Supplementary material

Supplementary Table 1 Search strategy.
Ovid

Database(s): Embase 1988 to 2019 Week 41, EBM Reviews - Cochrane Central Register of Controlled Trials October 2019, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to October 09, 2019, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, and Daily 1946 to October 09, 2019

Search Strategy:

#	Searches
1	exp Necrosis/
2	exp Pancreas/ or exp Pancreatitis/
3	1 and 2
4	((pancrea* adj3 (necros* or necroti*)) or (pancrea* adj3 fluid* adj3 collection*) or "walled-off necros*" or "walled-off necroti*").mp.
5	3 or 4
6	(((endoscop* or transmural*) adj3 drain*) or ((metal* or plastic*) adj3 stent*) or "AXIOS stent*" or "double pigtail plastic stent*" or "endoscopic necrosectom*" or "lumen apposing metal stent*" or "metal stent*" or "plastic stent*" or "self-expanding metal stent*").mp.
7	5 and 6
8	limit 7 to english language [Limit not valid in CDSR; records were retained]
9	limit 8 to yr="1990 -Current"
10	9 not "conference abstract".pt.
11	(exp animals/ or exp nonhuman/) not exp humans/
12	((alpaca or alpacas or amphibian or amphibians or animal or animals or antelope or armadillo or armadillos or avian or baboon or baboons or beagle or beagles or bee or bees or bird or birds or bison or bovine or buffalo or buffaloes or buffalos or "c elegans" or "Caenorhabditis elegans" or camel or camels or canine or canines or carp or cats or cattle or chick or chicken or chickens or chicks or chimp or chimpanze or chimpanzees or chimps or cow or cows or "D melanogaster" or "dairy calf" or "dairy calves" or deer or dog or dogs or donkey or donkeys or drosophila or "Drosophila melanogaster" or duck or duckling or ducklings or ducks or equid or equids or equine or equines or feline or felines or ferret or ferrets or finch or finches or fish or flatworm or flatworms or fox or foxes or frog or frogs or "fruit flies" or "fruit fly" or "G mellonella" or "Galleria mellonella" or geese or gerbil or gerbils or goat or goats or goose or gorilla or gorillas or hamster or hamsters or hare or hares or heifer or heifers or horse or horses or insect or insects or jellyfish or kangaroo or kangaroos or kitten or kittens or lagomorph or lagomorphs or lamb or lambs or llama or llamas or macaque or macaques or macaw or macaws or marmoset or marmosets or mice or minipig or minipigs or mink or minks or monkey or monkeys or mouse or mule or mules or nematode or nematodes or octopus or octopuses or orangutan or "orang-utan" or orangutans or "orang-utans" or oxen or parrot or parrots or pig or pigeon or pigeons or piglet or piglets or pigs or porcine or primate or primates or quail or rabbit or rabbits or rat or rats or reptile or reptiles or rodent or rodents or ruminant or ruminants or salmon or sheep or shrimp or slug or slugs or

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	swine or tamarin or tamarins or toad or toads or trout or urchin or urchins or vole or voles or waxworm or waxworms or worm or worms or xenopus or "zebra fish" or zebrafish) not (human or humans)).mp.
13	10 not (11 or 12)
14	limit 13 to (editorial or erratum or letter or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in Embase,CCTR,CDSR,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]
15	from 14 keep 1-93
16	13 not 15
17	remove duplicates from 16

Scopus

1	TITLE-ABS-KEY((pancrea* W/3 (necros* or necroti*)) OR (pancrea* W/3 fluid* W/3 collection*) OR "walled-off necros*" OR "walled-off necroti*")
2	TITLE-ABS-KEY(((endoscop* or transmural*) W/3 drain*) OR ((metal* or plastic*) W/3 stent*) OR "AXIOS stent*" OR "double pigtail plastic stent*" OR "endoscopic necrosectom*" OR "lumen apposing metal stent*" OR "metal stent*" OR "plastic stent*" OR "self-expanding metal stent*")
3	PUBYEAR AFT 1989 AND LANGUAGE(english)
4	1 and 2 and 3
5	TITLE-ABS-KEY((alpaca OR alpacas OR amphibian OR amphibians OR animal OR animals OR antelope OR armadillo OR armadillos OR avian OR baboon OR baboons OR beagle OR beagles OR bee OR bees OR bird OR birds OR bison OR bovine OR buffalo OR buffaloes OR buffalos OR "c elegans" OR "Caenorhabditis elegans" OR camel OR camels OR canine OR canines OR carp OR cats OR cattle OR chick OR chicken OR chickens OR chicks OR chimp OR chimpanze OR chimpanzees OR chimps OR cow OR cows OR "D melanogaster" OR "dairy calf" OR "dairy calves" OR deer OR dog OR dogs OR donkey OR donkeys OR drosophila OR "Drosophila melanogaster" OR duck OR duckling OR ducklings OR ducks OR equid OR equids OR equine OR equines OR feline OR felines OR ferret OR ferrets OR finch OR finches OR fish OR flatworm OR flatworms OR fox OR foxes OR frog OR frogs OR "fruit flies" OR "fruit fly" OR "G mellonella" OR "Galleria mellonella" OR geese OR gerbil OR gerbils OR goat OR goats OR goose OR gorilla OR gorillas OR hamster OR hamsters OR hare OR hares OR heifer OR heifers OR horse OR horses OR insect OR insects OR jellyfish OR kangaroo OR kangaroos OR kitten OR kittens OR lagomorph OR lagomorphs OR lamb OR lambs OR llama OR llamas OR macaque OR macaques OR macaw OR macaws OR marmoset OR marmosets OR mice OR minipig OR minipigs OR mink OR minks OR monkey OR monkeys OR mouse OR mule OR mules OR nematode OR nematodes OR octopus OR octopuses OR orangutan OR "orang-utan" OR orangutans OR "orang-utans" OR oxen OR parrot OR parrots OR pig OR pigeon OR pigeons OR piglet OR piglets OR pigs OR porcine OR primate OR primates OR quail OR rabbit OR rabbits OR rat OR rats OR reptile OR reptiles OR rodent OR rodents OR ruminant OR ruminants OR salmon OR sheep OR shrimp OR slug OR slugs OR swine OR tamarin OR tamarins OR toad OR toads OR trout OR urchin OR

