

Supplementary materials

Supplementary Table 1 Results of the subgroup analysis for overall PEP

Outcomes	Studies	RR	95%CI	P value	Heterogeneity	GRADE
Overall PEP (50 comparisons)	30	0.85	0.69-1.04	0.12	79%	Moderate
After removing high-impact studies (47 comparisons)	27	0.82	0.66-1.00	0.05	80%	Moderate
Indomethacin alone <i>vs</i> Control	21	0.87	0.62-1.21	0.40	84%	Moderate
Indomethacin combined <i>vs</i> Control	5	0.39	0.22-0.68	< 0.01	61%	Moderate
Indomethacin alone <i>vs</i> Indomethacin combined	14	1.12	0.94-1.34	0.20	36%	High
Indomethacin alone <i>vs</i> Placebo	8	0.61	0.42-0.87	< 0.01	51%	Moderate
Indomethacin combined <i>vs</i> Placebo	4	0.41	0.21-0.78	< 0.01	61%	Moderate
Indomethacin alone <i>vs</i> Salin/Salin combined	5	1.27	0.65-2.48	0.48	64%	Moderate
Indomethacin alone <i>vs</i> Glycerin/epinephrine or combined	7	0.53	0.33-0.84	< 0.01	67%	Moderate
Indomethacin <i>vs</i> Pancreatic duct stent combined	2	1.36	1.07-1.73	0.01	0%	High
Patients aged < 60 years	19	0.92	0.70-1.21	0.56	83%	Moderate
Patients aged > 60 years	11	0.74	0.55-1.00	0.05	65%	Moderate
Selected patients	13	0.83	0.60-1.13	0.23	85%	Moderate
Unselected patients	17	0.86	0.67-1.10	0.23	64%	Moderate
Single-center studies	21	0.78	0.58-1.06	0.11	82%	Moderate

Multi-center studies	9	1.02	0.81-1.27	0.88	62%	Moderate
Double-arm RCTs	23	0.84	0.68-1.04	0.10	68%	Moderate
Multiple-arm RCTs	7	0.82	0.55-1.22	0.33	85%	Moderate

Supplementary Table 2 Multivariate analysis outcomes of included studies

Ref.	Age > 40	Fem	Prior	History	Difficu	Pancreat	Biliary	Trainee	Pancreat
		ale	cholecys	of	lt	ic	sphincte	involve	ic duct
			t	pancrea	cannu	sphincte	rotomy	ment	stent
				ti		rotomy			
Roma no et al	NA	0.31 (0.9 1, 1.05)	0.4 (0.17, 0.9)	0.27 (0.1, 0.73)	0.32 (0.14, 0.72)	0.09 (0.03, 0.27)	0.43 (0.18, 1.02)	NA	NA
Patai et al	0.17(0.03, 0.952)	0.42 (0.2 5, 0.9)	0.27 (0.07, 1.06)	NA	NA	0.24 (0.06,0.85)	NA	NA	NA
Elmu nzer et al	0.5 (0.1, 0.9)	0.6(0.2, 1.8)	NA	0.9 (0.30, 1.50)	0.5 (0.1, 0.9)	0.5 (-0.1, 1.10)	0.91 (0.71, 1.25)	1.3 (0.8, 2.2)	1.43 (1.11, 2.0)
Leve nick et al	NA	NA	NA	1.38(0.1 4, 13.37)	0.82(0.3 3, 2.04)	0.46(0.09, 2.31)	0.62(0.20, 1.90)	1.03(0.65, 1.63)	1.32(0.55, 3.46)
Li et al	0.36 (0.17, 0.78)	0.42 (0.1 6, 1.12)	0.50 (0.21, 1.20)	NA	NA	NA	NA	NA	NA
Guha et al	0.25 (0.03, 2.24)	0.75 (0.0 5,	NA	NA	NA	NA	NA	NA	4.67 (0.55, 39.57)

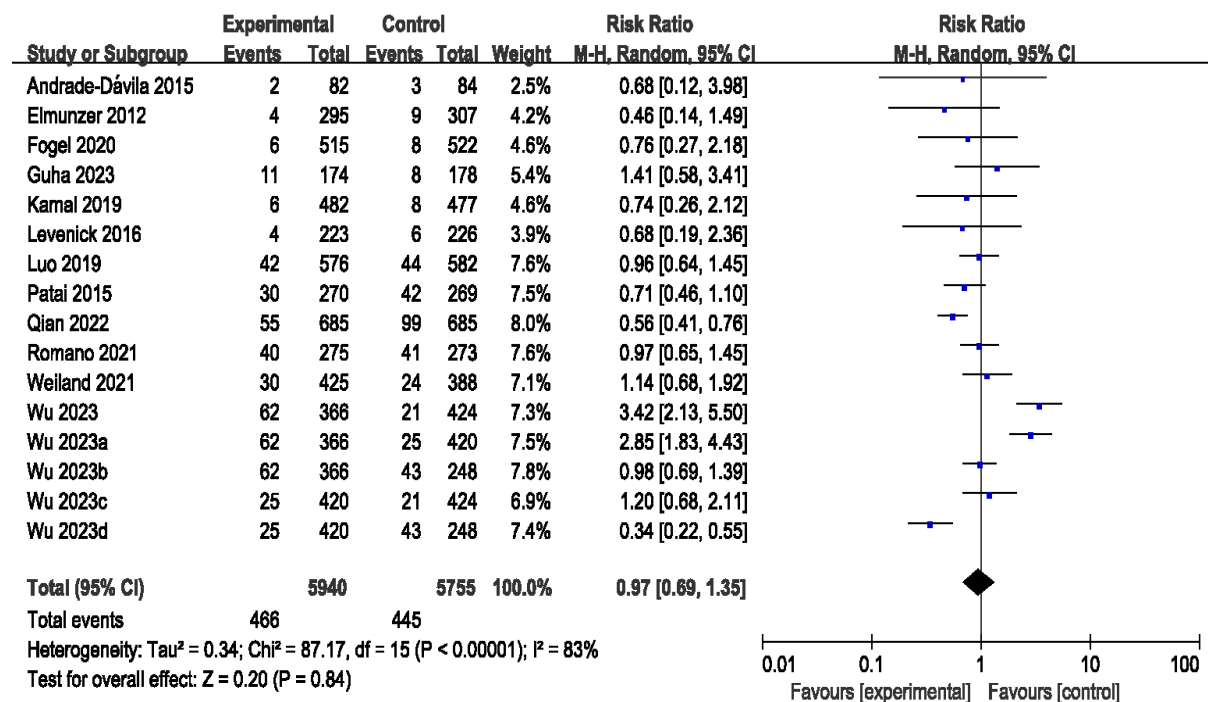
			11.6							
			5)							
Sotou dehm anesh <i>et al</i>	0.47 (0.09,2.53)		0.58 (0.2 2,1.5 3)	NA	NA	NA	0.55 (0.1- 2.94)	NA	NA	NA
Andr ade- Dávil a <i>et al</i>	1.43 3.16)	(0.65, 4,	2.38 (0.8 6.69)	NA	NA	0.23 (0.09, 0.60)	NA	0.75 (0.34, 1.66)	NA	NA
Qian <i>et al</i>	0.67 1.72)	(0.26- 9- 0.90)	0.51 (0.2 0.90)	NA	NA	NA	NA	NA	NA	NA
Döbr önte <i>et al</i>	0.69 2.11)	(0.22, 4, 1.58)	0.83 (0.4 1.58)	NA	NA	0.54 (0.16, 1.82)	NA	NA	NA	NA
Kama l <i>et al</i>	0.79 1.66)	(0.37, 7,1.6 6)	0.79 (0.3 7,1.6 6)	NA	0.78 (0.06, 10.37)	0.97 (0.58, 1.62)	0.61 (0.03, 12.80)	0.99 (0.58, 1.69)	0.95 (0.55, 1.65)	NA
Elmu nzer <i>et al</i>	0.65 0.88)	(0.49, 8,1.5 3)	1.16 (0.8 8,1.5 3)	NA	0.71 (0.46, 1.11)	0.77 (0.6, 1.00)	0.38 (0.20, 0.73)	0.84 (0.66, 1.07)	0.08 (0.03, 0.18)	1.32 (1.04, 1.67)

Luo <i>et al</i>	1.82 3.13)	(1.06- (1.05, 3.17)	1.83 3.1	NA	0.64(0.0 6-6.39)	1.93(0.8 3-4.49)	0.32(0.04 -2.55)	NA	1.66(0.85 -3.26)	3.66(1.09 -12.25)
Lai <i>et al</i>	NA		0.88 (0.48, 16.04)	NA	NA	0.63(0.0 8,5.21	NA	0.87(0.6,1 .25)	NA	NA
Weiland <i>et al</i>	0.77 1.29)	(0.44, (0.47- 1.44)	0.83 (0.47- 1.44)	NA	1.64 (0.18- 32.00)	0.81 (0.45- 1.42)	NA	NA	1.03 (0.04- 25.3)	2.26 (0.19- 46.80)
Hatami <i>et al</i>	NA		NA	0.50 (0.07, 3.58)	NA	0.24 (0.11, 3.8)	0.12 (0.04, 0.32)	NA	NA	NA

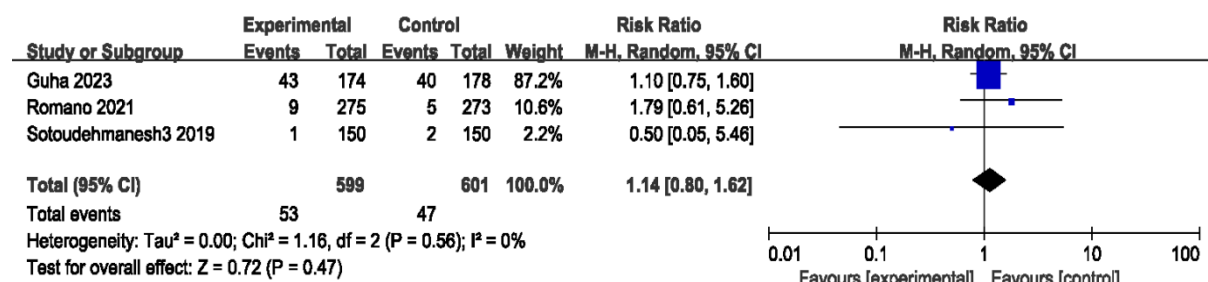
Supplementary Table 3 Defining factors of high-risk ERCP patients

