Appendix: C

~~Supplementary~~ Table 1: Agents excluded from the analysis since they were evaluated in only 1 Randomized control trial.

Odds ratio of less than 1 indicates the pharmacological agent to be protective.

* Odds ratio for the incidence of post ERCP pancreatitis (PEP) compared to placebo, ** compared to Hyoscine, # compared to Glucagon

Pharmacological agent	Agent details	Author Year	Number of patients in treatment arm	Odds ratio for the incidence of PEP
Aprepitant	Neurokinin-1 receptor antagonist	Shah 2012[1]	34	2.48 (0.12-1.52)*
Aprotinin	Trypsin inhibitor	Brust 1977[2]	22	2.25 (0.69-7.32)*
Platelet Activation Factor (PAF) Acetylhydrolase	Hydrolyzes PAF to a biologically inactive metabolite	Sherman 2009[3]	401	0.82 (0.53-1.27)*
Beta-Carotene	Precursor of Vitamin A	Lavy 2004[4]	141	1.06 (0.50-2.22)*
Botulinum toxin	Clostridium derived toxin	Gorelick 2004[5]	12	0.44 (0.08-2.39)*
5 Fluorouracil	Antimetabolite	Tao 2004[6]	80	0.23 (0.05-1.12)*
Glucagon	Hormone	Chang 1995[7]	23	0.82 (0.13-5.41)**
Hyoscine	Anticholinergic	Chang 1995[7]	29	1.21 (0.18-7.94)[#]
Lidocaine	Local anesthetic	Schwartz 2004[8]	145	1.46 (0.45-4.71)*
Losartan	Angiotensin II receptor antagonist	Bexelius 2012[9]	38	1.37 (0.45-4.170*
Magnesium sulphate	Inorganic salt	Ding 2012[10]	60	0.11 (0.01-0.91)*
Pentoxifylline	Xanthine derivative	Kapetanos 2007[11]	158	1.90 (0.62-5.79)*
Qingyi Decoction	Chinese herbal medicine	Liu 2009[12]	39	0.21 (0.02-1.84)*
Salmon Calcitonin	Salmon derived calcitonin hormone	Odes 1977[13]	17	0.76 (0.09-6.17)*
Selenium	Micronutrient	Wollschlager 1999[14]	20	0.63 (0.09-4.24)*
Semapimod	Inhibits nitric oxide synthesis in macrophages	Westerloo 2008[15]	121	0.57 (0.26-1.27)*
Udenafil	Phosphodiesterase type 5 inhibitor	Oh 2011[16]	137	1.03 (0.43-2.46)*
Valdecoxib	Non-steroidal anti-inflammatory agent	Bhatia 2011[17]	121	0.96 (0.42-2.19)*

~~Supplementary~~ **Table 2:** Characteristics of randomized trials that met the inclusion criteria and were included in analysis.

NR- none reported, PEP – post-ERCP pancreatitis, i.v – intravenous, s.c – sub cutaneous, i.m – intramuscular, PEP definition in quotes is obtained directly from each study ; Consensus definition for PEP (see *Cotton PB, Lehman G, Vennes J, et al. Endoscopic sphincterotomy complications and their management: an attempt at consensus. Gastrointest Endosc 1991;37:383-93*).

Author Year	Age (in years)	Female (%)	Definition of post-ERCP pancreatitis (PEP) as reported in the study	Treatments evaluated	N	PEP %	Severe PEP %	Mortality due to PEP %
Abbasinazari 2011[18]	NR	60.8	"Definition of post-ERCP pancreatitis in present study was based on a consensus criteria; mild: amylase concentration at least 3x above upper limit of normal at more than 24 hrs after procedure requiring admission for 2-3 days, moderate: admission for 4-10 days and severe: admission for more than 10 days."	Allopurinol – oral, 300 mg - 3 hrs before ERCP and 300 mg immediately before ERCP	29	10.34	0	0
				Placebo	45	11.1	0	0
Alveyn 1991[19]	Mean= 56	51.06	"Abdominal pain and plasma amylase>1000u/l"	Ciprofloxacin - oral, 750 mg- single dose 90 min before ERCP	24	8.3	NR	0
				Placebo	23	13.04	NR	0
Andriulli 2002[20] (Includes only high-risk patients)	Mean= 58	52.3	"Diagnosis of post-ERCP pancreatitis was made when both abdominal pain, requiring administration of analgesic medication and lasting for at least 24 hrs after endoscopy, and a persistent increase in serum amylase occurred. By using established criteria, serum amylase was considered to be significantly elevated when greater than 5- and 3-fold increases above the upper normal limit were recorded, respectively at 4 and 24 hrs after the procedure"	Somatostatin- i.v., 750 µg 30 min before the endoscopic session and for 2 hrs afterwards	183	11.5	0	0
				Gabexate – i.v., 500 mg 30 min before the endoscopic session and for 2 hrs afterwards	197	8.1	0.51	0
				Placebo	199	6.5	0.5	0
Andriulli 2004[21]	Mean= 65.34	48.7	"Patients were considered to have post-ERCP pancreatitis when both abdominal pain requiring analgesic use and lasting for at least 24 hrs after endoscopy and a persistent increase in serum amylase levels occurred. Serum amylase level was considered significantly increased when >5- and 3-fold elevations above the upper limits of normal at 4 and 24 hrs after the procedure were recorded, respectively"	Somatostatin-i.v., 750 µg/min 30 min before the endoscopic session and for 6 hrs afterwards	351	6.3	0	0
				Gabexate-i.v., 500 mg 30 min before the endoscopic session and for 6 hrs afterwards	381	5.77	1.05	0.78
				Placebo	395	4.8	0	1.01
Arcidiacono 1994[22]	Mean= 62	54.30	"Acute pancreatitis was defined as the combination of an increase in serum amylase greater than three times the upper limit of normal, with abdominal pain, nausea, and vomiting."	Octreotide – s.c., 0.1mg of octreotide acetate s.c. 120 and 30 min before ERCP and four hrs after the endoscopic procedure.	75	6.67	0	0
				Placebo	76	6.58	2.63	0
Arvanitidis 2004[23]	Mean= 63	40.44	"Procedure-induced pancreatitis was diagnosed when there was hyperamylasemia (serum amylase levels above 500 IU/L) and persistent abdominal pain that required >1 night of hospitalization."	Somatostatin - i.v., bolus injection of somatostatin 4µg/kg bodyweight plus 500mL normal saline over 12 hrs.	118	1.69	0	0
				Somatostatin - i.v., 3 mg of somatostatin infused over 12 h (starting 1 h before the procedure) and bolus i.v. normal saline.	116	1.72	0	0
				Placebo	122	9.84	0	0

Author Year	Age (in years)	Female (%)	Definition of post-ERCP pancreatitis (PEP) as reported in the study	Treatments evaluated	N	PEP %	Severe PEP %	Mortality due to PEP %
Arvanitidis 1998 A[24]	Mean= 63	57.53	Unclear	Octreotide- s.c., 0.1mg of octreotide at 30 min before and 8 and 16 hrs after the procedure.	37	10.81	0	0
				Placebo	36	11.11	0	0
Arvanitidis 1998 B[25]	Mean= 64.5	59.37	"We defined acute pancreatitis as the combination of elevated amylase with abdominal pain and tenderness."	Nifedipine – oral, 10 mg nifedipine 2 hrs before and 8 and 16 hrs after the procedure	47	10.6	NR	NR
				Placebo	49	8.16	NR	NR
Awad 2000[26]	Mean= 32	60	"Post-ERCP, blood samples were taken 4, 8, and 24 hrs for levels of amylase and lipase."	Octreotide- s.c., 1 ml at start of endoscopy, and at 8 and 16 hrs post-ERCP	25	4	0	0
				Placebo	22	0	0	0
Baldazzi 1994[27]	Mean= 59.75	66	“Amylase>800IU/L, Lipase >200IU/L, leukocytes>15,000, AST>250IU/L”	Octreotide – s.c., 0.1mg, 45 min before ERCP and 6 hrs after ERCP	50	2	NR	NR
				Placebo	50	6	NR	NR
Barkay 2008[28]	Mean= 64.5	59.04	"Defined as pain persisting for 24 hrs and associated with a threefold increase in serum amylase"	Heparin- s.c., deep injection of 5,000IU in the abdominal fat layer 20 to 30 min before ERCP	51	7.84	1.96	0
				Placebo	54	7.40	3.7	0
Beauchant 2008[29]	Mean= 52	72.11	"Occurrence of acute pancreatitis during the month following ERCP, as defined by epigastric pain and a rise in serum amylase and/or lipase concentration to more than three times the normal upper limit 24 hrs after endoscopy, in accordance with international consensus"	Nitroglycerine – i.v., nitroglycerin bolus of 0.1 mg, then 35 µg/kg per minute intravenously (maximum dose 9mg) for 6 hrs	105	9.5	1.9	0
				Placebo	103	14.56	3.88	0
Bhatia 2011[17]	Mean= 42.25	64.23	"Defined by the presence of pain persisting for 24 hrs post-ERCP, and associated with a rise in serum amylase levels to more than 3 times the upper limit of normal"	GTN- transdermal patch 10 mg/ hr- patch was applied 30 min before the procedure and removed after 24 hrs	124	9.67	0	0
				Placebo	126	10.32	0	0
Binmoeller 1992[30]	Mean= 59.5	47.34	"Defined by clinical features consistent with acute pancreatitis beginning after ERCP and lasting for at least 24 hrs, associated with an increase in serum amylase and/or lipase greater than three times the upper limit of normal"	Octreotide – i.v., five min before ERCP as a bolus injection of 100 µg and immediately after ERCP as a s.c. injection of 100 µg	121	1.65	0	0
				Placebo	124	1.61	0	0
Bordas 1987[31]	Mean= 59.5	40	"Pancreatitis was diagnosed when there was the simultaneous appearance of hyperlipasemia and hyperamylasemia as defined, upper abdominal pain, nausea and/or vomiting associated ileus that did not resolve within 18 hrs after the procedure and required prolongation of hospital stay."	Somatostatin- i.v., doses of 4µg/kg body weight. The i.v. injection was carried out on identification of the papilla and before introduction of the catheter	80	2.5	0	0
				Placebo	80	10	0	0
Bordas 1988[32]	Mean= 65	54.54	Pancreatitis was considered to occur when there was a simultaneous appearance of upper abdominal pain, nausea and vomiting, associated with a marked reduction of peristalsis and a rise in lipase and amylase plasma levels.	Somatostatin - i.v., single dose of 4 µg/kg body weight-, 2-3 min before introduction of the endoscope	17	0	0	0
				Placebo	16	12.5	0	0

