nieuwenhuijse 2014 (46)	High-flexion total knee arthroplasty	Invasive	Flexion	Orthopaedic	2	1	1	1	2	Yes
Nieuwenhuijse 2014 (46)	Gender-specific total knee arthroplasty	Invasive	Flexion-extension range	Orthopaedic	2	1	1	1	2	Yes
Nikooie 2019 (47)	Second generation antipsychotics	Drug	Sedation	Drug safety	2	2	1	2	2	Yes

Nikooie 2019 (47)	Second generation antipsychotics	Drug	Neurologic outcomes	Drug safety	2	2	1	2	2	Yes
Ochen 2019 (48)	Surgery for achilles tendon rupture	Invasive	Re-rupture	Orthopaedic	1	2	2	1	2	Yes
Ochen 2019 (48)	Surgery for achilles tendon rupture	Invasive	Complications	Orthopaedic	1	2	2	1	2	Yes
Pittas 2010 (49)	High vitamin D	Nutrition	Hypertension	Cardiovascular disease	2	3	3	1	3	Yes
Raman 2013 (50)	Carotid endarterectomy	Invasive	Ipsilateral stroke	Cardiovascular disease	2	1	2	1	2	Yes
Raman 2013 (50)	Carotid endarterectomy	Invasive	Stroke	Cardiovascular disease	2	1	2	1	2	Yes
Raman 2013 (50)	Carotid artery stenting	Invasive	Periprocedural stroke	Cardiovascular disease	2	2	2	1	2	Yes
Schweizer 2013 (51)	Nasal deconolization	Drug	Surgical site infection	Infectiological	2	2	1	1	2	Yes
Schweizer 2013 (51)	Glycopeptide prophylaxis	Drug	Surgical site infection	Infectiological	2	2	2	1	2	Yes
Silvain 2012 (52)	Enoxaparin	Drug	All-cause mortality	All-cause mortality	2	1	2	1	2	Yes
Silvain 2012 (52)	Enoxaparin	Drug	Major bleeding	Drug safety	2	1	2	1	2	Yes
Silvain 2012 (52)	Enoxaparin	Drug	All-cause mortality or myocardial infarction	Cardiovascular disease	2	1	2	1	2	Yes
Suthar 2012 (53)	Antiretroviral therapy	Drug	Tuberculosis infection	Infectiological	2	3	3	1	3	Yes
Te Morenga 2013 (54)	High sugar intake	Nutrition	Weight gain	Metabolic	2	1	2	1	2	Yes
Te Morenga 2013 (54)	High sugar intake	Nutrition	Body Mass Index	Metabolic	2	2	2	1	2	Yes
Thomas 2010 (55)	Influenza vaccines	Vaccine	Influenza-like illness	Infectiological	2	3	3	1	3	Yes
Tickell-Painter 2017 (56)	Mefloquine	Drug	Discontinuation due to adverse effects	Drug safety	2	1	1	1	2	Yes

Tickell-Painter 2017 (56)	Mefloquine	Drug	Serious adverse events or effects	Drug safety	3	1	1	2	3	Yes
Tickell-Painter 2017 (56)	Mefloquine	Drug	Nausea	Drug safety	3	1	1	1	3	Yes
Tricco 2018 (57)	Live-attenuated zoster vaccines	Vaccine	Suspected Herpes Zoster	Infectiological	2	2	2	1	2	Yes
Vinceti 2018 (58)	High selenium	Nutrition	Cancer	Oncological	2	3	3	2	3	Yes
Vinceti 2018 (58)	High selenium	Nutrition	Cancer mortality	Oncological	2	3	3	1	3	Yes
Vinceti 2018 (58)	High selenium	Nutrition	Colorectal cancer	Oncological	2	3	3	1	3	Yes
Wilson 2011 (59)	Training for traditional birth attendants/ assistance by traditional birth attendants	Birth assistance	Perinatal mortality	All-cause mortality	1	2	3	1	3	Yes
Wilson 2011 (59)	Training for traditional birth attendants/ assistance by traditional birth attendants	Birth assistance	Neonatal mortality	All-cause mortality	1	2	3	1	3	Yes
Wilson 2019 (60)	Unicompartmental knee arthroplasty	Invasive	Venous thrombo-embolism	Orthopaedic	2	1	1	1	2	Yes
Wilson 2019 (60)	Unicompartmental knee arthroplasty	Invasive	Flexion-extension range	Orthopaedic	2	1	1	1	2	Yes
Wilson 2019 (60)	Unicompartmental knee arthroplasty	Invasive	Operation duration	Orthopaedic	2	1	1	1	2	Yes
Yank 2011 (61)	Recombinant factor VII	Drug	All-cause mortality	All-cause mortality	2	2	1	1	2	Yes
Yank 2011 (61)	Recombinant factor VII	Drug	Thrombo-embolism	Drug safety	2	2	1	1	2	Yes
Zhang 2016 (62)	Everolimus-eluting bioresorbable vascular scaffold	Invasive	Stent thrombosis	Cardiovascular disease	2	1	1	1	2	Yes

Zhang 2016 (62)	Everolimus-eluting bioresorbable vascular scaffold	Invasive	All-cause mortality	All-cause mortality	2	1	1	1	2	Yes
Zhang 2016 (62)	Everolimus-eluting bioresorbable vascular scaffold	Invasive	Coronary heart disease mortality	Cardiovascular disease	2	1	1	1	2	Yes
Zhang 2017 (63)	Percutaneous coronary intervention	Invasive	All-cause mortality	All-cause mortality	2	2	1	1	2	Yes
Zhang 2017 (63)	Percutaneous coronary intervention	Invasive	Cardiovascular mortality	Cardiovascular disease	2	2	1	1	2	Yes
Zhang 2017 (63)	Percutaneous coronary intervention	Invasive	Myocardial infarction	Cardiovascular disease	2	2	1	1	2	Yes
Ziff 2015 (64)	Digoxin	Drug	All-cause mortality	All-cause mortality	3	1	1	1	3	Yes
Ziff 2015 (64)	Digoxin	Drug	Cardiovascular mortality	Cardiovascular disease	3	1	1	1	3	Yes
Ziff 2015 (64)	Digoxin	Drug	Hospital admission	Drug safety	2	1	1	1	2	Yes

DDP 4: Dipeptidylpeptidase-4; DHA and EPA: Docosahexaenoic acid and eicosapentaenoic acid; HIV: human immunodeficiency virus; NSTEMI-ACS: Non-ST-Segment Elevation Acute Coronary Syndromes; PI/ECO: population – intervention/exposure – comparator – outcome ; SGLT-2: Sodium dependent glucose transporter 2.

**Table S3:** Differences between published (reported) effect estimates and re-calculated effect estimates

Reference	Intervention / Exposure (as defined by the authors)	Outcome (as defined by the authors)	RCTs		Cohort Studies	
			Reported*	Recalculated (RE and inverse-variance model)	Reported*	Recalculated (RE and inverse-variance model)
			RR/HR/OR or MD (95% CI)	RR/HR/OR or MD (95% CI)	RR/HR/OR or MD (95% CI)	RR/HR/OR or MD (95% CI)
Aburto 2013 (2)	Low sodium	Cardiovascular disease	-	-	RR: 0.89 (0.75, 1.08)	RR: 0.90 (0.75, 1.08)
Ahmad 2015 (3)	Intra-aortic balloon pump	Mortality	-	-	-	OR: 1.02 (0.67, 1.56) <sup>1</sup>
Alipanah 2018 (5)	Self-administered therapy	Treatment success	-	RR: 0.95 (0.87, 1.03) <sup>1</sup>	RR: 0.81 (0.73, 0.89)	RR: 0.81 (0.74, 0.88)
Alipanah 2018 (5)	Self-administered therapy	Treatment completion	RR: 0.79 (0.56, 1.11)	RR: 0.79 (0.57, 1.09)	RR: 1.10 (0.90, 1.35)	RR: 1.10 (0.91, 1.33)
Alipanah 2018 (5)	Self-administered therapy	Mortality	-	-	RR: 1.35 (1.00, 1.84)	RR: 1.35 (1.00, 1.83)
Anglemyer 2013 (6)	Antiretroviral therapy	HIV Infection	RR: 0.11 (0.04, 0.32)	RR: 0.11 (0.04, 0.30)	RR: 0.58 (0.35, 0.96)	RR: 0.59 (0.36, 0.97)
Barnard 2015 (8)	Surgical abortion by mid-level providers	Failure or incomplete abortion	RR: 2.97 (0.21, 41.82)	RR: 2.84 (0.24, 32.97)	-	RR: 2.47 (1.44, 4.23) <sup>1</sup>
Barnard 2015 (8)	Surgical abortion by mid-level providers	Complications	RR: 0.99 (0.17, 5.7)	RR: 0.94 (0.14, 6.44)	-	RR: 1.30 (0.57, 2.96) <sup>1</sup>
Barnard 2015 (8)	Surgical abortion by mid-level providers	Abortion failure and complications	RR: 3.07 (0.16, 59.08)	RR: 2.93 (0.19, 44.15)	-	RR: 1.33 (0.78, 2.27) <sup>1</sup>
Bellemain-Appaix 2012 (9)	Clopidogrel pretreatment for percutaneous coronary intervention	All-cause mortality	OR: 0.80 (0.57, 1.11)	OR: 0.80 (0.58, 1.10)	-	OR: 0.79 (0.53, 1.18) <sup>2</sup>
Bellemain-Appaix 2012 (9)	Clopidogrel pretreatment for percutaneous coronary intervention	Major bleeding	-	-	-	OR: 1.03 (0.69, 1.53) <sup>2</sup>

Bellemain-Appaix 2012 (9)	Clopidogrel pretreatment for percutaneous coronary intervention	Coronary heart disease	-	-	-	OR: 0.76 (0.60, 0.95) <sup>2</sup>
Bellemain-Appaix 2014 (10)	P2Y12 inhibitor pretreatment in non-ST elevation acute coronary syndrome	All-cause mortality	OR: 0.92 (0.43, 1.98)	OR: 0.90 (0.71, 1.14)	-	OR: 0.69 (0.35, 1.32) <sup>2</sup>
Bellemain-Appaix 2014 (10)	P2Y12 inhibitor pretreatment in non-ST elevation acute coronary syndrome	Major bleeding	OR: 1.45 (0.97, 2.15)	OR: 1.43 (1.16, 1.76)	-	OR: 1.13 (0.92, 1.39) <sup>2</sup>
Bellemain-Appaix 2014 (10)	P2Y12 inhibitor pretreatment in non-ST elevation acute coronary syndrome	Main composite ischemic endpoint	OR: 0.85 (0.67, 1.07)	OR: 0.87 (0.73, 1.04)	-	OR: 0.78 (0.56, 1.08)
Bolland 2015 (12)	High-calcium	All fractures	RR: 0.90 (0.83, 0.96)	RR: 0.90 (0.83, 0.97)	-	RR: 1.02 (0.93, 1.12)
Bolland 2015 (12)	High-calcium	Vertebral fracture	-	-	RR: 1.40 (1.10, 1.90)	RR: 1.40 (1.10, 1.78)
Bolland 2015 (12)	High-calcium	Hip fracture	-	-	-	RR: 1.09 (0.91, 1.30) <sup>3</sup>
Brenner 2014 (13)	Sigmoidoscopy	Colorectal cancer mortality	-	-	RR: 0.59 (0.45, 0.76)	RR: 0.59 (0.45, 0.77)
Brenner 2014 (13)	Sigmoidoscopy	Colorectal cancer incidence	RR: 0.82 (0.75, 0.89)	RR: 0.82 (0.75, 0.90)	-	RR: 0.50 (0.37, 0.67) <sup>1</sup>
Chowdhury 2012 (14)	High omega-3	Cerebrovascular disease	RR: 0.98 (0.89, 1.08)	RR: 0.99 (0.90, 1.08)	RR: 0.90 (0.80, 1.01)	RR: 0.89 (0.89, 0.99)
Chowdhury 2014a (15)	High $\alpha$ -linolenic acid	Coronary heart disease	-	-	RR: 0.99 (0.86, 1.14)	RR: 0.99 (0.87, 1.13)
Chung 2016 (18)	High calcium	Cardiovascular mortality	-	RR: 1.05 (0.82, 1.33) <sup>3</sup>	-	RR: 0.97 (0.86, 1.09)



Fenton 2018 (20)	Radiation therapy	Erectile dysfunction	-	-	-	RR: 1.30 (1.19, 1.43) <sup>1</sup>
Fenton 2018 (20)	Radical Prostatectomy	Urinary incontinence	RR: 2.27 (1.82, 2.84)	RR: 2.25 (1.80, 2.82)	-	RR: 2.91 (1.80, 4.71) <sup>1</sup>
Fenton 2018 (20)	Radical Prostatectomy	Erectile dysfunction	RR: 1.60 (1.23, 2.07)	RR: 1.60 (1.24, 2.07)	-	RR: 1.49 (1.33, 1.66) <sup>1</sup>
Filippini 2017 (21)	Disease-modifying drugs	Conversion to clinically definite multiple sclerosis	-	HR: 0.52 (0.46, 0.60) <sup>4</sup>	-	HR: 0.48 (0.30, 0.78) <sup>4</sup>
Fluri 2010 (22)	Extracranial-intracranial arterial bypass	Mortality	-	-	-	OR: 0.97 (0.58, 1.62) <sup>1,7</sup>
Fluri 2010 (22)	Extracranial-intracranial arterial bypass	Any stroke	-	OR: 0.44 (0.06, 3.24) <sup>7</sup>	-	OR: 0.76 (0.49, 1.17) <sup>1,7</sup>
Fluri 2010 (22)	Extracranial-intracranial arterial bypass	Death or dependency	-	-	OR: 0.80 (0.50, 1.29) <sup>7</sup>	OR: 0.81 (0.50, 1.31) <sup>7</sup>
Gargiulo 2016 (23)	Transcatheter aortic valve implantation	Early mortality	OR: 0.80 (0.51, 1.25)	OR: 0.80 (0.58, 1.11)	-	OR: 1.08 (0.84, 1.39) <sup>1</sup>
Gargiulo 2016 (23)	Transcatheter aortic valve implantation	Mid-term mortality	OR: 0.90 (0.64, 1.26)	OR: 0.90 (0.71, 1.13)	-	-
Gargiulo 2016 (23)	Transcatheter aortic valve implantation	Long-term mortality	OR: 1.03 (0.65, 1.62)	OR: 1.03 (0.77, 1.37)	OR: 1.70 (1.23, 2.35)	OR: 1.70 (1.31, 2.20)
Hartling 2013 (24)	Treating Gestational Diabetes Mellitus	Birth weight > 4000g	-	-	-	RR: 0.69 (0.31, 1.54) <sup>3</sup>
Hartling 2013 (24)	Treating Gestational Diabetes Mellitus	Shoulder dystocia	-	-	RR: 0.38 (0.19, 0.78)	RR: 0.38 (0.18, 0.80)
Henderson 2019 (25)	Treating asymptomatic bacteriuria	Pyelonephritis	-	-	-	RR: 0.29 (0.15, 0.57) <sup>3</sup>
Higgins 2016 (26)	Bacillus Calmette-Guérin vaccination	Mortality	-	RR: 0.67 (0.40, 1.14) <sup>1</sup>	-	-
Higgins 2016 (26)	Measles containing vaccines	Mortality	-	-	-	RR: 0.53 (0.40, 0.70) <sup>1</sup>
Hopley 2010 (27)	Total hip arthroplasty	Reoperation	-	-	-	RR: 0.45 (0.19, 1.08) <sup>1</sup>

Hopley 2010 (27)	Total hip arthroplasty	Dislocation	-	-	-	RR: 0.79 (0.27, 2.35) <sup>1</sup>
Jamal 2013 (29)	Non-calcium-based phosphate binders	Mortality	RR: 0.78 (0.61, 0.98)	RR: 0.78 (0.62, 0.98)	-	-
Jefferson 2010 (30)	Parenteral influenza vaccine	Influenza-like illness	-	-	-	RR: 0.76 (0.66, 0.87) <sup>3</sup>
Jefferson 2010 (30)	Parenteral influenza vaccine	Influenza	-	-	-	RR: 0.51 (0.27, 0.97) <sup>3</sup>
Jefferson 2012 (31)	Inactivated influenza vaccines	Influenza	-	-	-	RR: 0.20 (0.10, 0.39) <sup>1</sup>
Jefferson 2012 (31)	Inactivated influenza vaccines	Influenza-like illness	-	-	-	RR: 0.29 (0.07, 1.15) <sup>1</sup>
Kansagara 2013 (34)	Transfusion	Mortality	RR: 0.94 (0.61, 1.42)	RR: 0.94 (0.62, 1.43)	-	RR: 2.49 (1.40, 4.43) <sup>1</sup>
Keag 2018 (35)	Caesarean section	Urinary incontinence	-	-	OR: 0.56 (0.47, 0.66)	OR: 0.56 (0.48, 0.66)
Keag 2018 (35)	Caesarean section	Fecal incontinence	OR: 3.07 (0.90, 10.49)	OR: 3.07 (0.90, 10.47)	-	-
Li 2014 (37)	Exenatide	Acute pancreatitis/ Admission for acute pancreatitis	RR: 0.86 (0.22, 3.37)	RR: 0.86 (0.22, 3.39)	-	RR: 0.92 (0.69, 1.22) <sup>3</sup>
Li 2016 (38)	DDP-4 Inhibitors	Heart failure	RR: 0.90 (0.61, 1.35)	RR: 0.95 (0.60, 1.50)	-	RR: 1.10 (1.04, 1.17) <sup>3</sup>
Matthews 2018 (39)	Tamoxifen	Heart failure	RR: 0.52 (0.33, 0.71)	RR: 0.52 (0.33, 0.79)	RR: 0.84 (0.65, 1.07)	RR: 0.85 (0.66, 1.09)
Menne 2019 (40)	SGLT-2 inhibitors	Acute kidney injury	-	-	OR: 0.40 (0.33, 0.48)	OR: 0.40 (0.31, 0.52)
Mesgarpour 2017 (41)	Erythropoiesis stimulating agents	Venous thromboembolism	-	-	RR: 1.87 (0.59, 5.92)	RR: 1.92 (0.64, 5.76)
Mesgarpour 2017 (41)	Erythropoiesis stimulating agents	Mortality	RR: 0.81 (0.71, 0.93)	RR: 0.82 (0.71, 0.93)	RR: 1.07 (0.65, 1.77)	RR: 1.08 (0.66, 1.78)
Molnar 2015 (43)	Neoral (cyclosporine)	Acute rejection of kidney transplant	OR: 1.23 (0.64, 2.36)	OR: 1.25 (0.61, 2.56)	-	OR: 0.46 (0.25, 0.86) <sup>1</sup>

Navarese 2013 (44)	Early intervention for NSTEMI-ACS	Myocardial infarction	OR: 1.15 (0.65, 2.01)	OR: 1.16 (0.67, 2.00)	-	-
Nelson 2010 (45)	Caesarean section	Anal incontinence, feces	-	-	-	OR: 0.91 (0.72, 1.16) <sup>1</sup>
Nelson 2010 (45)	Caesarean section	Anal incontinence, flatus	-	-	-	OR: 1.02 (0.87, 1.20) <sup>1</sup>
Nieuwenhuijse 2014 (46)	Ceramic-on-ceramic bearings for total hip arthroplasty	Harris Hip Score	-	MD: -0.23 (-1.09, 0.63) <sup>4</sup>	-	MD: -0.50 (-2.09, 1.09) <sup>1,4</sup>
Nieuwenhuijse 2014 (46)	High-flexion total knee arthroplasty	Flexion (degrees)	-	MD: 1.68 (0.28, 3.08) <sup>4</sup>	-	MD: 3.78 (1.64, 5.92) <sup>1,4</sup>
Nieuwenhuijse 2014 (46)	Gender-specific total knee arthroplasty	Flexion-extension range (degrees)	-	MD: 1.40 (-0.18, 2.99) <sup>1,4</sup>	-	MD: 3.15 (-0.03, 6.34) <sup>1,4</sup>
Nikooie 2019 (47)	Second generation antipsychotics	Sedation	-	-	-	RR: 1.84 (0.40, 8.54) <sup>3</sup>
Nikooie 2019 (47)	Second generation antipsychotics	Neurologic outcomes	-	-	-	RR: 0.76 (0.59, 0.99) <sup>3</sup>
Ochen 2019 (48)	Surgery for achilles tendon rupture	Re-rupture	-	-	RR: 0.42 (0.28, 0.64)	RR: 0.42 (0.28, 0.65)
Ochen 2019 (48)	Surgery for achilles tendon rupture	Complications	RR: 3.26 (1.26, 8.41)	RR: 3.13 (1.33, 7.38)	-	-
Raman 2013 (50)	Carotid endarterectomy	Ipsilateral stroke	-	-	-	RR: 0.47 (0.05, 4.46) <sup>1</sup>
Raman 2013 (50)	Carotid endarterectomy	Any stroke	-	-	-	RR: 0.73 (0.43, 1.22) <sup>1</sup>
Raman 2013 (50)	Carotid artery stenting	Periprocedural stroke	-	RR: 1.75 (0.87, 3.52) <sup>3</sup>	-	RR: 1.91 (1.72, 2.11) <sup>1</sup>
Schweizer 2013 (51)	Nasal deconolization	Surgical site infection	RR: 0.63 (0.63, 1.13)	RR: 0.63 (0.36, 1.12)	-	RR: 0.40 (0.28, 0.57) <sup>1</sup>
Schweizer 2013 (51)	Glycopeptide prophylaxis	Surgical site infection	-	-	RR: 0.34 (0.11, 1.10)	RR: 0.35 (0.12, 1.03)
Silvain 2012 (52)	Enoxaparin	Mortality	-	RR: 0.88 (0.70, 1.10) <sup>4</sup>	-	RR: 0.50 (0.40, 0.62) <sup>1,4</sup>

Silvain 2012 (52)	Enoxaparin	Major bleeding	-	RR: 0.88 (0.62, 1.24) <sup>4</sup>		RR: 0.72 (0.56, 0.93) <sup>1,4</sup>
Silvain 2012 (52)	Enoxaparin	Death or Myocardial infarction	-	RR: 0.86 (0.74, 0.99) <sup>4</sup>		RR: 0.44 (0.35, 0.55) <sup>1,4</sup>
Suthar 2012 (53)	Antiretroviral therapy	Tuberculosis infection	-	HR: 0.50 (0.34, 0.75) <sup>1</sup>	-	-
Te Morenga 2013 (54)	High sugar intake	Weight gain (kg)	MD: 0.75 (0.30, 1.19)	MD: 0.74 (0.30, 1.19)	-	-
Te Morenga 2013 (54)	High sugar intake	Body Mass Index (kg/m <sup>2</sup> )	-	MD: -0.06 (-0.15, 0.04) <sup>1</sup>	-	-
Tickell-Painter 2017 (56)	Mefloquine	Discontinuation due to adverse effects	-	-	RR: 2.73 (1.83, 4.08)	RR: 2.73 (1.84, 4.06)
Tickell-Painter 2017 (56)	Mefloquine	Serious adverse events or effects	RR: 0.70 (0.14, 3.53)	RR: 0.68 (0.11, 4.27)	RR: 3.08 (0.39, 24.11)	RR: 3.09 (0.38, 24.95)
Tickell-Painter 2017 (56)	Mefloquine	Nausea	RR: 1.35 (1.05, 1.73)	RR: 1.34 (1.04, 1.71)	RR: 1.85 (1.42, 2.43)	RR: 1.86 (1.42, 2.42)
Tricco 2018 (57)	Live-attenuated zoster vaccines	Suspected Herpes Zoster	RR: 0.61 (0.48, 0.93)	RR: 0.60 (0.54, 0.66)	RR: 0.48 (0.27, 0.84)	RR: 0.48 (0.27, 0.83) <sup>5</sup>
Wilson 2011 (59)	Training for traditional birth attendants/ assistance by traditional birth attendants	Perinatal mortality	RR: 0.76 (0.64, 0.88)	RR: 0.77 (0.66, 0.89)	-	RR: 0.82 (0.38, 1.78) <sup>1</sup>
Wilson 2011 (59)	Training for traditional birth attendants/ assistance by traditional birth attendants	Neonatal mortality	RR: 0.79 (0.69, 0.88)	RR: 0.80 (0.71, 0.90)	-	RR: 0.80 (0.47, 1.37) <sup>1</sup>
Wilson 2019 (60)	Unilateral knee arthroplasty	Venous thromboembolism	-	-	-	RR: 0.42 (0.30, 0.57) <sup>1</sup>
Wilson 2019 (60)	Unilateral knee arthroplasty	Range of movement (degrees)	-	-	-	MD: -8.43 (-10.15, -6.71) <sup>1</sup>
Wilson 2019 (60)	Unilateral knee arthroplasty	Operation duration (minutes)	-	-	-	MD: -23.80 (-40.43, -1.17) <sup>1</sup>

Yank 2011 (61)	Recombinant factor VII	Mortality	-	RR: 1.40 (0.49, 4.02) <sup>4,6</sup>	-	RR: 0.91 (0.39, 2.12) <sup>4,6</sup>
Yank 2011 (61)	Recombinant factor VII	Thromboembolic events	-	RR: 2.04 (0.51, 8.84) <sup>4,6</sup>	-	RR: 1.81 (0.67, 4.87) <sup>4,6</sup>
Zhang 2016 (62)	Everolimus-eluting bioresorbable vascular scaffold	Stent thrombosis	OR: 2.05 (0.95, 4.43) <sup>7</sup>	OR: 1.97 (0.90, 4.29)	OR: 2.32 (1.06, 5.07) <sup>7</sup>	OR: 2.22 (1.00, 4.93)
Zhang 2016 (62)	Everolimus-eluting bioresorbable vascular scaffold	Mortality	OR: 0.96 (0.46, 2.00) <sup>7</sup>	OR: 0.71 (0.17, 3.01)	OR: 0.57 (0.23, 1.44) <sup>7</sup>	OR: 0.63 (0.24, 1.63)
Zhang 2016 (62)	Everolimus-eluting bioresorbable vascular scaffold	Cardiac death	OR: 1.40 (0.45, 4.33) <sup>7</sup>	OR: 1.39 (0.17, 11.14)	OR: 0.81 (0.38, 1.70) <sup>7</sup>	OR: 0.94 (0.43, 2.06)
Zhang 2017 (63)	Percutaneous coronary intervention	Mortality	-	-	HR: 1.08 (0.92, 1.26)	HR: 1.07 (0.92, 1.26)
Zhang 2017 (63)	Percutaneous coronary intervention	Cardiovascular mortality	HR: 1.00 (0.72, 1.39)	HR: 0.99 (0.71, 1.39)	HR: 1.08 (0.51, 2.29)	HR: 1.08 (0.51, 2.28)
Zhang 2017 (63)	Percutaneous coronary intervention	Myocardial infarction	HR: 1.39 (0.85, 2.27)	HR: 1.39 (0.86, 2.26)	HR: 2.01 (1.64, 2.45)	HR: 2.00 (1.65, 2.44)
Ziff 2015 (64)	Digoxin	Mortality	-	-	RR: 1.61 (1.31, 1.97)	RR: 1.60 (1.31, 1.96)
Ziff 2015 (64)	Digoxin	Cardiovascular mortality	RR: 1.01 (0.94, 1.08)	RR: 1.01 (0.94, 1.09)	RR: 2.53 (1.12, 5.71)	RR: 2.53 (1.12, 5.70)
Ziff 2015 (64)	Digoxin	Hospital admission	RR: 0.94 (0.90, 0.99)	RR: 0.96 (0.87, 1.05)	RR: 0.91 (0.87, 0.95)	RR: 0.92 (0.85, 0.99)

CI: confidence interval; DDP 4: Dipeptidylpeptidase-4; HIV: human immunodeficiency virus; HR: hazard ratio; MD: mean difference; NSTE-ACS: Non-ST-Segment Elevation Acute Coronary Syndromes; OR: odds ratio; RCT: randomized controlled trial; RE: random effects; RR: risk ratio; SGLT-2: Sodium dependent glucose transporter 2. \*some estimates were converted (detailed description is reported elsewhere (65)).

<sup>1</sup> Only re-calculated data is shown since we excluded some primary studies from the original estimate due to inappropriate study design.

<sup>2</sup> Pooled estimate includes observational analysis of randomized controlled trials.

<sup>3</sup> Primary studies were not pooled in the original paper.

<sup>4</sup> In the original paper cohort studies and randomized controlled trials were pooled together (sometimes without a subgroup).

<sup>5</sup> Re-analysis with unpublished data.

<sup>6</sup> Data converted (risk difference to risk ratio).

<sup>7</sup> In the original paper common effects were reported, we calculated estimates with random effects model.

**Table S4:** Reason for exclusion from the pooling scenario

<b>Systematic Review</b>	<b>Intervention/Exposure</b>	<b>Outcome</b>	<b>Reason for exclusion</b>
Abou-Setta 2011 (1)	Nerve block	Delirium (OR)	Forest plots not available
Abou-Setta 2011 (1)	Spinal anaesthesia	Mortality (OR)	Forest plots not available
Alexander 2017 (4)	High docosahexaenoic acid and eicosapentaenoic acid	Any coronary heart disease event (RR)	Forest plots not available
Alexander 2017 (4)	High docosahexaenoic acid and eicosapentaenoic acid	Fatal coronary heart disease events (RR)	Forest plots not available
Alexander 2017 (4)	High docosahexaenoic acid and eicosapentaenoic acid	Non-fatal coronary heart disease events (RR)	Forest plots not available
Chowdhury 2014b (16)	High vitamin D	Mortality (RR)	Forest plot not available for RCTs
Chung 2011 (17)	High vitamin D	Colorectal cancer (RR)	Forest plots not available
Chung 2011 (17)	High vitamin D	Breast cancer (RR)	Forest plots not available
Johnston 2019 (33)	Low red meat	Mortality (HR)	Forest plot not available for cohort studies
Johnston 2019 (33)	Low red meat	Cardiovascular mortality (HR)	Forest plot not available for cohort studies
Johnston 2019 (33)	Low red meat	Cardiovascular disease (HR)	Forest plot not available for cohort studies

HR: Hazard ratio; OR: Odds ratio; RCT: randomized controlled trial; RR: Risk ratio;

**Table S5:** Pooling results of bodies of evidence from cohort studies with RCTs based on random effects and common effect model, 95% prediction intervals, heterogeneity, test for subgroup difference, and Population (P), Intervention (I) /Exposure (E), Comparator (C) Outcome similarity degree.

Author, year, and reference	Intervention/ Exposure	Outcome	BoE CSs, n	Effect estimate (95% CI)	I <sup>2</sup> (%)/ tau <sup>2</sup>	Pooled effect estimate (95%) RE (95% prediction interval)	I <sup>2</sup> (%)/ tau <sup>2</sup>	Weight CS (%)	CS conclusion modified	Pooled effect estimate (95%) CE	Degree of PI/ECO similarity*
Aburto 2013 (2)	Low sodium	Mortality	7	RR: 0.94 (0.83, 1.06)	61/ 0.02	RR: 0.93 (0.83, 1.04) (0.68, 1.26)	47/ 0.02	95.0	No	RR: 0.94 (0.88, 1.00)	2
Aburto 2013 (2)	Low sodium	Cardiovascular disease	9	RR: 0.90 (0.75, 1.08)	78/ 0.07	RR: 0.89 (0.75, 1.06) (0.49, 1.62)	74/ 0.07	91.3	No	RR: 0.86 (0.80, 0.93)	2
Ahmad 2015 (3)	Intra-aortic balloon pump	Mortality	14	OR: 1.02 (0.57, 1.82)	97/ 1.03	OR: 1.02 (0.67, 1.56) (0.14, 7.32)	95/ 0.86	62.2	No	OR: 0.76 (0.72, 0.82)	1
Alipanah 2018 (5)	Self-administered therapy	Treatment success	16	RR: 0.81 (0.74, 0.88)	91/ 0.02	RR: 0.84 (0.78, 0.90) (0.62, 1.14)	89/ 0.02	80.9	No	RR: 0.92 (0.90, 0.94)	3
Alipanah 2018 (5)	Self-administered therapy	Treatment completion	14	RR: 1.10 (0.91, 1.33)	86/ 0.07	RR: 1.02 (0.84, 1.23) (0.51, 2.02)	88/0.10	75.6	No	RR: 1.12 (1.07, 1.17)	3
Alipanah 2018 (5)	Self-administered therapy	Mortality	23	RR: 1.35 (1.00, 1.83)	90/ 0.34	RR: 1.26 (0.95, 1.67) (0.37, 4.28)	88/ 0.33	90.2	No	RR: 1.26 (1.18, 1.34)	3
Anglemyer 2013 (6)	Antiretroviral therapy	HIV infection	9	RR: 0.59 (0.36, 0.97)	63/ 0.25	RR: 0.45 (0.26, 0.78) (0.09, 2.31)	75/ 0.42	88.2	No	RR: 0.72 (0.64, 0.82)	3
Azad 2017 (7)	Non-nutritive sweeteners	BMI	1	MD: 0.77 (0.47, 1.07)	NA	MD: 0.23 (-0.77, 1.23) (-3.88, 4.34)	79/ 0.65	38.6	Yes	MD: 0.53 (0.26, 0.80)	2
Barnard 2015 (8)	Surgical abortion by mid-level providers	Failure or incomplete abortion	2	RR: 2.47 (1.44, 4.23)	0/ 0.00	RR: 2.23 (1.15, 4.32) (0.24, 20.54)	33/ 0.15	65.5	No	RR: 2.14 (1.35, 3.39)	2
Barnard 2015 (8)	Surgical abortion by mid-level providers	Complications	2	RR: 1.30 (0.57, 2.96)	70/ 0.26	RR: 1.31 (0.70, 2.42) (0.17, 10.11)	32/ 0.13	90.3	No	RR: 1.51 (1.05, 2.17)	2

Barnard 2015 (8)	Surgical abortion by mid-level providers	Abortion failure and complications	3	RR: 1.33 (0.78, 2.27)	74/ 0.16	RR: 1.36 (0.83, 2.21) (0.29, 6.32)	65/ 0.17	80.5	No	RR: 1.43 (1.12, 1.82)	2
Bellemain-Appaix 2012 (9)	Clopidogrel pretreatment for percutaneous coronary intervention	Mortality	8	OR: 0.79 (0.53, 1.18)	79/ 0.23	OR: 0.77 (0.57, 1.04) (0.30, 2.02)	66/ 0.17	69.3	No	OR: 0.65 (0.57, 0.75)	2
Bellemain-Appaix 2012 (9)	Clopidogrel pretreatment for percutaneous coronary intervention	Major bleeding	8	OR: 1.03 (0.69, 1.53)	64/ 0.16	OR: 1.04 (0.81, 1.33) (0.54, 2.03)	46/ 0.08	59.6	No	OR: 1.07 (0.92, 1.24)	2
Bellemain-Appaix 2012 (9)	Clopidogrel pretreatment for percutaneous coronary intervention	Major coronary event	8	OR: 0.76 (0.60, 0.95)	82/ 0.08	OR: 0.76 (0.65, 0.89) (0.45, 1.29)	69/ 0.05	64.0	No	OR: 0.78 (0.73, 0.85)	2
Bellemain-Appaix 2014 (10)	P2Y12 inhibitor pretreatment in non-ST elevation acute coronary syndrome	Mortality	4	OR: 0.69 (0.35, 1.32)	35/ 0.17	OR: 0.90 (0.75, 1.07) (0.65, 1.24)	10/ 0.01	33.2	No	OR: 0.91 (0.80, 1.04)	2
Bellemain-Appaix 2014 (10)	P2Y12 inhibitor pretreatment in non-ST elevation acute coronary syndrome	Major bleeding	4	OR: 1.13 (0.92, 1.39)	0/ 0.00	OR: 1.27 (1.10, 1.47) (1.05, 1.54)	0/ 0.00	50.3	No	OR: 1.27 (1.10, 1.47)	2
Bellemain-Appaix 2014 (10)	P2Y12 inhibitor pretreatment in non-ST elevation acute coronary syndrome	Main composite ischemic endpoint	4	OR: 0.78 (0.56, 1.08)	65/ 0.07	OR: 0.84 (0.72, 0.98) (0.56, 1.26)	52/ 0.02	45.0	Yes	OR: 0.85 (0.78, 0.93)	2
Bloomfield 2016 (11)	Mediterranean diet	Breast cancer	13	RR: 0.96 (0.90, 1.03)	52/ 0.01	RR: 0.95 (0.89, 1.02) (0.78, 1.17)	57/ 0.01	99.1	No	RR: 0.98 (0.95, 1.02)	2
Bolland 2015 (12)	High calcium	All fractures	5	RR: 1.02 (0.93, 1.12)	68/ 0.01	RR: 0.94 (0.88, 1.00) (0.78, 1.14)	50/ 0.01	42.0	No	RR: 0.99 (0.96, 1.02)	2
Bolland 2015 (12)	High calcium	Vertebral fracture	1	RR: 1.40 (1.10, 1.78)	NA	RR: 0.94 (0.79, 1.11) (0.65, 1.34)	22/ 0.02	23.3	Yes	RR: 0.98 (0.87, 1.11)	2
Bolland 2015 (12)	High calcium	Hip fracture	6	RR: 1.09 (0.91, 1.30)	50/ 0.03	RR: 1.02 (0.89, 1.18) (0.67, 1.56)	46/ 0.04	57.2	No	RR: 0.98 (0.91, 1.07)	2



Brenner 2014 (13)	Sigmoidoscopy, screening for CRC	Colorectal cancer mortality	1	RR: 0.59 (0.45, 0.77)	NA	RR: 0.70 (0.64, 0.77) (0.60, 0.82)	0/ 0.00	12.7	No	RR: 0.70 (0.64, 0.77)	1
Brenner 2014 (13)	Sigmoidoscopy, screening for CRC	Colorectal cancer incidence	2	RR: 0.50 (0.37, 0.69)	0/ 0.00	RR: 0.78 (0.69, 0.89) (0.55, 1.11)	65/ 0.01	11.0	No	RR: 0.79 (0.74, 0.84)	2
Chowdhury 2012 (14)	High omega-3-fatty acids	Cerebrovascular disease	10	RR: 0.89 (0.80, 0.99)	17/ 0.01	RR: 0.93 (0.85, 1.01) (0.78, 1.10)	21/ 0.00	59.3	Yes	RR: 0.95 (0.89, 1.01)	2
Chowdhury 2014a (15)	High $\alpha$ -linolenic acid	Coronary event	7	RR: 0.99 (0.88, 1.11)	61/ 0.02	RR: 0.99 (0.88, 1.11) (0.72, 1.37)	54/ 0.02	78.6	No	RR: 1.01 (0.95, 1.08)	3
Chowdhury 2014a (15)	High omega-3-fatty acids	Coronary event	16	RR: 0.87 (0.78, 0.97)	76/ 0.03	RR: 0.90 (0.83, 0.97) (0.66, 1.22)	61/ 0.02	61.9	No	RR: 0.93 (0.89, 0.97)	3
Chowdhury 2014a (15)	High omega-6-fatty acids	Coronary event	8	RR: 0.98 (0.90, 1.06)	54/ 0.01	RR: 0.94 (0.87, 1.03) (0.73, 1.21)	56/0.01	70.0	No	RR: 0.96 (0.94, 1.01)	3
Chung 2016 (18)	High calcium	Cardiovascular disease mortality	6	RR: 0.97 (0.86, 1.09)	37/ 0.01	RR: 0.99 (0.92, 1.07) (0.86, 1.15)	11/ 0.00	89.9	No	RR: 1.01 (0.95, 1.07)	2
Ding 2017 (19)	High dairy	Systolic blood pressure	27	MD: -0.11 (-0.20, -0.02)	30/ 0.01	MD: -0.11 (-0.20, -0.03) (-0.34, 0.11)	24/ 0.01	98.8	No	MD: -0.16 (-0.21, -0.11)	2
Fenton 2018 (20)	Radiation therapy	Erectile dysfunction	7	RR: 1.30 (1.19, 1.43)	31/ 0.00	RR: 1.24 (1.09, 1.41) (0.83, 1.86)	70/ 0.02	85.7	No	RR: 1.23 (1.15, 1.32)	2
Fenton 2018 (20)	Radical Prostatectomy	Urinary incontinence	5	RR: 2.91 (1.80, 4.71)	67/ 0.18	RR: 2.54 (1.97, 3.27) (1.28, 5.03)	51/ 0.06	52.1	No	RR: 2.46 (2.08, 2.90)	2
Fenton 2018 (20)	Radical Prostatectomy	Erectile dysfunction	6	RR: 1.49 (1.33, 1.66)	63/ 0.01	RR: 1.53 (1.37, 1.70) (1.07, 2.18)	75/ 0.02	65.1	No	RR: 1.50 (1.42, 1.58)	2
Filippini 2017 (21)	Disease-modifying drugs	Conversion to clinically definite multiple sclerosis	2	HR: 0.48 (0.30, 0.78)	62/ 0.08	HR: 0.53 (0.47, 0.59) (0.46, 0.61)	0/ 0.00	70.0	No	HR: 0.53 (0.47, 0.59)	2
Fluri 2010 (22)	Extracranial-intracranial arterial bypass	Mortality	11	OR: 0.97 (0.58, 1.62)	0/ 0.00	OR: 0.84 (0.66, 1.06) (0.64, 1.09)	0/ 0.00	20.3	No	OR: 0.84 (0.66, 1.06)	2

Fluri 2010 (22)	Extracranial-intracranial arterial bypass	Any stroke	15	OR: 0.76 (0.49, 1.17)	2/ 0.02	OR: 0.77 (0.50, 1.17) (0.29, 2.05)	29/ 0.17	67.5	No	OR: 0.95 (0.78, 1.16)	2
Fluri 2010 (22)	Extracranial-intracranial arterial bypass	Death or dependency	8	OR: 0.81 (0.50, 1.31)	0/ 0.00	OR: 0.91 (0.73, 1.14) (0.70, 1.19)	0/ 0.00	20.6	No	OR: 0.91 (0.73, 1.14)	2
Gargiulo 2016 (23)	Transcatheter aortic valve implantation	Early mortality	29	OR: 1.08 (0.84, 1.39)	41/ 0.16	OR: 1.01 (0.81, 1.26) (0.47, 2.20)	39/ 0.13	81.6	No	OR: 1.02 (0.88, 1.19)	2
Gargiulo 2016 (23)	Transcatheter aortic valve implantation	Mid-term mortality	18	OR: 1.00 (0.81, 1.24)	46/ 0.08	OR: 0.96 (0.82, 1.13) (0.59, 1.58)	40/ 0.05	71.0	No	OR: 0.93 (0.83, 1.04)	2
Gargiulo 2016 (23)	Transcatheter aortic valve implantation	Long-term mortality	6	OR: 1.70 (1.31, 2.20)	0/ 0.00	OR: 1.28 (1.00, 1.65) (0.62, 2.66)	62/ 0.08	46.7	Yes	OR: 1.18 (1.03, 1.35)	2
Hartling 2013 (24)	Treating Gestational Diabetes Mellitus	Birth weight > 4000g	6	RR: 0.69 (0.31, 1.54)	88/ 0.64	RR: 0.58 (0.40, 0.86) (0.17, 2.01)	79/ 0.25	48.3	Yes	RR: 0.54 (0.46, 0.63)	2
Hartling 2013 (24)	Treating Gestational Diabetes Mellitus	Large-for-gestational age neonate	4	RR: 0.43 (0.27, 0.70)	58/ 0.13	RR: 0.47 (0.36, 0.62) (0.22, 1.02)	60/ 0.07	49.8	No	RR: 0.45 (0.39, 0.52)	2
Hartling 2013 (24)	Treating Gestational Diabetes Mellitus	Shoulder dystocia	4	RR: 0.38 (0.19, 0.75)	16/ 0.09	RR: 0.39 (0.26, 0.60) (0.23, 0.68)	0/ 0.00	50.1	No	RR: 0.39 (0.26, 0.60)	2
Henderson 2019 (25)	Treating asymptomatic bacteriuria	Pyelonephritis	2	RR: 0.29 (0.15, 0.57)	0/ 0.00	RR: 0.25 (0.16, 0.39) (0.07, 0.87)	48/ 0.28	15.1	No	RR: 0.30 (0.23, 0.40)	3
Higgins 2016 (26)	BCG	Mortality	8	RR: 0.46 (0.30, 0.69)	63/ 0.19	RR: 0.51 (0.36, 0.72) (0.18, 1.46)	67/ 0.19	70.1	No	RR: 0.57 (0.48, 0.68)	3
Higgins 2016 (26)	Measles containing vaccines	Mortality	13	RR: 0.53 (0.40, 0.70)	67/ 0.14	RR: 0.57 (0.45, 0.72) (0.27, 1.21)	58/ 0.11	80.4	No	RR: 0.65 (0.57, 0.74)	3
Hopley 2010 (27)	Total hip arthroplasty	Reoperation	6	RR: 0.45 (0.19, 1.08)	23/ 0.28	RR: 0.66 (0.33, 1.32) (0.13, 3.42)	34/ 0.39	56.1	No	RR: 0.72 (0.43, 1.20)	2
Hopley 2010 (27)	Total hip arthroplasty	Dislocation	5	RR: 0.79 (0.27, 2.35)	18/ 0.28	RR: 1.20 (0.52, 2.76) (0.28, 5.08)	12/ 0.17	63.7	No	RR: 1.16 (0.54, 2.52)	2

Hopley 2010 (27)	Total hip arthroplasty	Deep infection	4	RR: 0.91 (0.25, 3.28)	0/ 0.00	RR: 1.37 (0.64, 2.94) (0.50, 3.73)	0/ 0.00	35.9	No	RR: 1.37 (0.64, 2.94)	2
Hüpfl 2010 (28)	Chest-compression- only cardio- pulmonary resuscitation	Survival	7	RR: 0.96 (0.83, 1.11)	0/ 0.00	RR: 1.04 (0.92, 1.19) (0.83, 1.31)	13/ 0.01	61.9	No	RR: 1.05 (0.93, 1.18)	3
Jamal 2013 (29)	Non-calcium-based phosphate binders	Mortality	3	RR: 0.89 (0.78, 1.00)	0/ 0.00	RR: 0.87 (0.77, 0.97) (0.67, 1.12)	28/ 0.01	49.1	Yes	RR: 0.89 (0.82, 0.96)	2
Jefferson 2010 (30)	Parenteral influenza vaccine	Influenza-like illness	30	RR: 0.76 (0.66, 0.87)	57/ 0.07	RR: 0.73 (0.64, 0.82) (0.43, 1.22)	54/ 0.06	85.6	No	RR: 0.70 (0.65, 0.75)	3
Jefferson 2010 (30)	Parenteral influenza vaccine	Influenza	10	RR: 0.51 (0.27, 0.97)	64/ 0.52	RR: 0.51 (0.32, 0.80) (0.13, 2.02)	59/ 0.34	68.7	No	RR: 0.60 (0.47, 0.78)	2
Jefferson 2012 (31)	Inactivated influenza vaccines	Influenza	1	RR: 0.20 (0.10, 0.39)	NA	RR: 0.37 (0.26, 0.53) (0.15, 0.92)	44/ 0.11	15.2	No	RR: 0.34 (0.27, 0.43)	2
Jefferson 2012 (31)	Inactivated influenza vaccines	Influenza-like illness	2	RR: 0.29 (0.07, 1.15)	95/ 1.43	RR: 0.56 (0.46, 0.68) (0.33, 0.94)	87/ 0.04	34.8	Yes	RR: 0.74 (0.71, 0.77)	2
Jin 2012 (32)	High total flavonoids	Colorectal neoplasms	3	RR: 1.00 (0.80, 1.25)	66/ 0.02	RR: 1.03 (0.88, 1.20) (0.56, 1.88)	56/ 0.01	69.6	No	RR: 1.02 (0.93, 1.13)	3
Kansagara 2013 (34)	Transfusion	Mortality	11	RR: 2.49 (1.40, 4.43)	97/ 0.94	RR: 1.84 (1.10, 3.07) (0.20, 16.54)	96/ 1.00	74.4	No	RR: 3.32 (3.03, 3.65)	3
Keag 2018 (35)	Caesarean section	Urinary incontinence	8	OR: 0.56 (0.48, 0.66)	70/ 0.04	OR: 0.58 (0.50, 0.68) (0.36, 0.94)	68/ 0.04	90.0	No	OR: 0.62 (0.57, 0.67)	3
Keag 2018 (35)	Caesarean section	Fecal incontinence	5	OR: 1.04 (0.73, 1.48)	72/ 0.10	OR: 1.11 (0.78, 1.58) (0.38, 3.26)	71/ 0.12	93.6	No	OR: 1.11 (0.94, 1.31)	3
Kredo 2014 (36)	Antiretroviral therapy by nurses	Mortality	2	RR: 1.23 (1.14, 1.33)	0/ 0.00	RR: 1.13 (0.94, 1.36) (0.13, 9.93)	76/ 0.02	64.7	Yes	RR: 1.17 (1.10, 1.26)	3

Kredo 2014 (36)	Antiretroviral therapy by nurses	Attrition	2	RR: 0.30 (0.05, 1.94)	98/ 1.77	RR: 0.43 (0.21, 0.86) (0.00, 2691.24)	95/ 0.35	65.6	Yes	RR: 0.75 (0.71, 0.79)	3
Kredo 2014 (36)	Nurses for maintenance of antiretroviral therapy	Mortality	1	RR: 0.19 (0.05, 0.78)	NA	RR: 0.61 (0.28, 1.35) (0.00, 2756.46)	56/ 0.28	20.2	Yes	RR: 0.79 (0.54, 1.16)	3
Li 2014 (37)	Exenatide	Acute pancreatitis/ Admission for acute pancreatitis	2	RR: 0.92 (0.69, 1.22)	0/ 0.00	RR: 0.92 (0.69, 1.22) (0.64, 1.32)	0/ 0.00	96.0	No	RR: 0.92 (0.69, 1.21)	2
Li 2016 (38)	DDP-4 Inhibitors	Heart failure	4	RR: 1.10 (1.04, 1.17)	0/ 0.00	RR: 1.10 (1.04, 1.17) (1.03, 1.16)	0/ 0.00	98.4	No	RR: 1.10 (1.04, 1.17)	2
Li 2016 (38)	DDP-4 Inhibitors	Hospital admission for heart failure	6	OR: 0.85 (0.74, 0.97)	33/ 0.01	OR: 0.94 (0.83, 1.08) (0.66, 1.36)	55/ 0.02	58.1	Yes	OR: 0.97 (0.90, 1.05)	2
Matthews 2018 (39)	Tamoxifen	Heart failure	2	RR: 0.85 (0.66, 1.09)	10/ 0.00	RR: 0.74 (0.53, 1.04) (0.02, 29.27)	59/ 0.05	70.5	No	RR: 0.75 (0.61, 0.92)	3
Menne 2019 (40)	SGLT-2 inhibitors	Acute kidney injury	5	OR: 0.40 (0.31, 0.52)	39/ 0.03	OR: 0.58 (0.49, 0.69) (0.41, 0.99)	27/ 0.05	36.9	No	OR: 0.62 (0.56, 0.68)	2
Mesgarpour 2017 (41)	Erythropoiesis stimulating agents	Venous thromboembolism	5	RR: 1.92 (0.64, 5.76)	75/ 1.03	RR: 1.26 (0.76, 2.10) (0.20, 8.14)	84/ 0.70	28.4	No	RR: 1.71 (1.45, 2.01)	2
Mesgarpour 2017 (41)	Erythropoiesis stimulating agents	Mortality	7	RR: 1.08 (0.66, 1.78)	91/ 0.35	RR: 0.88 (0.64, 1.21) (0.21, 3.71)	92/ 0.46	33.5	No	RR: 2.20 (2.15, 2.25)	2
Moberley 2013 (42)	Pneumococcal polysaccharide vaccines	Invasive pneumococcal disease	2	OR: 0.57 (0.36, 0.89)	0/ 0.00	OR: 0.40 (0.26, 0.61) (0.18, 0.85)	12/ 0.07	51.9	No	OR: 0.42 (0.29, 0.59)	2
Molnar 2015 (43)	Neoral (cyclosporine)	Acute rejection of kidney transplant	2	OR: 0.46 (0.25, 0.86)	5/ 0.02	OR: 0.74 (0.36, 1.54) (0.04, 12.62)	56/ 0.29	50.4	Yes	OR: 0.71 (0.46, 1.10)	2
Navarese 2013 (44)	Early intervention for NSTEMI-ACS	Mortality	4	OR: 0.80 (0.63, 1.02)	78/ 0.04	OR: 0.82 (0.69, 0.97) (0.54, 1.24)	45/ 0.03	74.8	Yes	OR: 0.86 (0.80, 0.94)	2
Navarese 2013 (44)	Early intervention for NSTEMI-ACS	Myocardial infarction	3	OR: 0.86 (0.69, 1.08)	86/ 0.03	OR: 0.97 (0.77, 1.22) (0.48, 1.94)	81/ 0.08	49.4	No	OR: 0.90 (0.83, 0.97)	2

