

APPENDICES 1-17

Appendix 1. Inclusion criteria for interventions and comparator groups.....	2
Appendix 2. Study characteristics	3
Appendix 3. Frequencies for specific drugs and drug combinations	8
Appendix 4. Patient characteristics.....	9
Appendix 5. Cochrane EPOC Risk-of-bias appraisal results	13
Appendix 6. Aggregate EPOC risk-of-bias appraisal results	16
Appendix 7. McHarm appraisal results.....	17
Appendix 8. Aggregate McHarm appraisal results	19
Appendix 9 Comparison adjusted funnel plots	20
Appendix 10. Definitions of arrhythmia	21
Appendix 11. Network meta-analysis for all outcomes for all time periods	22
Appendix 12. Plot of the surface under the cumulative ranking (SUCRA) curves for the 9 treatments included in Arrhythmia.	24
Appendix 13: Subgroup analysis for Arrhythmia and Delirium.....	25
Appendix 14. Network meta-analysis results for Delirium.	28
Appendix 15. Definitions of delirium	29
Appendix 16. Plot of the surface under the cumulative ranking (SUCRA) curves for the 6 treatments included in Delirium.....	30
Appendix 17. Included studies in our review versus previous systematic reviews	31

Appendix 1. Inclusion criteria for interventions and comparator groups

<p>Intervention:</p> <p>5-HT3 receptor antagonist with or without dexamethasone (Ondansetron, Granisetron, Dolasetron, Tropisetron, Ramosetron, Palonosetron)</p>	<p>Eligible comparators:</p> <p>I. Different 5-HT3 antagonist with or without Dexamethasone</p> <p>II. Antiemetic comparator listed below with or without Dexamethasone</p> <p>III. Same 5-HT3 antagonist given at different dose, formula, and/or timing or same 5-HT3 with Dexamethasone</p> <p>IV. Same 5-HT3 antagonist given in combination with one of the comparators below</p> <p>V. Different 5-HT3 antagonist given in combination with one of the comparators below</p>				
<p>Antiemetic comparators included:</p>					
<p>Benzamides</p> <p>Metoclopramide</p>	<p>Phenothiazine</p> <p>Perphenazine Promethazine</p>	<p>Butyrophenones</p> <p>Haloperidol Droperidol</p>	<p>Antihistamines</p> <p>Dimenhydrinate Cyclizine</p>	<p>NK-1</p> <p>Aprepitant Casopitant Rolapitant</p>	<p>Steroids</p> <p>Dexamethasone</p>
<p>Abbreviations: 5-HT3, Serotonin; NK-, Neurokinin-1 receptor antagonists; NaSSA, Noradrenergic and specific serotonergic antidepressant.</p>					

Appendix 2. Study characteristics

Author, year	Country of conduct	Study conduct period	Study duration (hours)	Setting	Interventions examined	Outcomes Reported
<i>Randomized clinical trials (n=112)</i>						
Choi, 2012	South Korea	NR	48	NR	Ondansetron + Dexamethasone, Ramosetron + Dexamethasone	Mortality
Wang, 2012	China (Taiwan)	NR	24	NR	Dexamethasone, Haloperidol + Dexamethasone, Ondansetron + Dexamethasone	QT Interval, Arrhythmia
Ekinci, 2011	Turkey	February 2007 - March 2008	48	NR	Droperidol, Metoclopramide, Ondansetron, Placebo, Tropisetron	Arrhythmia
El-deeb, 2011b	Egypt	NR	24	NR	Granisetron + Dexamethasone, Placebo	Arrhythmia
Gan, 2011	USA, Canada	NR	119	NR	Ondansetron, Placebo, Rolapitant	Mortality
Gupta, 2011	India	October 2008 - April 2009	NR	Hospital	Ondansetron, Placebo	QT Interval
Park, 2011	Republic of Korea	June 2010 - September 2010	24	Hospital	Ondansetron, Palonosetron	Mortality
Ryu, 2011	South Korea	NR	48	NR	Ramosetron, Tropisetron	QT Interval
Sahoo, 2011	India	September 2008 - December 2008	1	NR	Ondansetron, Placebo	Arrhythmia
Bilgin, 2010	Turkey	NR	24	NR	Dexamethasone, Metoclopramide, Ondansetron, Placebo	Mortality
Choi, 2010	Korea	September 2008 - February 2009	48	NR	Ondansetron, Placebo, Ramosetron	Arrhythmia
Jee, 2010	Korea	NR	36	NR	Metoclopramide + Dexamethasone, Ondansetron + Dexamethasone	Delirium, Arrhythmia
Jokela, 2010	Finland	December 2007 - January 2009	24	Hospital	Ondansetron, Placebo	Delirium
Mehta, 2010	Canada	February 2008 - March 2009	2	NR	Droperidol, Ondansetron, Ondansetron + Droperidol, Placebo	QT Interval
Shakya, 2010	India	NR	2	NR	Ondansetron, Placebo	Delirium
Singla, 2010	Belgium, Canada, Germany, Hungary, Spain, USA.	NR	119	Multi-centre	Casopitant, Ondansetron, Ondansetron + Casopitant	Mortality
Feng, 2009	Taiwan	NR	24	NR	Haloperidol, Ondansetron, Ondansetron + Haloperidol	QT Interval
Jain, 2009	India	NR	24	NR	Granisetron, Ondansetron, Placebo	Delirium

Riad, 2009	Saudi Arabia	NR	24	NR	Granisetron + Dexamethasone, Ondansetron + Dexamethasone, Placebo	Arrhythmia
Rosow, 2009	USA	NR	NR	Hospital	Haloperidol, Ondansetron	Delirium, QT Interval
Candiotti, 2008	USA, Romainia	NR	72	NR	Palonosetron, Placebo	Mortality, QT Interval
Choi, 2008	South Korea	September 2006 - June 2007	48	NR	Ondansetron, Ramosetron	Mortality
Contreras- Dominguez, 2008	Chile	December 2003 - February 2006	48	Hospital	Dexamethasone, Droperidol, Granisetron, Metoclopramide, Placebo, Tropisetron	Arrhythmia
Kovac, 2008	Germany, Poland, Czech Republic	NR	72	Multi-centre	Palonosetron, Placebo	Mortality, QT Interval
Owczuk, 2008	Poland	NR	0	NR	Ondansetron, Placebo	Arrhythmia
Piper, 2008	Germany, Switzerland	1999 - 2004	24	NR	Dolsetron, Droperidol, Placebo	Delirium, Arrhythmia
Said-Ahmed, 2008	Egypt	NR	24	NR	Granisetron, Placebo	Arrhythmia
Bestas, 2007	Turkey	NR	24	Medical center	Granisetron, Ondansetron, Placebo	Mortality
Diemunsch, 2007	North America (including USA), South America, Europe, Australia, Asia	May 2004 - April 2005	48	NR	Aprepitant, Ondansetron	QT Interval, Arrhythmia
Gan, 2007	Multicentred	September 2003 - November 2004	48	NR	Aprepitant, Ondansetron	QT Interval
Han, 2007	Korea	NR	48	NR	Ondansetron	Arrhythmia
Lee, 2007	Republic of China (Taiwan)	NR	24	NR	Haloperidol, Ondansetron	QT Interval, Arrhythmia
Oksuz, 2007	Turkey	NR	24	NR	Granisetron, Metoclopramide, Ondansetron	Mortality
Rusch, 2007	Germany	NR	24	Hospital	Dolsetron, Dolsetron + Dexamethasone, Haloperidol, Haloperidol + Dexamethasone	Delirium
Sagir, 2007	Turkey	NR	0.25	NR	Granisetron, Placebo	Delirium
Sandhu, 2007	Thailand	NR	24	NR	Metoclopramide, Ondansetron	Mortality
Siddik-Sayyid, 2007	Lebanon	NR	24	Medical center	Granisetron, Ondansetron, Placebo	Arrhythmia
Bridge, 2006	USA	NR	24	Hospital	Dolsetron, Granisetron, Ondansetron	Mortality
Chan, 2006	USA, Hong Kong, New Zeland	September 2002 - June 2004	48	NR	Droperidol, Ondansetron, Ondansetron + Droperidol, Placebo	Arrhythmia
Kelsaka, 2006	Turkey	NR	NR	NR	Ondansetron, Placebo	Arrhythmia
Sarvela, 2006	Finland	January 2003 - November 2003	24	NR	Ondansetron, Placebo, Tropisetron	Delirium
Tosun, 2006	Turkey	NR	24	NR	Placebo, Tropisetron	Delirium
D'Angelo, 2005	USA	March 2002 - August 2002	24	Multi-centre	Granisetron, Placebo	Mortality
Gan, 2005	USA	NR	24	NR	Granisetron + Dexamethasone,	Mortality, Arrhythmia

					Ondansetron + Dexamethasone	
Khalil, 2005	USA, Canada	NR	24	Multi-centre	Ondansetron, Placebo	Delirium, Arrhythmia
Kocamanoglu, 2005	Turkey	NR	24	NR	Droperidol, Granisetron, Granisetron + Dexamethasone, Granisetron + Droperidol, Placebo	Mortality
Kontrimaviciute, 2005	Lithuania	NR	24	Hospital	Ondansetron, Placebo	Arrhythmia
Pirat, 2005	Turkey	NR	24	NR	Ondansetron, Placebo	Arrhythmia
Treschan, 2005	Germany	NR	24	NR	Ondansetron, Placebo	Arrhythmia
White, 2005 [†]	USA	NR	24	NR	Palonosetron, Placebo	QT Interval
Apfel, 2004 (CR: Jokela, 2009)	Germany, USA, Finland, UK, Turkey, Slovakia	February 2000 - July 2002	24	NR	Dexamethasone, Droperidol, Droperidol + Dexamethasone, Ondansetron, Ondansetron + Dexamethasone, Ondansetron + Droperidol	QT Interval
Binstock, 2004	USA	NR	24	NR	Ondansetron, Placebo	Arrhythmia
Eberhart, 2004	Germany	NR	24	NR	Dolsetron, Dolsetron + Droperidol, Droperidol, Placebo	Arrhythmia
Hanaoka, 2004	Japan	NR	24	Multi-centre	Granisetron, Placebo	Arrhythmia
Samakarndi, 2004	Saudi Arabia	NR	24	NR	Dexamethasone, Ondansetron, Ondansetron + Dexamethasone, Placebo	Arrhythmia
Charuluxananan, 2003	Thailand	NR	24	Hospital	Ondansetron, Placebo	Arrhythmia
Loewen, 2003	Canada	May 2000 - December 2001	24	NR	Dolsetron, Droperidol	Delirium
O'Brien, 2003	UK	NR	24	Hospital	Cyclizine, Ondansetron, Placebo	Arrhythmia
Argiriadou, 2002	Greece	NR	12	Hospital	Ondansetron, Placebo, Tropisetron	Arrhythmia
Gurkan, 2002	Turkey	NR	6	NR	Ondansetron, Placebo	Arrhythmia
Dabbous, 2001	Lebanon	NR	24	NR	Droperidol, Metoclopramide, Ondansetron	Delirium
Kathirvel, 2001	India	NR	24	NR	Ondansetron, Placebo	Delirium
Subramaniam, 2001	India	NR	24	NR	Dexamethasone, Ondansetron, Placebo	Arrhythmia
Ahmed, 2000	UK	NR	24	NR	Ondansetron, Ondansetron + Cyclizine, Placebo	Arrhythmia
Charuluxananan, 2000	Thailand	NR	4	Hospital	Ondansetron, Placebo	Delirium
Jensen, 2000	australia	NR	24	Hospital	Placebo, Tropisetron	Delirium
Kreisler, 2000	USA	NR	24	NR	Droperidol, Ondansetron, Promethazine	Delirium
Philip, 2000	USA	NR	24	Multi-centre	Dolsetron, Placebo	Arrhythmia
Zarate, 2000	USA	NR	24	NR	Dolsetron, Ondansetron	Delirium
Koivuranta, 1999	Finland	NR	24	Hospital	Ondansetron, Tropisetron	Delirium
McCall, 1999	USA	NR	8	NR	Dimenhydrinate, Ondansetron, Placebo	Delirium
Sinha, 1999	India	NR	48	Hospital	Ondansetron, Placebo	Delirium
Tsui, 1999	China	NR	48	Hospital	Ondansetron, Placebo,	Mortality