Author Year	Age (in years)	Female (%)	Definition of post-ERCP pancreatitis (PEP) as reported in the study	Treatments evaluated	N	PEP %	Severe PEP %	Mortality due to PEP %
Bordas 1998[33]	Mean= 59.5	60.95	"Pancreatitis was diagnosed when there was the simultaneous appearance of hyperlipasemia and hyperamylasemia as defined, upper abdominal pain, nausea and/or vomiting associated ileus that did not resolve within 18 hrs after the procedure and required prolongation of hospital stay."	Somatostatin – i.v., bolus injection (4 µg/kg body weight) was carried out on identification of the papilla and before introduction of the catheter	52	3.85	NR	NR
				Placebo	53	15.09	NR	NR
Borsch 1984[34]	NR	NR	NR	Somatostatin – i.v., 6000 µg total, infusion from beginning of ERCP and continued for 24 hrs	10	10	NR	NR
				Placebo	10	10	NR	NR
Budzynska 2001[35]	Mean= 58.5	71	"When new or worsening abdominal pain occurred and the serum amylase and lipase concentrations were three times higher than the upper limit 24 h after the procedure"	Prednisone – oral, 40mg, 15 hrs and 3 hrs before ERCP	100	12	3	0
				Allopurinol – oral, 200mg, 15 hrs and 3 hrs before ERCP	99	12.12	1	0
				Placebo	101	7.92	0	0
Cavallini 1996[36]	Mean= 60.35	55.50	"Acute pancreatitis was considered to be present if serum amylase or lipase levels (or both) were five times greater than the upper limits of normal in association with the onset of pancreatic pain"	Gabexate – i.v., 1 gm continuous infusion, 30 to 90 min before the endoscopy session and continuing for 12 hrs afterwards	208	2.40	0	0
				Placebo	210	7.6	2.38	0.47
Chan 2008[37]	Mean= 62.7	45.86	"Post-ERCP pancreatitis was defined as abdominal pain associated with serum amylase level at least 3 times the normal value at 24 hrs or more after ERCP, requiring admission or prolongation of planned admission"	Somatostatin – i.v., 250 µg infusion before ERCP, followed by continuous infusion with somatostatin 250 µg/hour for 12 hrs	44	6.81	NR	0
				Somatostatin – i.v., 250 µg infusion before ERCP, with no subsequent infusion	40	2.5	NR	0
				Placebo-	49	4.08	NR	0
Chen 2005[38]	Mean= 53.3	46.53	“After ERCP, if amylase >500IU/ml, with pancreatic type abdominal pain for >24 hrs”	Ulinastatin – i.v., 100,000 IU, 1 day before ERCP, day of ERCP and day after, as infusion	112	8.03	NR	0
				Octreotide – s.c., 0.1 mg, 30 min before ERCP and 4 hrs after ERCP	110	2.73	NR	0
				Placebo	124	3.22	NR	0
Cheon 2007[39]	Mean= 45.8	66.67	"Post-ERCP pancreatitis was diagnosed when new-onset or increased abdominal pain caused an unplanned admission of an outpatient or a prolonged hospital stay of a planned admission of an inpatient and was associated with a serum amylase level increase at least 3-fold above normal at approximately 18 hrs after the procedure"	Diclofenac – oral, 30 to 90 min before ERCP and 4 to 6 hrs after ERCP	105	16.19	0.95	0
				Placebo	102	16.67	0.98	0

| Author Year | Age (in years) | Female (%) | Definition of post-ERCP pancreatitis (PEP) as reported in the study | Treatments evaluated | N | PEP % | Severe PEP % | Mortality due to PEP % |

De Palma 1999[40]	Mean= 58.6	47.26	"Procedure-induced pancreatitis was defined as persistent abdominal pain that required >1 night of hospitalization and a serum concentration of pancreatic enzymes (amylase or lipase) that was two or more times the upper limit of normal"	Hydrocortisone – i.v., 100 mg of immediately before ERCP, as continuous i.v. administration	263	5.7	0.76	0
				Placebo	266	4.89	0.37	0
Deviere 2001[41]	Mean= 60.3	56.9	"Clinical pancreatitis was defined as hyper hydrolasemia (amylase/lipase levels >3X normal) associated with new or worsened abdominal pain persisting more than 4 hrs after ERCP."	recombinant human IL -10 - i.v., 4 µg/kg 30 min before the procedure	48	10.41	0	0
				recombinant human IL-10 - i.v., 20 µg/kg 30 min before the procedure	44	6.82	0	0
				Placebo	45	24.45	4.45	0
Devereaux 2003[42]	NR	NR	NR	Secretin – i.v., 0.2 µg/kg body weight, before ERCP	16	0	NR	NR
				Placebo	13	0	NR	NR
Doboronte 2012[43]	Mean= 66.8	66.2%	"Per consensus definition"	Indomethacin – rectal, 100 mg, before ERCP	130	8.46	NR	0
				Placebo	98	11.22	NR	0
Dumot 1998[44]	NR	NR	"Procedure-induced pancreatitis was defined as new or worsened abdominal pain associated with serum concentration of pancreatic enzymes (amylase or lipase) that was two or more times the upper limit of normal or a baseline level in cases where previously elevated."	Methylprednisone – i.v., 125 mg of methylprednisolone as a bolus 15-30 min before the procedure	129	12.4	NR	0
				Placebo	126	8.73	NR	0
Dumot 2001[45]	Mean= 54	57.5	"Pancreatitis was defined as abdominal pain radiating to the back associated with elevated amylase or lipase two or more times the upper limit of normal (260 IU/L) requiring hospitalization for ≥2 days."	IL – 10 - i.v., 8 µg/ kg was administered as a bolus 15 min before the procedure	101	10.89	NR	NR
				Placebo	99	9.1	NR	NR
Duvnjak 1999[46]	Mean= 55	59.33	"ERCP-pancreatitis was defined as the presence of abdominal pain, tenderness, nausea, and vomiting beginning after ERCP and lasting for at least 24 hrs, associated with an increase in serum amylase and/or lipase levels greater than threefold upper limit"	Octreotide – s.c., 0.5 mg, one hour prior to the endoscopic procedure	104	3.85	0	NR
				Placebo	105	9.5	0	Placebo
Elmunzer 2012[47] (Includes only high risk patients)	Mean= 45.2	79.1	"Post ERCP pancreatitis was diagnosed if there was a new onset of pain in the upper abdomen, an elevation of pancreatic enzymes of at least three times the upper limit of the normal range, 24 hrs after the procedure and hospitalization for at least 2 nights."	Indomethacin – rectal, immediately after ERCP, 2 rectal suppositories of 50 mg each	295	9.15	1.01	0
				Placebo	307	16.94	0.97	0
Fujishiro 2006[48]	Mean= 64.9	100	Patients were diagnosed as having post-ERCP pancreatitis when they showed at least two of the following: (i) serum amylase concentration threefold greater than the upper limit of normal; (ii) continuous abdominal pain or tenderness after ERCP for more than 24 hrs, (iii) ultrasonography and/or CT findings of acute pancreatitis	Gabexate – i.v., continuous infusion of gabexate (300 mg, 3 times within 13 hrs, beginning from 1 hr before ERCP	46	4.35	NR	0
				Ulinastatin – i.v., short-term infusion of ulinastatin (150 000 units) given 3 times, at 1 hr before, during, and 11 hrs after the ERCP procedure. In addition, a continuous infusion of 1500mL solution was administered for 13 hrs.	46	6.52	NR	0
				Ulinastatin - i.v., short-term infusion of ulinastatin (50 000 units) at the same time points as patients in group B, together with the continuous infusion of 1500mL solution.	47	8.51	NR	0

Author Year	Age (in years)	Female (%)	Definition of post-ERCP pancreatitis (PEP) as reported in the study	Treatments evaluated	N	PEP %	Severe PEP %	Mortality due to PEP %
Gong 2004[49]	NR	NR	After ERCP, if amylase >500IU/ml, with abdominal pain of pancreatic type for >24 hrs	Ulinastatin – i.v., 200,000 IU, given for 3 days	68	7.35	NR	
				Octreotide – s.c., 0.1 mg 30 min before ERCP and 4 hr after ERCP	34	11.76	NR	
				Placebo	62	14.52	NR	
Gorgul 1998[50]	Mean= 47.2	52.2	Unclear	Somatostatin – i.v.-3.5 g/kg at the start of ERCP and at 250 gm infusion for 4 h	30	0	NR	0
				Octreotide – s.c., 3x100 g/day on the day of ERCP	30	0	NR	NR
				Placebo	30	0	NR	NR
Guelrud 1990[51]	NR	NR	"Upper abdominal pain with epigastric tenderness and at least 3 fold increase over normal values of serum amylase and lipase."	Somatostatin – i.v., 3000 µg Infusion started 1 hr prior to dilation and maintained for a total of 12 hrs	8	25	NR	
				Placebo	8	75	NR	
Hao 2009[52]	Mean= 63.85	58.11	"Post-ERCP pancreatitis was defined as a disease with sustained pancreatitis symptoms (such as abdominal pain) and high-amylase value over the normal value after ERCP."	GTN – sublingual, 5 mg, 5 min before the procedure	38	7.89	NR	0
				Placebo	36	25	NR	0
Hardt 2000[53]	Mean= 58.95	59.32	"Post-ERCP-pancreatitis was defined as 3-fold increase of amylase above upper limit and presence of abdominal pain during 24 hrs or need for analgesics as suggested elsewhere"	Octreotide – s.c., 200µg, day before ERCP at 10pm, day of ERCP at 6am, 2pm, and 10pm, day after ERCP at 6am	29	10.34	NR	0
				Placebo	30	13.33	NR	0
Jowell 2011[54]	Mean= 55.5	56.84	"Persistent post procedural pain clinically consistent with pancreatitis.	Secretin – i.v., 16 µg, before intubating the esophagus	413	8.72	0.24	NR
				Placebo	431	15.08	0.23	NR
Kaffes 2006[55]	Mean= 62.5	63.52	"A diagnosis of post-ERCP pancreatitis was made if the abdominal pain was typical of post-ERCP pancreatitis and was associated with a greater than 3-fold elevation of serum amylase above the upper limit of normal at 24 hrs after the procedure"	GTN – transdermal, 5mg patch over 24 hrs, starting 60 min before commencement of the ERCP	155	7.09	0	0
				Placebo	163	6.13	0	0
Katsinelos 2000[56]	Mean= 65.03	71.42	"Defined as severe epigastric pain and abdominal tenderness requiring narcotic analgesics and associated with serum amylase levels greater than thrice the normal upper limit, requiring hospitalization for a period longer than 24 hrs after the endoscopic procedure."	Octreotide – i.v., 100 mg, 30 min before and after ERCP as a bolus injection	73	5.48	0	0
				Placebo	74	8.10	0	0
Katsinelos 2005[57]	Median = (65,67) in the two arms respectively	51.44	"Defined as the presence of abdominal pain attributable to pancreatitis, together with a need for an unplanned hospitalization or an extension of a planned hospitalization by at least 2 days, and a serum amylase at least 3 times above the upper limit of normal at 24 hrs after the procedure."	Allopurinol- oral, 600 mg, 15 hrs and 3 hrs before ERCP	125	3.20	0	0
				Placebo	118	17.80	1.69	1.69