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	urchins OR vole OR voles OR waxworm OR waxworms OR worm OR worms OR xenopus OR "zebra fish" OR zebrafish) AND NOT (human OR humans))
6	4 and not 5
7	DOCTYPE(le) OR DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh) OR DOCTYPE(ab)
8	6 and not 7
9	PMID(0*) OR PMID(1*) OR PMID(2*) OR PMID(3*) OR PMID(4*) OR PMID(5*) OR PMID(6*) OR PMID(7*) OR PMID(8*) OR PMID(9*)
10	8 and not 9

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Supplementary Table 2 Assessment of methodologic quality of studies utilizing a modified Newcastle-Ottawa Scale.

Study	Year	Question 1		Question 2		Question 3		Question 4		Question 5		Methodologic Quality
		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	
Kumar [1]	2014	X		X		X			X	X		Moderate
Lin [2]	2014	X		X		X		X		X		Good
Rana [3]	2014	X		X			X		X		X	Poor
Rana [4]	2015	X			X	X			X		X	Poor
Rinninella [5]	2015	X		X		X		X		X		Good
Smoczynski [6]	2015	X			X	X		X		X		Moderate
Walter [7]	2015	X		X			X	X		X		Moderate
Sharaiha [8]	2016	X		X		X		X		X		Good
Siddiqui [9]	2016	X		X		X		X		X		Good
Storm [10]	2016		X	X			X	X		X		Poor
Thompson [11]	2016	X		X		X			X	X		Moderate
Adler [12]	2017		X	X		X			X		X	Poor
Bang [13]	2017	X		X		X		X		X		Good
Bapaye [14]	2017	X		X			X	X		X		Moderate
Bekkali [15]	2017	X			X		X	X		X		Poor
He [16]	2017	X		X		X		X		X		Good
Rana [17]	2017	X			X		X		X		X	Poor
Ren [18]	2017	X			X	X			X		X	Poor
Siddiqui [19]	2017	X		X		X		X		X		Good
Tarantino [20]	2017	X		X		X		X		X		Good
Watanabe [21]	2017	X		X		X		X		X		Good
Yoo [22]	2017		X	X		X		X		X		Moderate
Abu Dayyeh [23]	2018	X		X		X		X		X		Good
Garcia-Alonso [24]	2018	X			X	X		X		X		Moderate
Law [25]	2018	X		X			X	X		X		Moderate
Shekhar [26]	2018	X		X		X		X		X		Good
Venkatachalapathy [27]	2018	X		X		X		X		X		Good
Yang [28]	2018	X		X		X		X		X		Good
Bang [29]	2019	X		X		X		X		X		Good

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Study	Year	Question 1		Question 2		Question 3		Question 4		Question 5		Methodologic Quality
		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	
Chen [30]	2019	X		X		X		X		X		Good

Questions:

1. Did the patient(s) represent the whole case(s) of the medical center? Cases included represented the general population of walled-off-necrosis.

2. Was the diagnosis correctly made? Based on the revised Atlanta criteria.

3. Was follow-up long enough for outcomes to occur? Reported adequate follow-up time.

4. Were all important data cited in the report? Reported resolution and at least 2 outcomes.

5. Was the outcome correctly ascertained? Provided definition of resolution.

Supplementary material

Supplementary Table 3 Status of studies included in Bazerbachi 2018 [31].