						Tropisetron	
Diemunsch, 1998	France	NR	24	NR		Dolsetron, Placebo	Arrhythmia
Goodarzi, 1998	USA	NR	48	NR		Droperidol, Ondansetron, Placebo	Mortality
Hamid, 1998	Canada	NR	24	NR		Dimenhydrinate, Ondansetron, Placebo	Arrhythmia
Morris, 1998	Australia, Canada, Denmark, France, Germany, Iceland, Israel, Netherlands, Norway, South Africa, Sweden, UK	NR	24	Multi-centre		Metoclopramide, Ondansetron, Placebo	Mortality
Scholz, 1998	Germany	NR	24	NR		Ondansetron, Placebo, Tropisetron	Arrhythmia
Tramer, 1998	Switzerland	NR	48	Hospital		Ondansetron, Placebo	Arrhythmia
Diemunsch, 1997b	France	NR	24	NR		Dolsetron, Placebo	Arrhythmia
Diemunsch, 1997c	Europe	NR	24	NR		Dolsetron, Placebo	Arrhythmia, Mortality
Graczyk, 1997	USA	NR	24	NR		Dolsetron, Placebo	QT Interval
Klockgether- Radke, 1997	Germany	NR	24	NR		Droperidol, Ondansetron, Placebo	Arrhythmia
Koivuranta, 1997	Finland	NR	24	Hospital		Droperidol, Ondansetron, Placebo	Delirium
Korttila, 1997	finland	NR	24	Multi-centre		Dolsetron, Ondansetron, Placebo	Arrhythmia
Kovac, 1997	USA	NR	24	NR		Dolsetron, Placebo	QT Interval
Mikawa, 1997	Japan	NR	24	NR		Granisetron, Placebo	Arrhythmia
Monagle, 1997	Australia	NR	24	NR		Metoclopramide, Ondansetron	Arrhythmia
Morton, 1997	Denmark, Sweden, UK, France, Belgium, Germany, Norway.	NR	24	Multi-centre		Ondansetron, Placebo	Arrhythmia
Patel, 1997	USA	NR	24	Multi-centre		Ondansetron, Placebo	Delirium
Purhonen, 1997	Finland	NR	48	Hospital		Droperidol, Placebo, Tropisetron	Arrhythmia
Rung, 1997	USA	NR	24	Multi-centre		Ondansetron, Placebo	Mortality
Scuderi, 1997	USA	NR	24	NR		Droperidol, Metoclopramide, Ondansetron, Placebo	Arrhythmia
Taylor, 1997	UK	NR	144	Multi-centre		Granisetron, Placebo	Mortality, Arrhythmia
Ulusoy, 1997	Turkey	nr	24	Hospital		Ondansetron, Placebo	Delirium
Warriner, 1997	Canada	NR	24	Multi-centre		Dolsetron, Placebo	Mortality, Arrhythmia
Ali-melkkila, 1996	Finland	NR	24	Hospital		Metoclopramide, Placebo, Tropisetron	Mortality
Capouet, 1996	Belgium	NR	24	Multi-centre		Placebo, Tropisetron	QT Interval, Arrhythmia
Kovac, 1996 (CR: Pearman, 1994c)	USA	NR	24	NR		Ondansetron, Placebo	Delirium
Naguib, 1996	Saudi Arabia	NR	24	NR		Granisetron, Metoclopramide, Ondansetron, Placebo, Tropisetron	Mortality
Rose, 1996a	USA	NR	24	NR		Ondansetron, Placebo	Mortality
Desilva, 1995	USA	NR	4	NR		Droperidol, Metoclopramide, Ondansetron, Perphenazine, Placebo	Delirium
Litman, 1995	USA	NR	24	Hospital		Droperidol, Ondansetron	Delirium
Paech, 1995	Australia	NR	24	Hospital		Droperidol, Ondansetron, Placebo	Delirium
Paxton, 1995a	Ireland	NR	24	NR		Droperidol, Ondansetron, Placebo	Arrhythmia

Kaufmann, 1994	Switzerland, USA	NR	35	NR	Droperidol, Metoclopramide, Placebo, Tropisetron	Delirium
Ummerhofer, 1994	Switzerland	NR	24	Hospital	Ondansetron, Placebo	Delirium
Dupeyron, 1993	Belgium, Denmark, France	NR	24	NR	Ondansetron, Placebo	Arrhythmia
Helmers, 1993	Netherlands, Ireland, Sweden, UK, South Africa, France,	NR	24	NR	Ondansetron, Placebo	Mortality, Arrhythmia
Raphael, 1993	UK	NR	24	NR	Metoclopramide, Ondansetron	Delirium
Du Pen, 1992 (CR: Scuderi, 1993)	USA	NR	24	Multi-centre	Ondansetron, Placebo	Delirium
Kovac, 1992 (CRs: McKenzie, 1993a; Pearman, 1994a)	USA	NR	24	Multi-centre	Ondansetron, Placebo	Delirium
<i>Non-randomized clinical trials (n=2)</i>						
Charbit, 2005	France	NR	3	Hospital	Droperidol, Ondansetron	QT prolongation, Arrhythmia
Lerman, 1996	Canada	NR	24	Hospital	Dolasetron	QT prolongation
<i>Controlled before-after studies (n=1)</i>						
Wagner, 2007	USA	NR	24	Medical center	Ondansetron, Placebo	Delirium
<i>Cohort studies (n=0)</i>						
Note: †Unpublished data (White, 2005).						
Abbreviations: CR, companion report; NR, not reported; UK, United Kingdom; USA United States of America.						

Appendix 3. Frequencies for specific drugs and drug combinations

<i>Intervention/ Comparator:</i>	% of arms (n=367)	% of studies (n=115)
Ondansetron	26.16	68.7
Placebo	23.71	74.78
Dolasetron	10.62	13.04
Granisetron	5.99	12.17
Droperidol	5.72	20
Tropisetron	5.45	13.04
Metoclopramide	3.81	12.17
Palonosetron	3.27	3.48
Ondansetron + Dexamethasone	1.91	6.09
Dexamethasone	1.63	5.22
Ramosetron	1.36	2.61
Aprepitant	1.09	1.74
Granisetron + Dexamethasone	1.09	3.48
Haloperidol	1.09	3.48
Rolapitant	1.09	0.87
Ondansetron + Casopitant	0.82	0.87
Ondansetron + Droperidol	0.82	2.61
Dimenhydrinate	0.54	1.74
Haloperidol + Dexamethasone	0.54	1.74
Casopitant	0.27	0.87
Cyclizine	0.27	0.87
Dolasetron + Dexamethasone	0.27	0.87
Dolasetron + Droperidol	0.27	0.87
Droperidol + Dexamethasone	0.27	0.87
Granisetron + Droperidol	0.27	0.87
Metoclopramide + Dexamethasone	0.27	0.87
Ondansetron + Cyclizine	0.27	0.87
Ondansetron + Haloperidol	0.27	0.87
Perphenazine	0.27	0.87
Promethazine	0.27	0.87
Ramosetron + Dexamethasone	0.27	0.87

Appendix 4. Patient characteristics

Author, year	Sample size	Age Category	% female	ASA status	Surgery type	H/o motion sickness	H/o PONV	Comorbidities
<i>Randomized clinical trials (n=112)</i>								
Choi, 2012	120	Adults	100	I or II	Orthopaedic	YES	YES	NR
Wang, 2012	130	Adults	100	I or II	Miscellaneous	YES	YES	NR
Ekinci, 2011	100	Adults	100	I or II or III	Obstetrics & Gynaecological	NR	NR	NR
El-deeb, 2011b	160	Adults	100	I or II	Obstetrics & Gynaecological	NR	NR	NR
Gan, 2011	619	Adults	100	I or II or III	Miscellaneous	YES	YES	NR
Gupta, 2011	136	Adults	62	I or II	Miscellaneous	NR	NR	NR
Park, 2011	90	Adults	100	I or II	Obstetrics & Gynaecological	YES	YES	NR
Ryu, 2011	124	Adults	54	I or II	Gastrointestinal	NR	NR	Cardiovascular, liver disease
Sahoo, 2011	52	Adults	100	I	Obstetrics & Gynaecological	NR	NR	NR
Bilgin, 2010	160	Adults	100	I or II	Obstetrics & Gynaecological	NR	NR	NR
Choi, 2010	279	Adults & Elderly	39	NR	Cardiovascular	YES	YES	NR
Jee, 2010	100	Adults	100	I or II	Obstetrics & Gynaecological	YES	YES	NR
Jokela, 2010	80	Adults	100	I or II or III	Obstetrics & Gynaecological	YES	YES	NR
Mehta, 2010	80	Children	50	I or II	Miscellaneous	NR	NR	NR
Shakya, 2010	80	Adults	63	I or II	Miscellaneous	NR	NR	NR
Singla, 2010	702	Adults	100	NR	Miscellaneous	YES	YES	NR
Feng, 2009	192	Adults	74	I or II	Gastrointestinal	YES	YES	NR
Jain, 2009	87	Adults	29.9	I or II	Neurological	NR	NR	NR
Riad, 2009	100	Children	48	I or II	Eye	NR	NR	NR
Rosow, 2009	244	Adults & Elderly	66	I or II or III	Miscellaneous	NR	NR	NR
Candiotti, 2008	546	Adults & Elderly	95	I or II or III	Miscellaneous	YES	YES	NR
Choi, 2008	94	Adults	100	NR	Orthopaedic	YES	YES	NR
Contreras-Dominguez, 2008	150	Adults	49	I or II	Gastrointestinal	NR	YES	NR
Kovac, 2008	544	Adults	100	I or II or III	Miscellaneous	YES	YES	NR
Owczuk, 2008	71	Adults	11	I or II	Miscellaneous	NR	NR	NR
Piper, 2008	83	Adults	56	I or II	General dentistry, oral and maxillofacial surgery and orthodontics	YES	YES	NR
Said-Ahmed, 2008	50	Adults	100	I or II	Obstetrics & Gynaecological	NR	NR	NR
Bestas, 2007	90	Adults	77	I or II	Gastrointestinal	NR	NR	NR
Diemunsch, 2007	892	Adults & Elderly	91	I or II or III	Miscellaneous	YES	YES	NR
Gan, 2007	766	Adults & Elderly	94	I or II or III	Miscellaneous	YES	YES	NR
Han, 2007	80	Adults	100	I	Obstetrics & Gynaecological	NR	NR	NR
Lee, 2007	86	Adults	100	I or II	Obstetrics & Gynaecological	YES	YES	NR
Oksuz, 2007	75	Adults & Elderly	65	I or II	Gastrointestinal	NR	YES	NR
Rusch, 2007	228	Adults & Elderly	49	I or II or III	Miscellaneous	NR	YES	NR
Sagir, 2007	80	Adults	0.7	I or II	Urological	NR	NR	NR
Sandhu, 2007	80	Adults	71	I or II	Gastrointestinal	NR	NR	NR
Siddik-Sayyid, 2007	129	Adults	100	I or II	Obstetrics &	NR	NR	Obesity