Author Year	Age (in years)	Female (%)	Definition of post-ERCP pancreatitis (PEP) as reported in the study	Treatments evaluated	N	PEP %	Severe PEP %	Mortality due to PEP %
Katsinelos 2005 B[58]	Mean= 63.9	61.45	"Post-ERCP pancreatitis was defined as follows: presence of abdominal pain attributed to pancreatitis, together with a need for an unplanned hospitalization or an extension of a planned hospitalization by at least 2 days, and a serum amylase at least 3 times above the upper limit of normal at 24 hrs after the procedure."	N acetylcysteine – i.v., 70 mg/kg 2 hrs before, and 35 mg/kg at 4-hour intervals for a total of 24 hrs after the endoscopic procedure	124	12.10	0	0
				Placebo	125	9.60	0	0
Khoshbaten 2008[59]	Mean= 58.5	53	"A diagnosis of acute pancreatitis was made based on a serum amylase level greater than fourfold the upper limit of normal for the reference laboratory (>800IU/L) in conjunction with epigastric pain, back pain, and epigastric rebound tenderness."	Diclofenac – rectal, 100 mg immediately on entering the recovery room	50	4	NR	NR
				Placebo	50	26	NR	NR
Kwanngern 2005[60]	Mean= 57.51	51.67	"The patients were diagnosed as having pancreatitis when they had elevation of serum amylase more than 2.5 times normal (24 hrs from procedure) together with new or worsened epigastric or subcostal pain with or without radiation to the back."	Hydrocortisone – i.v., 100 mg, 1 hour before procedure	61	1.64	NR	0
				Placebo	59	11.86	NR	0
Kwon 2012[61]	Mean= 66.2	56.61	New onset abdominal pain within 24 hrs of ERCP with 3 times elevation of amylase above normal limit and hospitalization	Gabexate – i.v., 600 mg, 30 min before procedure and continued for 12 hrs	73	6.85	4.11	0
				Nafamostat - i.v., 50 mg dissolved in 500 mL of 5% dextrose solution, beginning 30 min before the ERCP and continuing for 12 hrs after	88	5.68	2.27	0
				Placebo	81	6.17	2.46	0
Lee 2008[62]	Mean= 62.5	48.85	"Pancreatitis was defined as abdominal pain and tenderness persisting for at least 24 hrs after ERCP, with a raised amylase or lipase level more than 3 times the upper normal limit."	Somatostatin –i.v., 3 mg in 500ml normal saline, infused for 12 hrs starting 30 min before ERCP	193	3.63	0	0
				Placebo	198	9.6	0	0
Li 2007[63]	Mean= 54.89	48.08	"Acute pancreatitis was defined as serum amylase levels more than three times the upper limit of normal, with pancreatic pain (pain of the epigastric and periumbilical region often radiating to the back) for at least 24 h."	Octreotide – i.v., 0.3 mg given 1 hr before the endoscopic examination and continued 6 hr thereafter, followed by 0.1 mg s.c.at 6 and 12 hrs after the i.v. injection	414	2.42	NR	NR
				Placebo	418	5.26	NR	NR
Liu 2009[12]	NR	50	Amylase >/= 3 times elevated compared to normal, and abdominal pain for >24 hrs	Octreotide – s.c., 0.1 mg 30 min before ERCP and 4 hrs after ERCP	42	0	NR	0
				Placebo	44	11.36	NR	0
Manes 2007[64]	Mean= 63.34	39.55	"post-ERCP pancreatitis was defined as an at-least 3-fold increase in serum amylase at 24 hrs, with typical pain and with symptoms impressive enough to require admission to the hospital (or extension of an existing admission)."	Gabexate – i.v., 500 mg beginning within 1 hr before ERCP and continuing for 6 hrs	203	3.94	NR	0
				Gabexate- i.v., 500 mg beginning within 1 hr after ERCP and continuing for 6 hrs	203	3.45	NR	0
				Placebo	202	9.41	NR	0.49

Author Year	Age (in years)	Female (%)	Definition of post-ERCP pancreatitis (PEP) as reported in the study	Treatments evaluated	N	PEP %	Severe PEP %	Mortality due to PEP %
Matsushita 2009[65]	Mean =61.35	47.57	"Elevated serum amylase and/or lipase levels (more than a threefold increase of the normal upper limit) associated with at least two clinical symptoms (abdominal pain or tenderness, backache, nausea, and vomiting) after the procedure for 24 hrs."	Epinephrine – spray, 10 ml of 0.02% epinephrine solution sprayed directly on the major papilla with the use of a sprinkler catheter	185	0	0	0
				Placebo	185	2.17	0	0
Milewski 2006[66]	NR	62.26	"New onset of abdominal pain persisting for more than 24 h after the procedure, and elevation of serum pancreatic enzymes 5 times above the normal limit."	N-acetylcysteine – oral, two 600 mg doses, 24 hrs and 12 hrs before ERCP and 600 mg was given i.v., twice a day for two days after the ERCP	55	7.27	NR	NR
				Placebo	51	11.76	NR	NR
Manolako-paulos[67] 2002	Median =(62,65, 64)	59.41	"ERCP-induced pancreatitis was defined as the combination of new or worse, severe and persistent, and epigastric or peri umbilical pain associated with serum amylase greater than 3 times the upper limit of normal that required hospitalization for more than 24 hrs after the procedure."	Octreotide – s.c., 100 µg, 30 min before ERCP	112	9.82	0	0
				Hydrocortisone – i.v., 100 mg, 30 min before ERCP	113	7.08	0	0
				Placebo	115	13.04	0	0
Montano-Loza 2007[68]	Mean= 53.24	66.67	Amylase 3 times above the normal limit and the patient presents with abdominal pain radiating towards the back, with nausea or vomiting.	Indomethacin – rectal, 100 mg, 2 hrs before procedure	75	5.33	NR	0
				Placebo	75	16	NR	0
Montano-Loza 2006[69]	NR	NR	Amylase 3 times above the normal limit and the patient presents with abdominal pain radiating towards the back, with nausea or vomiting.	Indomethacin – rectal, 100 mg, before ERCP	61	4.91	NR	NR
				Placebo	56	14.29	NR	NR
Moreto 2003[70]	Mean= 65.95	39.58	"Pain persisting for 24 hrs (graded as absent, mild, moderate, severe) associated with a 3-fold increase in serum amylase and/or lipase."	GTN – transdermal, 15 mg patch applied 30 - 40 min before ERCP, removed after 24 hrs	71	4.22	NR	NR
				Placebo	73	15.07	NR	NR
Mosler 2005[71]	Mean= 51.85	72.33	"Post-ERCP pancreatitis was diagnosed when new-onset or increased abdominal pain lasted for more than 24 hrs, caused an unplanned admission of an outpatient for more than one night, or prolonged a planned admission of an inpatient, and was associated with a serum amylase level increase of at least 3 times above normal, at approximately 18 hrs (the next morning) after the procedure"	Allopurinol – oral, 600 mg, 4 hrs before ERCP and 300 mg 1 hr before ERCP	355	12.96	NR	0.56
				Placebo	346	12.14	NR	0.57
Murray 2003[72]	Mean= 56.5	65	"A diagnosis of acute pancreatitis was made on the basis of a serum amylase level >4 times the upper level of normal for the reference laboratory (>800 IU/L) in conjunction with epigastric pain, back pain, and epigastric rebound tenderness."	Diclofenac – rectal, 100mg, immediately on entering the recovery area after ERCP	110	6.36	NR	0
				Placebo	110	15.45	NR	0
Niederau 1994[73]	NR	NR	Unclear	Cefotaxime – i.v., 2 g, 15 min before ERCP	50	4	NR	0
				Placebo	50	6	NR	0
Nikolopoulo 1995[74]	Mean= 64	50	"ERCP associated pancreatitis was defined by clinical features consistent with acute pancreatitis beginning after ERCP and lasting for at least 24 hrs, associated with an increase in serum amylase greater than 3 times the upper normal limits".	Octreotide – s.c., 100 µg, 5 min before ERCP and later 12 hrs after ERCP as s.c.	20	5	NR	NR
				Placebo	18	11.11	NR	NR