Navarese 2013 (44)	Early intervention for NSTEMI-ACS	Major bleeding	3	OR: 1.12 (0.69, 1.82)	92/ 0.17	OR: 0.92 (0.68, 1.24) (0.39, 2.15)	70/ 0.11	56.3	No	OR: 1.00 (0.88, 1.13)	2
Nelson 2010 (45)	Caesarean section	Anal incontinence, feces	12	OR: 0.91 (0.72, 1.16)	0/ 0.00	OR: 0.92 (0.74, 1.16) (0.72, 1.19)	0/ 0.00	90.0	No	OR: 0.92 (0.74, 1.16)	3
Nelson 2010 (45)	Caesarean section	Anal incontinence, flatus	4	OR: 1.02 (0.87, 1.20)	0/ 0.00	OR: 1.00 (0.86, 1.16) (0.78, 1.28)	0/ 0.00	90.3	No	OR: 1.00 (0.86, 1.16)	3
Nieuwenhuijse 2014 (46)	Ceramic-on-ceramic bearings for total hip arthroplasty	Harris Hip Score	3	MD: -0.50 (-2.09, 1.09)	62/ 1.08	MD: -0.29 (-0.96, 0.38) (-1.81, 1.22)	32/ 0.31	40.7	No	MD: -0.20 (-0.66, 0.26)	2
Nieuwenhuijse 2014 (46)	High-flexion total knee arthroplasty	Flexion (degrees)	26	MD: 3.78 (1.64, 5.92)	78/ 19.12	MD: 2.91 (1.56, 4.27) (-4.42, 10.25)	73/ 12.7	53.2	No	MD: 2.49 (1.84, 3.14)	2
Nieuwenhuijse 2014 (46)	Gender-specific total knee arthroplasty	Flexion-extension range (degrees)	2	MD: 3.15 (-0.03, 6.34)	29/ 1.58	MD: 1.80 (0.40, 3.21) (-0.53, 4.14)	9/ 0.40	25.6	Yes	MD: 1.85 (0.54, 3.16)	2
Nikooie 2019 (47)	Second generation antipsychotics	Sedation	3	RR: 1.84 (0.40, 8.54)	34/ 0.84	RR: 1.29 (0.95, 1.74) (0.91, 1.83)	0/ 0.00	6.0	No	RR: 1.29 (0.95, 1.74)	2
Nikooie 2019 (47)	Second generation antipsychotics	Neurologic outcomes	5	RR: 0.76 (0.59, 0.99)	0/ 0.00	RR: 0.73 (0.57, 0.93) (0.56, 0.95)	0/ 0.00	91.0	No	RR: 0.73 (0.57, 0.93)	2
Ochen 2019 (48)	Surgery for achilles tendon rupture	Re-rupture	18	RR: 0.42 (0.28, 0.65)	30/ 0.19	RR: 0.43 (0.31, 0.60) (0.20, 0.96)	21/ 0.12	69.6	No	RR: 0.65 (0.54, 0.79)	2
Ochen 2019 (48)	Surgery for achilles tendon rupture	Complications	15	RR: 2.93 (2.28, 3.75)	0/ 0.00	RR: 2.72 (1.84, 4.02) (0.84, 8.82)	41/ 0.28	57.8	No	RR: 2.63 (2.13, 3.27)	2
Pittas 2010 (49)	High vitamin D	Hypertension	3	RR: 0.57 (0.41, 0.79)	0/ 0.00	RR: 0.68 (0.43, 1.07) (0.10, 4.51)	77/ 0.14	61.8	Yes	RR: 1.00 (0.95, 1.05)	3
Raman 2013 (50)	Carotid endarterectomy	Ipsilateral stroke	2	RR: 0.47 (0.05, 4.46)	83/ 2.19	RR: 0.70 (0.51, 0.97) (0.29, 1.69)	38/ 0.05	11.9	Yes	RR: 0.72 (0.58, 0.89)	2
Raman 2013 (50)	Carotid endarterectomy	Any stroke	3	RR: 0.73 (0.43, 1.22)	0/ 0.00	RR: 0.67 (0.57, 0.79) (0.53, 0.84)	0/ 0.00	9.7	Yes	RR: 0.67 (0.57, 0.79)	2

Raman 2013 (50)	Carotid artery stenting	Periprocedural stroke	5	RR: 1.91 (1.72, 2.11)	7/ 0.00	RR: 1.91 (1.74, 2.10) (1.69, 2.16)	0/ 0.00	98.2	No	RR: 1.91 (1.74, 2.10)	2
Schweizer 2013 (51)	Nasal deconolization	Surgical site infection	6	RR: 0.40 (0.28, 0.57)	0/ 0.00	RR: 0.48 (0.33, 0.69) (0.18, 1.26)	44/ 0.15	52.4	No	RR: 0.54 (0.42, 0.69)	2
Schweizer 2013 (51)	Glycopeptide prophylaxis	Surgical site infection	7	RR: 0.35 (0.12, 1.03)	80/ 1.44	RR: 0.71 (0.48, 1.05) (0.22, 2.27)	62/ 0.25	38.5	No	RR: 1.04 (0.66, 1.24)	2
Silvain 2012 (52)	Enoxaparin	Mortality	7	RR: 0.50 (0.40, 0.62)	0/ 0.00	RR: 0.64 (0.49, 0.82) (0.32, 1.26)	46/ 0.08	48.9	No	RR: 0.66 (0.56, 0.77)	2
Silvain 2012 (52)	Enoxaparin	Major bleeding	7	RR: 0.72 (0.56, 0.93)	0/ 0.00	RR: 0.81 (0.66, 1.00) (0.49, 1.37)	30/ 0.05	42.5	Yes	RR: 0.84 (0.72, 0.98)	2
Silvain 2012 (52)	Enoxaparin	Death or Myocardial infarction	7	RR: 0.44 (0.35, 0.55)	0/ 0.00	RR: 0.67 (0.55, 0.81) (0.37, 1.21)	58/ 0.07	34.3	No	RR: 0.77 (0.71, 0.85)	2
Suthar 2012 (53)	Antiretroviral therapy	Tuberculosis infection	9	HR: 0.32 (0.25, 0.41)	27/ 0.03	HR: 0.35 (0.29, 0.44) (0.22, 0.57)	26/ 0.03	78.9	No	HR: 0.37 (0.31, 0.44)	3
Te Morenga 2013 (54)	High sugar intake	Weight gain (kg)	4	MD: 0.31 (-0.07, 0.68)	99/ 0.14	MD: 0.51 (0.26, 0.75) (-0.36, 1.37)	99/ 0.14	42.0	Yes	MD: 0.59 (0.58, 0.60)	2
Te Morenga 2013 (54)	High sugar intake	BMI (kg/m <sup>2</sup> )	4	MD: -0.02 (-0.05, 0.00)	74/ 0.00	MD: -0.02 (-0.05,-0.00) (-0.05, 0.09)	58/ 0.00	5.0	No	MD: -0.01 (-0.03, -0.00)	2
Thomas 2010 (55)	Influenza vaccines	Influenza-like illness	1	RR: 0.31 (0.26, 0.36)	NA	RR: 0.53 (0.31, 0.89) (0.08, 3.48)	94/ 0.28	24.5	No	RR: 0.48 (0.43, 0.53)	3
Tickell-Painter 2017 (56)	Mefloquine	Discontinuation due to adverse effects	9	RR: 2.73 (1.84, 4.06)	31/ 0.11	RR: 2.78 (2.05, 3.77) (1.57, 4.91)	15/ 0.04	79.2	No	RR: 2.85 (2.19, 3.71)	2
Tickell-Painter 2017 (56)	Mefloquine	Serious adverse events or effects	2	RR: 3.09 (0.38, 24.95)	0/ 0.00	RR: 1.31 (0.33, 5.23) (0.14, 12.39)	0/ 0.00	43.7	No	RR: 1.31 (0.33, 5.23)	3
Tickell-Painter 2017 (56)	Mefloquine	Nausea	3	RR: 1.86 (1.42, 2.42)	0/ 0.00	RR: 1.56 (1.30, 1.87) (1.16, 2.09)	0/ 0.00	46.3	No	RR: 1.56 (1.30, 1.87)	3

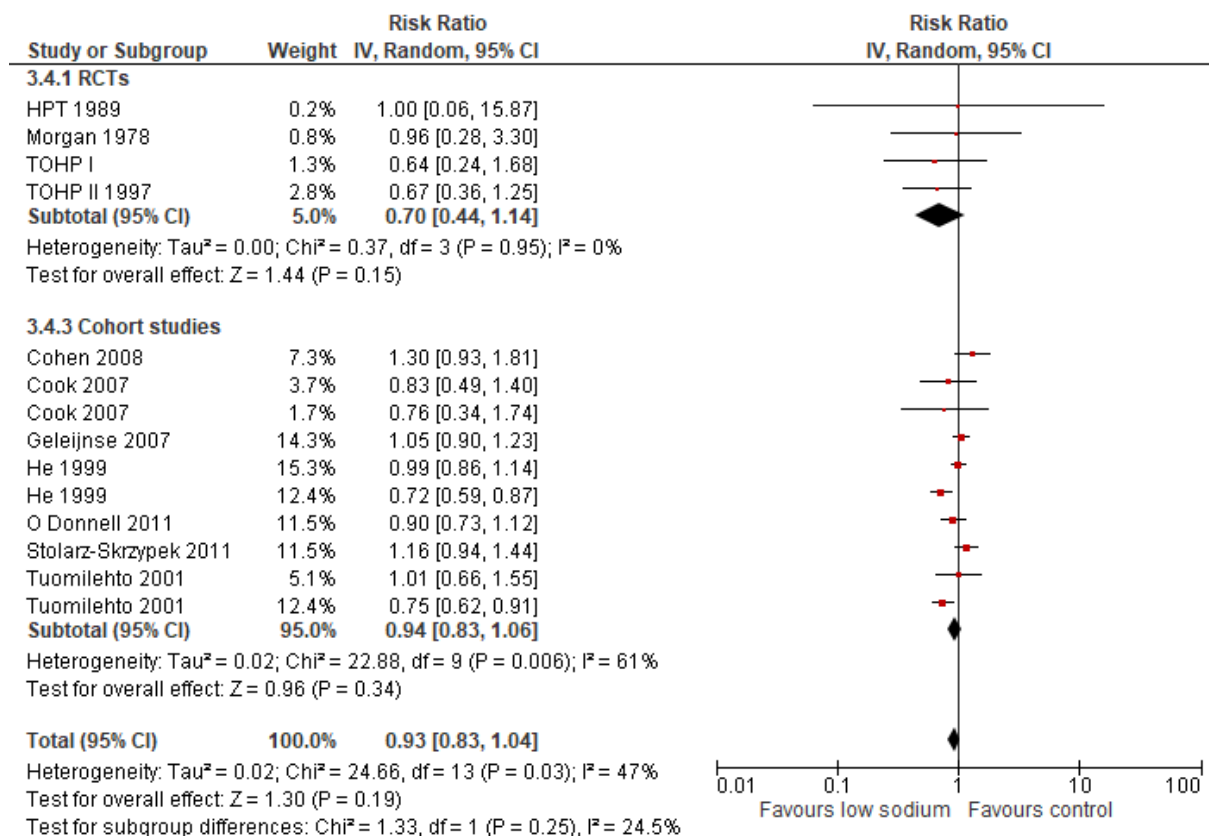
Tricco 2018 (57)	Live-attenuated zoster vaccines	Suspected Herpes Zoster	3	RR: 0.48 (0.27, 0.83)	99/ 0.24	RR: 0.55 (0.40, 0.77) (0.20, 1.52)	97/ 0.14	56.6	No	RR: 0.72 (0.70, 0.74)	2
Vinceti 2018 (58)	Selenium	Any cancer	7	RR: 0.72 (0.55, 0.93)	46/ 0.06	RR: 0.86 (0.73, 1.01) (0.52, 1.42)	64/ 0.04	45.7	Yes	RR: 0.94 (0.88, 1.01)	3
Vinceti 2018 (58)	Selenium	Cancer mortality	7	RR: 0.76 (0.59, 0.97)	66/ 0.07	RR: 0.78 (0.64, 0.95) (0.44, 1.39)	65/ 0.05	73.2	No	RR: 0.88 (0.80, 0.96)	3
Vinceti 2018 (58)	Selenium	Colorectal cancer	6	RR: 0.82 (0.72, 0.94)	0/ 0.00	RR: 0.83 (0.74, 0.94) (0.73, 0.95)	0/ 0.00	85.6	No	RR: 0.83 (0.74, 0.94)	3
Wilson 2011 (59)	Training for traditional birth attendants/ assistance by traditional birth attendants	Perinatal mortality	1	RR: 0.82 (0.38, 1.78)	NA	RR: 0.77 (0.67, 0.89) (0.53, 1.13)	52/ 0.01	3.0	Yes	RR: 0.79 (0.73, 0.86)	3
Wilson 2011 (59)	Training for traditional birth attendants/ assistance by traditional birth attendants	Neonatal mortality	2	RR: 0.80 (0.47, 1.37)	0/ 0.00	RR: 0.80 (0.73, 0.88) (0.67, 0.95)	14.0/ 0.00	3.0	Yes	RR: 0.80 (0.74, 0.87)	3
Wilson 2019 (60)	Unilateral knee arthroplasty	Venous thromboembolism	8	RR: 0.42 (0.30, 0.57)	24/ 0.04	RR: 0.43 (0.33, 0.55) (0.29, 0.64)	8/ 0.01	98.1	No	RR: 0.45 (0.37, 0.54)	2
Wilson 2019 (60)	Unilateral knee arthroplasty	Range of movement (degrees)	11	MD: -8.43 (-10.15, -6.71)	86/ 6.20	MD: -7.60 (-9.27, -5.93) (-13.98, -1.22)	91/ 7.85	77.8	No	MD: -8.29 (-8.63, -7.95)	2
Wilson 2019 (60)	Unilateral knee arthroplasty	Operation duration (minutes)	8	MD: -23.80 (-40.43, -7.17)	99/ 491.19	MD: -17.07 (-29.11, -5.04) (-63.37, 29.23)	98/ 365.45	69.8	No	MD: -11.25 (-12.71, -9.97)	2
Yank 2011 (61)	Recombinant factor VII	Mortality	2	RR: 0.91 (0.39, 2.12)	0/ 0.00	RR: 1.08 (0.56, 2.09) (0.25, 4.59)	0/ 0.00	60.6	No	RR: 1.08 (0.56, 2.09)	2
Yank 2011 (61)	Recombinant factor VII	Thromboembolic events	2	RR: 1.81 (0.67, 4.87)	0/ 0.00	RR: 1.88 (0.85, 4.16) (0.33, 10.76)	0/ 0.00	64.5	No	RR: 1.88 (0.85, 4.16)	2

Zhang 2016 (62)	Everolimus-eluting bioresorbable vascular scaffold	Stent thrombosis	3	OR: 2.22 (1.00, 4.93)	0/ 0.00	OR: 2.09 (1.20, 3.64) (1.04, 4.18)	0/ 0.00	48.9	Yes	OR: 2.09 (1.20, 3.64)	2
Zhang 2016 (62)	Everolimus-eluting bioresorbable vascular scaffold	Mortality	4	OR: 0.63 (0.24, 1.63)	0/ 0.00	OR: 0.73 (0.34, 1.57) (0.18, 2.97)	15/ 0.20	48.3	No	OR: 0.82 (0.42, 1.60)	2
Zhang 2016 (62)	Everolimus-eluting bioresorbable vascular scaffold	Cardiac death	4	OR: 0.94 (0.43, 2.06)	0/ 0.00	OR: 1.05 (0.53, 2.12) (0.42, 2.63)	0/ 0.00	78.6	No	OR: 1.05 (0.53, 2.12)	2
Zhang 2017 (63)	Percutaneous coronary intervention	Mortality	17	HR: 1.07 (0.92, 1.26)	37/ 0.03	HR: 1.05 (0.93, 1.20) (0.73, 1.52)	32/ 0.03	74.4	No	HR: 1.08 (0.98, 1.19)	2
Zhang 2017 (63)	Percutaneous coronary intervention	Cardiovascular mortality	5	HR: 1.08 (0.51, 2.28)	78/ 0.49	HR: 1.05 (0.69, 1.59) (0.29, 3.81)	72/ 0.25	48.8	No	HR: 1.33 (1.09, 1.62)	2
Zhang 2017 (63)	Percutaneous coronary intervention	Myocardial infarction	5	HR: 2.00 (1.65, 2.44)	0/ 0.00	HR: 1.69 (1.22, 2.33) (0.71, 4.03)	57/ 0.12	46.3	No	HR: 1.66 (1.42, 1.94)	2
Ziff 2015 (64)	Digoxin	Mortality	8	RR: 1.60 (1.31, 1.96)	63/ 0.05	RR: 1.38 (1.15, 1.66) (0.77, 2.49)	75/ 0.06	69.8	No	RR: 1.08 (1.03, 1.14)	3
Ziff 2015 (64)	Digoxin	Cardiovascular mortality	3	RR: 2.53 (1.12, 5.70)	96/ 0.48	RR: 1.71 (1.04, 2.80) (0.26, 11.38)	96/ 0.29	58.1	No	RR: 1.15 (1.08, 1.22)	3
Ziff 2015 (64)	Digoxin	Hospital admission	4	RR: 0.92 (0.85, 0.99)	64/ 0.00	RR: 0.93 (0.88, 0.98) (0.80, 1.09)	61/ 0.00	62.2	No	RR: 0.92 (0.89, 0.95)	2

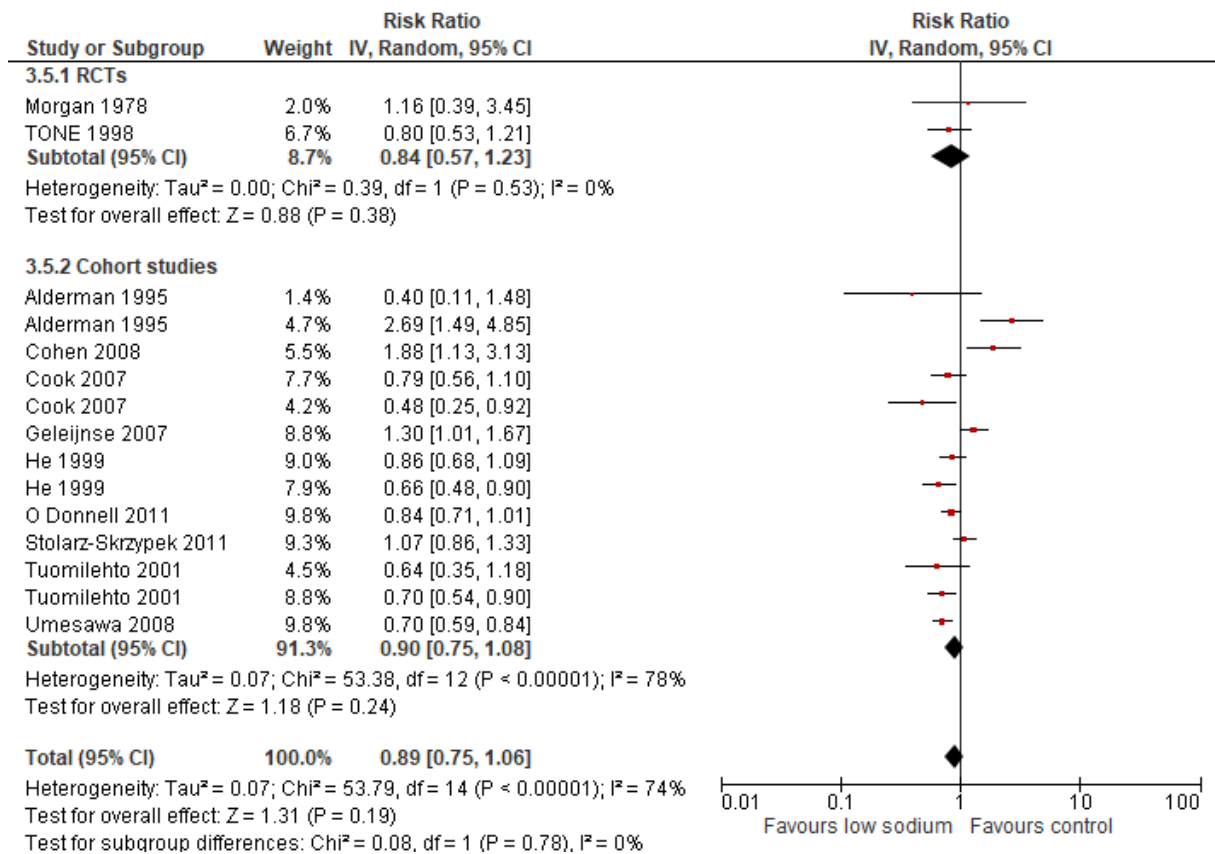
BCG: Bacillus Calmette-Guérin; BMI: Body Mass Index; BoE: Bodies of Evidence; CE: Common Effects; CI: Confidence Interval; CRC: Colorectal Cancer; CS: Cohort Studies; DDP 4: Dipeptidylpeptidase-4; HIV: Human Immunodeficiency Virus; HR: Hazard Ratio; MD: Mean Difference; NA: Not Applicable; NSTE-ACS: Non-ST-Segment Elevation Acute Coronary Syndromes; OR: Odds Ratio; PI/ECO: Population – Intervention/Exposure – Comparator – Outcome; RCT: Randomized Controlled Trial; RE: Random Effects; RR: Risk Ratio; SGLT-2: Sodium Dependent Glucose Transporter 2;

\* PI/ECO similarity degree: 1=more or less identical; 2=similar but not identical; 3=broadly similar;

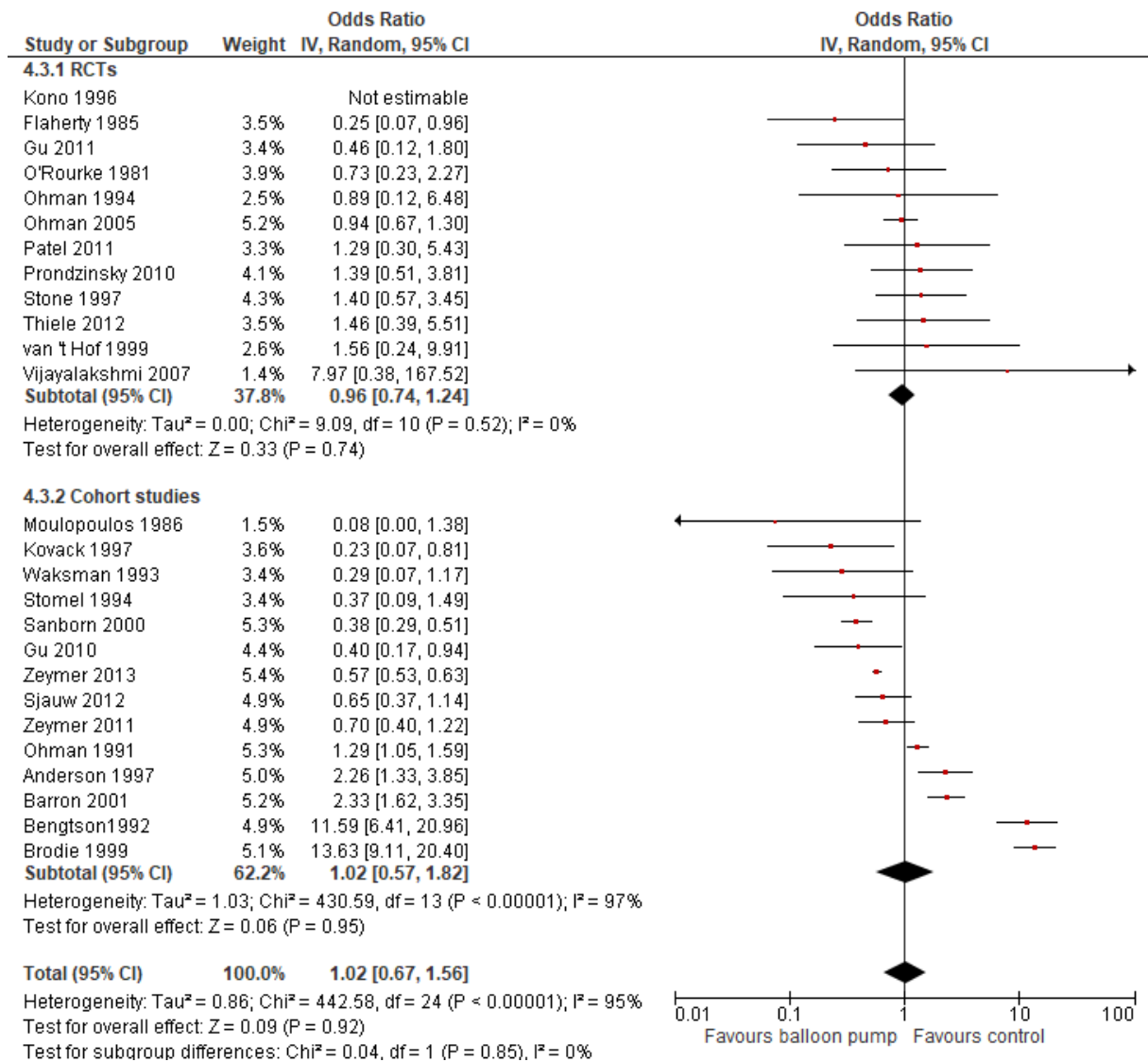




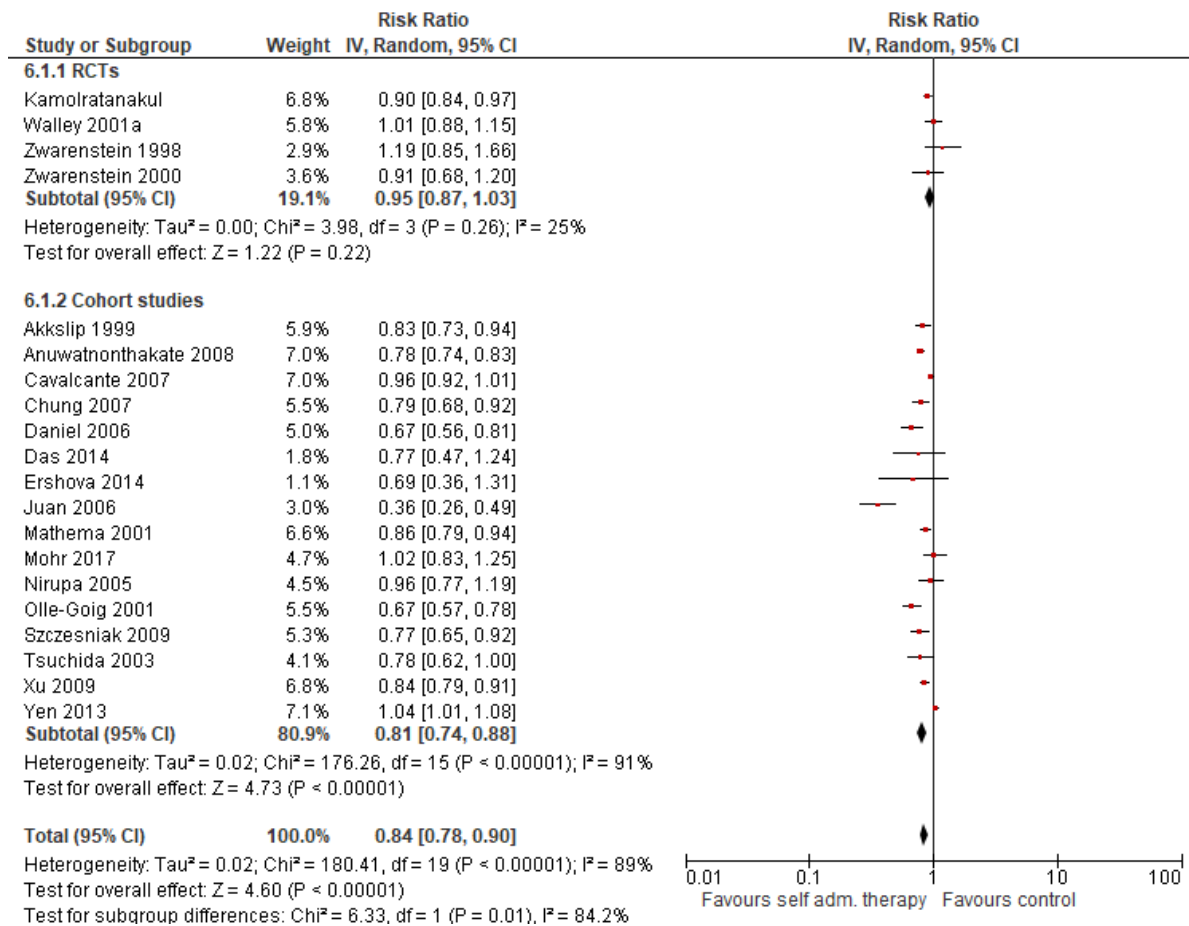
**Figure S1:** Aburto 2013; Intervention/ Exposure: Low sodium; Outcome: All-cause mortality



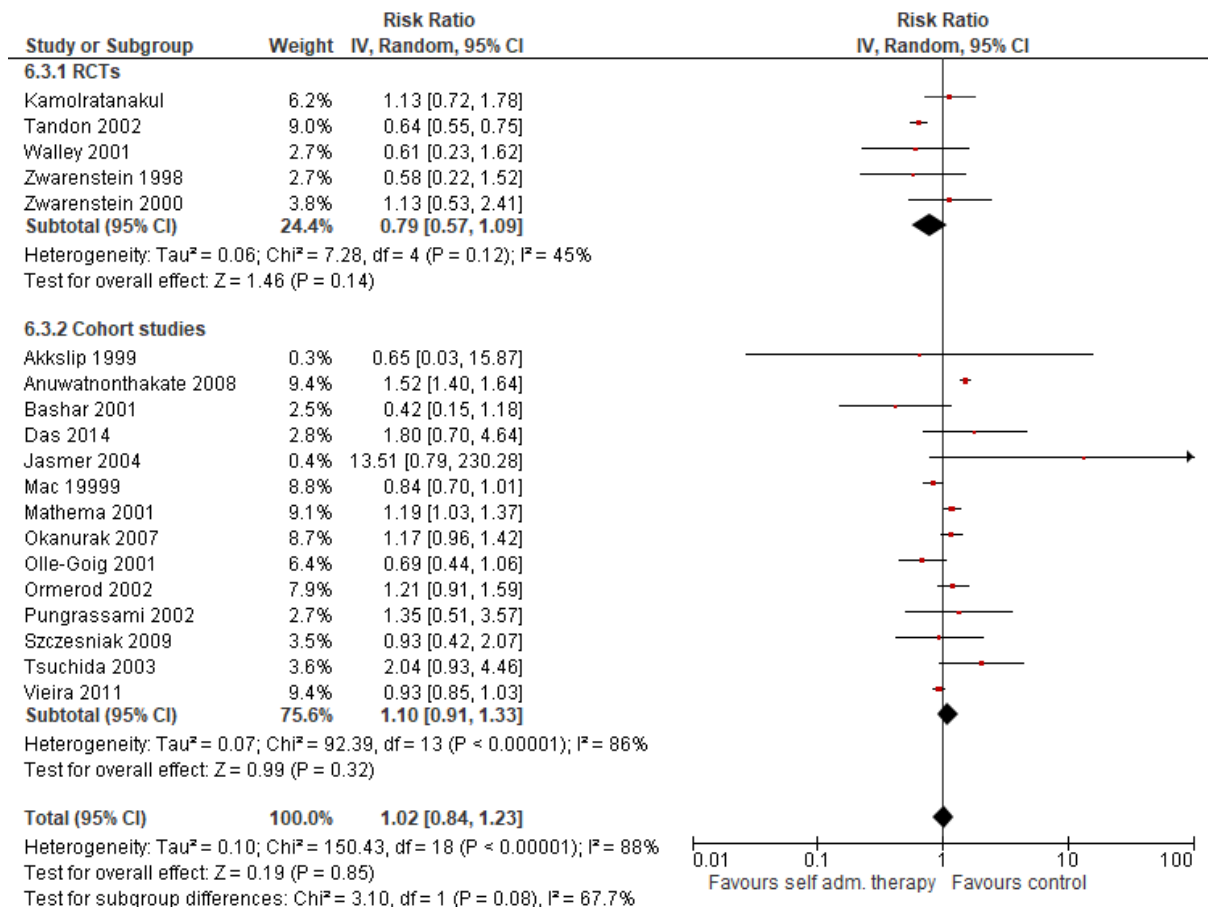
**Figure S2:** Aburto 2013; Intervention/ Exposure: Low-sodium; Outcome: Cardiovascular disease



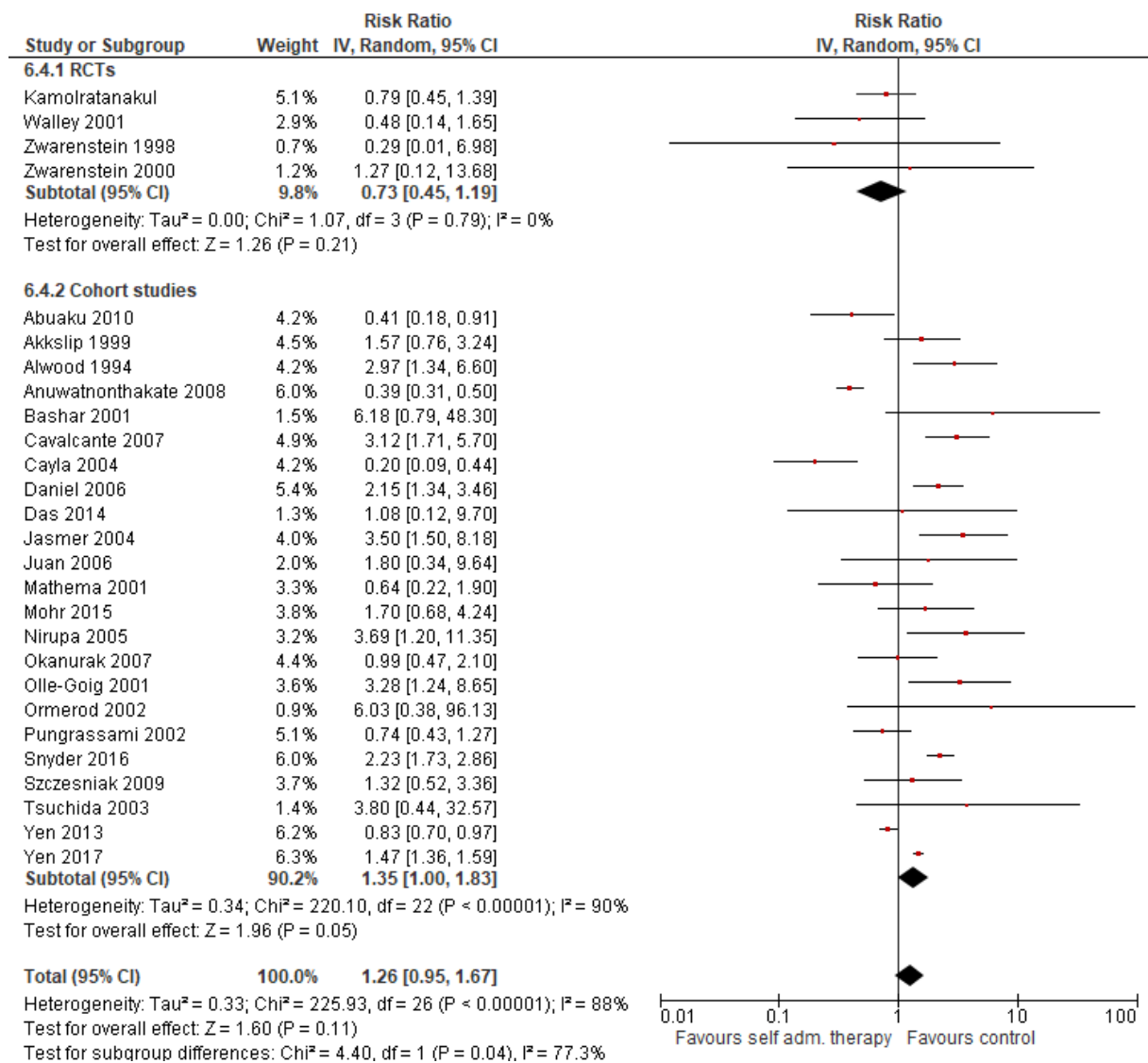
**Figure S3:** Ahmad 2015; Intervention/ Exposure: Intra-aortic balloon pump; Outcome: All-cause mortality



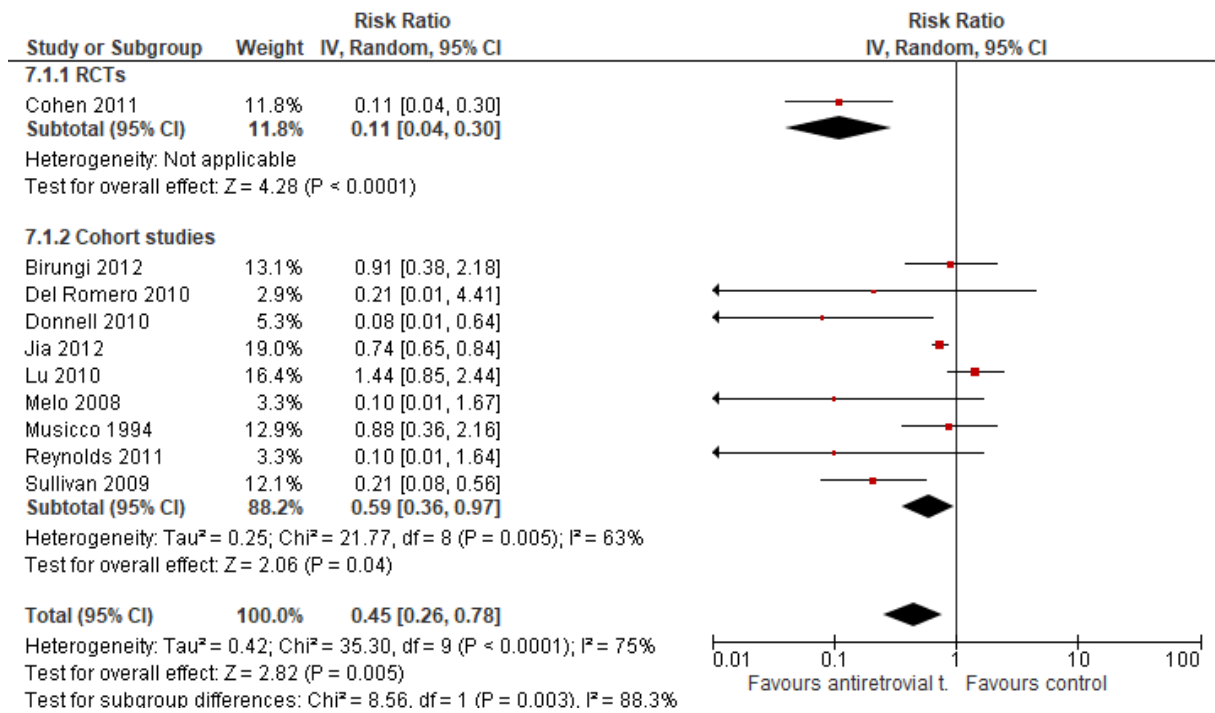
**Figure S4:** Alipanah 2018; Intervention/ Exposure: Self-administered therapy; Outcome: Treatment success (Risk Ratio >1 indicates a favorable effect)



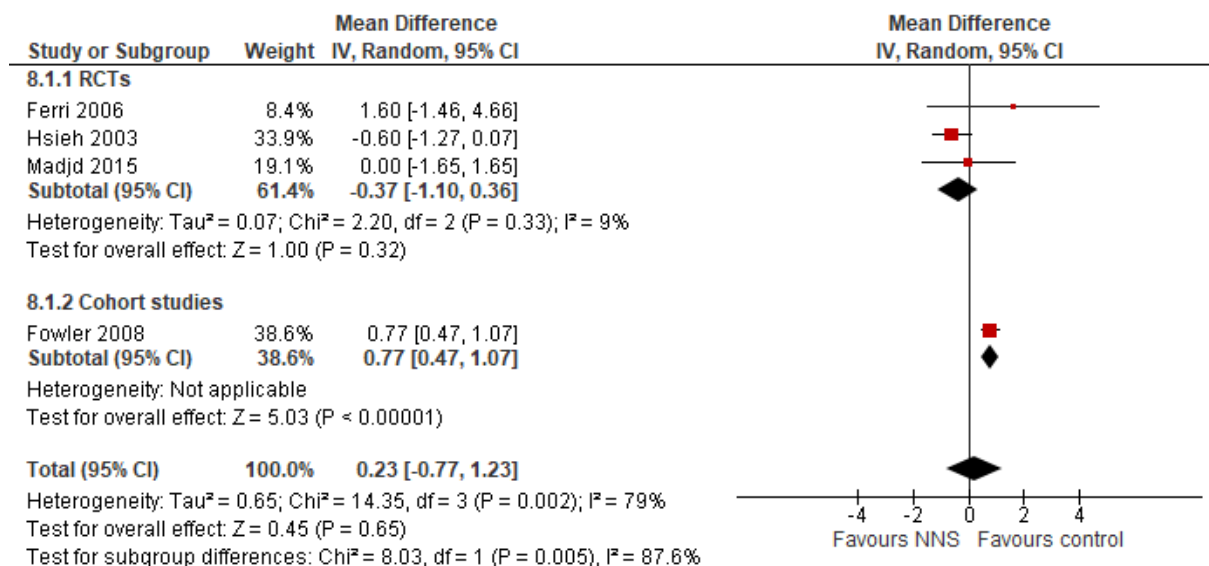
**Figure S5:** Alipanah 2018; Intervention/ Exposure: Self-administered therapy; Outcome: Treatment completion (Risk Ratio >1 indicates a favorable effect)



**Figure S6:** Alipanah 2018; Intervention/ Exposure: Self-administered therapy; Outcome: All-cause mortality

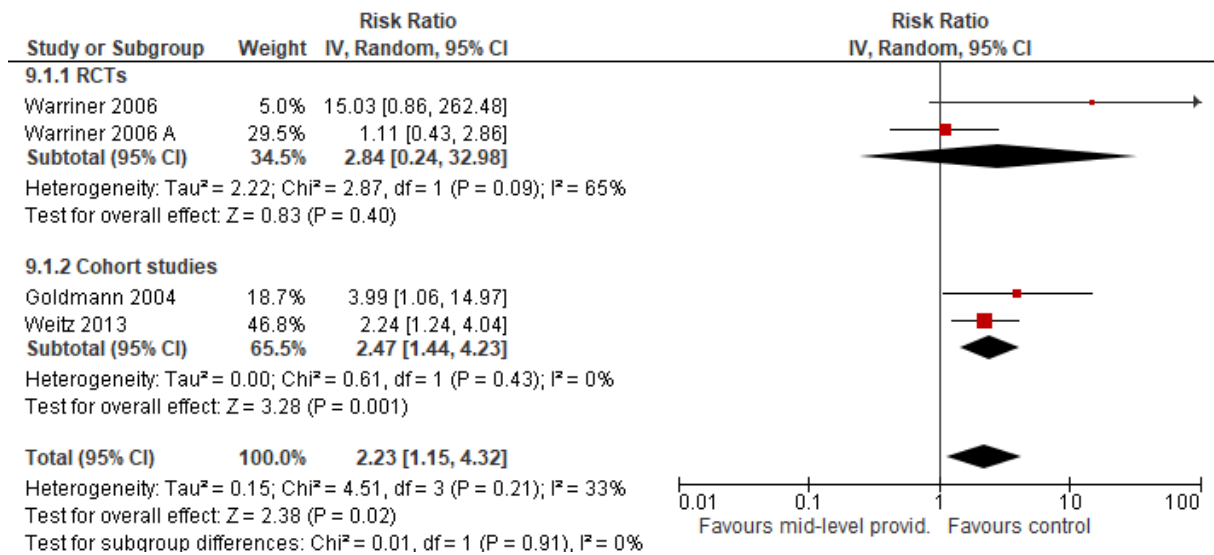


**Figure S7:** Anglemyer 2013; Intervention/ Exposure: Antiretroviral therapy; Outcome: HIV infection

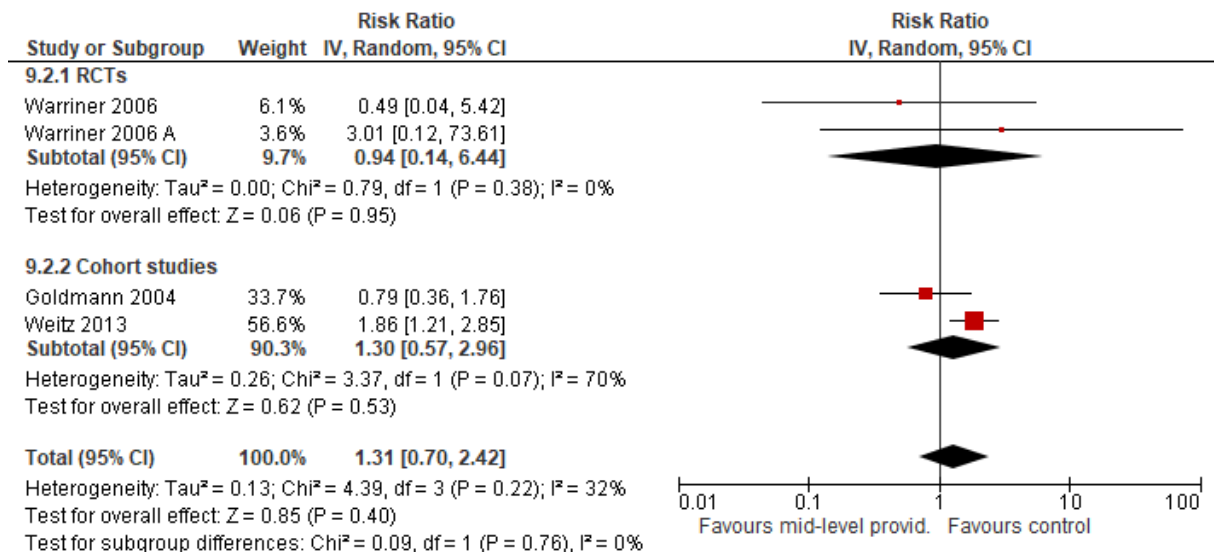


**Figure S8:** Azad 2017; Intervention/ Exposure: Nonnutritive sweeteners; Outcome: Body Mass Index

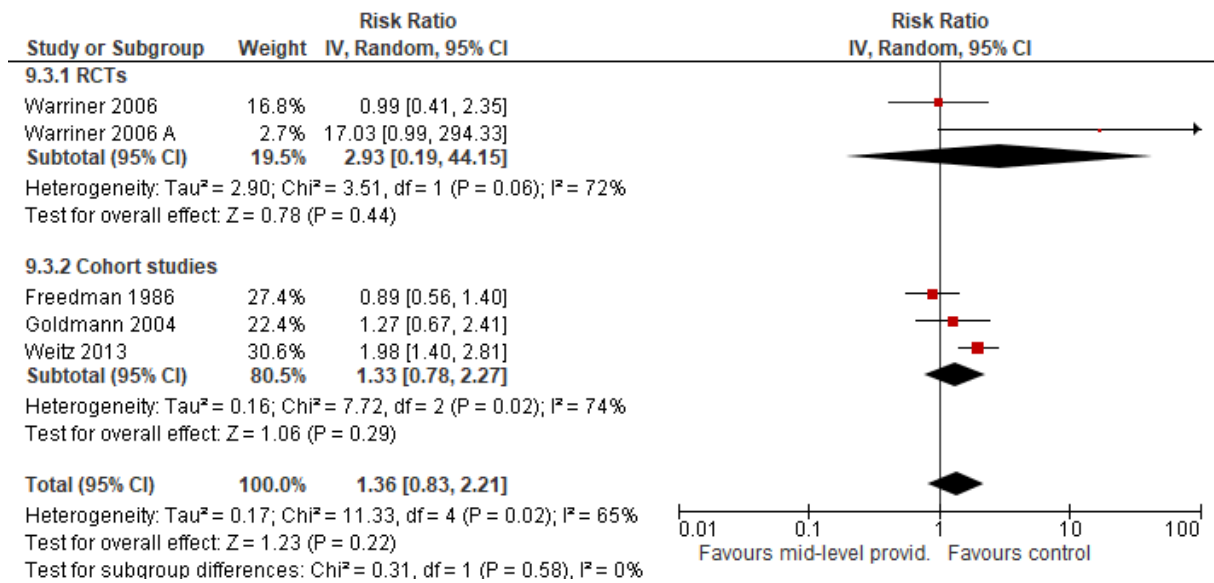




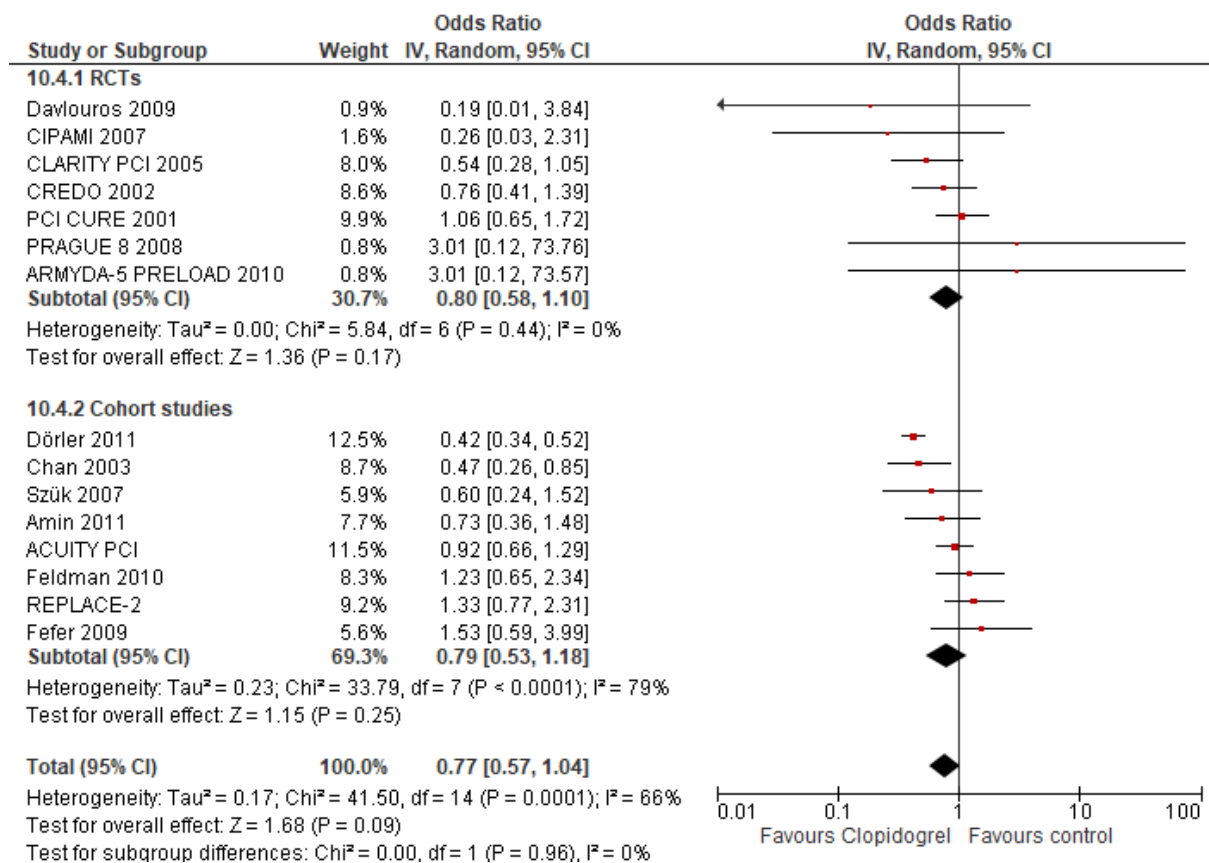
**Figure S9:** Barnard 2015; Intervention/ Exposure: Surgical abortion by mid-level providers; Outcome: Failure or incomplete abortion