Risk Factor Type	Risk Factor
Definite factors	Suspected sphincter of Oddi dysfunction
	Prior post-ERCP pancreatitis
	Pancreatic duct injection
	Difficult cannulation
	Pre-cut or pancreatic sphincterotomy
	Ampullectomy
	Balloon dilation of an intact biliary sphincter
Likely factors	Female sex
	Younger age
	Normal bilirubin
	Nondilated common bile duct
	Absence of chronic pancreatitis
	Multiple guidewire passages
	Recurrent pancreatitis
	End-stage renal disease

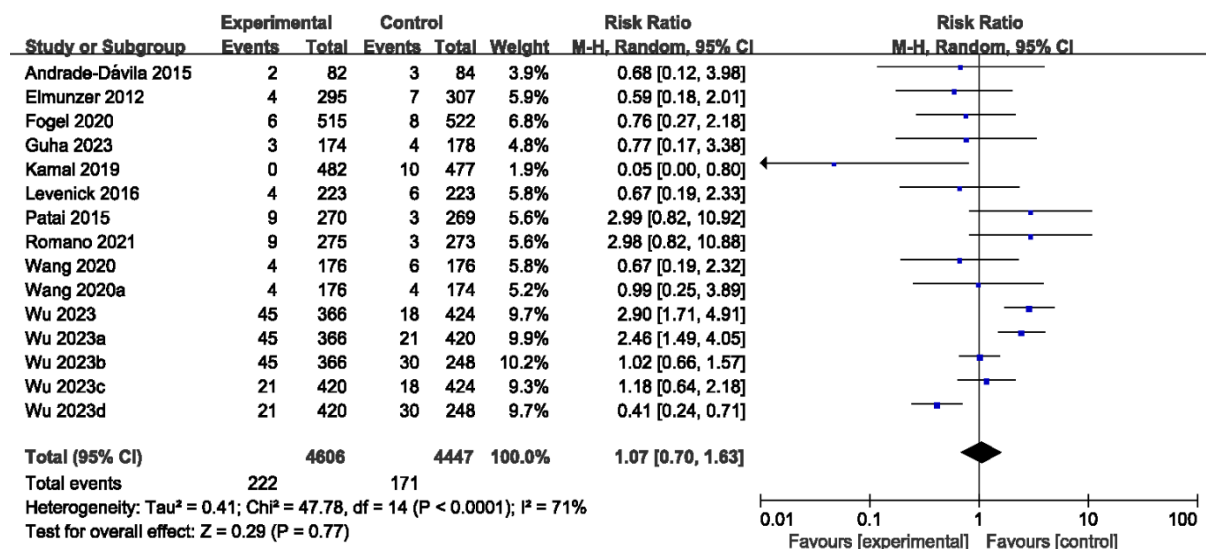
As per the ESGE/ ASGE guidelines the presence of ≥ 1 definite or ≥ 2 likely risk factors for high-risk ERCP patients for PEP.



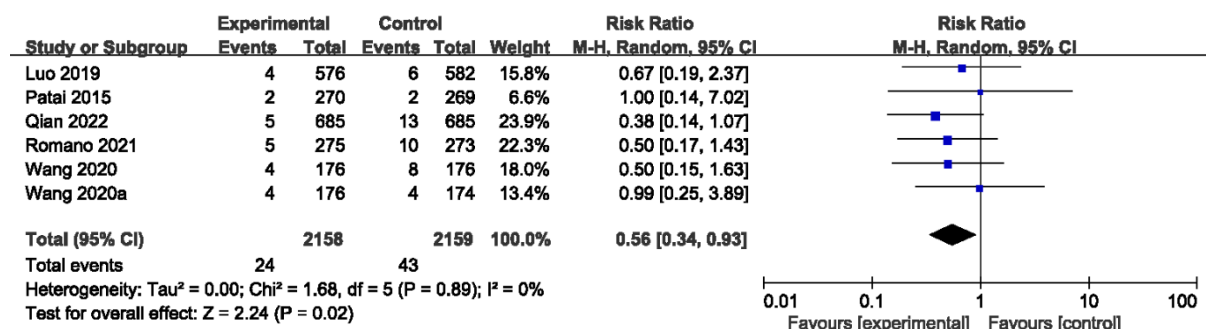
Supplementary Figure 1 Forest plot of adverse events.



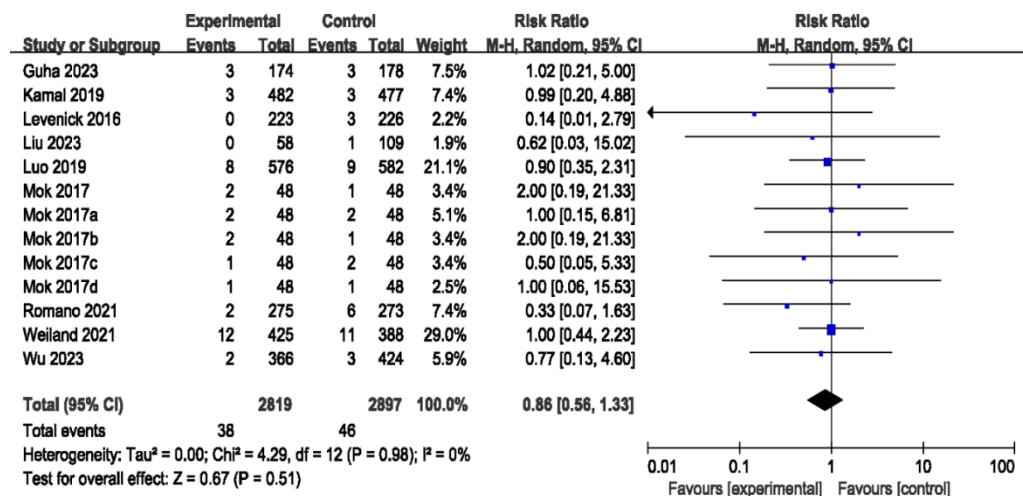
Supplementary Figure 2 Forest plot of Abdominal pain



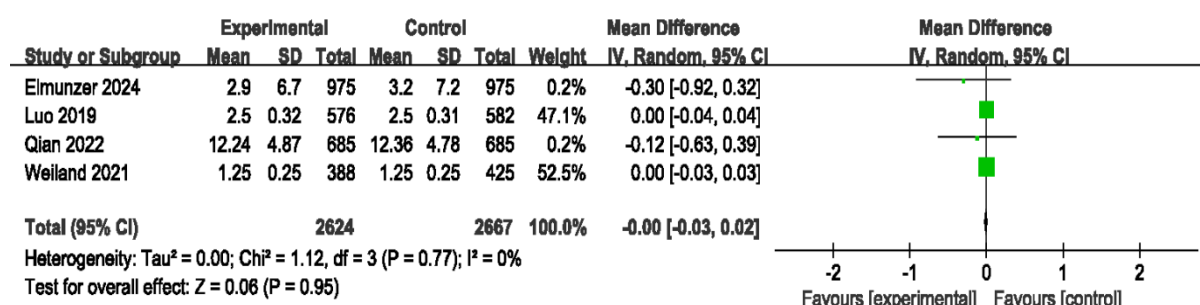
Supplementary Figure 3 Forest plot of bleeding.



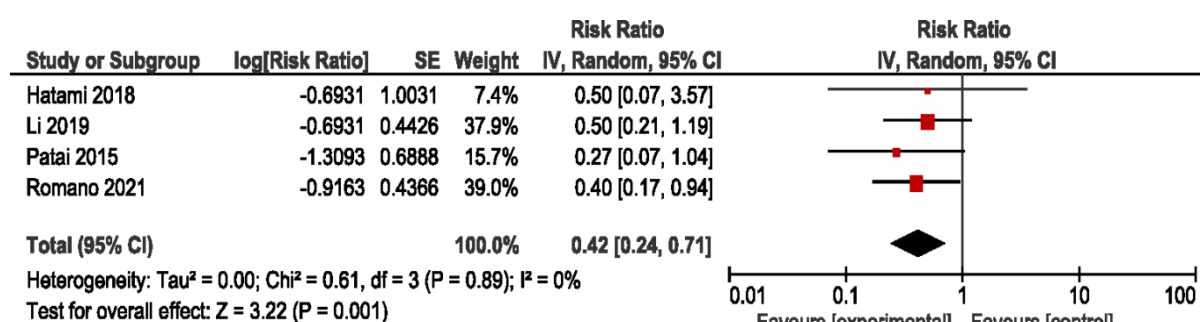
Supplementary Figure 4 Forest plot of cholangitis.



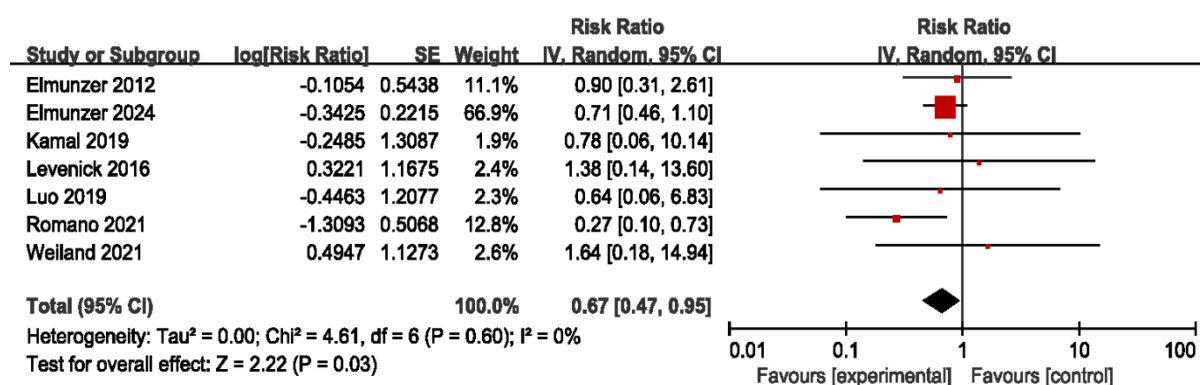
Supplementary Figure 5 Forest plot of mortality rate.