Author Year	Age (in years)	Female (%)	Definition of post-ERCP pancreatitis (PEP) as reported in the study	Treatments evaluated	N	PEP %	Severe PEP %	Mortality due to PEP %
Nojgaard 2009[75]	Mean= 66	41.20	“Per consensus definition”	GTN- transdermal, 15 mg, 30 - 40 min before ERCP, removed after 24 hrs	401	4.49	1.24	0.24
				Placebo	405	7.16	0.74	0.24
Otsuka 2012[76]	Median = 75, 72	49.03	“Per consensus definition”	Diclofenac – rectal, 50 mg, 30 min before ERCP	51	3.92	0	0
				Placebo	53	18.87	0	0
Park 2011[77]	Mean= 63.5	46.39	"Post-ERCP pancreatitis was defined as typical abdominal pain combined with an increase in serum amylase level more than 3 times the normal limit at 24 hrs or more after ERCP, requiring admission or prolongation of planned admission."	Nafamostat – i.v., 20 mg beginning 1 hr before the ERCP and continuing for 24 hrs	198	4.04	0	NR
				Nafamostat – i.v., 50 mg beginning 1 hr before the ERCP and continuing for 24 hrs	197	5.08	0	NR
				Placebo	200	13	0	NR
Persson 1992[78]	Mean= 61.5	50	"Injection pancreatitis in these cases is defined as alteration of any of the following parameters: elevated levels of serum amylase, elevated levels of urinary amylase and serum lipase and/or clinical signs of pancreatitis such as upper right abdominal pain, nausea and vomiting and sometimes fever."	Somatostatin – i.v., starting 30 min before ERCP, dose of 300 µg per hr for 3 hrs and dose of 140 µg for 4 hrs	26	15.38	NR	0
				Placebo	28	17.86	NR	0
Poon 2003[79]	Median = 69, 67	49.26	"New or worsened abdominal pain and tenderness persisting for more than 24 hrs after endoscopy with a raised serum amylase level more than three times the upper normal limit (110 IU/l) at 24 hrs."	Somatostatin - i.v., 250 µg, starting immediately after diagnostic ERCP but before therapeutic procedures	135	4.44	0	0
				Placebo	135	1.33	0	0
Poon 1999[80]	Mean= 62.75	53.64	"ERCP pancreatitis was defined as abdominal pain and tenderness persisting for at least 24 hrs after ERCP with a raised amylase or lipase level more than 3 times the upper normal limit."	Somatostatin - i.v., 3 mg infused over 12 hrs starting 30 min, before ERCP and continuing for 12 hrs	109	2.75	NR	0
				Placebo	111	9.91	NR	0
Prat 2002[81]	Mean= 65.8	45.16	“Acute pancreatitis was defined as upper abdominal pain associated with hyperamylasemia and/or hyperlipasemia (enzyme levels 3 times the upper normal value), regardless of the duration of pain.”	Nifedipine – oral, 20-mg tablet of long-acting nifedipine was given at least 3 hrs and no more than 6 hrs before the procedure. A second tablet was administered within 6 hrs after the procedure	76	13.16	NR	NR
				Placebo	79	17.72	NR	NR
Rabenstein 2004[82]	Mean= 57.5	69.87	"Post-ERCP pancreatitis was defined according to consensus criteria: elevation of serum amylase at least 3-fold above the upper normal value at 24 hrs and significant pain (VAS (visual analogue scale) +3 or continuous/recurrent need of pain medication for at least 24 hrs)."	Heparin – s.c., 3000 IU, two hrs before ERCP. A second dose was given 24 hrs after the initial administration.	221	8.14	0.45	0.45
				Placebo	227	8.81	0	0
Raty 2001[83]	Mean= 61	58.09	"The diagnosis of acute pancreatitis was based on clinical findings, an increase in serum amylase activity of threefold or more (1900 IU/L) over the upper normal range, increased CRP level, and increased leukocyte count, and signs of cholangitis were lacking"	Ceftazidime – i.v., 2 g, 30 min before ERCP	155	2.58	NR	0
				Placebo	160	9.38	NR	0
Romagnuolo 2008[84]	Median = 53.9, 55.5	58.70	"PEP diagnosis required the presence of typical pancreatic pain (epigastric pain often radiating into the back and associated with nausea and/or vomiting), in association with a serum lipase or amylase level greater than 2 times the upper limit of normal."	Allopurinol – oral, 300 mg, 20 min before ERCP	293	54.61	0.68	0
				Placebo	293	4.09	0.68	0

Author Year	Age (in years)	Female (%)	Definition of post-ERCP pancreatitis (PEP) as reported in the study	Treatments evaluated	N	PEP %	Severe PEP %	Mortality due to PEP %
Russo 1992[85]	Mean= 66.1	55	Amylase elevated to 5 times the normal, pancreatic type of abdominal pain for 24 hrs	Octreotide – s.c., 0.1mg, 60 min before ERCP and 8 hrs after ERCP	50	8	NR	NR
				Placebo	50	4	NR	NR
Saari 1988[86]	Mean= 49.15	41.02	Pain and serum amylase > 600 U/L	Somatostatin – i.v., 1000 µg as initial 250 µg bolus, followed by 250 µg per hour for 3 hrs	17	11.76	NR	NR
				Placebo	22	18.18	NR	NR
Sand 1993[87]	Mean= 61.5	59.03	"The criteria for clinical diagnosis of acute pancreatitis were nausea with or without vomiting and prolonged epigastric pain, tenderness in palpation and serum total amylase activity 3 times over the normal upper limit."	Nifedipine – oral, 20 mg, 3 times at 8-hr intervals, first dose given 3-6 hrs before the examination	82	3.65	NR	NR
				Placebo	84	3.41	NR	NR
Senol 2009[88]	Mean= 59.8	46.25	"Acute pancreatitis was defined as serum amylase > 3 times the upper limit of normal associated with epigastric pain, back pain, and epigastric tenderness."	Diclofenac – i.m., 75 mg, immediately after procedure	40	7.5	NR	NR
				Placebo	40	1.75	NR	NR
Sherman 2003[89]	Mean= 51.2	64.48	"Post-ERCP pancreatitis was diagnosed when new-onset or increased abdominal pain lasted for more than 24 hrs, caused an unplanned hospitalization of an outpatient for more than 1 night or prolonged a planned hospitalization of an inpatient, and was associated with an increase in serum amylase level of at least 3 times greater than the normal upper limit at approximately 18 hrs (the next morning) after the procedure."	Prednisone – oral, 40 mg, 15 hrs and 3 hrs before ERCP	555	1.66	6	NR
				Placebo	560	13.57	5	NR
Sherman 2009[90] (Includes only high risk patients)	Mean= 50.6	78.30	"Post- ERCP acute pancreatitis was diagnosed when new-onset or increased abdominal pain versus patient's baseline developed within 48 hrs after ERCP and caused an unplanned admission of an outpatient for 2 or more nights (or prolonged the hospitalization of an inpatient by 2 or more nights) and was also associated with increased serum amylase level of at least 3 times greater than the normal upper limit after ERCP."	IL – 10- i.v., 8 µg/kg of recombinant human IL-10, as a single injection 15 to 30 min before the ERCP	91	15.38	4.39	1.1
				IL – 10- i.v., 20 µg /kg of recombinant human IL-10, as a single injection 15 to 30 min before the ERCP	109	22.02	0.92	0
				Placebo	105	14.28	2.86	0.95
Song 2005[91]	Mean= 47.6	57.5	Amylase elevated for >24 hour after ERCP and the patient has abdominal pain, vomiting	Ulinastatin – i.v., 200,000 U infusion, 1 hr before ERCP	20	0	NR	0
				Placebo	20	10	NR	0
Sotoudeh-manesh[92] 2007	Mean= 58.25	53.88	"Acute pancreatitis was defined as a serum amylase more than 3 times the upper limit of normal associated with epigastric pain, back pain, and epigastric tenderness."	Indomethacin – rectal, 100 mg, immediately before ERCP	245	2.86	0	0
				Placebo	245	6.12	0	0
Sternlieb[93] 1992	Mean= 59.2	72.15	"Clinical pancreatitis was defined as the combination of an abnormal amylase and/or lipase, and abdominal pain with at least localized tenderness"	Octreotide - i.v., 100 µg at the beginning of procedure and another 100 µg 45 mins later	37	35.13	NR	NR
				Placebo	42	11.90	NR	NR
Sudhindran 2001[94]	Mean= 63.7	64.97	"Acute pancreatitis was defined as a serum amylase level greater than 1000 units/ml at 6 hrs in association with a visual analog pain score of more than 5."	GTN – sub lingual, 2ml, 5 min before ERCP	96	7.30	NR	NR
				Placebo	101	16.83	NR	NR

