Communication from the ASGE Standards of Practice Committee

GUIDELINE

ASGE American Society for Gastrointestinal Endoscopy

American Society for Gastrointestinal Endoscopy guideline on the role of endoscopy in the management of chronic pancreatitis: methodology and review of evidence

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This document was reviewed and approved by the Governing Board of the American Society for Gastrointestinal Endoscopy.

This guideline document was prepared by the Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy using the best available scientific evidence and considering a multitude of variables including but not limited to adverse events, patient values, and cost implications. The purpose of these guidelines is to provide the best practice recommendations that may help standardize patient care, improve patient outcomes, and reduce variability in practice. We recognize that clinical decision-making is complex. Guidelines therefore are not a substitute for a clinician's judgment. Such judgements may at times seem contradictory to our guidance because of many factors that are impossible to fully consider by guideline developers. Any clinical decisions should be based on the clinician's experience, local expertise, resource availability, and patient values and preferences. This document is not a rule and should not be construed as establishing a legal standard of care or as encouraging, advocating for, mandating, or discouraging any particular treatment. Our guidelines should not be used in support of medical complaints, legal proceedings, and/or litigation, as they were not designed for this purpose.

Chronic pancreatitis (CP) is a progressive and irreversible fibroinflammatory disorder of the pancreas that may result in chronic abdominal pain and exocrine and endocrine insufficiency.[1,2] Morphologically, CP may be characterized by the development of pancreatic duct (PD) stones and PD strictures or complicated by the development of biliary strictures and pseudocysts. Although the pain in CP is multifactorial and complex, some patients may have pain from an obstructed PD with resultant ductal hypertension and pancreatic inflammation and may benefit from endoscopic therapy.[3] Therefore, the American Society for Gastrointestinal Endoscopy (ASGE) aimed to develop evidence-based guidelines for the role of endoscopy in the management of CP using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology.[4,5] In formulating these guidelines, we conducted extensive literature reviews, including formal systematic reviews of the literature and meta-analyses. To make all information we collected and analyzed readily accessible, this guideline is presented in 2 documents: Methodology and Review of Evidence (presented here) and Summary and Recommendations.

METHODS

The aim of this document is to describe the methodology used in this process and to provide a detailed review of the evidence used to inform the guideline panel. It details the formulation of clinical questions, literature searches, data analyses, panel composition, evidence profiles, and other considerations such as cost-effectiveness, patient preferences, and health equity. For each clinical question, this document includes outcomes of interest, pooled-effects estimates, and evidence that was considered by the panel in making the final recommendations. A separate publication of Summary and Recommendations provides a summary of the main findings and final recommendations

of the ASGE Standards of Practice Committee for the role of endoscopy in the management of CP.

Formulation of clinical questions

The panel addressed 6 questions (including subquestions) relevant to the role of endoscopy in the management of CP using the GRADE methodology (Table 1). For these questions, we followed the PICO format: P, population in question; I, intervention; C, comparator; and O, outcomes of interest. For all clinical questions, potentially relevant patient-important outcomes were identified a priori and rated as "critical," "important," or "not important" for decision-making through a consensus process. The "critical" and "important" outcomes were retained for the evidence review.

Literature search and study selection criteria

For each PICO question, we searched for existing systematic reviews of available randomized controlled trials (RCTs). We performed systematic reviews and meta-analyses to address PICO questions 1, 2, and 5, for which RCTs were available. Only systematic reviews were performed for PICO questions 3, 4 (observational comparative cohort studies), and 6 (1 RCT only) because of low sample sizes.

A health sciences librarian devised the search strategy and systematically searched the following: Ovid MEDLINE, EMBASE (Elsevier), and the Cochrane Library (Wiley) separately on November 12, 2021 for each PICO question. The filters were applied to include only RCTs, meta-analyses, systematic reviews, and prospective or retrospective comparative studies published after January 1, 2001 in English on human subjects. A combination of subject headings (when available) and keywords were used and are provided in Appendix 1 (available online at www.giejournal.org). Cross-referencing and forward searches of the citations from articles fulfilling the inclusion criteria and other pertinent articles were performed after the date of search until December 31, 2022. Eligible studies contained the population of interest, intervention, comparators, and associated outcomes of the PICO questions. Citations were imported into EndNote x9.2 (Clarivate Analytics, Philadelphia, Pa, USA) and duplicates were removed using the Bramer method[6] and uploaded into Covidence (Melbourne, Australia) for screening. Studies were first screened by title and abstract and then by full text by 2 independent reviewers (S.G.S. and J.D.M.), and all conflicts were resolved by discussion.

Data extraction and statistical analysis

Two independent reviewers (S.G.S. and A.C.) extracted data from the eligible studies using Microsoft Excel (Microsoft Corporation, Redmond, Wash, USA). The primary effect measures were based on a priori–identified outcomes of interest. Meta-analytic summary statistics were performed including odds ratios (ORs) and cumulative difference in means for PICO questions 1, 2, and 5. We narratively summarized findings from eligible studies for PICO questions 3, 4, and 6. We used the DerSimonian and Laird random-effects model for meta-analysis of all outcomes in anticipation of heterogeneity among the source studies. Statistical heterogeneity was quantified using the I^2 and Q statistics. Significant heterogeneity was defined at $I^2 > 50\%$ and significant P value (<.05) on the Q statistic. Meta-analyses with high I^2 values and wide confidence intervals (CIs) underwent sensitivity analysis. Publication bias was assessed if there were more than 10 studies for the specific PICO question.[7] Two reviewers (S.G.S. and A.C.) assessed the risk of bias among RCTs using the Cochrane RoB 2.0 tool and ROBINS-I tool for nonrandomized observational cohort studies.[8,9] Statistical analyses were performed using STATA 17.0 (StataCorp, College Station, Tex, USA).

Panel composition and conflict of interest management. On January 21, 2023, we assembled a panel of stakeholders to review evidence and make recommendations in a virtual meeting. The panel consisted of lead authors (S.G.S. and J.D.M.), content experts independent of the Standards of Practice Committee (C.F. and N.Z.), a GRADE methodologist (B.J.Q.), and Standards of Practice Committee members with expertise in methodology and systematic reviews and meta-analyses, chaired by a committee chair (B.J.Q.). A patient representative (Michele Knoy) from the National Pancreas Foundation was also included.

All panel members were required to disclose potential financial and intellectual conflicts of interest, which were addressed according to ASGE policies set forth in the ASGE & Journal Policy for Managing Declared Conflicts of Interest found at https://www.asge.org/docs/default-source/default-document-library/coi-full-policy-for-asge-and-publications_edd_2-10-20.pdf. Panel members who received funding for any technologies or companies associated with any of the PICO questions or had other relevant conflicts of interest were asked to declare their conflicts before the discussion and did not vote on the final recommendation addressing that specific PICO question. In addition, the lead authors and committee chair did not vote on final recommendations per Standards of Practice Committee protocol.

Certainty in the evidence

We used the GRADE approach to determine the certainty (quality) in the evidence and confidence in the effect estimates. With this approach, the certainty in effect estimates is categorized into 1 of 4 levels: high, moderate, low, and very low based on considerations of risk of bias, imprecision, inconsistency, indirectness, and publication bias (Table 2). The evidence profiles were generated using GRADEpro/GDT applications (https://gdt.guidelinedevelopment.org/app).

External review

The guideline was reviewed by the *Gastrointestinal Endoscopy* Editorial Board and the ASGE Governing Board and was made available for public comment for 30 days on the ASGE website.

TABLE 1. List of population, intervention, comparator, and outcome questions addressed

Population	Intervention	Comparator	Outcomes	Rating
1. Painful CP and obstructed main PD	Endoscopy	Surgery	1. Mortality 2. Pain relief 3. Technical success 4. Adverse events 5. Physical and mental quality of life 6. Diabetes 7. Exocrine insufficiency	Critical Critical Critical Critical Important Important Important
2. Painful CP on medical therapy undergoing CPB	EUS-guided CPB	Percutaneous CPB	1. Pain relief (at 1, 4, 12 wk) 2. Decrease in pain intensity 3. Adverse events	Critical Critical Critical
3. Patients with painful CP with main PD stones requiring lithotripsy and not undergoing ERCP alone for complete stone clearance				
3a.	Pancreatoscopy ± lithotripsy	Extracorporeal shock wave lithotripsy	1. Technical success 2. Clinical success 3. Number of procedures 4. Procedure time 5. Adverse events	Critical Critical Important Important Important
3b.	ESWL alone	Extracorporeal shock wave lithotripsy and ERCP	1. Mortality 2. Stone clearance 3. Pain relief 4. Adverse events	Critical Critical Critical Important
4. Patients with painful CP and main PD stricture undergoing ERCP and pancreatic duct stent placement				
4a. Initial treatment of dominant main PD stricture	Single plastic stent	Multiple plastic stents	1. Pain relief 2. Mortality 3. Number of ERCP sessions 4. Recurrence/recurrent stent placement 5. Exocrine insufficiency 6. Diabetes	Critical Critical Important Important Important Important
4b. Initial treatment of dominant main PD stricture	Single 10F plastic stent	≤8.5F plastic stent	1. Hospitalization for abdominal pain	Critical
4c. Treatment of persistent PD stricture	Single plastic stent	Fully covered self-expandable metal stent	1. Technical success 2. Clinical success 3. Stricture resolution 4. Pain relief 5. Stent exchange 6. Duration of stent placement 7. Number of ERCP sessions 8. Adverse effects	Critical Critical Critical Critical Important Important Important Important
5. CP complicated by benign biliary strictures and jaundice/elevated alkaline phosphatase >4 wk	Multiple plastic stents	Fully covered self-expandable metal stent	1. Number of ERCP sessions 2. Number of stents placed 3. Stricture resolution 4. ERCP time 5. Time to resolution 6. Adverse events 7. Mortality	Critical Important Critical Important Important Critical Critical
6. CP complicated by symptomatic pseudocysts	Endoscopic drainage	Surgical drainage	1. Treatment success 2. Recurrence 3. Adverse events 4. Length of hospital stay 5. Physical and mental quality of life 6. Reintervention	Critical Critical Critical Important Important Important

CP, Chronic pancreatitis; *PD*, pancreatic duct; *CPB*, celiac plexus block; *ESWL*, extracorporeal shockwave lithotripsy.