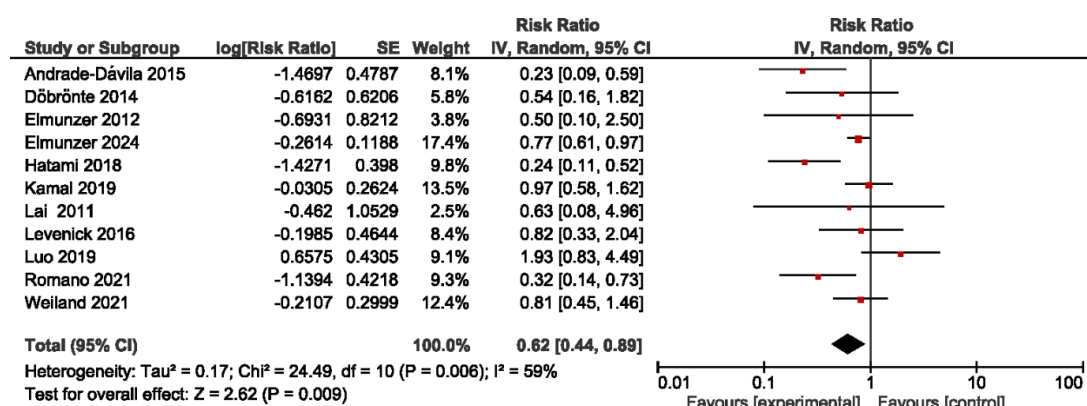
Supplementary Figure 6 Forest plot of hospital stay.



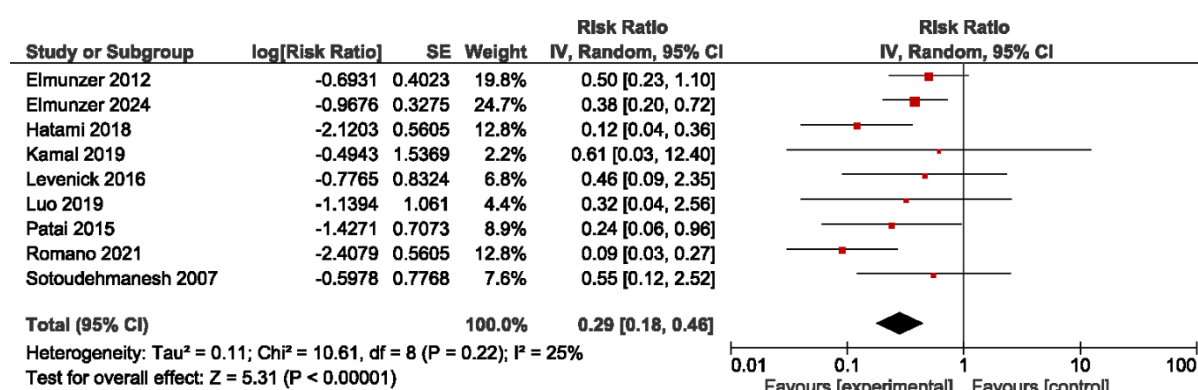
Supplementary Figure 7 Forest plot of prior cholecystectomy.



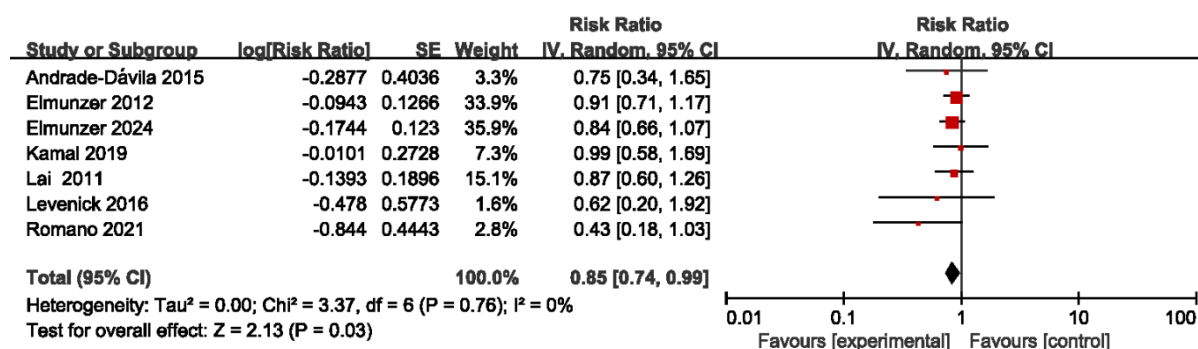
Supplementary Figure 8 Forest plot of the history of pancreatitis.



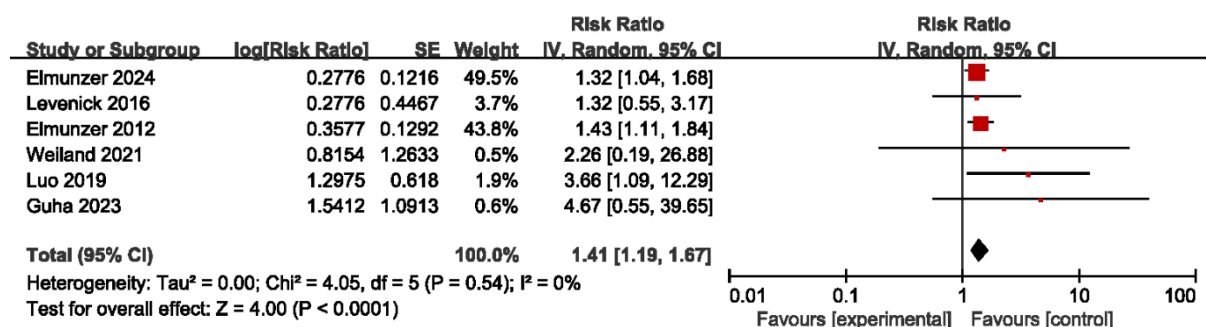
Supplementary Figure 9 Forest plot of difficult cannulation.



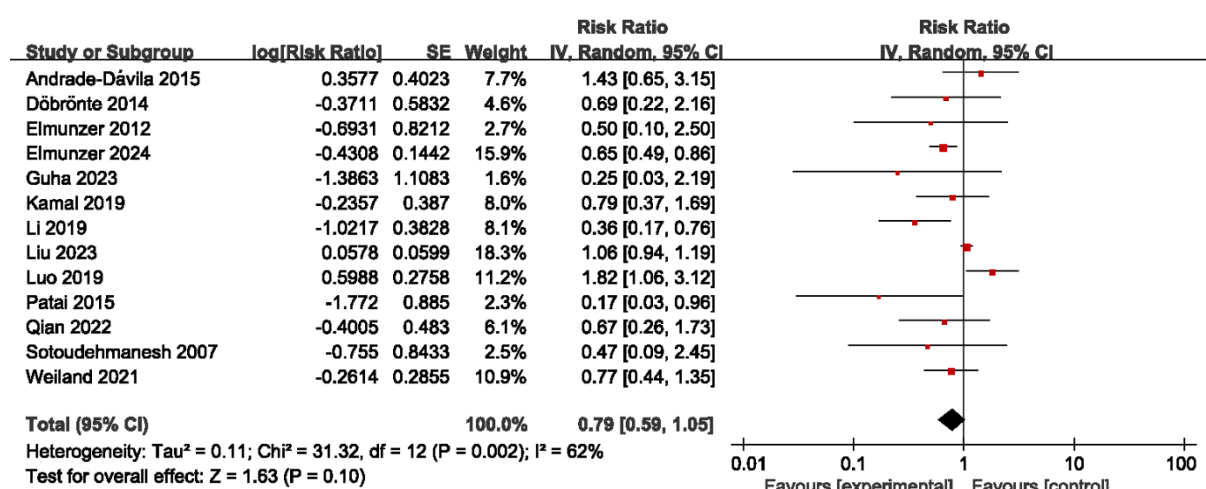
Supplementary Figure 10 Forest plot of pancreatic sphincterotomy.



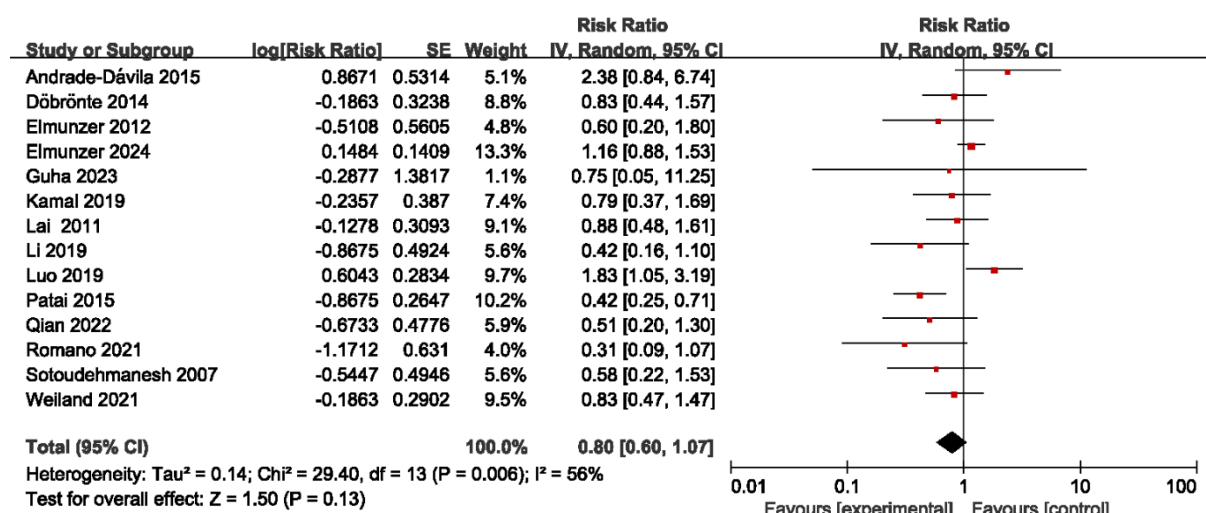
Supplementary Figure 11 Forest plot of biliary sphincterotomy.