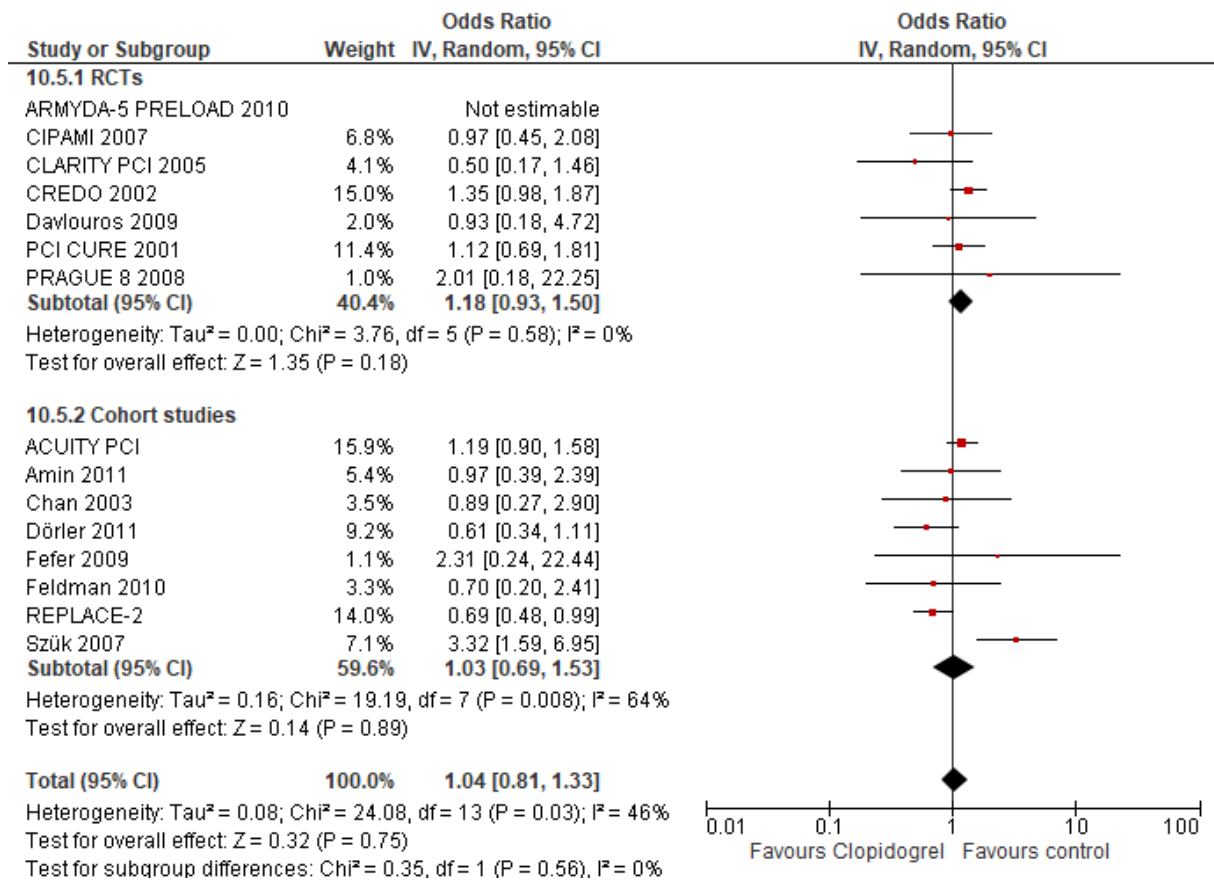
**Figure S10:** Barnard 2015; Intervention/ Exposure: Surgical abortion by mid-level providers; Outcome: Complications



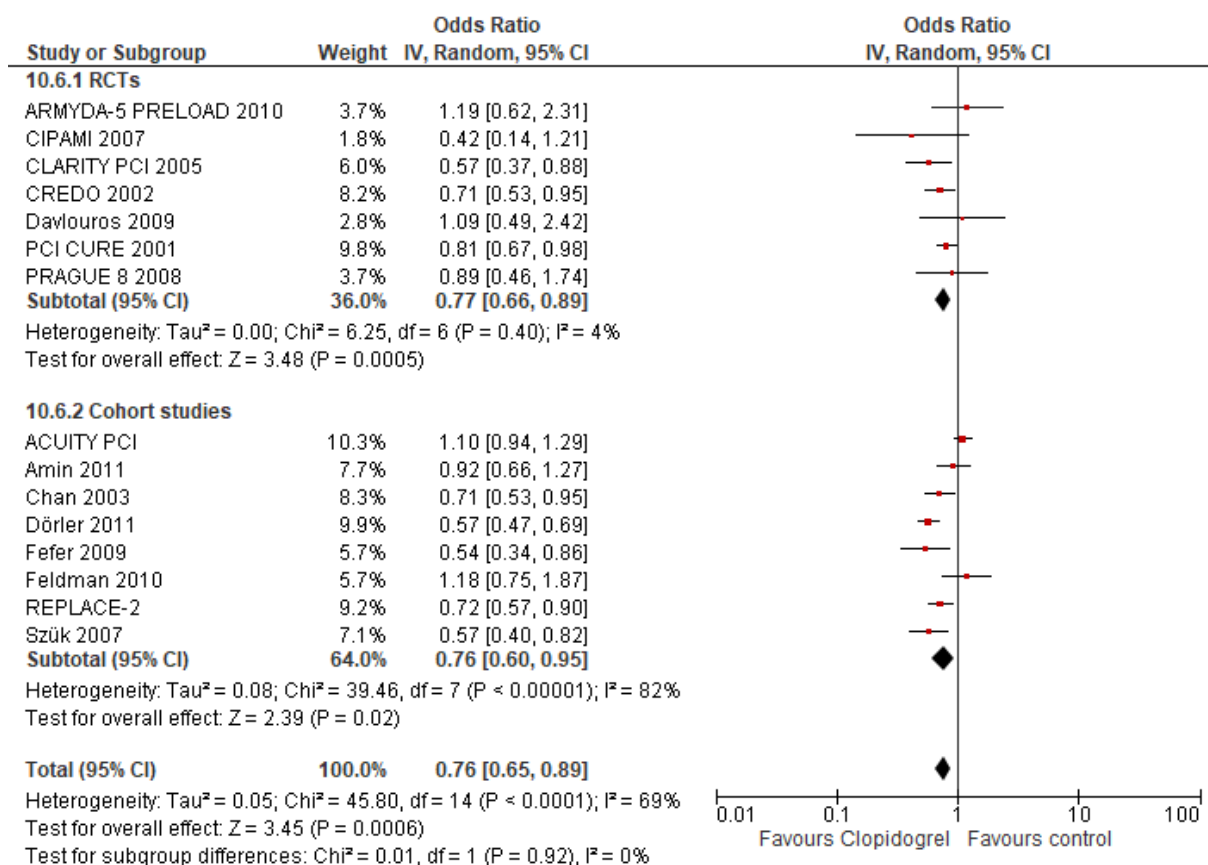
**Figure S11:** Barnard 2015; Intervention/ Exposure: Surgical abortion by mid-level providers; Outcome: Abortion failure and complications



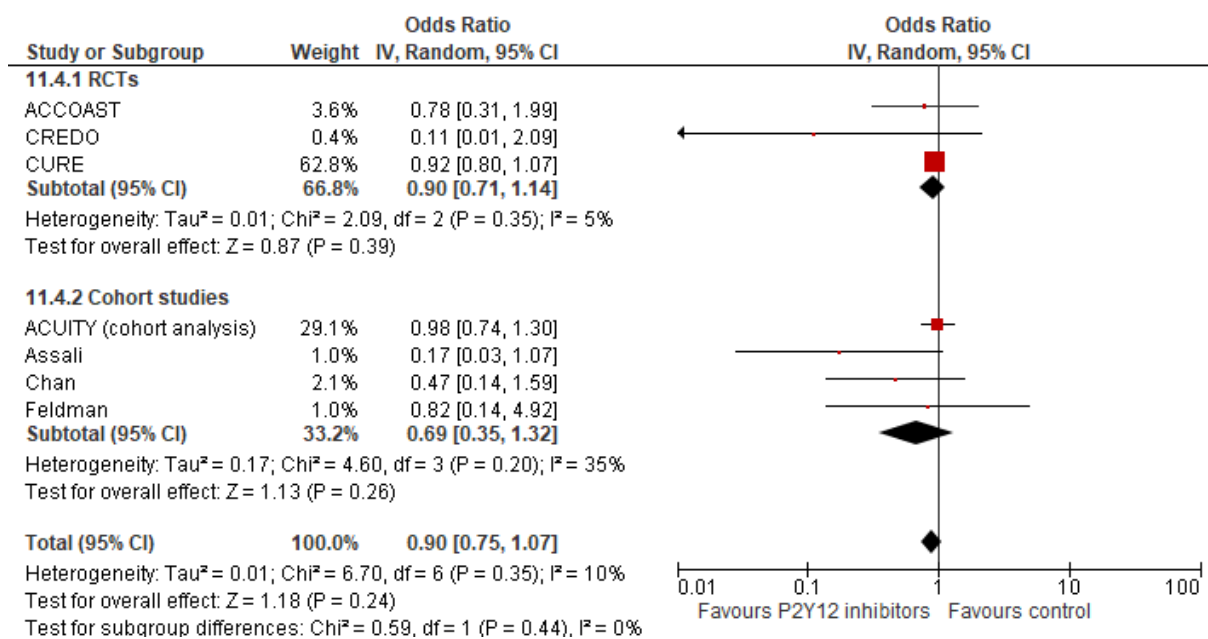
**Figure S12:** Bellemain-Appaix 2012; Intervention/ Exposure: Clopidogrel pretreatment for percutaneous coronary intervention; Outcome: All-cause mortality



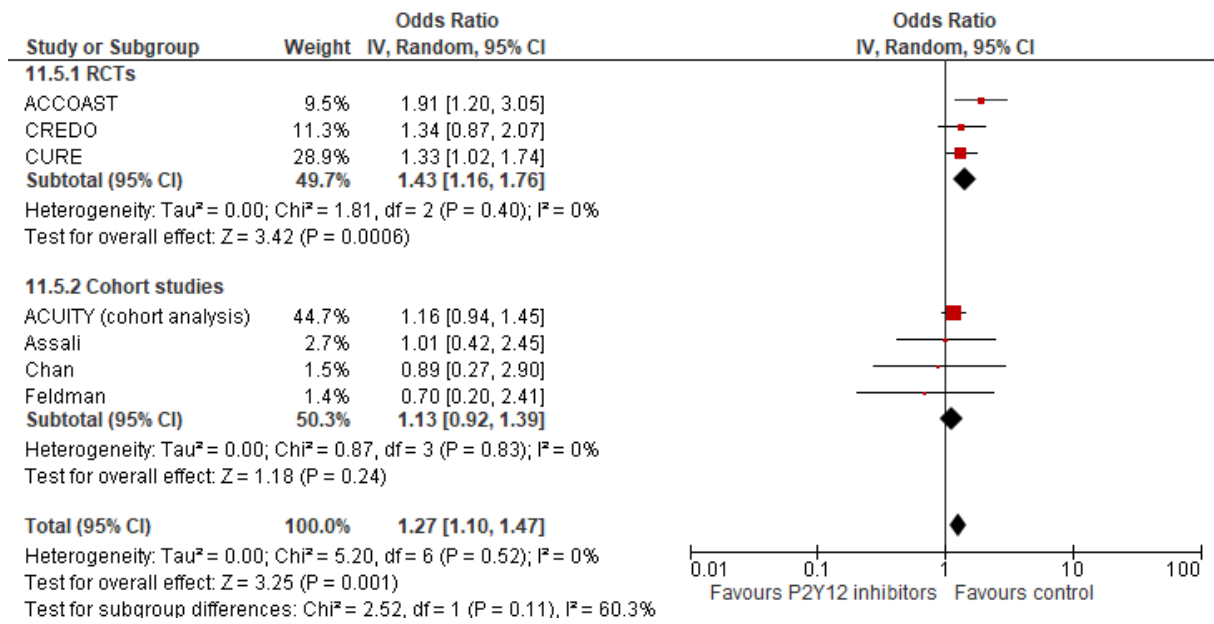
**Figure S13:** Bellemin-Appaix 2012; Intervention/ Exposure: Clopidogrel pretreatment for percutaneous coronary intervention; Outcome: Major bleeding



**Figure S14:** Bellemain-Appaix 2012; Intervention/ Exposure: Clopidogrel pretreatment for percutaneous coronary intervention; Outcome: Coronary heart disease

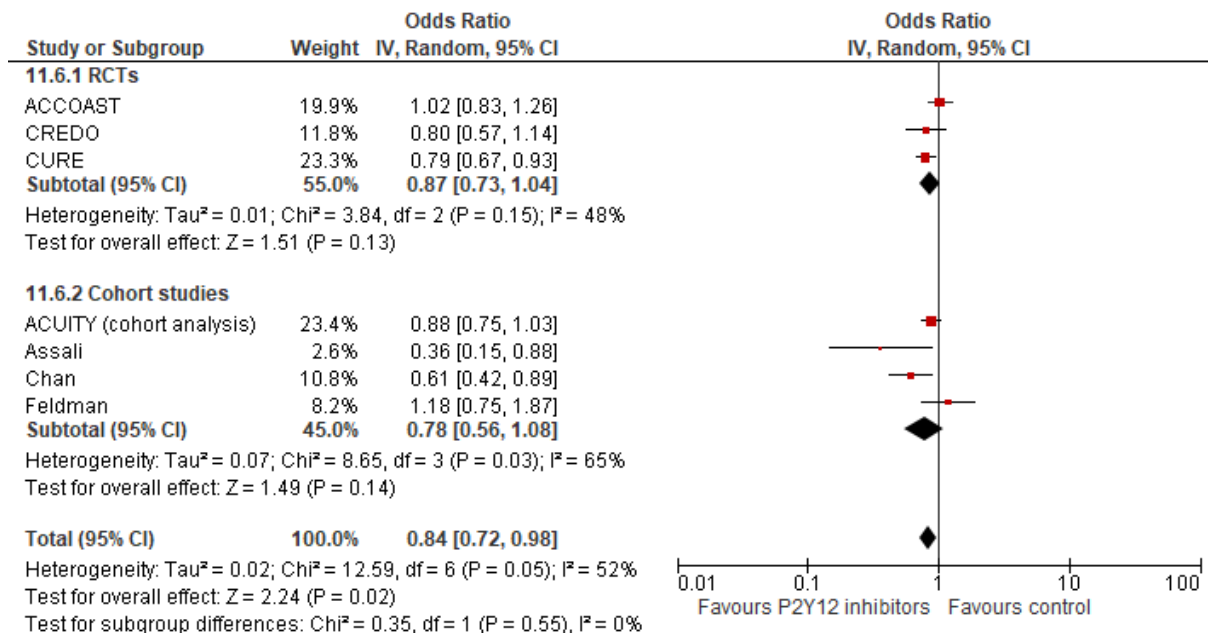


**Figure S15:** Bellemain-Appaix 2014; Intervention/ Exposure: P2Y12 inhibitor pretreatment in non-ST elevation acute coronary syndrome; Outcome: All-cause mortality

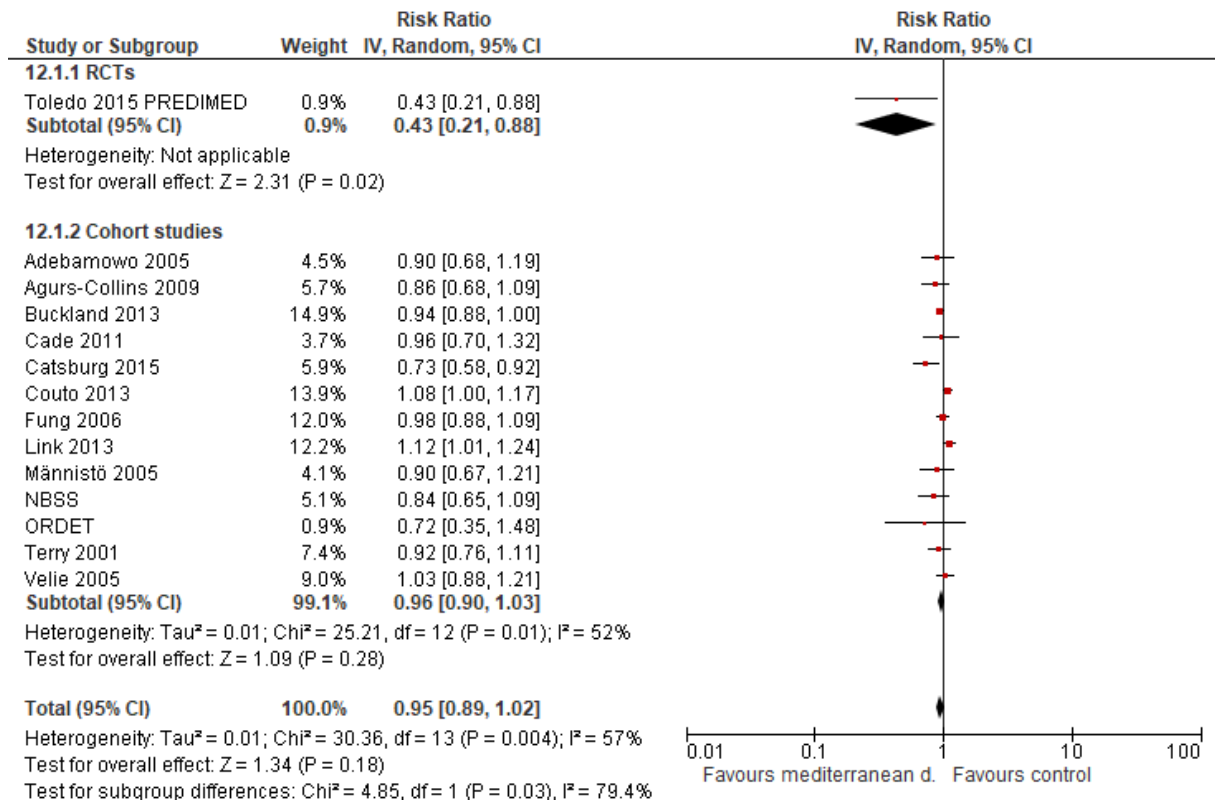


**Figure S16:** Bellemain-Appaix 2014; Intervention/ Exposure: P2Y12 inhibitor pretreatment in non-ST elevation acute coronary syndrome; Outcome: Major bleeding

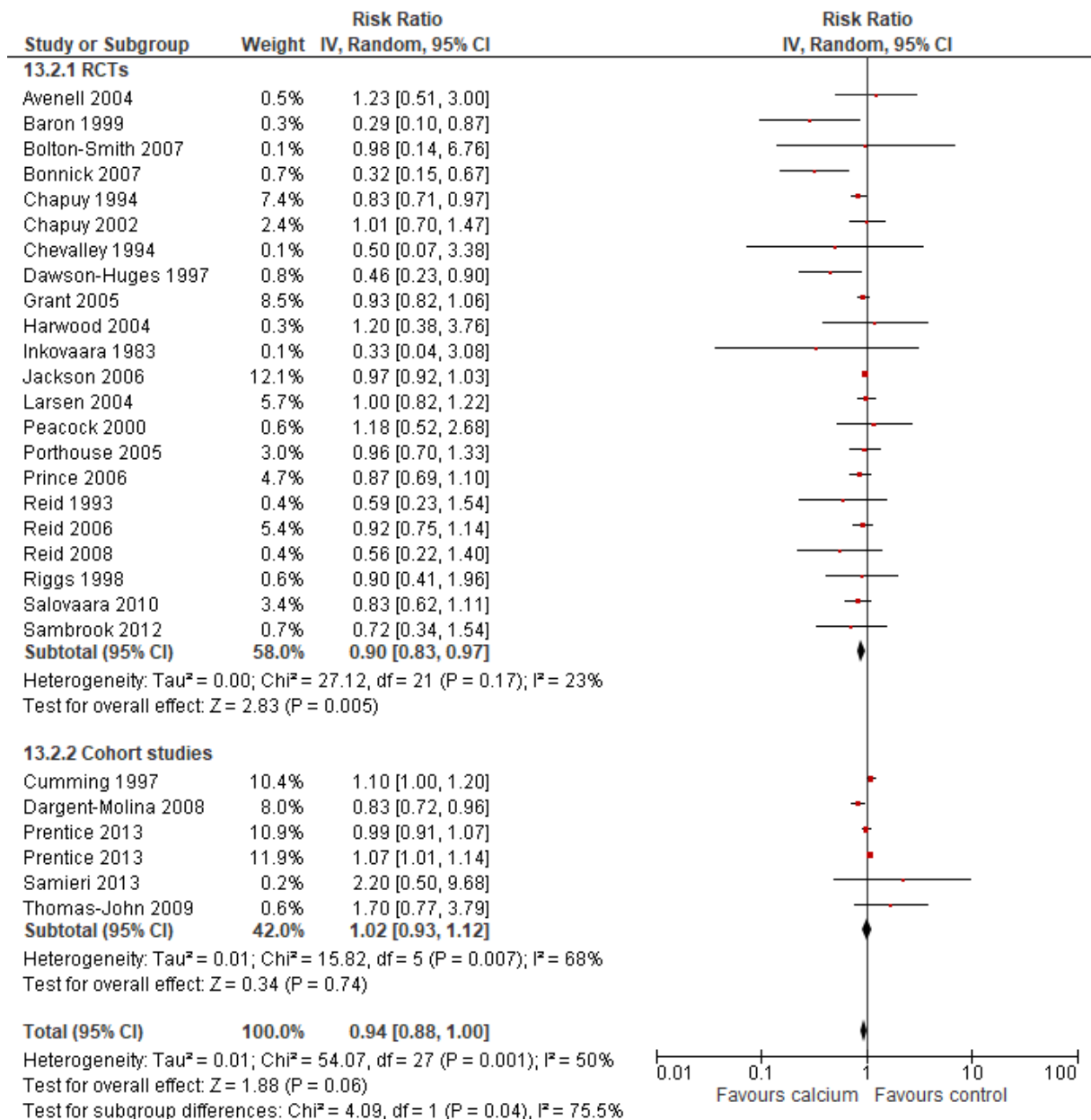




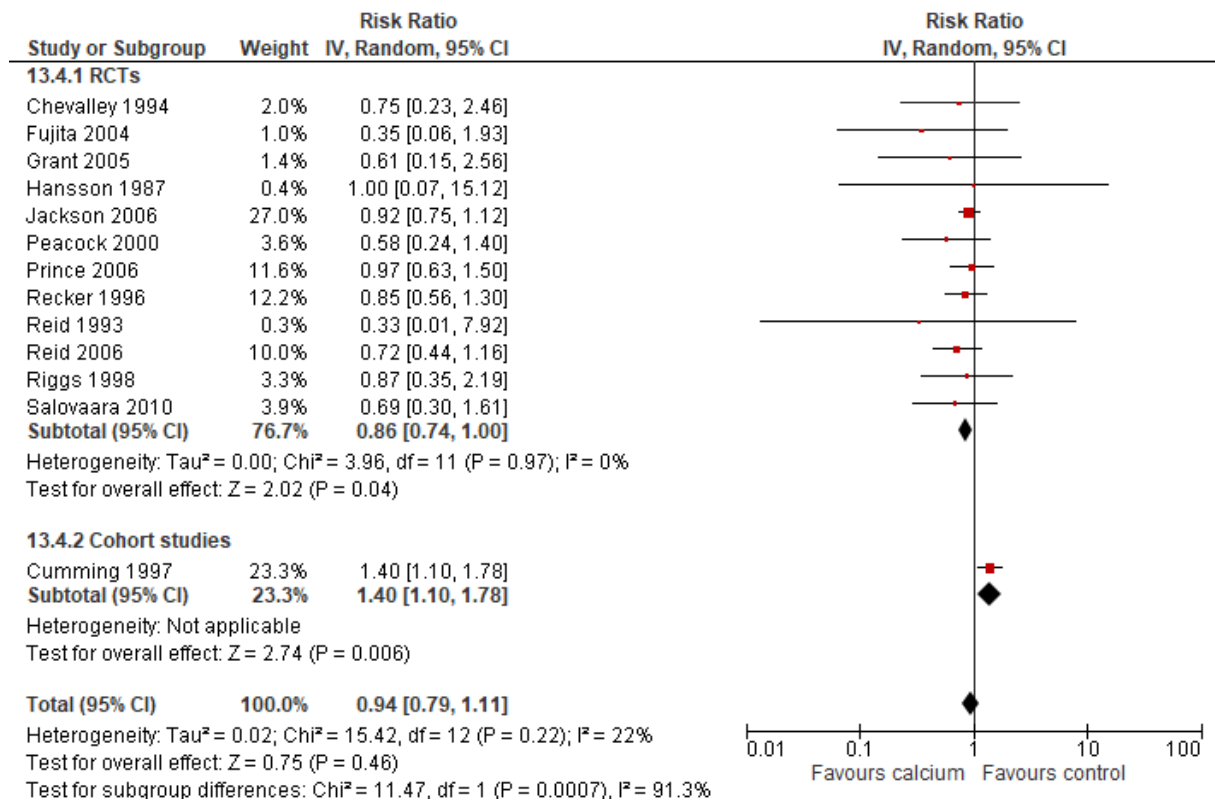
**Figure S17:** Bellemain-Appaix 2014; Intervention/ Exposure: P2Y12 inhibitor pretreatment in non-ST elevation acute coronary syndrome; Outcome: Main composite ischemic endpoint



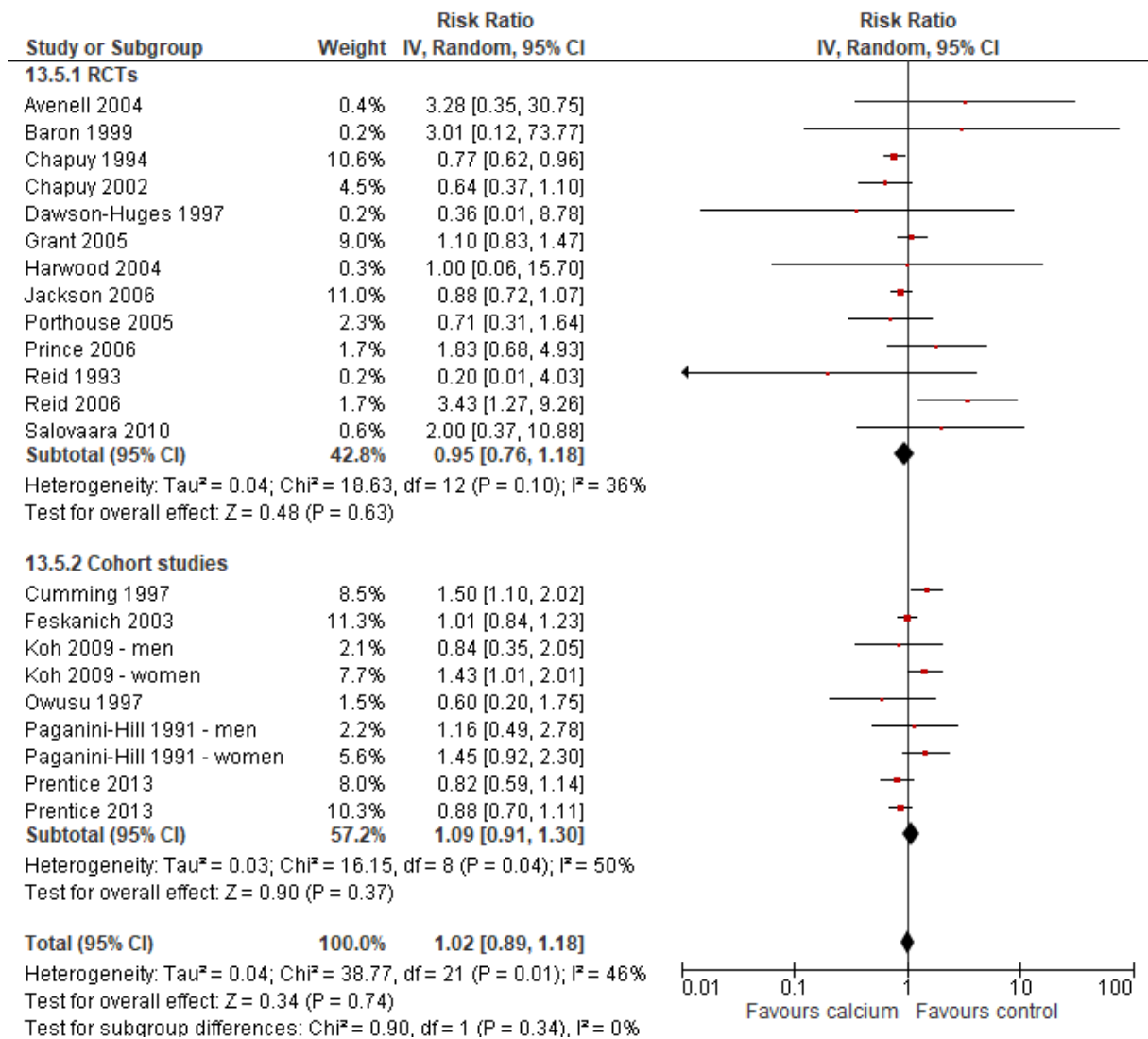
**Figure S18:** Bloomfield 2016; Intervention/ Exposure: Mediterranean diet; Outcome: Breast cancer



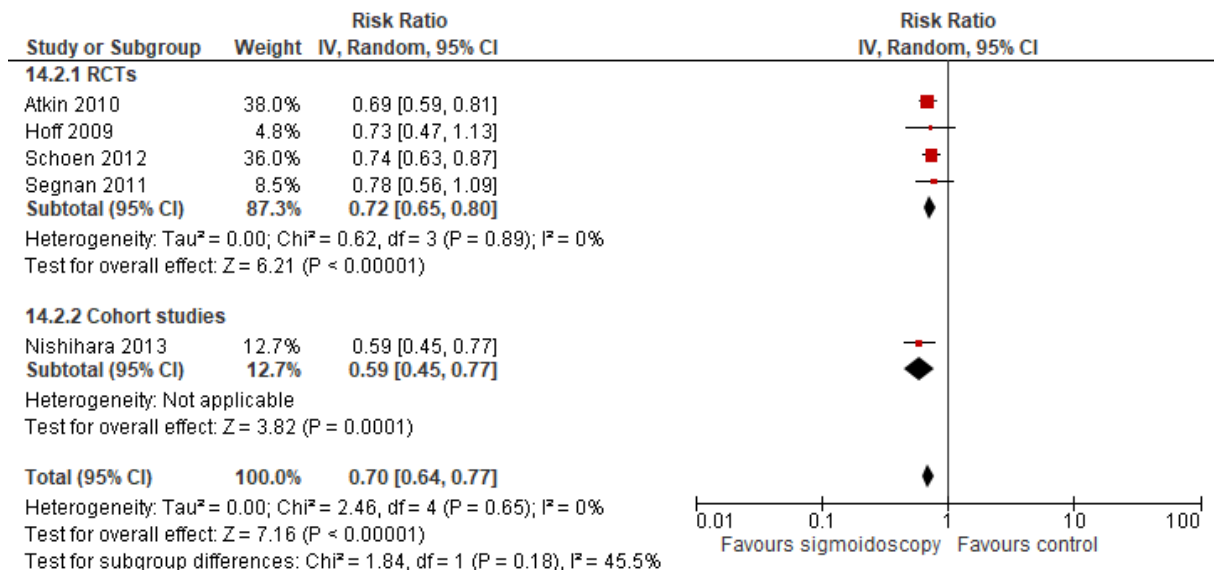
**Figure S19:** Bolland 2015; Intervention/ Exposure: High calcium; Outcome: All fractures



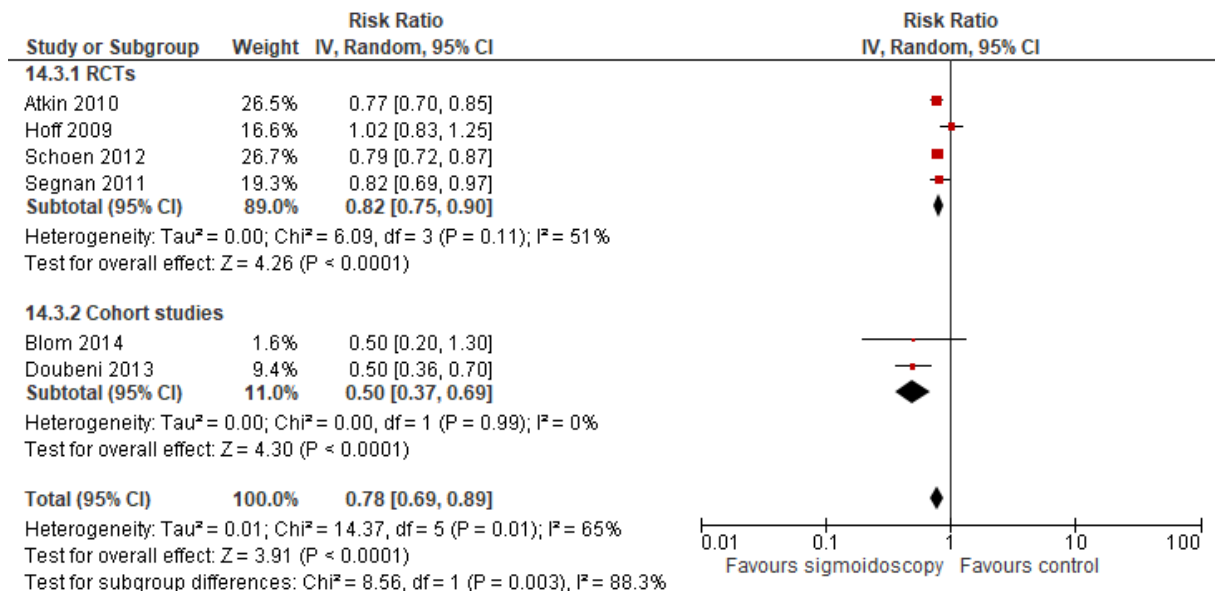
**Figure S20:** Bolland 2015; Intervention/ Exposure: High calcium; Outcome: Vertebral fracture



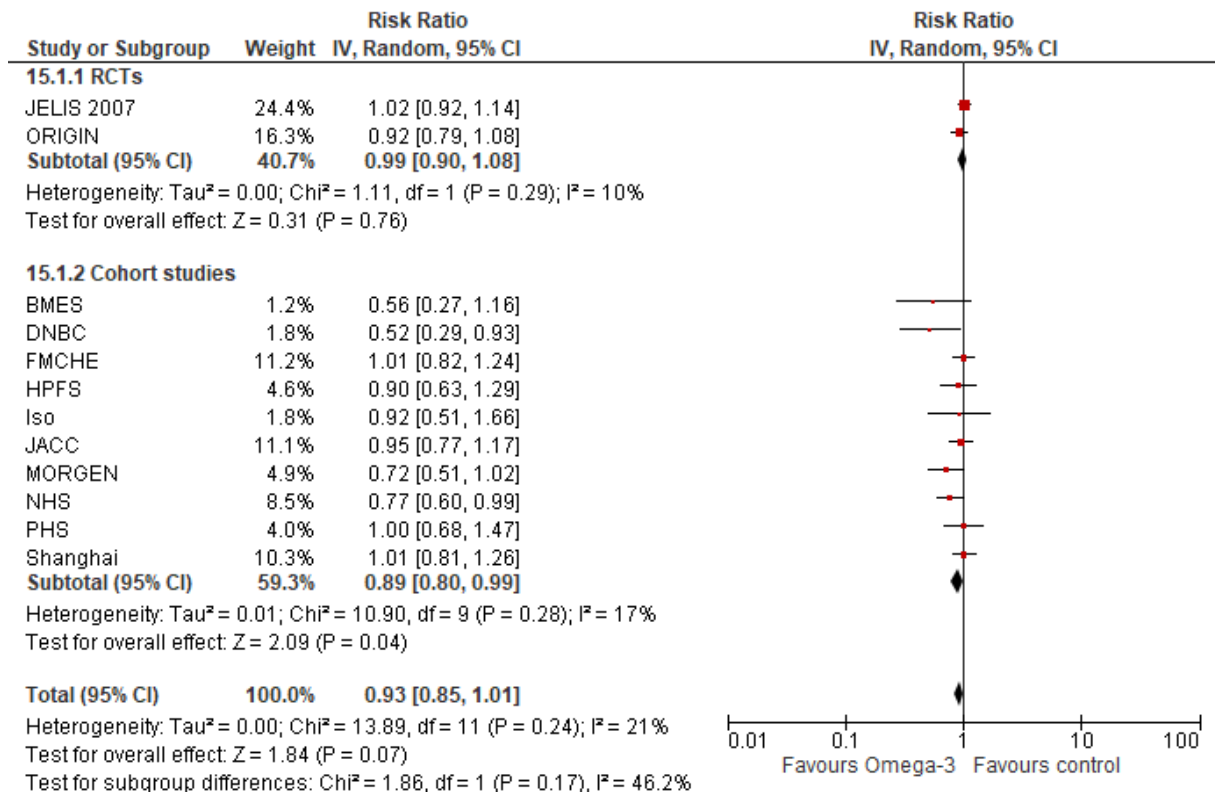
**Figure S21:** Bolland 2015; Intervention/ Exposure: High calcium; Outcome: Hip fracture



**Figure S22:** Brenner 2014; Intervention/ Exposure: Sigmoidoscopy; Outcome: Colorectal cancer mortality

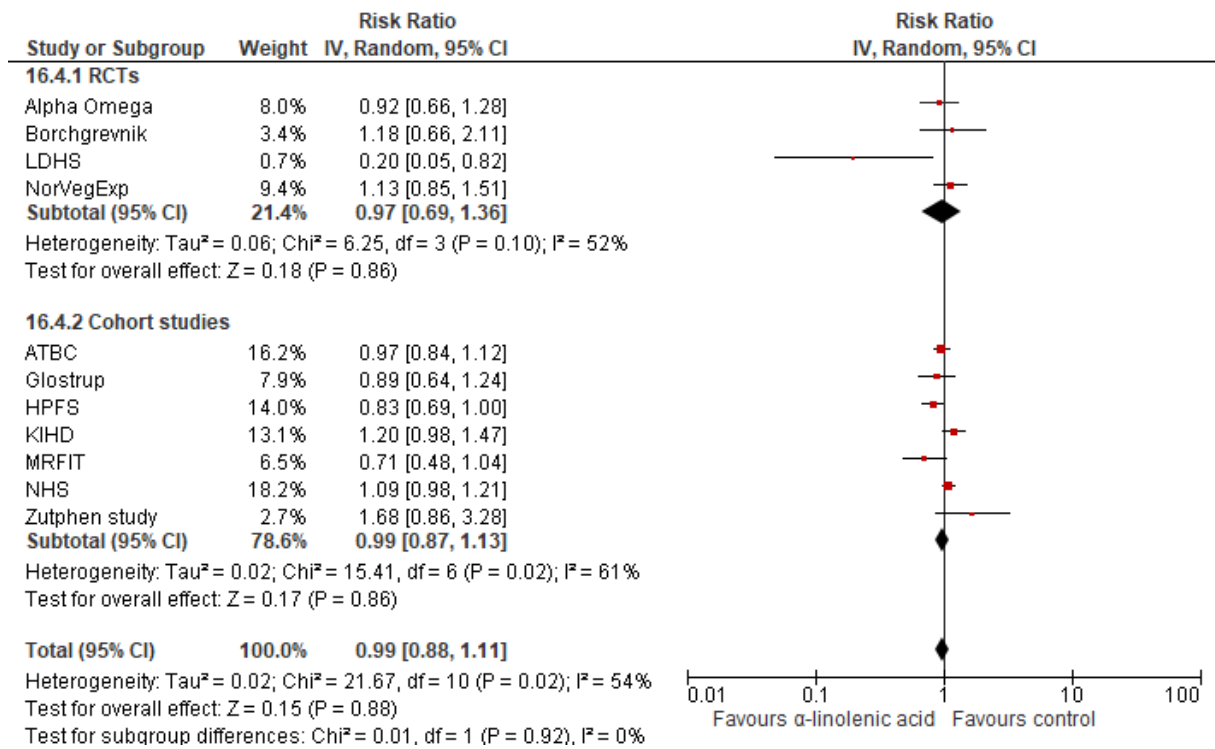


**Figure S23:** Brenner 2014; Intervention/ Exposure: Sigmoidoscopy; Outcome: Colorectal cancer incidence

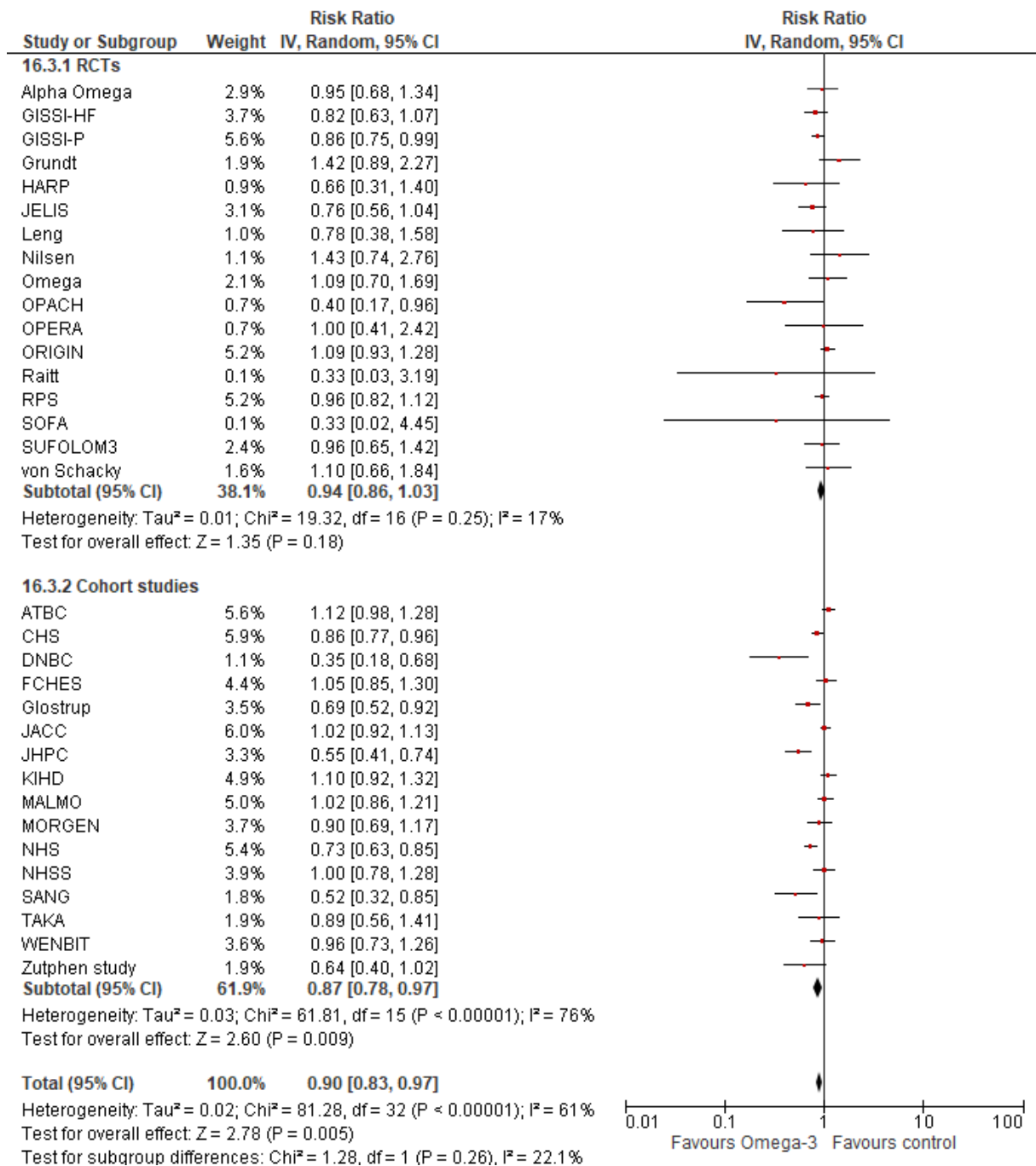


**Figure S24:** Chowdhury 2012; Intervention/ Exposure: High omega-3; Outcome: Cerebrovascular disease

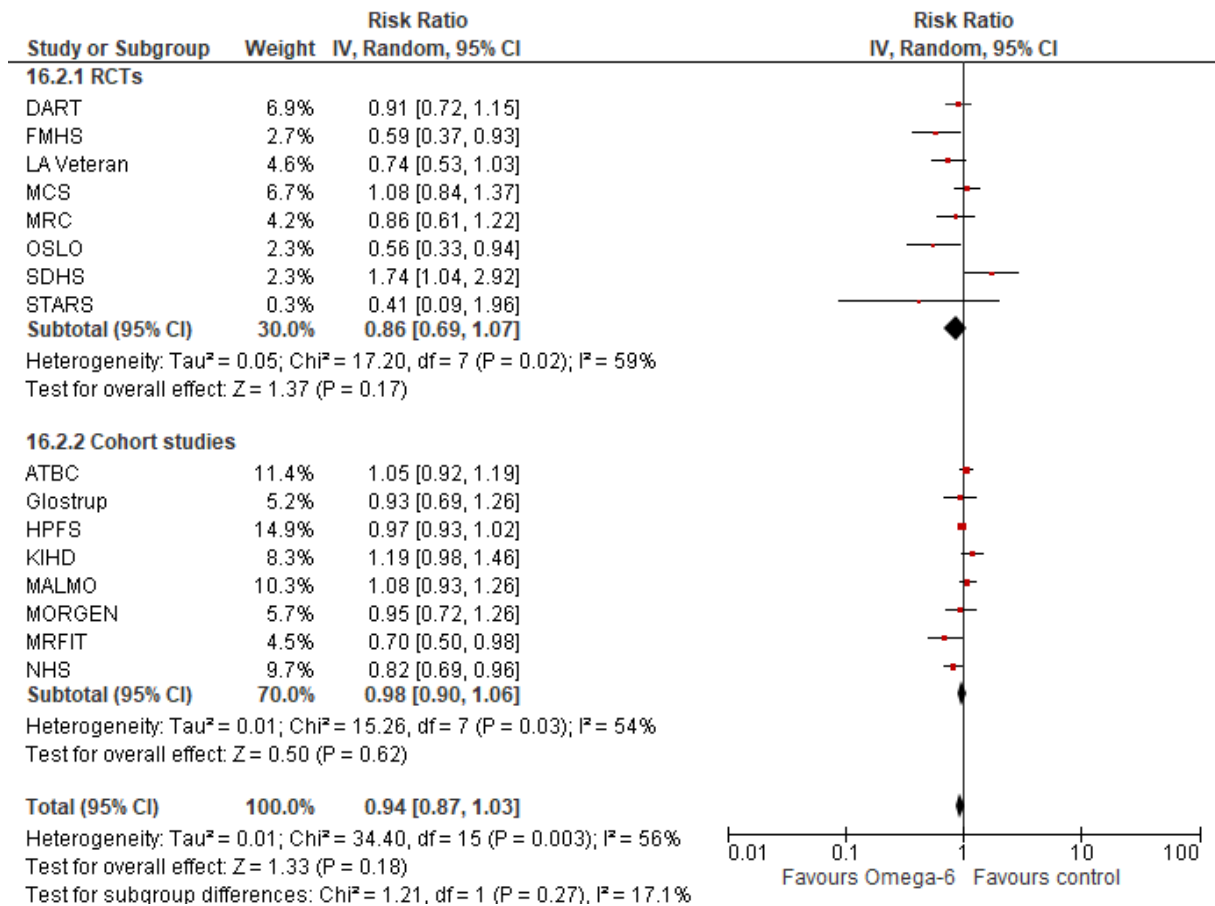




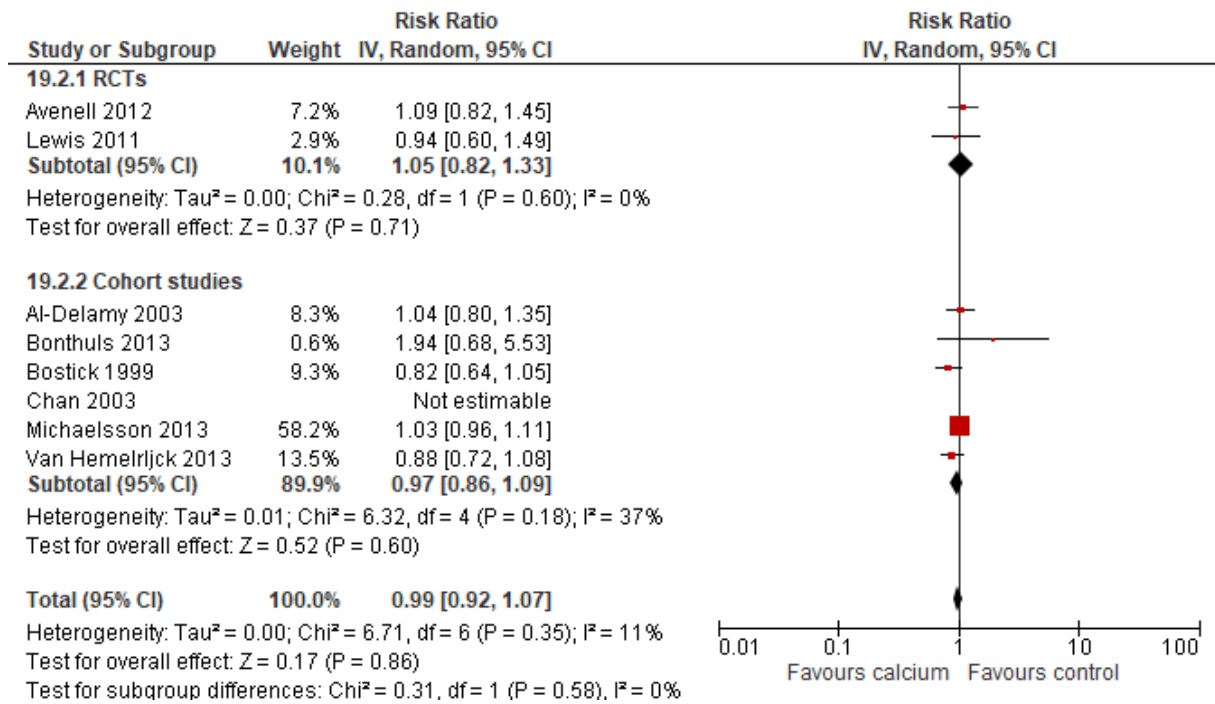
**Figure S25:** Chowdhury 2014a; Intervention/ Exposure: High  $\alpha$ -linolenic acid; Outcome: Coronary heart disease



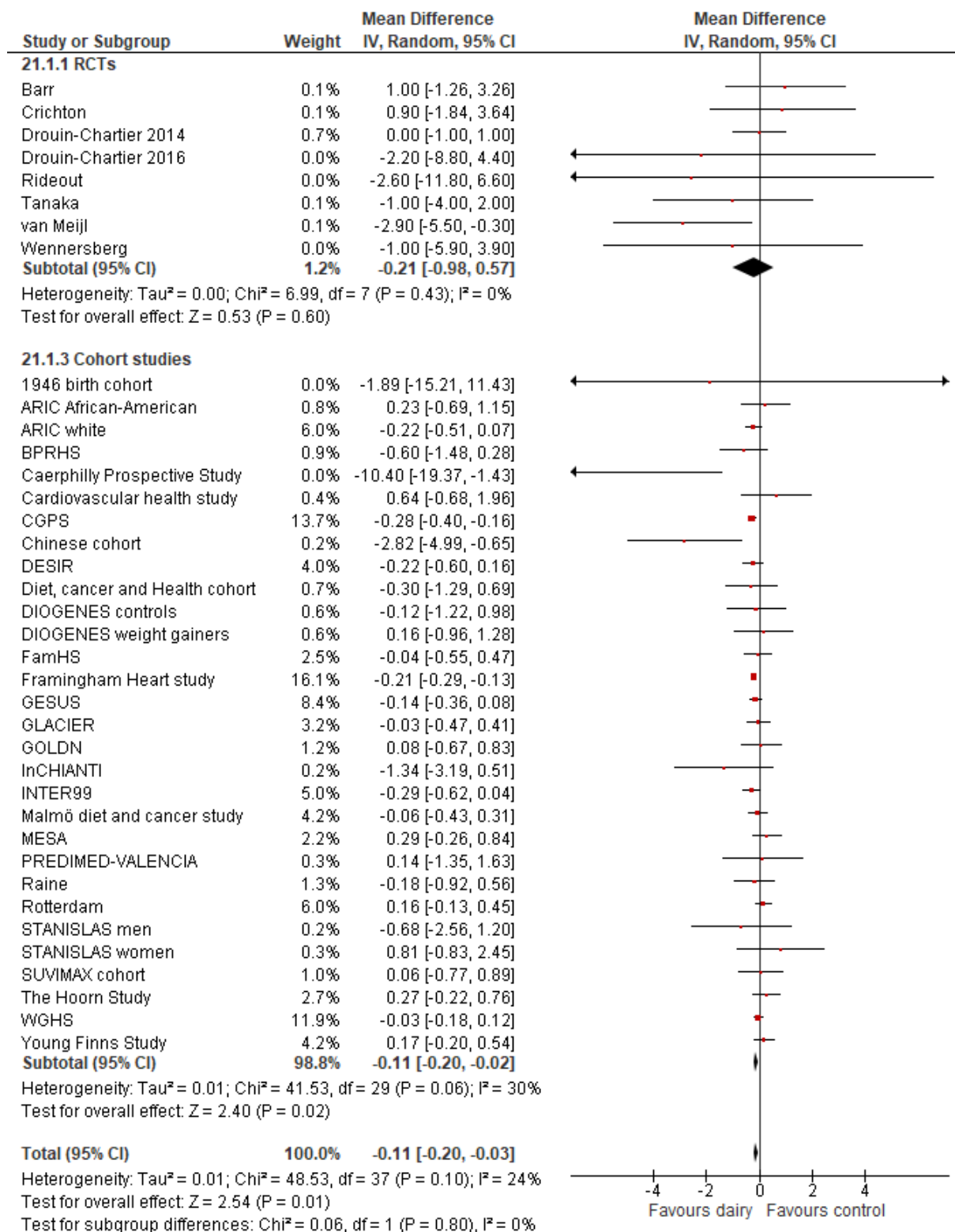
**Figure S26:** Chowdhury 2014a; Intervention/ Exposure: High omega-3; Outcome: Coronary heart disease



