

#### Appendix 4. Search strategy for MEDLINE/Ovid

- 1 exp Surgical Procedures, Operative/
- 2 su.fs. or (surger\* or surgical\*).tw,kf.
- 3 (curettage or debridement or electrosurger\* or fasciotom\* or Keratectom\* or laparotom\* or lymph node excision or mastectom\* or metastasectom\* or microsurger\* or myotom\* or neurosurgical procedure\* or orthopedic procedure\* or amputation or Osteotom\* or pelvic exenteration or pneumonectom\* or prosthesis implantation or reoperation or splenectom\* or symphysiotom\* or transplantation).tw,kf.
- 4 or/1-3
- 5 ((opioid\* or opiate\*) adj3 (sparing or minimi?ation or free)).tw,kf.
- 6 (multimodal adj5 (an?esthes\* or analges\*)).tw,kf.
- 7 5 or 6
- 8 analgesics/ or exp analgesics, non-narcotic/
- 9 exp Adrenergic alpha-2 Receptor Agonists/
- 10 Caffeine/
- 11 exp anti-inflammatory agents/
- 12 exp Adrenal Cortex Hormones/
- 13 exp Cyclooxygenase 2 Inhibitors/
- 14 exp Adrenergic beta-Antagonists/
- 15 Receptors, N-Methyl-D-Aspartate/ai [Antagonists & Inhibitors]
- 16 magnesium compounds/ or magnesium sulfate/
- 17 exp Anticonvulsants/
- 18 (Lidocaine or Alpha-2 Receptor Agonist\* or Caffeine or Corticosteroid\* or Beta block\* or NMDA receptor antagonist\* or Magnesium or Acetaminophen or NSAID\* or Anticonvulsant\* or anticonvulsant\* or Antidepressant\* or gabapentinoid\* or cox-2 inhibitor\*).tw,kf.
- 19 Dexmedetomidine/ or lidocaine/ or ketamine/ or Propanolamines/ or Clonidine/
- 20 (Pregabalin or Gabapentin or Carbamazepine or Carbazepin or Esmolol or Propanolamine\* or Metoprolol or Labetolol or Clonidine or Dexmedetomidine or Catapressan or Caffeine or Ketamine or Dextromethorphan or Dexamethasone or Methylprednisolone or hydrocortison\* or Prednisone or magnesium or Amitriptyline or Duloxetine or Tryptophan or Bicifadine or Desipramine or fluoxetine or Venlafaxine or Citalopram).ti.
- 21 or/8-20
- 22 perioperative period/ or intraoperative period/ or exp Administration, Intravenous/ or Combined Modality Therapy/
- 23 (perioperat\* or peri operat\* or intra operat\* or intraoperat\*).tw,kf.
- 24 (an?esthes\* adj2 induction).tw,kf.
- 25 or/22-24
- 26 21 and 25
- 27 7 or 26
- 28 4 and 27
- 29 randomized controlled trial.pt.
- 30 controlled clinical trial.pt.
- 31 random\*.tw.

32 placebo.ab.  
33 clinical trials as topic.sh.  
34 trial.ti.  
35 or/29-34  
36 exp animals/ not humans/  
37 35 not 36  
38 28 and 37  
39 38 use medall

**Search strategy for Embase**

- 40 exp \*surgery/  
41 (surg\* or surgical\*).tw.  
42 (curettage or debridement or electrosurger\* or fasciotom\* or Keratectom\* or laparotom\* or lymph node excision or mastectom\* or metastasectom\* or microsurger\* or myotom\* or neurosurgical procedure\* or orthopedic procedure\* or amputation or Osteotom\* or pelvic exenteration or pneumonectom\* or prosthesis implantation or reoperation or splenectom\* or symphysiotom\* or transplantation).tw.  
43 40 or 41 or 42  
44 ((opioid\* or opiate\*) adj3 (sparing or minimi?ation or free)).tw.  
45 (multimodal adj5 (an?esthes\* or analges\*)).tw.  
46 44 or 45  
47 exp \*analgesic agent/  
48 exp \*alpha 2 adrenergic receptor stimulating agent/  
49 \*caffeine/  
50 exp \*antiinflammatory agent/  
51 exp \*corticosteroid/  
52 exp \*cyclooxygenase 2 inhibitor/  
53 exp \*beta adrenergic receptor blocking agent/  
54 exp \*n methyl dextro aspartic acid receptor stimulating agent/  
55 \*magnesium/  
56 \*magnesium sulfate/  
57 exp \*anticonvulsive agent/  
58 (Lidocaine or Alpha-2 Receptor Agonist\* or Caffeine or Corticosteroid\* or Beta block\* or NMDA receptor antagonist\* or Magnesium or Acetaminophen or NSAID\* or Anti-convulsant\* or anticonvulsant\* or Antidepressant\* or gabapentinoid\* or cox-2 inhibitor\*).tw.  
59 \*dexmedetomidine/  
60 \*lidocaine/  
61 \*ketamine/