					Gynaecological			
Bridge, 2006	194	Adults	100	NR	Miscellaneous	NR	NR	NR
					Obstetrics &			
Chan, 2006	394	Adults	100	I or II	Gynaecological	YES	YES	NR
Kelsaka, 2006	50	Adults	25	I or II	Orthopaedic	NR	NR	NR
					Obstetrics &			
Sarvela, 2006	87	Adults	100	NR	Gynaecological	NR	NR	NR
Tosun, 2006	125	Children	49	I or II	Eye	NR	NR	NR
					Obstetrics &			
D'Angelo, 2005	121	Adults	100	I or II or III	Gynaecological	YES	YES	NR
					Obstetrics &			
Gan, 2005	176	Adults	100	I or II or III	Gynaecological	YES	YES	NR
					Obstetrics &			
Khalil, 2005	670	Children	24	I or II or III	Miscellaneous	YES	YES	NR
					Obstetrics &			
Kocamanoglu, 2005	150	Adults	100	I or II	Gynaecological	YES	YES	NR
					Obstetrics &			
Kontrimaviciute, 2005	34	Adults	100	I or II	Gynaecological	NR	YES	NR
Pirat, 2005	150	Adults	0	I	Miscellaneous	NR	NR	NR
Treschan, 2005	142	All groups	56	I or II	Eye	YES	YES	NR
					Obstetrics &			
White, 2005 [†]	372	NR	100	NR	Gynaecological	NR	NR	NR
Apfel, 2004 (CR: Jokela, 2009)	260	Adults	81	NR	Miscellaneous	YES	YES	NR
Binstock, 2004	101	Children	42	I or II	Miscellaneous	NR	NR	NR
					Obstetrics &			
Eberhart, 2004	304	Adults & Elderly	52	I or II or III	Eye	YES	YES	NR
					Obstetrics &			
Hanaoka, 2004	315	Adults	95	I or II or III	Miscellaneous	YES	NR	NR
Samakarndi, 2004	80	Children	49	I or II	Eye	NR	NR	NR
					Obstetrics &			
Charuluxananan, 2003	180	Adults	100	I or II	Gynaecological	NR	NR	NR
Loewen, 2003	71	Adults	100	NR	Breast	YES	YES	NR
O'Brien, 2003	150	Children	NR	I or II	Miscellaneous	YES	YES	NR
Argiriadou, 2002	87	Adults	76	I or II	Gastrointestinal	NR	NR	NR
Gurkan, 2002	150	Adults	53	I or II	Miscellaneous	NR	NR	NR
Dabbous, 2001	173	Adults	77	I or II	Gastrointestinal	YES	YES	Diabetes
					Obstetrics &			
Kathirvel, 2001	152	Adults & Children	38	I or II	Neurological	NR	NR	NR
Subramaniam, 2001	135	Children	54	I or II	Eye	NR	YES	NR
					Obstetrics &			
Ahmed, 2000	139	Adults	100	NR	Gynaecological	YES	YES	NR
					Obstetrics &			
Charuluxananan, 2000	80	Adults	100	I or II	Gynaecological	NR	NR	NR
					General dentistry, oral and maxillofacial surgery and orthodontics			
Jensen, 2000	71	Children	41	I or II		YES	NR	NR
Kreisler, 2000	31	Adults	81	NR	Miscellaneous	NR	YES	NR
					Obstetrics &			
Philip, 2000	1030	Adults	70	I or II or III	Miscellaneous	YES	YES	NR
Zarate, 2000	200	Adults	44	I or II	Miscellaneous	YES	YES	NR
					Obstetrics &			
Koivuranta, 1999	428	Adults	82	I or II or III	Miscellaneous	YES	YES	NR
McCall, 1999	73	Children	53	I or II	Eye	NR	NR	NR
					Obstetrics &			
Sinha, 1999	40	Adults	47	I or II or III	Neurological	NR	YES	NR
					Obstetrics &			
Tsui, 1999	121	Adults	100	I or II or III	Gynaecological	NR	NR	NR
					Obstetrics &			
Diemunsch, 1998	793	Adults	100	I or II or III	Gynaecological	YES	YES	NR
Goodarzi, 1998	81	Children	43	I or II	Orthopaedic	NR	NR	NR
					General dentistry, oral and maxillofacial surgery and orthodontics			
Hamid, 1998	71	Children	55	I or II		NR	YES	NR
					Obstetrics &			
Morris, 1998	1044	Adults	100	I or II or III	Gynaecological	NR	YES	NR
Scholz, 1998	842	Adults &	74	I or II	Miscellaneous	YES	YES	NR

		Elderly		or III				
Tramer, 1998	157	Children	49	NR	Eye	YES	YES	
Diemunsch, 1997b	281	Adults	100	I or II	Obstetrics & Gynaecological	NR	YES	NR
Diemunsch, 1997c	337	Adults	95	I or II	Obstetrics & Gynaecological	NR	YES	NR
Graczyk, 1997	635	Adults	100	I or II	Obstetrics & Gynaecological	NR	YES	NR
Klockgether-Radke, 1997	120	Children	48	I or II	Eye	NR	NR	NR
Koivuranta, 1997	439	Adults & Elderly	100	I or II or III	Miscellaneous	YES	YES	Migraines
Korttila, 1997	517	Adults	94	I or II or III	Miscellaneous	YES	YES	NR
Kovac, 1997	620	Adults	83	I or II or III	Miscellaneous	YES	YES	NR
Mikawa, 1997	200	Adults & Elderly	100	I	Obstetrics & Gynaecological	NR	YES	NR
Monagle, 1997	91	Adults	100	NR	Obstetrics & Gynaecological	NR	YES	NR
Morton, 1997	427	Children	51	I or II	General dentistry, oral and maxillofacial surgery and orthodontics	NR	YES	NR
Patel, 1997	429	Children	37	I or II or III	Miscellaneous	YES	YES	NR
Purhonen, 1997	146	Adults	100	I or II or III	Miscellaneous	YES	YES	NR
Rung, 1997	121	Adults & Elderly	69	I or II or III	Miscellaneous	YES	YES	NR
Scuderi, 1997	160	Children	52	I or II	Eye	NR	YES	NR
Taylor, 1997	523	Adults & Elderly	89	I or II or III	Multiple types included	YES	YES	NR
Ulusoy, 1997	40	Adults	37	I or II	Miscellaneous	NR	NR	NR
Warriner, 1997	374	Adults & Elderly	100	I or II	Obstetrics & Gynaecological	YES	YES	NR
Ali-melkkila, 1996	120	Adults	42	I or II or III	Eye	NR	YES	NR
Capouet, 1996	385	Adults	100	I or II	Miscellaneous	YES	YES	NR
Kovac, 1996 (CR: Pearman, 1994c)	30	Adults	100	I or II	Obstetrics & Gynaecological	NR	NR	NR
Naguib, 1996	48	Adults	100	I or II	Obstetrics & Gynaecological	NR	NR	NR
Rose, 1996a	136	Children	44	I or II	General dentistry, oral and maxillofacial surgery and orthodontics	NR	NR	NR
Desilva, 1995	50	Adults	70	I or II	Gastrointestinal	NR	NR	NR
Litman, 1995	57	Children	40	I or II	Eye	YES	YES	NR
Paech, 1995	259	Adults	100	NR	Obstetrics & Gynaecological	NR	YES	NR
Paxton, 1995a	60	Children	47	NR	Ear, nose and larynx	NR	NR	NR
Kaufmann, 1994	286	Adults	54	I or II	Orthopaedic	NR	NR	NR
Ummerhofer, 1994	200	Children	34	I or II	Miscellaneous	NR	NR	NR
Dupeyron, 1993	243	Adults & Elderly	100	I or II or III	Obstetrics & Gynaecological	NR	NR	Cardiovascular, urological
Helmers, 1993	923	Adults	100	I or II or III	Obstetrics & Gynaecological	NR	NR	NR
Raphael, 1993	123	Adults	100	NR	Obstetrics & Gynaecological	YES	YES	NR
Du Pen, 1992 (CR: Scuderi, 1993)	500	All groups	11	I or II	Miscellaneous	NR	NR	NR
Kovac, 1992 (CRs: McKenzie, 1993a; Pearman, 1994a)	580	Adults	100	I or II	Obstetrics & Gynaecological	NR	YES	NR
<i>Non-randomized clinical trials (n=2)</i>								
Charbit, 2005	85	Adults	60	NR	Miscellaneous	NR	NR	NR

Lerman, 1996	28	Children	32	I or II	Otolaryngological	NR	NR	NR
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Controlled before-after studies (n=1)

Wagner, 2007	66	Children	54	I or II	Eye	NR	NR	NR
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Note: †Unpublished data (White, 2005).

Abbreviations: ASA, American Society of Anaesthesiologists physical classification system; NR, not reported or No; CR, companion report; PONV, post-operative nausea and vomiting; H/o, History of.

Appendix 5. Cochrane EPOC Risk-of-bias appraisal results

Author, year	1	2	3	4	5	6	7	8	9
<i>Randomized clinical trials (n=112)</i>									
Choi, 2012	Low	Low	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
Wang, 2012	Low	High	Unclear	Low	Low	Low	Unclear	Unclear	Unclear
Ekinci, 2011	Low	Unclear	Unclear	Low	Low	Low	Low	Unclear	Unclear
El-deeb, 2011b	Low	Low	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
Gan, 2011	Low	Low	Unclear	Low	High	Low	Unclear	Low	Low
Gupta, 2011	Low	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Unclear	Unclear
Park, 2011	Low	Unclear	Unclear	Low	Low	Low	Low	Unclear	Low
Ryu, 2011	Low	Low	Unclear	Low	Low	Low	Low	Low	Low
Sahoo, 2011	Low	Unclear	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
Bilgin, 2010	Low	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear
Choi, 2010	Low	Low	Low	Low	High	Unclear	Low	Unclear	Unclear
Jee, 2010	Low	Unclear	Unclear	Low	Unclear	Unclear	Unclear	Unclear	Unclear
Jokela, 2010	Low	Unclear	Unclear	Low	High	Low	Low	Unclear	Unclear
Mehta, 2010	Low	Low	Low	Low	High	Low	Low	Unclear	Unclear
Shakya, 2010	Unclear	Unclear	Unclear	Low	Unclear	Unclear	Unclear	Unclear	Low
Singla, 2010	Unclear	Unclear	Unclear	Low	Low	Low	Unclear	Low	Unclear
Feng, 2009	Low	Low	Low	Low	Low	Low	Low	Unclear	Low
Jain, 2009	Low	Unclear	Unclear	Low	High	Unclear	Unclear	Unclear	Unclear
Riad, 2009	Unclear	Low	Unclear	Low	Low	Low	Low	Unclear	Low
Rosow, 2009	Unclear	High	Unclear	Low	Low	Low	Unclear	Unclear	High
Candiotti, 2008	Low	Low	Low	Low	Low	Unclear	Low	Unclear	Unclear
Choi, 2008	Low	Low	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
Contreras-Dominguez, 2008	Unclear	Unclear	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
Kovac, 2008	Low	Unclear	Unclear	Low	Unclear	Unclear	Low	Unclear	Unclear
Owczuk, 2008	Low	Unclear	Unclear	Low	Low	Unclear	Low	Unclear	Unclear
Piper, 2008	Unclear	Low	Unclear	Low	Unclear	Low	Low	Low	Low
Said-Ahmed, 2008	Unclear	Low	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
Bestas, 2007	Unclear	Unclear	Unclear	Low	Low	Low	Low	Unclear	Unclear
Diemunsch, 2007	Low	Low	Unclear	Low	Unclear	Low	Unclear	Low	High
Gan, 2007	Low	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear
Han, 2007	Unclear	Unclear	Unclear	Low	Low	Low	Unclear	Unclear	Unclear
Lee, 2007	Low	Low	Low	Low	Low	Low	Low	Unclear	Low
Oksuz, 2007	Unclear	Unclear	Unclear	Low	Low	Low	Low	Unclear	Low
Rusch, 2007	Low	Unclear	Low	Low	Unclear	Low	Unclear	Unclear	Low
Sagir, 2007	Low	Low	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
Sandhu, 2007	Unclear	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear
Siddik-Sayyid, 2007	Low	Low	Unclear	Low	Low	Low	Low	Unclear	Low
Bridge, 2006	Unclear	Low	Unclear	Low	Unclear	Unclear	Low	Unclear	Unclear
Chan, 2006	Low	Low	Low	Low	Low	Low	Low	Unclear	Low
Kelsaka, 2006	Unclear	Unclear	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
Sarvela, 2006	Unclear	Low	Low	Low	High	Low	Low	Unclear	Unclear
Tosun, 2006	Unclear	Unclear	Unclear	Low	Unclear	Unclear	Unclear	Unclear	Unclear
D'Angelo, 2005	Low	Low	Unclear	High	Low	Low	Low	Unclear	Unclear
Gan, 2005	Low	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear
Khalil, 2005	Unclear	High	Low	Low	High	Unclear	Unclear	Unclear	High
Kocamanoglu, 2005	Unclear	Unclear	Low	Low	Unclear	Low	Low	Unclear	Unclear
Kontrimaviciute, 2005	Unclear	Unclear	Unclear	Low	Unclear	Unclear	Unclear	Unclear	Unclear
Pirat, 2005	Unclear	Unclear	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
Treschan, 2005	Low	Low	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
White, 2005 [†]	Unclear	Unclear	Unclear	Low	Unclear	Unclear	Unclear	Unclear	Unclear
Apfel, 2004 (CR: Jokela, 2009)	Low	Low	Unclear	Unclear	Low	Low	Low	Unclear	Low
Binstock, 2004	Unclear	Unclear	Unclear	High	Low	Unclear	Low	Unclear	Unclear
Eberhart, 2004	Unclear	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear
Hanaoka, 2004	Unclear	Low	Unclear	Low	High	Unclear	Unclear	Unclear	Unclear
Samakarndi, 2004	Unclear	Unclear	Low	Unclear	Low	Low	Low	Unclear	Unclear
Charuluxananan, 2003	Low	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear

Loewen, 2003	Low	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear
O'Brien, 2003	Unclear	Unclear	Unclear	Unclear	Low	Unclear	Low	Unclear	Unclear
Argiriadou, 2002	Low	Low	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
Gurkan, 2002	Low	Unclear	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
Dabbous, 2001	Low	Low	Unclear	Low	High	Low	Low	Unclear	Unclear
Kathirvel, 2001	Low	Unclear	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
Subramaniam, 2001	Low	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear
Ahmed, 2000	Low	Unclear	Unclear	Low	Low	Low	Low	Unclear	Unclear
Charuluxananan, 2000	Low	Low	Unclear	Low	Unclear	Unclear	Low	Unclear	Unclear
Jensen, 2000	Low	Unclear	Unclear	Unclear	Low	Low	Low	Unclear	Low
Kreislser, 2000	Unclear	Unclear	Unclear	Low	High	Low	Low	Unclear	High
Philip, 2000	Unclear	Unclear	Unclear	Low	Low	Unclear	Low	Unclear	Low
Zarate, 2000	Low	Unclear	Unclear	Low	Low	Low	Unclear	Unclear	Unclear
Koivuranta, 1999	Unclear	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear
McCall, 1999	Unclear	Unclear	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
Sinha, 1999	Low	Unclear	Unclear	Low	High	Low	Low	Unclear	Unclear
Tsui, 1999	Unclear	Unclear	Unclear	Low	Unclear	Low	Unclear	Unclear	Low
Diemunsch, 1998	Unclear	Unclear	Unclear	Low	Low	Unclear	Low	Unclear	Unclear
Goodarzi, 1998	Unclear	Unclear	Unclear	Low	Low	Low	Low	Unclear	Unclear
Hamid, 1998	Low	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear
Morris, 1998	Unclear	Unclear	Unclear	Low	Unclear	Unclear	Unclear	Unclear	Unclear
Scholz, 1998	Unclear	Low	Unclear	Low	Low	Unclear	Unclear	Unclear	Unclear
Tramer, 1998	Low	Unclear	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
Diemunsch, 1997b	Unclear	Low	Low	Low	Unclear	Unclear	Low	Unclear	Unclear
Diemunsch, 1997c	Unclear	Unclear	Low	Low	Unclear	Unclear	Low	Unclear	Unclear
Graczyk, 1997	Unclear	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear
Klockgether-Radke, 1997	Unclear	Unclear	Unclear	Low	Unclear	Unclear	Low	Unclear	Unclear
Koivuranta, 1997	Low	Unclear	Unclear	High	Low	Low	Low	Unclear	Unclear
Korttila, 1997	Unclear	Unclear	Unclear	Low	Low	Unclear	Unclear	Unclear	Unclear
Kovac, 1997	Low	Low	Low	High	Low	Unclear	Low	Unclear	Unclear
Mikawa, 1997	Unclear	Unclear	Low	Low	Unclear	Low	Low	Unclear	Unclear
Monagle, 1997	Unclear	Low	Low	Low	Low	Low	Unclear	Unclear	Unclear
Morton, 1997	Unclear	Unclear	Unclear	Low	Low	Unclear	Low	Unclear	Unclear
Patel, 1997	Unclear	Unclear	Unclear	Low	Low	Low	Low	Unclear	Unclear
Purhonen, 1997	Unclear	Low	Low	Low	Low	Low	Unclear	Unclear	Unclear
Rung, 1997	Low	Low	Low	Low	Unclear	Unclear	Low	Unclear	Unclear
Scuderi, 1997	Low	Unclear	Unclear	Low	Unclear	Unclear	Low	Unclear	Unclear
Taylor, 1997	Low	Unclear	Low	Low	High	Unclear	Unclear	Unclear	Unclear
Ulusoy, 1997	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Unclear	Unclear
Warriner, 1997	Unclear	Unclear	Unclear	Low	Low	Unclear	Low	Unclear	Unclear
Ali-melkkila, 1996	Unclear	Unclear	Unclear	Low	Low	Unclear	Low	Unclear	Unclear
Capouet, 1996	Unclear	Low	Unclear	Low	Unclear	Unclear	Low	Unclear	Unclear
Kovac, 1996 (CR: Pearman, 1994c)	Unclear	Unclear	Unclear	Low	Unclear	Unclear	Low	Unclear	Unclear
Naguib, 1996	Unclear	Low	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
Rose, 1996a	Unclear	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear
Desilva, 1995	Unclear	Low	Low	Low	High	Low	Low	Unclear	Unclear
Litman, 1995	Low	Unclear	Unclear	Low	Unclear	Unclear	Unclear	Unclear	Unclear
Paech, 1995	Low	Unclear	Unclear	Low	Low	Unclear	Low	Unclear	Unclear
Paxton, 1995a	Unclear	Unclear	Unclear	Low	Unclear	Unclear	Low	Unclear	Low
Kaufmann, 1994	Low	Low	Unclear	High	Low	Low	Low	Unclear	Unclear
Ummerhofer, 1994	Low	Low	Unclear	Low	Unclear	Low	Low	Unclear	Unclear
Dupeyron, 1993	Unclear	Unclear	Unclear	Low	Unclear	Unclear	Low	Unclear	Unclear
Helmers, 1993	Unclear	Unclear	Unclear	Low	Low	Unclear	Unclear	Unclear	Unclear
Raphael, 1993	Unclear	Unclear	Low	Low	Low	Unclear	Unclear	Unclear	Unclear
Du Pen, 1992 (CR: Scuderi, 1993)	Unclear	Unclear	Low	High	Unclear	Unclear	Low	Unclear	Unclear
Kovac, 1992 (CRs: McKenzie, 1993a; Pearman, 1994a)	Unclear	Unclear	Low	Low	Low	Unclear	Low	Unclear	Unclear

Non-randomized clinical trials (n=2)

Charbit, 2005	High	High	Low	Low	Unclear	Low	Low	Unclear	Unclear
Lerman, 1996	High	High	Unclear	Low	Unclear	High	Low	Unclear	Unclear

Controlled before-after studies (n=1)

Wagner, 2007 High High Unclear High High High Unclear Unclear High

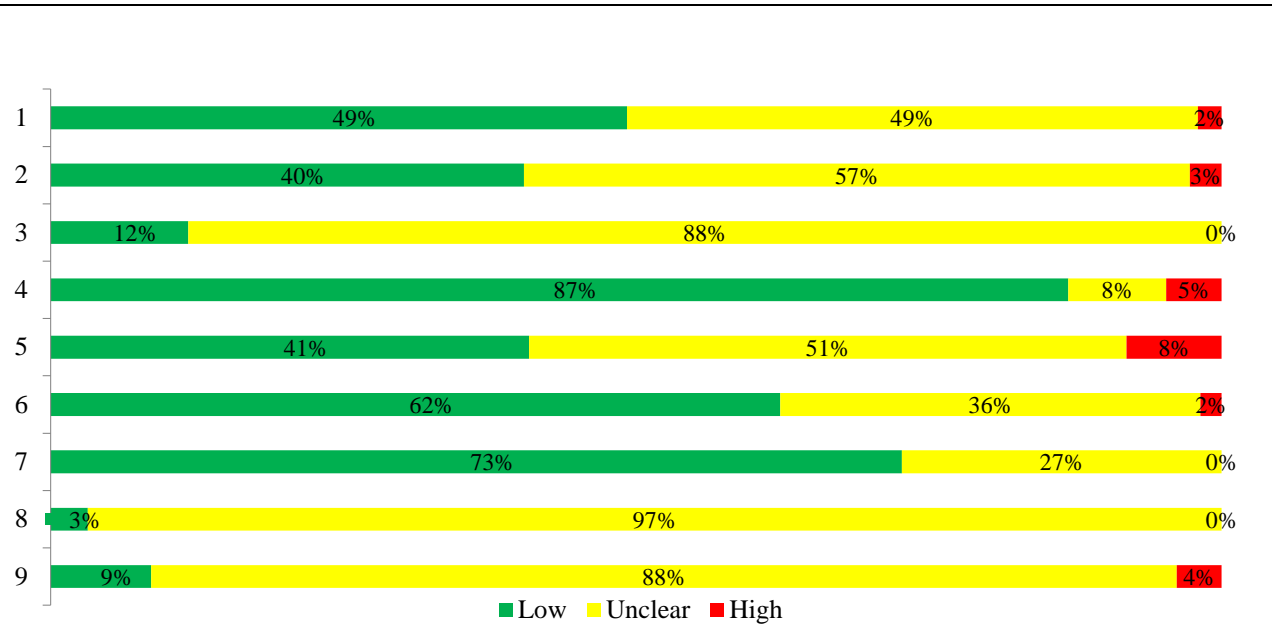
Note: †Unpublished data.

Abbreviations: CR, companion report; EPOC, Effective Practice and Organization of Care; High, high risk; Low, low risk; Unclear, unclear risk .

Items:

1. Random sequence generation
 2. Allocation concealment
 3. Similar baseline outcome measures
 4. Similar baseline characteristics
 5. Incomplete outcome data
 6. Blinding of outcome assessor
 7. Contamination
 8. Selective outcome reporting
 9. Other bias
-

Appendix 6. Aggregate EPOC risk-of-bias appraisal results



Abbreviations: EPOC, Effective Practice and Organization of Care; High, High risk of bias; Low, Low risk of bias; Unclear, Unclear risk of bias.

Items:

1. Random sequence generation
2. Allocation concealment
3. Similar baseline outcome measures
4. Similar baseline characteristics
5. Incomplete outcome data
6. Blinding
7. Contamination
8. Selective outcome reporting
9. Other bias

Appendix 7. McHarm appraisal results

Author, year	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
<i>Randomized clinical trials</i>															
Wang, 2012	P	U	U	U	P	U	U	U	P	C	P	C	U	C	U
Ekinci, 2011	P	U	U	U	P	U	U	U	U	P	C	U	U	C	C
El-deeb, 2011b	P	U	U	U	P	U	U	U	U	U	U	U	U	C	P
Sahoo, 2011	U	U	U	U	C	U	U	U	C	P	C	U	U	C	P
Choi, 2010	P	U	U	U	P	U	P	U	U	P	P	P	U	P	U
Jokela, 2010	P	U	U	U	C	U	C	C	C	C	C	C	C	C	C
Mehta, 2010	P	U	U	U	C	U	C	C	C	C	U	C	U	U	U
Shakya, 2010	P	U	U	U	U	U	U	U	U	P	P	U	U	C	U
Feng, 2009	P	U	U	U	C	U	U	U	C	P	C	C	U	C	P
Jain, 2009	P	U	U	U	C	U	P	P	P	P	C	C	U	C	U
Riad, 2009	U	U	U	U	C	U	P	U	C	P	U	U	U	C	P
Candiotti, 2008	U	U	U	U	U	U	U	U	U	U	C	C	P	C	U
Contreras-Dominguez, 2008	P	U	U	U	C	U	C	C	C	P	C	U	U	C	U
Kovac, 2008	U	U	U	U	U	U	U	U	U	U	C	U	C	C	C
Owczuk, 2008	P	U	U	U	C	U	U	U	C	P	U	C	U	U	P
Piper, 2008	U	U	U	U	U	U	U	U	U	U	C	U	U	C	U
Said-Ahmed, 2008	P	U	U	U	C	U	C	P	C	P	C	U	U	U	P
Aouad, 2007	P	U	U	U	P	U	C	P	C	C	C	C	U	C	C
Balki, 2007	P	U	U	U	C	U	U	U	P	P	C	C	U	C	C
Diemunsch, 2007	P	U	U	U	C	U	P	U	C	P	C	C	C	C	C
Gan, 2007	P	U	U	C	C	U	P	U	C	C	C	C	C	C	P
Han, 2007	P	U	U	U	P	U	C	C	P	C	U	C	U	C	U
Lee, 2007	P	U	U	U	P	U	C	C	C	P	P	C	U	C	U
Rusch, 2007	U	U	U	U	C	U	P	P	C	P	C	C	C	C	P
Sagir, 2007	C	U	U	U	P	U	U	U	U	P	C	U	U	C	C
Siddik-Sayyid, 2007	P	U	U	U	P	U	C	C	C	P	P	U	U	P	U
Chan, 2006	P	U	U	U	C	U	P	U	C	P	C	C	U	C	P
Kelsaka, 2006	U	U	U	U	U	U	U	U	C	U	U	U	U	U	U
Sarvela, 2006	U	U	U	U	C	P	U	U	C	P	U	C	U	U	P
Tosun, 2006	P	U	U	U	C	NA	C	C	C	U	C	U	U	C	C
Gan, 2005	P	U	U	C	P	U	C	P	U	U	C	C	C	C	P
Khalil, 2005	P	U	U	U	C	NA	P	U	C	U	C	P	P	C	C
Kontrimaviciute, 2005	U	U	U	U	P	U	U	U	P	P	C	U	U	C	U
Pirat, 2005	C	U	U	U	P	U	C	C	C	P	C	U	U	C	U
Treschan, 2005	U	U	U	U	C	U	U	U	C	P	C	U	U	U	P
Binstock, 2004	P	U	U	U	C	U	U	U	C	U	C	P	U	P	C
Eberhart, 2004	P	U	U	U	U	U	U	U	U	U	C	C	U	C	U
Hanaoka, 2004	P	C	U	U	P	U	C	U	P	P	U	C	C	C	U
Samakarndi, 2004	U	U	U	U	C	U	U	U	C	P	U	U	U	U	P
Charuluxananan, 2003	P	U	U	U	C	U	P	U	C	P	C	C	C	C	C
Loewen, 2003	P	U	U	U	C	U	C	C	U	C	C	C	U	C	U
O'Brien, 2003	P	U	U	U	P	U	C	C	C	U	P	C	C	C	U
Gurkan, 2002	P	U	U	U	P	U	U	U	C	P	U	U	U	C	P
Dabbous, 2001	P	U	U	U	U	U	U	U	U	U	C	U	U	C	U
Kathirvel, 2001	P	U	U	U	P	U	C	C	P	U	C	C	C	C	U
Subramaniam, 2001	U	U	U	U	C	U	U	U	C	P	C	U	U	C	P
Ahmed, 2000	U	U	U	U	C	U	C	U	C	U	C	C	C	U	P
Charuluxananan, 2000	U	U	U	U	U	U	P	U	P	U	U	U	U	U	P
Jensen, 2000	U	U	U	U	C	U	U	U	C	P	C	C	U	C	P
Kreisler, 2000	P	U	U	U	P	U	P	U	U	U	C	U	U	C	U
Philip, 2000	P	U	U	U	P	U	U	U	U	C	P	C	U	U	C
Zarate, 2000	P	U	U	U	C	U	C	C	C	U	U	U	U	U	C
Koivuranta, 1999	U	U	U	U	C	U	C	C	C	U	C	C	U	C	U
McCall, 1999	P	U	U	U	P	U	P	U	U	C	C	P	C	C	U
Sinha, 1999	U	U	U	P	P	U	U	U	P	U	C	C	U	C	U
Diemunsch, 1998	P	U	U	U	C	U	U	U	C	P	C	U	U	C	C
Hamid, 1998	U	U	U	U	U	U	U	U	U	U	U	P	U	U	U
Tramer, 1998	C	U	U	U	C	NA	C	C	P	C	C	C	U	C	C