Author (year)	Status	Rationale
Abu Dayyeh (2018) [23]	Kept LAMS only	Mixed EUS for DPPS
Lakhtakia (2017) [32]	Dropped	No DPPS, LAMS were non-AXIOS
Ang (2016) [33]	Dropped	Had DPPS, LAMS were non-AXIOS, no results given for endpoints of interest
Sharaiha (2016) [8]	Kept	
Siddiqui (2017) [19]	Kept	
Siddiqui (2016) [9]	Kept	
Smocyzinski (2016) [34]	Dropped	Duplicate data
Storm (2016) [10]	Kept	
Thompson (2016) [11]	Kept	
Sharma (2016) [35]	Dropped	Mixed EUS, no EUS-stratified results
Keane (2016) [36]	Dropped	No results given for endpoints of interest
Gornals (2016) [37]	Dropped	Duplicate data
Bang (J Pediatr Gastroenterol 2016) [38]	Dropped	Duplicate data
Bang (Dig Endosc 2017) [13]	Kept LAMS only	Mixed EUS for DPPS
Bang (Gut 2017) [39]	Dropped	Interim data, replaced by Bang (2019)
Albers (2016) [40]	Dropped	No DPPS, LAMS were non-AXIOS
Walter (2015) [7]	Kept	
Smocyzinski (2015) [6]	Kept	
Smith (2015) [41]	Dropped	No DPPS and no LAMS
Rana (2014) [3]	Kept	
Schmidt (2015) [42]	Dropped	Mixed EUS, no EUS-stratified results
Rinninella (2015) [5]	Kept	
Rana (2015) [4]	Kept	
Mukai (Endosc Ultrasound 2015) [43]	Dropped	No DPPS, LAMS were non-AXIOS
Bapaye (2017) [14]	Kept	
Nabi (2017) [44]	Dropped	No DPPS, LAMS were non-AXIOS
Mukai (Endoscopy 2015) [45]	Dropped	Too few patients: 2 DPPS, 3 LAMS
Jagielski (2015) [46]	Dropped	Duplicate data
Hugget (2015) [47]	Dropped	No DPPS, LAMS were non-AXIOS
Chandran (2015) [48]	Dropped	No DPPS, LAMS were non-AXIOS
Smocyzinski (2014) [49]	Dropped	No EUS
Saxena (2014) [50]	Dropped	No DPPS and no LAMS
Mukai (GIE 2014)	Dropped	Used multiple gateway technique for DPPS patients, cannot separate AXIOS from LAMS data
Lin (2014) [2]	Kept	
Kumar (2014) [1]	Kept	
Attam (2014) [51]	Dropped	No DPPS, LAMS were non-AXIOS
Yamamoto (2013) [52]	Dropped	No DPPS, LAMS were non-AXIOS
Varadarajulu (2011) [53]	Dropped	Mixed EUS, no EUS-stratified results
Gardner (2011) [54]	Dropped	Mixed EUS, no EUS-stratified results
Gardner (2009) [55]	Dropped	Mixed EUS, no EUS-stratified results
Papachristou (2007) [56]	Dropped	Mixed EUS, no EUS-stratified results

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Supplementary Table 4 Definitions of WON size across studies.

Size of Long Axis	Maximal Dimension/Diameter/ Size	Other	Not Defined	Not Collected/ Recorded
Bang [13]	Abu Dayyeh [23]	Bang [29] – Provided both transverse and anteroposterior axes measurements	Adler [12]	He [16]
Siddiqui [19]	Bapaye [14]	Law [25] - Diameter	Bekkali [15]	Rana [4]
Siddiqui [9]	Rinninella [5]	Ren [18] - Cyst size in 2 dimensions, e.g. 7 x 8 cm	Chen [30]	Storm [10]
Watanabe [21]	Venkatachalapathy [27]	Sharaiha [8] - Diameter	Garcia-Alonso [24]	Thompson [11]
Yang [28]		Tarantino [20] – Diameter	Kumar [1]	
Yoo [22]			Lin [2]	
			Rana [3]	
			Rana [17]	
			Shekhar [26]	
			Smocyzinski [6]	
			Walter [7]	

WON, walled-off necrosis.

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Supplementary Table 5 Analysis of heterogeneity by outcome and stent type in all (comparative and non-comparative) studies.

Stent	Outcome	# of Studies	# of Patients	I^2 (95% CI)
LAMS	Bleeding	14	741	76.1 (60.0, 85.8)
Plastic	Bleeding	10	381	71.8 (46.5, 85.2)
LAMS	Perforation	12	545	17.7 (0.0, 57.0)
Plastic	Perforation	6	287	0.0 (0.0, 68.9)
LAMS	Stent Migration	15	788	81.6 (70.7, 88.4)
Plastic	Stent Migration	5	318	68.3 (18.2, 87.7)
LAMS	Stent Occlusion	13	730	86.6 (78.8, 91.5)
Plastic	Stent Occlusion	4	239	90.1 (77.6, 95.6)
LAMS	WON Resolution	16	827	66.5 (43.4, 80.2)
Plastic	WON Resolution	15	614	82.8 (72.9, 89.1)

LAMS, lumen-apposing metal stents; WON, walled-off necrosis.

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Supplementary Table 6 Definitions of bleeding across studies.