TABLE 2. Grading of Recommendations, Assessment, Development, and Evaluation categories of quality of evidence

Grading of Recommendations, Assessment, Development, and Evaluation quality of evidence	Meaning	Interpretation
High	We are confident that the true effect lies close to that of the estimate of the effect.	Further research is very unlikely to change our confidence in the estimate of the effect.
Moderate	We are moderately confident in the estimate of the effect; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.	Further research is likely to have an impact on our confidence in the estimate of the effect and may change the estimate.
Low	Our confidence in the estimate of the effect is limited; the true effect may be substantially different from the estimate of the effect.	Further research is very likely to have an impact on our confidence in the estimate of the effect and is likely to change the estimate.
Very low	We have very little confidence in the estimate of the effect; the true effect is likely to be substantially different from the estimate of the effect.	Any estimate of the effect is very uncertain.

RESULTS

Question 1: In patients with painful CP and an obstructed main PD, how does endoscopic therapy compare with surgical management for pain relief?

Recommendation 1:

a. In patients with painful CP and an obstructed main PD with no contraindications to surgery, the ASGE suggests surgical evaluation before initiation of endoscopic management.

b. Otherwise, in patients with contraindications to surgery or those who prefer a less-invasive approach, the ASGE suggests endoscopic management as the initial approach.

(Conditional recommendation/low to moderate quality of evidence)

We performed a systematic review and meta-analysis of studies in CP patients with a main PD obstruction. A search through November 12, 2021 yielded 185 citations that were screened by 2 independent reviewers (S.G.S. and J.D.M.) (Appendix 1). Six studies were assessed for eligibility, of which 4 RCTs fulfilled the inclusion criteria.[10-15] We conducted a meta-analysis of RCTs, which included 3 of the 4 RCTs because 1 study included the same population but with a shorter follow-up period. These RCTs compared the outcomes of surgical intervention with endotherapy in 199 CP patients with obstructed main PDs.[10-15]

CP was diagnosed based on imaging studies, exocrine pancreatic insufficiency, or both in these patients. Most patients had pain that was nonresponsive to conservative management.[10-15] The common criteria for exclusion included prolonged opioid use, prior surgical or endoscopic intervention, suspected malignancy, poor surgical candidacy (American Society of Anesthesiologists class IV, severe portal hypertension, etc), or pregnancy (Supplementary Table 1, available online at www.giejournal.org).[10-15] Endoscopic procedures included a combination of pancreatic ductal sphincterotomy, dilation of strictures, PD stent placement, and lithotripsy and/or stone extraction.[10-15] Surgical procedures included drainage procedures such as pancreatojejunostomy (majority) and duodenum-preserving pancreatic head resection, distal pancreatectomy, and pylorus-preserving pancreatoduodenectomy.[10-15] Patient characteristics and study outcomes are summarized in Supplementary Tables 2 and 3 (available online at www.giejournal.org).

Outcomes

For this clinical question, the outcomes of interest were mortality, pain relief (quantified using Izbicki and Melzack scores[16,17]), technical success, adverse events, quality of life, and pancreatic function (Figs. 1 and 2). These results are summarized in an evidence profile (Table 3).

1. *Mortality.* No intervention-related deaths were reported in either group.[11,12,15] Overall observed deaths between endoscopic and surgical groups also lacked statistical difference. The RCTs led by Cahen et al[11,12] reported 4 overall deaths in the surgery group compared with 3 in the endoscopy group, whereas Issa et al[15] reported no deaths in either group.
2. *Technical success.* The technical success of endotherapy was significantly lower than surgical intervention (OR, .07; 95% CI, .02-.24; $I^2 = 0\%$) (Fig. 2A).[11,15]
3. *Adverse events.* Adverse events were reported to be similar in both groups (OR, 2.31; 95% CI, .31-17.30; $I^2 = 81.78\%$) (Fig. 2B).[11,12,15]
4. *Duration of hospital stay.* Among all eligible studies, duration of hospital stay lacked statistical difference in both the endoscopic and surgical groups and varied in the 5 studies that were individually analyzed (Table 3). Moreover, no trend favoring endoscopic or surgical intervention was observed in these studies.[10-15]

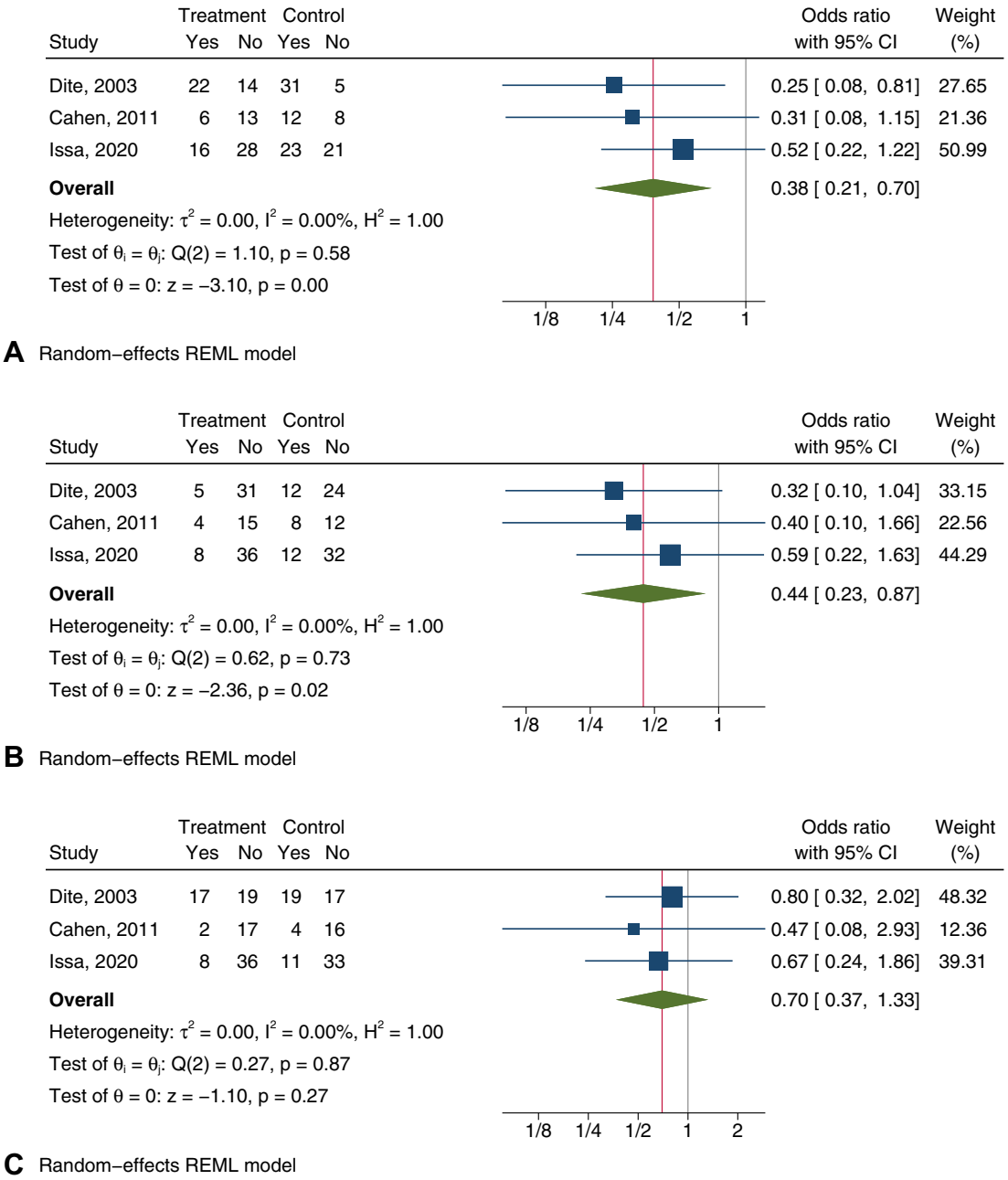


Figure 1. Among patients with painful chronic pancreatitis and obstructed main pancreatic duct who underwent endotherapy versus surgery, the odds of (**A**) any pain relief, (**B**) complete pain relief, and (**C**) partial pain relief are shown. *CI*, Confidence interval.

5. Pain relief
   a. *Any pain relief.* Based on the random-effects model, significantly lower odds of any pain relief were observed in CP patients undergoing endotherapy as compared with surgery (OR, .38; 95% CI, .21-.70); $I^2 = 0.\%$) (Fig. 1A).[10,12,15]
   b. *Complete pain relief.* Significantly lower complete pain relief was observed in endotherapy patients as compared with surgical patients (OR, .44; 95% CI, .23-.87; $I^2 = 0\%$) (Fig. 1B).[10,12,15]
   c. *Partial pain relief.* No difference in partial pain relief was found in the endoscopic versus surgical groups (OR, .70; 95% CI, .37-1.33; $I^2 = 0\%$) (Fig. 1C).[10,12,15]
6. Quality of life
   a. *Physical quality of life.* We observed statistically significant lower physical quality of life scores on the 36-Item Short Form Health Survey (mean difference, –3.66; 95% CI, –7.29 to .04; $I^2 = 0\%$; $P = .05$) in patients undergoing endotherapy as compared with surgery (Fig. 2C).[10-12,15]