Author Year	Age (in years)	Female (%)	Definition of post-ERCP pancreatitis (PEP) as reported in the study	Treatments evaluated	N	PEP %	Severe PEP %	Mortality due to PEP %
Talwar 2005[95]	Mean= 64	69.23	Unclear	GTN – topical on papilla, 5 ml, upon visualization of the papilla	52	1.92	NR	NR
				Placebo	52	0	NR	NR
Testoni 1988[96]	NR	NR	Epigastric pain, amylase elevation more than 5 times the normal values, leucocytosis	Somatostatin- i.v, 6500 µg, 250 µg/hour for 26 hrs starting 2 hrs before ERCP	27	7.41	NR	NR
				Placebo	27	1.85	NR	NR
Testoni 2001[97] (Includes only high risk patients)	Mean= 51.75	60.68	"Clinical features considered indicative of acute pancreatitis were pancreatic like pain persisting for at least 24 hrs after the procedure, with serum amylase more than 5 times the normal upper limit with or without leucocytosis."	Octreotide – s.c., 200 µg, 4 dose pretreatments at 800 hrs, 1600 hrs, 0000 hrs the day before and at 800 hrs on the day of the procedure	58	17.24	0	0
				Placebo	56	25	0	0
Testoni 1996[98]	Mean= 63.33	65.6	Acute pancreatitis confirmed on computer tomography	Octreotide – s.c., 200 µg, 3 dose pretreatments at 800 hrs, 1600 hrs, 0000 hrs the day before the procedure	30	0	NR	NR
				Placebo	30	10	NR	NR
Thomopoulos 2006[99]	Mean= 69.8	102	"Post ERCP pancreatitis was diagnosed when a clinical syndrome of abdominal pain for at least 1 day and hyperamylasemia that required hospitalization were developed."	Octreotide – s.c., 500 µg, 4 dose pretreatments at 800 hrs, 1600 hrs, 0000 hrs the day before; at 800 hrs on the day of the procedure and at 1600 hrs after the procedure.	100	2	0	NR
				Placebo	101	8.9	NR	NR
Torres 2009[100]	Mean= 53.15	58.82	"If the serum amylase was above 600 UI/L or three times above the normal value and the patient had a sharp pain irradiating to the back and nausea or vomiting, the diagnosis of PEP was established in the absence of radiological evidence of a pneumo peritoneum or emphysema in the retroperitoneal space through a plain radiologic examination of the abdomen or CT scan."	Allopurinol – oral, 300 mg, at 15 hrs and 3 hrs before ERCP	85	2.35	0	0
				Placebo	85	9.41	0	NR
Tsujino 2005[101]	Mean= 65	39.9	"Acute pancreatitis was defined as abdominal pain persisting for at least 24 hrs after the procedure associated with a high serum amylase or lipase level equivalent to at least 3 times the upper limit of normal 18 hrs after the procedure."	Ulinastatin – i.v., 150,000 U, administered 10 min just before ERCP	204	2.94	0	0
				Placebo	202	7.42	0	0
Tulassay 1998[102]	Mean= 61.35	63.55	"Pancreatic injury was assessed by clinical symptoms such as pain, fever and abdominal tenderness."	Octreotide – s.c., 0.1 mg, prior to and 45 min after ERCP	599	7.68	NR	NR
				Placebo	600	8	NR	NR
Tulassay 1991[103]	Mean= 49	55.56	NR	Octreotide – s.c., 0.1 mg, 45 min before ERCP	29	0	NR	NR
				Placebo	34	0	NR	NR
Ueki 2007[104]	Mean= 63.5	30.88	"Post ERCP pancreatitis was defined as abdominal pain persisting for at least 24 h after the ERCP associated with the elevation of serum amylase, lipase and/or elastase 1 levels to at least three times the upper limit of normal at 18h after the ERCP."	Ulinastatin – i.v., 150,000 U, 60 to 90 min before ERCP and continued until 22 hrs after the procedure	34	2.94	0	0
				Gabexate – i.v., 600 mg, 60 to 90 min before ERCP and continued until 22 hrs after the procedure	34	2.94	0	0
Ung 2011[105]	Mean= 64	48.23	"Per Consensus definition"	Heparin – s.c., 5000 IU, 4hrs before ERCP and 4hrs, 18 hrs after ERCP	41	2.44	NR	0
				Placebo	44	6.82	NR	0

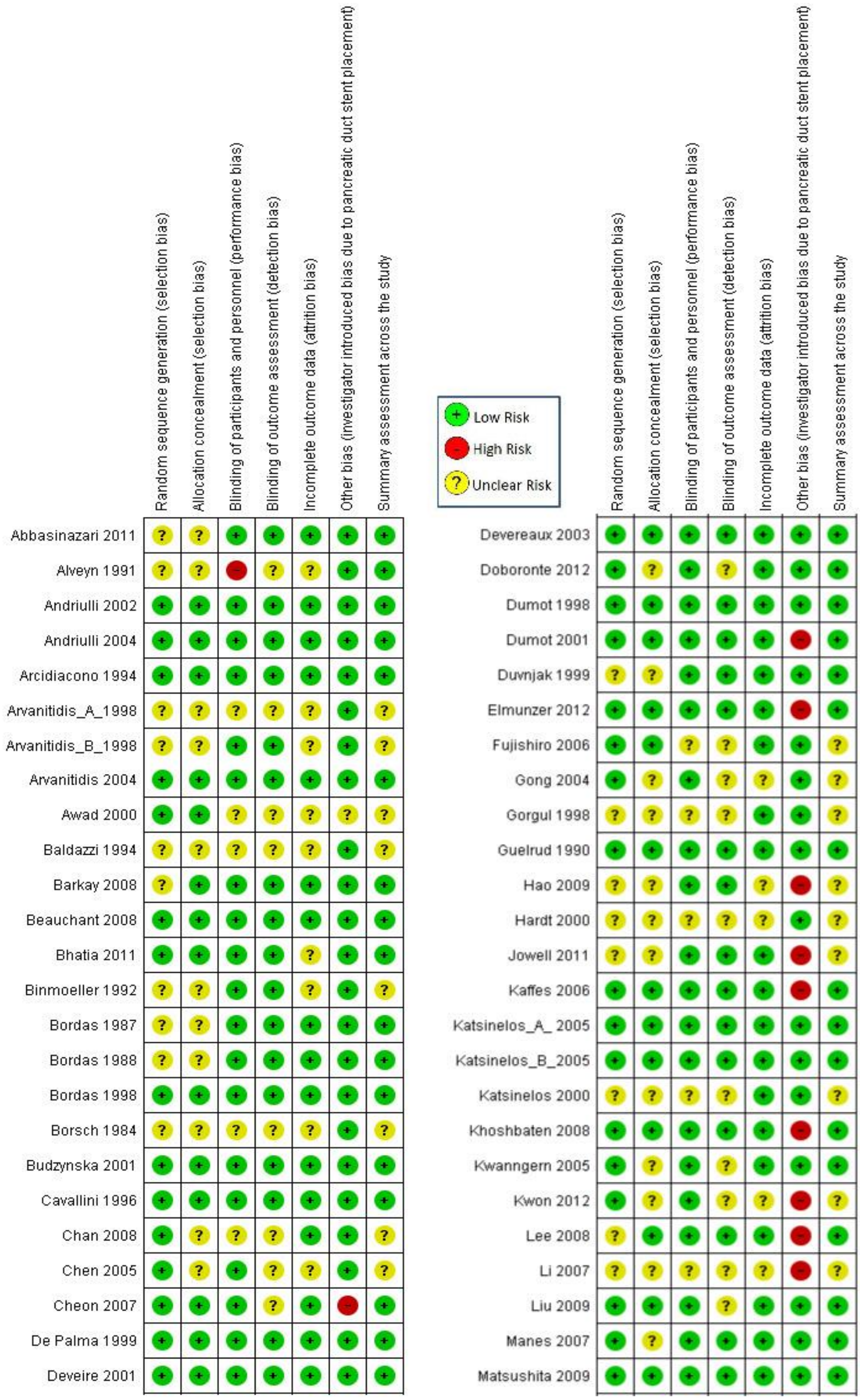
Author Year	Age (in years)	Female (%)	Definition of post-ERCP pancreatitis (PEP) as reported in the study	Treatments evaluated	N	PEP %	Severe PEP %	Mortality due to PEP %
Wei 2009[106]	NR	NR	Continuous abdominal pain with amylase>500 IU (normal 115 IU)	Gabexate – i.v., 200 mg started 30 min before ERCP and continued for 12 hrs	160	5	NR	NR
				Somatostatin – i.v., 60 mg started 30 min before ERCP and continued for 24 hrs	160	3.75	NR	NR
				Placebo	30	6.67	NR	NR
Wollschlager 1999[14]	NR	NR	"Post ERCP pancreatitis defined when amylase, lipase or CRP increased to more than twice the normal level. In addition, were added an acute abdominal pain and an ultrasound-morphological proof of condition for this definition."	Metronidazole/Ofloxacin –i.v., 0.5/0.2 g, before and 6 hrs after ERCP	20	10	NR	NR
				Placebo	20	15	NR	NR
Wehrmann 2001[107]	Mean= 55	58.71	"Defined according to consensus recommendations."	GTN - Topical, 10 mg of GTN diluted in 10 ml of sterile water was sprayed directly onto the papillary orifice	40	7.5	NR	NR
				Placebo	40	10	NR	NR
Xiong 2006[108]	Mean= 62	53.37	"Post ERCP pancreatitis was defined as new or worsened abdominal pain for more than 24 hrs after endoscopy with more than 5 fold increase in serum amylase level (4 hrs) or a 3 fold increase (24 hrs) above the upper normal limit."	Gabexate – i.v., 300 mg, starting 30 min before ERCP and continuing 4 hrs after ERCP	98	3.06	NR	0
				Placebo	95	10.53	NR	0
Xu Hua 2011[109]	Mean= 59.6	44.84	"We defined post ERCP pancreatitis as a combination of elevated serum amylase levels (more than a threefold increase of the normal upper limit) associated with at least two clinical symptoms (abdominal pain or tenderness, backache, nausea, and vomiting) after the procedure for 6–24 hrs."	Epinephrine – topical, 20 mL irrigation with epinephrine diluted to 0.02% in saline sprayed over the entire papilla	461	1.95	0	0
				Placebo	480	6.46	0	0
Yasuda 1987[110]	Mean= 54	46.43	Unclear	Ulinastatin – i.v., 50,000 U infusion 60 min before ERCP	28	0	NR	NR
				Gabexate – i.v., 200mg, 60 min before ERCP	28	0	NR	NR
Yoo 2008[111] (Includes only high risk patients)	Mean= 63.5	45.81	"Acute pancreatitis was defined as the presence of abdominal pain typical of pancreatitis at 24 hrs post ERCP with hyperamylasemia (amylase 3 times the upper limit of normal)."	Ulinastatin – i.v., 100,000 U, just after ERCP for 5.5 hrs	119	6.72	0	0
				Placebo	108	5.56	0	0
Yoo 2011[112]	Mean= 62.5	50.00	"Post-ERCP pancreatitis was diagnosed when new-onset or increased abdominal pain lasted for more than 24 hrs, associated with a serum amylase level increase of at least 3 times higher than normal at approximately 24 hrs after the procedure."	Nafamostat – i.v., 50 mg beginning 1 hour before the ERCP and continuing for 6 hrs after	143	2.80	0	NR
				Placebo	143	9.09	0	NR
Yusuf 1999[113]	Median = (51.4, 46.7)	56.67	"After the procedure, right upper abdominal pain, nausea and vomiting. A threefold increase in the serum amylase level compared to the baseline level and of leukocyte count above 10,000/mm were established as the diagnostic criteria for acute ERCP related pancreatitis."	Somatostatin – i.v., 250 µg per hour starting 30 min prior to ERCP and for 6 hrs	15	0	NR	NR
				Placebo	15	0	NR	NR