Defined	Defined as Requiring Transfusion	Not Defined in Methods, but Bleeding Event(s) Described as Follows in the Results	Not Defined	Not Collected/ Recorded
Garcia-Alonso [24] Any GI bleed presenting as hematemesis, melena, hematochezia, or rectal bleeding, with endoscopic or radiologic documentation of the fistula as the source of bleeding	Bapaye [14]	Abu Dayyeh [23] -Bleeding requiring endoscopic intervention -Bleeding requiring IR -Bleeding requiring surgery	Adler [12]	Bang [13]
He [16] -GI Bleeding: 500 ml of blood/24 hours) -Intra-abdominal bleeding: requiring surgical, radiologic, or endoscopic intervention	Kumar [1]	Law [25] "significant"	Bekkali [15]	Rana [3]
Rinninella [5] Any hemorrhagic event requiring endotherapy, radiologic interventions, blood product transfusion, or inpatient observation		Lin [2] "bleeding from puncture site"	Ren [18]	Rana [17]
Sharaiha [8] Graded according to American Society for GI Endoscopy lexicon severity grading system		Shekhar [26] Resolved, with or without intervention	Smocyzinski [6]	Rana [4]
		Siddiqui [9] "self-limiting"	Storm [10]	
Thompson [11] Bleeding requiring subsequent endoscopic or radiologic procedures for hemostasis		Siddiqui [19] "bleeding at stent site"	Tarantino [20]	
		Walter [7] "self-limited device-related bleeding"	Yoo [22]	
		Bang [29] Various descriptions		
		Venkatachalapathy [27] – Bleeding requiring transfusion and embolization		
		Yang [28] – "self-limited bleeding," "bleeding from the initial LAMS insertion tract required embolization,"		

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Supplementary Table 7 Definitions of perforation across studies.

Pneumoperitoneum on Imaging plus Peritoneal Signs	Perforation of WON Wall or Capsule	Not Defined in Methods, but Described as Follows in the Results	Not Defined	Not Collected/ Recorded
Rinninella [5]	Kumar [1]	Abu Dayyeh [23] - Perforation requiring surgery; Perforation managed non-surgically	Bekkali [15]	Bang [13]
	Thompson [11]	Adler [12] - "perforation from the creation of cystenterostomy"	Chen [30]	Bapaye [14]
		Bang [29] – Perforation and peritoneal leakage of pancreatic fluid collection contents	Garcia-Alonso [24]	Law [25]
		Gardner [55] - "luminal perforations"	He [16]	Lin [2]
		Sharaiha [8] - Graded according to American Society for GI Endoscopy lexicon severity grading system	Ren [18]	Rana [3]
		Siddiqui [19] - "The perforations were not a result of the stent design but a result of operator stent maldeployment"	Tarantino [20]	Rana [17]
		Smocyzinski [6] - "Perforation of the GI tract occurred during fistulotomy formation"	Walter [7]	Rana [4]
		Watanabe [21] - events of "pneumoperitoneum" and "puncture into another organ" described	Yang [28]	Shekhar [26]
			Yoo [22]	Siddiqui [9]
				Storm [10]
				Venkatachalapathy [27]

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Supplementary Table 8 Definitions of stent migration across studies.

Stent Migration Within or Outside of WON	Need to Retrieve Stent from Within WON or Enteral Lumen	Other Definitions	Not Defined in Methods, but Described as Follows in the Results	Not Defined	Not Collected/ Recorded
Bang [13]	Rinninella [5]	Bang [29] – Migration into the gastrointestinal tract	Bapaye [14] - "outward migration"	Adler [12]	Kumar [1]
Law [25]		Bekkali [15] - Defined according to Lakhtakia et al.† [32]	He [16] - "stent migration during direct endoscopic necrosectomy"; "stent migration into fistula tract"; "spontaneous stent migration"	Chen [30]	Lin [2]
		Garcia-Alonso [24] - radiologic and/or endoscopic confirmation of spontaneous dislodgment of the LAMS, appearing after the deployment of the stent and unrelated to the index or further endoscopic procedures through the stent; further classified as symptomatic or asymptomatic, internal or external	Sharaiha [8] - "All migrations occurred during DEN"	Ren [18]	Rana [3]
		Law [25] - Dislodgement during necrosectomy	Siddiqui [19] - "stent migration out of the WON cavity"	Siddiqui [9]	Rana [17]
		Tarantino [20] - Interprocedural dislodgement of stent with worsening of clinical conditions	Yoo [22] - "spontaneous migration into the enteral lumen after resolution of WONs"	Smocyzinski [6]	Rana [4]
		Venkatachalapathy [27] - Migration of stent without manipulation. Clinically significant or insignificant.		Storm [10]	Shekhar [26]
		Yang [28] – Interval change in the position (inward towards the gastrointestinal lumen or		Walter [7]	Thompson [11]

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outward towards the PFC) of the LAMS	Watanabe [21]

†Clinically insignificant
– spontaneous external migration of stent after complete resolution of WON
Clinically significant
– internal migration – migration of the stent into the cavity, with or without persistent WON
– external migration – migration of the stent with persistent WON

WON, walled-off necrosis; LAMS, lumen-apposing metal stent; PFC, pancreatic fluid collection.