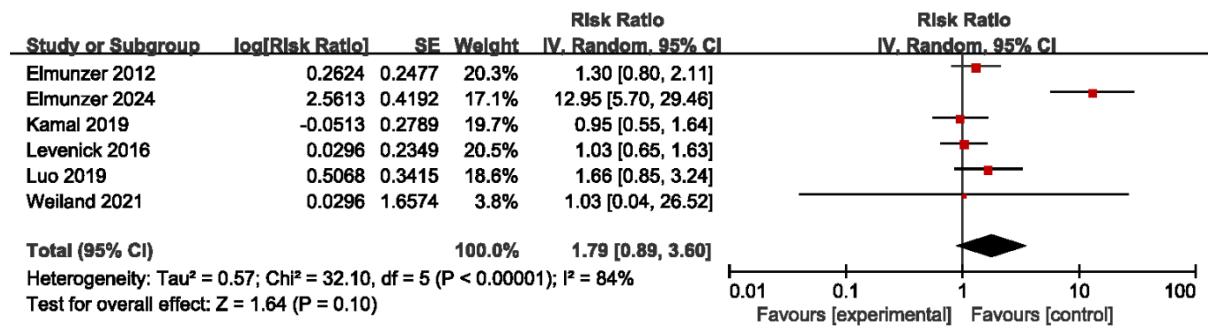
Supplementary Figure 12 Forest plot of pancreatic duct stent.



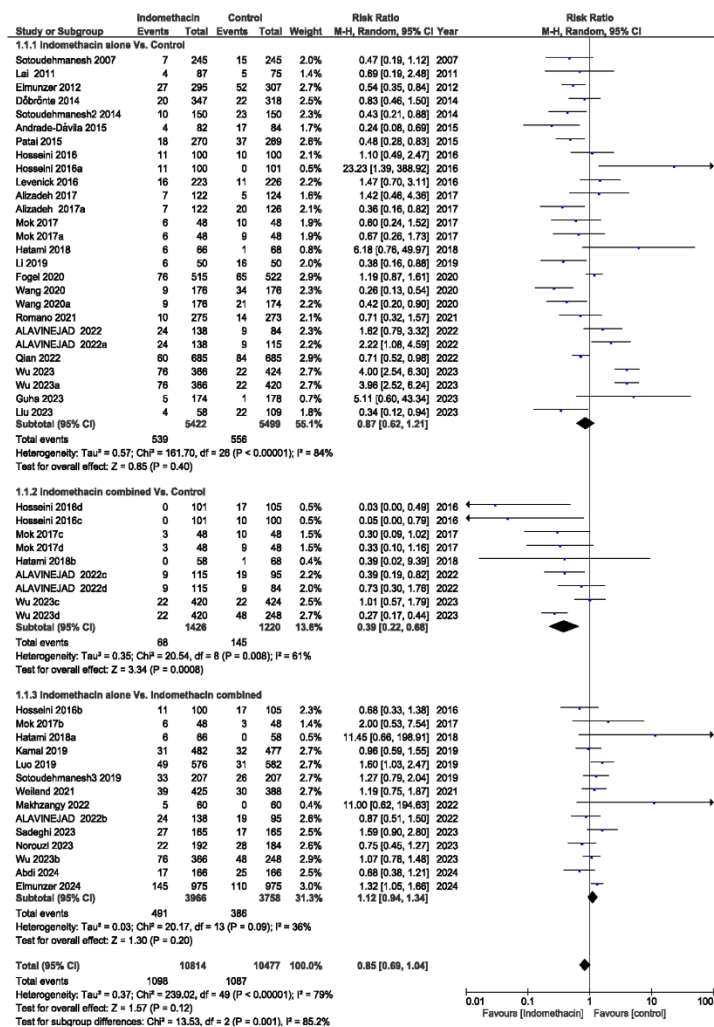
Supplementary Figure 13 Forest plot of patient age >40 years.



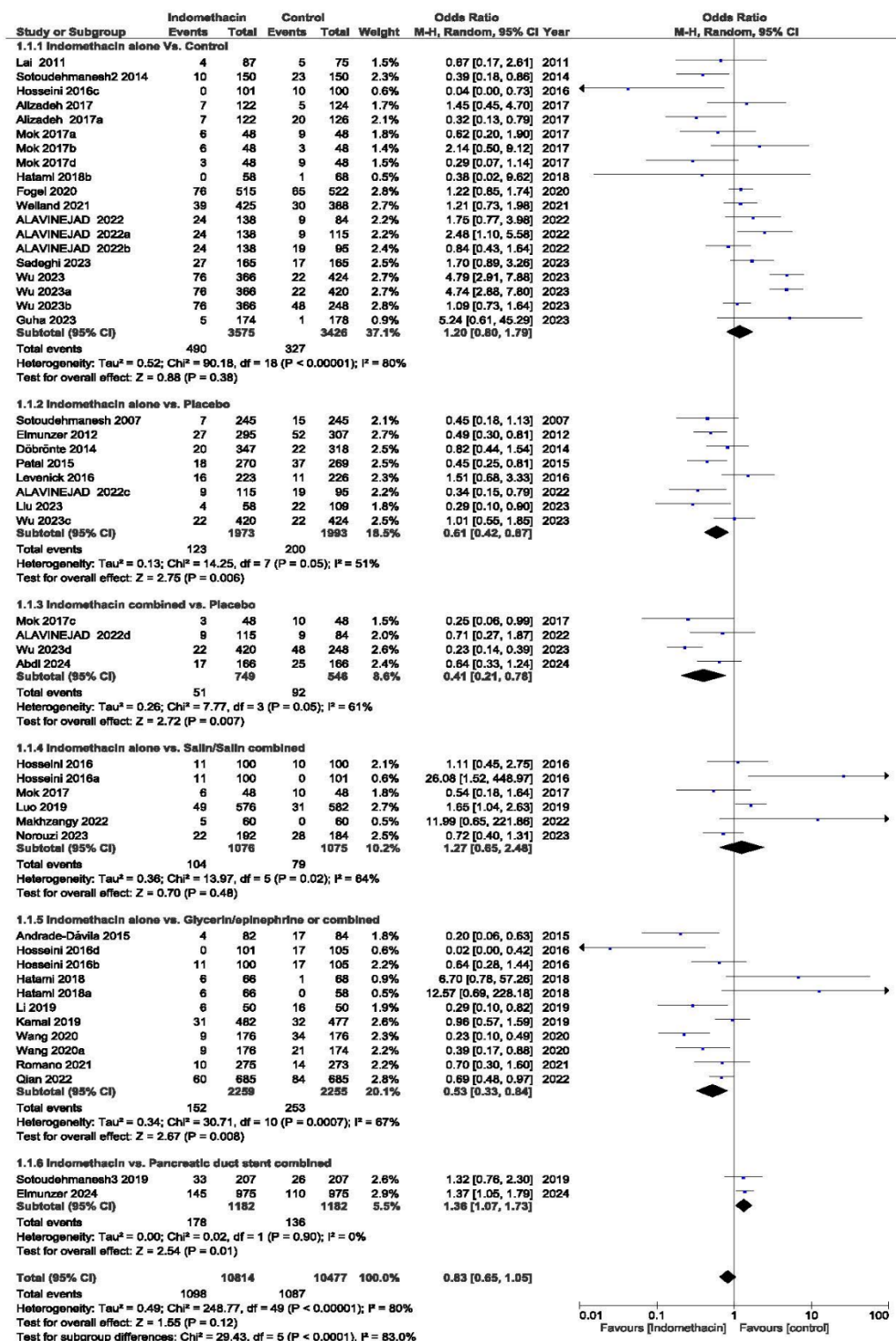
Supplementary Figure 14 Forest plot of female sex.



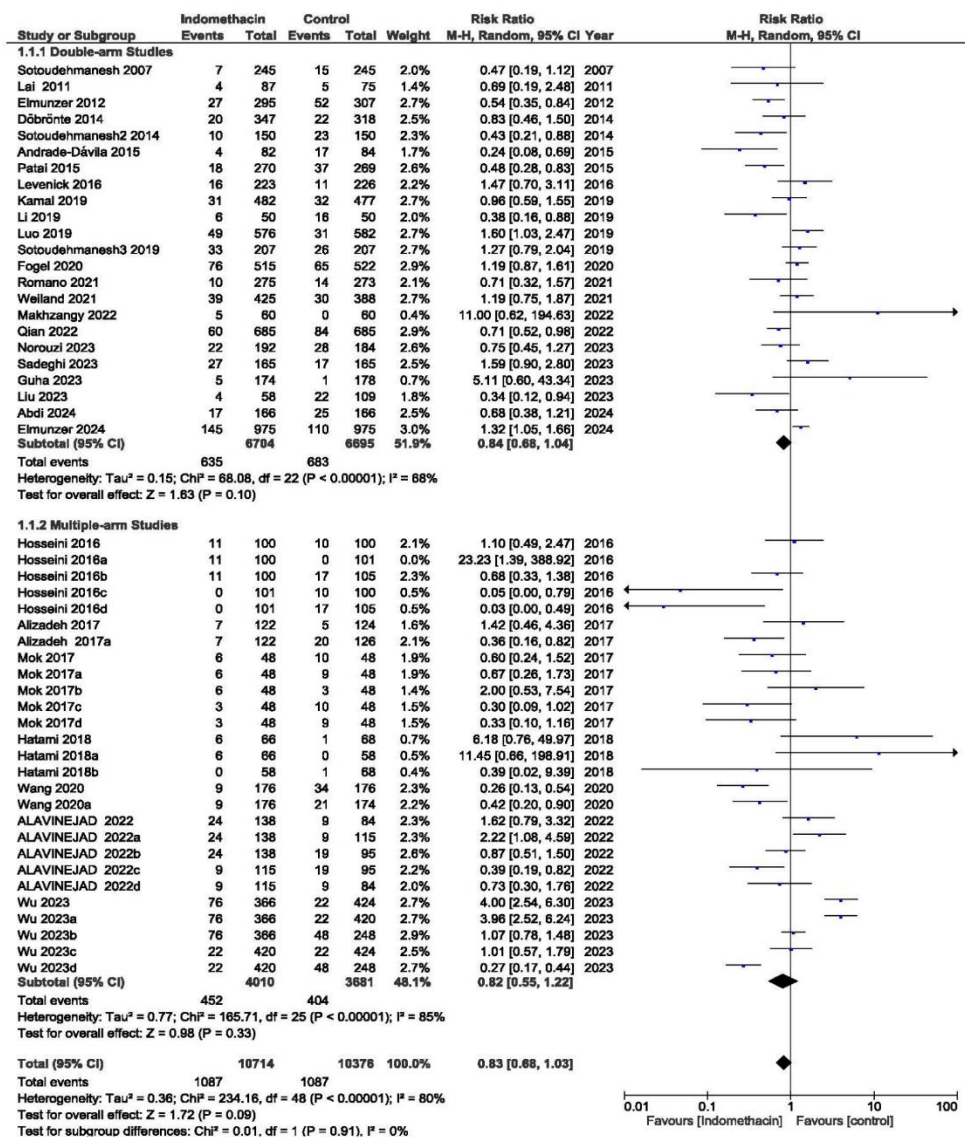
Supplementary Figure 15 Forest plot of trainee involvement.