- 62 \*propranolamine derivative/  
63 \*clonidine/  
64 (Pregabalin or Gabapentin or Carbamazepine or Carbazepin or Esmolol or Propranolamine\* or Metoprolol or Labetolol or Clonidine or Dexmedetomidine or Catapressan or Caffeine or Ketamine or Dextromethorphan or Dexamethasone or Methylprednisolone or hydrocortison\* or Prednisone or magnesium or Amitriptyline or Duloxetine or Tryptophan or Bicifadine or Desipramine or fluoxetine or Venlafaxine or Citalopram).ti.  
65 or/47-64  
66 \*perioperative period/  
67 intraoperative period/  
68 (perioperat\* or peri operat\* or intra operat\* or intraoperat\*).tw.  
69 anesthesia induction/  
70 \*intravenous drug administration/  
71 (an?esthes\* adj1 induction).tw.  
72 or/66-71  
73 65 and 72  
74 46 or 73  
75 43 and 74  
76 random\*.tw. or placebo\*.mp. or double-blind\*.tw. or trial.ti.  
77 75 and 76  
78 (exp animal/ or nonhuman/) not exp human/  
79 77 not 78  
80 79 use emczd

**Search strategy for CENTRAL**

- 81 exp Surgical Procedures, Operative/  
82 su.fs. or (surger\* or surgical\*).tw,kw.  
83 (curettage or debridement or electrosurger\* or fasciotom\* or Keratectom\* or laparotom\* or lymph node excision or mastectom\* or metastasectom\* or microsurger\* or myotom\* or neurosurgical procedure\* or orthopedic procedure\* or amputation or Osteotom\* or pelvic exenteration or pneumonectom\* or prosthesis implantation or reoperation or splenectom\* or symphysiotom\* or transplantation).tw,kw.  
84 or/81-83  
85 ((opioid\* or opiate\*) adj3 (sparing or minimi?ation or free)).tw,kw.  
86 (multimodal adj5 (an?esthes\* or analges\*)).tw,kw.  
87 85 or 86  
88 analgesics/ or exp analgesics, non-narcotic/  
89 exp Adrenergic alpha-2 Receptor Agonists/  
90 Caffeine/  
91 exp anti-inflammatory agents/  
92 exp Adrenal Cortex Hormones/  
93 exp Cyclooxygenase 2 Inhibitors/  
94 exp Adrenergic beta-Antagonists/  
95 Receptors, N-Methyl-D-Aspartate/ai [Antagonists & Inhibitors]  
96 magnesium compounds/ or magnesium sulfate/  
97 exp Anticonvulsants/  
98 (Lidocaine or Alpha-2 Receptor Agonist\* or Caffeine or Corticosteroid\* or Beta block\* or NMDA receptor antagonist\* or Magnesium or Acetaminophen or NSAID\* or Anti-convulsant\* or anticonvulsant\* or Antidepressant\* or gabapentinoid\* or cox-2 inhibitor\*).tw,kw.  
99 Dexmedetomidine/ or lidocaine/ or ketamine/ or Propanolamines/ or Clonidine/  
100 (Pregabalin or Gabapentin or Carbamazepine or Carbazepin or Esmolol or Propanolamine\* or Metoprolol or Labetolol or Clonidine or Dexmedetomidine or Catapressan or Caffeine or Ketamine or Dextromethorphan or Dexamethasone or Methylprednisolone or hydrocortison\* or Prednisone or magnesium or Amitriptyline or

- Duloxetine or Tryptophan or Bicyclanil or Desipramine or fluoxetine or Venlafaxine or Citalopram).ti.
- 101 or/88-100
- 102 perioperative period/ or intraoperative period/ or exp Administration, Intravenous/ or Combined Modality Therapy/
- 103 (perioperat\* or peri operat\* or intra operat\* or intraoperat\*).tw,kw.
- 104 (an?esthes\* adj2 induction).tw,kw.
- 105 or/102-104
- 106 101 and 105
- 107 87 or 106
- 108 84 and 107
- 109 108 use cctr
- 110 39 or 80 or 109