Supplementary Table 9 Definitions of WON resolution in included studies.

Absent	CRR + SR	CRR	SR	WON Size ≤ 2 CM + SR	WON Size ≤ 3 CM + SR	RI + SR
Adler [12]	Abu Dayyeh [23]	He [16]	Kumar [1]	Bang [13]	Chen [30]	Bapaye [14]
Garcia-Alonso [24]	Bang [29]	Rinninella [5]	Storm [10]	Law [25]	Smoczynski [6]	
Rana [3]	Bekkali [15]	Sharaiha [8]	Venkatachalapathy [27]	Lin [2]	Yang [28]	
Rana [4]	Shekhar [26]			Walter [7]		
Rana [17]	Siddiqui [19]			Watanabe [21]		
Ren [18]	Siddiqui [9]					
	Tarantino [20]					
	Thompson [11]					
	Yoo [22]					

CRR, complete radiologic resolution; SR, symptom resolution; RI, radiologic improvement; WON, walled-off necrosis.

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Supplementary Table 10 Summary of efficacy and safety meta-analytic outcomes for LAMS (all EUS-guided) vs. DPPS (with or without EUS guidance, including eight additional studies: Papachristou 2017 [56], Gardner 2009 [55], Gardner 2011 [54], Varadarajulu 2011 [53], Smoczynski 2014 [49], Schmidt 2015 [42], Sharma 2016 [35], Jagielski 2018 [57])

	LAMS (EUS-guided only)			DPPS (with and without EUS guidance)			*P* value
	N studies	N patients	% (95% CI)	N studies	N patients	% (95% CI)	
Safety Outcomes							
Bleeding	14	741	2.5% (0.7%, 5.5%)	19	903	9.0% (5.1%, 13.9%)	0.009
Perforation	12	545	0.5% (0.0%, 1.3%)	13	735	2.6% (1.3%, 4.4%)	0.005
Stent migration	15	788	5.9% (2.6%, 10.6%)	11	601	5.3% (2.6%, 9.0%)	0.82
Stent occlusion	13	73 0	3.8% (0.9%, 8.7%)	6	310	7.0% (1.1%, 17.4%)	0.47
Efficacy Outcomes							
Resolution of WON	16	827	87.4% (83.0%, 91.3%)	25	1162	83.8% (78.1%, 88.9%)	0.30
Number of procedures to achieve resolution	2	115	2.09 (1.05, 3.13)	10	308	1.83 (1.54, 2.11)	0.64
Total unique studies or patients	17	899		26	1173		

LAMS, lumen-apposing metal stent; EUS, endoscopic ultrasound; DPPS, double-pigtail plastic stents; WON, wall-off necrosis.

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Supplementary Table 11 Publication bias testing.

	Rank correlation test of funnel plot asymmetry (Begg and Mazumdar)		Rank correlation test of funnel plot asymmetry (with continuity correction) (Begg and Mazumdar)		Linear regression test of funnel plot asymmetry (Eggers)	
Outcome	**LAMS**	**DPPS**	**LAMS**	**DPPS**	**LAMS**	**DPPS**
Bleeding	0.74	0.53	0.78	0.59	0.63	0.61
Perforation	0.63	0.57	0.68	0.71	0.15	0.94
Occlusion	1.00	0.33	1.00	0.46	0.73	0.24
Migration	0.43	0.17	0.46	0.31	0.17	0.059
Resolution	0.39	0.11	0.42	0.12	0.23	0.026
Number of Procedures *	--	0.57	--	0.71	--	0.42

All numbers are *P* values from the rank correlation or linear regression tests for funnel plot symmetry.
* - the test could not be conducted for the LAMS studies because only two studies were available.
LAMS, lumen-apposing metal stent; DPPS, double-pigtail plastic stent.