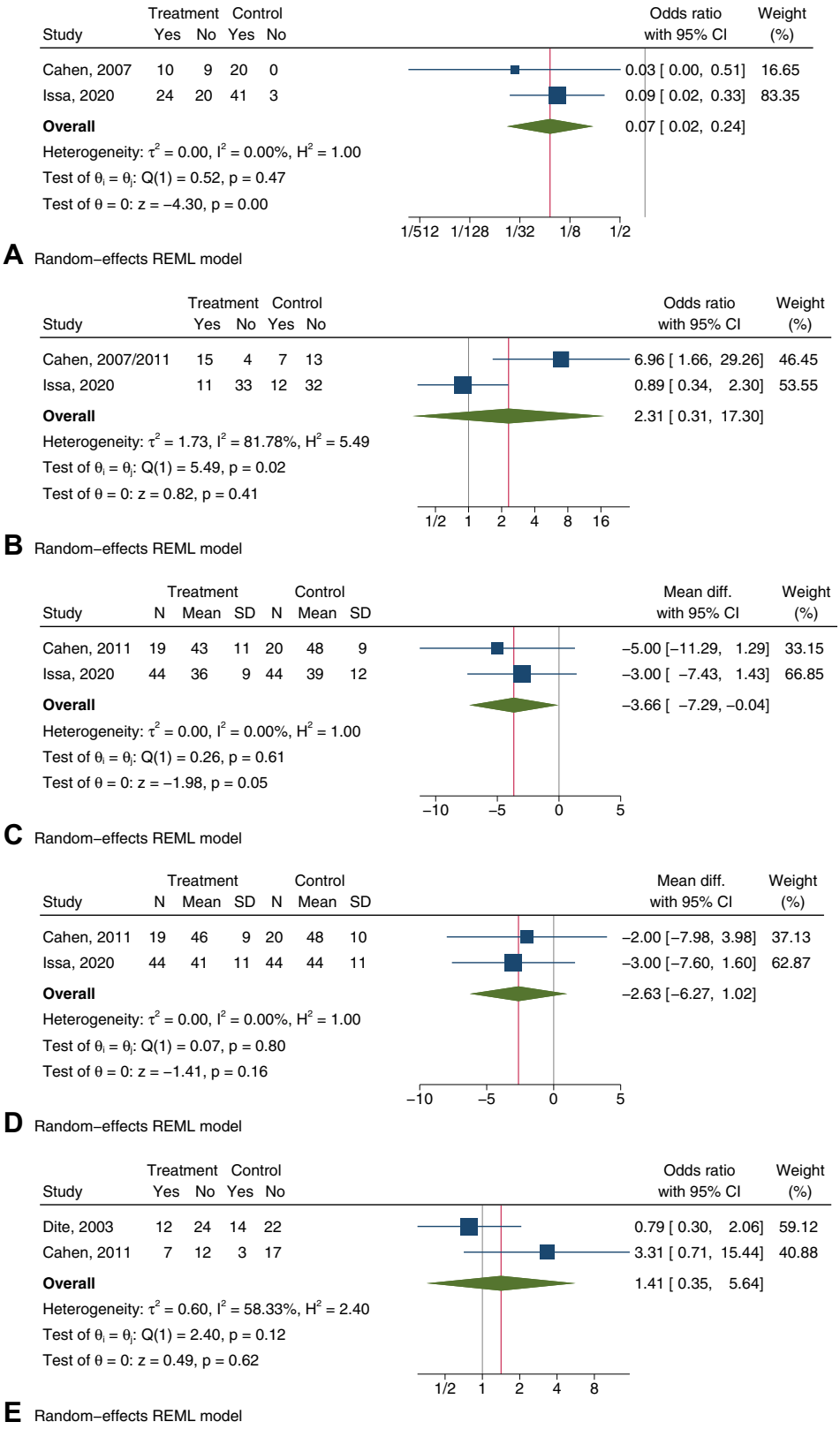


Figure 2. Among patients with painful chronic pancreatitis and obstructed main pancreatic duct who underwent endotherapy versus surgery, odds of (**A**) technical success, (**B**) adverse events, (**C**) mean difference in physical quality of life, (**D**) mean difference in mental quality of life, and (**E**) worsened endocrine dysfunction (diabetes) are shown. *CI*, Confidence interval; *SD*, standard deviation.

b. *Mental quality of life.* No statistical difference was found in the mental quality of life scores on the 36-Item Short Form health Survey (mean difference, –2.63; 95% CI, –6.27 to 1.02; $I^2 = 0\%$; $P = .16$) in patients undergoing endotherapy as compared with surgery (Fig. 2D).[10-12,15]

7. Pancreatic function
   a. *Exocrine pancreatic insufficiency.* No significant worsening or improvement in exocrine pancreatic function measured by fecal elastase <200 μg/g was observed as a consequence of endotherapy versus surgery among eligible studies.[12,14]
   b. *Endocrine pancreatic insufficiency.* No difference was seen in worsened endocrine dysfunction (diabetes) in patients undergoing endotherapy as compared with patients undergoing surgery (OR, 1.41; 95% CI, .35-5.64; $I^2 = 58.33\%$) (Fig. 2E).[10-12]

Sensitivity analysis

The meta-analyses with ≥3 studies underwent sensitivity analysis through the leave-1-out meta-analyses method. The studies describing any pain relief and complete or partial pain relief had low event rates and large CIs that did not alter significantly after removal of individual studies (Supplementary Fig. 1A-C, available online at www.giejournal.org). A sensitivity analysis for outcomes described by only 2 RCTs could not be performed.

Certainty in the evidence

For the outcomes of pain relief, technical success, adverse events, and quality of life, the risk of bias was nonserious (Supplementary Fig. 2, available online at www.giejournal.org). For determination of worsened diabetes, Dite et al[10] had a high risk of bias in the selective reporting domain. Only overall mortality had serious inconsistencies in the results between studies. The certainty of most outcomes were downgraded to low to moderate given the imprecision because of low sample size, event rates, and wide CIs as shown in the evidence profile (Table 3).

Other considerations

No significant differences occurred in the costs of endoscopic and surgical interventions in all eligible studies.[12-15] However, Kempeneers et al[18] performed a cost-effectiveness analysis among the patients included in the multicenter Dutch ESCAPE trial. The primary outcomes were the costs per unit decrease in the Izbicki pain score and gain in quality-adjusted life-years. This study showed that early surgery was more cost-effective than the endoscopy-first approach. Early surgery had a probability percentage of 88.4% of being more cost-effective than the endoscopy-first approach at a willingness-to-pay threshold of €0 per day per unit decrease on the Izbicki pain score. The probability percentage per additional gained quality-adjusted life-years was 75.7% at a willingness-to-pay threshold of €50,000.

Discussion

Pain is the predominant symptom of CP and an important predictor of quality of life.[19] The pain in CP is multifactorial; however, a subset of patients may have pain from obstruction of the PD resulting in increased intraductal pressure.[20] Hence, ductal decompression, either by the endoscopic or surgical approach, may provide durable relief of pain. When comparing both approaches, a systematic review and meta-analysis of the RCTs showed that in patients with uncomplicated painful CP with an obstructed PD, surgery was superior to endoscopic therapy in providing any pain relief or complete pain relief, with better technical success and greater improvement in physical quality of life.[10-12,15] However, no differences in mortality, adverse events, length of hospitalization, impact on endocrine or exocrine function, or difference in improvement in mental quality of life scores were found. As noted above, a cost-effective analysis study showed that the surgical approach was more cost-effective than the endoscopic approach.[18]

It should be noted that only 199 patients were included in all RCTs combined, and complete pain relief was achieved in only 49 of these patients (24.6%), emphasizing the multifactorial nature of pain in CP.[10-12,15] In these studies, patients were included if they had an obstructed PD, were surgical candidates, and were refractory to medical analgesia. Except for the study by Issa et al,[15] many patients were opioid dependent. In the surgical group, approximately two-thirds of patients only had a drainage procedure (ie, a pancreaticojejunostomy). In the endoscopy group, patients had a combination of ERCP with or without extracorporeal shock wave lithotripsy (ESWL).

Interventions during ERCP were variable and included pancreatic sphincterotomy, stricture dilation, PD stent placement, and stone extraction.[10-12,15] Most patients underwent ERCPs every 3 months for at least 12 months. In these trials, no subgroup analyses evaluated outcomes based on the type of endoscopic interventions, use of lithotripsy, or type of surgery (drainage or resection procedures). However, in a recent multicenter Dutch study,[15] in patients in whom complete ductal clearance was achieved endoscopically, the reduction in the pain score was comparable with the surgical group. Pancreatoscopy with intraductal lithotripsy was not used in this trial. Hence, it is possible that as newer endoscopic modalities become available, the proportion of patients who may achieve complete ductal clearance and relief of obstruction may increase.

Based on the data presented above, the panel suggested that when patients fail conservative medical treatment, a multidisciplinary discussion should ensue involving medical pancreatologists, pancreatic surgeons, interventional endoscopists, radiologists, and pain specialists. Regardless of the therapy chosen, the decision requires an ongoing discussion among all stakeholders, repeated assessment of treatment response, and careful longitudinal follow-up. Based on the recent Dutch study,[15] early surgery appears to be beneficial. Despite the superiority of a surgical approach,

TABLE 3. Evidence profile on population, intervention, comparator, outcome question 1: endotherapy compared with surgery in patients with painful chronic pancreatitis and obstructed main pancreatic duct

Certainty assessment						
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**
Overall mortality (18-92 mo of follow-up)						
3	Randomized trials	Not serious	Serious*	Not serious	Very serious†	None
Intervention-related deaths						
3	Randomized trials	Not serious	Not serious	Not serious	Extremely serious†	None
Any pain relief (based on Izbicki score, Melzack score) (follow-up: range, 18-92 mo)						
3	Randomized trials	Not serious‡	Not serious	Not serious	Serious†	None
Complete pain relief (follow-up: range, 18-92 mo)						
3	Randomized trials	Not serious§	Not serious	Not serious	Serious†	None
Technical success (follow-up: range, 18-92 mo)						
2	Randomized trials	Not serious‖	Not serious	Not serious	Serious†	None
Adverse event (follow-up: range, 18-92 mo)						
3	Randomized trials	Not serious‖	Not serious¶	Not serious	Serious**	None
Mean physical health quality of life (follow-up: range, 18-92 mo)						
2	Randomized trials	Not serious	Not serious	Not serious	Very serious††	None
Mean mental health quality of life (follow-up: range, 18-92 mo)						
2	Randomized trials	Not serious	Not serious‡	Not serious	Very serious‖	None
New-onset diabetes mellitus (follow-up: range, 18-92 mo)						
2	Randomized trials	Serious¶	Not serious‡	Not serious	Serious*	None
Improved exocrine pancreatic insufficiency (follow-up: range, 18-92 mo)						
2	Randomized trials	Not serious†	Not serious	Not serious	Extremely serious**	None
Worsened exocrine pancreatic insufficiency (follow-up: range, 18-92 mo)						
2	Randomized trials	Not serious†	Not serious	Not serious	Very serious*	None
Partial pain relief (follow-up: range, 18-92 mo)						
3	Randomized trials	Not serious††	Not serious	Not serious	Very serious§	None
Duration of hospital stay (days)						
5	Randomized trials	Not serious‡‡	Not serious	Serious§§	Serious‖‖	None

RCT, Randomized controlled trial; *CI*, confidence interval; *MD*, mean difference; *OR*, odds ratio.