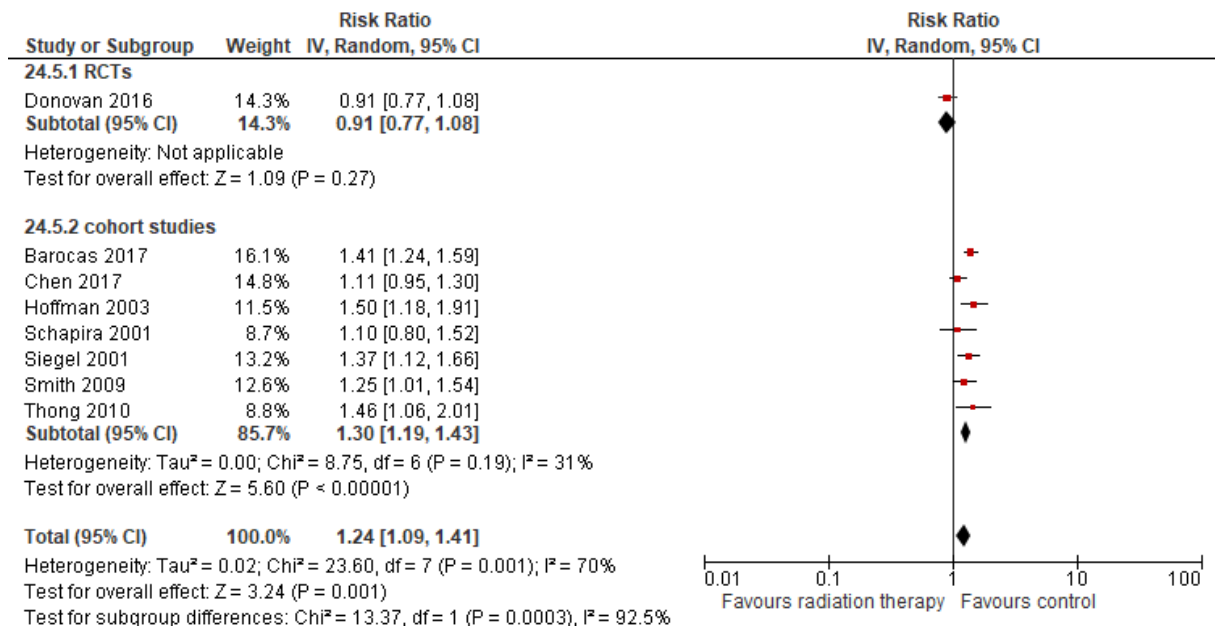
**Figure S27:** Chowdhury 2014a; Intervention/ Exposure: Omega-6; Outcome: Coronary heart disease



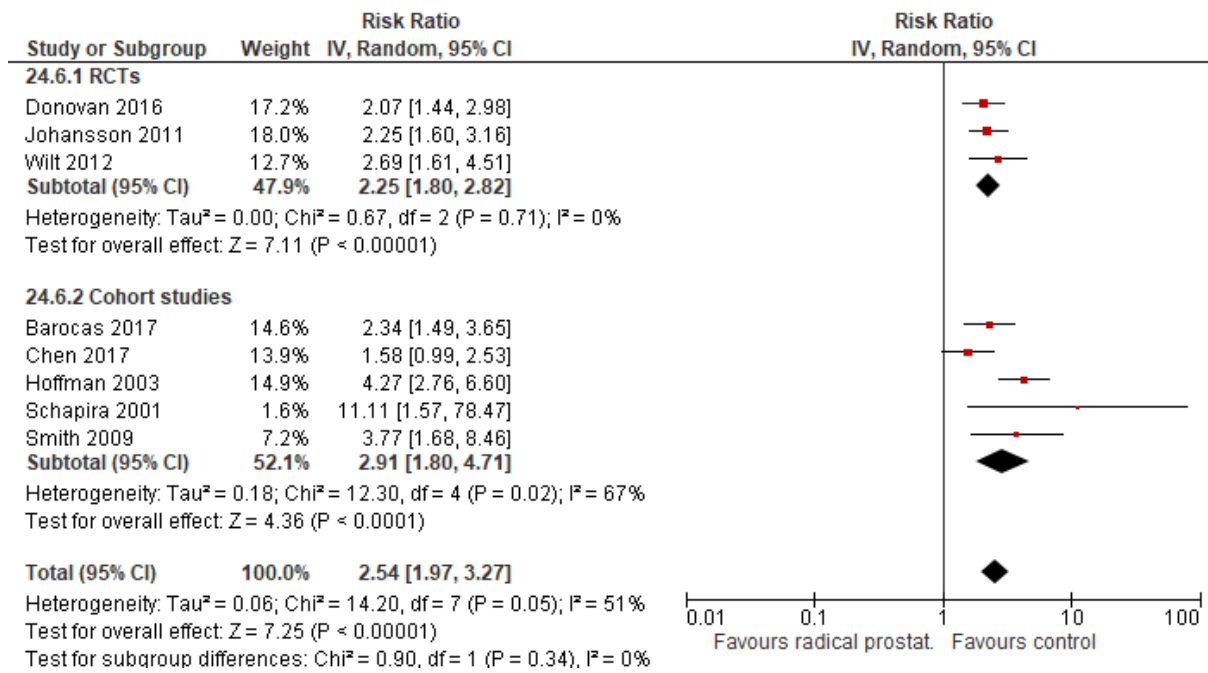
**Figure S28:** Chung 2016; Intervention/ Exposure: High calcium; Outcome: Cardiovascular mortality



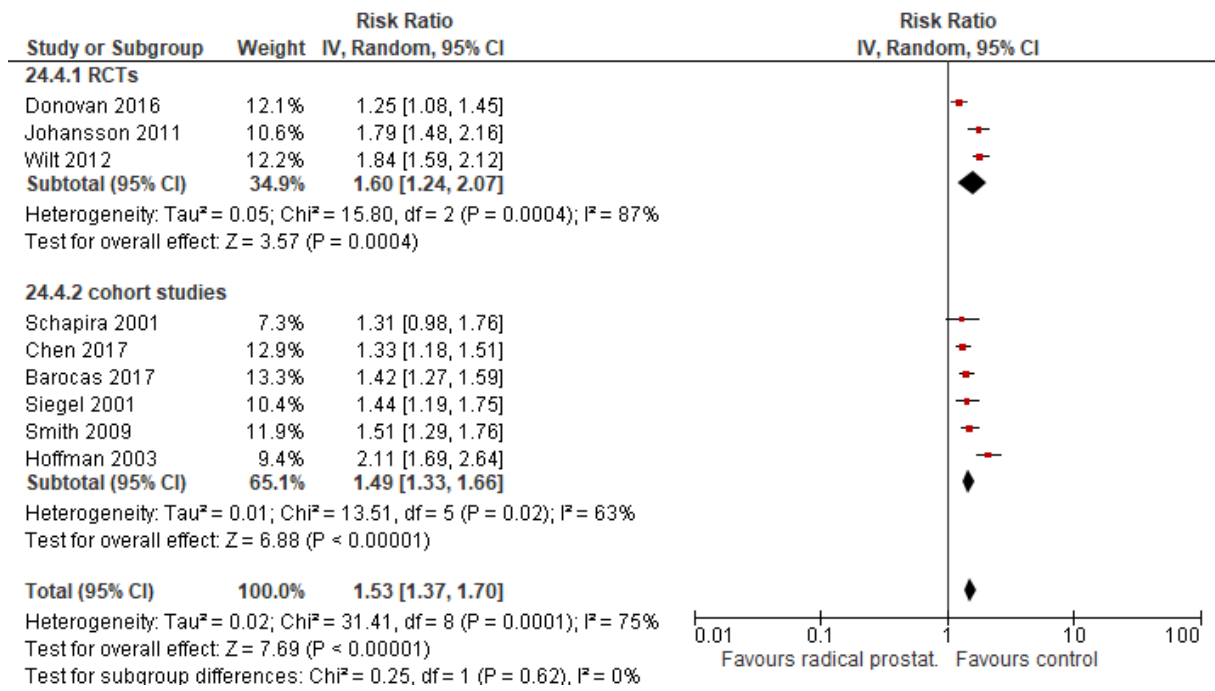
**Figure S29:** Ding 2017; Intervention/ Exposure: High dairy; Outcome: Systolic blood pressure



**Figure S30:** Fenton 2018; Intervention/ Exposure: Radiation therapy; Outcome: Erectile dysfunction

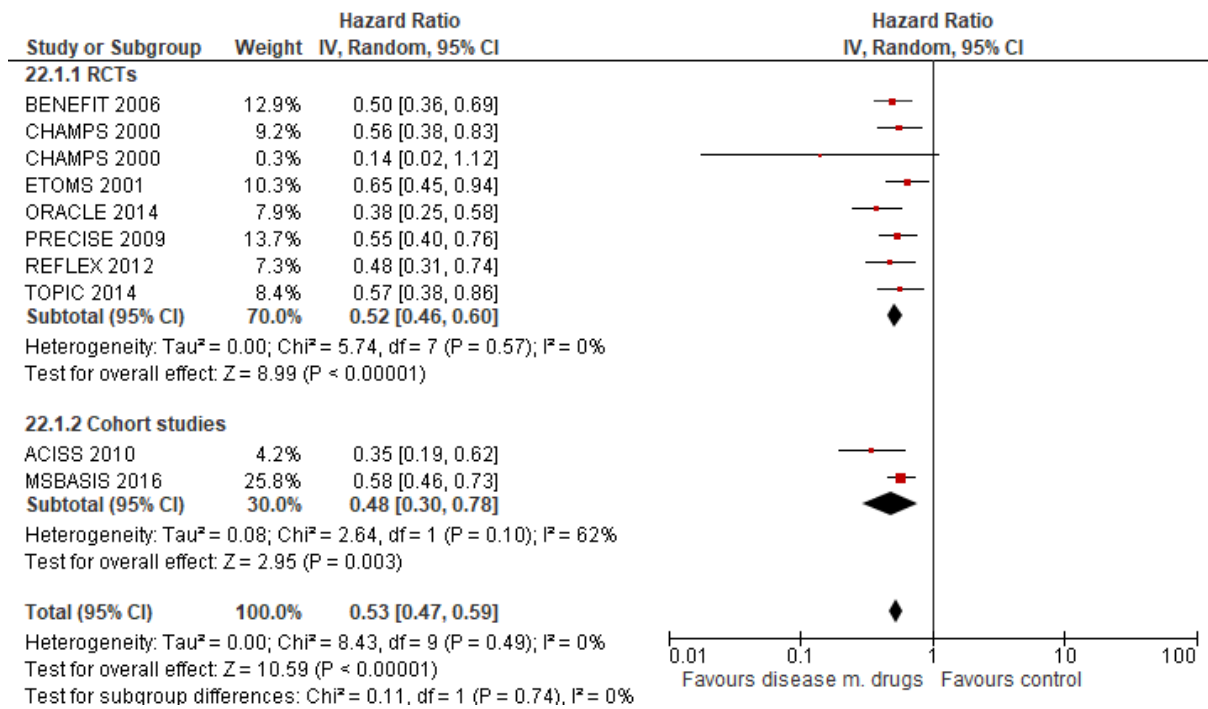


**Figure S31:** Fenton 2018; Intervention/ Exposure: Radical prostatectomy; Outcome: Urinary incontinence

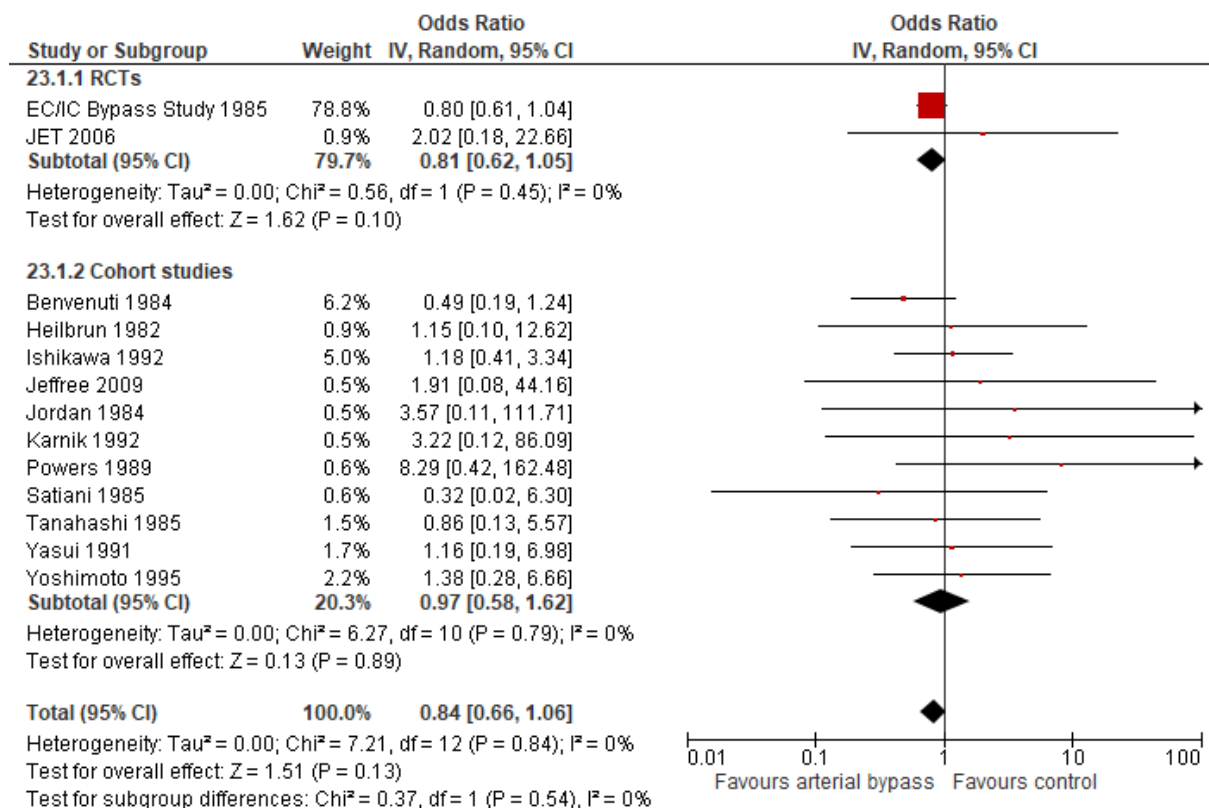


**Figure S32:** Fenton 2018; Intervention/ Exposure: Radical Prostatectomy; Outcome: Erectile dysfunction

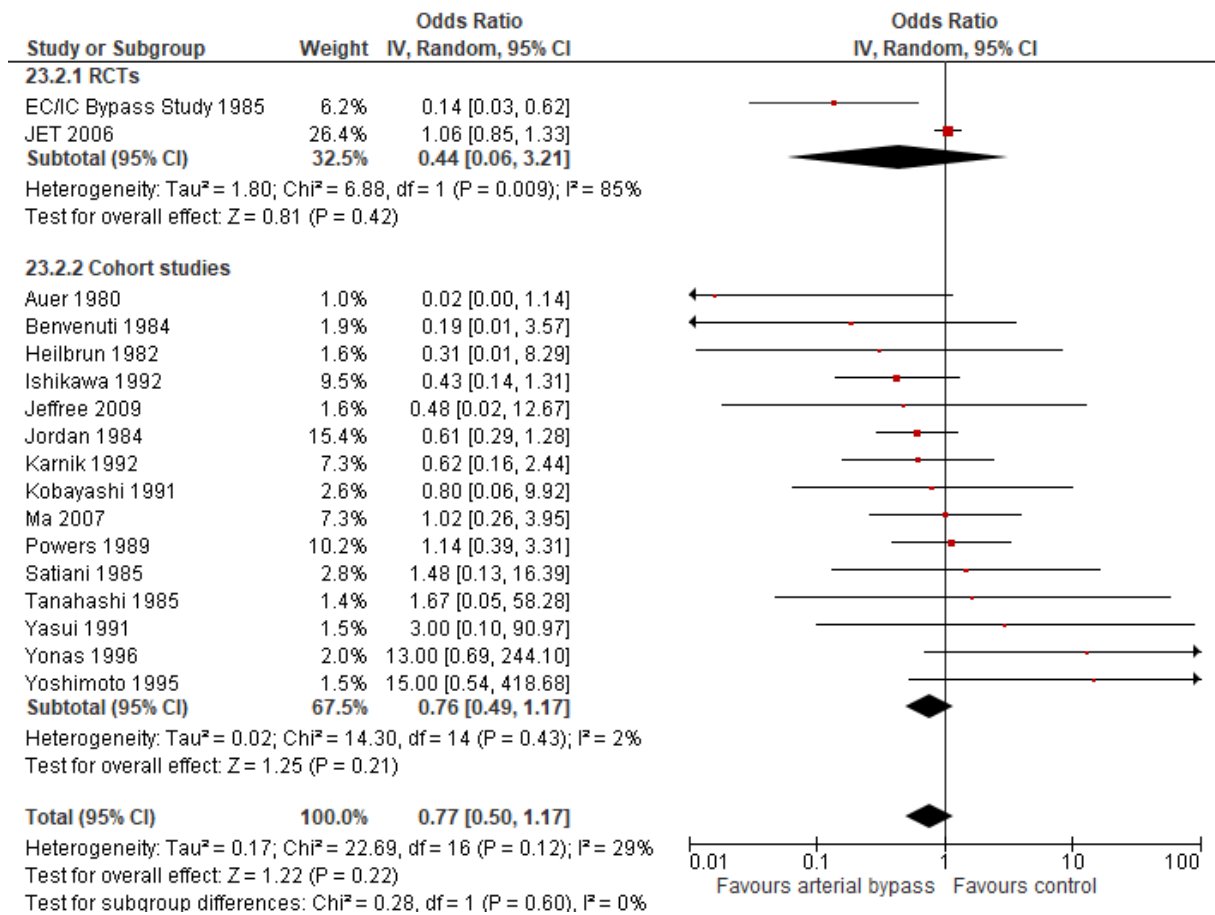




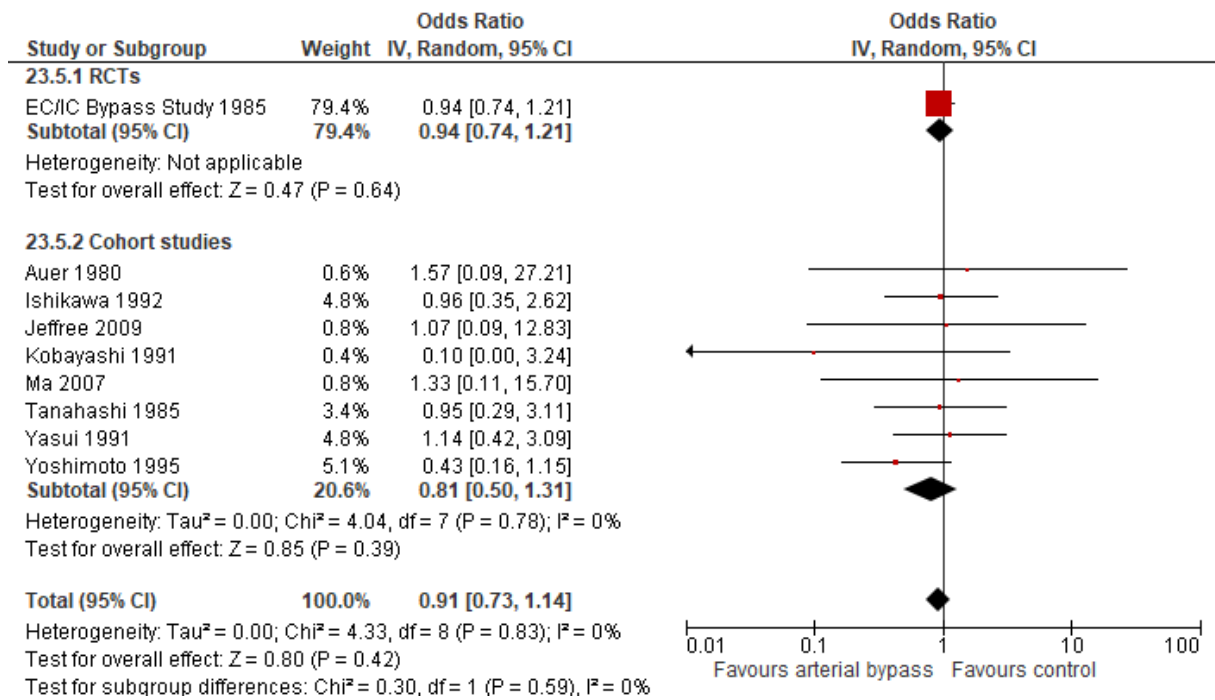
**Figure S33:** Filippini 2017; Intervention/ Exposure: Disease-modifying drugs; Outcome: Conversion to clinically definite multiple sclerosis



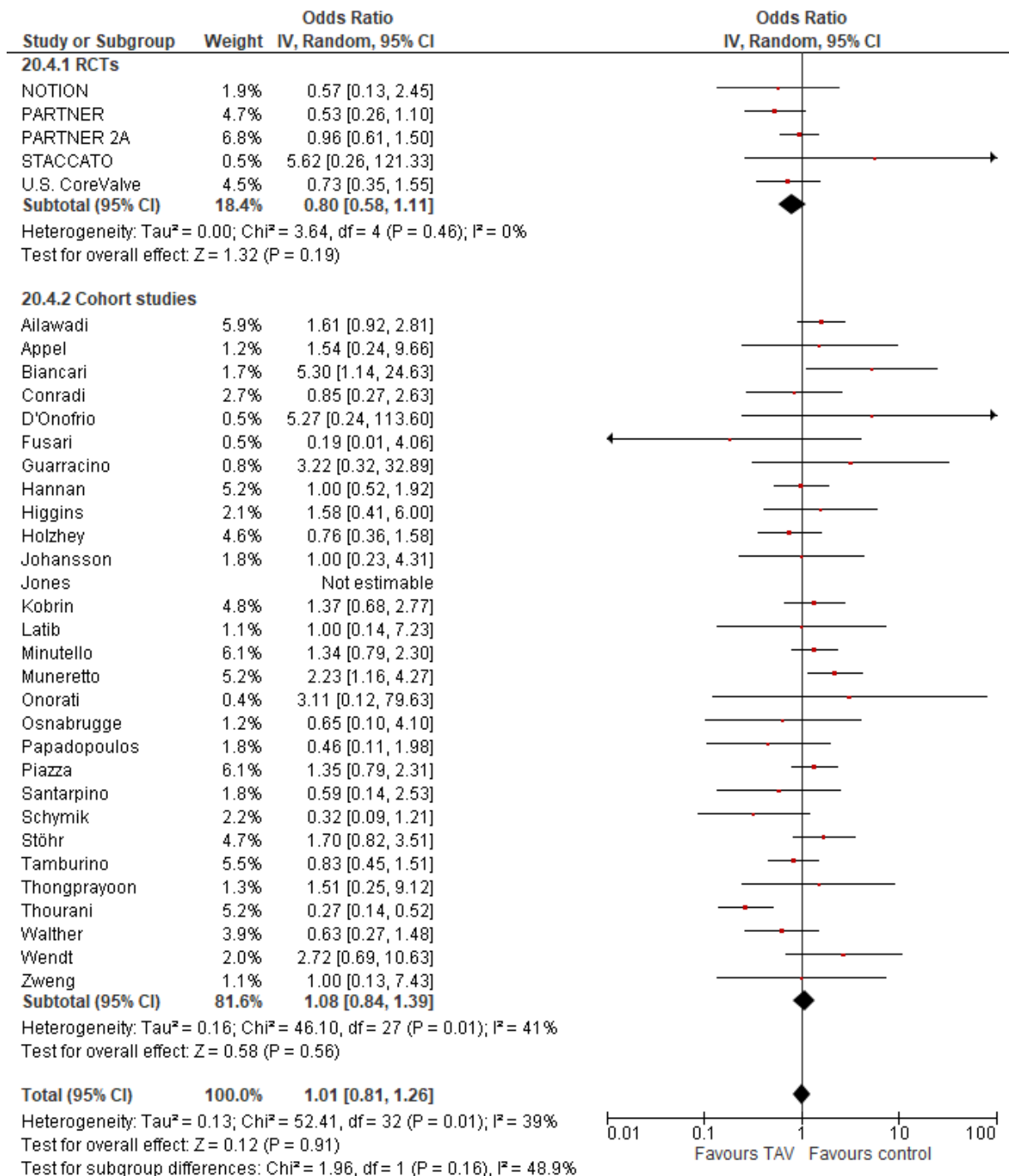
**Figure S34:** Fluri 2010; Intervention/ Exposure: Extracranial-intracranial arterial bypass; Outcome: All-cause mortality



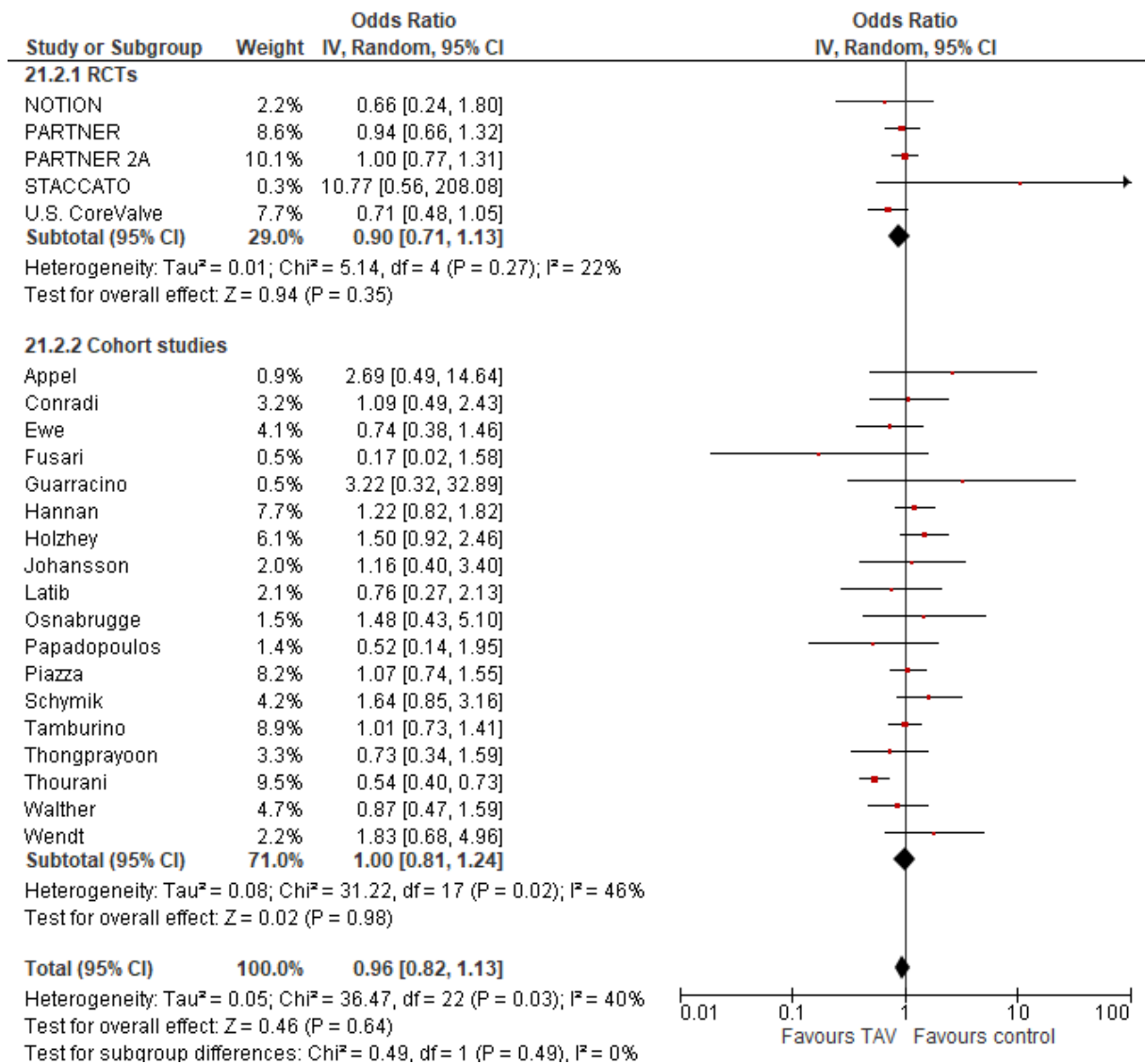
**Figure S35:** Fluri 2010; Intervention/ Exposure: Extracranial-intracranial arterial bypass; Outcome: Stroke



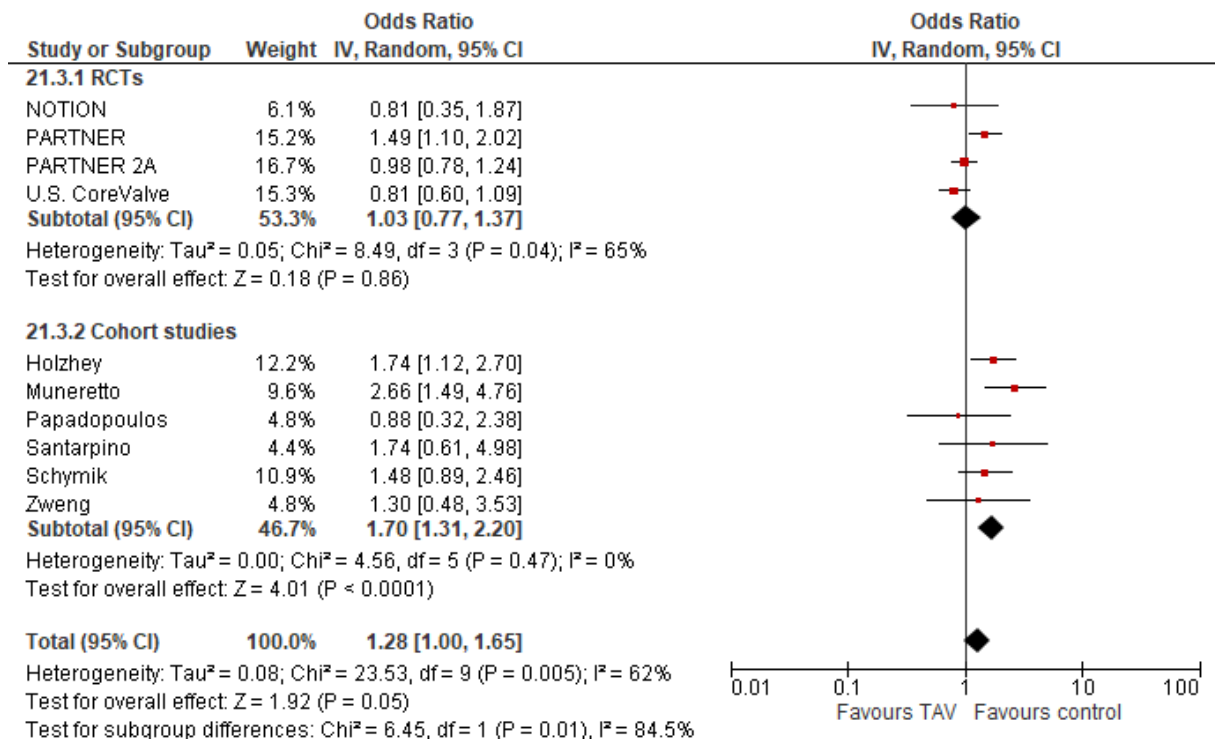
**Figure S36:** Fluri 2010; Intervention/ Exposure: Extracranial-intracranial arterial bypass; Outcome: Stroke mortality or dependency



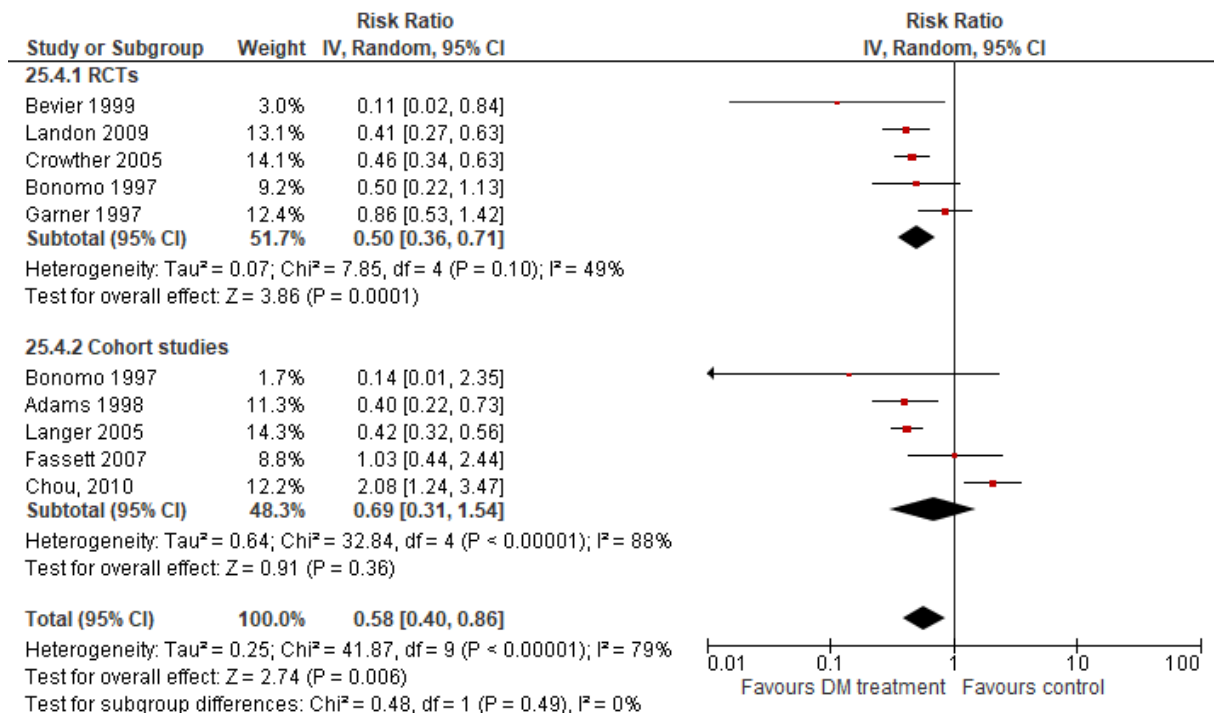
**Figure S37:** Gargiulo 2016; Intervention/ Exposure: Transcatheter aortic valve implantation; Outcome: Early all-cause mortality



**Figure S38:** Gargiulo 2016; Intervention/ Exposure: Transcatheter aortic valve implantation; Outcome: Mid-term all-cause mortality

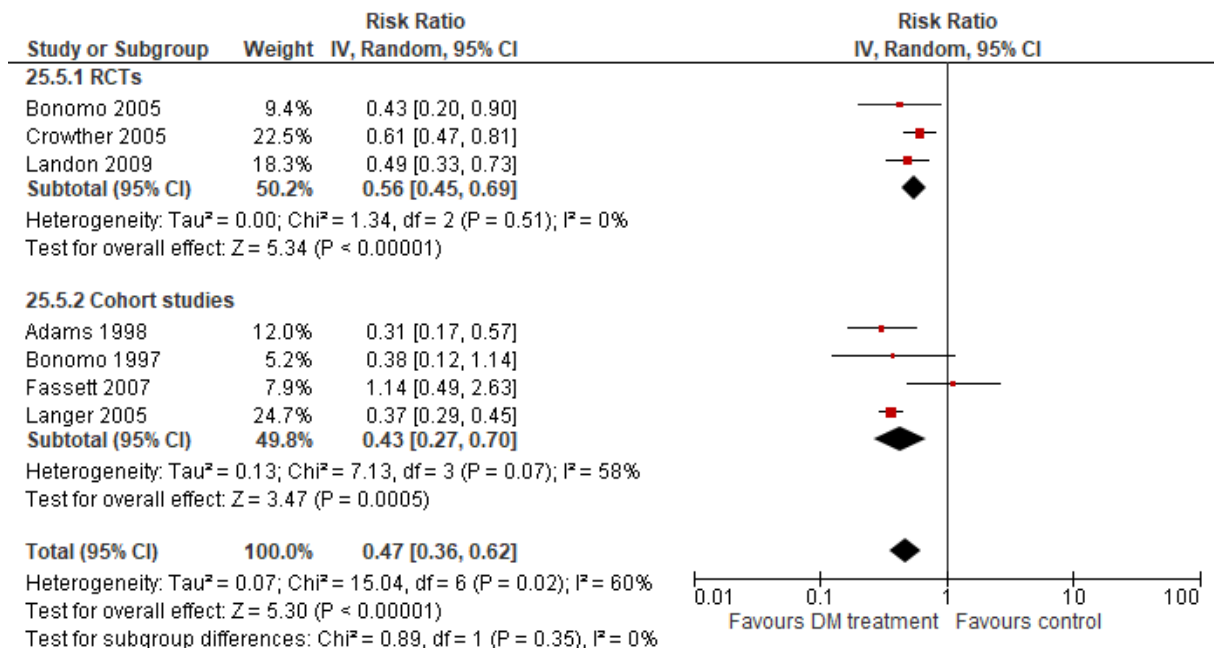


**Figure S39:** Gargiulo 2016; Intervention/ Exposure: Transcatheter aortic valve implantation; Outcome: Long-term all-cause mortality

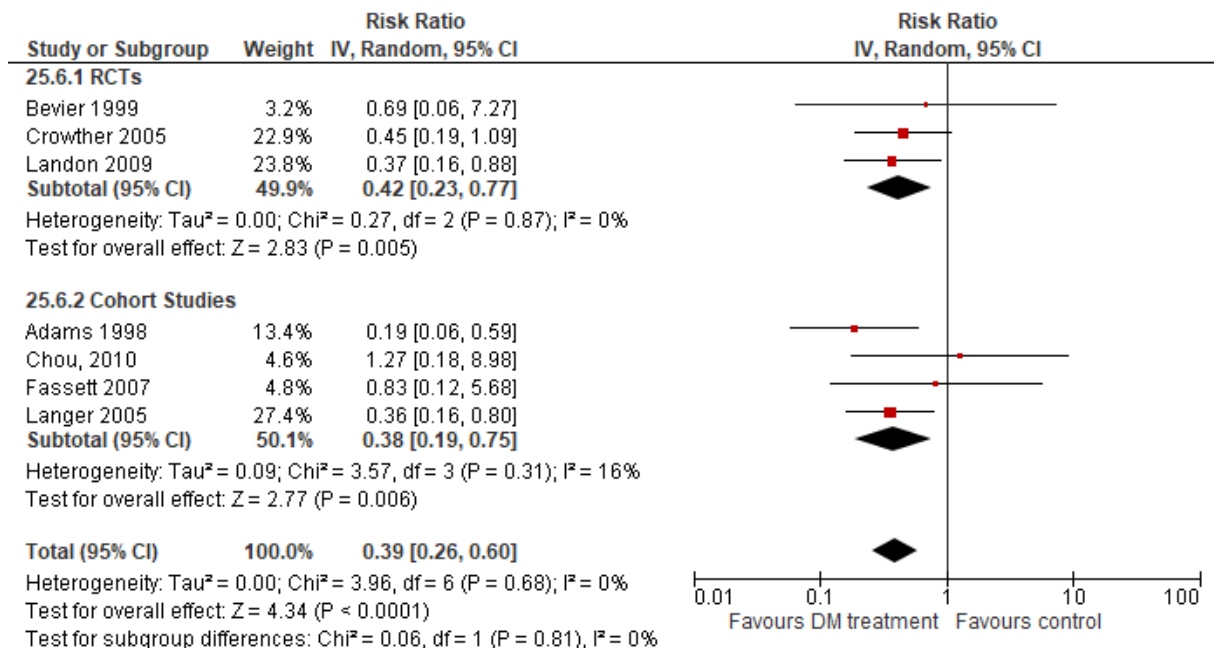


**Figure S40:** Hartling 2013; Intervention/ Exposure: Treating gestational diabetes mellitus; Outcome: High birth weight

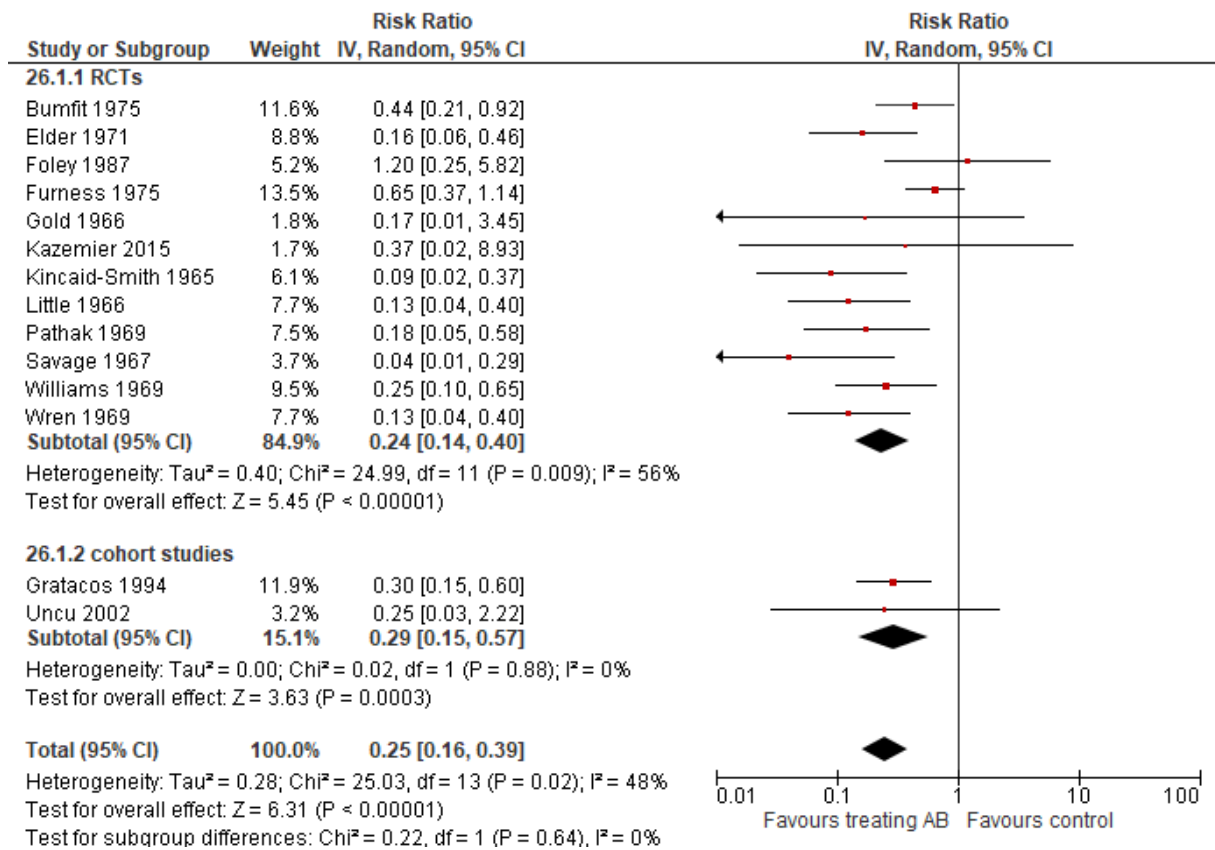




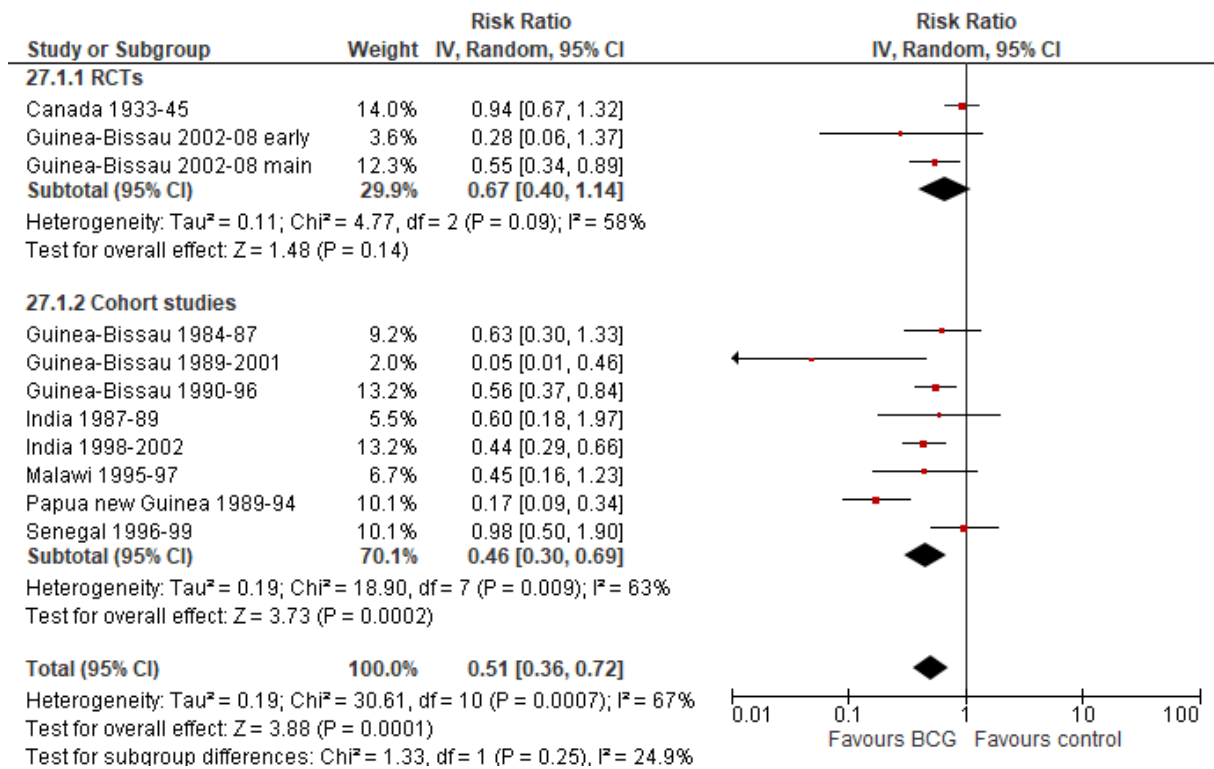
**Figure S41:** Hartling 2013; Intervention/ Exposure: Treating gestational diabetes mellitus; Outcome: Large-for-gestational age neonate



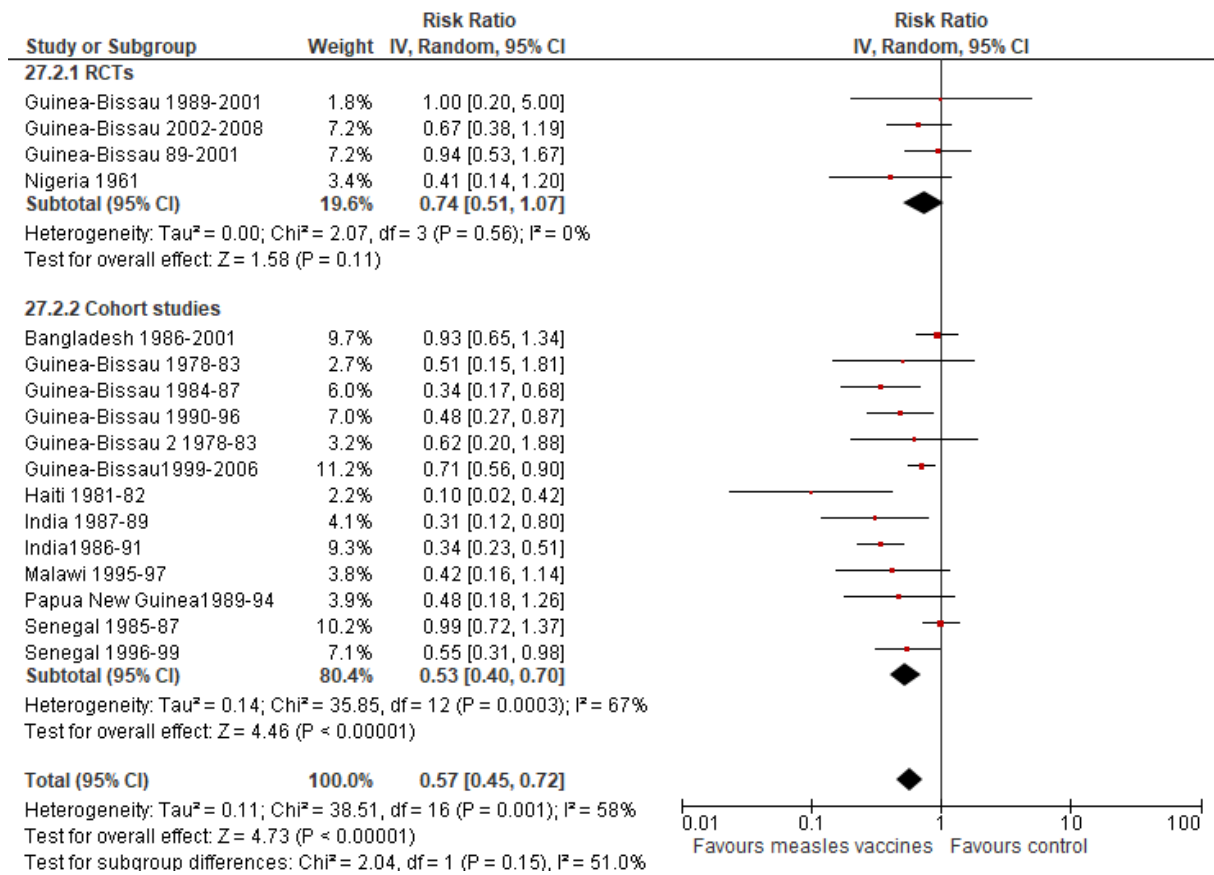
**Figure S42:** Hartling 2013; Intervention/ Exposure: Treating gestational diabetes mellitus; Outcome: Shoulder dystocia



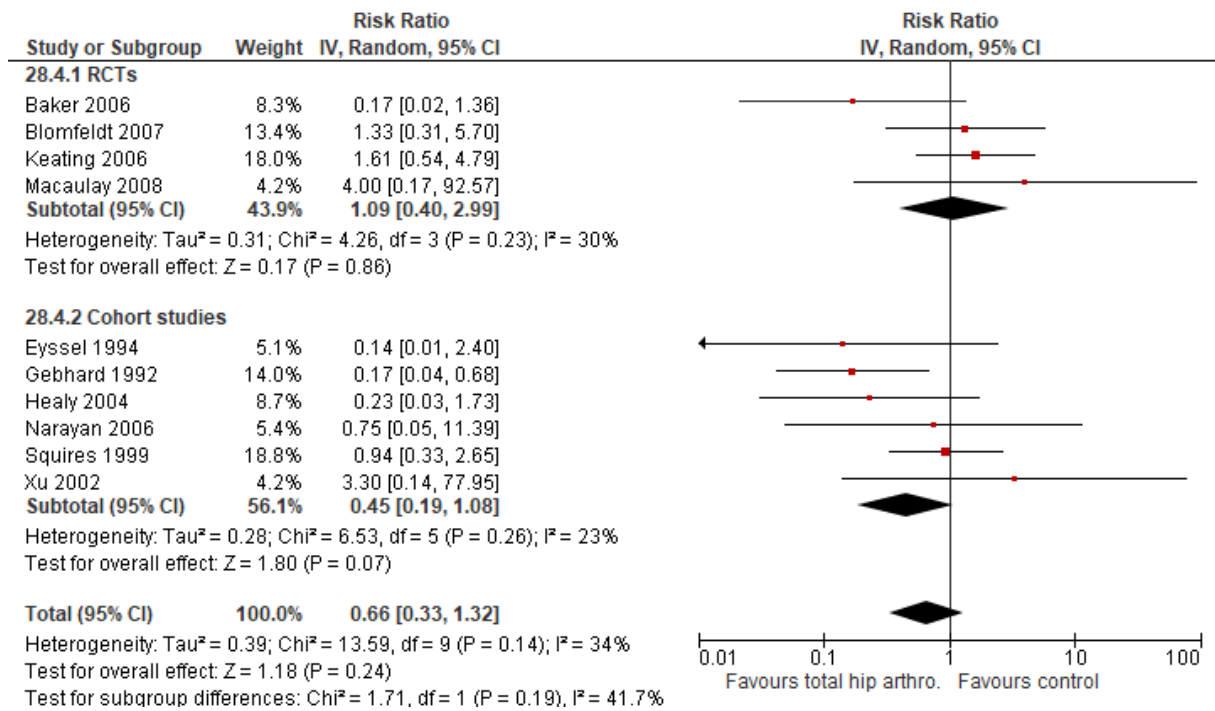
**Figure S43:** Henderson 2019; Intervention/ Exposure: Treating asymptomatic bacteriuria; Outcome: Pyelonephritis