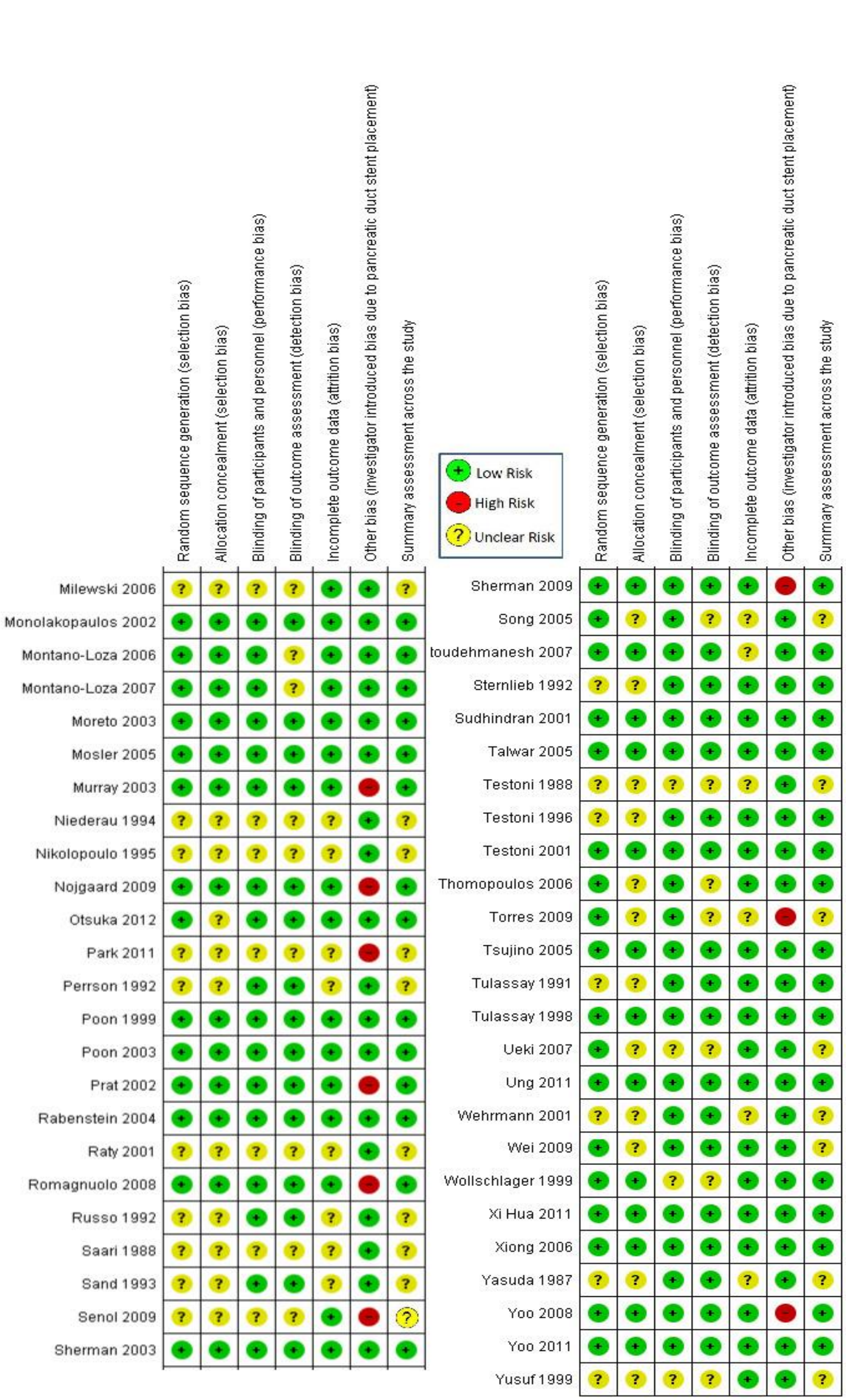
~~Supplementary~~ Table 3: Odds ratios (95% probability intervals) comparing agents with each other to prevent post-ERCP pancreatitis ordered by the results in the rankogram.

Results are odds ratios (OR) with 95% PI (probability interval) between the column defining agent and row defining agent. OR below the diagonal are from Network Meta-Analysis and above the diagonal are Bayesian meta-analysis of trials or OR calculated from single trials. OR of less than 1 favors the column defining agent. The common comparator, placebo is placed first in the diagonal followed by other agents ordered by their ranks of performance. (ALLO – Allopurinol, ANTI – Antibiotics, EPI – Topical epinephrine, GAB – Gabexate, GTN – Glyceryl trinitrate, HEP – Heparin, NAC- N-acetylcysteine, NAF – Nafamostat, NIF – Nifedipine, OCT – Octreotide, SEC – Secretin, STER – Steroids, SOM – Somatostatin, ULIN – Ulinastatin, NE – Not estimable)

PLACEBO	3.82 (0.95-90.91)	2.09 (0.70-8.35)	2.33 (1.51-4.35)	2.67 (2.04-3.48)	0.81 (0.16-24.13)	2.16 (1.31-4.08)	1.64 (1.02-2.91)	1.46 (0.32-3.30)	1.02 (0.36-5.31)	0.74 (0.20-6.38)	0.88 (0.30-3.74)	1.29 (0.54-4.28)	1.23 (0.30-5.34)	0.91 (0.28-5.12)	1.29 (0.86-2.08)	0.98 (0.54-2.42)
4.05 (1.55-16.05)	**EPI**															
2.41 (1.17-5.90)	0.42 (0.13-2.18)	**NAF**					0.82 (0.23-2.95)									
2.18 (0.94-6.61)	0.69 (0.11-2.28)	1.15 (0.27-3.35)	**ANTI**													
2.39 (1.57-3.90)	0.62 (0.14-1.74)	1.04 (0.37-2.38)	0.86 (0.34-2.90)	**NSAIDs**												
1.61 (0.63-5.64)	0.28 (0.08-1.89)	0.56 (0.18-2.78)	0.58 (0.18-3.28)	0.64 (0.23-2.48)	**SEC**											
2.12 (1.44-3.30)	0.55 (0.13-1.53)	0.92 (0.34-2.06)	0.76 (0.30-2.52)	0.84 (0.48-1.63)	1.38 (0.36-3.77)	**SOM**		0.98 (0.39-2.97)							NE	
1.67 (1.05-2.83)	0.44 (0.10-1.24)	0.73 (0.26-1.66)	0.60 (0.23-2.07)	0.66 (0.36-1.36)	1.11 (0.28-3.05)	0.76 (0.42-1.46)	**GAB**									
1.64 (1.04-2.79)	0.43 (0.10-1.22)	0.73 (0.25-1.66)	0.59 (0.23-2.03)	0.65 (0.35-1.34)	1.09 (0.27-3.02)	0.83 (0.41-1.48)	1.05 (0.49-1.98)	**GTN**					0.32 (0.06-5.92)			
1.10 (0.49-3.12)	0.34 (0.06-1.10)	0.57 (0.14-1.61)	0.40 (0.13-1.90)	0.44 (0.18-1.39)	0.86 (0.16-2.75)	0.50 (0.21-1.56)	0.62 (0.25-2.04)	0.63 (0.26-2.06)	**HEP**							
0.91 (0.37-2.86)	0.16 (0.04-1.00)	0.49 (0.11-1.45)	0.32 (0.10-1.73)	0.36 (0.14-1.28)	0.74 (0.12-2.47)	0.41 (0.16-1.42)	0.51 (0.19-1.86)	0.52 (0.20-1.89)	0.75 (0.30-2.49)	**NAC**						
0.97 (0.42-2.76)	0.17 (0.05-1.00)	0.51 (0.12-1.42)	0.35 (0.11-1.68)	0.39 (0.15-1.25)	0.76 (0.14-2.44)	0.44 (0.18-1.38)	0.55 (0.22-1.81)	0.56 (0.22-1.84)	0.71 (0.24-3.26)	0.82 (0.27-4.19)	**NIF**					
1.33 (0.79-2.44)	0.36 (0.08-1.03)	0.60 (0.20-1.41)	0.48 (0.18-1.72)	0.53 (0.27-1.16)	0.90 (0.22-2.55)	0.60 (0.32-1.28)	0.74 (0.38-1.71)	0.76 (0.39-1.73)	1.30 (0.38-3.26)	1.59 (0.42-4.31)	1.48 (0.43-3.83)	**ALLO**				1.01 (0.43-2.37)
1.22 (0.68-2.47)	0.34 (0.07-1.00)	0.56 (0.18-1.39)	0.44 (0.16-1.68)	0.49 (0.24-1.15)	0.85 (0.19-2.46)	0.55 (0.28-1.27)	0.69 (0.35-1.60)	0.70 (0.34-1.72)	1.24 (0.34-3.23)	1.50 (0.37-4.14)	1.40 (0.39-3.70)	0.85 (0.40-2.20)	**ULIN**		0.89 (0.20-10.86)	
1.05 (0.53-2.41)	0.18 (0.06-0.92)	0.50 (0.14-1.31)	0.38 (0.13-1.57)	0.42 (0.19-1.11)	0.76 (0.16-2.28)	0.47 (0.22-1.22)	0.59 (0.26-1.61)	0.60 (0.27-1.65)	0.76 (0.28-3.01)	0.88 (0.31-3.87)	0.86 (0.31-3.46)	0.73 (0.32-2.09)	0.77 (0.32-2.33)	**IL-10**		
1.27 (0.89-1.89)	0.33 (0.08-0.89)	0.55 (0.20-1.20)	0.46 (0.18-1.45)	0.50 (0.29-0.94)	0.82 (0.22-2.20)	0.57 (0.34-1.04)	0.79 (0.40-1.38)	0.72 (0.41-1.42)	1.19 (0.38-2.82)	1.45 (0.42-3.70)	1.35 (0.43-3.27)	0.99 (0.47-1.83)	1.07 (0.48-2.07)	1.26 (0.49-2.68)	**OCT**	1.43 (0.55-3.69)
0.98 (0.55-1.60)	0.27 (0.06-0.77)	0.46 (0.16-1.07)	0.37 (0.14-1.30)	0.41 (0.22-0.87)	0.69 (0.17-1.95)	0.46 (0.25-0.96)	0.58 (0.30-1.28)	0.59 (0.30-1.30)	0.75 (0.30-2.49)	1.22 (0.33-3.26)	1.13 (0.33-2.86)	0.71 (0.36-2.62)	0.75 (0.36-1.90)	1.05 (0.38-2.39)	0.78 (0.43-1.57)	**STER**