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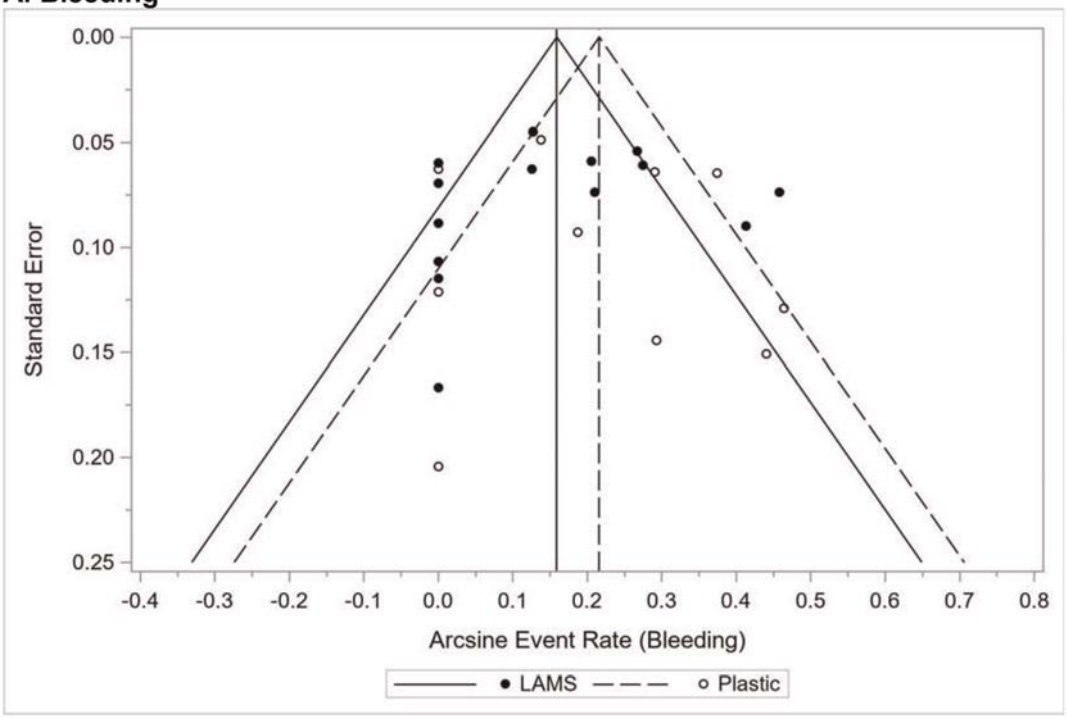
Supplementary Fig. 1 Funnel plots for studies of LAMS compared to DPPS safety and efficacy outcomes. **a** Bleeding. **b** Perforation. **c** Stent migration. **d** stent occlusion; **e** Overall WON resolution. **f** number of endoscopic procedures to achieve resolution.

A. Bleeding



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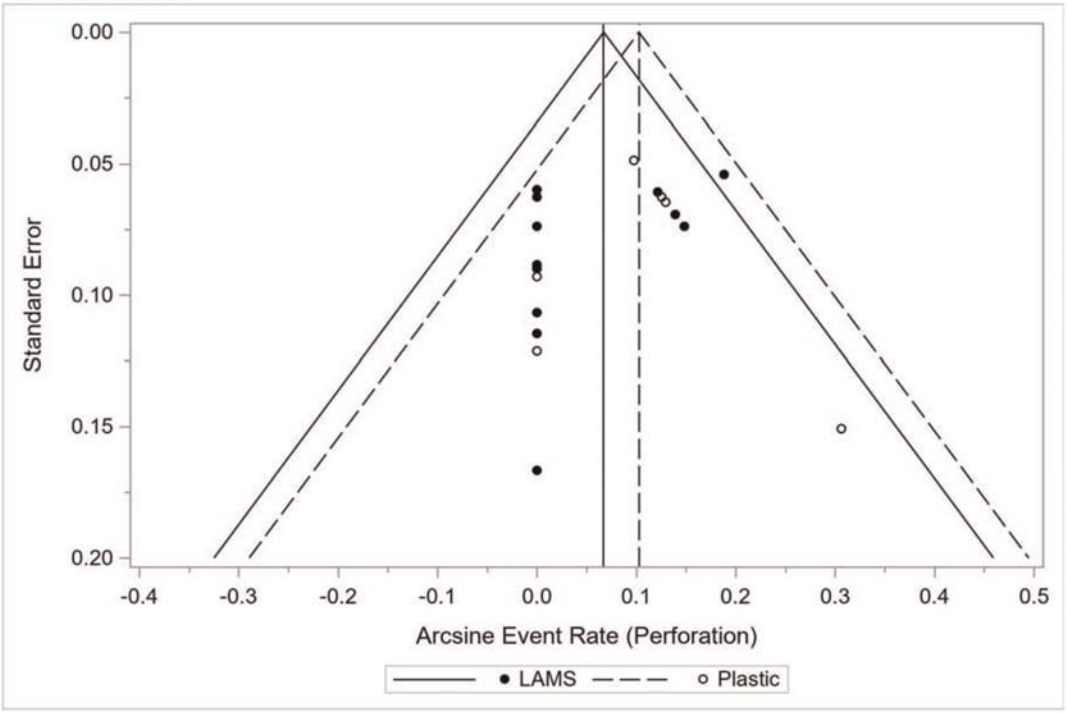
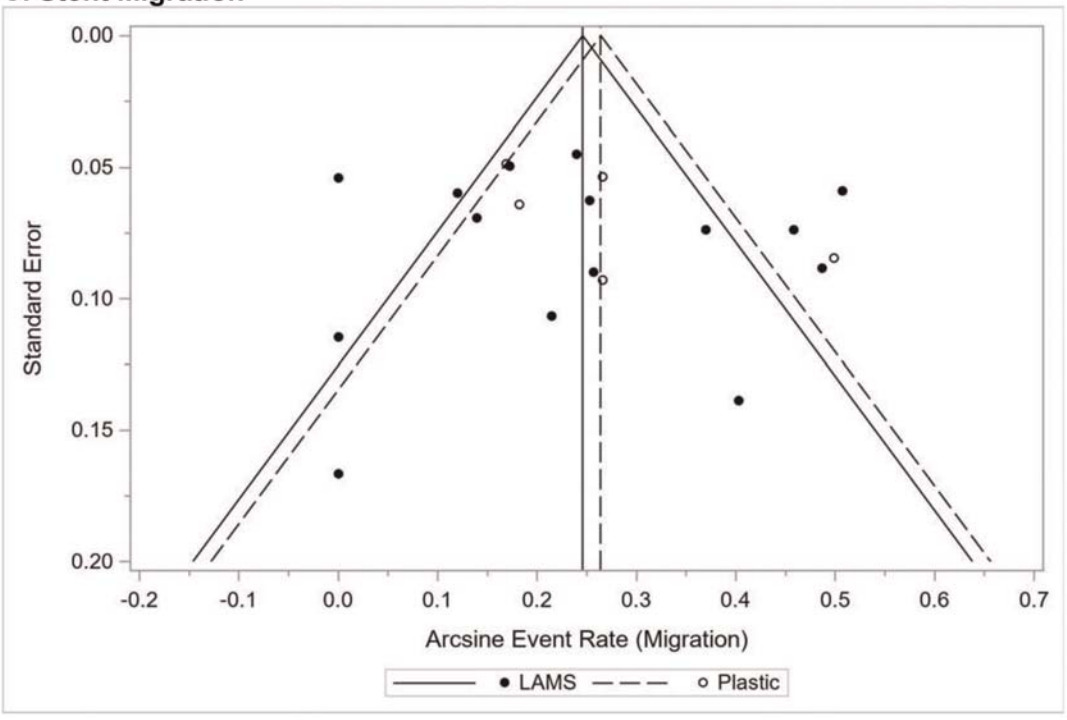
B. Perforation