Diemunsch, 1997b	P	U	U	U	C	U	U	U	C	P	C	U	C	C	C
Diemunsch, 1997c	P	U	U	U	P	U	U	U	U	C	C	U	C	C	C
Graczyk, 1997	P	U	U	U	C	U	U	U	C	P	C	U	U	C	C
Klockgether-Radke, 1997	C	U	U	U	P	U	U	U	P	P	C	U	U	C	C
Koivuranta, 1997	P	U	U	P	C	U	U	U	C	U	C	C	C	C	P
Korttila, 1997	P	U	U	U	C	NA	U	U	C	P	C	C	C	C	P
Kovac, 1997	P	U	U	U	C	P	P	U	C	P	C	U	C	C	C
Mikawa, 1997	P	U	U	U	C	NA	P	U	C	P	C	P	U	C	C
Monagle, 1997	U	U	U	U	P	P	P	P	P	P	U	P	U	U	C
Morton, 1997	U	U	U	U	U	U	U	U	C	U	C	C	U	C	C
Patel, 1997	P	U	U	U	C	C	C	P	C	U	C	C	U	C	U
Purhonen, 1997	C	U	U	U	P	U	U	U	P	P	U	C	U	C	P
Scuderi, 1997	P	U	U	U	C	U	U	U	C	P	P	U	U	C	P
Taylor, 1997	U	U	U	C	P	P	C	P	P	U	C	P	U	C	U
Ulusoy, 1997	P	U	U	U	P	U	U	U	C	U	C	U	U	C	P
Warriner, 1997	U	U	U	C	C	U	U	U	C	P	C	U	U	C	C
Capouet, 1996	U	U	U	U	P	P	C	P	C	U	C	P	U	C	U
Kovac, 1996 (CR: Pearman 1994)	P	U	U	U	P	P	C	P	C	P	C	C	U	C	C
Scholz, 1996	U	U	U	U	U	U	U	U	C	P	C	U	U	C	P
Desilva, 1995	P	U	U	U	P	U	P	U	U	U	C	C	U	C	C
Litman, 1995	U	U	U	U	C	U	U	U	C	U	U	U	U	P	C
Paech, 1995	P	U	U	U	C	NA	P	U	C	C	C	P	U	C	C
Paxton, 1995a	U	U	U	U	P	U	P	U	C	P	U	U	U	U	P
Kaufmann, 1994	P	U	U	U	P	U	C	C	C	P	C	C	U	C	C
Ummenhofer, 1994	U	U	U	U	C	U	P	U	C	P	U	U	U	C	P
Dupeyron, 1993	U	U	U	U	C	C	P	P	U	U	C	U	U	C	U
Helmers, 1993	P	U	U	C	C	C	P	U	C	P	C	P	U	C	U
Raphael, 1993	U	U	U	U	C	C	U	U	C	P	C	C	P	C	P
Du Pen, 1992	P	U	U	U	NA	C	P	U	P	U	C	U	U	C	U
Kovac, 1992 (CR: Mckenzie, 1993a)	P	U	U	U	P	U	P	U	C	P	C	U	C	C	C

Non-randomized clinical trials

Charbit, 2005	P	U	U	U	C	U	C	U	C	C	C	U	U	C	C
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Controlled before-after studies

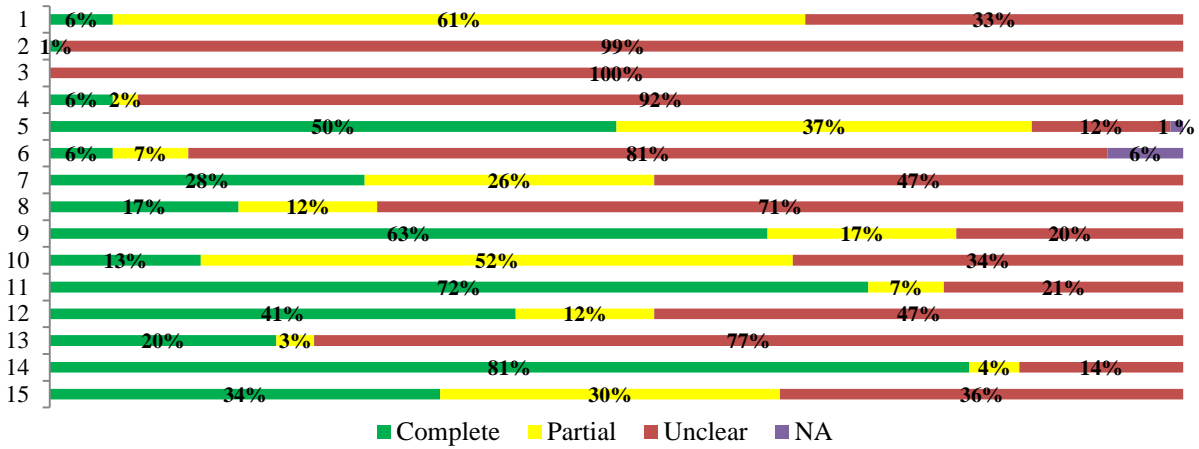
Wagner, 2007	U	U	U	U	P	U	U	U	C	U	C	U	U	C	U
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Abbreviations: C, complete; NA, not applicable; P, partial; U, unclear.

Items:

1. Were the harms pre-defined using standard or precise definitions?
2. Were serious events precisely defined?
3. Were severe events precisely defined?
4. Were the number of deaths in each study group specified or were the reason(s) for unclear specifying given?
5. Was the mode of harms collection specified as active?
6. Was the mode of harms collection specified as passive?
7. Did the study specify who collected the harms?
8. Did the study specify the training or background of who ascertained the harms?
9. Did the study specify the timing and frequency of collection of the harms?
10. Did the authors use standard scales or checklists for harms collection?
11. Did the authors specify if the harms reported encompass all the events collected or a selected sample?
12. Was the overall number of participants that withdrew or were lost to follow-up, including each reason why, specified for each study group?
13. Was the number of participants who withdrew due to harms specified for each study group?
14. Did the author(s) specify the number and type of harmful events for each study group?
15. Did the author(s) specify the type of analyses undertaken for harms data?

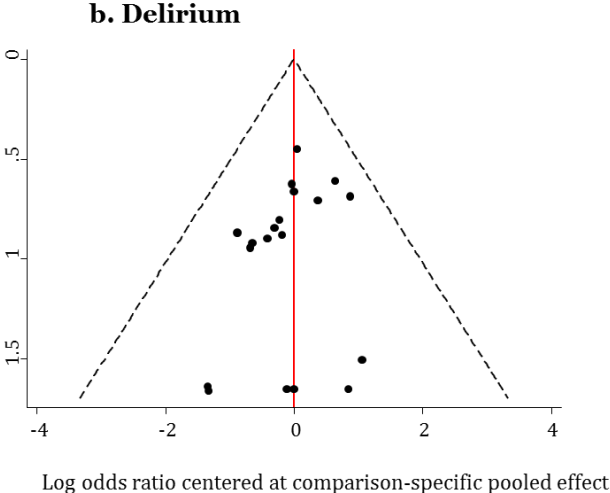
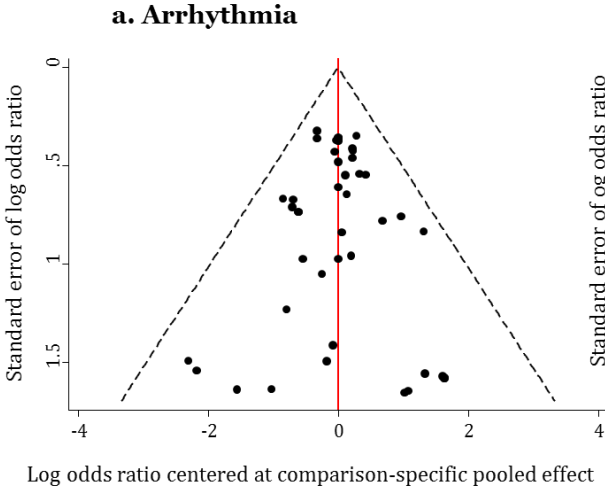
Appendix 8. Aggregate McHarm appraisal results



Items:

1. Were the harms pre-defined using standard or precise definitions?
2. Were serious events precisely defined?
3. Were severe events precisely defined?
4. Were the number of deaths in each study group specified or were the reason(s) for unclear specifying given?
5. Was the mode of harms collection specified as active?
6. Was the mode of harms collection specified as passive?
7. Did the study specify who collected the harms?
8. Did the study specify the training or background of who ascertained the harms?
9. Did the study specify the timing and frequency of collection of the harms?
10. Did the authors use standard scales or checklists for harms collection?
11. Did the authors specify if the harms reported encompass all the events collected or a selected sample?
12. Was the overall number of participants that withdrew or were lost to follow-up, including each reason why, specified for each study group?
13. Was the number of participants who withdrew due to harms specified for each study group?
14. Did the author(s) specify the number and type of harmful events for each study group?
15. Did the author(s) specify the type of analyses undertaken for harms data?