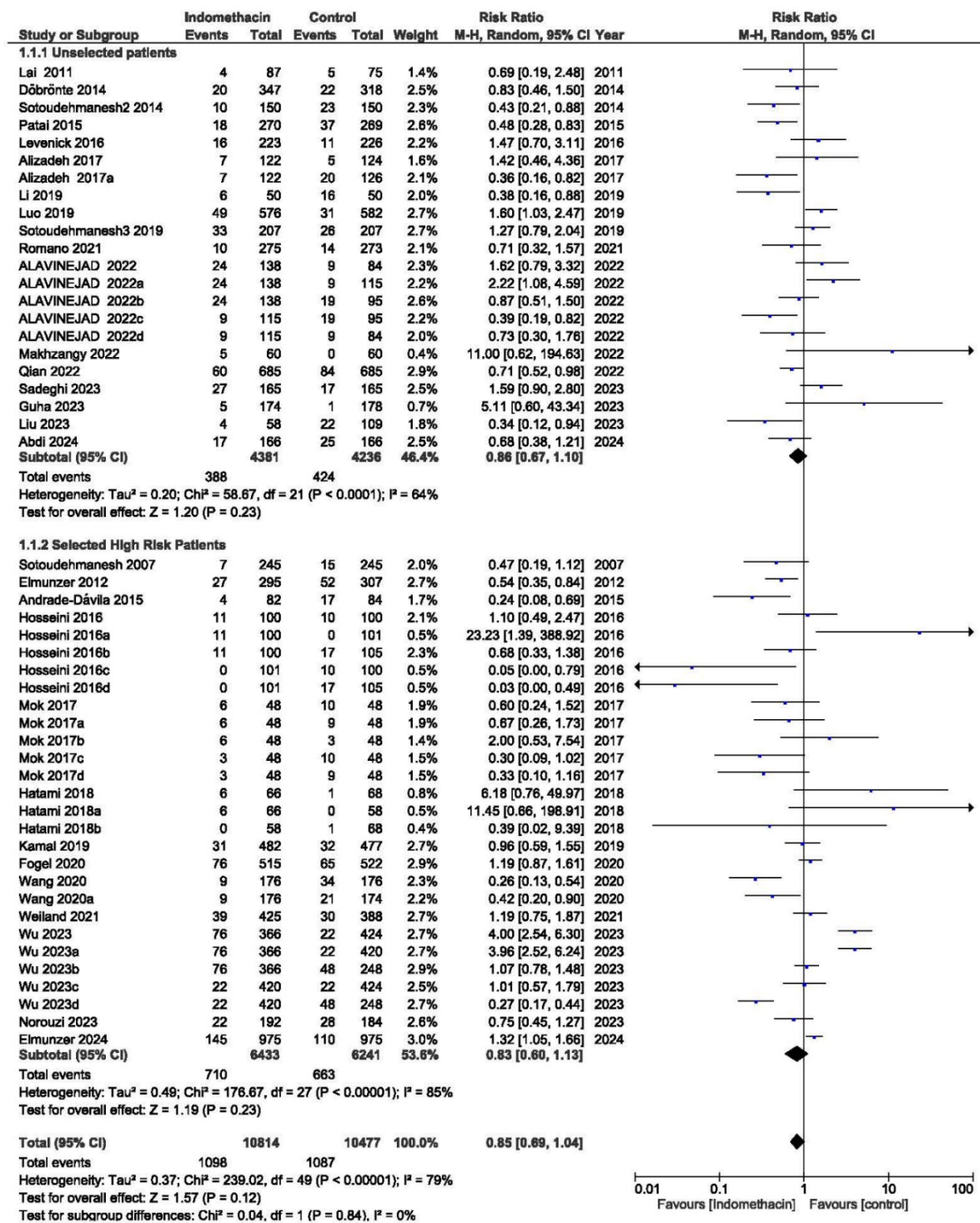
Supplementary Figure 16 Forest plot of Indo. Alone versus Indo. Combined.



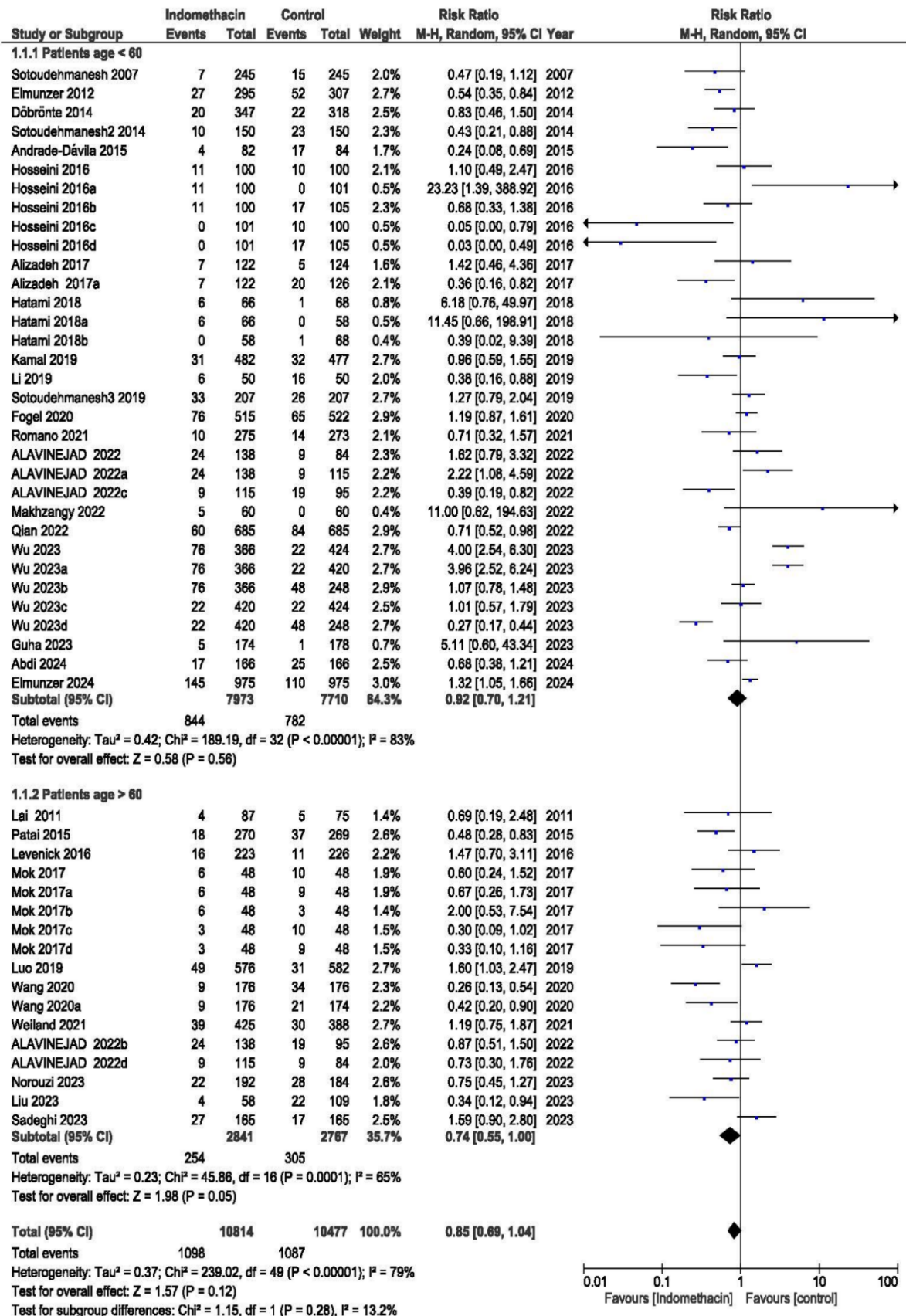
Supplementary Figure 17 Forest plot of Indo. versus Placebo , Indo. versus saline/saline combined/ glycerin/epinephrine or combined.