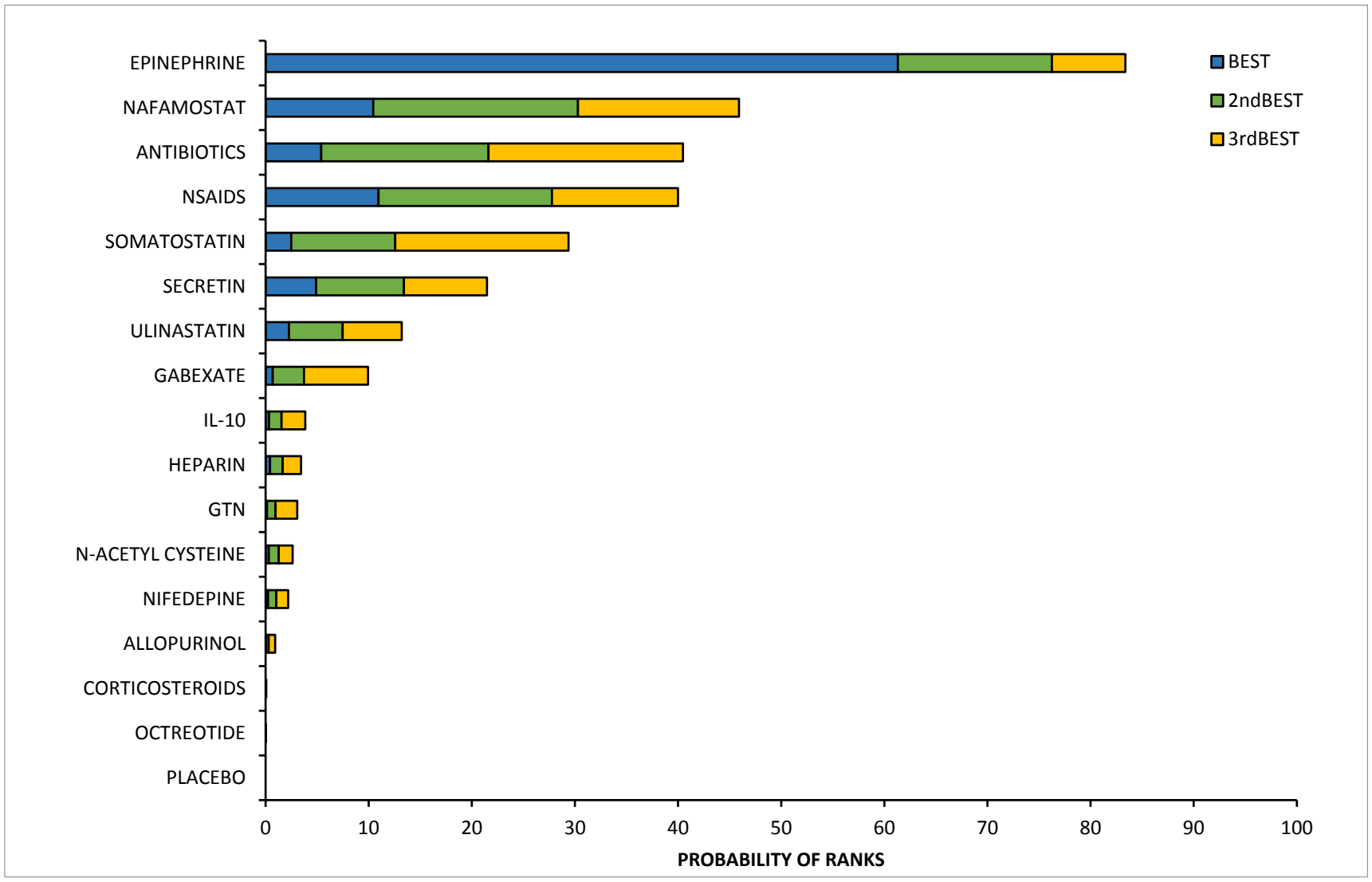
~~Supplementary~~ Figure 1: Assessment of risk of bias in the trials used in analysis, using the Cochrane Collaboration's tool for assessing risk of bias




Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Other bias (investigator introduced bias due to pancreatic duct stent placement)
Summary assessment across the study
Low Risk
High Risk
Unclear Risk
Milewski 2006
Monolakopaulos 2002
Montano-Loza 2006
Montano-Loza 2007
Moreto 2003
Mosler 2005
Murray 2003
Niederau 1994
Nikolopoulo 1995
Nojgaard 2009
Otsuka 2012
Park 2011
Perrson 1992
Poon 1999
Poon 2003
Prat 2002
Rabenstein 2004
Raty 2001
Romagnuolo 2008
Russo 1992
Saari 1988
Sand 1993
Senol 2009
Sherman 2003
Sherman 2009
Song 2005
toudehmanesh 2007
Sternlieb 1992
Sudhindran 2001
Talwar 2005
Testoni 1988
Testoni 1996
Testoni 2001
Thomopoulos 2006
Torres 2009
Tsujino 2005
Tulassay 1991
Tulassay 1998
Ueki 2007
Ung 2011
Wehrmann 2001
Wei 2009
Wollschlager 1999
Xi Hua 2011
Xiong 2006
Yasuda 1987
Yoo 2008
Yoo 2011
Yusuf 1999

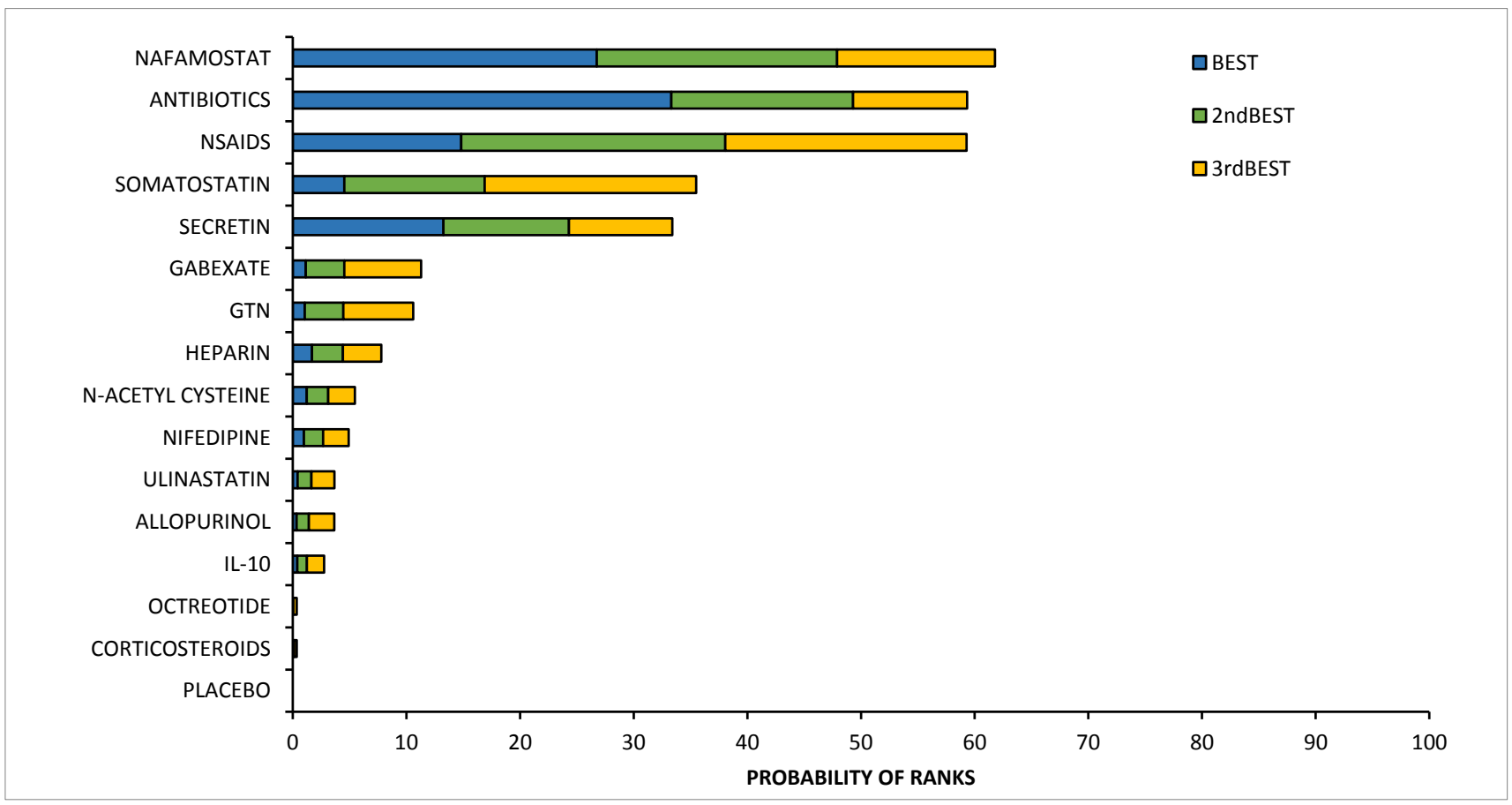
~~Supplementary~~ Figure 2 – Exploring source of heterogeneity: Rankograms comparing all the pharmacologic agents used in analysis to compare efficacy in preventing post-ERCP pancreatitis (PEP), after excluding Randomized controlled trials which included only high risk patients.

The vertical axis lists the agents evaluated and horizontal axis lists the probability of achieving the best, second best, or the third best rank. The agent having the longest bar indicates the best performing agent.