## Search strategy for Web of science

1. (TS=(surg\*)) OR TS=(( curettage or debridement or electrosurger\* or fasciotom\* or Keratectom\* or laparotom\* or lymph node excision or mastectom\* or metastasectom\* or microsurger\* or myotom\* or neurosurgical procedure\* or orthopedic procedure\* or amputation or Osteotom\* or pelvic exenteration or pneumonectom\* or prosthesis implantation or reoperation or splenectom\* or symphysiotom\* or transplantation ))
2. TS((((opioid\* or opiate\*) NEAR/3 (sparing or minimi?ation or free)))
3. (TS=(multimodal NEAR/5 (an\$esthes\* or analges\*)))
4. (#2) OR #3
5. (TS=(nonnarcotic analges\* )) OR TS=(non narcotic analges\*)
6. TS=((Pregabalin or Gabapentin or Carbamazepine or Carbazepin or Esmolol or Propranolamine\* or Metoprolol or Labetolol or Clonidine or Dexmedetomidine or Catapresan or Caffeine or Ketamine or Dextromethorphan or Dexamethasone or Methylprednisolone or hydrocortison\* or Prednisone or magnesium or Amitriptyline or Duloxetine or Tryptophan or Bicifadine or Desipramine or fluoxetine or Venlafaxine or Citalopram))
7. (TS=(Nonsteroid\* anti-inflammatory)) OR TS=(Nonsteroid\* antiinflammatory)
8. TS=((Lidocaine or Alpha-2 Receptor Agonist\* or Caffeine or Corticosteroid\* or Beta block\* or NMDA receptor antagonist\* or Magnesium or Acetaminophen or NSAID\* or Anti-convulsant\* or anticonvulsant\* or Antidepressant\* or gabapentinoid\* or cox-2 inhibitor\*))
9. (((#5) OR #6) OR #7) OR #8
10. TS=(intravenous) OR TS=(an\$esthes\* NEAR/2 induction)
11. ALL=(perioperat\* or peri operat\* or intra operat\* or intraoperat\*)
12. (#10) OR #11
13. (#9) AND #12
14. (#13) OR #4
15. (#1) AND #14
16. TS=((randomised OR randomized OR randomisation OR randomisation OR placebo\* OR (random\* AND (allocat\* OR assign\* ) OR (blind\* AND (single OR double OR treble OR triple) )) )
17. TS=((animal or animals or pisces or fish or fishes or catfish or catfishes or sheatfish or silurus or arius or heteropneustes or clarias or gariepinus or fathead minnow or fathead minnows