Appendix 9. Comparison adjusted funnel plots



Appendix 10. Definitions of arrhythmia

Study	Definition of arrhythmia
Sahoo, 2012	No definition for bradycardia reported
El-Deeb, 2011b	No definition for bradycardia reported
Choi, 2010	'Episodes of arrhythmias (i.e., atrial fibrillation or flutter, paroxysmal supraventricular tachycardia, atrial or ventricular premature contraction, or ventricular tachycardia) observed via ECG during the ICU stay were also recorded'; No specific definitions provided
Ekinci, 2009	No definition for tachycardia reported
Raid, 2009	No definition for OCR requiring atropine reported
Owczuk, 2008	No definition for bradycardia requiring atropine reported
Kelsaka, 2006	No definition for bradycardia reported
Gan, 2005	No definition for bradycardia reported
Kahlil, 2005	No definition for 'tachycardia & nodal arrhythmia' reported
Treschan, 2005	No definition for OCR reported
Binstock, 2004	No definition for tachycardia reported
Eberhart, 2004	No definition for bradycardia (OCR) requiring atropine reported
Hanaoka, 2004	No definition for ventricular fibrillation (cardiac arrest) reported
Samarkandi, 2004	No definition for OCR requiring atropine reported
Philip, 2000	No definition for 'sinus arrhythmia' reported
Subramaniam, 2000	No definition for OCR requiring atropine reported
Tramer, 1998	'A significant OCR was defined as an acute decrease in heart rate of 20% or greater associated with traction on an eye muscle'
Diemunsch, 1997b	No definition for bradycardia reported
Klockgether-Radke, 1997	No definition for 'OCR' reported
Korttila, 1997	No definition for bradycardia reported
Morton, 1997	No definition for bradycardia reported
Purhonen, 1997	Bradycardia defined as 'heart rate <50 bpm'
Capouet, 1996	No definition for 'bradycardia treated with an anticholinergic' reported
Hennes, 1996	No definition for bradycardia reported
Paxton, 1995a	No definition of nodal rhythms reported
Helmerts, 1993	No definition for bradycardia reported

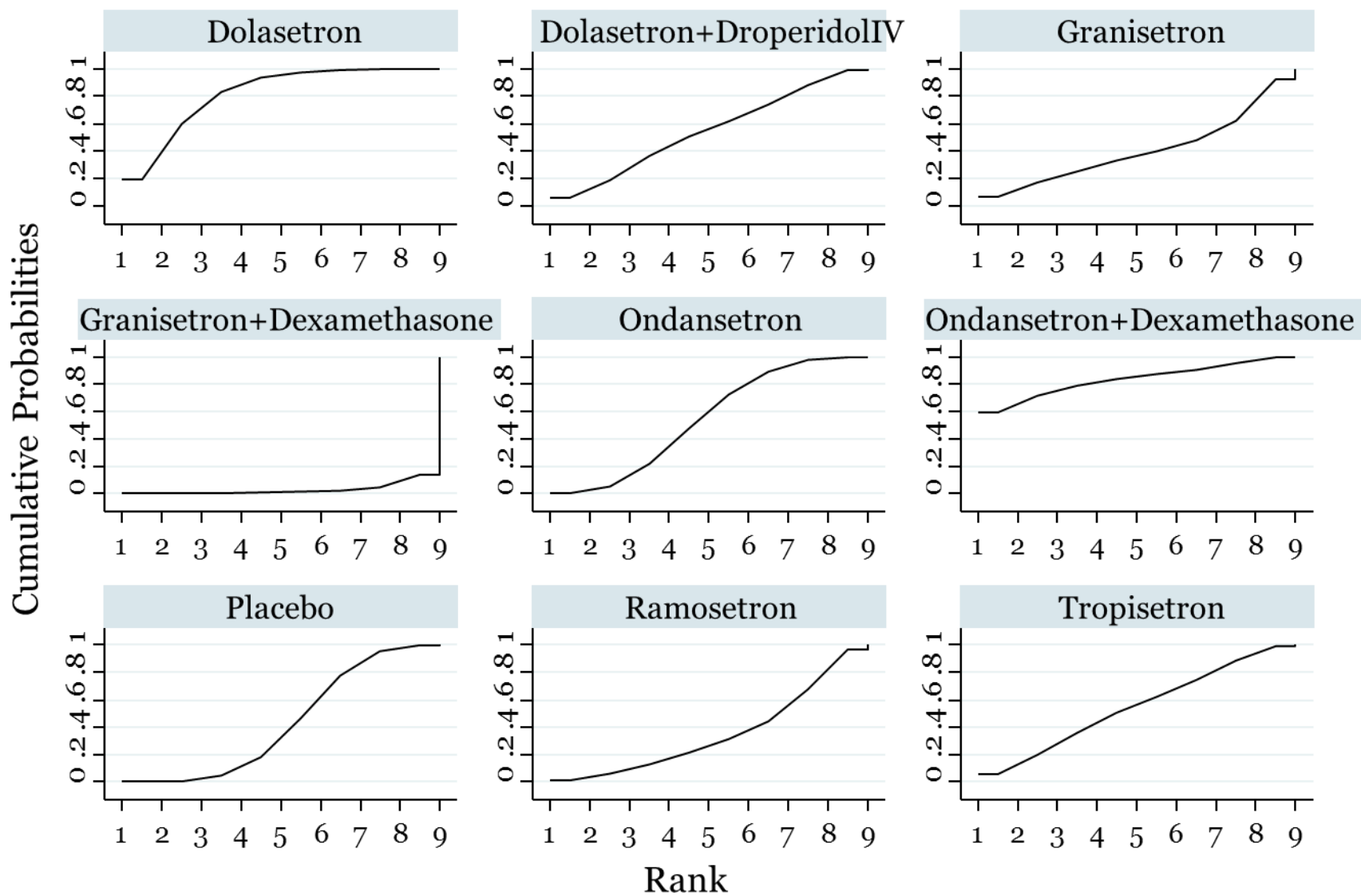
Abbreviations: Bpm, beats per minute; ECG, electrocardiogram; ICU, intensive care unit; OCR, oculocardiac reflex.

Appendix 11. Network meta-analysis for all outcomes for all time periods

<i>Treatment Comparison</i>	<i># of studies</i>	<i>MA estimate: OR (95% CI)</i>	<i>NMA estimate: OR (95% CI)</i>	<i># of studies</i>	<i>MA estimate: OR (95% CI)</i>	<i>NMA estimate: OR (95% CI)</i>
Arrhythmia (all ages) - 31 RCTs and 6,623 patients				Arrhythmia (children) - 9 RCTs and 1,572 patients		
Ondansetron vs Placebo	18	0.93 (0.70–1.23)	0.92 (0.69–1.21)	8	1.12 (0.54–2.33)	1.09 (0.56–2.14)
Granisetron vs Placebo	2	1.12 (0.40–3.11)	1.12 (0.40–3.11)	NA	NA	NA
Dolasetron vs Placebo	7	0.67 (0.45–1.00)	0.68 (0.46–1.01)	NA	NA	NA
Tropisetron vs Placebo	4	0.93 (0.48–1.79)	0.91 (0.49–1.68)	NA	NA	NA
Ondansetron+DEX vs Placebo	2	0.78 (0.19–3.14)	0.52 (0.16–1.68)	2	0.78 (0.19–3.14)	0.72 (0.20–2.66)
Ramosectron vs Placebo	1	1.36 (0.66–2.80)	1.15 (0.61–2.15)	NA	NA	NA
Granisetron+DEX vs Placebo	2	2.63 (0.75–9.29)	2.96 (1.11–7.94)	1	4.89 (1.15–20.79)	5.15 (1.33–19.91)
Dolasetron+DROP vs Placebo	1	0.91 (0.45–1.84)	0.91 (0.48–1.73)	NA	NA	NA
Granisetron vs Ondansetron	NA	NA	1.22 (0.43–3.53)	NA	NA	NA
Dolasetron vs Ondansetron	1	0.73 (0.28–1.87)	0.74 (0.46–1.18)	NA	NA	NA
Tropisetron vs Ondansetron	1	1.10 (0.33–3.65)	0.99 (0.52–1.90)	NA	NA	NA
Ondansetron+DEX vs Ondansetron	1	0.63 (0.09–4.24)	0.56 (0.17–1.86)	1	0.63 (0.09–4.24)	0.66 (0.17–2.59)
Ramosectron vs Ondansetron	1	1.07 (0.53–2.15)	1.25 (0.67–2.34)	NA	NA	NA
Granisetron+DEX vs Ondansetron	NA	NA	3.23 (1.17–8.95)	NA	NA	4.71 (1.08–20.46)
Dolasetron+DROP vs Ondansetron	NA	NA	0.99 (0.49–1.99)	NA	NA	NA
Dolasetron vs Granisetron	NA	NA	0.61 (0.20–1.81)	NA	NA	NA
Tropisetron vs Granisetron	NA	NA	0.81 (0.25–2.66)	NA	NA	NA
Ondansetron+DEX vs Granisetron	NA	NA	0.46 (0.10–2.19)	NA	NA	NA
Ramosectron vs Granisetron	NA	NA	1.02 (0.31–3.39)	NA	NA	NA
Granisetron+DEX vs Granisetron	NA	NA	2.64 (0.64–10.92)	NA	NA	NA
Dolasetron+DROP vs Granisetron	NA	NA	0.81 (0.24–2.70)	NA	NA	NA
Tropisetron vs Dolasetron	NA	NA	1.34 (0.64–2.77)	NA	NA	NA
Ondansetron+DEX vs Dolasetron	NA	NA	0.76 (0.22–2.64)	NA	NA	NA
Ramosectron vs Dolasetron	NA	NA	1.69 (0.81–3.53)	NA	NA	NA
Granisetron+DEX vs Dolasetron	NA	NA	4.37 (1.51–12.62)	NA	NA	NA
Dolasetron+DROP vs Dolasetron	1	1.33 (0.63–2.77)	1.34 (0.69–2.58)	NA	NA	NA
Ondansetron+DEX vs Tropisetron	NA	NA	0.57 (0.15–2.15)	NA	NA	NA
Ramosectron vs Tropisetron	NA	NA	1.26 (0.53–3.01)	NA	NA	NA
Granisetron+DEX vs Tropisetron	NA	NA	3.27 (1.02–10.43)	NA	NA	NA
Dolasetron+DROP vs Tropisetron	NA	NA	1.00 (0.41–2.43)	NA	NA	NA
Ramosectron vs Ondansetron+DEX	NA	NA	2.22 (0.59–8.42)	NA	NA	NA
Granisetron+DEX vs Ondansetron+DEX	2	8.10 (1.92–34.13)	5.75 (1.71–19.34)	1	7.67 (1.47–40)	7.12 (1.66–30.63)
Dolasetron+DROP vs Ondansetron+DEX	NA	NA	1.76 (0.46–6.77)	NA	NA	NA

Granisetron+DEX vs Ramosetron	NA	NA	2.59 (0.81–8.31)	NA	NA	NA
Dolasetron+DROD vs Ramosetron	NA	NA	0.79 (0.32–1.95)	NA	NA	NA
Dolasetron+DROD vs Granisetron+DEX	NA	NA	0.31 (0.09–0.99)	NA	NA	NA
Between-study heterogeneity	0.01			0.02		
Design-by-treatment interaction model for inconsistency (χ^2, d.f., P-value, heterogeneity)	3.49 (10, 0.968, 0.01)			0.13 (2, 0.938, 0.32)		
	Delirium (all ages) - 18 RCTs and 3,652 patients			Delirium (children) - 4 RCTs and 1,220 patients		
Ondansetron vs Placebo	11	0.84 (0.53–1.32)	0.83 (0.53–1.31)	2	0.83 (0.19–3.60)	0.77 (0.23–2.61)
Granisetron vs Placebo	3	0.29 (0.08–1.08)	0.30 (0.08–1.12)	NA	NA	NA
Dolasetron vs Placebo	1	3.34 (0.13–85.47)	3.34 (0.13–85.52)	NA	NA	NA
Tropisetron vs Placebo	3	1.45 (0.58–3.66)	1.45 (0.58–3.66)	2	1.35 (0.45–4.01)	1.38 (0.39–4.8)
Dolasetron+DEX vs Placebo	NA	NA	3.54 (0.11–116.45)	NA	NA	NA
Granisetron vs Ondansetron	NA	NA	0.36 (0.09–1.43)	NA	NA	NA
Dolasetron vs Ondansetron	NA	NA	4.00 (0.15–105.86)	NA	NA	NA
Tropisetron vs Ondansetron	NA	NA	1.74 (0.62–4.88)	NA	NA	1.78 (0.32–9.9)
Dolasetron+DEX vs Ondansetron	NA	NA	4.24 (0.13–143.81)	NA	NA	NA
Dolasetron vs Granisetron	NA	NA	11.13 (0.34–368.08)	NA	NA	NA
Tropisetron vs Granisetron	NA	NA	4.85 (0.97–24.11)	NA	NA	NA
Dolasetron+DEX vs Granisetron	NA	NA	11.80 (0.28–492.67)	NA	NA	NA
Tropisetron vs Dolasetron	NA	NA	0.44 (0.01–12.68)	NA	NA	NA
Dolasetron+DEX vs Dolasetron	1	1.06 (0.29–3.88)	1.06 (0.29–3.88)	NA	NA	NA
Dolasetron+DEX vs Tropisetron	NA	NA	2.43 (0.07–90.26)	NA	NA	NA
Between-study heterogeneity	0.00			0.18		
Design-by-treatment interaction model for inconsistency (χ^2, d.f., P-value, heterogeneity)	0.31 (2, 0.857, 0.00)			NA		
Abbreviations: DEX dexamethasone, DROD droperidol (intravenous), METO Metoclopramide (intravenous), PONV post-operative nausea and vomiting.						

Appendix 12. Plot of the surface under the cumulative ranking (SUCRA) curves for the 9 treatments included in Arrhythmia.