C. Stent Migration



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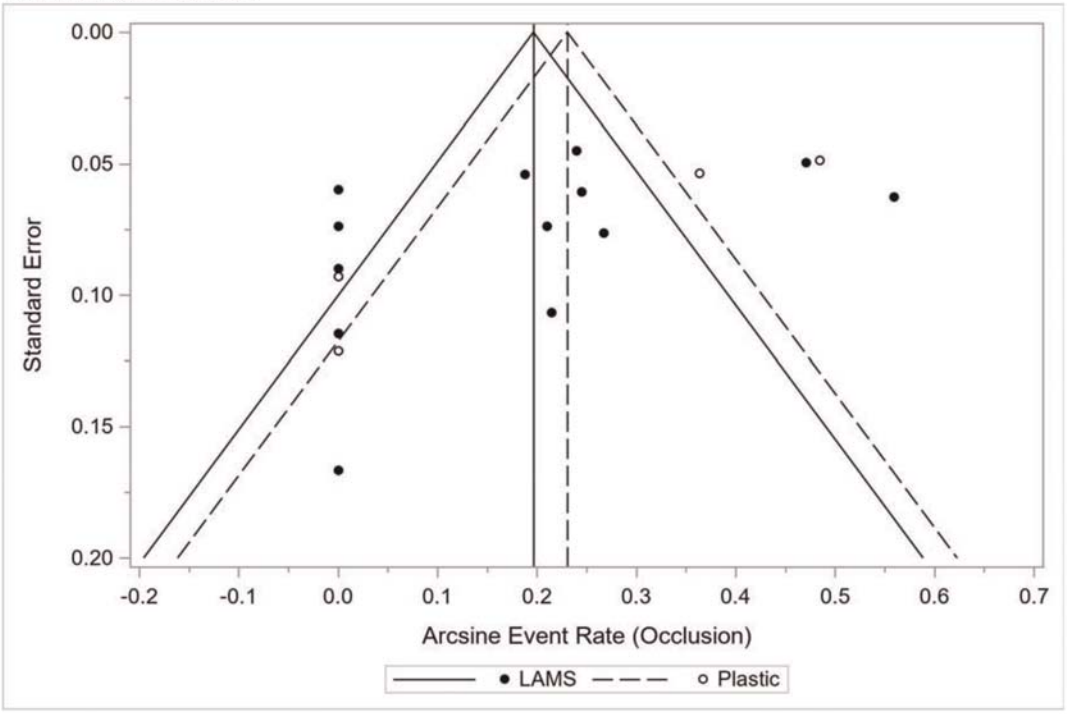
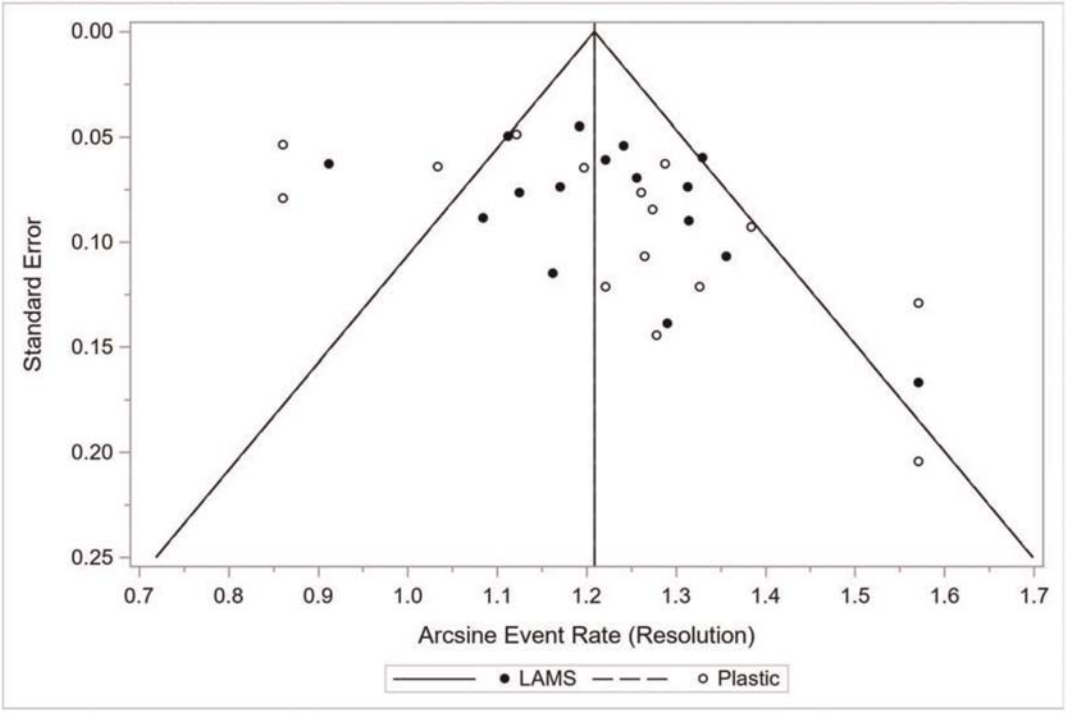
D. Stent Occlusion