*Low number of events and small sample size of included studies.

†Two RCTs (Cahen et al, 2007 and 2011)[11,12] had some concerns for deviation from the intended intervention. Unlikely that pooled estimate is affected by risk of bias.

‡The magnitude of statistical heterogeneity was low (I^2 < 40%) and study estimates 95% CIs overlap.

§Low number of events and sample size of included studies. Pooled-effects 95% CI includes considerable benefit and harm.

‖Small sample size and lower bound of 95% CI includes half minimal clinically important difference (5 unit) for mental component summary score of the 36-item Short Form Survey.

¶One RCT (Dite et al, 2003)[10] was at a high risk of bias because of selective reporting domain. All RCTs were judged to have some concerns because of deviation from the intended intervention. Risk of bias might be the main reason for the observed heterogeneity.

**Wide CIs, based on a small number of events with small sample sizes. Rated down 3 levels because the 95% CIs for the pooled estimate varies considerably, suggesting a large benefit to considerable harm.

††One RCT (Dite et al, 2003)[10] was at a high risk of bias because of selective reporting domain. All RCTs were judged to have some concerns because of deviation from the intended intervention. Decided not to rate down for risk of bias as the weight for the 1 study at a high risk of bias was ∼40%.

‡‡Despite the 2 observational studies being at high risk of bias because of confounding, decided not to rate down for risk of bias because there was no difference between findings from low risk of bias trials and observational studies.

§§Non-U.S.–based studies.

‖‖Wide CIs, based on a small number of patients.

TABLE 3. Continued

No. of patients		Effect		Certainty	Importance
Endotherapy	**Surgery**	**Relative (95% CI)**	**Absolute (95% CI)**		
3 RCTs reported overall deaths without statistical difference: Cahen et al (2011)[12] 2 endo vs 4 surgery, Cahen et al (2007)[11] 1 endo vs 0 surgery, Issa et al (2020)[15] 0 in both groups				⨁◯◯◯ Very low	CRITICAL
3 RCTs (Cahen 2007,[11] 2011[12]; Issa 2020[15]), 0 deaths				⨁◯◯◯ Very low	CRITICAL
44/99 (44.4%)	66/100 (66.0%)	OR .38 (.21-.70)	235 fewer per 1000 (from 370 fewer to 84 fewer)	⨁⨁⨁◯ Moderate	CRITICAL
17/99 (17.2%)	32/100 (32.0%)	OR .44 (.23-.87)	148 fewer per 1000 (from 222 fewer to 30 fewer)	⨁⨁⨁◯ Moderate	CRITICAL
34/63 (54.0%)	61/64 (95.3%)	OR .07 (.02-.24)	366 fewer per 1000 (from 664 fewer to 123 fewer)	⨁⨁⨁◯ Moderate	CRITICAL
26/63 (41.3%)	19/64 (29.7%)	OR 2.31 (.31-17.30)	197 more per 1000 (from 181 fewer to 583 more)	⨁⨁⨁◯ Moderate	CRITICAL
63	64		MD 3.66 lower (7.29 lower to .04 lower)	⨁⨁◯◯ Low	IMPORTANT
63	64		MD 2.63 lower (6.27 lower to 1.02 higher)	⨁⨁◯◯ Low	IMPORTANT
19/55 (34.5%)	17/56 (30.4%)	OR 1.41 (.35-5.64)	77 more per 1000 (from 171 fewer to 407 more)	⨁⨁◯◯ Low	IMPORTANT
• Cahen (2011)[12] 0 vs 2 ($P = .13$) • Kawashima (2018)[14] 3 vs 1 ($P = .55$) • Overall no improvement				⨁◯◯◯ Very low	IMPORTANT
• Cahen (2011)[12] 6 endo vs 2 surgery ($P = .13$) • Kawashima (2018)[14] 4 vs 1 ($P = .55$) • Overall no worsening				⨁⨁◯◯ Low	IMPORTANT
27/99 (27.3%)	34/100 (34.0%)	OR .70 (.37-1.33)	75 fewer per 1000 (from 180 fewer to 67 more)	⨁⨁◯◯ Low	IMPORTANT
• Cahen (2007 and 2011)[11,12] 13 days endo vs 11 days surgery, $P = .33$ • Issa (2020)[15] 10 vs 11, $P = .57$ • Hirota (2011)[13] 29 vs 18, $P = .11$ • Kawashima (2018)[14] 18 vs 23, $P = .38$ • Overall no statistical difference between the 2 groups in 5 studies; all non-U.S. studies				⨁⨁◯◯ Low	IMPORTANT

the panel noted that many patients and their surgeons prefer starting with the less-invasive endoscopic route before surgical management. An endoscopic approach may be preferred in patients in whom there is a high likelihood of complete relief of ductal obstruction (stone clearance, resolution of PD strictures), such as in patients with uncomplicated obstruction in the head, neck, or body of the pancreas, because pain relief in these patients is comparable with the surgical group.[18] Also, many patients may not be optimal surgical candidates because of comorbidities, age considerations, and other contraindications to surgery. Surgery may be considered first when endoscopic treatment is likely to be unsuccessful such as when the disease is in the tail of the pancreas or if there is dense calcification and large stone burden not amenable to endoscopic treatment.[21] However, successful surgical outcomes are highly dependent on the availability of a skilled and high-volume pancreatic surgeon, which may be restricted to specialized centers. Although no studies are available to provide guidance on the timing of surgery when endoscopic treatment fails, the panel suggested that early surgery should be considered over repeated unsuccessful ERCPs.

In summary, for patients who are surgical candidates, early surgical evaluation should be considered based on

TABLE 4. Evidence profile on population, intervention, comparator, outcome question 2: EUS-guided celiac plexus block vs percutaneous celiac plexus block in patients with painful chronic pancreatitis

Certainty assessment						
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**
Pain relief (1 wk) (Santosh et al: decrease in VAS by 3 points/10; Gress at al: decrease in pain score not specified and decrease in use of pain meds)						
2	Randomized trials	Serious*	Not serious	Not serious	Serious†	None
Pain relief (4 wk)						
2	Randomized trials	Serious†	Not serious	Not serious	Serious†	None
Pain relief (12 wk)						
2	Randomized trials	Serious	Not serious	Not serious	Serious†	None
Pain intensity defined by median pain score on VAS (follow-up: mean 12 wk)						
2	Randomized trials	Serious*	Not serious	Not serious	Serious‡	None
Adverse events						
2	Randomized trials	Serious†	Not serious	Not serious	Serious†	None
Noncomparative data on efficacy of EUS-guided celiac block in CP (systematic review and meta-analysis)						
8	Observational studies	Not serious	Not serious	Serious	Not serious	None

RCT, Randomized controlled trial; *CI*, confidence interval; *OR*, odds ratio; *VAS*, visual analog scale.
*Concerns from the Santosh et al (2009)[23] study in the randomization process, deviation from the intended intervention, and measurement of outcomes and judged to be at high risk of bias for selection of reported outcomes.
†Low number of events and small sample size of included studies.
‡Small sample size of the trial not meeting the optimal information size.

current evidence. For patients who prefer to avoid surgical interventions, we suggest endoscopic approach first. These recommendations are conditional with a low to moderate quality of evidence.

Question 2: Should an EUS-guided or percutaneous (PC) approach be used in patients with painful CP undergoing celiac plexus block (CPB)?

Recommendation 2: In patients with painful CP in whom a decision is made to proceed with a CPB, the ASGE suggests an EUS-guided over a PC approach.

(Conditional recommendation/low quality of evidence)

A systematic review and meta-analysis was performed to address the main outcomes of interest for this clinical question. After a systematic literature search (Appendix 1), 62 studies and conference abstracts were screened by 2 investigators (S.G.S. and J.D.M.) and 12 studies were identified for full-text screening. A systematic search and cross-referencing identified 2 RCTs that compared EUS-guided CPB (EUS-CPB) and PC CPB among 74 patients with intractable abdominal pain not responding to medical therapy[22,23]; these results are summarized in Supplementary Tables 1 and 2. PC CPB was performed with either fluoroscopic or CT guidance. The studies excluded patients with CP complicated by abscess, pseudocyst, or biliary stricture. The outcomes of interest were the proportion of patients with pain relief at 1-, 4-, and 12-week intervals; improvement in pain intensity based on a visual analog scale (VAS), and adverse effects (Supplementary Table 3).

Outcomes

For this clinical question, the outcomes of interest were pain relief and adverse events. These results are summarized below and in an evidence profile (Table 4).

1. Pain relief
   a. Based on the random-effects model, no significant differences in pain relief were found at 1 week from EUS-CPB (36/37) compared with PC CPB (31/37) (OR, 5.17; 95% CI, .16-170.6; $I^2 = 63.63\%$) (Fig. 3A).[22,23]

TABLE 4. Continued

No. of patients		Effect		Certainty	Importance
EUS-guided celiac plexus block	Percutaneous celiac plexus block	Relative (95% CI)	Absolute (95% CI)		
36/37 (97.3%)	31/37 (83.8%)	OR 5.17 (.16-170.60)	126 more per 1000 (from 385 fewer to 161 more)	⨁⨁◯◯ Low	CRITICAL
30/37 (81.1%)	13/37 (35.1%)	OR 8.11 (2.77-23.75)	463 more per 1000 (from 249 more to 577 more)	⨁⨁◯◯ Low	CRITICAL
13/37 (35.1%)	4/37 (10.8%)	OR 4.33 (1.24-15.08)	236 more per 1000 (from 23 more to 538 more)	⨁⨁◯◯ Low	CRITICAL
Santosh (2009), RCT (EUS 27, percutaneous fluoroscopy 29) EUS-VAS median pain scores 1 vs percutaneous 7; $P = .044$ Gress (1999), RCT (EUS 10, percutaneous CT 8) EUS-VAS pain scores 1 vs percutaneous CT-guided 9 (out of 10); $P = .02$				⨁⨁◯◯ Low	CRITICAL
3/37 (8.1%)	4/37 (10.8%)	OR .65 (.06-7.51)	35 fewer per 1000 (from 101 fewer to 368 more)	⨁⨁◯◯ Low	CRITICAL
• Systematic review of 8 studies (283 patients) • 7 days to 15 weeks of follow-up, VAS • Response rate 59.45% (95% CI, 54.51–64.30), Cochran's Q test: $P = .58$ • No publication bias				⨁◯◯◯ Very low	IMPORTANT

b. Significantly higher odds of pain relief were found among patients undergoing EUS-CPB (30/37) compared with PC CPB (13/37) at 4 weeks (OR, 8.11; 95% CI, 2.77-23.75; $I^2 = .00\%$) and at 12 weeks (13/37 vs 4/37: OR, 4.33; 95% CI, 1.24-15.08; $I^2 = .00\%$) (Fig. 3B and C).[22,23]

c. The pain score assessed by the median VAS score was compared among patients undergoing EUS-CPB versus PC CPB.[22,23] In the study by Santosh et al,[23] the median VAS score was significantly lower among those undergoing EUS-CPB (1/10) as compared with PC CPB (7/10; $P = .04$). Similarly, Gress et al[22] showed significantly lower pain scale scores among the EUS-CPB group (1/10) versus the PC CPB group (9/10; $P = .02$).[22]