or pimephales or promelas or cichlidae or trout or trouts or char or chars or salvelinus or salmo or oncorhynchus or guppy or guppies or millionfish or poecilia or goldfish or goldfishes or carassius or auratus or mullet or mullets or mugil or curema or shark or sharks or cod or cods or gadus or morhua or carp or carps or cyprinus or carpio or killifish or eel or eels or anguilla or zander or sander or lucioperca or stizostedion or turbot or turbots or psetta or flatfish or flatfishes or plaice or pleuronectes or platessa or tilapia or tilapias or oreochromis or sarotherodon or common sole or dover sole or solea or zebrafish or zebrafishes or danio or rerio or seabass or dicentrarchus or labrax or morone or lamprey or lampreys or petromyzon or pumpkinseed or pumpkinseeds or lepomis or gibbosus or herring or clupea or harengus or amphibia or amphibian or amphibians or anura or salientia or frog or frogs or rana or toad or toads or bufo or xenopus or laevis or bombina or epidalea or calamita or salamander or salamanders or newt or newts or triturus or reptilia or reptile or reptiles or bearded dragon or pogona or vitticeps or iguana or iguanas or lizard or lizards or anguis fragilis or turtle or turtles or snakes or snake or aves or bird or birds or quail or quails or coturnix or bobwhite or colinus or virginianus or poultry or poultries or fowl or fowls or chicken or chickens or gallus or zebra finch or taeniopygia or guttata or canary or canaries or serinus or canaria or parakeet or parakeets or grasskeet or parrot or parrots or psittacine or psittacines or shelduck or tadorna or goose or geese or branta or leucopsis or woodlark or lullula or flycatcher or ficedula or hypoleuca or dove or doves or geopelia or cuneata or duck or ducks or greylag or graylag or anser or harrier or circus pygargus or red knot or great knot or calidris or canutus or godwit or limosa or lapponica or meleagris or gallopavo or jackdaw or corvus or monedula or ruff or philomachus or pugnax or lapwing or peewit or plover or vanellus or swan or cygnus or columbianus or bewickii or gull or chroicocephalus or ridibundus or albigularis or great tit or parus or aythya or fuligula or streptopelia or risoria or spoonbill or platalea or leucorodia or blackbird or turdus or merula or blue tit or cyanistes or pigeon or pigeons or columba or pintail or anas or starling or sturnus or owl or athene noctua or pochard or ferina or cockatiel or nymphiacus or hollandicus or skylark or alauda or tern or sterna or teal or crecca or oystercatcher or haematopus or ostralegus or shrew or shrews or sorex or araneus or crocidura or russula or european mole or talpa or chiroptera or bat or bats or eptesicus or serotinus or myotis or dasycneme or daubentonii or pipistrelle or pipistrellus or cat or cats or felis or catus or feline or dog or dogs or canis or canine or canines or otter or otters or lutra or badger or badgers or meles or fitchew or fitch or fomart or foulmart or ferrets or ferret or polecat or polecats or mustela or putorius or weasel or weasels or fox or foxes or vulpes or common seal or phoca or vitulina or grey seal or halichoerus or horse or horses or equus or equine or equidae or donkey or donkeys or mule or mules or pig or pigs or swine or swines or hog or hogs or boar or boars or porcine or piglet or piglets or sus or scrofa or llama or llamas or lama or glama or deer or deers or cervus or elaphus or cow or cows or bos taurus or bos indicus or bovine or bull or bulls or cattle or bison or bisons or sheep or sheeps or ovis aries or ovine or lamb or lambs or mouflon or mouflons or goat or goats or capra or caprine or chamois or rupicapra or leporidae or lagomorpha or lagomorph or rabbit or rabbits or oryctolagus or cuniculus or laprine or hares or lepus or rodentia or rodent or rodents or murinae or mouse or mice or mus or musculus or murine or woodmouse or apodemus or rat or rats or rattus or norvegicus or guinea pig or guinea pigs or cavia or porcellus or hamster or hamsters or mesocricetus or cricetus or gerbil or gerbils or jird or jirds or meriones or



unguiculatus or jerboa or jerboas or jaculus or chinchilla or chinchillas or beaver or beavers or castor fiber or castor canadensis or sciuridae or squirrel or squirrels or sciurus or chipmunk or chipmunks or marmot or marmots or marmota or suslik or susliks or spermophilus or cynomys or cottonrat or cottonrats or sigmodon or vole or voles or microtus or myodes or glareolus or primate or primates or prosimian or prosimians or lemur or lemurs or lemuridae or loris or bush baby or bush babies or bushbaby or bushbabies or galago or galagos or anthropoidea or anthropoids or simian or simians or monkey or monkeys or marmoset or marmosets or callithrix or cebuella or tamarin or tamarins or saguinus or leontopithecus or squirrel monkey or squirrel monkeys or saimiri or night monkey or night monkeys or owl monkey or owl monkeys or douroucoulis or aotus or spider monkey or spider monkeys or ateles or baboon or baboons or papio or rhesus monkey or macaque or macaca or mulatta or cynomolgus or fascicularis or green monkey or green monkeys or chlorocebus or vervet or vervets or pygerythrus or hominoidea or ape or apes or hylobatidae or gibbon or gibbons or siamang or siamangs or nomascus or symphalangus or hominidae or orangutan or orangutans or pongo or chimpanzee or chimpanzees or pan troglodytes or bonobo or bonobos or pan paniscus or gorilla or gorillas or troglodytes))