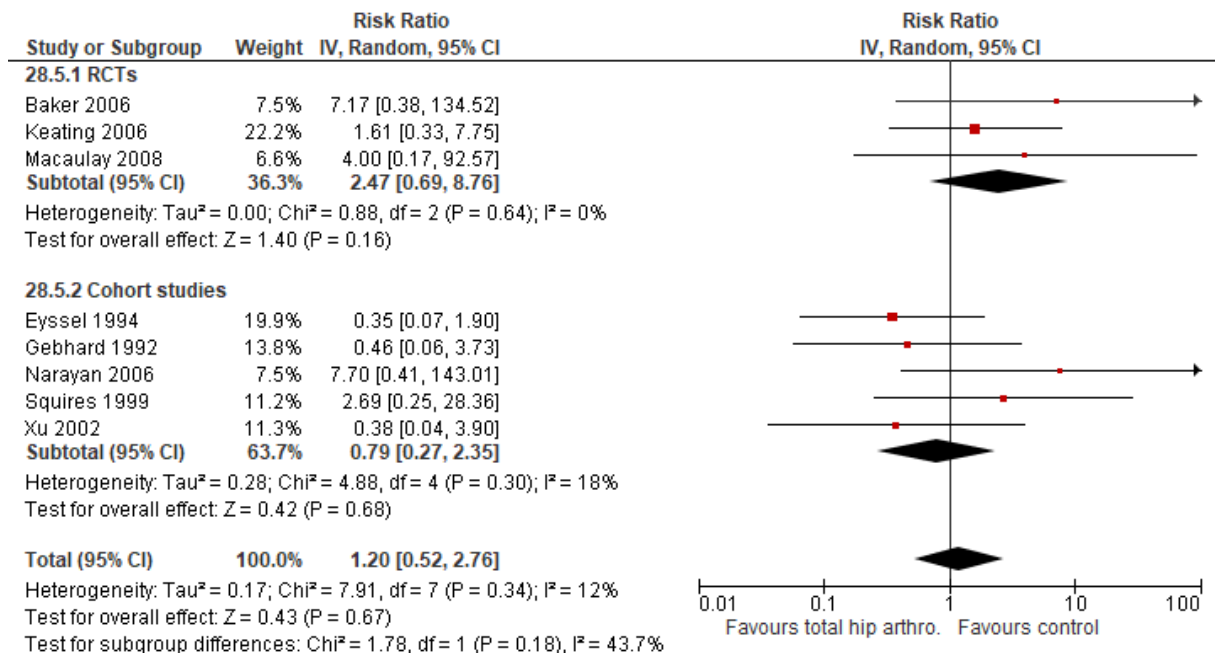
**Figure S44:** Higgins 2016; Intervention/ Exposure: Bacillus Calmette-Guérin vaccination; Outcome: All-cause mortality



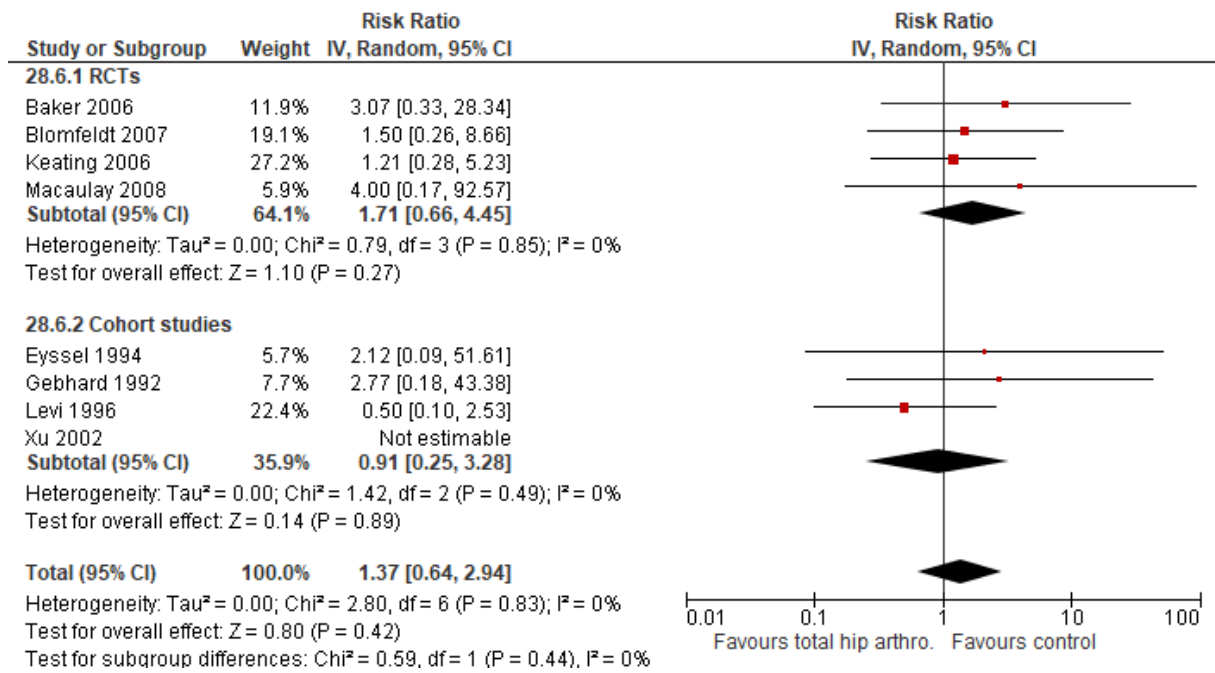
**Figure S45:** Higgins 2016; Intervention/ Exposure: Measles containing vaccines; Outcome: All-cause mortality



**Figure S46:** Hopley 2010; Intervention/ Exposure: Total hip arthroplasty; Outcome: Reoperation

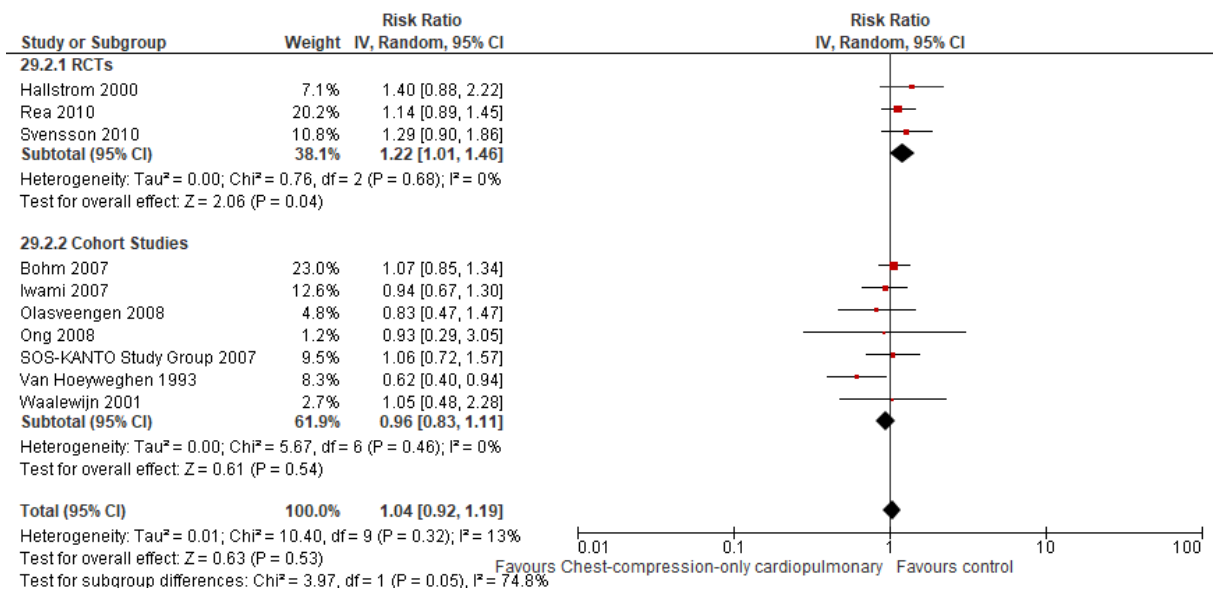


**Figure S47:** Hopley 2010; Intervention/ Exposure: Total hip arthroplasty; Outcome: Dislocation

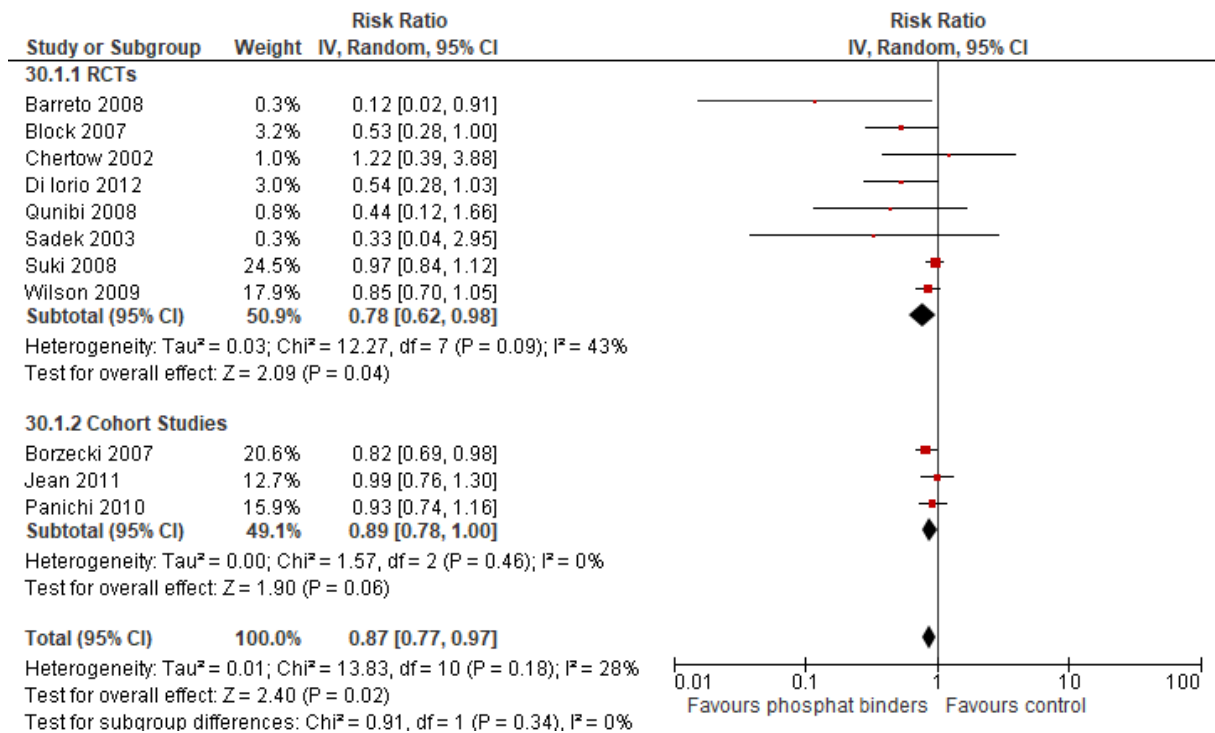


**Figure S48:** Hopley 2010; Intervention/ Exposure: Total hip arthroplasty; Outcome: Deep infection

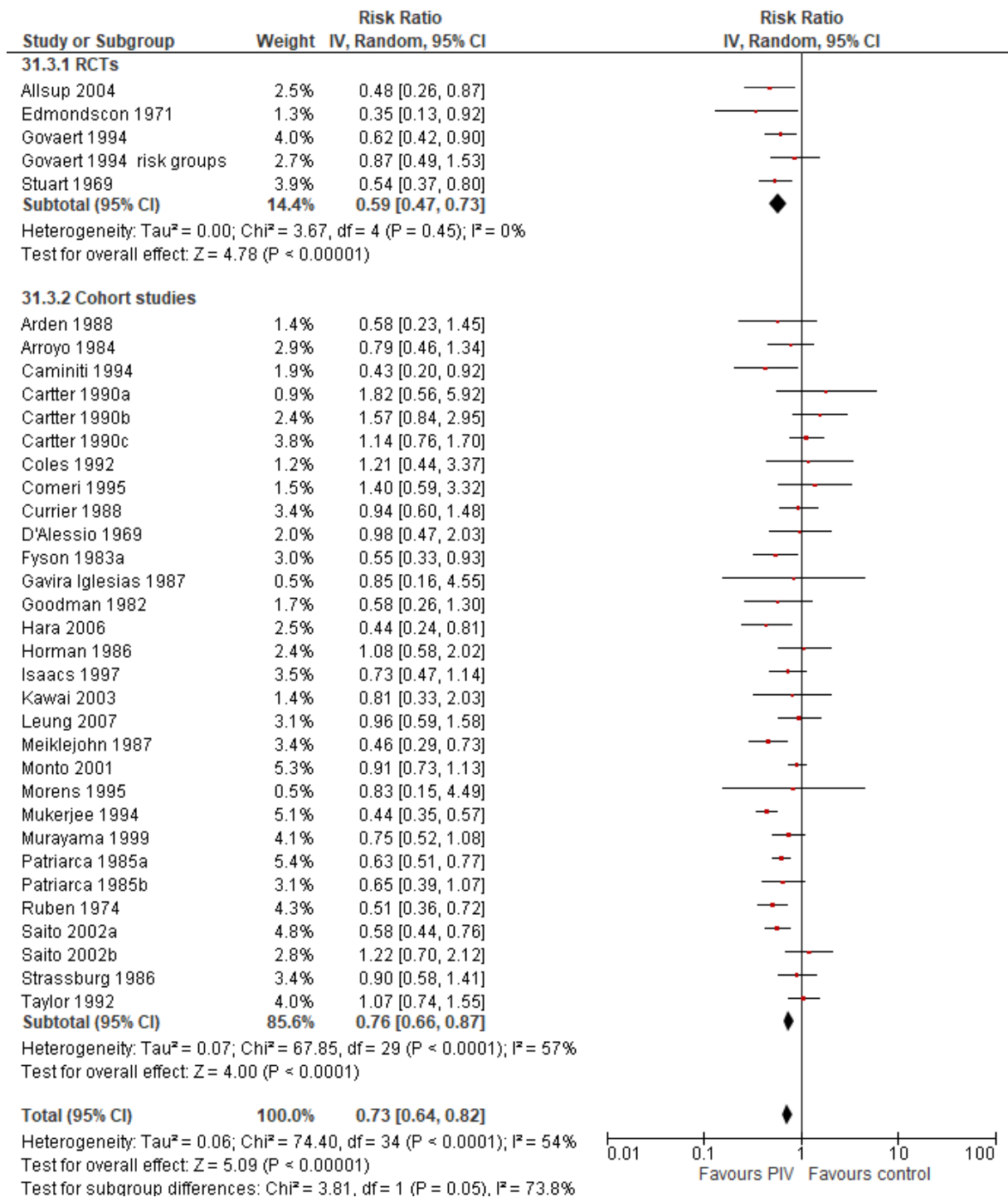




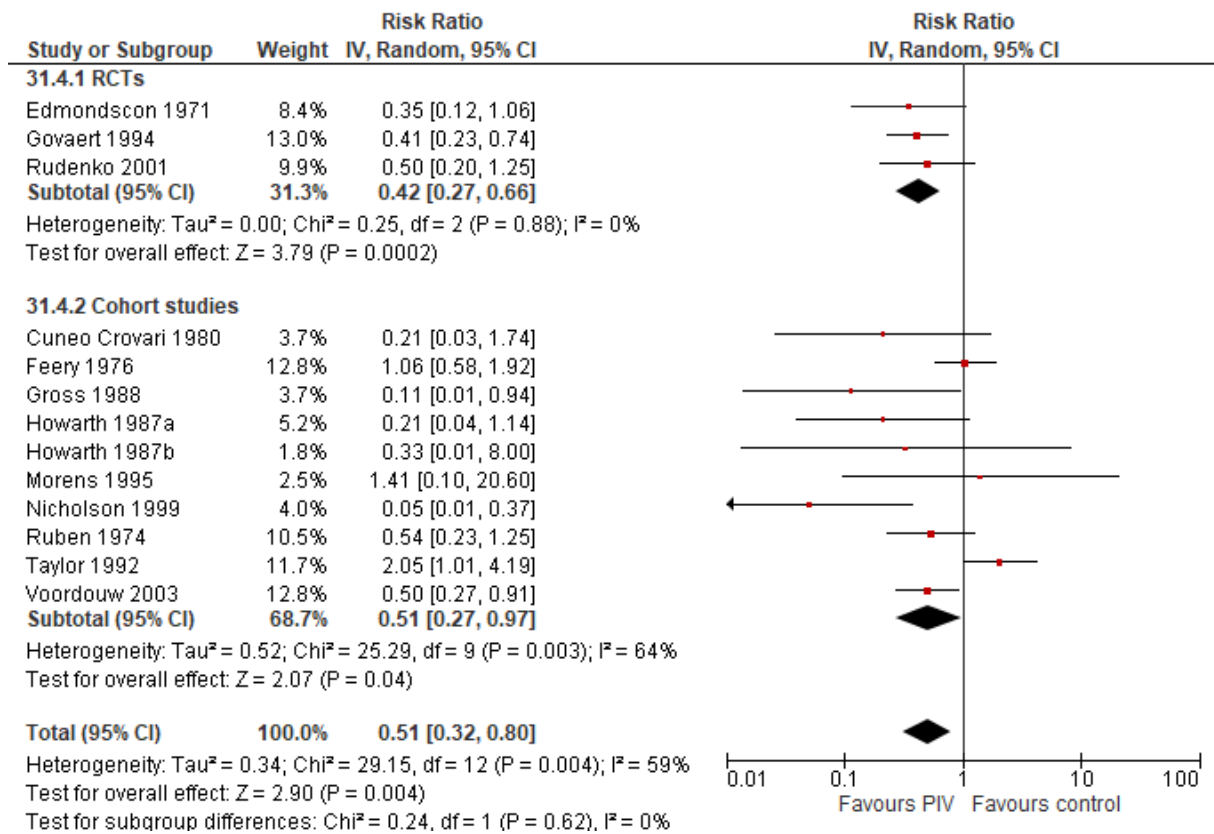
**Figure S49:** Hüpfl 2010; Intervention/ Exposure: Chest-compression-only cardiopulmonary resuscitation; Outcome: Survival (Risk Ratio >1 indicates a favorable effect)



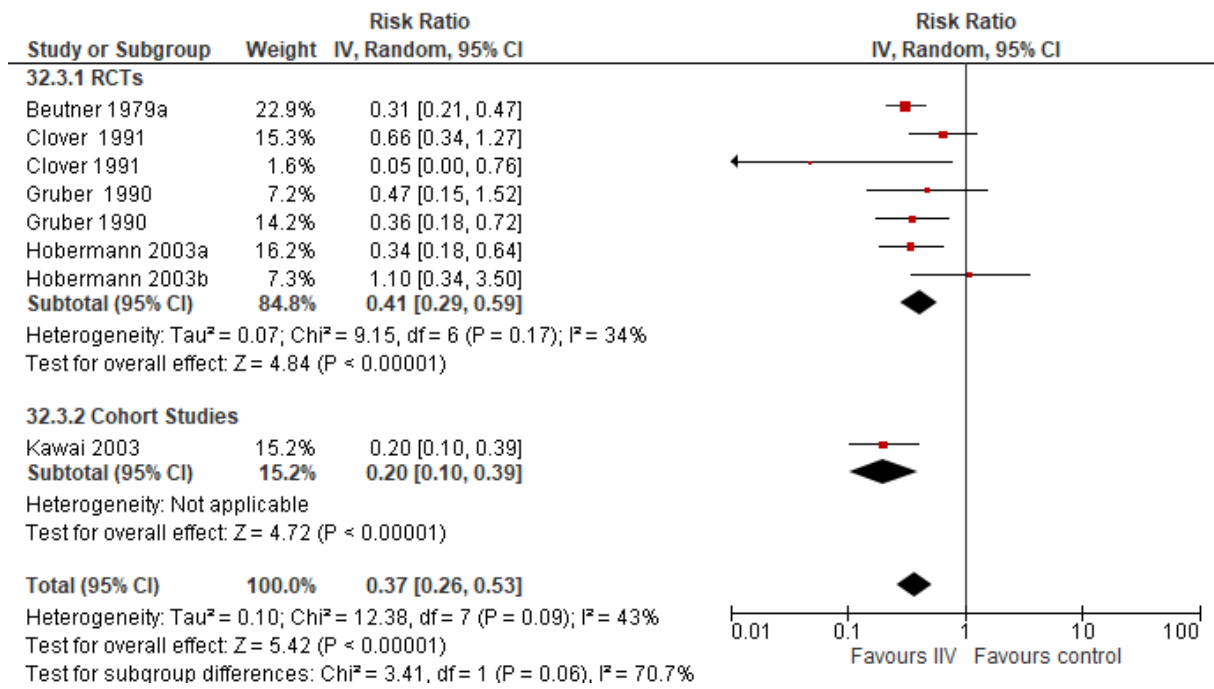
**Figure S50:** Jamal 2013; Intervention/ Exposure: Non-calcium-based phosphat binders; Outcome: All-cause mortality



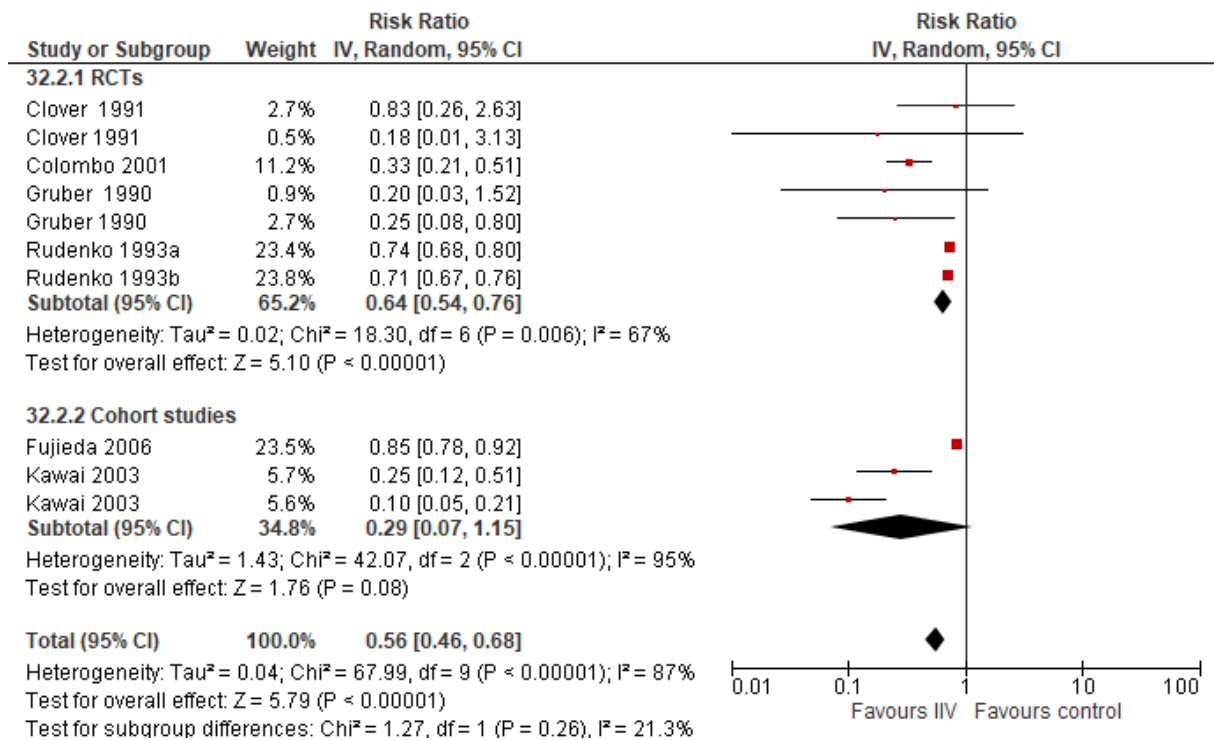
**Figure S51:** Jefferson 2010; Intervention/ Exposure: Parenteral influenza vaccine; Outcome: Influenza-like illness



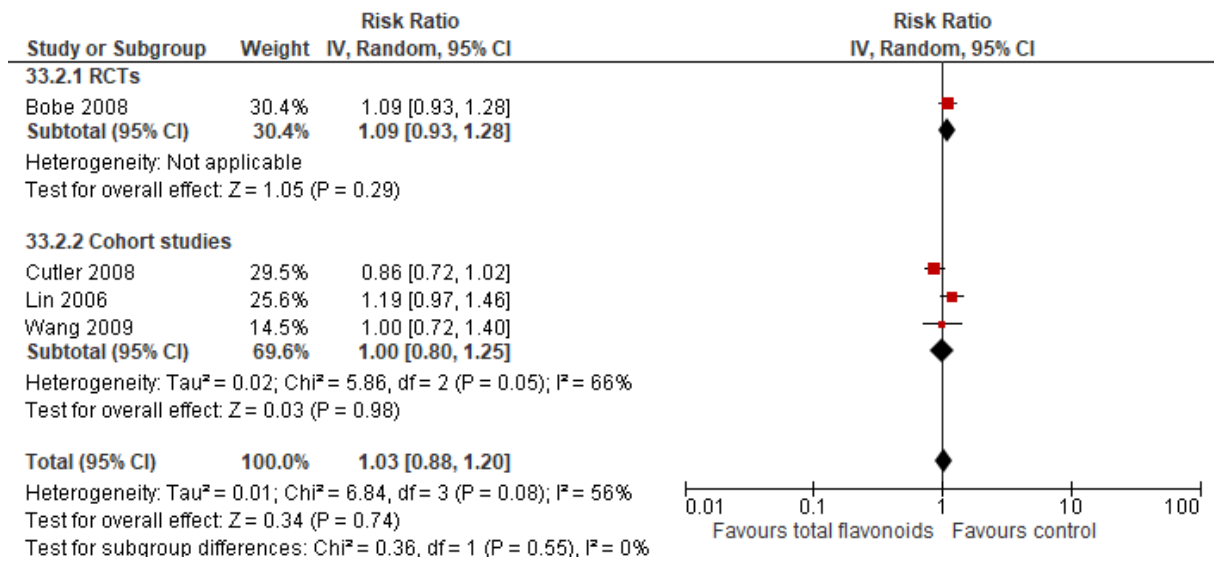
**Figure S52:** Jefferson 2010; Intervention/ Exposure: Parenteral influenza vaccine; Outcome: Influenza



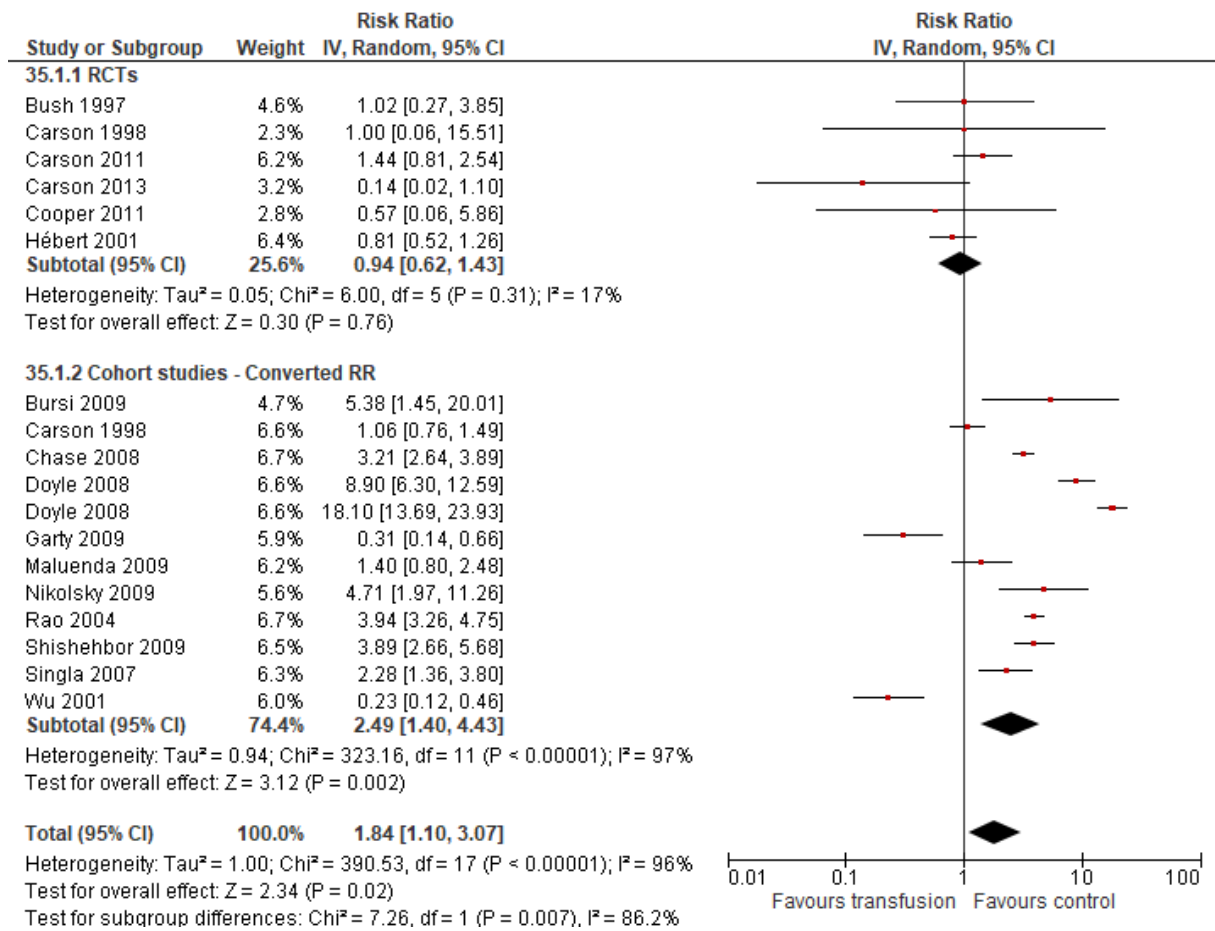
**Figure S53:** Jefferson 2012; Intervention/ Exposure: Inactivated influenza vaccines; Outcome: Influenza



**Figure S54:** Jefferson 2012; Intervention/ Exposure: Inactivated influenza vaccines; Outcome: Influenza-like illness

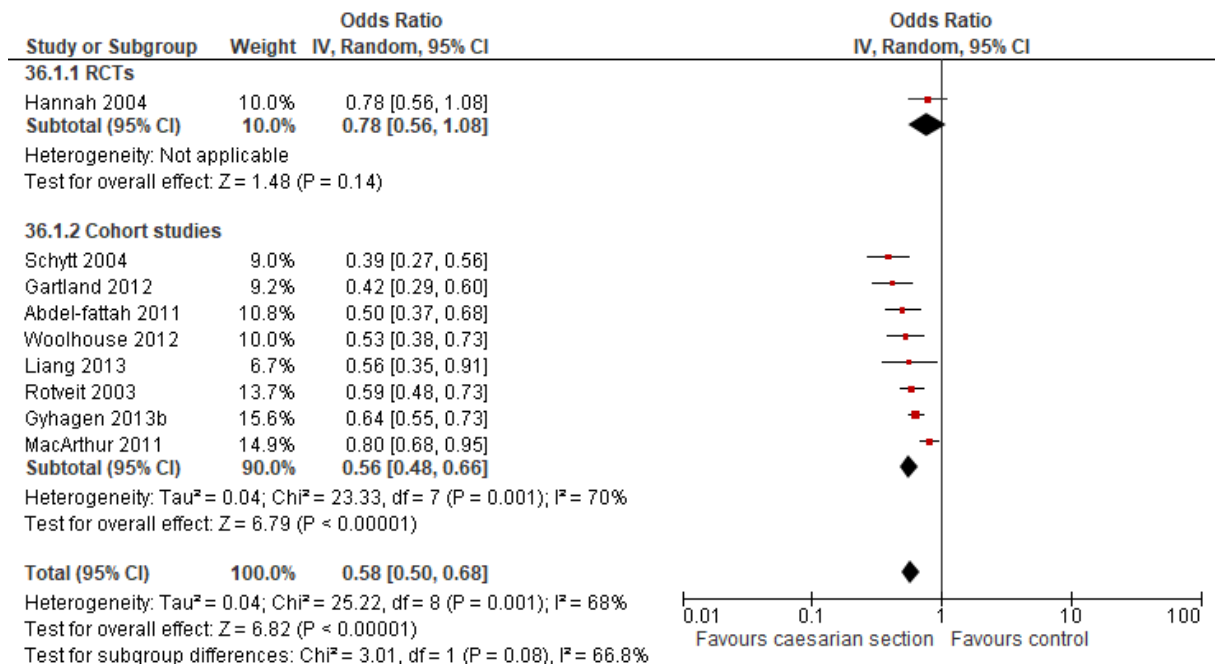


**Figure S55:** Jin 2012; Intervention/ Exposure: High total flavonoids; Outcome: Colorectal neoplasms

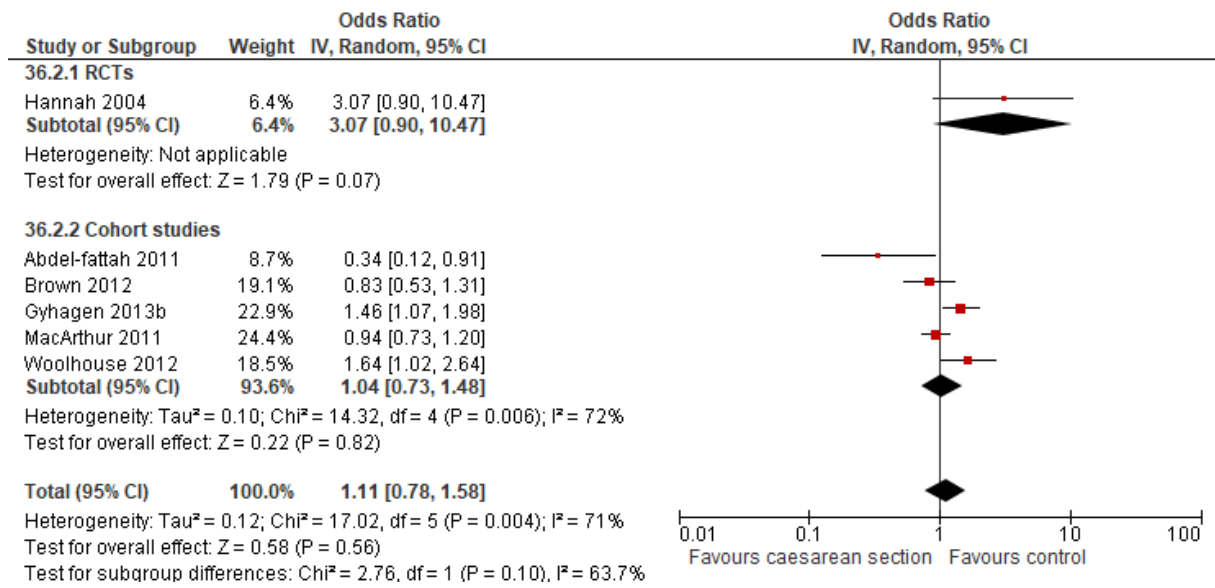


**Figure S56:** Kansagara 2013; Intervention/ Exposure: Transfusion; Outcome: All-cause mortality

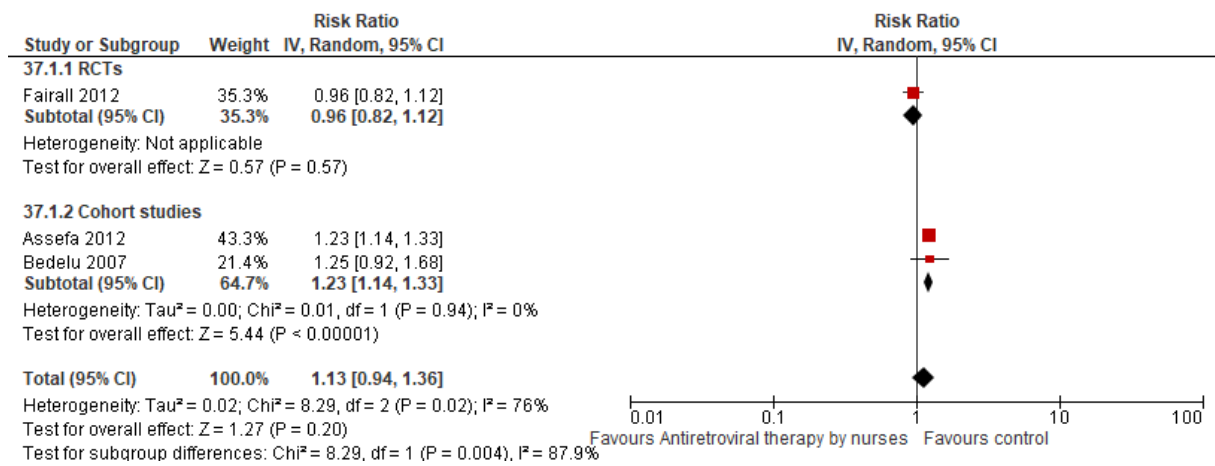




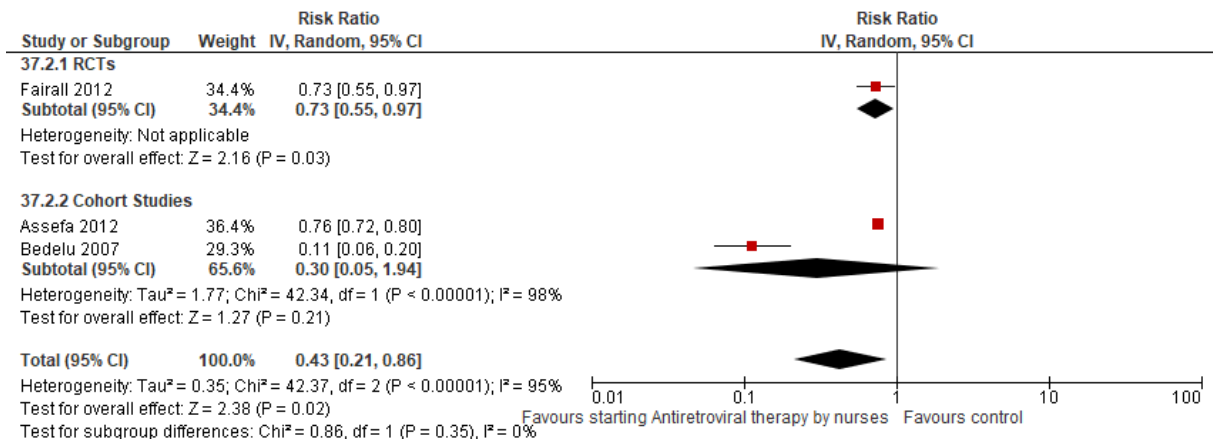
**Figure S57:** Keag 2018; Intervention/ Exposure: Caesarean section; Outcome: Urinary incontinence



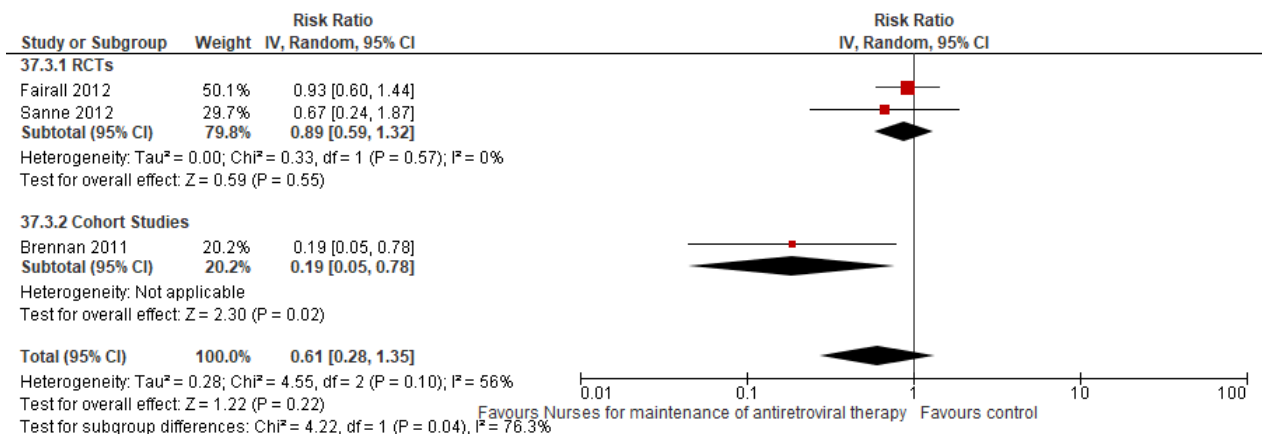
**Figure S58:** Keag 2018; Intervention/ Exposure: Caesarean section; Outcome: Fecal incontinence



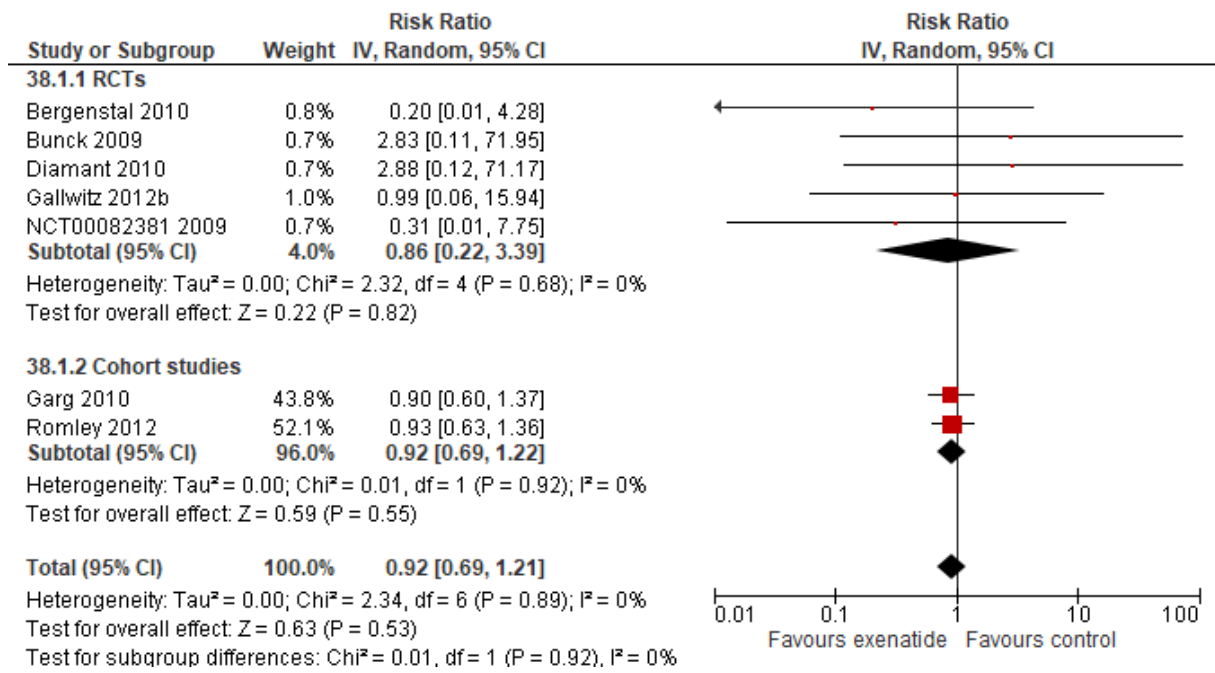
**Figure S59:** Kredo 2014; Intervention/ Exposure: Antiretroviral therapy by nurses; Outcome: All-cause mortality



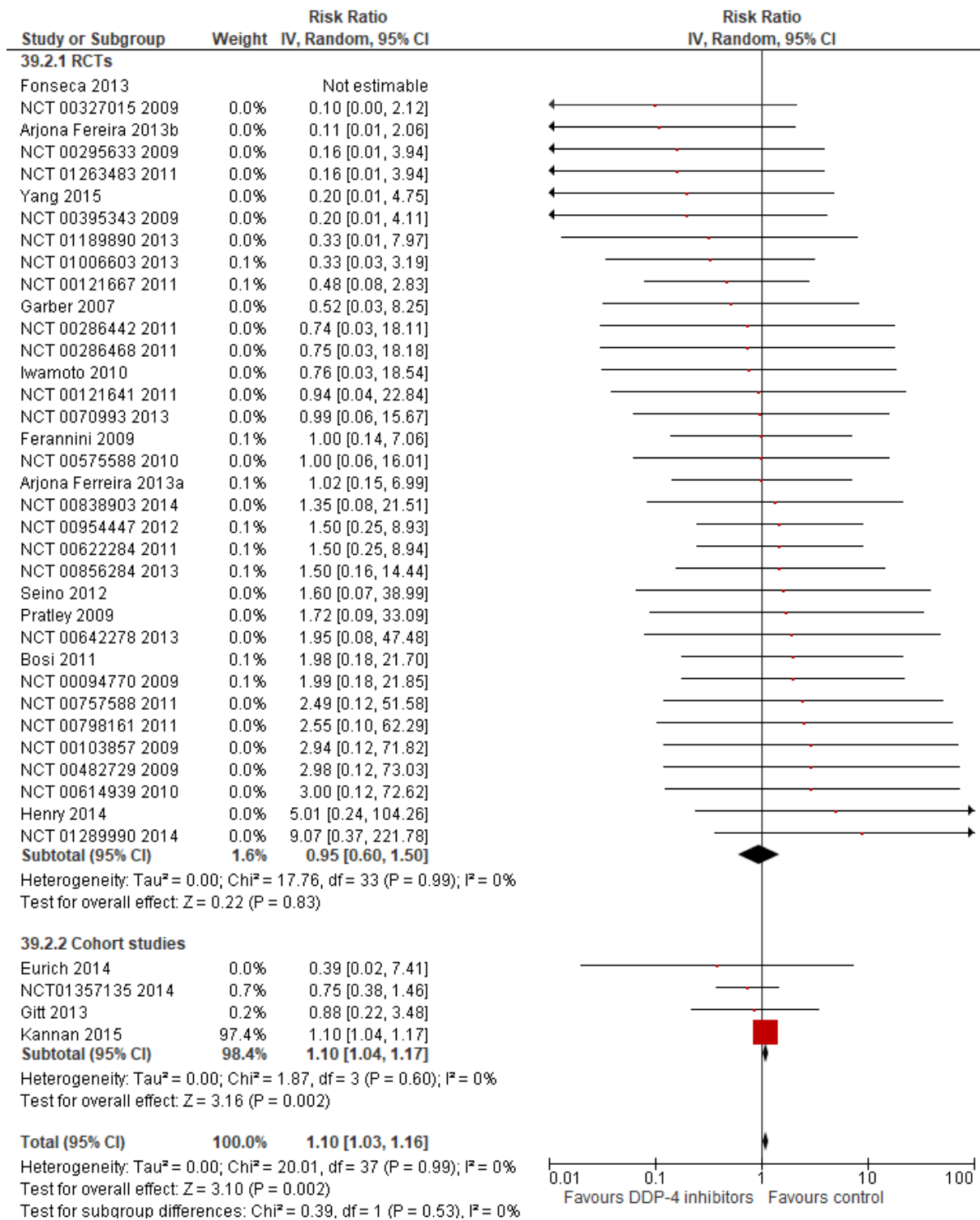
**Figure S60:** Kredo 2014; Intervention/ Exposure: Antiretroviral therapy by nurses; Outcome: Attrition



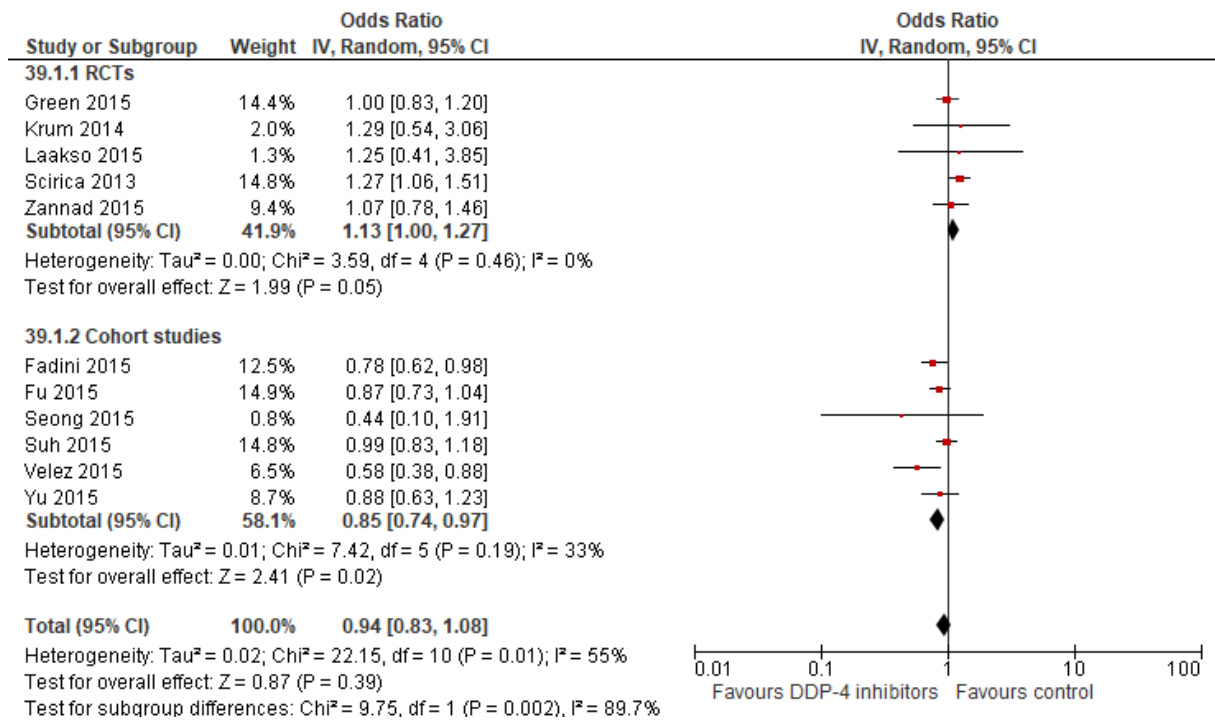
**Figure S61:** Kreda 2014; Intervention/ Exposure: Nurses for maintenance of antiretroviral therapy; Outcome: All-cause mortality