2. *Adverse events.* No statistical difference in adverse events was observed in the EUS-CPB group compared with the PC CPB group (OR, .65; 95% CI, .06-7.51; $P = .73$, $I^2 = 48.18\%$) (Fig. 3D).[22,23]

Certainty in the evidence

Despite being randomized trials, both eligible studies in this section were prone to bias (as assessed using the RoB 2 tool) because of concerns in the randomization process, deviation from the intended intervention, and measurement of outcomes (Supplementary Fig. 2). Additionally, imprecision because of low sample size and events and wide CIs caused the certainty in the evidence to be downgraded to low (Table 4). A sensitivity analysis was not done because only 2 RCTs were included.

Other considerations

No cost-effective analysis is available.

Discussion

The pain in CP is frequently treated with opioids. In spite of using high-potency opioids, many patients do not have adequate pain relief because multiple factors contribute to the pain in CP, especially central sensitization. Moreover, patients may experience significant side effects from long-term opioid use, which carries a substantial risk of narcotic dependence. Also, in patients with CP who do not have ductal obstruction, endoscopic or surgical drainage procedures are not beneficial. CPB is a modality in which the pain signals from upper abdominal organs reaching the celiac plexus can be temporarily interrupted using a combination of a local anesthetic with or without a steroid injection.[24] CPB has been shown to provide variable pain relief in pancreatic cancer and CP.[25] CPB can be administered with EUS guidance or a PC approach.

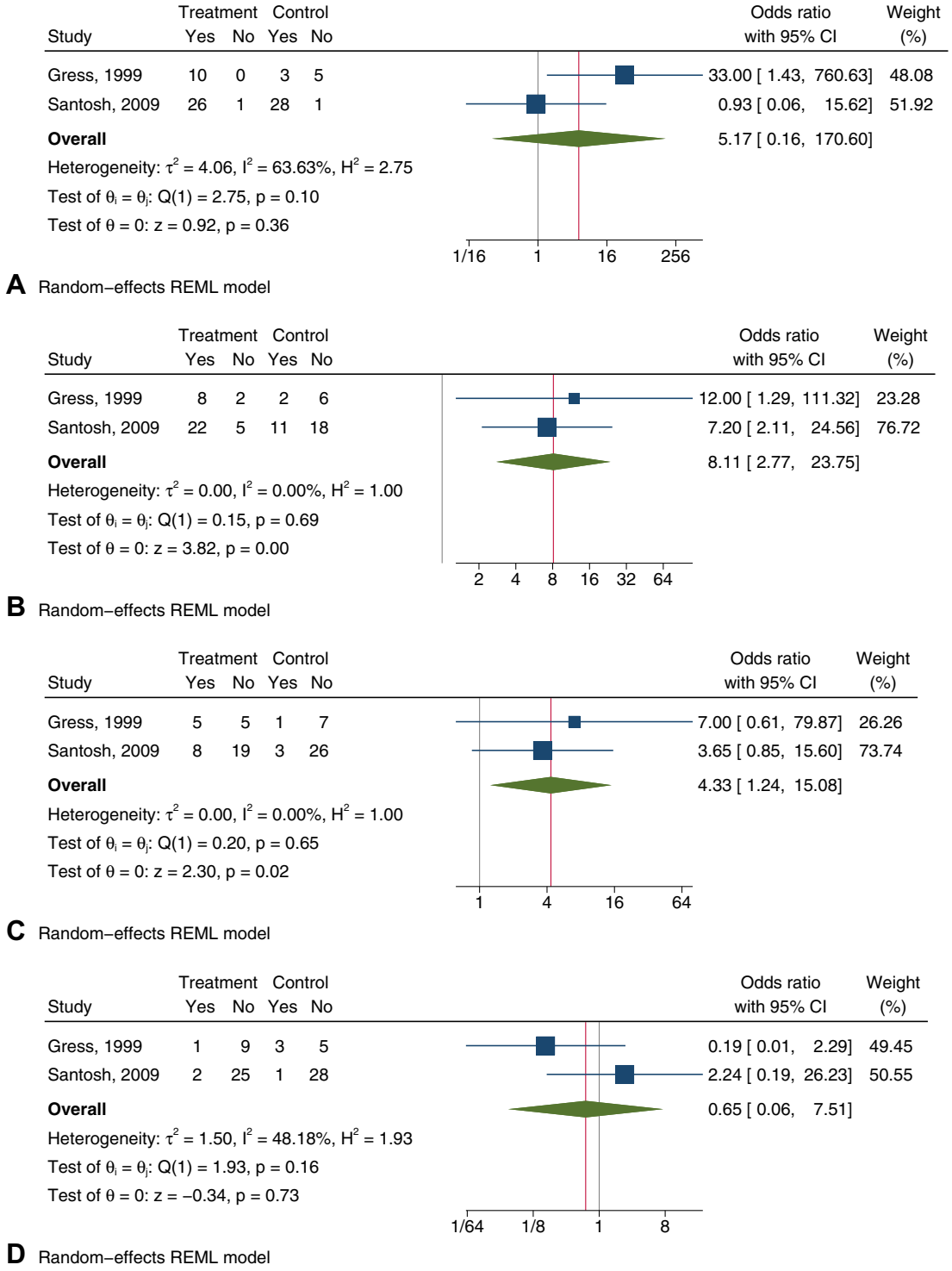


Figure 3. Odds ratio of pain control between EUS-guided celiac plexus block (CPB) versus percutaneous CPB at (**A**) 1 week, (**B**) 4 weeks, and (**C**) 12 weeks. **D,** Odds ratio of adverse events in EUS-guided CPB versus percutaneous CPB. *CI*, Confidence interval.

In the analysis of the 2 RCTs described above, EUS-CPB was more successful than PC CPB (either fluoroscopic or CT-guided) in providing pain relief in patients with CP who failed medical treatment, possibly because of better localization and targeting of the plexus by EUS.[22,23] Specifically, a higher proportion of patients experienced pain relief at weeks 4 and 12 after EUS-CPB. Also, the intensity of pain measured by the median VAS score was significantly lower in the EUS-CPB group compared with both fluoroscopic and CT-guided PC CPB, without any difference in adverse events. The quality of the evidence in the RCTs was low (as discussed above), and no cost analysis data are available.

It should be noted that the effectiveness of CPB for the treatment of pain in CP has not been rigorously studied. No studies have compared CPB with other treatment modalities, and no placebo or sham-controlled trials have been conducted. In a systematic review and meta-analysis of 8 single-arm, noncomparative studies in 283 CP patients, EUS-CPB for the treatment of pain was shown to have modest pain relief in 59.5% of patients (95% CI, 54.51-64.30), with a subgroup analysis showing that bilateral injection of the plexus provided better pain relief than unilateral injections.[25] In addition to not being consistently effective, pain relief with CPB is not sustained, and most patients return to their baseline pain in less than 6 months, including in the RCT by Santosh et al.[23] However, Sey et al[26] showed that patients who benefited from a single CPB injection may benefit from a subsequent injection when pain relief subsided after the first injection. Also, neurolysis of the celiac plexus with ethanol ablation has not been studied in CP because of the risk of serious neurologic side effects. Typical adverse events noted with CPB were transient hypotension, diarrhea, retroperitoneal abscess, and postprocedural pain, which occurred in 1.6% of 220 procedures carried out in 158 patients.[27] Based on these data, the panel suggested that CPB could be considered in CP patients with severe ongoing pain on maximum medical therapy, nonobstructive small duct disease, or with side effects to opioids or do not wish to take opioids.

In summary, low-quality evidence suggests that CPB may provide modest and nonsustained pain relief in CP patients with reasonable safety. In patients with painful CP in whom a decision is made to proceed with a CPB, the ASGE suggests an EUS-guided over a PC approach. The recommendation is conditional with a low quality of evidence.

Question 3: In patients with painful CP and main PD stones, what is the optimal approach in endoscopic management: ERCP alone, ERCP with pancreatoscopy and lithotripsy, or ERCP with ESWL?

Recommendation 3: In patients with painful CP and main PD stones, the ASGE suggests the management strategy should be based on stone size, location, and radiopacity:

a. For radiopaque stones >5 mm and in head, neck, and body of the pancreas, the ASGE suggests ERCP with or without pancreatoscopy or ESWL alone.
b. After ESWL and no spontaneous stone clearance after adequate fragmentation (defined as fragments <2-3 mm), the ASGE suggests adding ERCP (with or without pancreatoscopy) for stone clearance.
c. For radiopaque stones <5 mm, any radiolucent stone, or contraindications to ESWL, the ASGE suggests ERCP with or without pancreatoscopy.

(Conditional recommendation/very low to low quality of evidence)

To address the management strategy of PD stones, we evaluated studies comparing ESWL versus pancreatoscopy with electrohydraulic lithotripsy (EHL) and studies comparing ESWL alone versus ESWL followed by ERCP. We systematically reviewed the literature, and of 360 references, we identified 16 citations for full-text review. A systematic search and cross-reference yielded 4 original studies (1 RCT and 3 observational studies; Appendix 1) that were included in the final analysis.[28-31] These studies included adult CP patients with pancreaticolithiasis and abdominal pain. The exclusion criteria for these studies were the presence of a pancreatic fluid collection >2 cm, serum alkaline phosphatase levels greater than twice the normal value or cholangitis, age <18 years, pregnancy, and lactation (Supplementary Table 1). Details on patient characteristics and outcomes are outlined in Supplementary Tables 2 and 3. The median stone size was >5 mm in all studies.