E. WON Resolution



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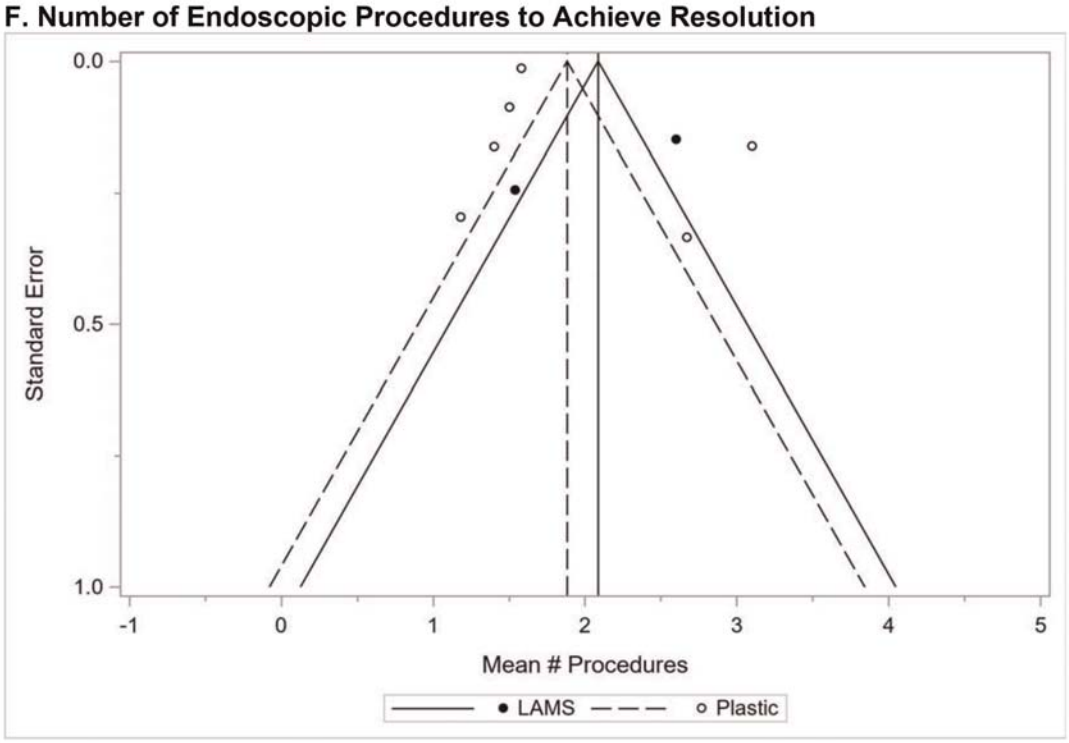

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