**Figure S62:** Li 2014; Intervention/ Exposure: Exenatide; Outcome: Acute pancreatitis

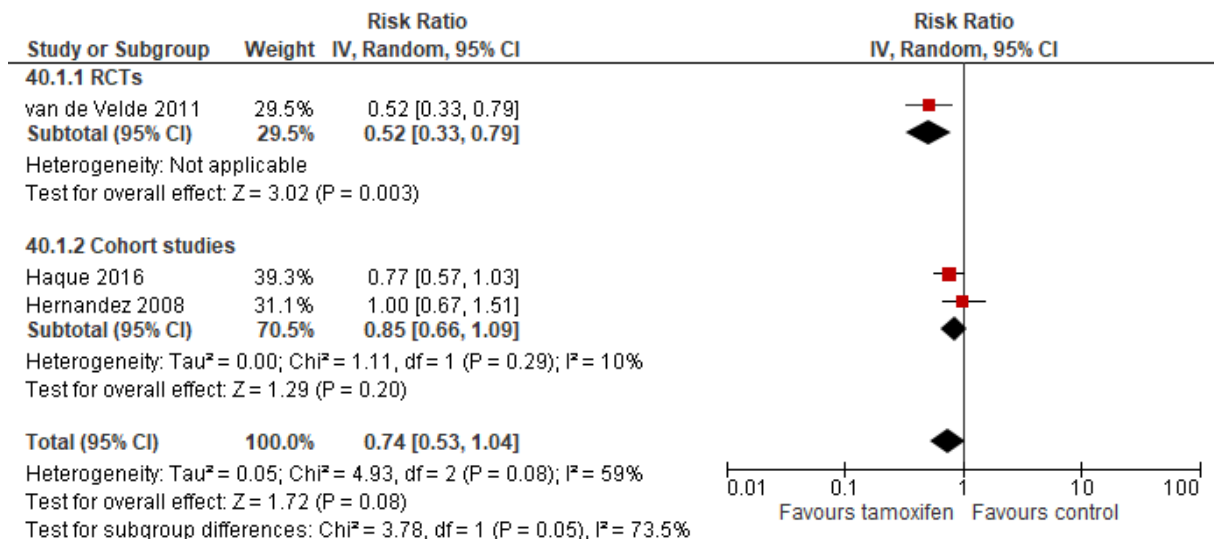


**Figure S63:** Li 2016; Intervention/ Exposure: DDP-4 inhibitors; Outcome: Heart failure

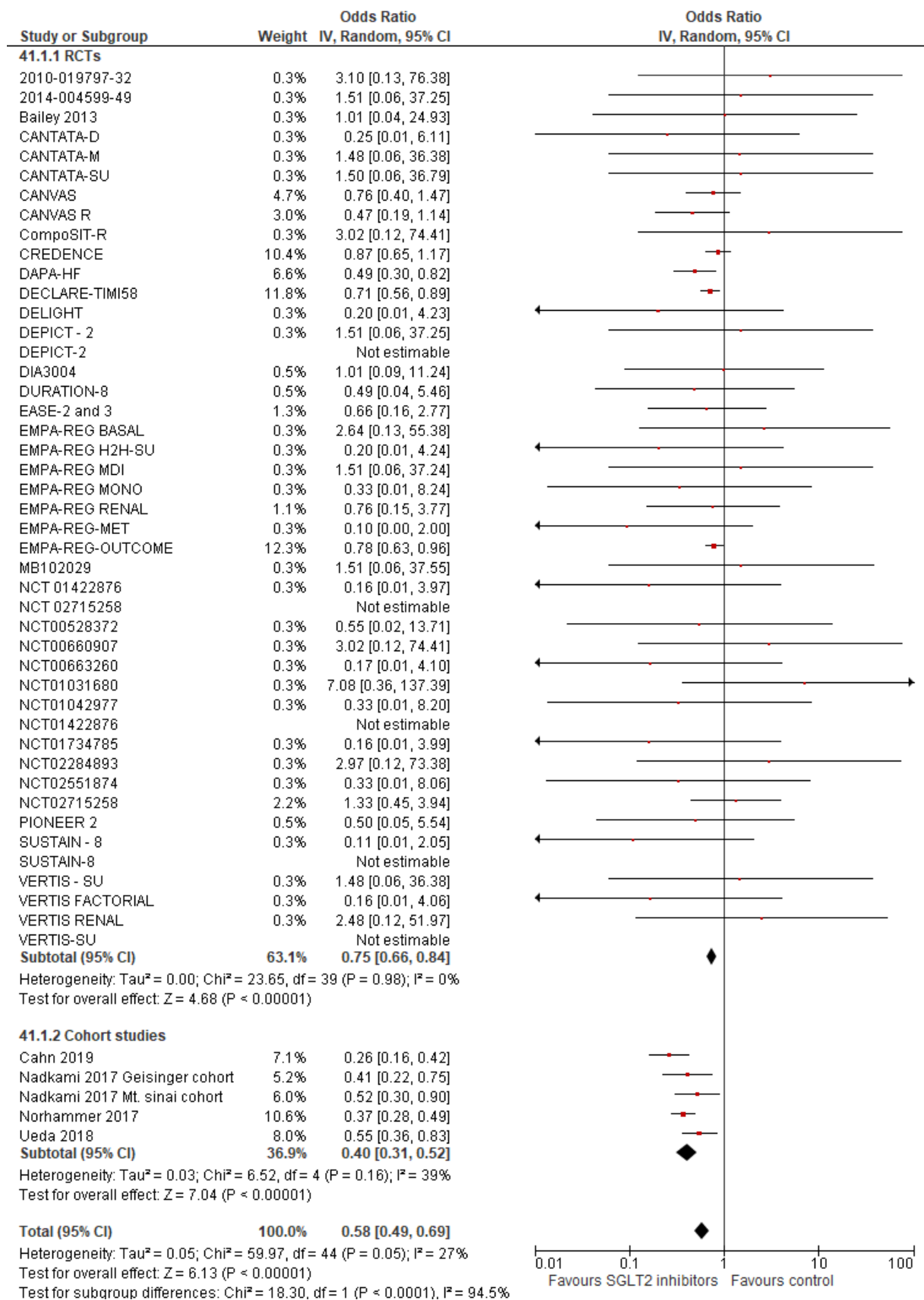


**Figure S64:** Li 2016; Intervention/ Exposure: DDP-4 inhibitors; Outcome: Hospital admission for heart failure

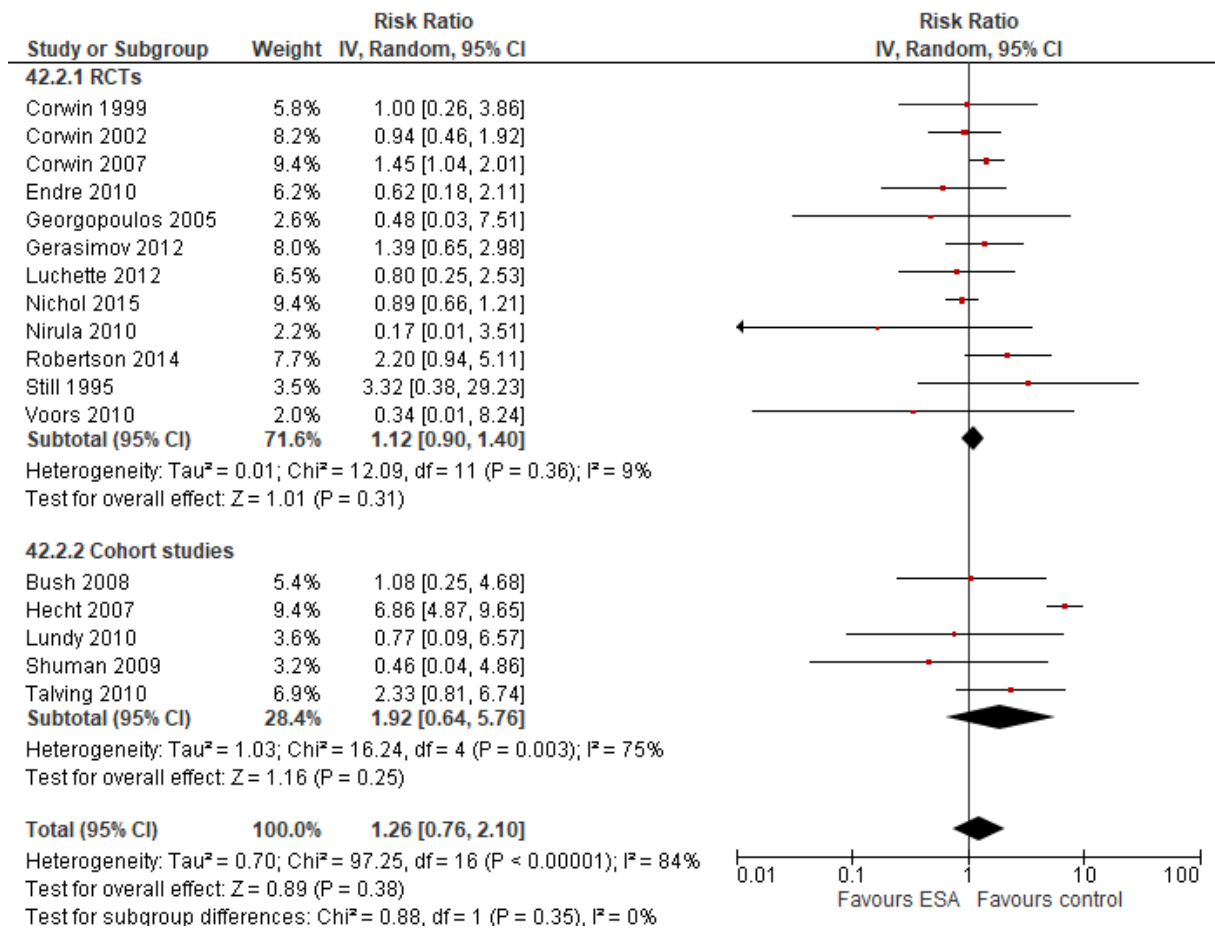




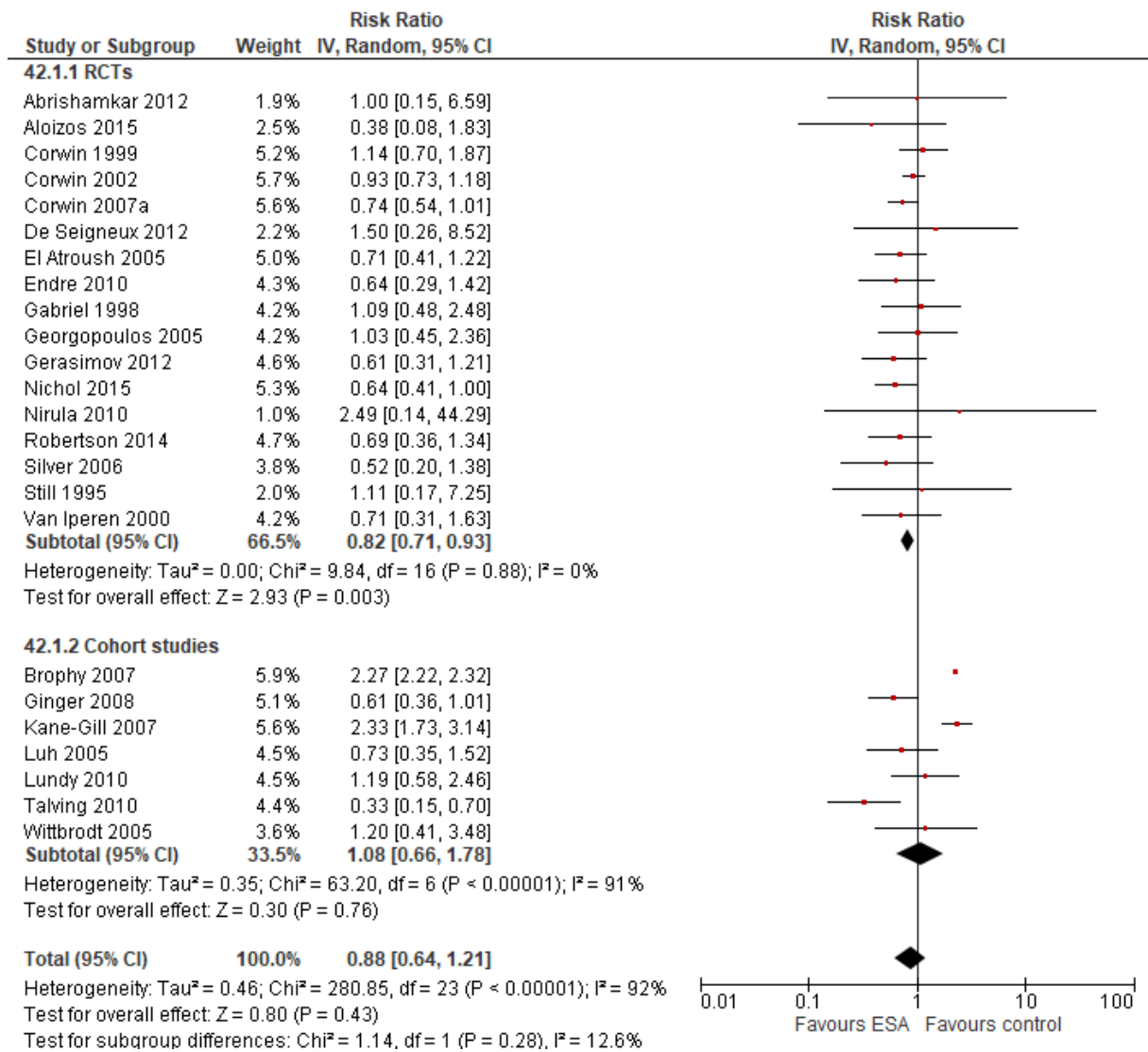
**Figure S65:** Matthews 2018; Intervention/ Exposure: Tamoxifen; Outcome: Heart failure



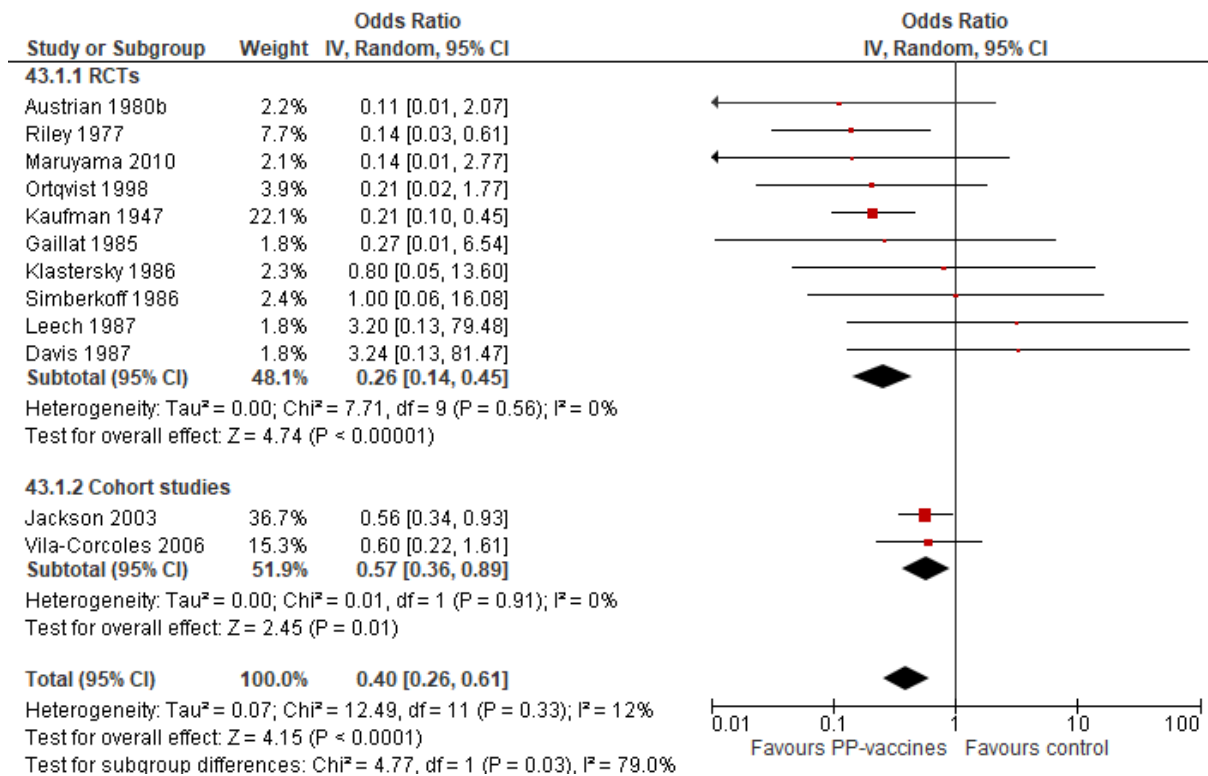
**Figure S66:** Menne 2019; Intervention/ Exposure: SGLT-2 inhibitors; Outcome: Acute kidney injury



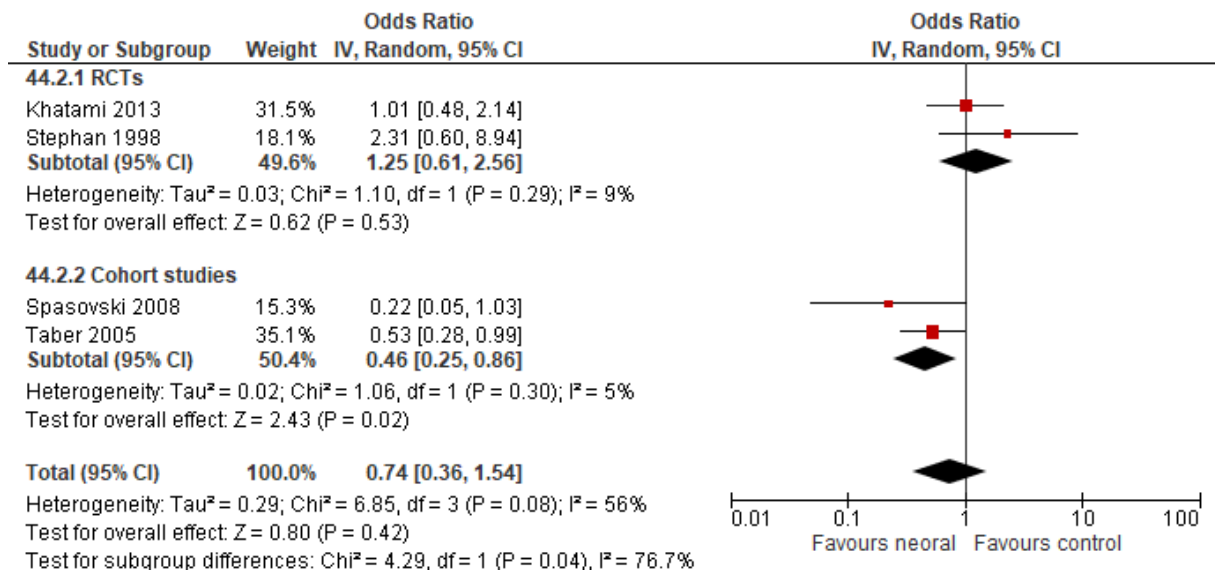
**Figure S67:** Mesgarpour 2017; Intervention/ Exposure: Erythropoiesis stimulating agents; Outcome: Venous thromboembolism



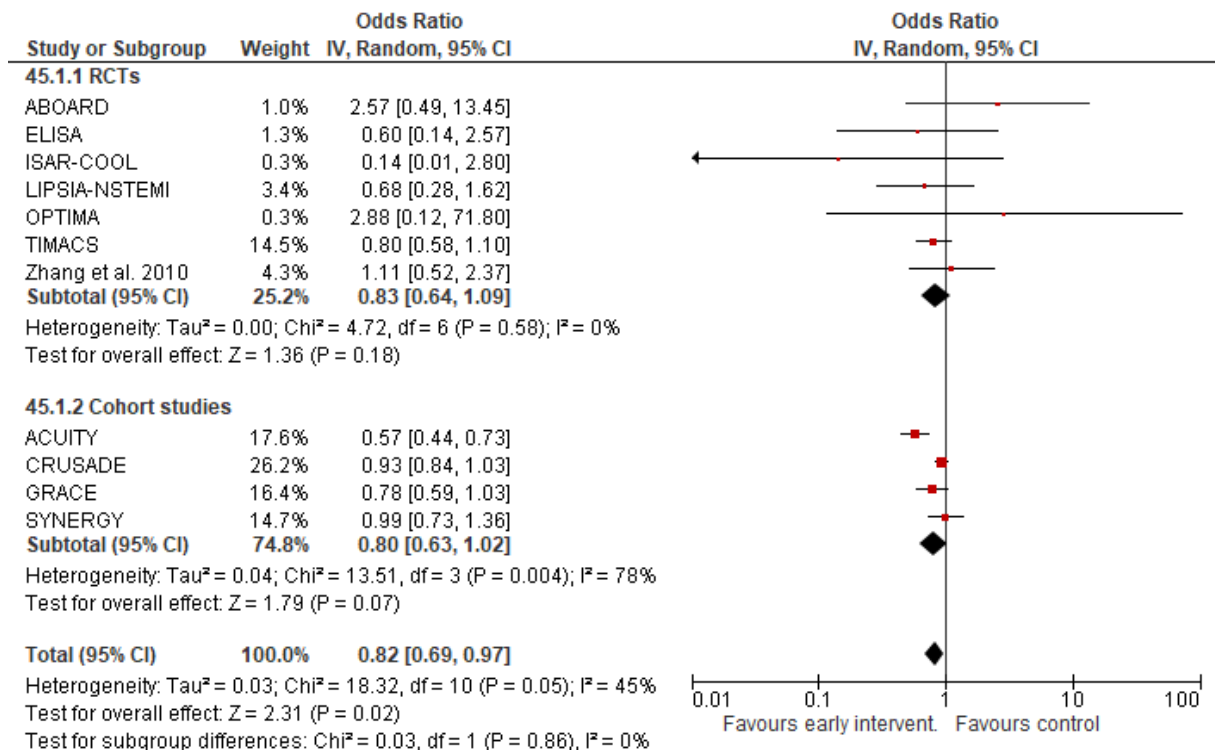
**Figure S68:** Mesgarpour 2017; Intervention/ Exposure: Erythropoiesis stimulating agents; Outcome: All-cause mortality



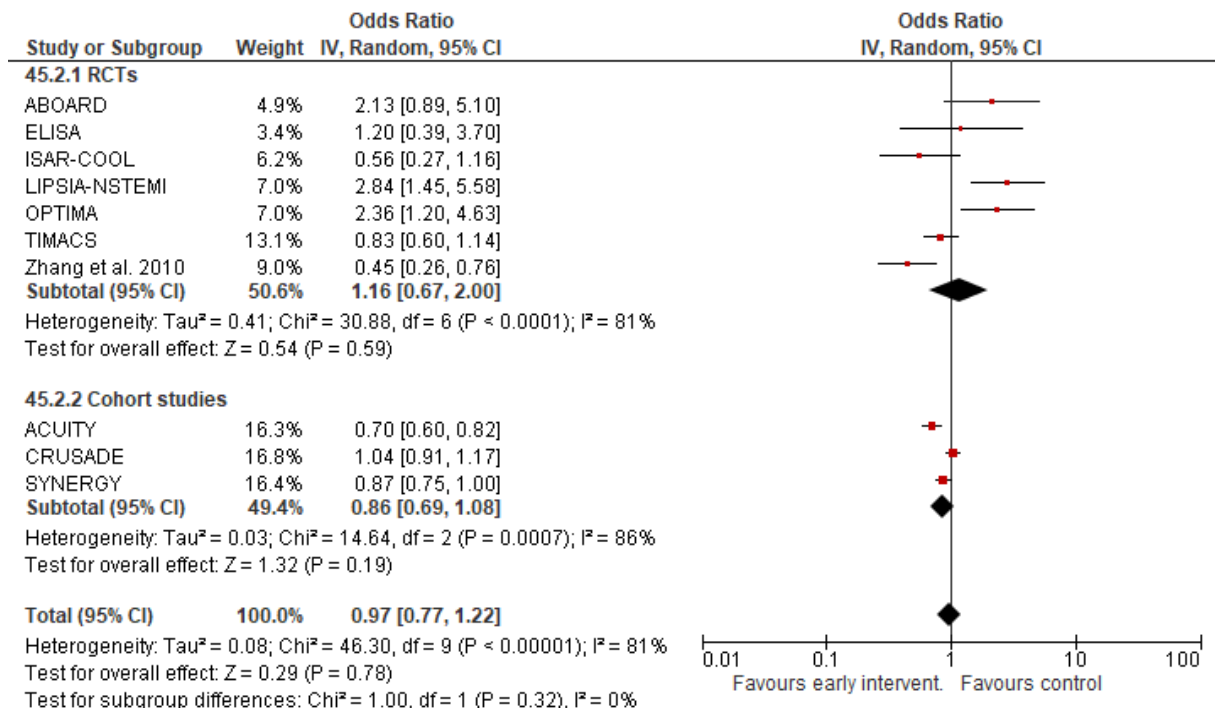
**Figure S69:** Moberley 2013; Intervention/ Exposure: Pneumococcal polysaccharide vaccines; Outcome: Invasive pneumococcal disease



**Figure S70:** Molnar 2015; Intervention/ Exposure: Neoral (Cyclosporin); Outcome: Acute rejection of kidney transplant

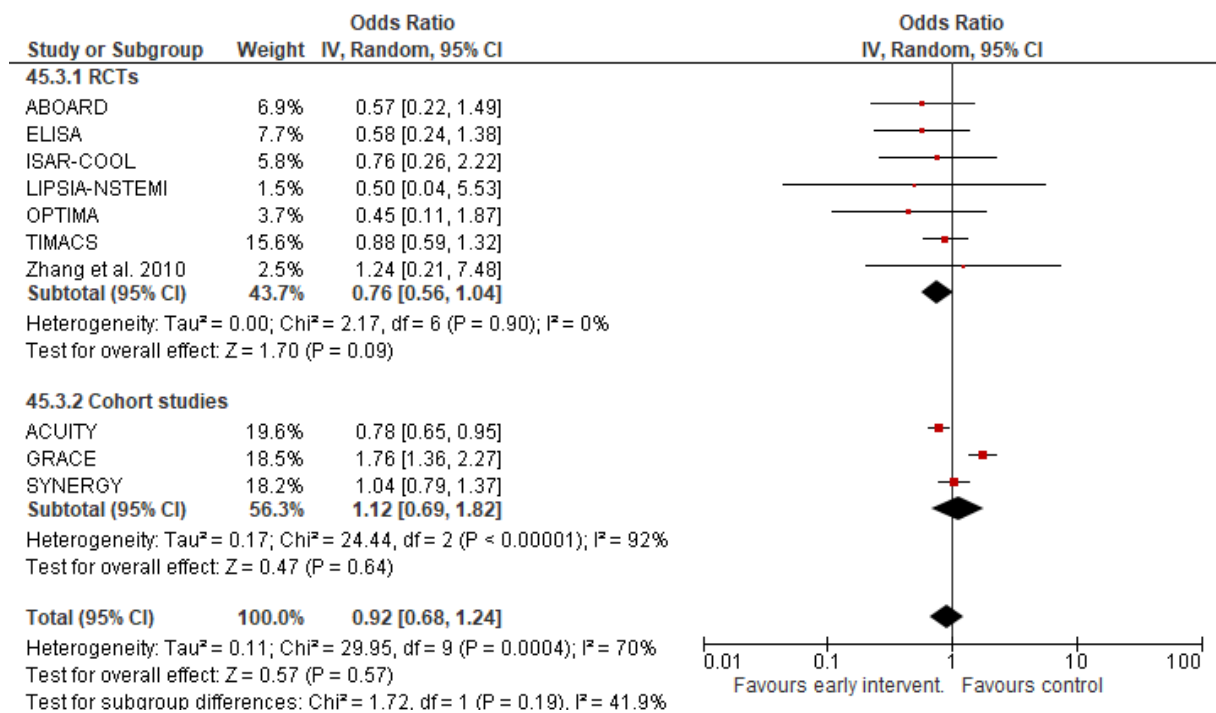


**Figure S71:** Navarese 2013; Intervention/ Exposure: Early intervention for NSTEMI-ACS; Outcome: All-cause mortality

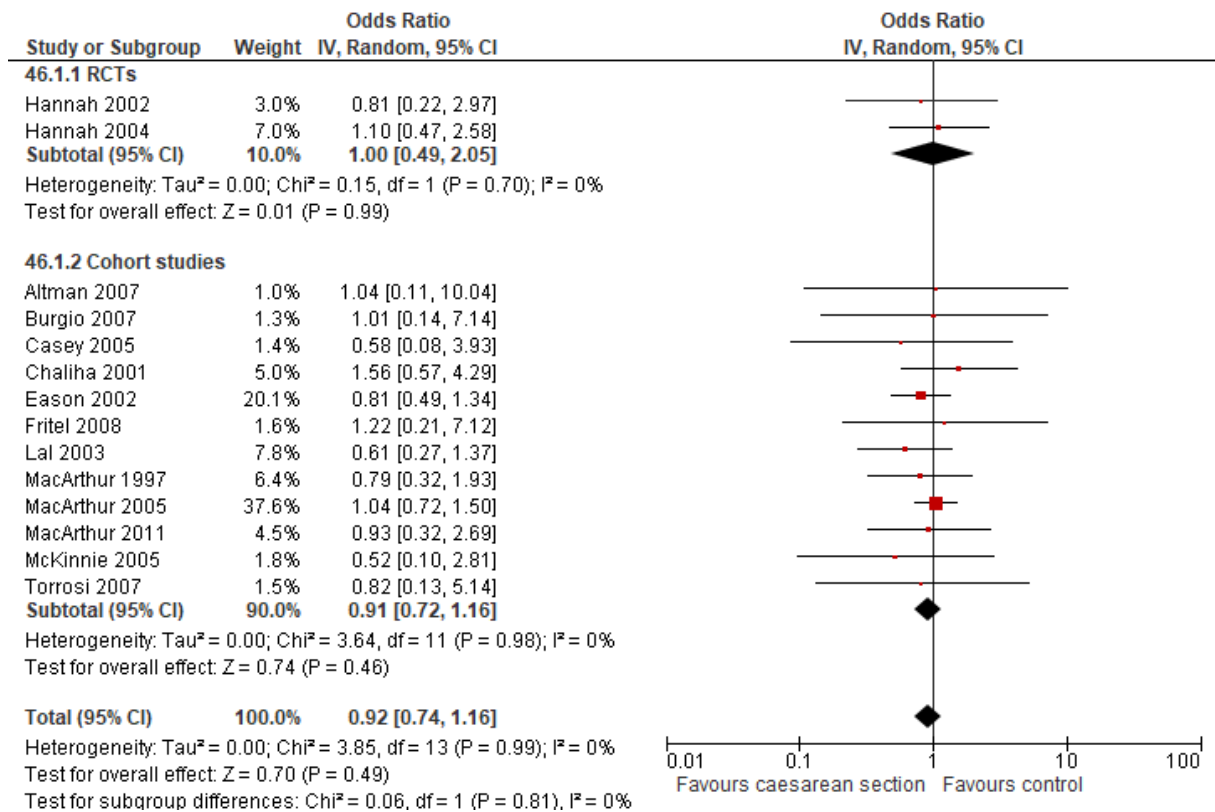


**Figure S72:** Navarese 2013; Intervention/ Exposure: Early intervention for NSTEMI-ACS; Outcome: Myocardial infarction

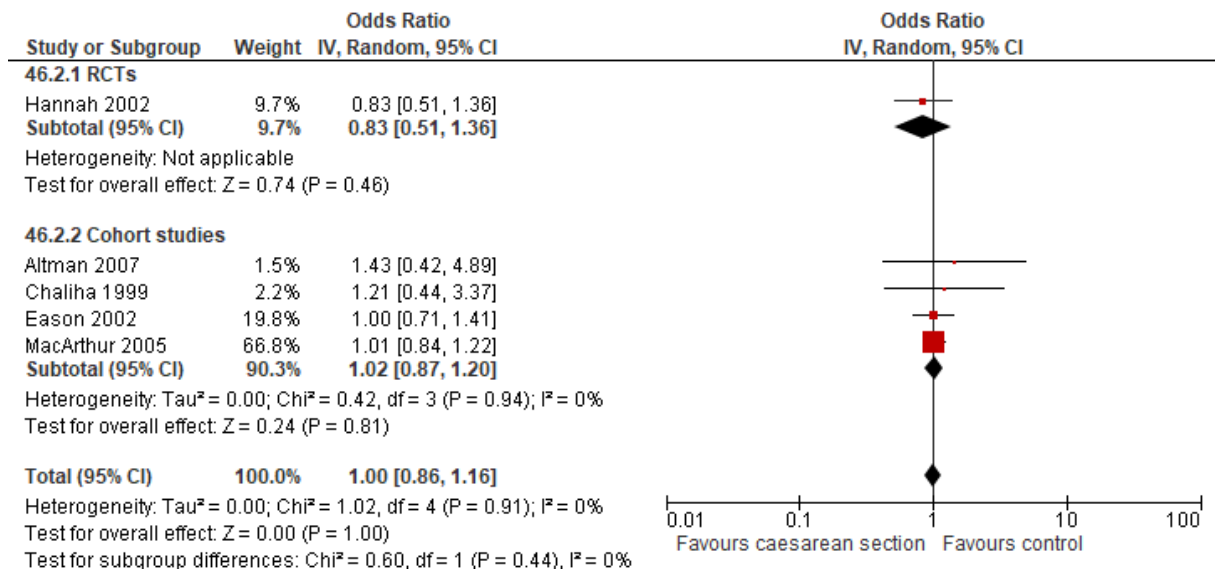




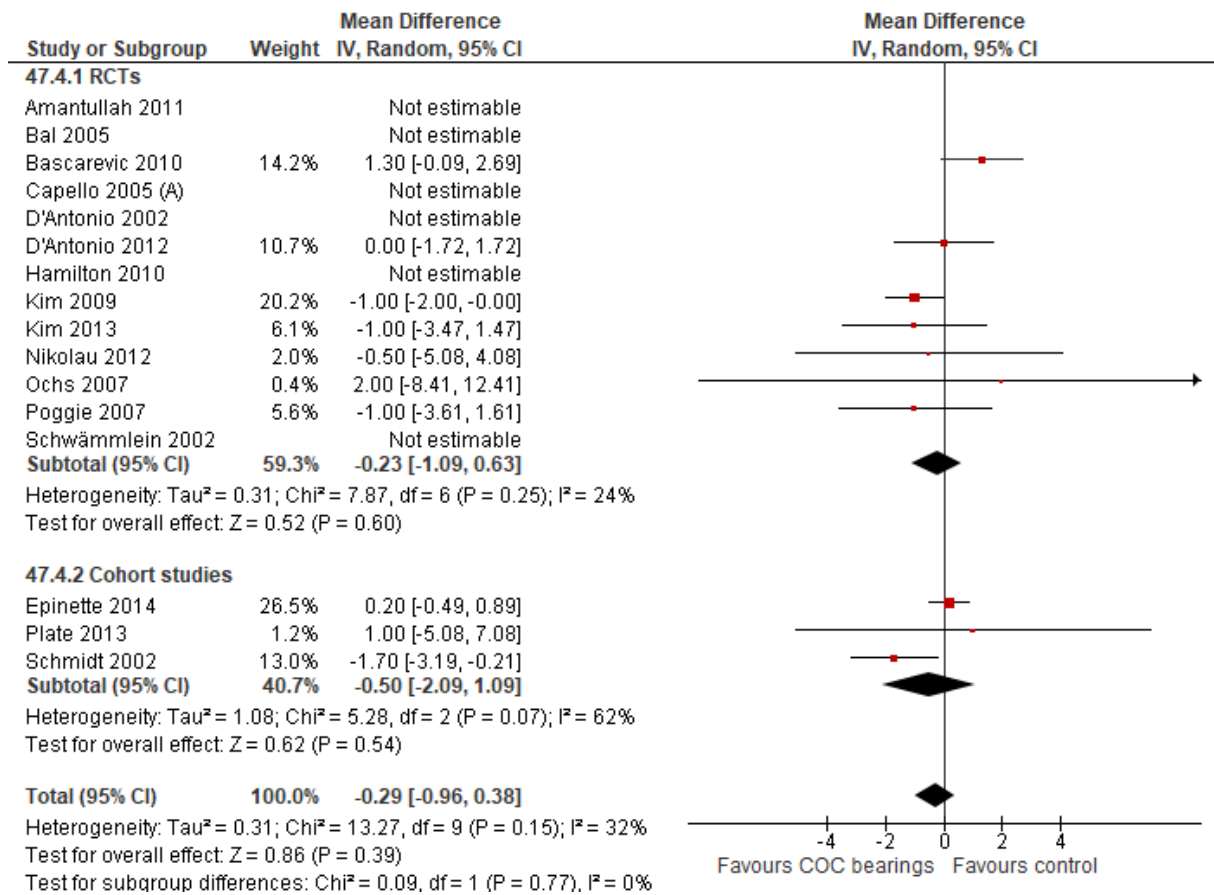
**Figure S73:** Navarese 2013; Intervention/ Exposure: Early intervention for NSTEMI-ACS; Outcome: Major bleeding



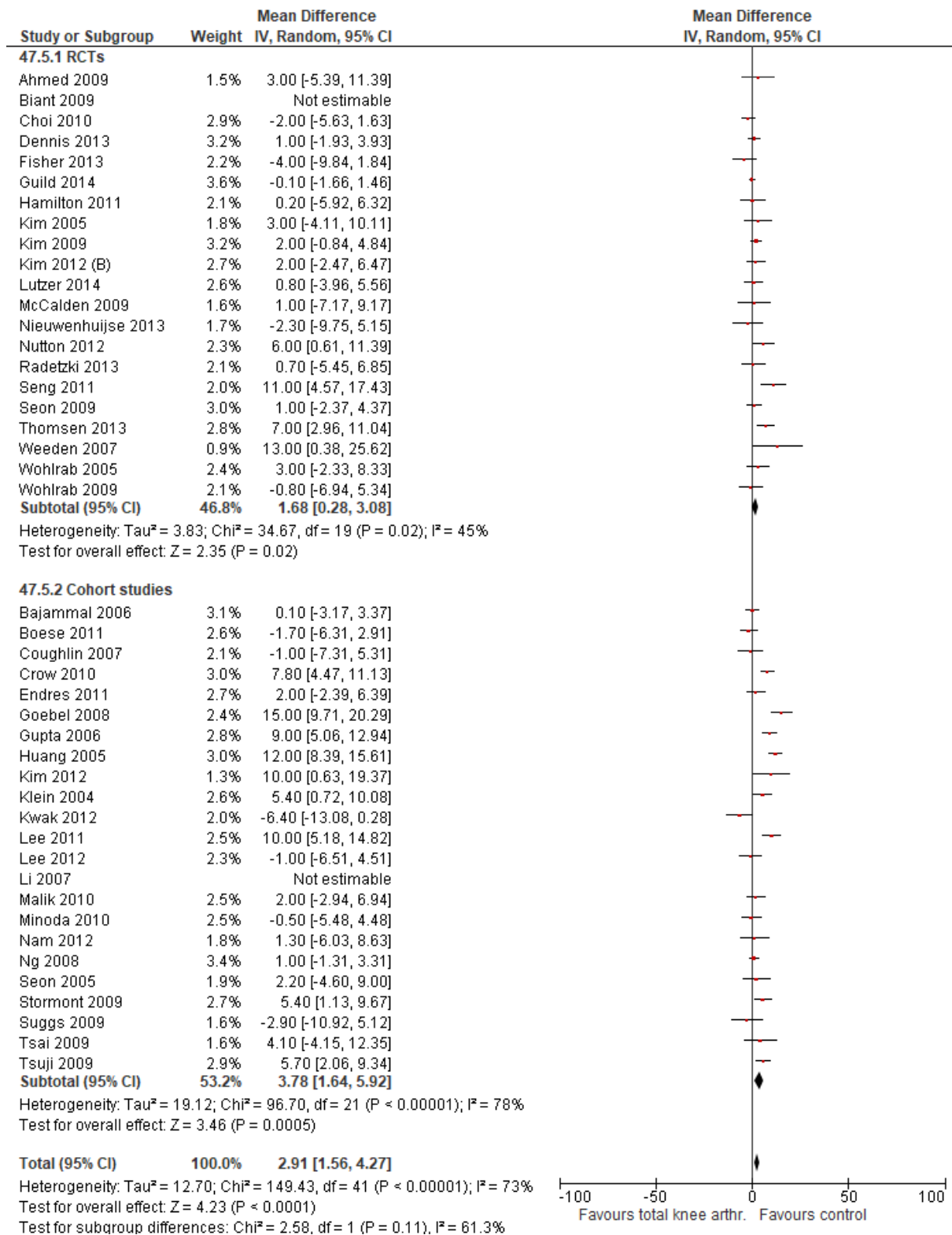
**Figure S74:** Nelson 2010; Intervention/ Exposure: Caesarean section; Outcome: Anal incontinence, feces



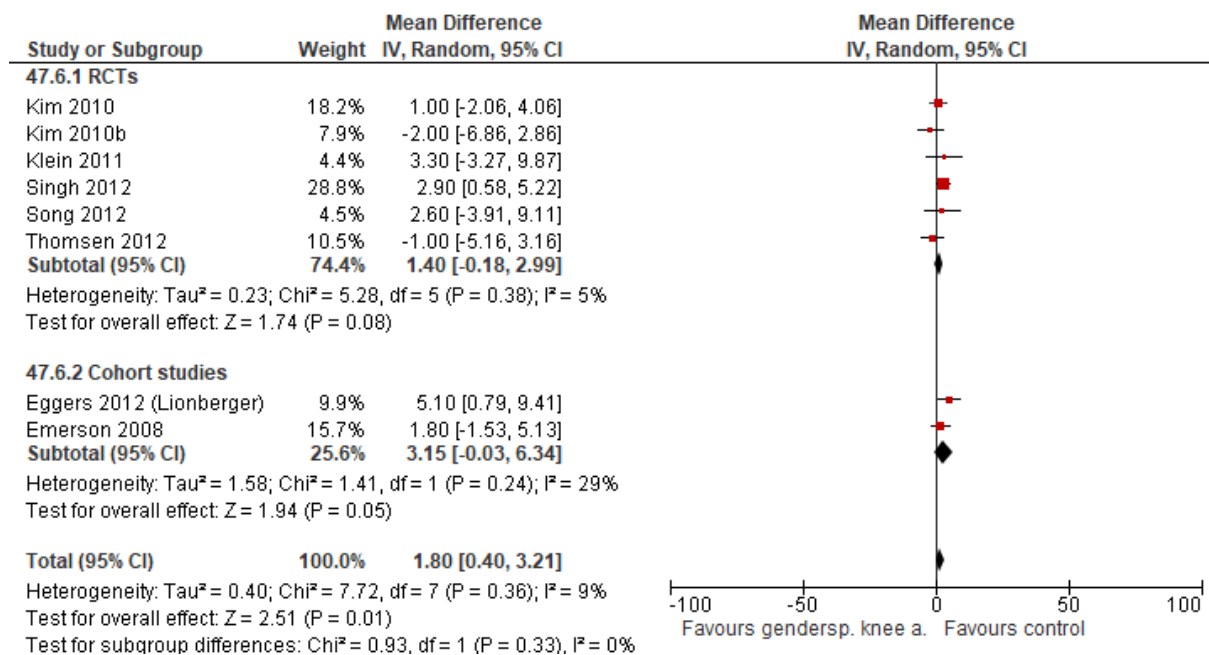
**Figure S75:** Nelson 2010; Intervention/ Exposure: Caesarean section; Outcome: Anal incontinence, flatus



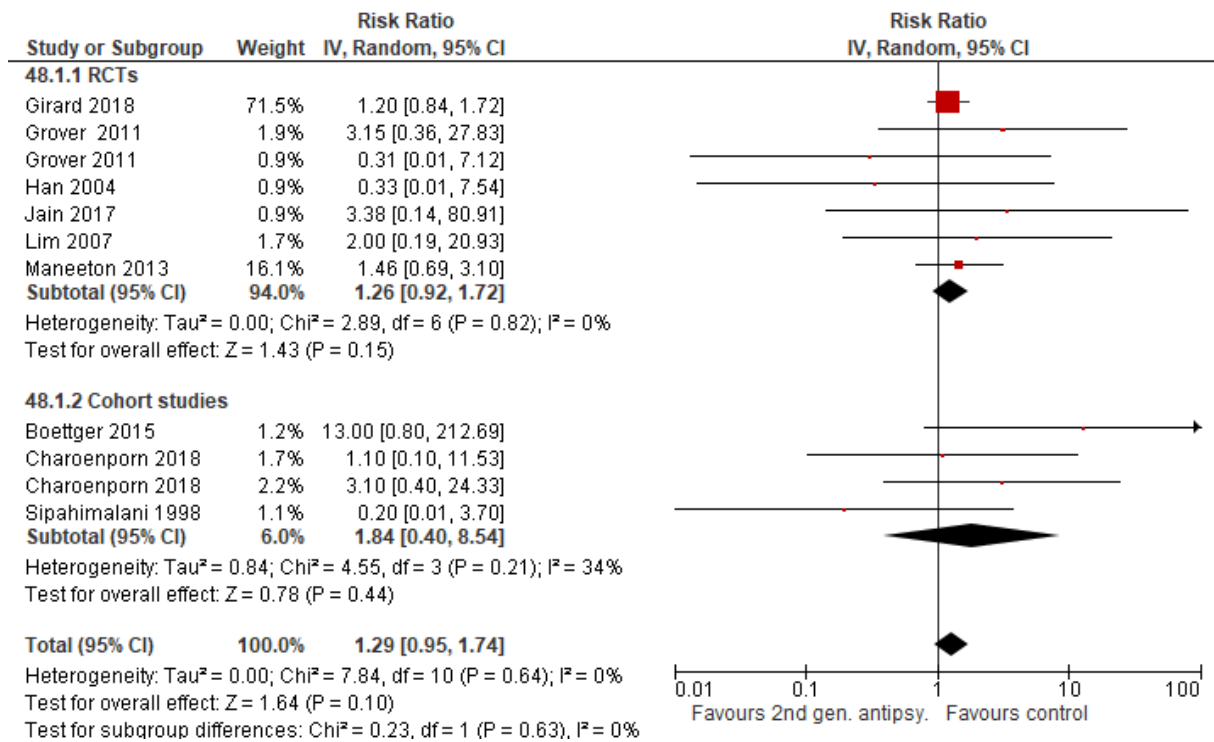
**Figure S76:** Nieuwenhuijse 2014; Intervention/ Exposure: Ceramic-on-ceramic bearings for total hip arthroplasty; Outcome: Harris Hip Score



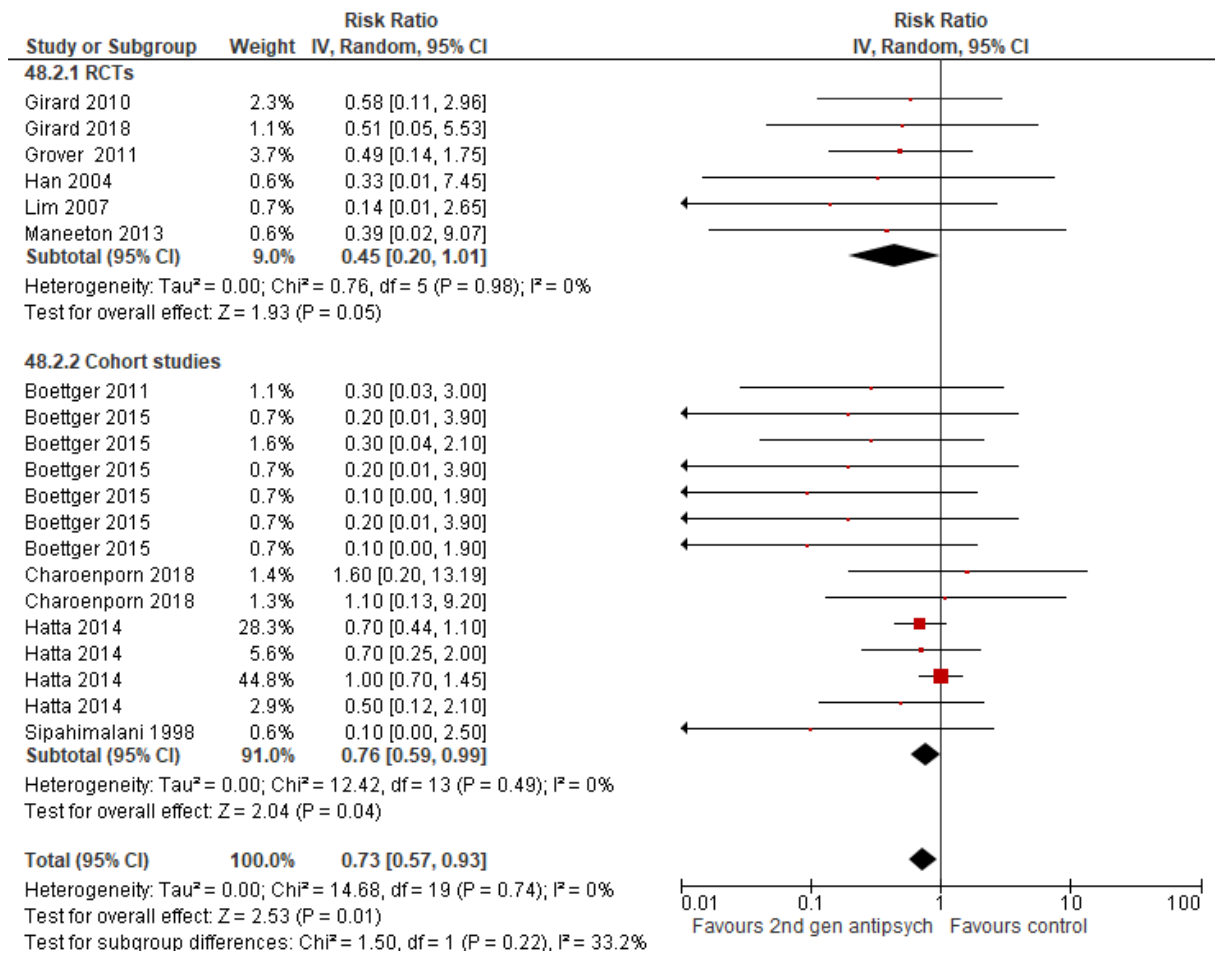
**Figure S77:** Nieuwenhuijse 2014; Intervention/ Exposure: High-flexion total knee arthroplasty; Outcome: Flexion in degrees



**Figure S78:** Nieuwenhuijse 2014; Intervention/ Exposure: Gender-specific total knee arthroplasty; Outcome: Flexion-extension range