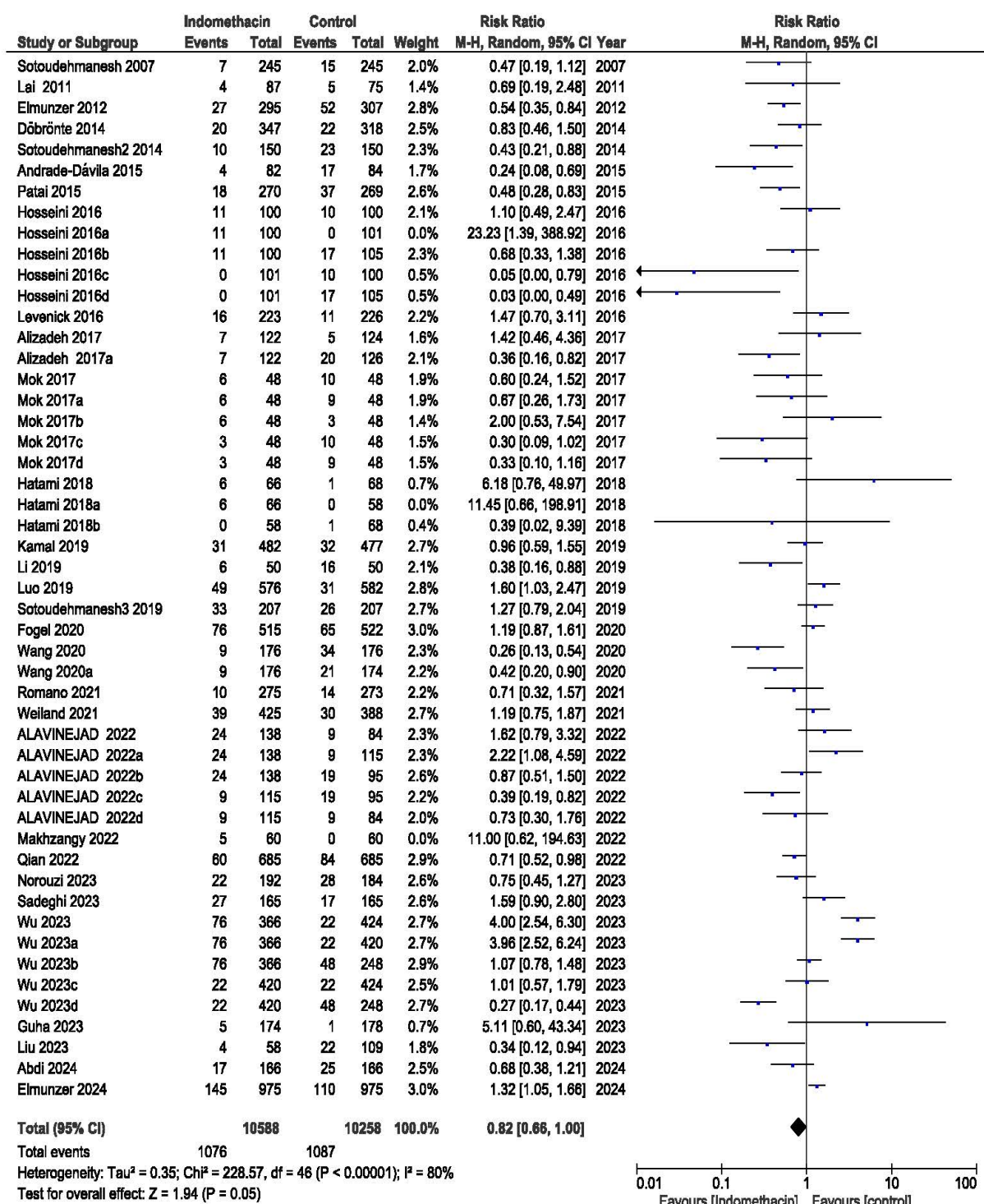
Supplementary Figure 18 Forest plot of study groups with two arms versus studies with multiple arms.



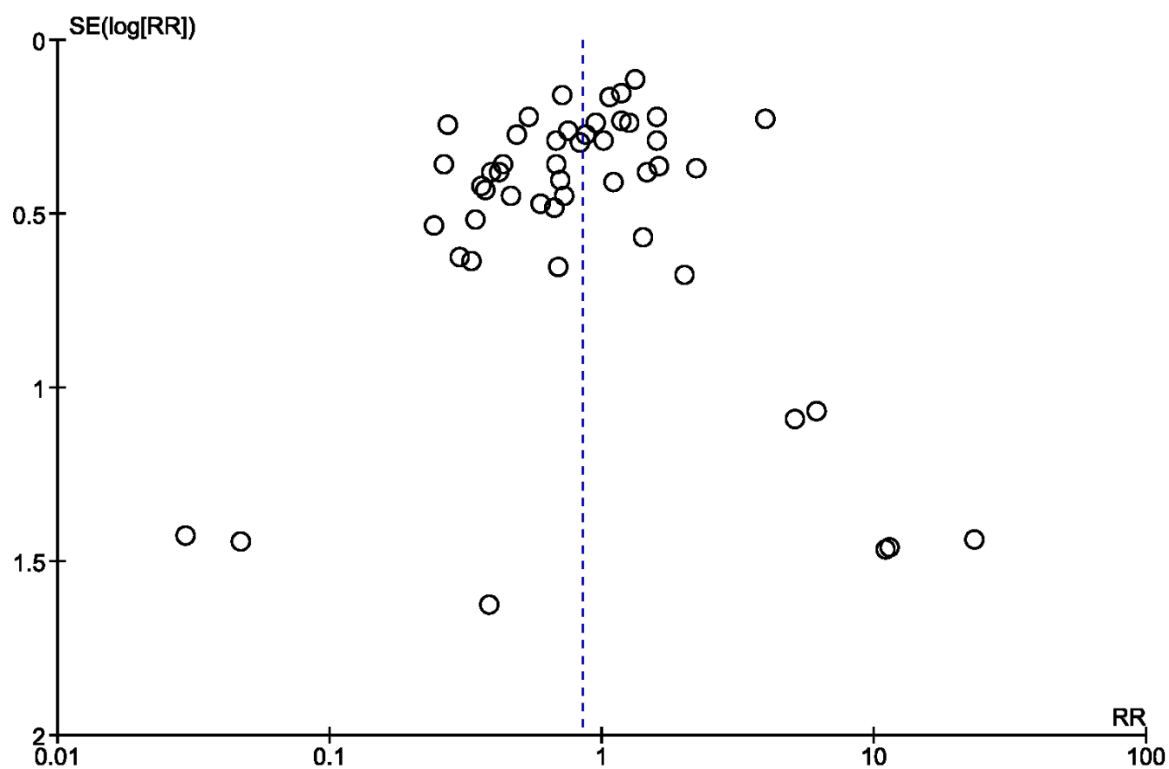
Supplementary Figure 19 Forest plot of selected patients *vs* unselected patients.



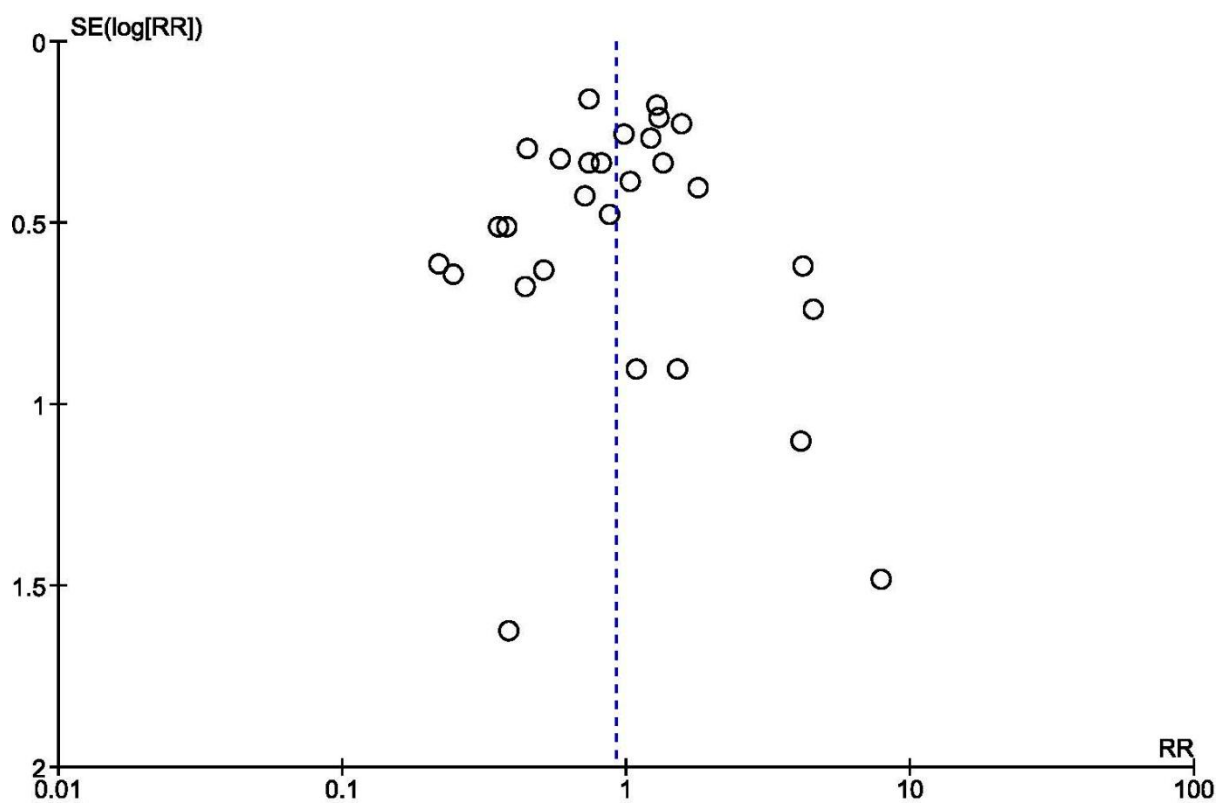
Supplementary Figure 20 Forest plot of patients aged < 60 vs > 60.