18. (#16) NOT #17

19. (#15) AND #18

**Search strategy for CINAHL**

- S1 (MH "Surgical Patients")
- S2 (MH "Surgery, Operative+")
- TI ( (curettage or debridement or electrosurger\* or fasciotom\* or Keratectom\* or laparotom\* or lymph node excision or mastectom\* or metastasectom\* or microsurger\* or myotom\* or neurosurgical procedure\* or orthopedic procedure\* or amputation or Osteotom\* or pelvic exenteration or pneumonectom\* or prosthesis implantation or reoperation or splenectom\* or symphysiotom\* or transplantation) ) OR AB ( (curettage or debridement or electrosurger\* or fasciotom\* or Keratectom\* or laparotom\* or lymph node excision or mastectom\* or metastasectom\* or microsurger\* or myotom\* or neurosurgical procedure\* or orthopedic procedure\* or amputation or Osteotom\* or pelvic exenteration or pneumonectom\* or prosthesis implantation or reoperation or splenectom\* or symphysiotom\* or transplantation) )
- S3
- S4 TI surger\* OR AB surger\* OR TI surgical\* OR AB surgical\*
- S5 S1 OR S2 OR S3 OR S4
- S6 opioid\* N3 sparing OR opioid\* N3 minimi\* OR opioid\* N3 free
- S7 opiate\* N3 sparing OR opiate\* N3 minimi\* OR opiate\* N3 free
- S8 multimodal N5 an\*esthes OR multimodal N5 analges\*
- S9 S6 OR S7 OR S8
- (MH "Analgesics") OR (MH "Analgesics, Nonnarcotic+") OR (MH "Anesthesia Adjuvants+")
- S10
- S11 (MH "Adrenergic Beta-Agonists+")
- S12 (MH "Caffeine")
- S13 (MH "Antiinflammatory Agents+")

S14 (MH "Adrenal Cortex Hormones+")

S15 (MH "Adrenergic Beta-Antagonists+")

S16 (MH "Magnesium Compounds+")

S17 (MH "Anticonvulsants+")

S18 (MH "Lidocaine")

S19 (MH "Ketamine")

S20 "Dexmedetomidine"

S21 (MH "Propranolamines")

S22 (MH "Clonidine")

TI ( (Lidocaine or Alpha-2 Receptor Agonist\* or Caffeine or Corticosteroid\* or Beta block\* or NMDA receptor antagonist\* or N-Methyl-D-aspartate receptor antagonist\* or Magnesium or Acetaminophen or NSAID\* or Anti-convulsant\* or anticonvulsant\* or Antidepressant\* or gabapentinoid\* or cox-2 inhibitor\* or Nonsteroidal anti-inflammatory\*) ) OR AB ( (Lidocaine or Alpha-2 Receptor Agonist\* or Caffeine or Corticosteroid\* or Beta block\* or NMDA receptor antagonist\* or N-Methyl-D-aspartate receptor antagonist\* or Magnesium or Acetaminophen or NSAID\* or Anti-convulsant\* or anticonvulsant\* or Antidepressant\* or gabapentinoid\* or cox-2 inhibitor\* or Nonsteroidal anti-inflammatory\*) )

S23 )

TI (Pregabalin or Gabapentin or Carbamazepine or Carbazepin or Esmolol or Propranolamine\* or Metoprolol or Labetolol or Clonidine or Dexmedetomidine or Catapressan or Caffeine or Ketamine or Dextromethorphan or Dexamethasone or Methylprednisolone or hydrocortison\* or Prednisone or magnesium or Amitriptyline or Duloxetine or Tryptophan or Bicifadine or Desipramine or fluoxetine or Venlafaxine or Citalopram)

S24

S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20  
S25 OR S21 OR S22 OR S23 OR S24

S26 (MH "Intraoperative Period")

- S27 (MH "Administration, Intravenous")
- S28 (MH "Combined Modality Therapy")
- S29 TI ( (perioperat\* or peri operat\* or intra operat\* or intraoperat\* ) OR AB ( (perioperat\* or peri operat\* or intra operat\* or intraoperat\* ) )
- S30 TI an\*esthes\* N2 induction OR AB an?esthes\* N2 induction
- S31 (MH "Anesthesia Induction")
- S32 S26 OR S27 OR S28 OR S29 OR S30 OR S31
- S33 S25 AND S32
- S34 S9 OR S33
- S35 S5 AND S34
- S36 (MH "Randomized Controlled Trials+") OR (MH "Double-Blind Studies") OR (MH "Triple-Blind Studies") OR (MH "Clinical Trials")
- S37 TI random\* OR AB random\* OR TI placebo OR AB placebo OR TI trial
- S38 (control W5 group)
- S39 (MH "Random Assignment")
- S40 S36 OR S37 OR S38 OR S39
- S41 S35 AND S40
- S42 (MH "Animals+")
- S43 (MH "Animal Studies")
- S44 TI animal model\*
- S45 S42 OR S43 OR S44

S46 (MH "Human")

S47 S45 NOT S46

S48 S41 NOT S47

S49 S41 NOT S47