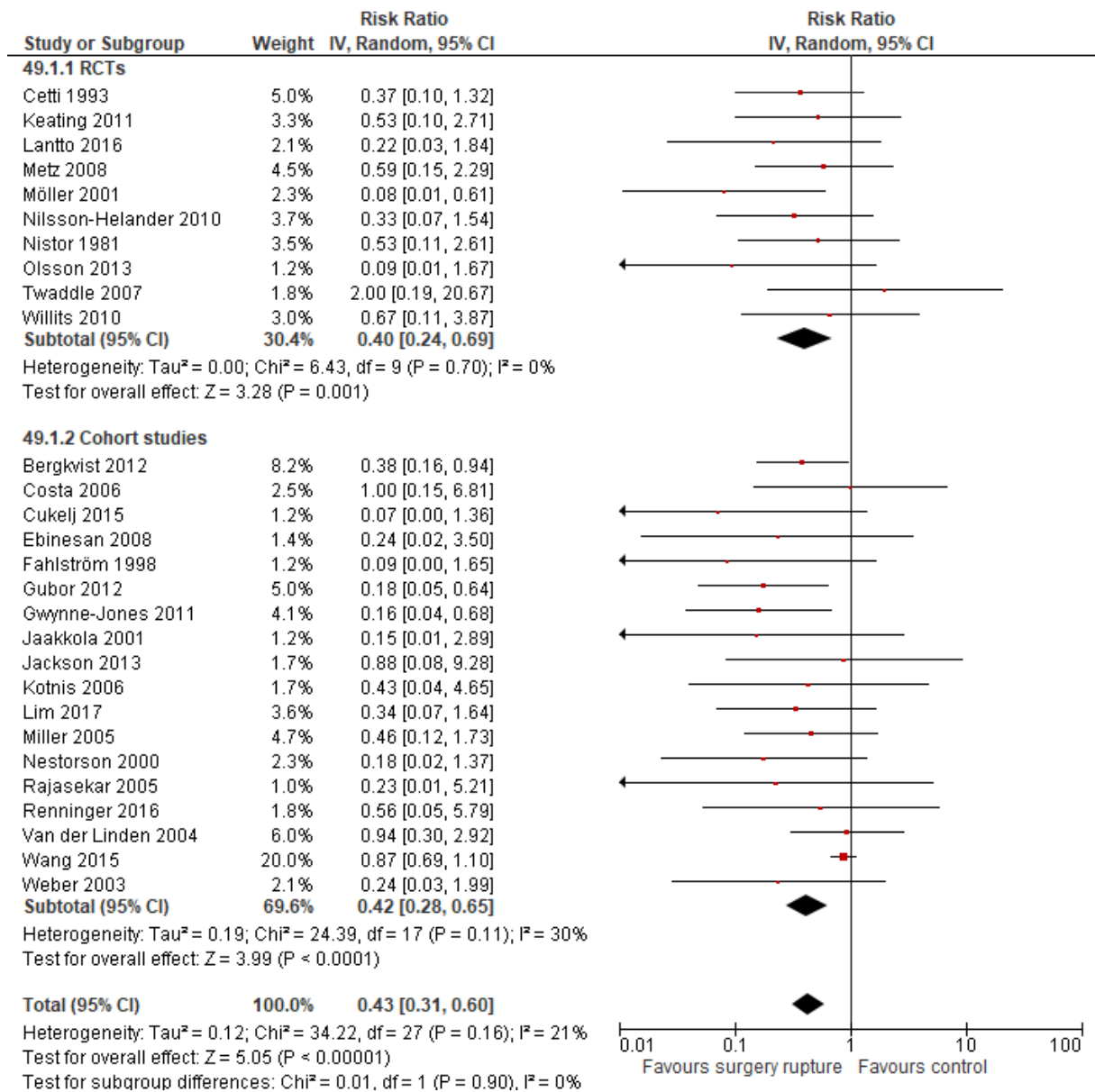


**Figure S79:** Nikooie 2019; Intervention/ Exposure: Second generation antipsychotics; Outcome: Sedation

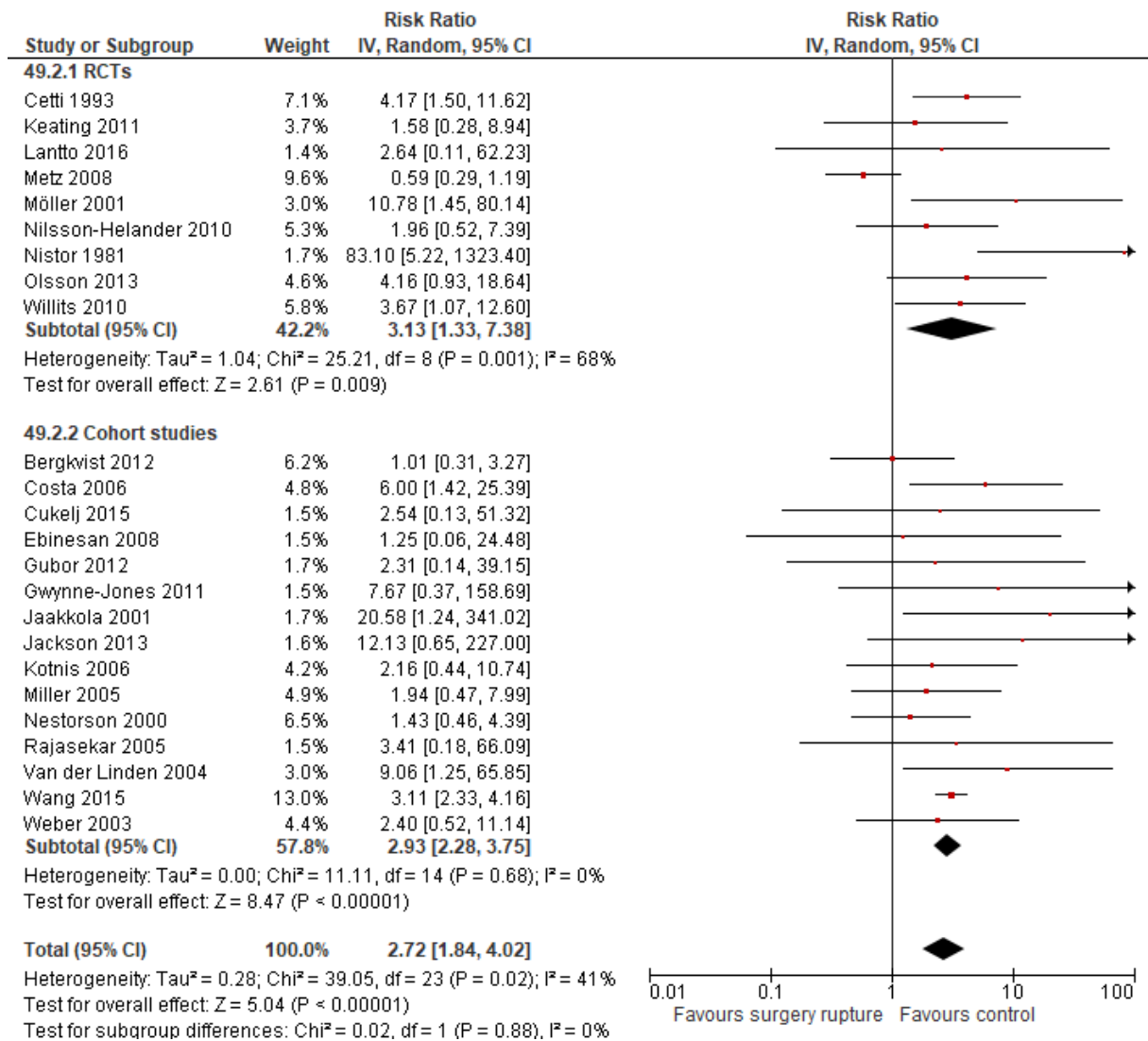


**Figure S80:** Nikooie 2019; Intervention/ Exposure: Second generation antipsychotics; Outcome: Neurologic outcomes

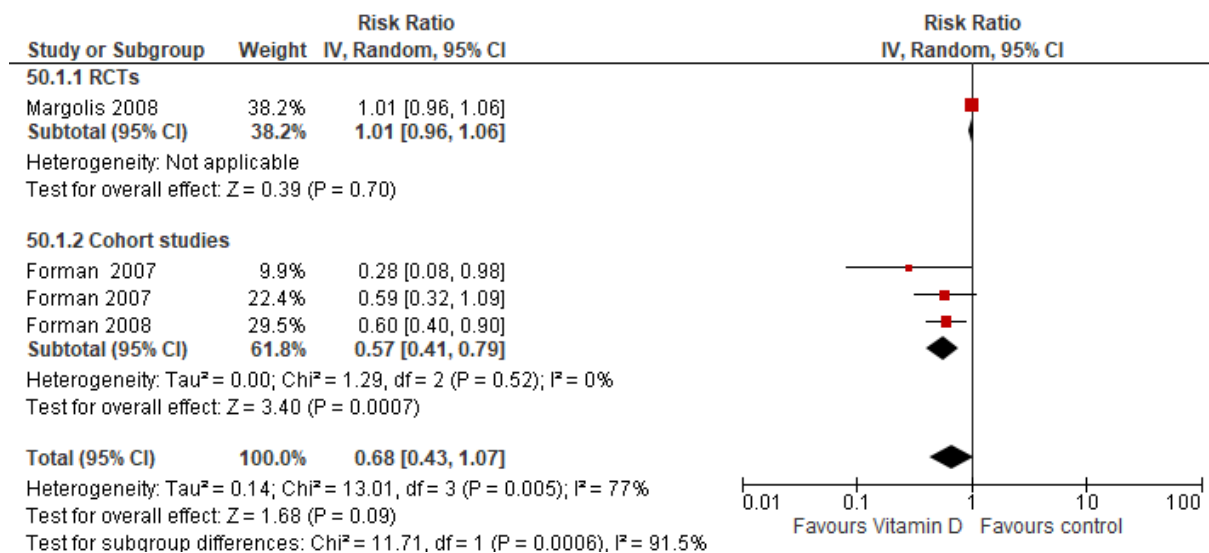




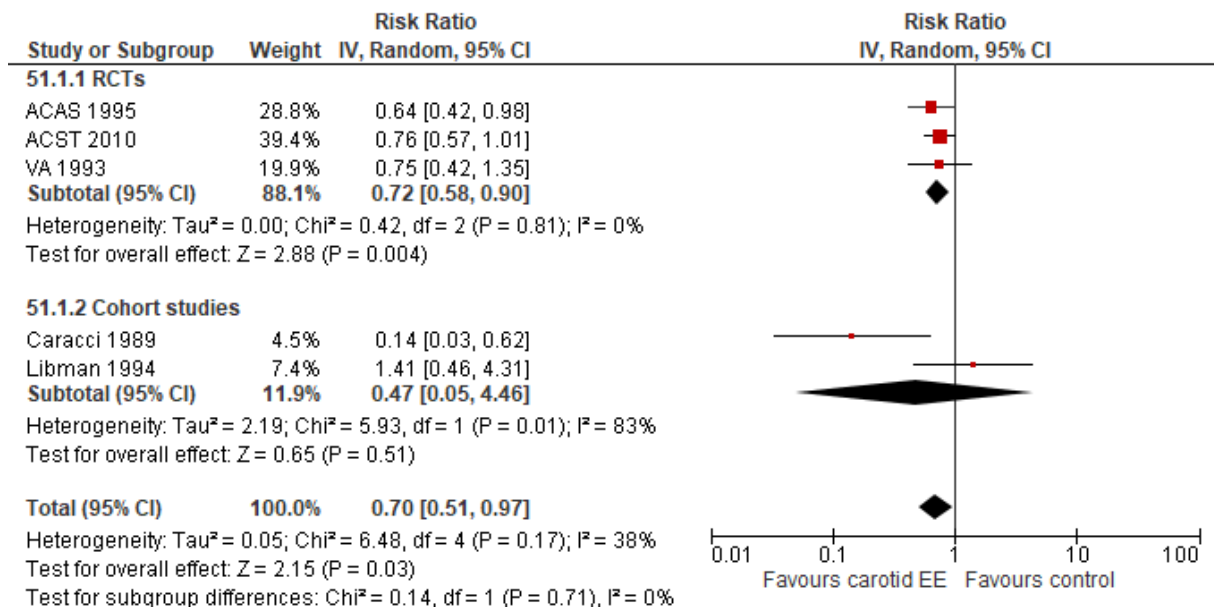
**Figure S81:** Ochen 2019; Intervention/ Exposure: Surgery for achilles tendon rupture; Outcome: Re-rupture



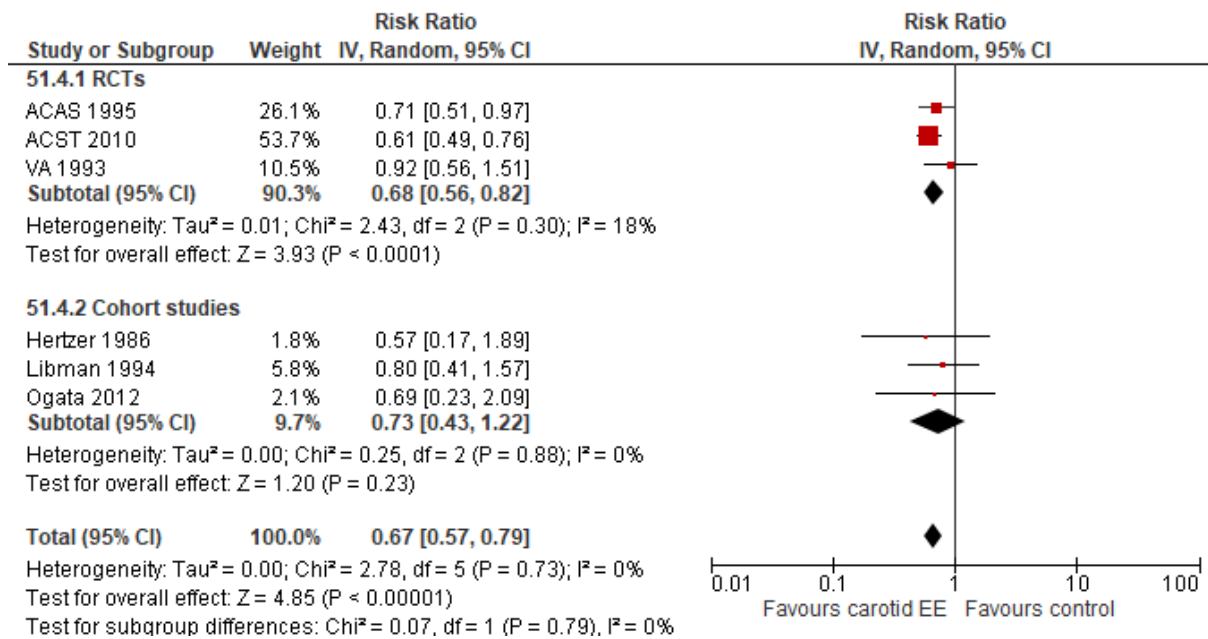
**Figure S82:** Ochen 2019; Intervention/ Exposure: Surgery for achilles tendon rupture; Outcome: Complications



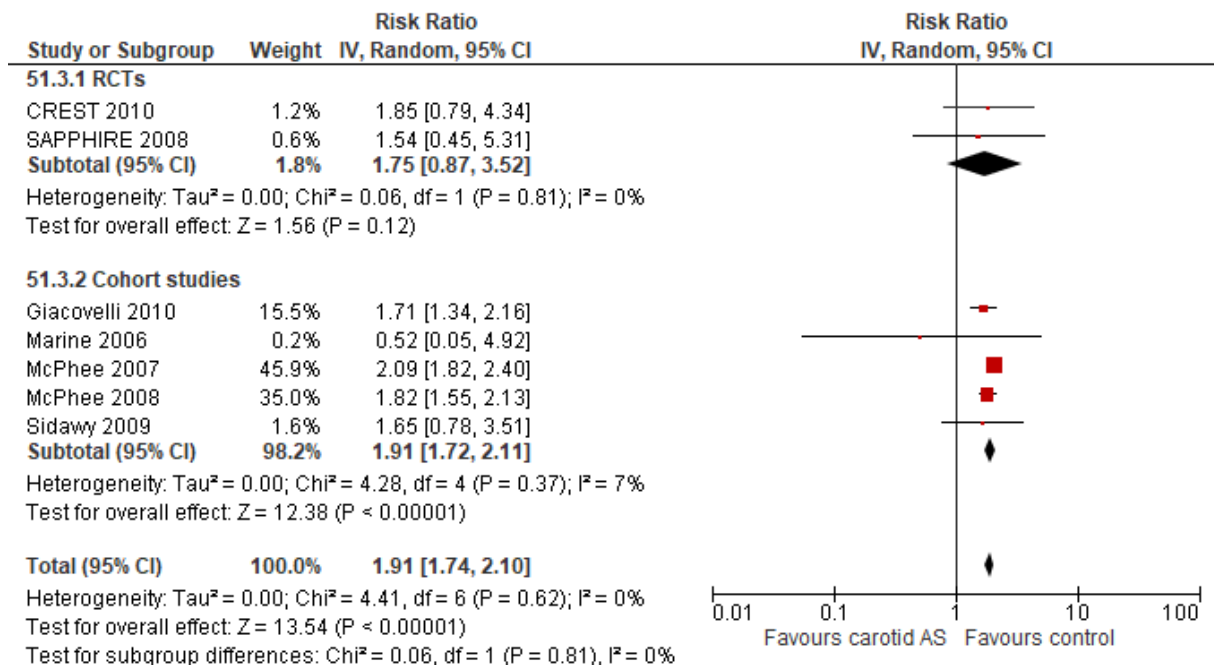
**Figure S83:** Pittas 2010; Intervention/ Exposure: High vitamin D; Outcome: Hypertension



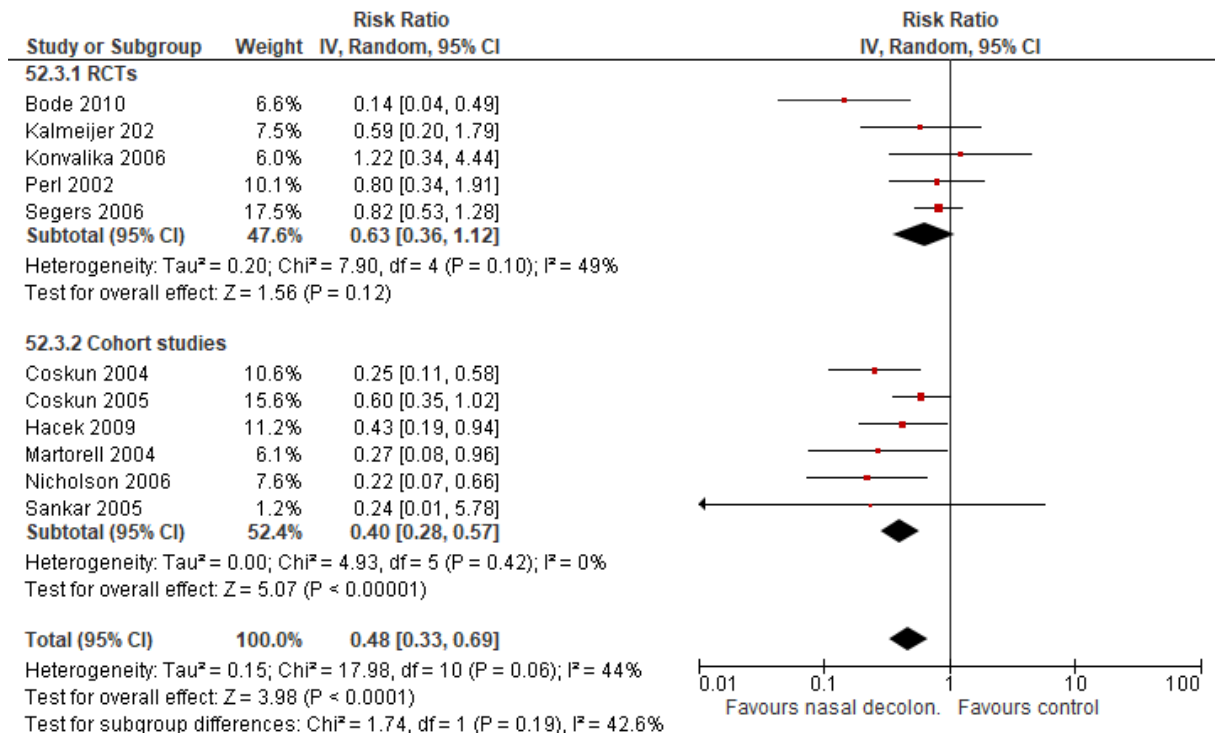
**Figure S84:** Raman 2013; Intervention/ Exposure: Carotid endarterectomy; Outcome: Ipsilateral stroke



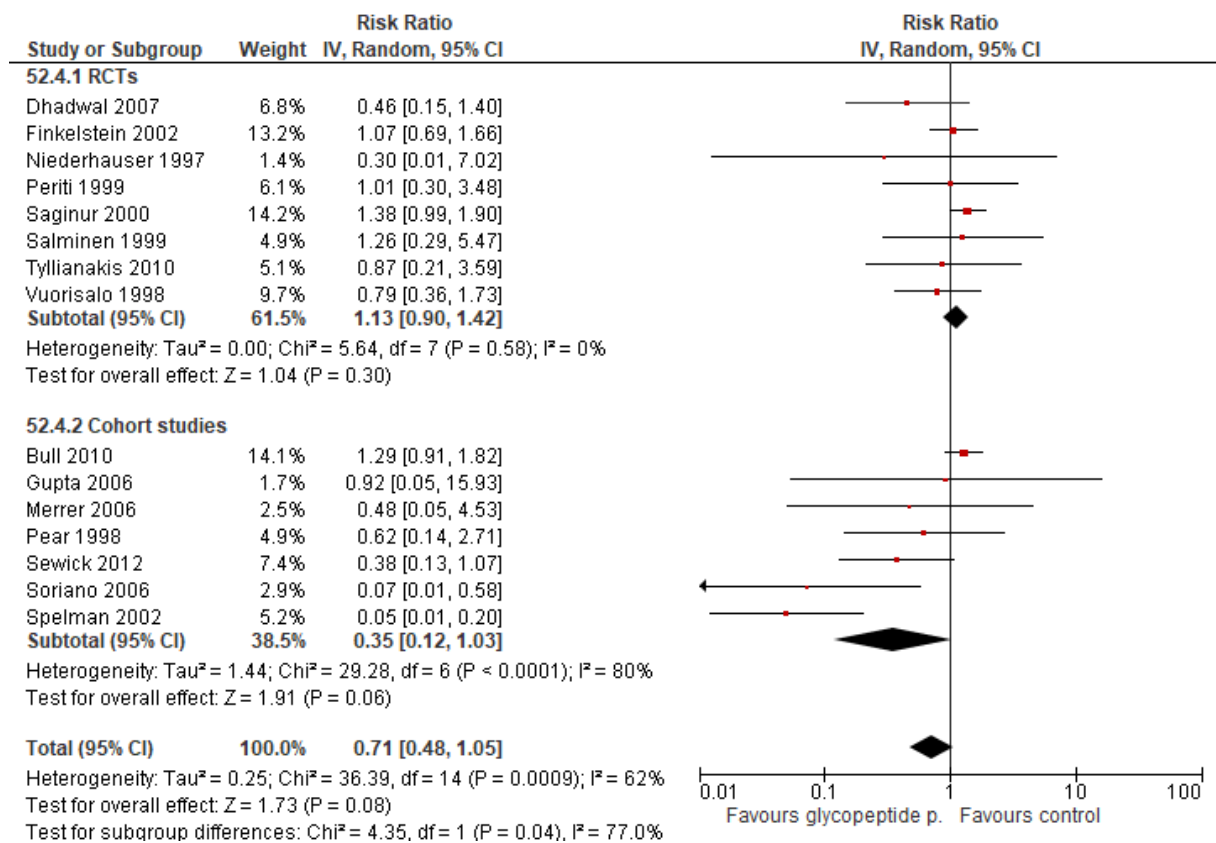
**Figure S85:** Raman 2013; Intervention/ Exposure: Carotid endarterectomy; Outcome: Stroke



**Figure S86:** Raman 2013; Intervention/ Exposure: Carotid artery stenting; Outcome: Periprocedural stroke

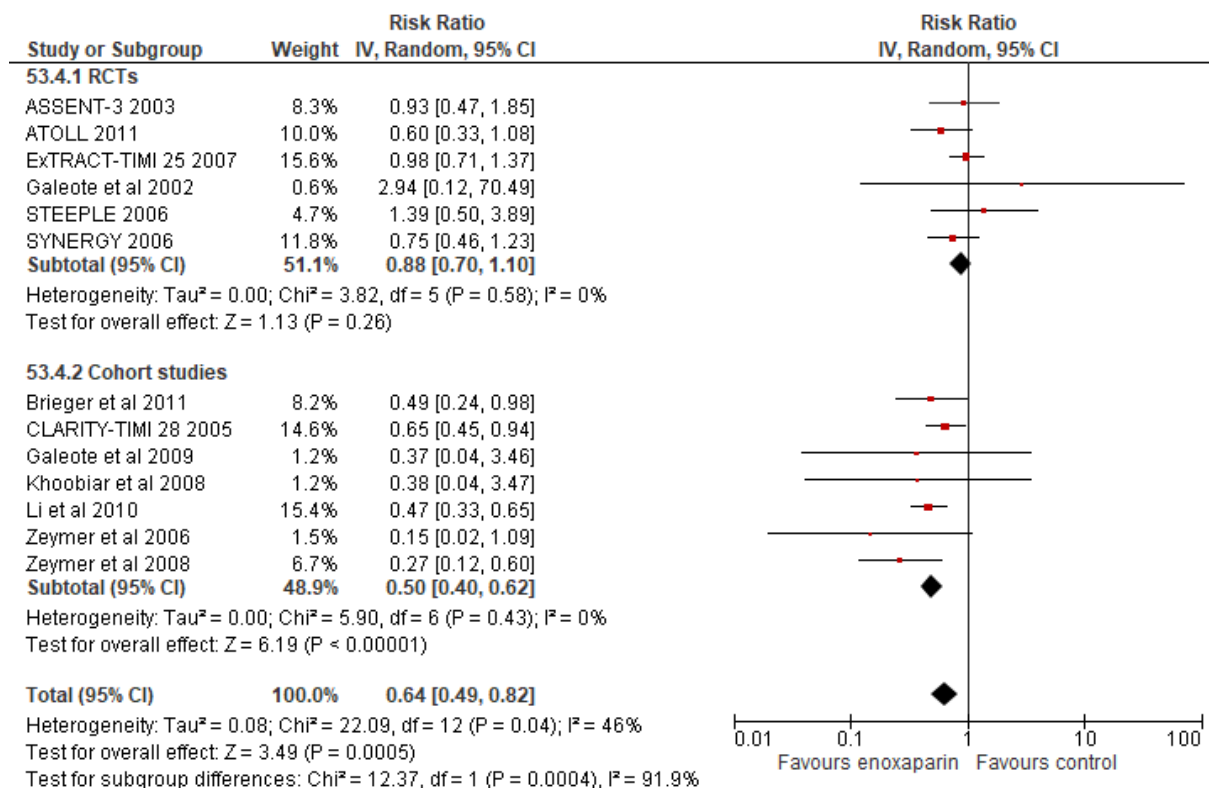


**Figure S87:** Schweizer 2013; Intervention/ Exposure: Nasal decontamination; Outcome: Surgical site infection

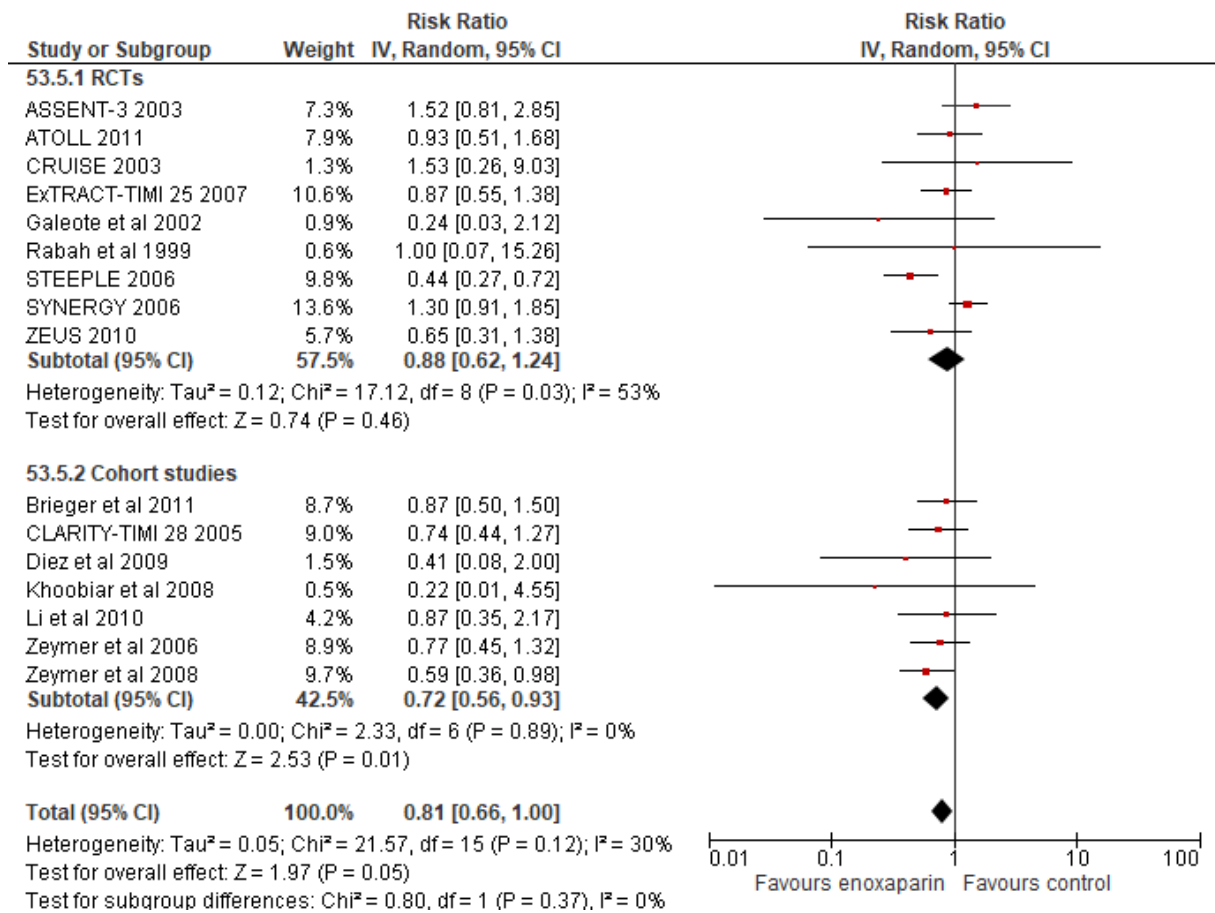


**Figure S88:** Schweizer 2013; Intervention/ Exposure: Glycopeptide prophylaxis; Outcome: Surgical site infection

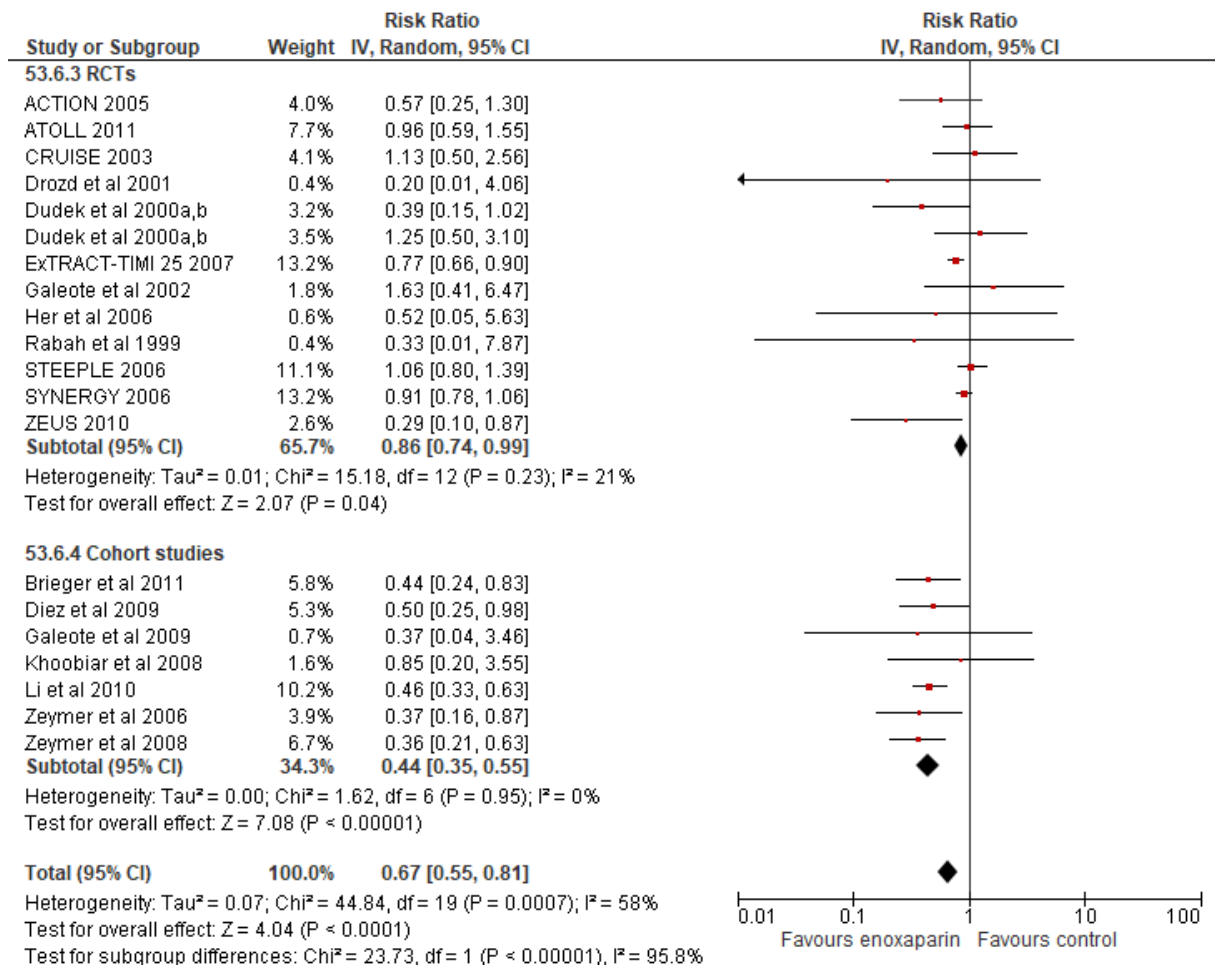




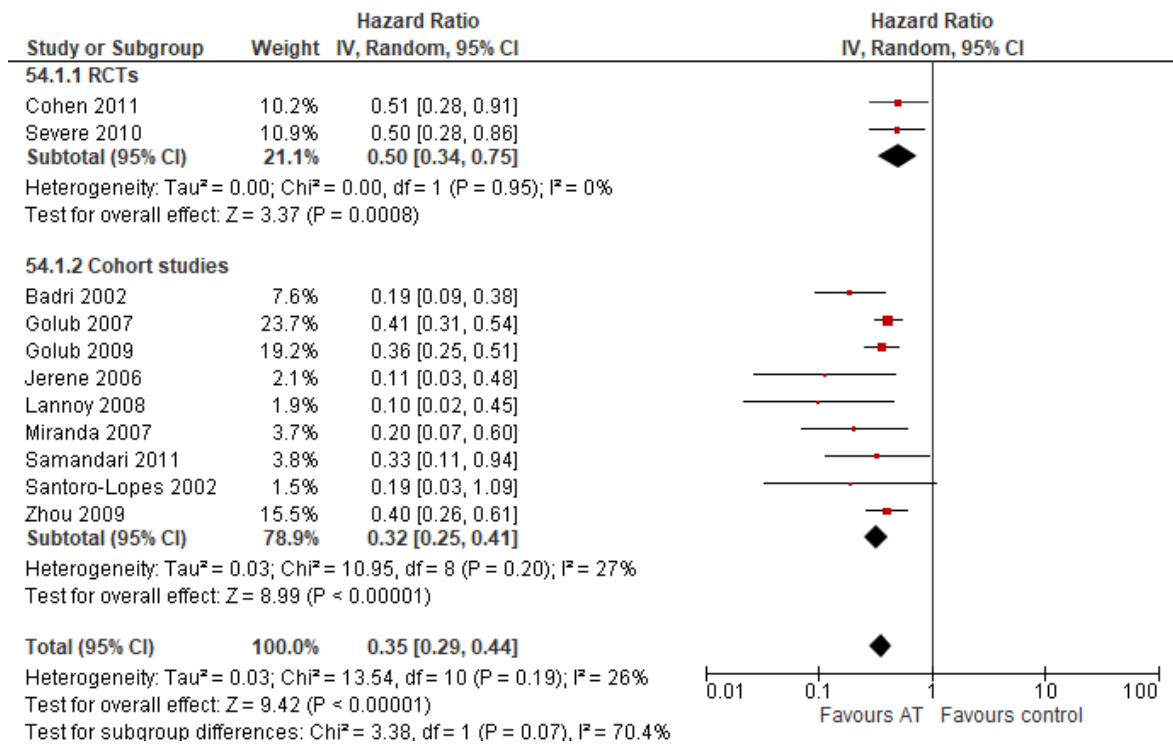
**Figure S89:** Silvain 2012; Intervention/ Exposure: Enoxaparin; Outcome: All-cause mortality



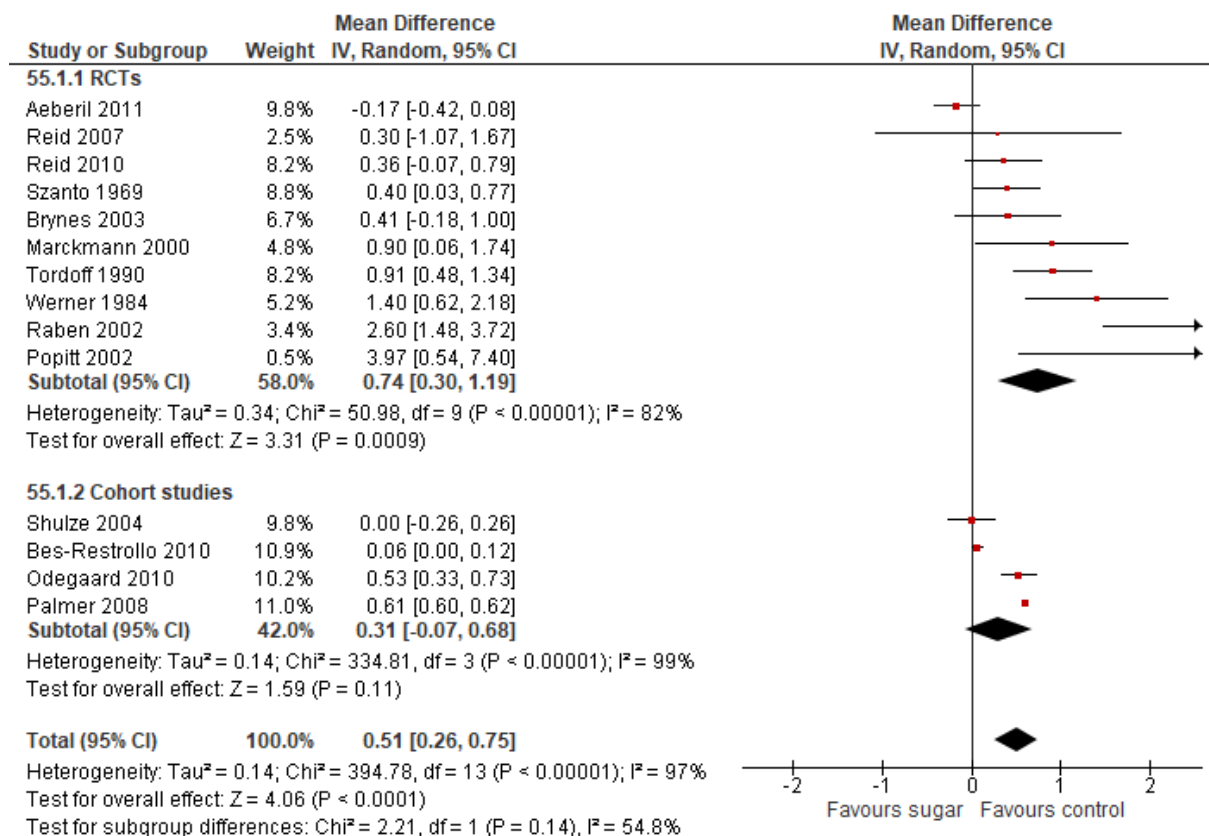
**Figure S90:** Silvain 2012; Intervention/ Exposure: Enoxaparin; Outcome: Major bleeding



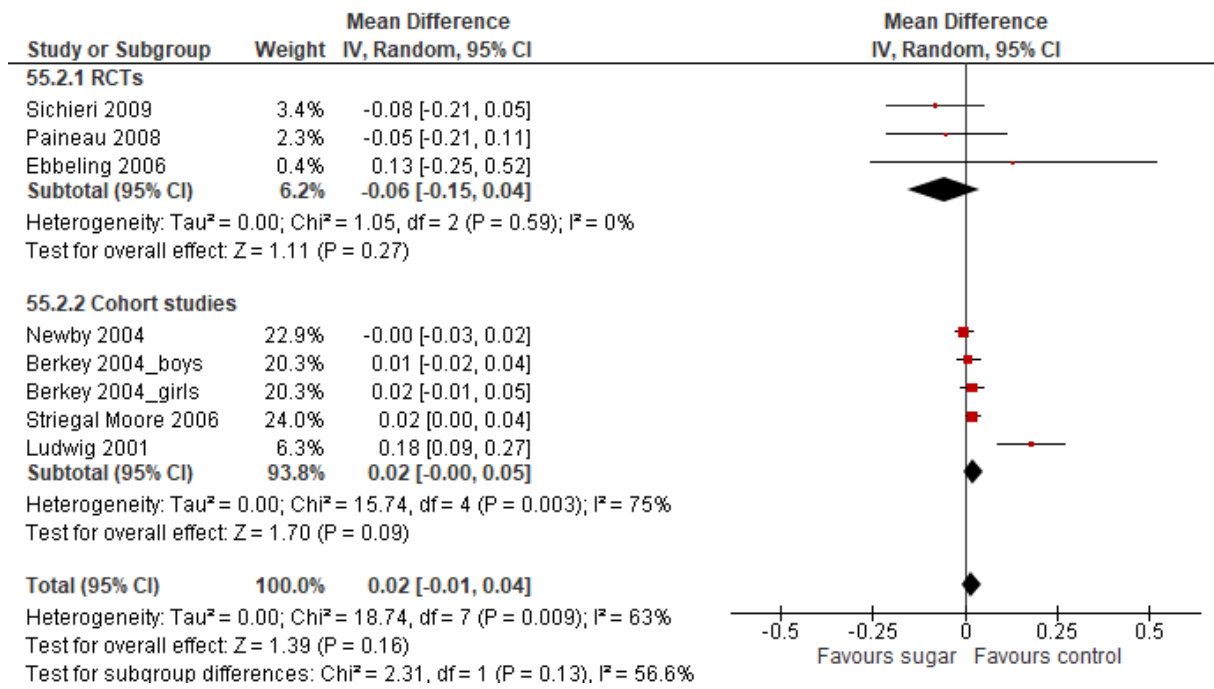
**Figure S91:** Silvain 2012; Intervention/ Exposure: Enoxaparin; Outcome: All-cause mortality or myocardial infarction



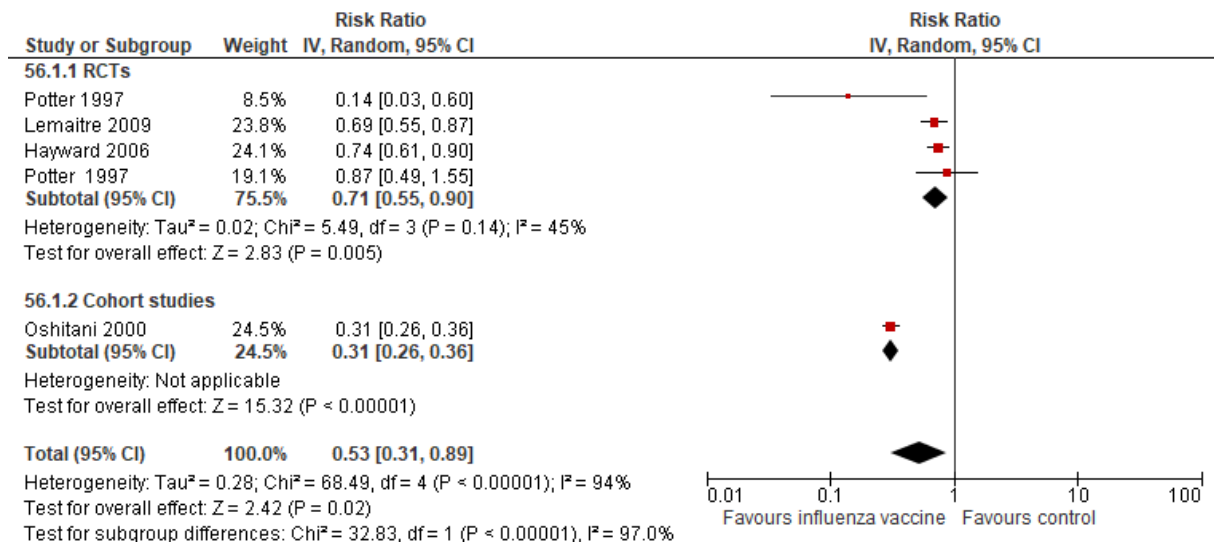
**Figure S92:** Suthar 2012; Intervention/ Exposure: Antiretroviral therapy; Outcome: Tuberculosis infection



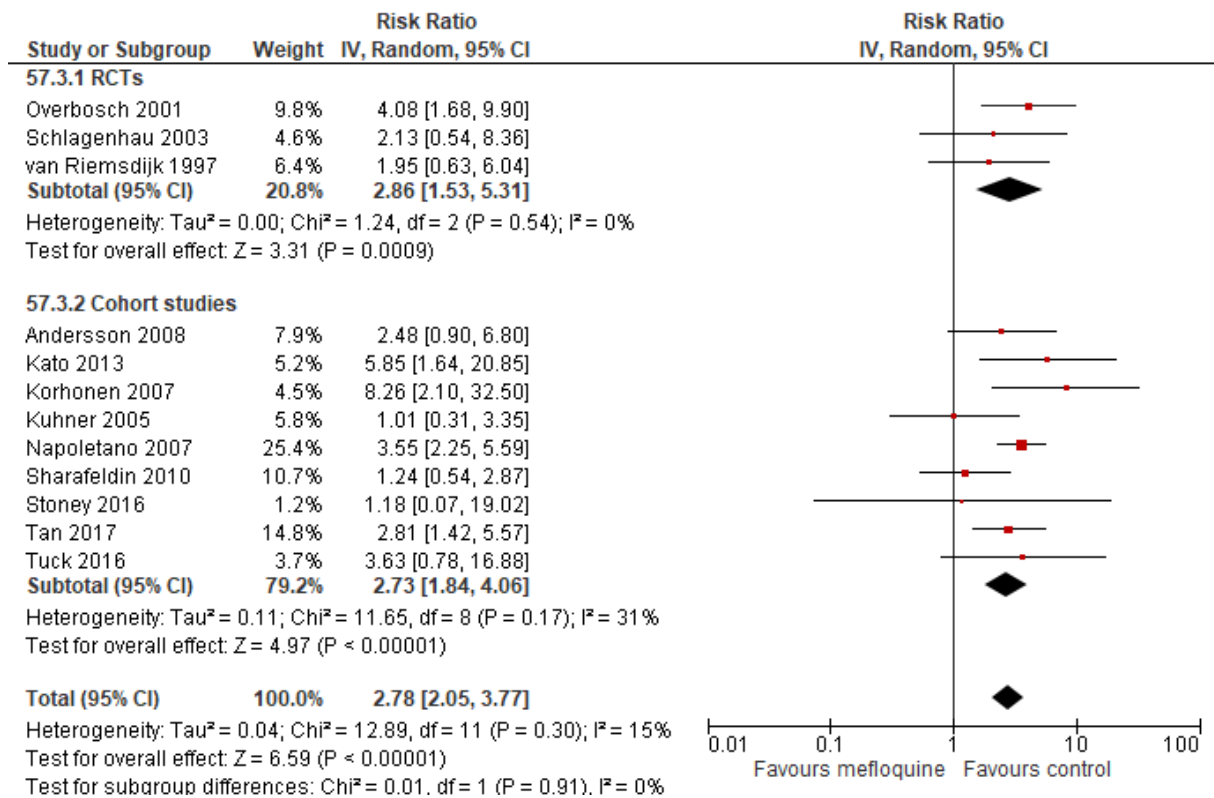
**Figure S93:** Te Morenga 2013; Intervention/ Exposure: High sugar intake; Outcome: Weight gain



**Figure S94:** Te Morenga 2013; Intervention/ Exposure: High sugar intake; Outcome: Body Mass Index

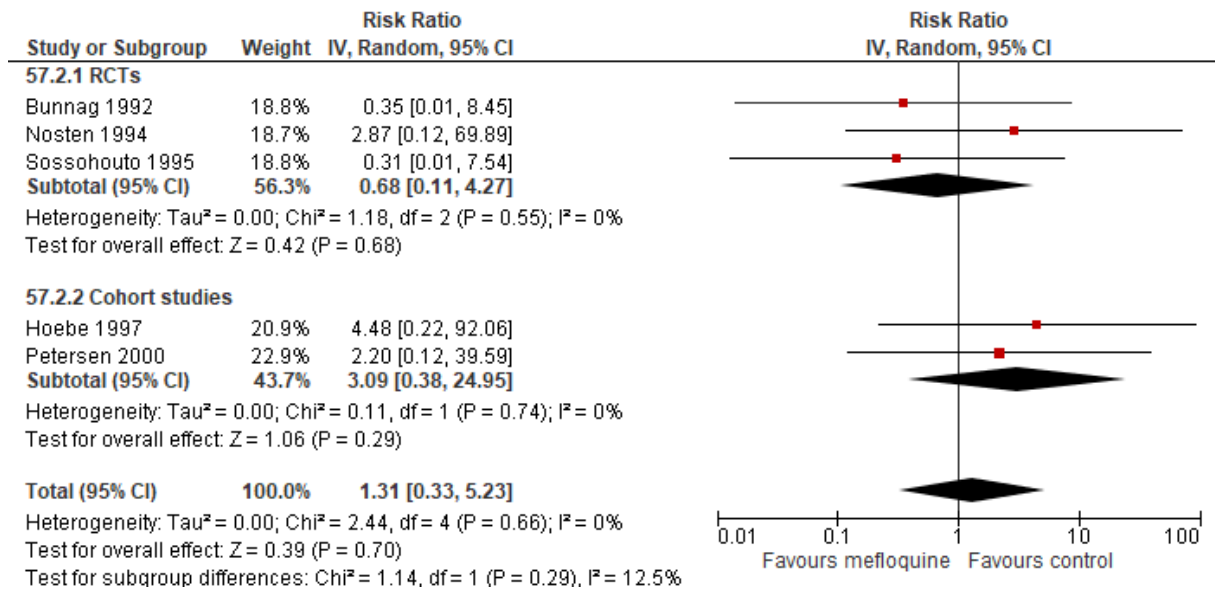


**Figure S95:** Thomas 2010; Intervention/ Exposure: Influenza vaccines; Outcome: Influenza-like illness

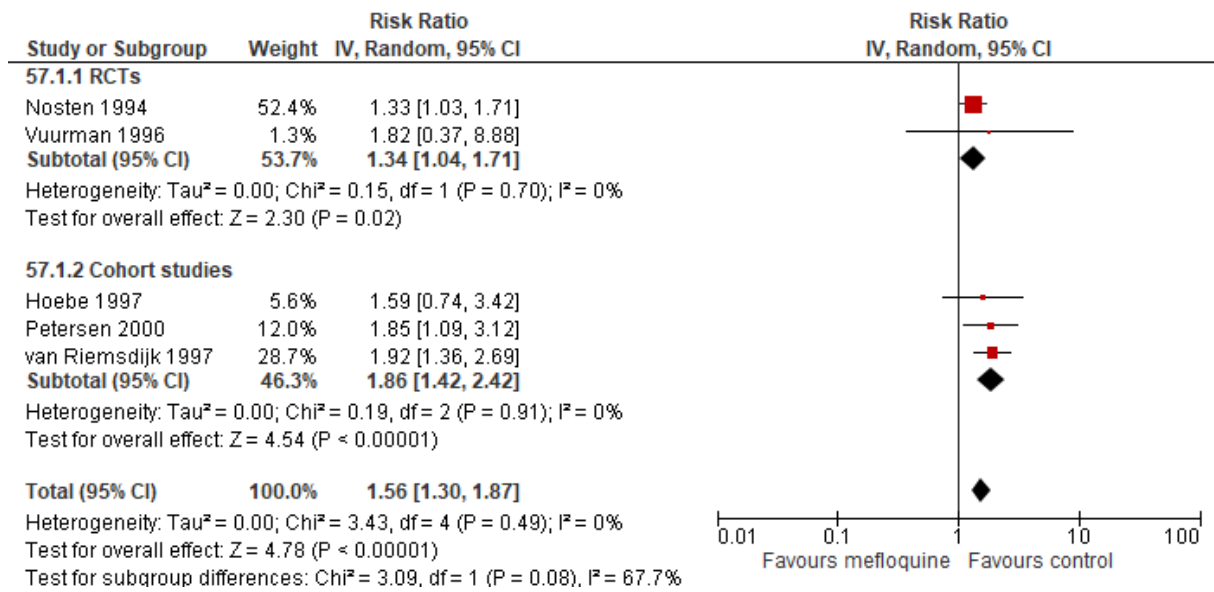


**Figure S96:** Tickell-Painter 2017; Intervention/ Exposure: Mefloquine; Outcome: Discontinuation due to adverse effects

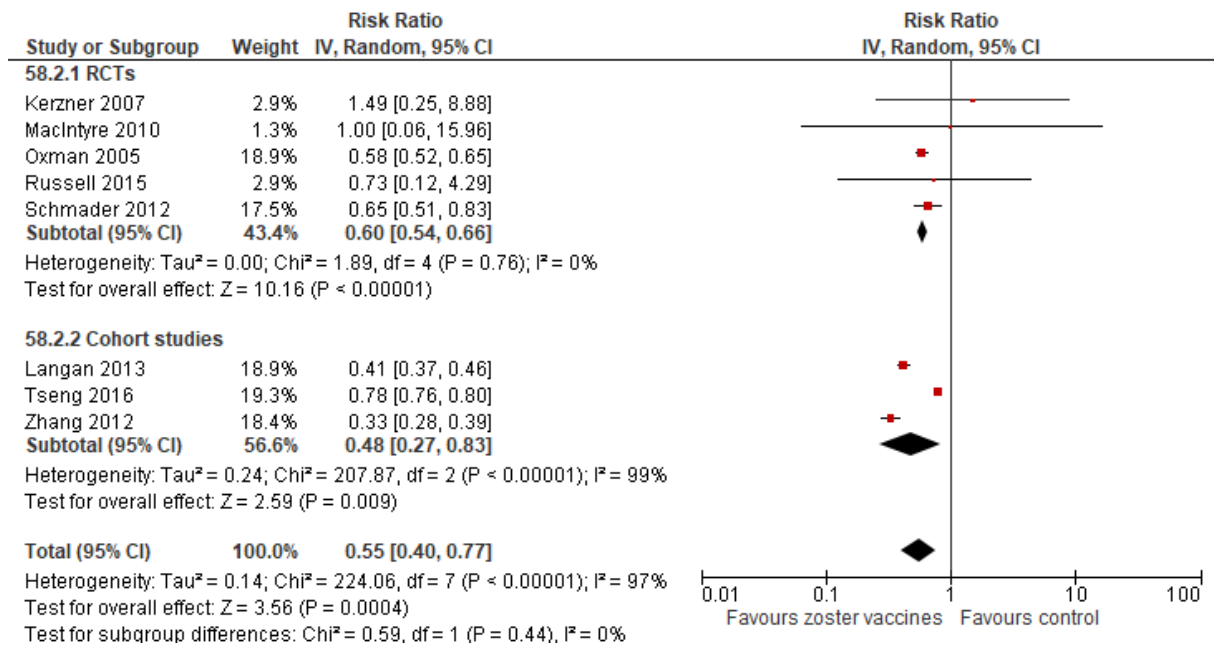




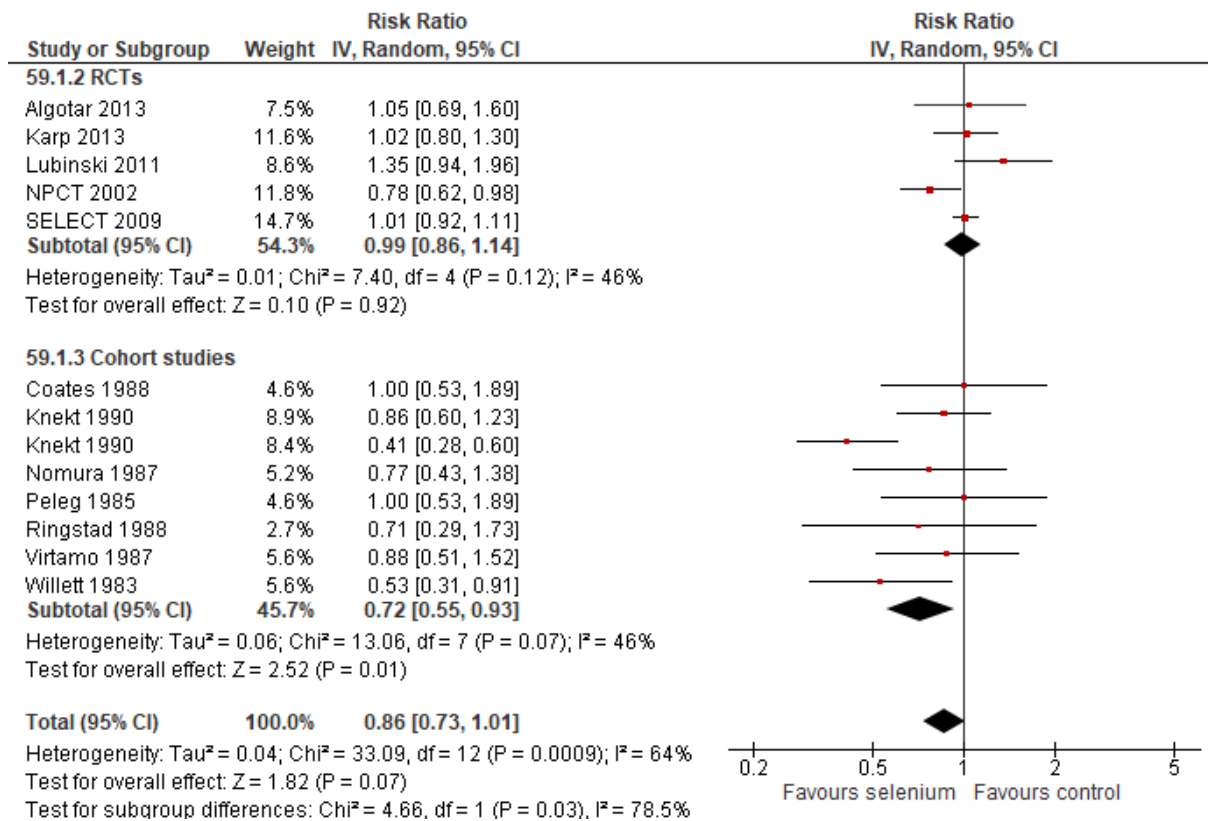
**Figure S97:** Tickell-Painter 2017; Intervention/ Exposure: Mefloquine; Outcome: Serious adverse events or effects