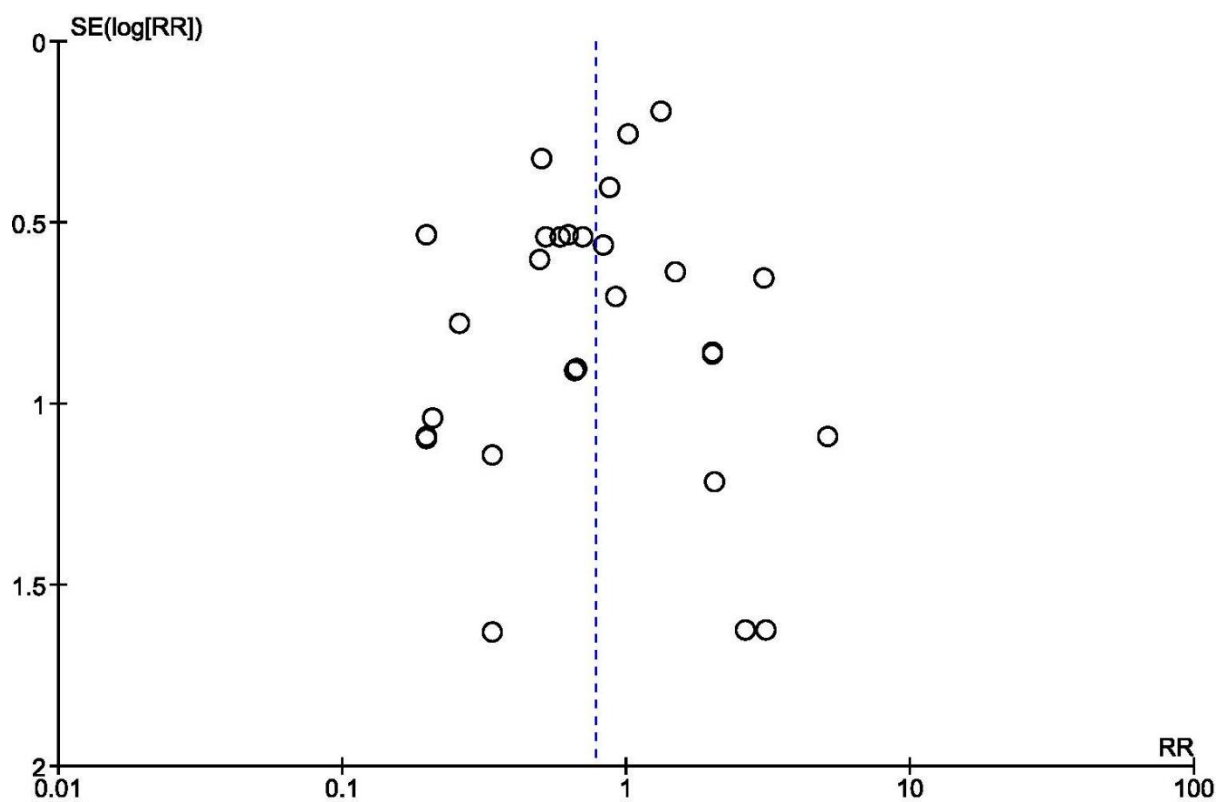
Supplementary Figure 21 Forest plot of PEP (high impact studies removed).



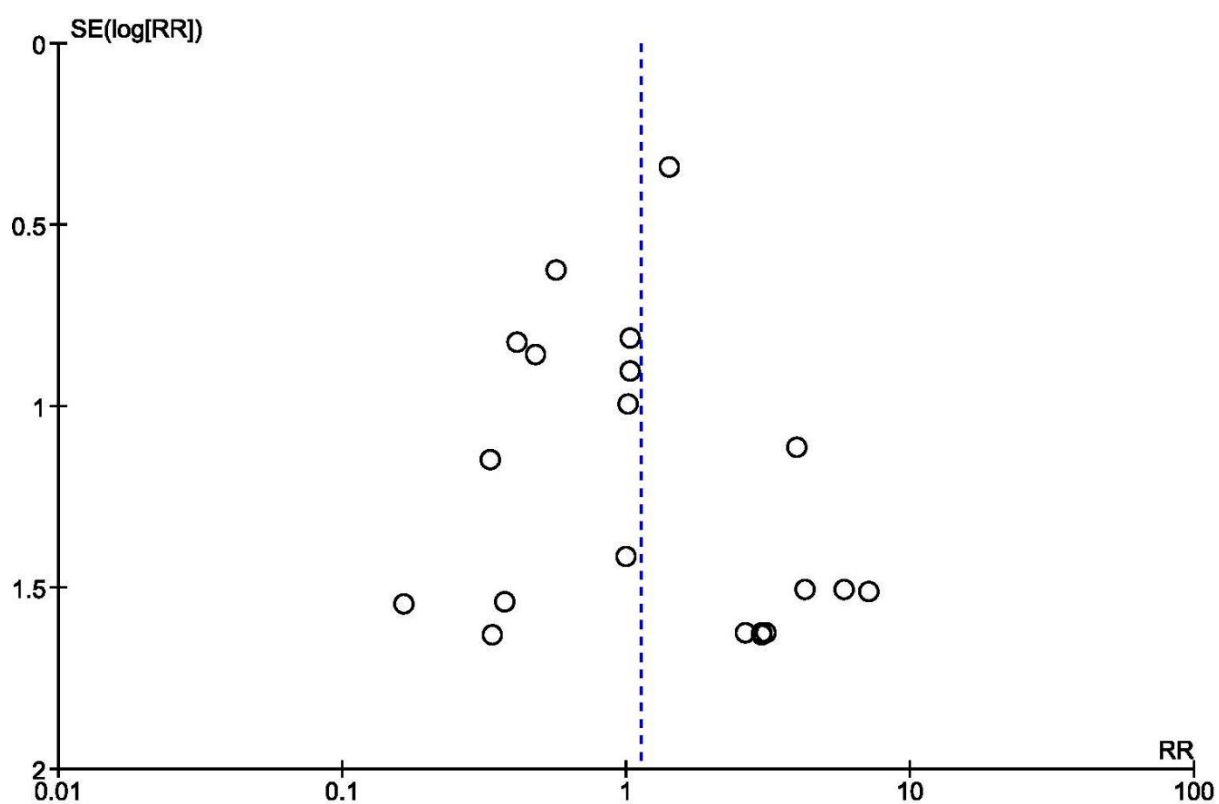
Supplementary Figure 22: Funnel plot of incidence of post-ERCP pancreatitis.



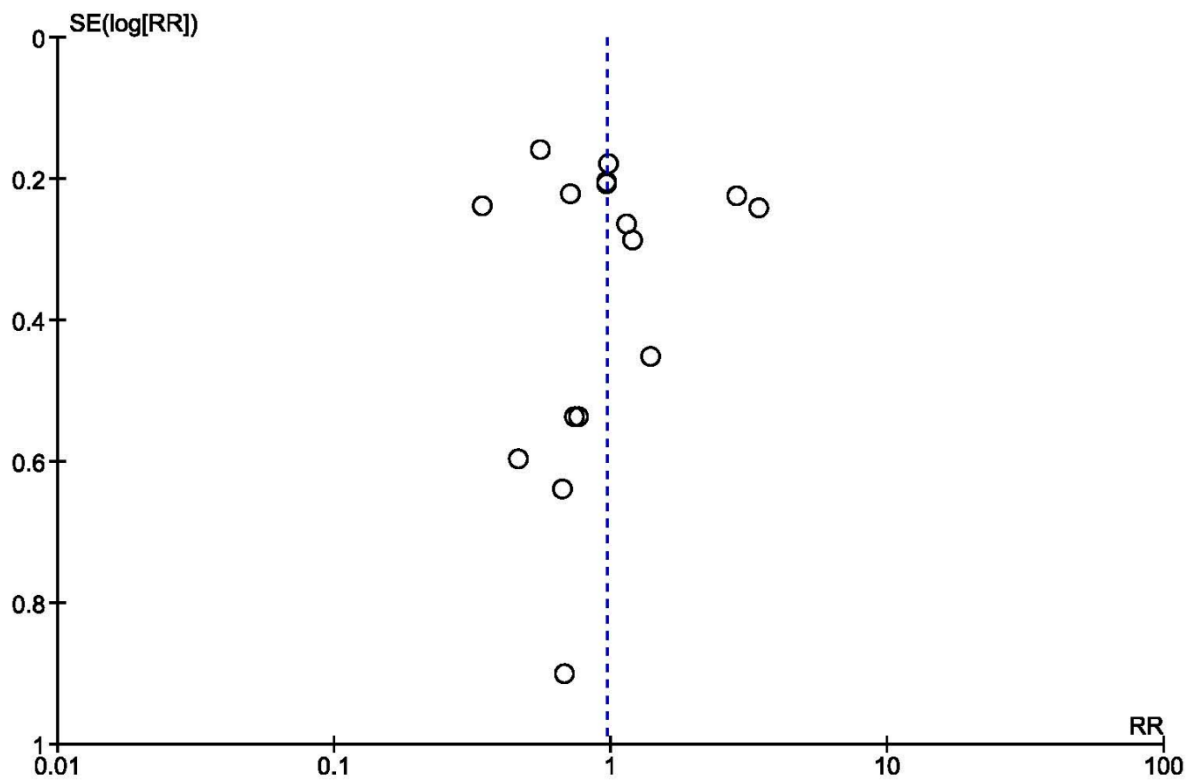
Supplementary Figure 23: Funnel plot of mild PEP.