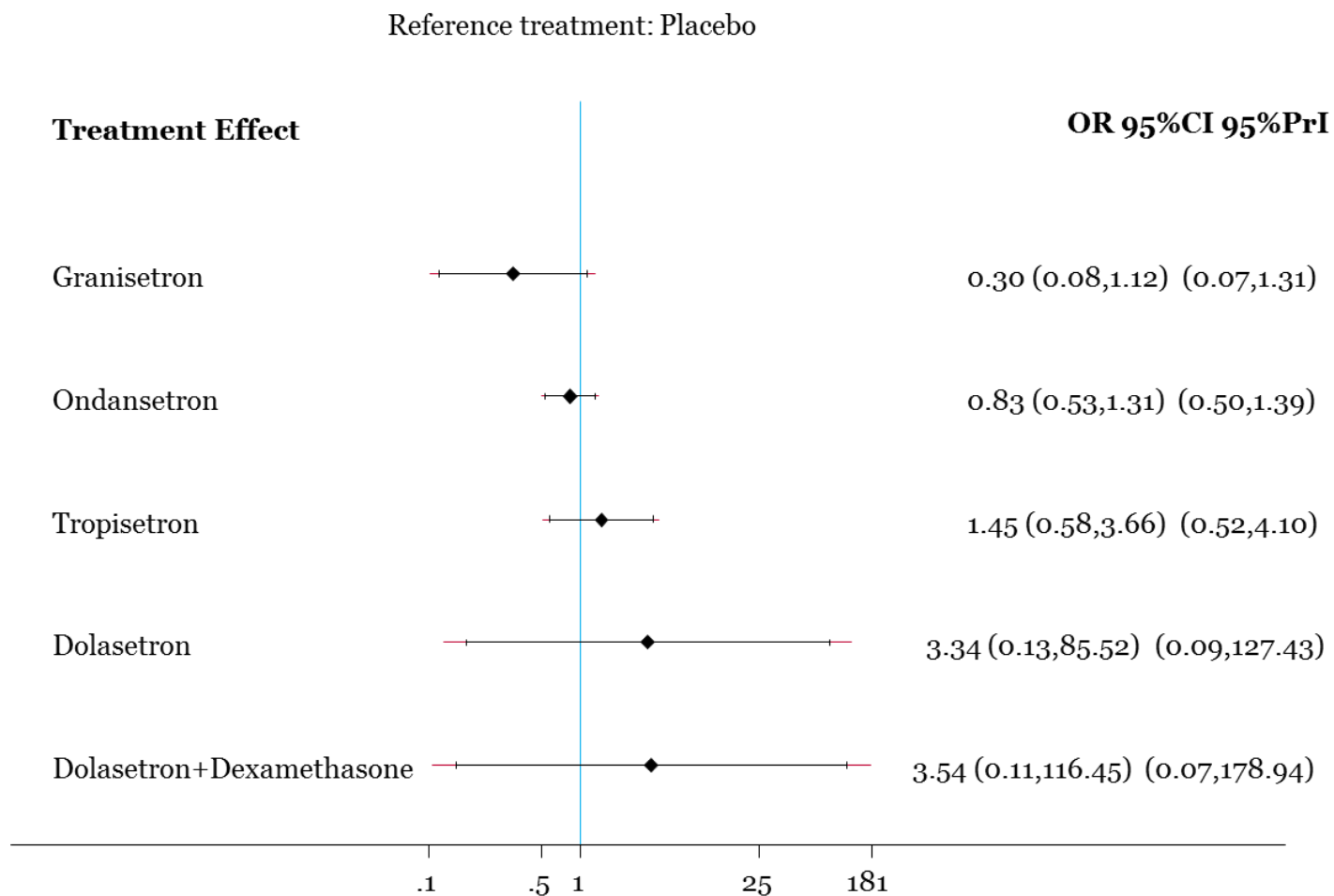
Appendix 13: Subgroup analysis for Arrhythmia and Delirium

<i>Treatment Comparison</i>	Intra surgery - RCTs only			All time periods - RCTs only - sensitivity analysis for Risk of Bias			All time periods - all study designs		
	<i># of studies</i>	<i>MA estimate: OR (95% CI)</i>	<i>NMA estimate: OR (95% CI)</i>	<i># of studies</i>	<i>MA estimate: OR (95% CI)</i>	<i>NMA estimate: OR (95% CI)</i>	<i># of studies</i>	<i>MA estimate: OR (95% CI)</i>	<i>NMA estimate: OR (95% CI)</i>
	Arrhythmia								
Ondansetron vs Placebo	16	0.89 (0.65-1.23)	0.87 (0.64-1.2)	18	0.93 (0.7-1.23)	0.92 (0.69-1.21)			
Granisetron vs Placebo	1	3.12 (0.13-77.52)	3.12 (0.13-77.37)	1	3.12 (0.13-77.52)	3.12 (0.13-77.36)			
Dolasetron vs Placebo	4	0.56 (0.34-0.92)	0.57 (0.35-0.93)	7	0.67 (0.45-1)	0.68 (0.46-1.01)			
Tropisetron vs Placebo	4	0.93 (0.48-1.79)	0.9 (0.49-1.66)	4	0.93 (0.48-1.79)	0.91 (0.49-1.68)			
Ondansetron+Dexamethasone vs Placebo	2	0.78 (0.19-3.14)	0.51 (0.16-1.66)	2	0.78 (0.19-3.14)	0.52 (0.16-1.68)			
Ramosetron vs Placebo	1	1.48 (0.73-3)	1.48 (0.73-3)	1	1.36 (0.66-2.8)	1.15 (0.61-2.15)			
Granisetron+Dexamethasone vs Placebo	2	2.63 (0.75-9.29)	2.95 (1.1-7.91)	2	2.63 (0.75-9.29)	2.96 (1.11-7.94)			
Dolasetron+DroperidolIV vs Placebo	1	0.91 (0.45-1.84)	0.84 (0.44-1.62)	1	0.91 (0.45-1.84)	0.91 (0.48-1.73)			
Granisetron vs Ondansetron	NA	NA	3.56 (0.14-89.88)	NA	NA	3.4 (0.14-85.46)			
Dolasetron vs Ondansetron	1	0.73 (0.28-1.87)	0.66 (0.38-1.14)	1	0.73 (0.28-1.87)	0.74 (0.46-1.18)			
Tropisetron vs Ondansetron	1	1.1 (0.33-3.65)	1.03 (0.53-1.99)	1	1.1 (0.33-3.65)	0.99 (0.52-1.9)			
Ondansetron+Dexamethasone vs Ondansetron	1	0.63 (0.09-4.24)	0.58 (0.17-1.94)	1	0.63 (0.09-4.24)	0.56 (0.17-1.86)			
Ramosetron vs Ondansetron	NA	NA	1.69 (0.78-3.67)	1	1.07 (0.53-2.15)	1.25 (0.67-2.34)			
Granisetron+Dexamethasone vs Ondansetron	NA	NA	3.38 (1.21-9.42)	NA	NA	3.23 (1.17-8.95)			
Dolasetron+DroperidolIV vs Ondansetron	NA	NA	0.96 (0.47-1.98)	NA	NA	0.99 (0.49-1.99)			
Dolasetron vs Granisetron	NA	NA	0.18 (0.01-4.75)	NA	NA	0.22 (0.01-5.54)			
Tropisetron vs Granisetron	NA	NA	0.29 (0.01-7.59)	NA	NA	0.29 (0.01-7.66)			
Ondansetron+Dexamethasone vs Granisetron	NA	NA	0.16 (0.01-5.01)	NA	NA	0.17 (0.01-5.07)			
Ramosetron vs Granisetron	NA	NA	0.47 (0.02-12.72)	NA	NA	0.37 (0.01-9.7)			
Granisetron+Dexamethasone vs Granisetron	NA	NA	0.95 (0.03-27.27)	NA	NA	0.95 (0.03-27.38)			
Dolasetron+DroperidolIV vs Granisetron	NA	NA	0.27 (0.01-7.17)	NA	NA	0.29 (0.01-7.7)			
Tropisetron vs Dolasetron	NA	NA	1.56 (0.72-3.4)	NA	NA	1.34 (0.64-2.77)			
Ondansetron+Dexamethasone vs Dolasetron	NA	NA	0.88 (0.25-3.17)	NA	NA	0.76 (0.22-2.64)			
Ramosetron vs Dolasetron	NA	NA	2.57 (1.09-6.06)	NA	NA	1.69 (0.81-3.53)			
Granisetron+Dexamethasone vs Dolasetron	NA	NA	5.13 (1.72-15.37)	NA	NA	4.37 (1.51-12.62)			
Dolasetron+DroperidolIV vs Dolasetron	1	1.33 (0.63-2.77)	1.46 (0.75-2.87)	NA	1.33 (0.63-2.77)	1.34 (0.69-2.58)			
Ondansetron+Dexamethasone vs Tropisetron	NA	NA	0.57 (0.15-2.14)	NA	NA	0.57 (0.15-2.15)			
Ramosetron vs Tropisetron	NA	NA	1.64 (0.64-4.21)	NA	NA	1.26 (0.53-3.01)			
Granisetron+Dexamethasone vs Tropisetron	NA	NA	3.29 (1.03-10.49)	NA	NA	3.27 (1.02-10.43)			
Dolasetron+DroperidolIV vs Tropisetron	NA	NA	0.94 (0.38-2.3)	NA	NA	1 (0.41-2.43)			
Ramosetron vs	NA	NA	2.9 (0.73-11.55)	NA	NA	2.22 (0.59-8.42)			

Ondansetron+Dexamethasone									
Granisetron+Dexamethasone vs Ondansetron+Dexamethasone	2	8.1 (1.92-34.13)	5.8 (1.73-19.51)	2	8.1 (1.92-34.13)	5.75 (1.71-19.34)			
Dolasetron+DroperidolIV vs Ondansetron+Dexamethasone	NA	NA	1.66 (0.43-6.4)	NA	NA	1.76 (0.46-6.77)			
Granisetron+Dexamethasone vs Ramosetron	NA	NA	2 (0.59-6.73)	NA	NA	2.59 (0.81-8.31)			
Dolasetron+DroperidolIV vs Ramosetron	NA	NA	0.57 (0.22-1.5)	NA	NA	0.79 (0.32-1.95)			
Dolasetron+DroperidolIV vs Granisetron+Dexamethasone	NA	NA	0.29 (0.09-0.93)	NA	NA	0.31 (0.09-0.99)			
Between-study heterogeneity			0.00			0.00			
Design-by-treatment interaction model for inconsistency (χ^2, d.f., P-value, heterogeneity)			2.88 (9, 0.969, 0.04)			3.46 (10, 0.968, 0.01)			
	Delirium								
Ondansetron vs Placebo	10	0.80 (0.50-1.28)	0.80 (0.5-1.27)	10	0.85 (0.54-1.35)	0.85 (0.54-1.35)	12	0.85 (0.54-1.34)	0.85 (0.54-1.34)
Granisetron vs Placebo	2	0.17 (0.02-1.51)	0.19 (0.02-1.64)	1	0.1 (0.01-1.92)	0.1 (0.01-1.92)	3	0.29 (0.08-1.08)	0.3 (0.08-1.12)
Dolasetron vs Placebo	1	3.34 (0.13-85.47)	3.34 (0.13-85.56)	1	3.34 (0.13-85.47)	3.34 (0.13-85.54)	1	3.34 (0.13-85.47)	3.34 (0.13-85.54)
Tropisetron vs Placebo	2	1.35 (0.45-4.01)	1.35 (0.45-4.01)	3	1.45 (0.58-3.66)	1.45 (0.58-3.66)	3	1.45 (0.58-3.66)	1.45 (0.58-3.66)
Dolasetron+DEX vs Placebo	NA	NA	0.24 (0.03-2.15)	NA	NA	3.54 (0.11-116.48)	NA	NA	3.54 (0.11-116.46)
Granisetron vs Ondansetron	NA	NA	4.2 (0.16-111.21)	NA	NA	0.12 (0.01-2.35)	NA	NA	0.35 (0.09-1.4)
Dolasetron vs Ondansetron	NA	NA	1.7 (0.52-5.56)	NA	NA	3.93 (0.15-103.99)	NA	NA	3.91 (0.15-103.41)
Tropisetron vs Ondansetron	NA	NA	17.46 (0.36-855.21)	NA	NA	1.71 (0.61-4.8)	NA	NA	1.7 (0.61-4.76)
Dolasetron+DEX vs Ondansetron	NA	NA	7.05 (0.63-78.61)	NA	NA	4.17 (0.12-141.28)	NA	NA	4.15 (0.12-140.47)
Dolasetron vs Granisetron	NA	NA	0.4 (0.01-12.37)	NA	NA	33.35 (0.41-2683.9)	NA	NA	11.12 (0.34-367.78)
Tropisetron vs Granisetron	NA	NA	NA	NA	NA	14.52 (0.66-321.2)	NA	NA	4.84 (0.97-24.09)
Dolasetron+DEX vs Granisetron	NA	NA	NA	NA	NA	35.35 (0.36-3434.22)	NA	NA	11.79 (0.28-492.21)
Tropisetron vs Dolasetron	NA	NA	NA	NA	NA	0.44 (0.01-12.68)	NA	NA	0.44 (0.01-12.69)
Dolasetron+DEX vs Dolasetron	NA	NA	NA	1	1.06 (0.29-3.88)	1.06 (0.29-3.88)	1	1.06 (0.29-3.88)	1.06 (0.29-3.88)
Dolasetron+DEX vs Tropisetron	NA	NA	NA	NA	NA	2.43 (0.07-90.28)	NA	NA	2.43 (0.07-90.26)
Between-study heterogeneity			0.00			0.00			0.00
Design-by-treatment interaction model for inconsistency (χ^2, d.f., P-value, heterogeneity)			0.63 (2, 0.729, 0.00)			NA			0.32 (2, 0.851, 0.00)

heterogeneity)									
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Appendix 14. Network meta-analysis results for Delirium.