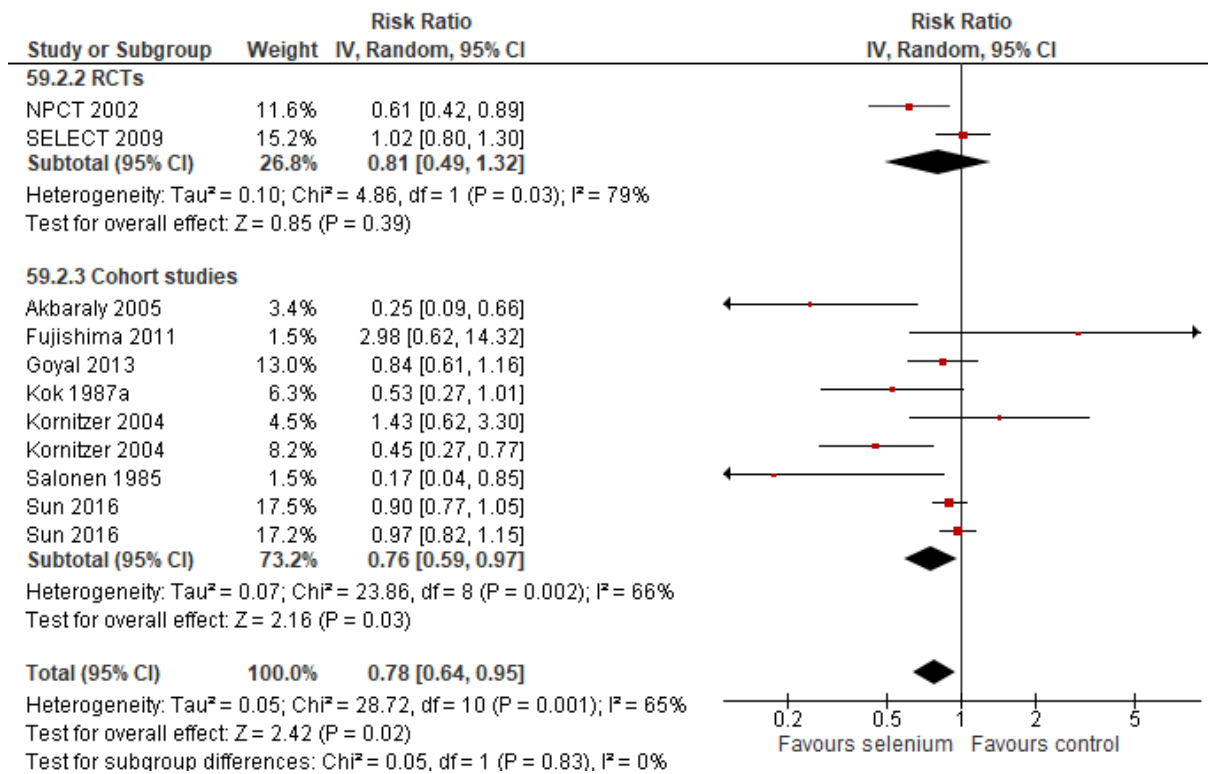
**Figure S98:** Tickell-Painter 2017; Intervention/ Exposure: Mefloquine; Outcome: Nausea



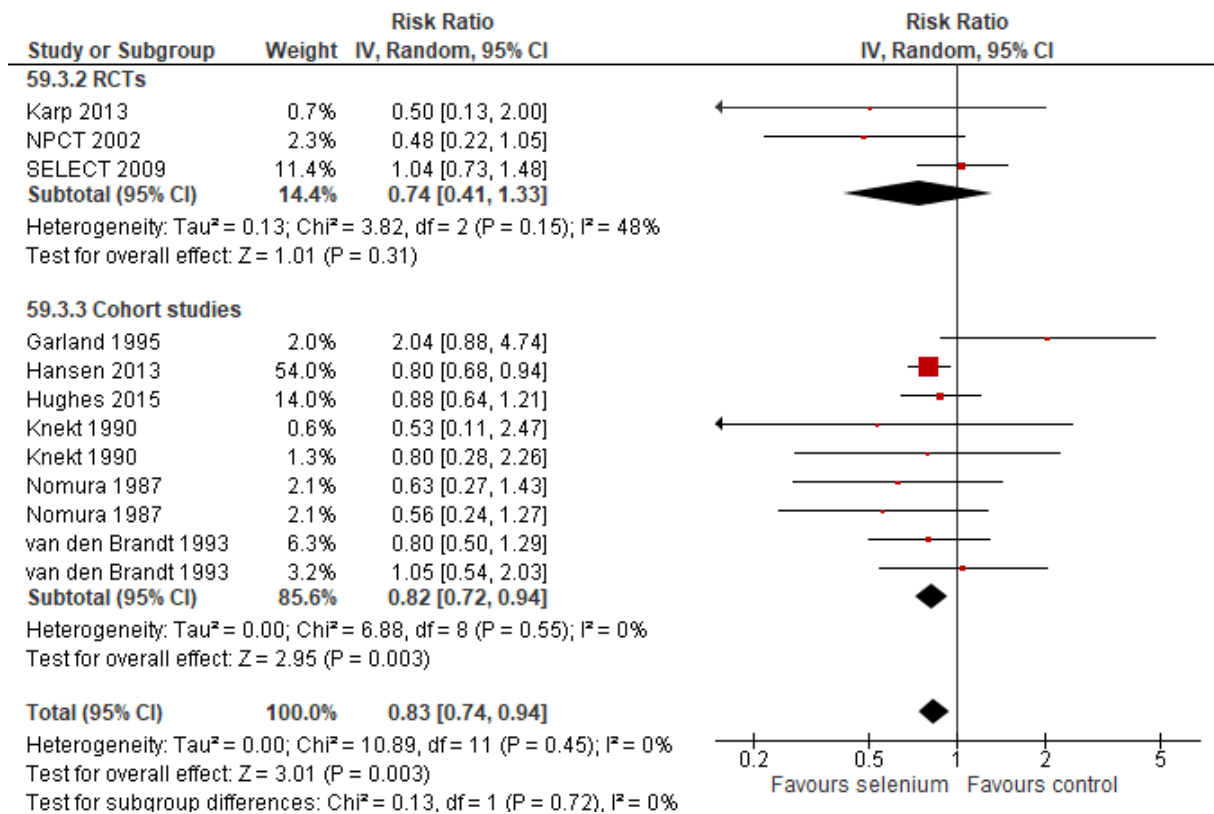
**Figure S99:** Tricco 2018; Intervention/ Exposure: Live-attenuated zoster vaccines; Outcome: Suspected Herpes Zoster



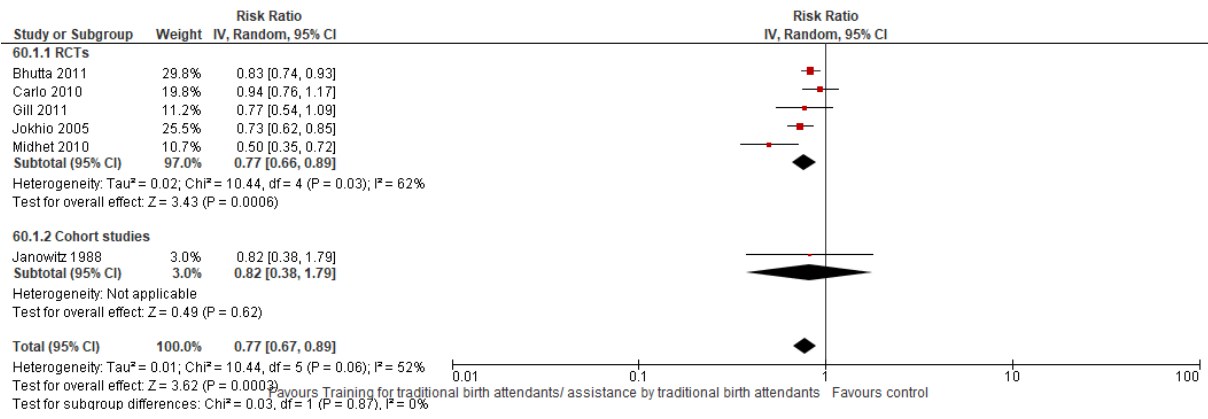
**Figure S100:** Vinceti 2018; Intervention/ Exposure: High selenium; Outcome: Cancer



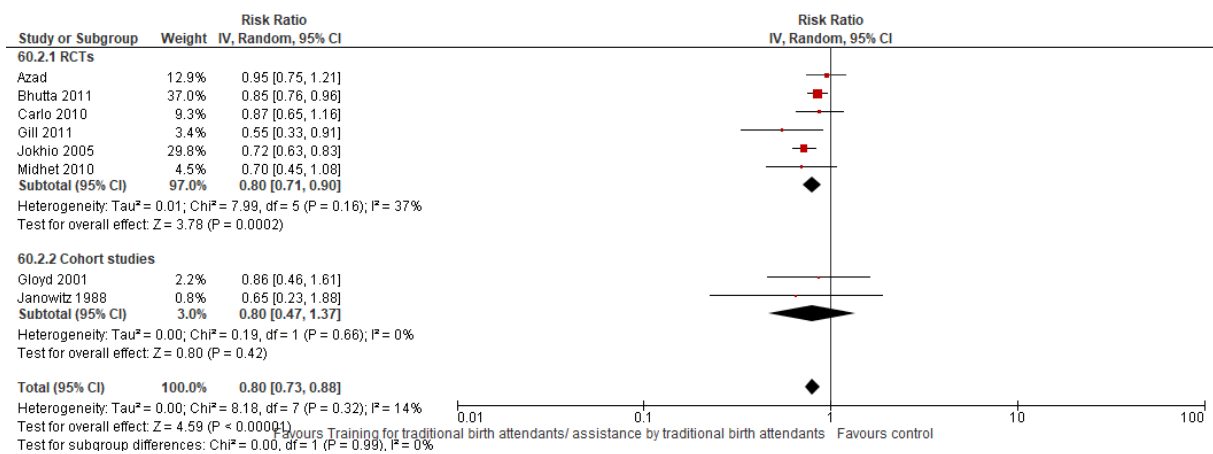
**Figure S101:** Vinceti 2018; Intervention/ Exposure: High selenium; Outcome: Cancer mortality



**Figure S102:** Vinceti 2018; Intervention/ Exposure: High selenium; Outcome: Colorectal cancer

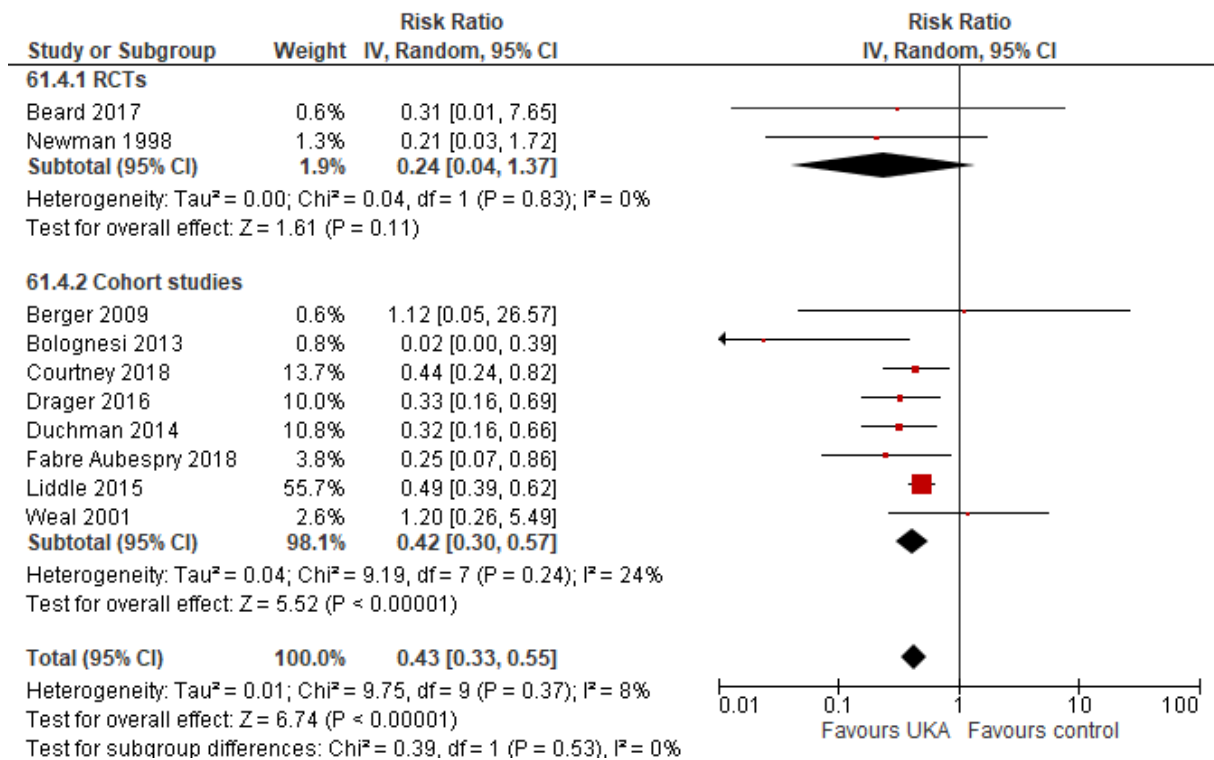


**Figure S103:** Wilson 2011; Intervention/ Exposure: Training for traditional birth attendants/ assistance by traditional birth attendants; Outcome: Perinatal mortality

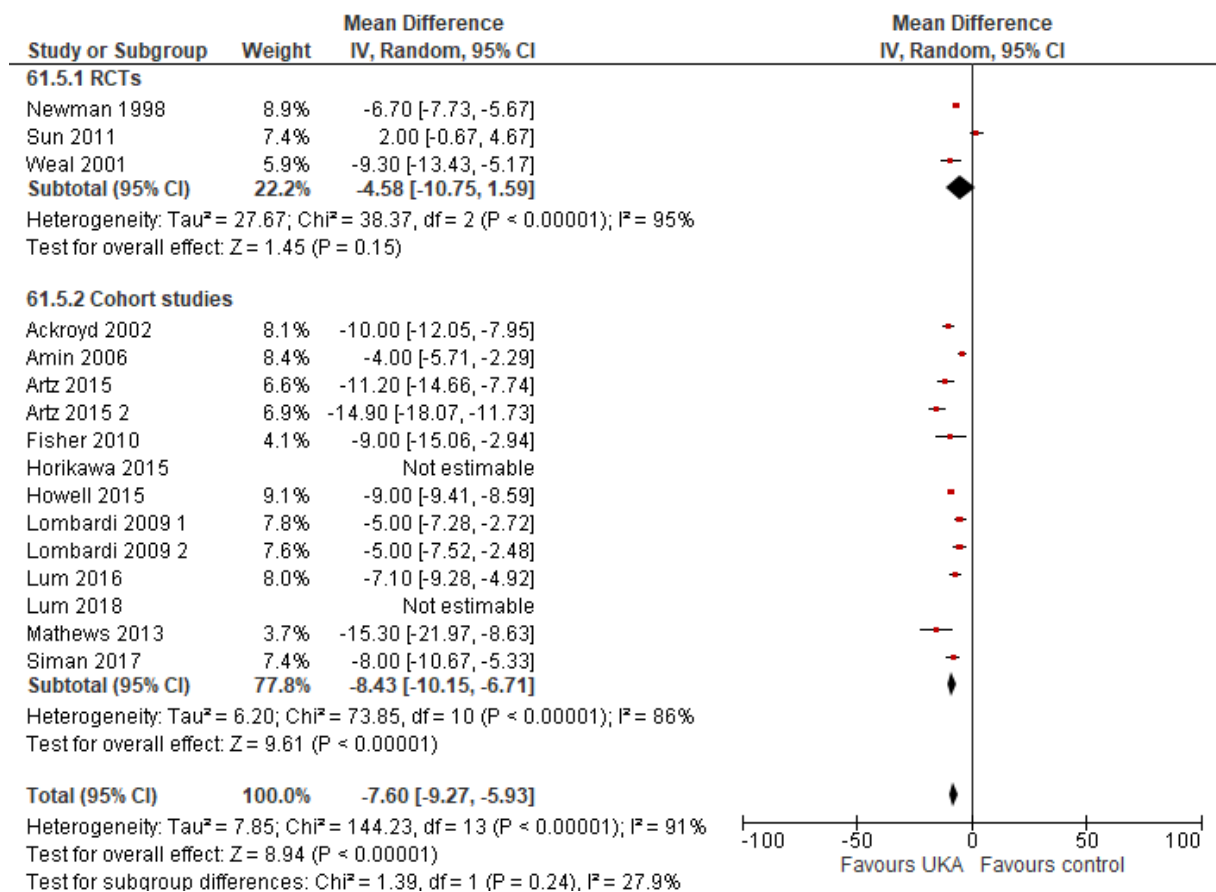


**Figure S104:** Wilson 2011; Intervention/ Exposure: Training for traditional birth attendants/ assistance by traditional birth attendants; Outcome: Neonatal mortality

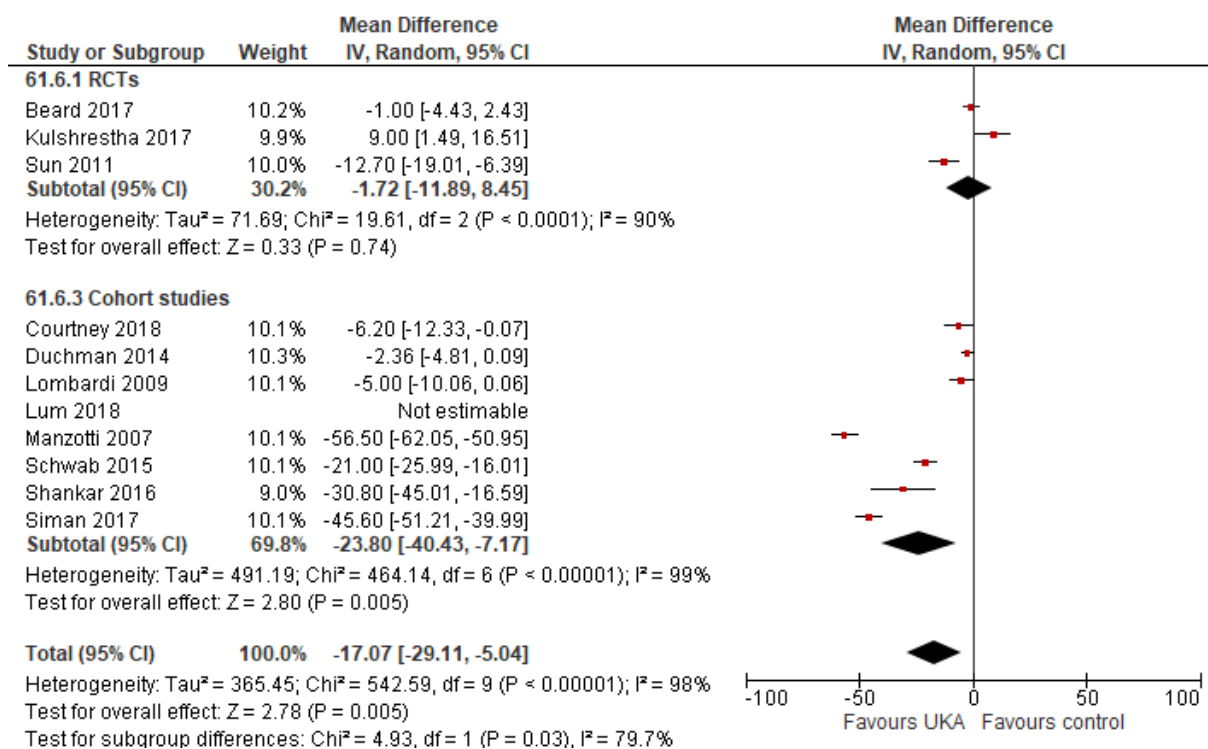




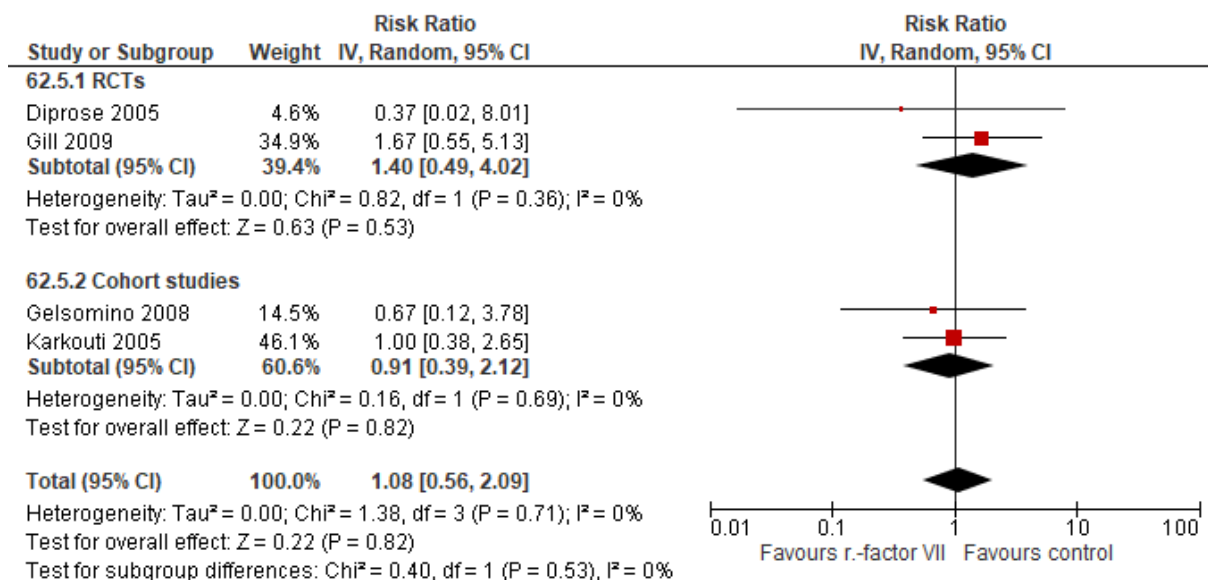
**Figure S105:** Wilson 2019; Intervention/ Exposure: Unicompartimental knee arthroplasty; Outcome: Venous thromboembolism



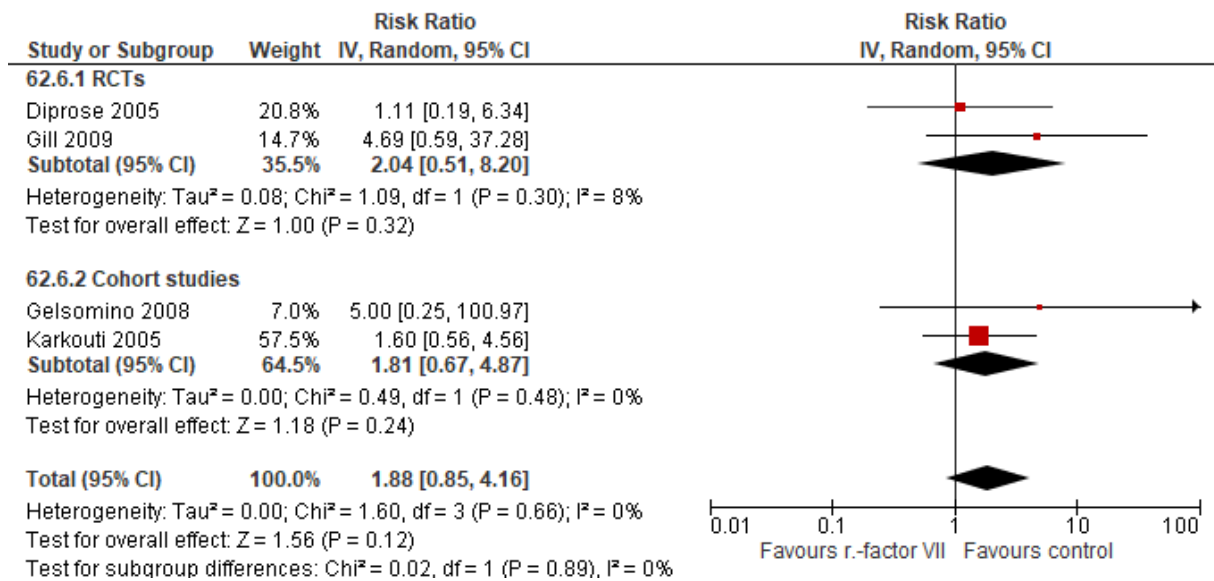
**Figure S106:** Wilson 2019; Intervention/ Exposure: Unicompartmental knee arthroplasty; Outcome: Flexion-extension range



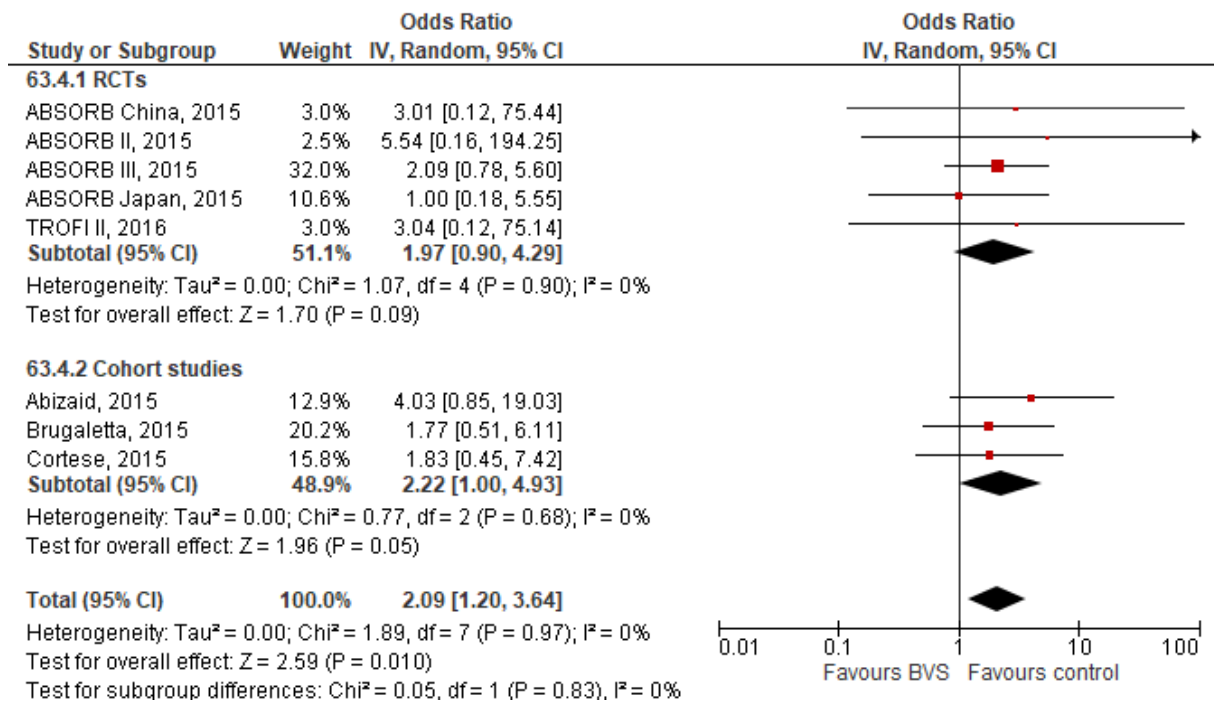
**Figure S107:** Wilson 2019; Intervention/ Exposure: Unicompartmental knee arthroplasty; Outcome: Operation duration



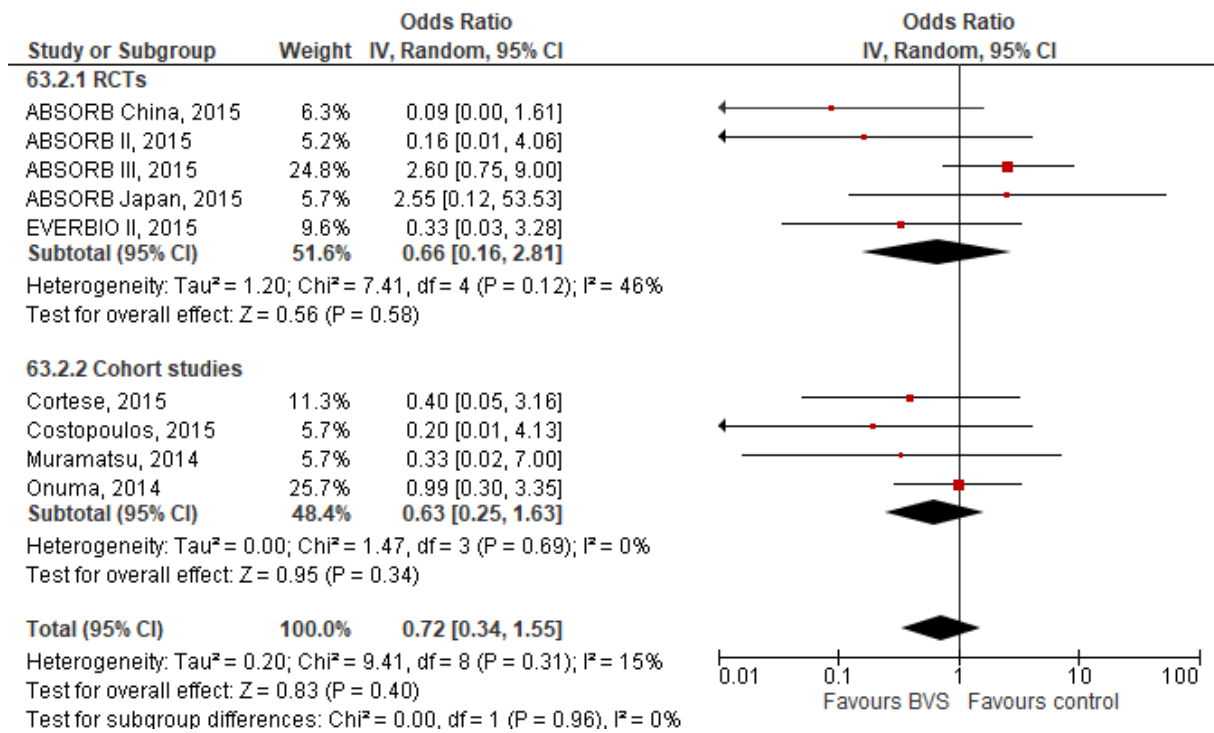
**Figure S108:** Yank 2011; Intervention/ Exposure: Recombinant factor VII; Outcome: All-cause mortality



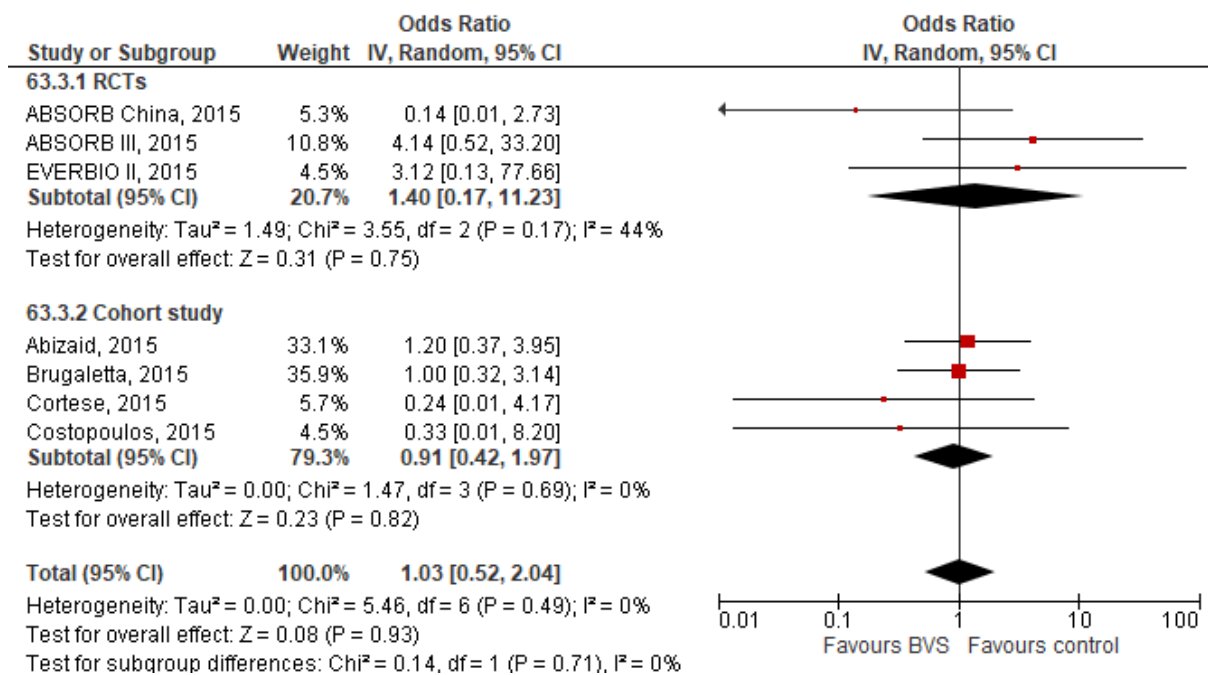
**Figure S109:** Yank 2011; Intervention/ Exposure: Recombinant factor VII; Outcome: Thromboembolism



**Figure S110:** Zhang 2016; Intervention/ Exposure: Everolimus-eluting bioresorbable vascular scaffold; Outcome: Stent thrombosis

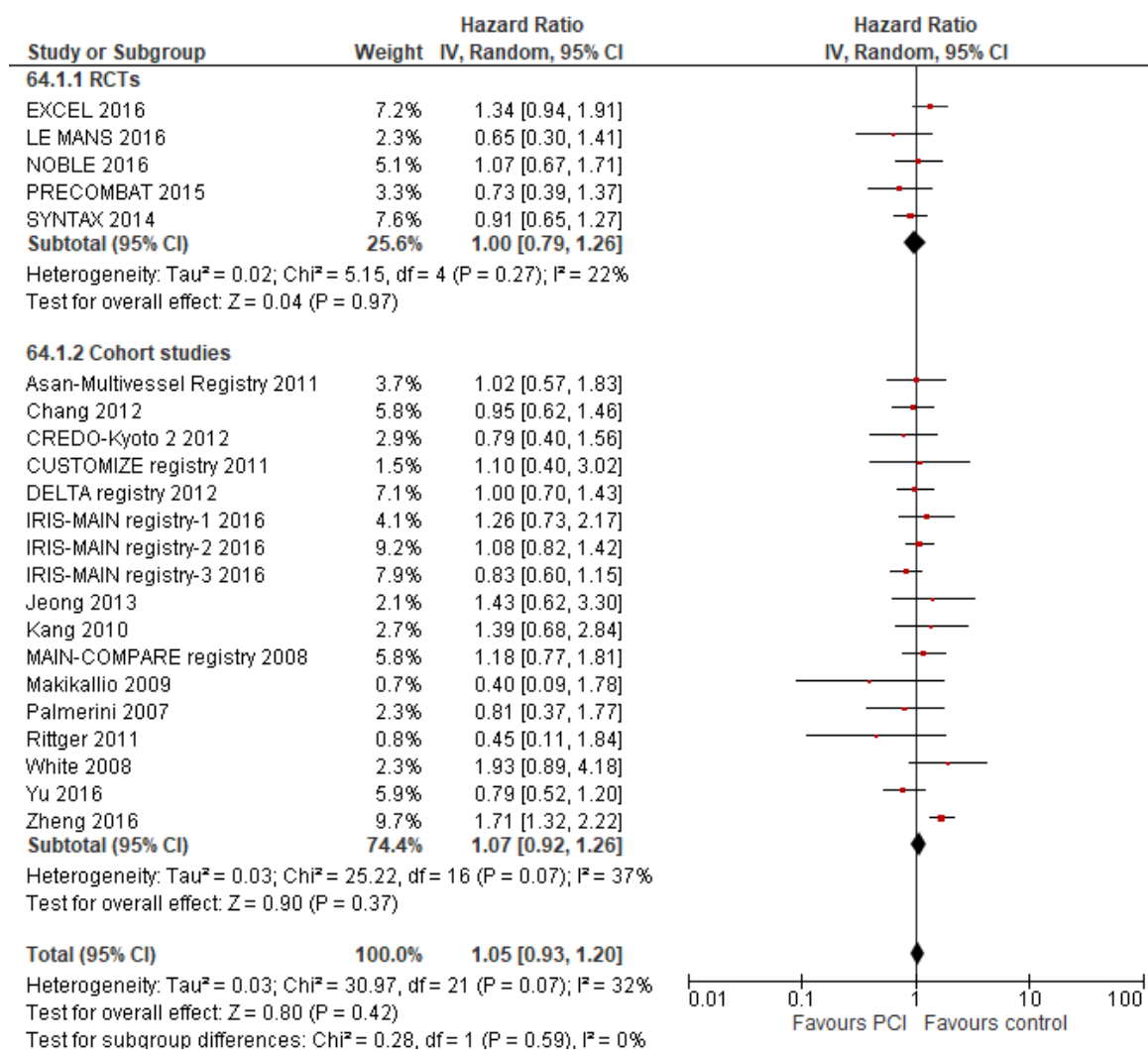


**Figure S111:** Zhang 2016; Intervention/ Exposure: Everolimus-eluting bioresorbable vascular scaffold; Outcome: All-cause mortality

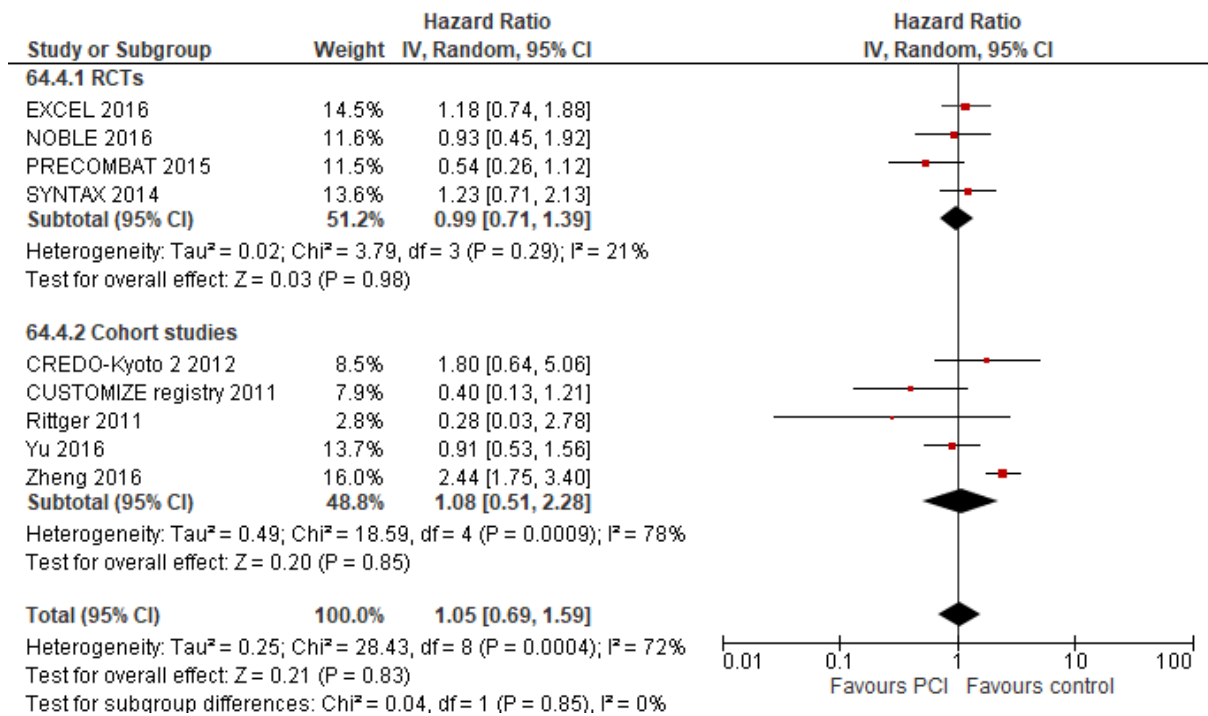


**Figure S112:** Zhang 2016; Intervention/ Exposure: Everolimus-eluting bioresorbable vascular scaffold; Outcome: Coronary heart disease mortality

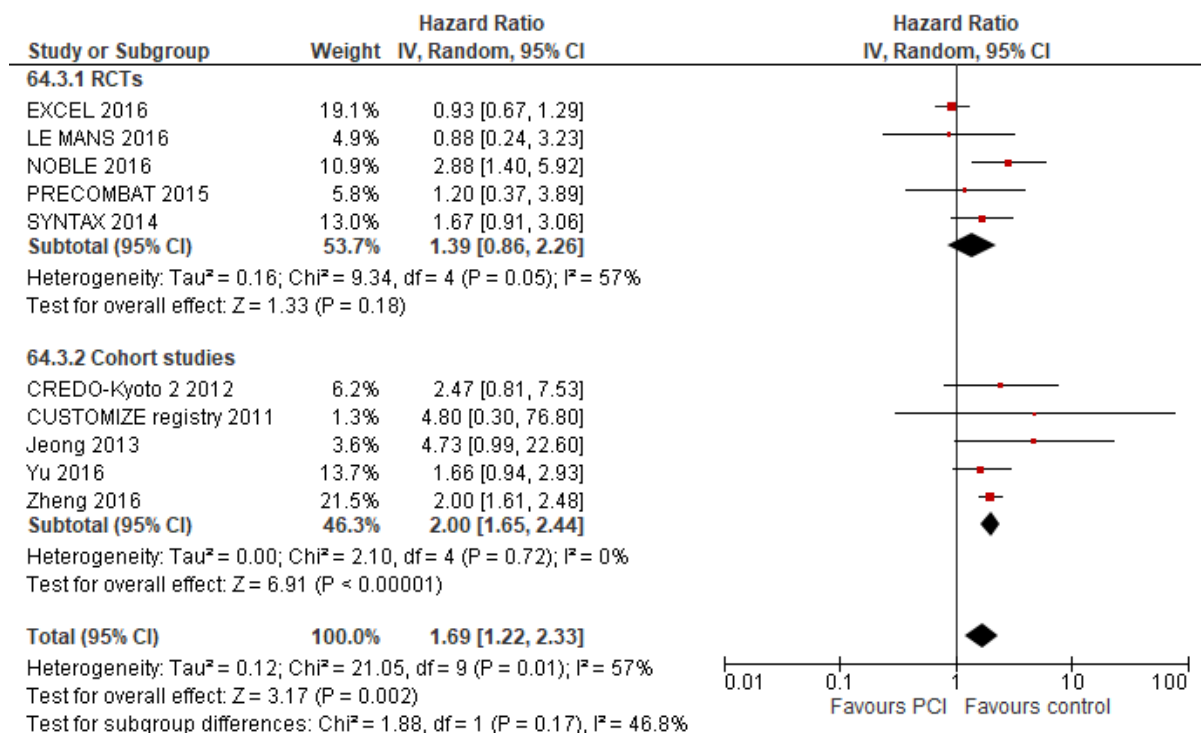




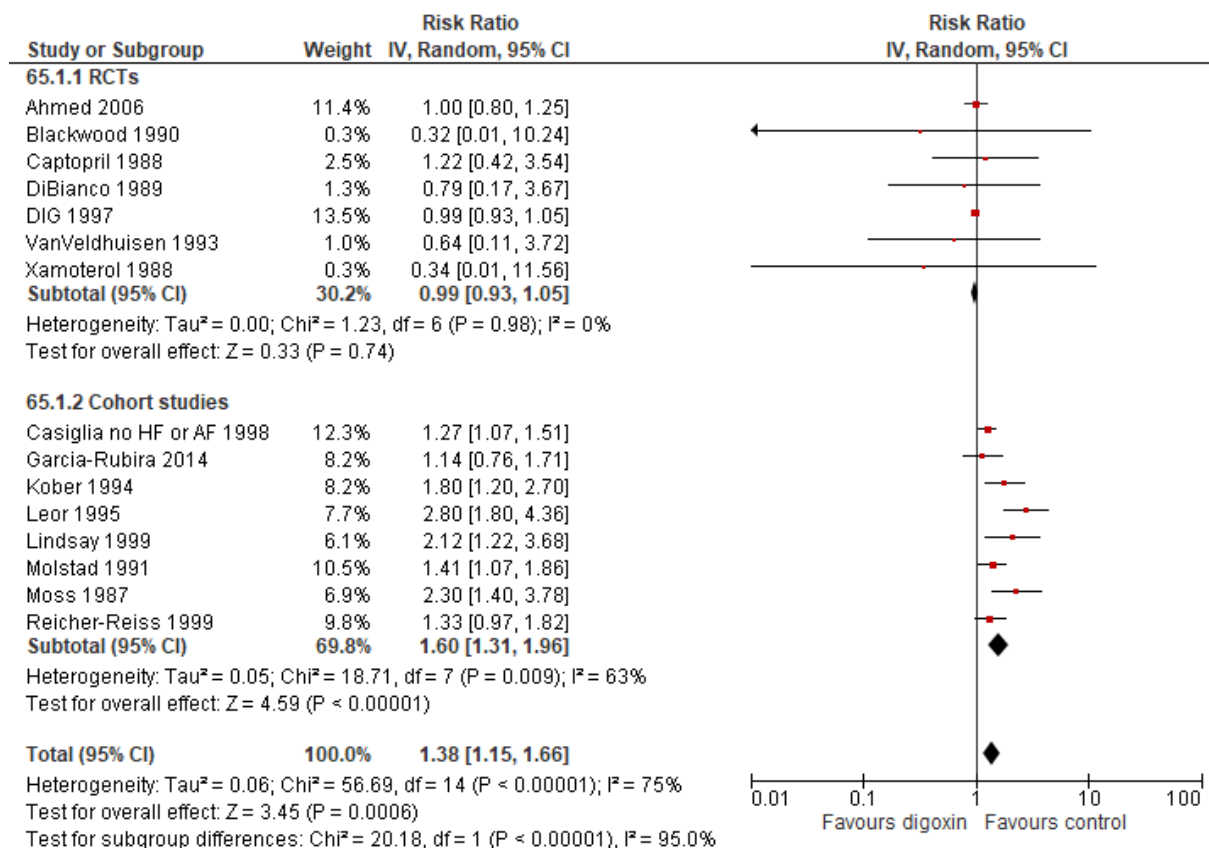
**Figure S113:** Zhang 2017; Intervention/ Exposure: Percutaneous coronary intervention; Outcome: All-cause mortality



**Figure S114:** Zhang 2017; Intervention/ Exposure: Percutaneous coronary intervention; Outcome: Cardiovascular mortality

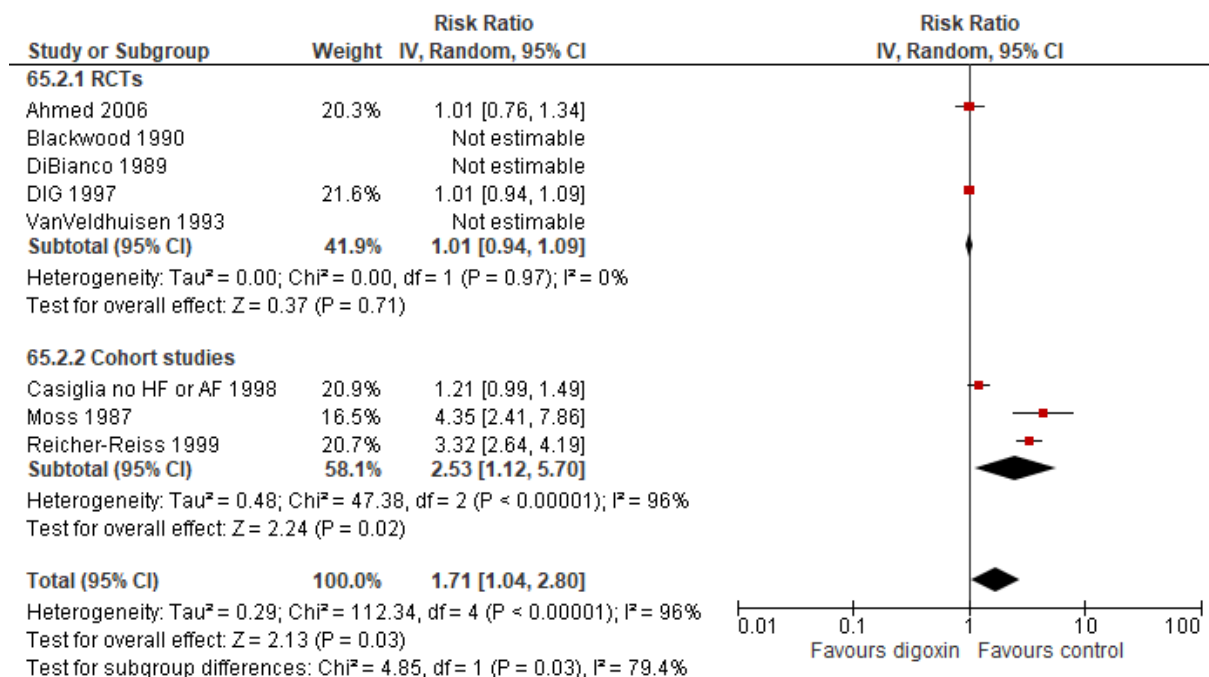


**Figure S115:** Zhang 2017; Intervention/ Exposure: Percutaneous coronary intervention; Outcome: Myocardial infarction

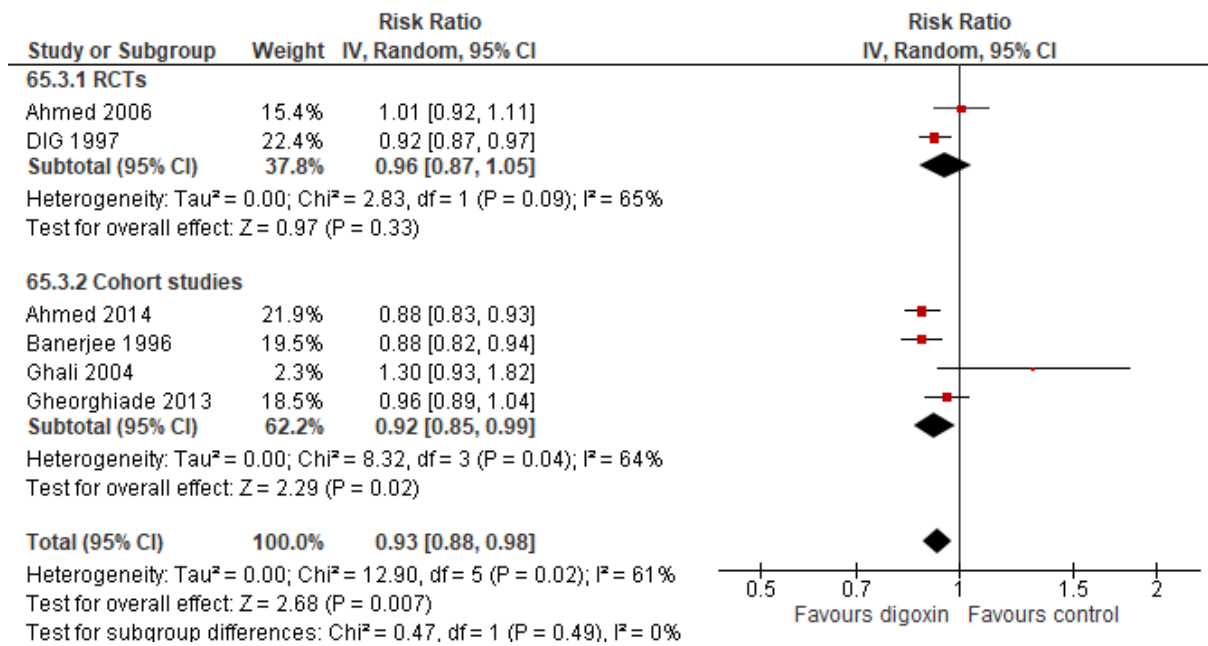


**Figure S116:** Ziff 2015; Intervention/ Exposure: Digoxin;

Outcome: All-cause mortality



**Figure S117:** Ziff 2015; Intervention/ Exposure: Digoxin; Outcome: Cardiovascular mortality



**Figure S118:** Ziff 2015; Intervention/ Exposure: Digoxin; Outcome: Hospital admission

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