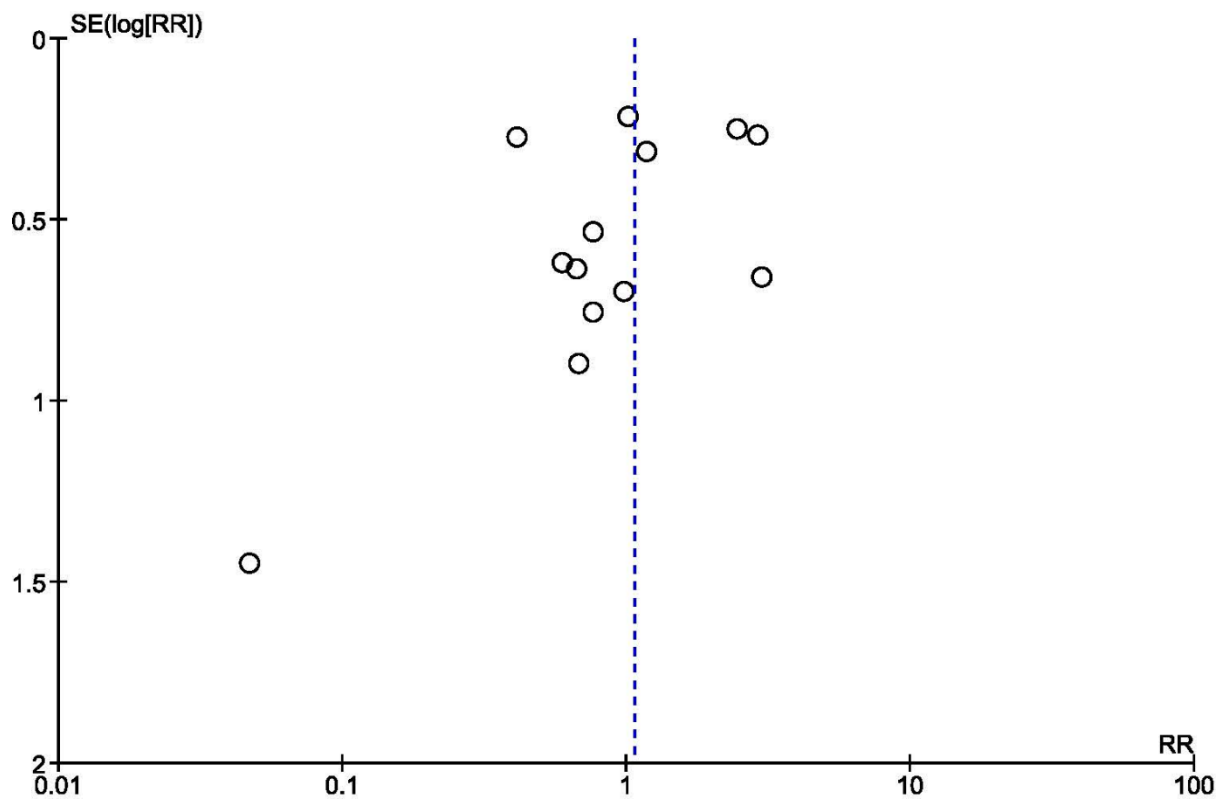
Supplementary Figure 24: Funnel plot of moderate PEP.



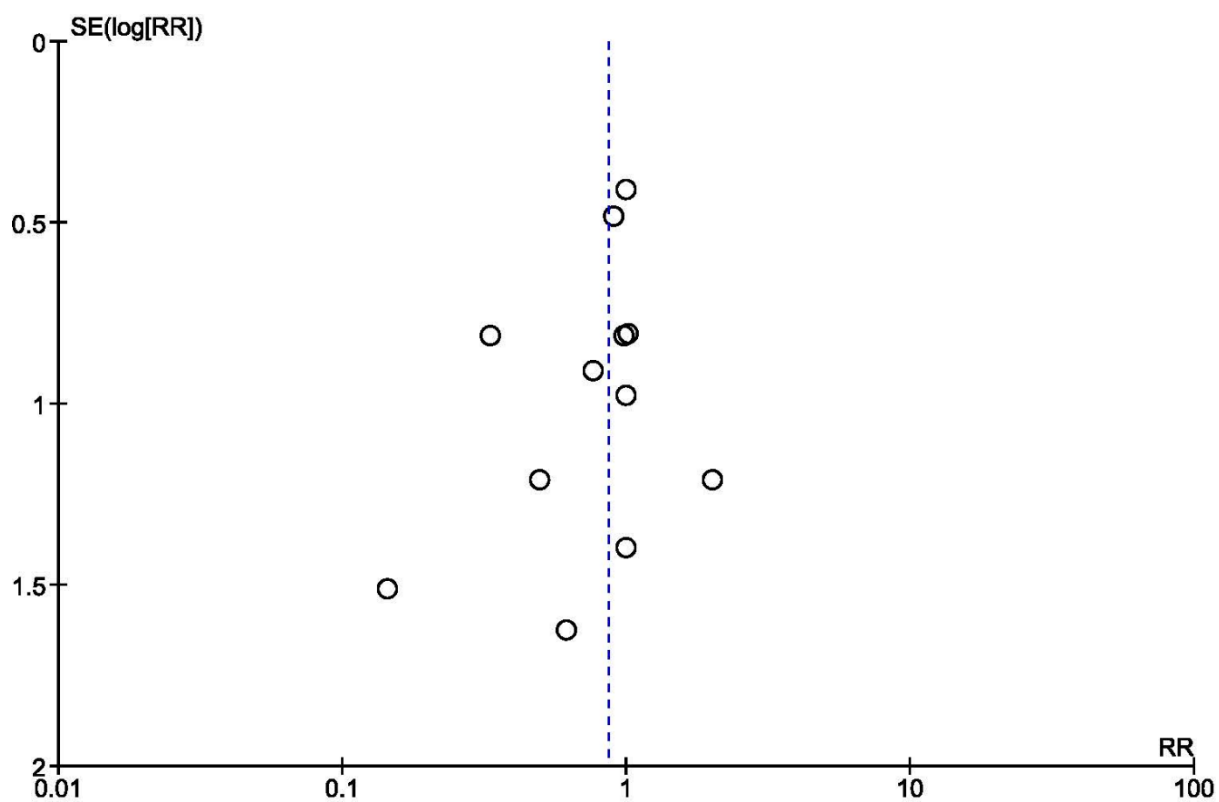
Supplementary Figure 25 Funnel plot Severe PEP.



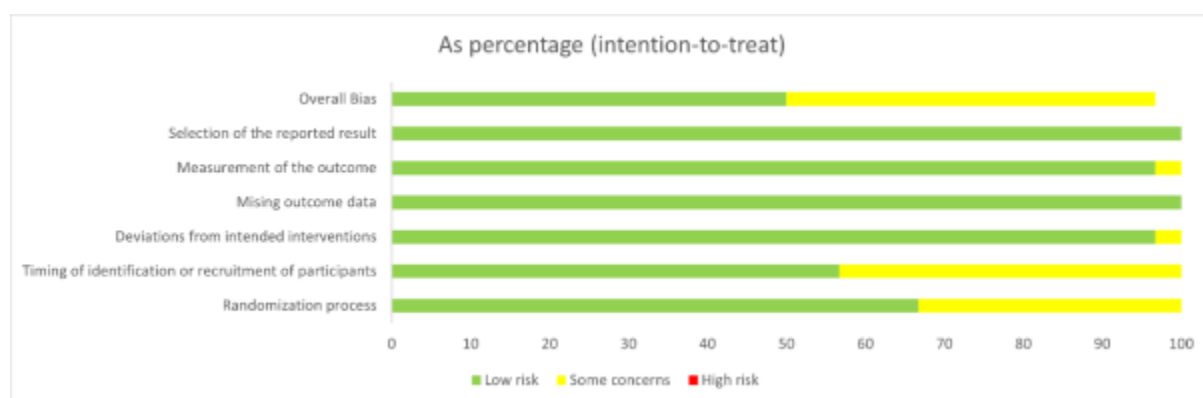
Supplementary Figure 26 Funnel plot of adverse events.



Supplementary Figure 27 Funnel plot of bleeding.



Supplementary Figure 28 Funnel plot of mortality rate



Intention-to-treat	Unique ID	D1a	D1b	D2	D3	D4	D5	Overall	
	Wang 2020	+	+	+	+	+	+	+	Low risk
	Romano 2021	+	+	+	+	+	+	+	Some concerns
	Patai 2015	+	+	+	+	+	+	+	High risk
	Elmunzer 2012	+	!	+	+	+	+	!	
	Levenick 2016	+	+	+	+	+	+	+	D1a Randomisation process
	Liu 2023	!	+	+	+	+	+	!	D1b Timing of identification or recruitment of participants
	Li 2019	+	!	+	+	+	+	!	D2 Deviations from the intended interventions
	Alizadeh 2017	+	+	+	+	+	+	+	D3 Missing outcome data
	ALAVINEJAD 2022	!	!	+	+	+	+	!	D4 Measurement of the outcome
	Guha 2023	!	!	+	+	+	+	!	D5 Selection of the reported result
	Sotoudehmanesh 2007	!	!	+	+	+	+	!	
	Andrade-Dóvila 2015	!	!	!	+	!	+	!	
	Qian 2022	+	+	+	+	+	+	+	
	Wu 2023	!	!	+	+	+	+	!	
	Döbrönte 2014	!	!	+	+	+	+	!	
	Fogel 2020	+	+	+	+	+	+	+	
	Norouzi 2023	+	+	+	+	+	+	+	
	Sadeghi 2023	!	!	+	+	+	+	!	
	Kamal 2019	+	+	+	+	+	+	+	
	Elmunzer 2024	+	+	+	+	+	+	+	
	Mahzangy 2022	+	!	+	+	+	+	!	
	Luo 2019	+	+	+	+	+	+	+	
	Hosseini 2016	+	+	+	+	+	+	+	
	Abdi 2024	+	!	+	+	+	+	!	
	Mok 2017	+	+	+	+	+	+	+	
	Sotoudehmanesh2 2014	+	+	+	+	+	+	+	
	Lai 2011	!	+	+	+	+	+	!	
	Sotoudehmanesh3 2019	+	+	+	+	+	+	+	
	Weiland 2021	!	!	+	+	+	+	!	
	Hatami 2018	+	!	+	+	+	+	!	

Supplementary Figure 29 Risk of bias results

Search strategy

Embase 2024 30 June

1# ('indomethacin'/exp OR indomethacin) AND ('pancreatitis'/exp OR pancreatitis)
890

2# 1# AND ('clinical article'/de OR 'clinical study'/de OR 'clinical trial'/de OR
'clinical trial topic'/de OR 'controlled clinical trial'/de OR 'controlled study'/de OR
'cross sectional study'/de OR 'double blind procedure'/de OR 'major clinical
study'/de OR 'multicenter study'/de OR 'multicenter study topic'/de OR
'observational study'/de OR 'prospective study'/de OR 'randomized controlled
trial'/de OR 'randomized controlled trial topic'/de OR 'single blind procedure'/de)
AND ('article'/it OR 'article in press'/it) 258

PubMed/MEDLINE

1# "indomethacin"[MeSH Terms] OR "indomethacin"[All Fields] OR
"indometacin"[All Fields] OR "indomethacine"[All Fields] 47228

2# "pancreas"[MeSH Terms] OR "pancreas"[All Fields] OR "pancreatic"[All Fields] OR
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Title,abstract,Keywords (indomethacin AND pancreatitis) 272

Lim (Eng and Article) 155

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