Outcomes

For this clinical question, the outcomes of interest were mortality, pain relief, technical success (defined as stone clearance), number of procedures, adverse events, and hospital length of stay. These results are summarized in an evidence profile (Table 5). Outcomes are presented below comparing pancreatoscopy with EHL versus ESWL[28] and ESWL alone versus ESWL and ERCP combined.[29-31]

1. *Pancreatoscopy with EHL versus ESWL.* Only 1 study compared pancreatoscopy with EHL with ESWL. This study, by Bick et al,[28] included 18 patients with pancreatoscopy and 240 patients with ESWL. The authors reported pain relief from pancreatoscopy in 93.8% of patients (15/18), which was similar to ESWL (82.7% [182/240], P = .43). No significant difference was found in stone clearance between pancreatoscopy (88.9%) and ESWL (86.7%, P = 1.0). This study also investigated stone clearance efficiency, which was defined as ≤2 procedures to clear stones. Pancreatoscopy had significantly higher stone clearance efficiency as compared with ESWL (OR, 5.24; 95% CI, 1.3-20.39), except for stones >10 mm where pancreatoscopy was significantly less efficient than ESWL (OR, .484; 95% CI, .256-.912). Pancreatoscopy had a significantly lower procedural time (101.6 ± 68 minutes) compared with ESWL (191.8 ± 111.6 minutes, P = .001). Also, significantly fewer procedures occurred in the pancreatoscopy group (1.6 [standard deviation = .6] vs 3.1 [standard deviation = 1.5], P < .001). No significant differences in procedure-related adverse events were observed between pancreatoscopy (5.6%) and ESWL (6.7%, P = 1.0).
2. *ESWL alone versus ESWL and ERCP combined.* Three studies were identified that informed this question. The relief in pain by ESWL and ESWL+ERCP was shown to be similar in an RCT by Dumoncaeu et al[29] (3.8 vs 3.7 points, respectively; P = .7) as well as an observational study by Vaysse et al[30] (29 [71%] vs 71 [78%], P = .4). Dumonceau et al showed 100% stone fragmentation in both

TABLE 5. Evidence profile on population, intervention, comparator, outcome question 3a: pancreatoscopy compared with ESWL for painful chronic pancreatitis with main pancreatic duct stones

Certainty assessment						
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**
Technical success, defined as complete stone clearance (comparative study pancreatoscopy 18 vs ESWL 240)						
1	Observational studies	Not serious	Not serious	Not serious	Serious	None
Clinical success (relief of pain): comparative study						
1	Observational studies	Not serious	Not serious	Not serious†	Serious†	None
Number of procedures: comparative study						
1	Observational studies	Not serious	Not serious	Not serious†	Serious†	None
Efficiency of stone clearance (total stone burden): defined as ≤2 procedures to clear stones: comparative study						
1	Observational Studies	Not serious	Not serious	Not serious	Serious†	None
Efficiency of clearing stones >10 mm: comparative study						
1	Observational studies	Not serious	Not serious	Not serious	Serious†	None
Adverse events: comparative study						
1	Observational studies	Not serious	Not serious	Not serious	Serious†	None
Adverse events: noncomparative study						
15	Observational studies	Not serious	Not serious	Serious*	Not serious	None

ESWL, Extracorporeal shock wave lithotripsy; *CI*, confidence interval; *OR*, odds ratio.
*Noncomparative.
†Small numbers, single center, retrospective.

ESWL (26 [100%]) and ESWL+ERCP (29 [100%]). Furthermore, main PD decompression (mean decrease in PD diameter, 1.7 mm; 95% CI, .9-2.6; $P < .001$) did not differ significantly ($P = .391$). The observational study by Vaysse et al also showed no difference in the rate of stone clearance ($P = .93$). These results were not consistent with the observational study by Suzuki et al,[31] which showed significantly higher stone clearance in the ESWL+ERCP group (203 [79.5%]) as compared with the ESWL group (99 [49.2%], $P < .05$). The adverse event rates of ESWL and ESWL+ERCP were compared in the RCT and lacked a significant difference (0 vs 1 [3%]).[29] Dumonceau et al described no intervention-related mortality in both the ESWL and ESWL+ERCP groups. However, non-CP–related deaths were reported in 4 patients who underwent ESWL and 7 who underwent ESWL+ERCP but without a statistical difference between the 2 groups. A longer duration of hospital stay without statistical significance was observed in patients who underwent ESWL+ERCP as compared with ESWL alone (8.6 days [16.5] vs 3.1 days [5.3], $P = .1$).[29]

Certainty in the evidence

For a comparison of pancreatoscopy versus ESWL, a single observational study was included that was rated down for low event rates and resulted in a very low quality of evidence (Table 5). For the ESWL versus ESWL with ERCP studies, the evidence was rated down because of risk of bias because of deviations from the intended intervention (Supplementary Fig. 2).[29-31] Moreover, low sample size and event rates resulted in rating down for imprecision. Thus, the quality of the evidence was low (Table 6).

Other considerations

There was no cost analysis available for the study comparing pancreatoscopy and ESWL. The cost of ESWL alone was significantly lower than ESWL+ERCP ($4092.66

TABLE 5. Continued

No. of patients		Effect			
Pancreatoscopy	ESWL	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
	• Pancreatoscopy 88.9% • ESWL 86.7% $P=1.000$			⨁◯◯◯ Very low	CRITICAL
	• Pancreatoscopy 93.8% • ESWL 82.7% ($P = .43$)			⨁◯◯◯ Very low	CRITICAL
	• Pancreatoscopy 1.6 (.6) • ESWL 3.1 (1.5) • $P < .001$			⨁◯◯◯ Very low	IMPORTANT
	• Pancreatoscopy > ESWL • OR 5.24 (1.3-20.39) • $P = .017$			⨁◯◯◯ Very low	IMPORTANT
	• Pancreatoscopy < ESWL • OR .484 (.256-.912) • $P = .025$			⨁◯◯◯ Very low	IMPORTANT
	• Pancreatoscopy 6.3% • ESWL 5.6% • $P = 1.000$ • Mostly mild adverse events			⨁◯◯◯ Very low	IMPORTANT
	• Total 43 events in 370 patients • 12% (8.7-15.5)			⨁◯◯◯ Very low	IMPORTANT

vs $12,939.3, $P < .001$); however, a cost-effective analysis was not performed.[29]

Discussion

A hallmark of CP is the development of pancreatic stones, which are typically calcified and radiopaque. Predictors of higher stone burden are male sex, heavy alcohol use, heavy smoking, and longer disease duration.[32] When located in the main PD, stones can cause obstruction and severe pain because of increased intraductal hypertension and pressure-induced ischemia.[33] Removal of stones at endoscopy relieves the obstruction and may improve pain.[34] Standard techniques of stone removal at ERCP using pancreatic sphincterotomy, dilation methods, and stone extraction using a balloon or basket are successful in less than 15% of CP patients.[31] Hence, stone extraction by ERCP alone is reserved for smaller stones (ie, <5 mm) or radiolucent stones that cannot be targeted by ESWL, typically located in the head, neck, and body of the pancreas.[31,35]

The evidence presented above addresses management strategies in patients with painful CP and main PD stones who are not candidates for conventional ERCP techniques alone and will likely require stone fragmentation for ductal clearance. Bick et al[28] compared 18 patients undergoing single-operator pancreatoscopy with intraductal lithotripsy with 240 patients who underwent ESWL in a single-center, comparative, observational cohort study. In their study, stones were >5 mm, and also a significantly higher number of pancreatoscopy patients had prior unsuccessful ERCPs and attempts at lithotripsy. No differences were found in the rates of stone clearance, improvement in pain, and adverse events between the 2 groups. However, the number of procedures required was significantly lower in the pancreatoscopy group with a significantly lower procedural time compared with the ESWL group. Efficiency of stone clearance, defined as ≤2 procedures required for stone clearance, was significantly improved for the pancreatoscopy group. However, ESWL was more efficient when stones were >10 mm. When comparing ESWL alone with ESWL and ERCP, both groups had similar success in pain relief.[29,30] Ductal clearance was similar in both groups in the RCT by Dumonceau et al[29] and the observational study by Vaysse et al.[30] However, rates of ductal clearance were lower in the ESWL alone group in the observational

TABLE 6. Evidence profile on population, intervention, comparator, outcome question 3b: ESWL alone compared with ERCP+ESWL in patients with painful chronic pancreatitis and main pancreatic duct stones

Certainty assessment						
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**
Overall mortality						
1	Randomized trials	Not serious	Not serious	Not serious	Very serious*	None
Stone clearance (assessed by pancreatic duct decompression on MRCP in RCTs, not stated in observational studies)						
3	Observational studies	Serious†	Serious‡	Not serious§	Serious*	None
Pain resolution/reduction						
2	Randomized trials	Not serious	Not serious	Not serious	Very serious*	None
Technical success (stone fragments <2-3 mm)						
1	Randomized trials	Serious‖	Not serious	Not serious	Serious*	None
Pain relapse						
1	Randomized trials	Not serious	Not serious	Not serious	Serious*	None
Adverse events						
1	Randomized trials	Not serious	Not serious	Not serious	Very serious*	None
Duration of hospital stay (days)						
1	Randomized trials	Not serious	Not serious	Not serious	Very serious	None
Weight gain						
1	Randomized trials	Not serious	Not serious	Not serious	Very serious*	None

RCT, Randomized controlled trial; *ESWL*, extracorporeal shock wave lithotripsy; *CI*, confidence interval; *PDAC*, pancreatic ductal adenocarcinoma.
*Low number of events and sample size of included studies.
†The 2 observational studies had serious concerns in risk of bias because of confounding, and Vaysse et al (2016)[30] only had data for 1 of the interventions.
‡Outcomes used to assess benefit differ across studies; 1 RCT reported no difference in a surrogate outcome, 1 observational study reported benefit in favor of the intervention, and the other reports large benefit in favor of the comparison.
§Despite using surrogate outcome in the RCT study, decided not to rate down further to avoid double penalizing for inconsistency and indirectness.
‖Some concerns in deviation from intended intervention. Study arms have different duration of follow-up and number of patients in each arm differ.