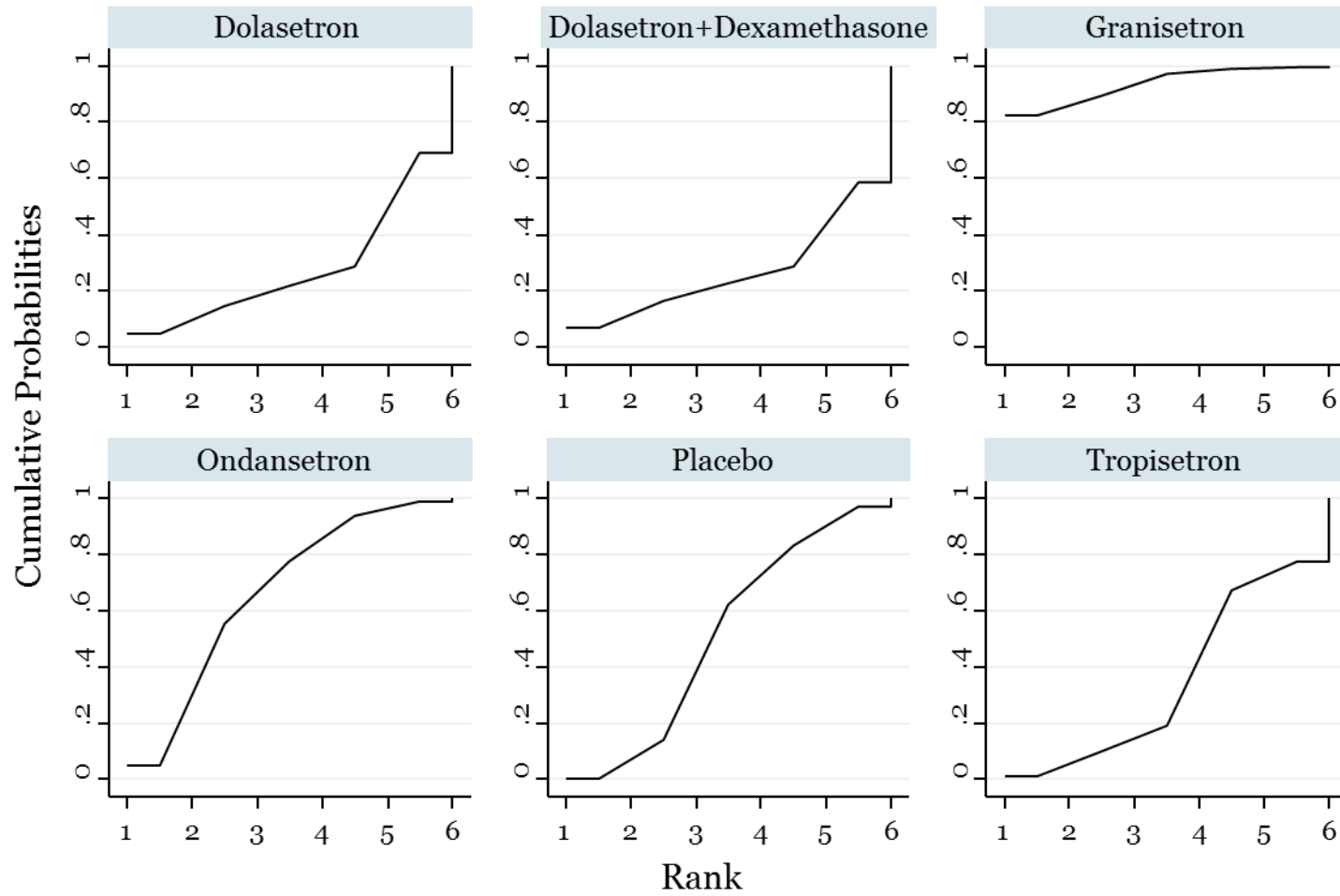
Network estimates using the random effects model and a common within-network heterogeneity

All treatments are compared to placebo. The black horizontal lines represent the 95% confidence intervals (CI) of the summary treatment effects and red horizontal lines the 95% predictive intervals (PrI). The results are presented on the odds ratio scale.

Appendix 15. Definitions of delirium

Study	Definition of delirium
Jain, 2009	Confusion unspecified
Piper, 2008	Restlessness, agitation unspecified
Sagir, 2007	Agitation unspecified
Wagner, 2007	Emergence delirium unspecified
Tosun, 2006	Agitation unspecified
Khalil, 2005	Agitation and aggressive behavior unspecified
Kathirvel, 2001	Confusion/Dizziness unspecified
Jensen, 2000	Restlessness unspecified
McCall, 1999	Emergence was scored as 'where 1 = calm emergence, 2 = slight agitation or delirium, 3 = moderate agitation or delirium, and 4 = extreme agitation or delirium'; Delirium was considered a score of 3,4
Sinha, 1999	Confusion unspecified
Koivuranta, 1997	Restlessness unspecified
Patel, 1997	Anxiety/agitation unspecified
Kovac, 1996 (CR: Pearman, 1994c)	Anxiety/agitation unspecified
Paech, 1995	Agitation unspecified
Kovac, 1992 (CR: Mckenzie, 1993a)	Anxiety/agitation unspecified

Appendix 16. Plot of the surface under the cumulative ranking (SUCRA) curves for the 6 treatments included in Delirium.



Appendix 17. Included studies in our review versus previous systematic reviews

Study	Tang, 2012 (NMA)	Carlisle, 2006 (Cochrane)	Rawlinson, 2012	# of patients
<i>Randomized clinical trials (n=112)</i>				
Choi, 2012	NO	NO	NO	120
Wang, 2012	NO	NO	NO	130
Ekinçi, 2011	NO	NO	NO	100
El-deeb, 2011b	NO	NO	NO	160
Gan, 2011	NO	NO	NO	619
Gupta, 2011	NO	NO	NO	136
Park, 2011	NO	NO	NO	90
Ryu, 2011	NO	NO	NO	124
Sahoo, 2011	NO	NO	NO	52
Bilgin, 2010	NO	NO	NO	160
Choi, 2010	NO	NO	NO	279
Jee, 2010	NO	NO	NO	100
Jokela, 2010	NO	NO	NO	80
Mehta, 2010	NO	NO	NO	80
Shakya, 2010	NO	NO	NO	80
Singla, 2010	NO	NO	NO	702
Feng, 2009	NO	NO	NO	192
Jain, 2009	NO	NO	NO	87
Riad, 2009	NO	NO	NO	100
Rosow, 2009	NO	NO	NO	244
Candiotti, 2008	NO	NO	NO	546
Choi, 2008	NO	NO	NO	94
Contreras-Dominguez, 2008	YES	NO	NO	150
Kovac, 2008	NO	NO	NO	544
Owczuk, 2008	NO	NO	NO	71
Piper, 2008	YES	NO	NO	83
Said-Ahmed, 2008	NO	NO	NO	50
Bestas, 2007	YES	NO	NO	90
Diemunsch, 2007	NO	NO	NO	892
Gan, 2007	NO	NO	NO	766
Han, 2007	NO	NO	NO	80
Lee, 2007	NO	NO	NO	86
Oksuz, 2007	NO	NO	NO	75
Rusch, 2007	NO	NO	NO	228
Sagir, 2007	NO	NO	NO	80
Sandhu, 2007	NO	NO	NO	80
Siddik-Sayyid, 2007	NO	NO	NO	129
Bridge, 2006	NO	NO	NO	194
Chan, 2006	NO	NO	NO	394
Kelsaka, 2006	NO	NO	NO	50
Sarvela, 2006	NO	NO	NO	87
Tosun, 2006	NO	YES	NO	125

D'Angelo, 2005	YES	NO	NO	121
Gan, 2005	NO	NO	NO	176
Khalil, 2005	NO	NO	NO	670
Kocamanoglu, 2005	YES	NO	NO	150
Kontrimaviciute, 2005	NO	NO	NO	34
Pirat, 2005	YES	NO	NO	150
Treschan, 2005	NO	NO	NO	142
White, 2005 ^f	NO	NO	NO	372
Apfel, 2004 (CR: Jokela, 2009)	NO	YES	YES	260
Binstock, 2004	NO	NO	NO	101
Eberhart, 2004	NO	NO	NO	304
Hanaoka, 2004	YES	NO	NO	315
Samakarndi, 2004	NO	NO	NO	80
Charuluxananan, 2003	NO	YES	NO	180
Loewen, 2003	NO	YES	NO	71
O'Brien, 2003	NO	YES	NO	150
Argiriadou, 2002	NO	YES	NO	87
Gurkan, 2002	NO	NO	NO	150
Dabbous, 2001	NO	NO	NO	173
Kathirvel, 2001	YES	YES	NO	152
Subramaniam, 2001	NO	YES	NO	135
Ahmed, 2000	NO	YES	NO	139
Charuluxananan, 2000	NO	NO	NO	80
Jensen, 2000	NO	YES	NO	71
Kreiser, 2000	NO	YES	NO	31
Philip, 2000	YES	YES	NO	1030
Zarate, 2000	NO	YES	NO	200
Koivuranta, 1999	NO	YES	NO	88
McCall, 1999	NO	YES	NO	100
Sinha, 1999	YES	YES	NO	40
Tsui, 1999	NO	YES	NO	121
Diemunsch, 1998	YES	YES	NO	793
Goodarzi, 1998	NO	YES	NO	81
Hamid, 1998	NO	YES	NO	71
Morris, 1998	NO	YES	NO	1044
Scholz, 1998	YES	YES	NO	842
Tramer, 1998	NO	YES	NO	157
Diemunsch, 1997b	NO	YES	NO	281
Diemunsch, 1997c	NO	NO	NO	337
Graczyk, 1997	NO	NO	NO	635
Klockgether-Radke, 1997	NO	YES	NO	120
Koivuranta, 1997	NO	YES	NO	439
Korttila, 1997	YES	YES	NO	517
Kovac, 1997	NO	NO	NO	620
Mikawa, 1997	YES	YES	NO	200
Monagle, 1997	NO	YES	NO	91
Morton, 1997	NO	YES	NO	427
Patel, 1997	NO	NO	NO	429

Purhonen, 1997	YES	YES	NO	146
Rung, 1997	NO	NO	NO	121
Scuderi, 1997	NO	YES	NO	160
Taylor, 1997	NO	NO	NO	523
Ulusoy, 1997	NO	NO	NO	40
Warriner, 1997	YES	YES	NO	374
Ali-melkkila, 1996	NO	NO	NO	120
Capouet, 1996	YES	YES	NO	385
Kovac, 1996 (CR: Pearman, 1994c)	YES	YES	NO	468
Naguib, 1996	YES	YES	NO	132
Rose, 1996a	NO	YES	NO	136
Desilva, 1995	NO	NO	NO	286
Litman, 1995	NO	YES	NO	57
Paech, 1995	NO	YES	NO	259
Paxton, 1995a	NO	YES	NO	60
Kaufmann, 1994	YES	YES	NO	286
Ummenhofer, 1994	NO	YES	NO	200
Dupeyron, 1993	NO	YES	NO	243
Helmers, 1993	NO	YES	NO	923
Raphael, 1993	NO	YES	NO	123
Du Pen, 1992 (CR: Scuderi, 1993)	NO	NO	NO	500
Kovac, 1992 (CRs: McKenzie, 1993a; Pearman, 1994a)	NO	NO	NO	580
<i>Non randomized clinical trials (n=2)</i>				
Charbit, 2005	NO	NO	NO	85
Lerman, 1996	NO	YES	NO	28
<i>Controlled before-after study (n=1)</i>				
Wagner, 2007	NO	NO	NO	66
Total included studies	66	217	4	

Note: †Unpublished data (White, 2005).

Abbreviations: CR, companion report; NMA, network meta-analysis; NO, study wasn't included in review; YES, study was included in review.