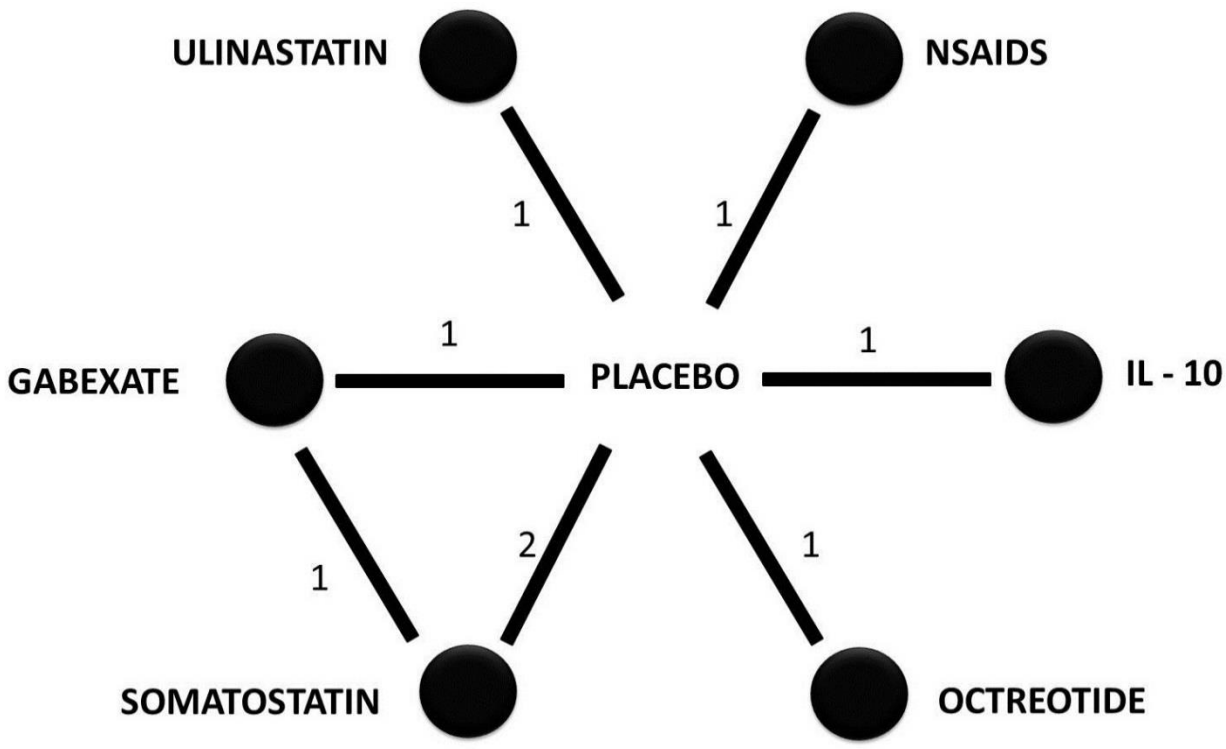
~~Supplementary~~ Figure 3 – Sensitivity analysis: Rankograms comparing pharmacologic agents used in analysis to compare efficacy in preventing post-ERCP pancreatitis (PEP), after excluding Randomized controlled trials which evaluated epinephrine.

The vertical axis lists the agents evaluated and horizontal axis lists the probability of achieving the best, second best, or the third best rank. The agent having the longest bar indicates the best performing agent.



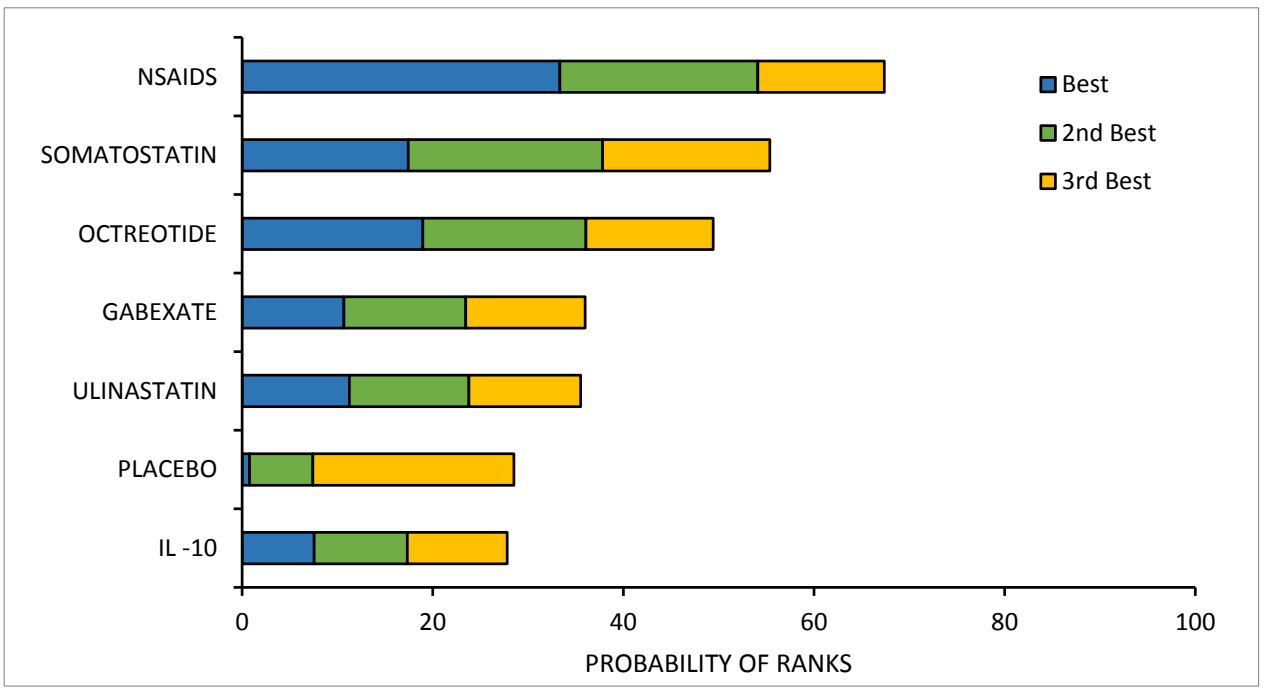
~~Supplementary~~ Figure 4 - Sensitivity analysis: Network of randomized controlled trials (RCT) comparing different pharmacologic agents for their efficacy in preventing post-ERCP pancreatitis among high risk patients.

Each circle represents an agent used in the analysis and the number on lines connecting agents indicate the number of RCTs (IL – Interleukin)



~~Supplementary~~ Figure 5 - Sensitivity analysis: Rankograms comparing the efficacy of pharmacologic agents evaluated in Randomized controlled trials including only high risk patients.

The vertical axis lists the agents evaluated and horizontal axis lists the probability of achieving the best, second best, or the third best rank. The agent having the longest bar indicates the best performing agent.



~~Supplementary~~ **Table 4** – **Sensitivity analysis** by stratifying the 16 agents into 30 sub-groups based on dosage and route of administration.

Lower and upper limits of odds ratios represent the limits of odds ratios from each of the trials in each sub-group, compared to placebo.

GTN – Glyceryl trinitrate, I.V. – intravenous, S.C. – subcutaneous, I.M. – intramuscular, hrs – hours, µg – microgram, mg – milligram

Agent name	Number of trials	Odds ratio	
		Lower limit	Upper limit
ALLOPURINOL	6	0.15 (0.05- 0.46)	1.60 (0.63 - 4.11)
ANTIBIOTICS	4	0.26 (0.08 - 0.79)	0.65 (0.10 - 4.08)
CORTICOSTEROIDS			
CORTICOSTEROIDS I.V.	5	0.12 (0.01 - 1.04)	1.48 (0.66 - 3.33)
CORTICOSTEROIDS ORAL	2	1.27 (0.91 - 1.76)	1.59 (0.62 - 4.06)
EPINEPHRINE			
EPINEPHRINE 10 ml	1	0.11 (0.01 - 2.03)	
EPINEPHRINE 20 ml	1	0.29 (0.14 - 0.61)	
GABEXATE	7	0.27 (0.07 - 1.01)	1.26 (0.59 - 2.70)
GTN			
TRANSDERMAL GTN	4	0.25 (0.07 - 0.93)	1.17 (0.48 - 2.83)
SUBLINGUAL GTN	2	0.26 (0.06 - 1.04)	0.39 (0.15 - 0.98)
TOPICAL GTN	2	0.73 (0.15 - 3.49)	3.06 (0.12 - 76.82)
I.V. GTN	1	0.62 (0.26 - 1.45)	
HEPARIN	3	0.34 (0.03 - 3.42)	1.06 (0.25 - 4.50)
IL-10			
IL-10 < 10 µg	2	0.36 (0.11 - 1.13)	1.09 (0.50 - 2.40)
IL-10 ≥ 10 µg	2	0.23 (0.06 - 0.88)	1.69 (0.83 - 3.45)
N ACETYLCYSTEINE	2	0.59 (0.16 - 2.22)	1.30 (0.58 - 2.89)
NAFAMOSTAT			
NAFAMOSTAT 20 mg	1	0.28 (0.12 - 0.64)	
NAFAMOSTAT 50 mg	3	0.29 (0.09 - 0.91)	0.92 (0.26 - 3.29)
NIFEDEPINE	3	0.70 (0.29 - 1.70)	1.34 (0.34 - 5.33)
NSAIDS			
RECTAL NSAIDS	8	0.12 (0.03 - 0.56)	0.49 (0.30 - 0.81)
ORAL NSAIDS	1	0.97 (0.46 - 2.02)	
I.M. NSAIDS	1	0.38 (0.09 - 1.60)	
OCTREOTIDE			
OCTREOTIDE S.C.	17	0.08 (0.00 - 1.58)	2.76 (0.11 - 71.15)
OCTREOTIDE I.V.	5	0.42 (0.03 - 5.08)	6.54 (0.77 - 55.72)
SECRETIN	2	0.54 (0.35 - 0.83)	
SOMATOSTATIN			
SOMATOSTATIN ≥ 12 hrs	8	0.11 (0.01 - 1.07)	1.72 (0.27 - 10.80)
SOMATOSTATIN < 12 hrs	6	0.60 (0.10 - 3.74)	1.85 (0.90 - 3.82)
SOMATOSTATIN BOLUS	6	0.16 (0.03 - 0.72)	0.60 (0.05 - 6.90)
ULINASTATIN			
ULINASTATIN ≥ 150,000	3	0.18 (0.01 - 4.01)	0.47 (0.15 - 1.48)
ULINASTATIN < 150,000	2	1.23 (0.41 - 3.65)	2.62 (0.78 - 8.76)

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