Japanese study by Suzuki et al.[31] Neither group showed differences in adverse events or mortality, but length of hospital stay was longer in the combined ESWL+ERCP group without statistical significance.

Some of the advantages of pancreatoscopy over ESWL are that stones, even if not radiopaque, can be fragmented under direct vision and the procedure can be combined with ERCP in a single session. However, pancreatoscopy is technically difficult in the presence of main PD strictures and when stones are located upstream from the stricture or in the tail of the pancreas because a 10F catheter is required to be advanced to the stone. A systematic review and meta-analysis of 15 noncomparative studies evaluated 2 types of lithotripsy during pancreatoscopy in 370 patients,[36] reporting high rates of clinical (relief of symptoms) and technical (complete ductal clearance) success of up to 90% in patients undergoing either EHL or laser lithotripsy at the time of pancreatoscopy. Common adverse events were postprocedure pain, fever, pancreatitis, bleeding, and/or perforation in 12% of patients. Moole et al[37] evaluated the efficacy of

TABLE 6. Continued

No. of patients		Effect			
ESWL alone	ERCP+ESWL	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
• Domonceau (2007)[29] 4 ESWL vs 7 ESWL+ERCP • 1 PDAC, rest unrelated • No significant difference • The intervention-related mortality was zero in both arms				⨁⨁◯◯ Low	CRITICAL
• RCT: No difference in MRCP decompression (pancreatic duct < 1.7 mm) between ESWL and ESWL+ERCP, $P = .391$ • Observational study: Suzuki (2013),[31] 99 patients (49.2%) in ESWL 203 patients (79.5%) in all ESWL+ERCP cases, $P < .05$ • Observational study: Vaysse (2016), $P = .93$ between groups				⨁◯◯◯ Very low	CRITICAL
• RCT: mean reduction in pain episodes • 3.8 points ESWL vs 3.7 points ESWL+ERCP, $P = .759$ • Observational study: pain resolution • 29 (71%) ESWL vs 71 (78%) ESWL+ERCP, $P = .37$				⨁⨁◯◯ Low	CRITICAL
RCT: both groups 100%				⨁⨁◯◯ Low	IMPORTANT
• RCT: 2-y follow up • 10 (38%) ESWL vs 13 (45%) ESWL+ERCP, $P = .633$ • 52-month follow up • 11 (42%) ESWL vs 13 (45%) ESWL+ERCP, $P = .851$				⨁⨁⨁◯ Moderate	IMPORTANT
RCT: 0 ESWL vs 1 ESWL+ERCP				⨁⨁◯◯ Low	IMPORTANT
RCT: 3.1 days ESWL vs 8.6 days ESWL+ERCP, $P = .099$				⨁⨁◯◯ Low	IMPORTANT
RCT: 3.9 kg ESWL vs 3.5 kg ESWL+ERCP, $P = .84$				⨁⨁◯◯ Low	IMPORTANT

ESWL in CP in a systematic review and meta-analysis including 27 studies with 3189 patients. They reported ductal clearance of up to 71% for stones >5 mm, with complete pain relief in approximately 52% of patients and partial relief in an additional 33% as well as a quality of life improvement in 88% at a median follow-up of 2 years. ERCP was combined in most studies, with adverse events occurring in less than 5%.[37] It should be noted that a clear shock wave pathway is required for ESWL without the interference by bones, calcified vessels, or lung tissue, and, in general, most patients require up to 3 ESWL sessions.[38] During the panel meeting, equity and feasibility issues of various modalities were discussed, recognizing that ESWL is not as readily available in the United States compared with Europe and Asia.

In summary, the panel suggested for radiopaque stones <5 mm or if PD stones are radiolucent and located in the head, neck, and body of the pancreas, ERCP alone (with or without pancreatoscopy) should be attempted first, because of the higher probability of ductal clearance. For all other cases where lithotripsy is required, either pancreatoscopy with lithotripsy or ESWL can be used depending on local availability. Pancreatoscopy may be more efficient than ESWL in ductal clearance, except when stones are >10 mm. These recommendations are conditional with very low to low quality of evidence.

Question 4: In patients with painful CP and main PD strictures undergoing ERCP, what is the optimal management strategy for PD stent placement?

Recommendation 4: In patients with painful CP and main PD strictures, the ASGE suggests the following management strategy:

a. *Number of stents.* The ASGE suggests placement of single over multiple plastic stents (PSs) for the initial treatment of a dominant PD stricture.
b. *Stent diameter.* The ASGE suggests the placement of the largest possible diameter PS that can be safely deployed in the initial treatment of a dominant PD stricture while avoiding forceful or traumatic placement, with a gradual upsizing if necessary.
c. *Use of metal stents.* The ASGE suggests against the routine use of fully covered self-expandable metal stents (FCSEMSs) for patients with persistent or refractory PD stricture who have failed initial stent placement.

(Conditional recommendation /very low quality of evidence)

To address the questions on stent placement (stent number, diameter, and type) for the treatment of main PD strictures, our search yielded 239 citations, of which 15 articles were selected for full-text review (Appendix 1). Three comparative observational cohort studies met the inclusion criteria and compared the utility of the number of stents (single vs multiple PSs), diameter of stents (10F vs 8.5F or smaller PSs), and type of stents (single PS vs FCSEMSs).[39-41] The strategies of stent placement were considered separately for the initial management of PD strictures as well as secondary treatment of persistent or refractory PD strictures. The inclusion and exclusion criteria of eligible studies are outlined in Supplementary Table 1. Patient characteristics, study design, and outcomes are described in Supplementary Tables 2 and 3. The outcomes reported in the 3 studies varied and are discussed below.[39-41]

Outcomes

1. *Number of stents: single versus multiple PSs.* Only 1 observational study by Papalavrentios et al[39] assessed the difference between single and multiple PSs. The study compared 3 groups: single PSs (n = 18), 1 or 2 PSs (n = 35), and 2 PSs (n = 32). When comparing 1 PS versus 1 or 2 PSs versus 2 PSs, a single PS had significantly higher odds of pain relief defined as an Izbicki score ≤10 at the end of the stent placement period (OR, 7.5; 95% CI, 1.46-38.70). Also, more patients in the 1 PS group had pain relief compared with the other groups (1 vs 1-2 vs 2: 88.2% vs 74.2% vs 50%, $P = .02$). A significantly lower median Izbicki score was seen in the 1 PS group (0) as compared with the 1 to 2 PS group (0 [5]) or 2 PS group (6 [15], $P = .03$). None of the patients undergoing use of 1 PS, 1 to 2 PSs, or 2 PSs had intervention-related mortality, and overall mortality did not differ significantly (5.5%, 2.9%, and 3.1%, respectively; $P = .87$).[39] No significant difference in exocrine pancreatic insufficiency was observed in patients undergoing pancreatic ductal stent placement with 1 PS (4 [22%]), 1 to 2 PSs (7 [20%]), or 2 PSs (14 [44%], $P = .89$).[39] No significant difference in endocrine pancreatic insufficiency was observed in patients undergoing pancreatic ductal stent placement with 1 PS (5 [28%]), 1 to 2 PSs (7 [20%]), or 2 PSs (16 [50%], $P = .56$).[39]
2. *Diameter of stents: single 10F PSs versus ≤8.5F PSs.* Endotherapy with pancreatic stent placement was assessed in 169 patients, and significantly fewer hospitalizations for abdominal pain were observed in patients in the 10F PS group (.8 [2.2]) as compared with the ≤8.5F PS group (1.5 [2.4], $P = .01$).[40] Also, a significantly lower proportion of patients were hospitalized in the 10F PS group versus the ≤8.5F PS group (8 [24%] vs 63 [49%], $P < .001$).
3. *Type of stents: single PS versus FCSEMSs.* We identified 1 study by Lee et al[41] that compared use of a single PS (n = 54) with FCSEMSs (n = 26) in CP patients with persistent PD strictures (present 3 months after initial PD stent placement). Lee et al assessed pain relief or clinical success through a median VAS score. A 50% reduction in the pain score before and after the stent insertion was similarly observed in 26 (100%) and 52 (96.3%) patients undergoing FCSEMS and PS insertion, respectively ($P = .32$). Successful stent placement did not differ between the FCSEMS group (n = 26 [100%]) and the PS group (n = 54 [100%]). Stricture resolution was significantly higher with FCSEMSs (20 [87.0%]) as compared with PSs (21 [42.0%], ($P < .001$).[41] The number of ERCP sessions was similar between the single PS group (3 [interquartile range {IQR}, 1-10]) and FCSEMS group (2 [IQR, 1-3], $P = .14$).[41] No significant differences occurred in the immediate adverse events in the single PS group (20/54 [37.0%]) as compared with the FCSEMS group (10/26 [38.5%], $P = .90$).[41] However, delayed adverse events including spontaneous stent migration (26.9% vs 3.7%, $P = .002$) and de novo strictures (23.1% vs 0%, $P < .001$) were significantly more common in the FCSEMS group.

Certainty in the evidence

There was serious risk of confounding bias from the studies by Lee et al[41] and Sauer et al,[40] whereas the study by Papalavrentios et al[39] had a low risk of bias (Supplementary Fig. 2). However, we observed a very serious risk of imprecision because of the small sample size and low event rates. Thus, the certainty of evidence from these eligible studies was downgraded to very low because of concerns with study quality and imprecision (Tables 7-9).

TABLE 7. Evidence profile on population, intervention, comparator, outcome question 4a: ERCP and single PS compared with multiple stents in initial treatment of patients with painful chronic pancreatitis and dominant main pancreatic duct stricture

Certainty assessment									
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Impact**	**Certainty**	**Importance**
Treatment outcome: reduction in Izbicki pain score <10: group A 1 PS (18) vs group B 1-2 PSs (35) vs group C 2 PSs (32): all 8.5F/10F									
1	Observational studies	Serious*	Not serious†	Not serious	Very serious‡	None	• 1 PS: 15 (88.2%) • 1/2 PSs: 23 (74.2%) • 2 PSs: 15 patients (50%) • $P = .02$ • 1 PS vs 2 PSs • OR 7.5 (1.46-38.70), $P = .04$	⨁◯◯◯ Very low	CRITICAL
Pain relief at end of treatment (14-22 mo)									
1	Observational studies	Serious*	Not serious	Not serious	Very serious§	None	Median Izbicki scores in group A (1 PS), 0 in group B (1 or 2 PSs), 6 in group C (2 PSs) $P = .03$	⨁◯◯◯ Very low	CRITICAL
Number of ERCP sessions									
1	Observational studies	Serious*	Not serious	Not serious	Very serious‡	None	• 3 sessions (IQR, 1-3) for 1 PS • 4 sessions (IQR, 3-5) for 1 or 2 PSs • 3 sessions (IQR, 2 to 3) for 2 PSs • $P < .001$ • 1/2 PS group had more sessions than others	⨁◯◯◯ Very low	IMPORTANT
Adverse effects: stent migration									
1	Observational studies	Serious*	Not serious	Not serious	Very serious‡	None	• 1 PS: 3 (17%) • 2 PSs: 9 (26%) • 3 PSs: 6 (19%) • $P = .87$	⨁◯◯◯ Very low	IMPORTANT
Overall mortality									
1	Observational studies	Not serious	Not serious	Not serious	Very serious‡	None	• 1 PS: 1 (5.5%) • 1/2 PSs: 2 (2.9%) • 2 PSs: 1 (3.1%) • $P = .87$ • No details of death provided • No intervention-related death in any of the study arms	⨁◯◯◯ Very low	CRITICAL
Recurrence requiring recurrent stent placement (after end of treatment with 84-mo follow-up)									
1	Observational studies	Serious*	Not serious	Serious‖	Very serious‡	None	• 1 PS: 7 (39%) • 1/2 PSs: 10 (29%) • 2 PSs: 13 (41%) • $P = .66$	⨁◯◯◯ Very low	IMPORTANT
Pancreatic exocrine insufficiency									
1	Observational studies	Not serious	Not serious	Not serious	Very serious‡	None	• 1 PS: 4 (22%) • 1/2 PSs: 7 (20%) • 2 PSs: 14 (44%) • $P = .89$	⨁◯◯◯ Very low	IMPORTANT

(*continued on the next page*)

TABLE 7. Continued

Certainty assessment									
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Impact**	**Certainty**	**Importance**
New-Onset diabetes									
1	Observational studies	Not serious	Not serious	Not serious	Very serious‡	None	• 1 PS: 5 (28%) • 1/2 PSs: 7 (20%) • 2 PSs: 16 (50%) • $P = .56$	⨁◯◯◯ Very low	IMPORTANT

PS, Plastic stent; *IQR*, interquartile range.
*One study (Lee et al, 2021)[41] had serious concerns for risk of bias because of confounding.
†Decided not to rate down further despite the inconsistency of findings between the 2 studies as risk of bias might be the source of inconsistency.
‡Low number of events and small sample size of included studies.
§Small sample size not meeting the optimal information size.
||Papalavrentios et al (2019)[39] reported recurrent stent placement instead of recurrence.

TABLE 8. Evidence profile on population, intervention, comparator, outcome question 4b: ERCP and single 10F PS compared with ≤8.5F PS in initial treatment of patients with painful chronic pancreatitis and dominant main pancreatic duct stricture

Certainty assessment									
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Impact**	**Certainty**	**Importance**
Hospitalization for abdominal pain in 10F PS vs ≤8.5F PS (follow-up: mean 36 mo)									
1	Observational studies	Serious*	Not serious	Not serious	Very serious†	None	• Total number of patients o 10F: 34 patients o < 8.5F: 129 patients: 5F (9) + 7F (120) • Number of patients hospitalized o 10F: 8 (24%) o < 8.5F: 63 (49%), $P <$ .001 • Number of hospitalizations (per follow-up time for each patient) o 10F: .8 (2.2) o < 8.5F: 1.5 (2.4), $P =$ .01	⨁◯◯◯ Very low	CRITICAL

PS, Plastic stent.
*Only one study - so serious risk of bias due to confounding.
†Low number of events and sample size.

Other considerations

A cost analysis was available in the PS versus FCSEMS study,[41] which showed no difference between the 2 groups (PS vs FCSEMS: $1596.9 [1000.8] vs $1455 [333.1], $P = .49$).

Discussion

The chronic and irreversible fibroinflammatory process that occurs in CP commonly results in main PD strictures associated with upstream dilation of the PD and can contribute to abdominal pain secondary to increased intraductal pressures.[34] The pain can, at times, be relieved by decompression of the PD by dilating the stricture and then placing a stent across it. Relief of pain after PD stent placement is common, but the short- and long-term results vary.[42] Unfortunately, up to 30% of patients may have ongoing pain after the stents are removed because the stricture may not resolve.[42] Resolution of PD strictures may require repeated ERCPs, usually at 3-month intervals for up to 6 to 12 months. At the follow-up ERCP, strictures are reassessed and a decision made on increasing the size of the stent, as needed.[43] Dominant PD strictures are those in which upstream dilation of the PD occurs (defined by PD diameter ≥6 mm).[44] Symptomatic strictures that do not resolve after 3 months and 1 year after stent placement with a single PS are referred to as persistent and refractory strictures, respectively.[41,45]

TABLE 9. Evidence profile on population, intervention, comparator, outcome question 4c: ERCP and single PS compared with FCSEMSs in patients with painful chronic pancreatitis and persistent pancreatic duct stricture

Certainty assessment									
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Impact**	**Certainty**	**Importance**
Technical success (stent placement) and clinical success (>50% reduction in visual analog scale): single PS (54) vs FCSEMSs (26) (follow-up: median 34 mo)									
1	Observational studies	Serious*	Not serious†	Not serious	Serious‡	None	• Technical o PS: 54 (100%) o FCSEMS: 26 (100%), $P = .99$ • Clinical o PS: 52 (100%) o FCSEMS: 26 (100%), $P = .320$ • Note PS size 5F or 7F in 70% of patients	⨁⨁◯◯ Low	CRITICAL
Stricture resolution									
1	Observational studies	Serious*	Not serious	Not serious	Serious‡	None	• Single PS: 21 (42.0%) • FCSEMS: 20 (87.0%), $P < .001$	⨁◯◯◯ Very low	CRITICAL
Pain relief									
1	Observational studies	Serious*	Not serious	Not serious	Serious§	None	• Single PS: 29 (53.7%) • FCSEMS: 20 (76.9%), $P = .046$	⨁◯◯◯ Very low	CRITICAL
Stent exchange									
1	Observational studies	Serious*	Not serious	Not serious	Serious‡	None	• Number of stent exchanges in entire group: o PS: 25 (46.3%) o FC-SEMS: 1 (3.8%), $P < .001$	⨁⨁◯◯ Low	IMPORTANT
Duration of stent placement									
1	Observational studies	Serious*	Not serious	Not serious	Serious§	None	• PS, 7.3 mo (IQR, 3.7-15.2) • FCSEMS, 4.9 mo (IQR, 4.0-6.5), $P = .022$	⨁⨁◯◯ Low	IMPORTANT
Number of ERCP sessions									
1	Observational studies	Serious*	Not serious	Not serious	Serious‡	None	• Single PS, 3 (IQR, 1-10) • FCSEMS, 2 (IQR, 1-3). $P = .140$	⨁⨁◯◯ Low	IMPORTANT
Adverse effects									
1	Observational studies	Serious*	Not serious	Not serious	Serious‡	None	• Immediate o PS 20/54 o FCSEMS 10/26 o P = .902 • Delayed o FCSEMS: more spontaneous migration and de novo main duct pancreatic strictures ($P < .001$)	⨁⨁◯◯ Low	IMPORTANT

(*continued on the next page*)

TABLE 9. Continued

Certainty assessment									
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Impact**	**Certainty**	**Importance**
Noncomparative study of FCSEMSs after prior PS and stone clearance for persistent strictures: Stent removal at 6 mo									
1	Observational studies	Not serious	Not serious	Not serious	Serious‖	None	Sherman et al Multicenter 2022 67 patients, 46 eligible for primary endpoint (other without significant pain) Technical success: placement of stent (97%) Primary endpoint: pain reduction, 12/46 (26.1%) less than performance goal of 53.3% Serious adverse events: 21/67 (31.3%) Stent migrations: 31 (47.7%) Recurrent stent placement: 7 patients Secondary/de novo stricture: 5 patients self-reported improvement in quality of life: 71.7% at 6 mo	⨁◯◯◯ Very low	

PS, Plastic stent; *FCSEMS,* fully covered self-expandable metal stent; *IQR,* interquartile range.
*One study (Lee et al, 2021)[41] had serious concerns for risk of bias because of confounding.
†Decided not to rate down further despite the inconsistency of findings between the 2 studies as risk of bias might be the source of inconsistency.
‡Low number of events and small sample size of included studies.
§Small sample size not meeting the optimal information size.
‖Noncomparative study, low numbers.

The evidence presented above addresses some of the available strategies for the initial management of dominant PD strictures and subsequent management of persistent PD strictures in patients with painful CP. For the initial treatment of a dominant PD stricture, a single PS had higher odds of providing pain relief than 1 or 2 PSs and 2 PSs. Moreover, a higher proportion of patients in the single PS group had pain relief compared with the other groups.[39] However, no significant differences in mortality, exocrine function, or endocrine function were found. It should be noted that in this study[39], in the 1 to 2 PS group, 31 of 35 patients were upgraded from 1 PS to 2 PSs at the follow-up ERCP. Also, when comparing 10F PSs with ≤8.5F PSs in a single observational cohort study, patients with smaller PSs had significantly more hospitalizations for abdominal pain per patient, with a significantly higher proportion of hospitalizations in this group.[40] Given the retrospective nature of the study, it is unclear whether a smaller stent was initially placed because the PD stricture was more stenosed and difficult to negotiate and therefore more likely to result in frequent hospitalizations for abdominal pain. In patients who have persistent strictures after 3 months of initial stent placement with a single PS, Lee et al[41] compared use of a single PS with FCSEMSs. It should be noted that in the single PS group 70% of the stents were 7F or less. In this observational non-RCT, pain relief, success rate of ERCPs, and immediate adverse events were similar in both groups. Although the rate of stricture resolution was significantly higher in the FCSEMS group, delayed adverse events such as spontaneous stent migration and de novo strictures were more common in the FCSEMS group.

Sofi et al[45] performed a systematic review and meta-analysis of several noncomparative (single-arm) studies comparing the efficacy and safety of multiple PSs and FCSEMSs in CP patients with symptomatic PD strictures refractory to treatment after 1 year of stent placement. The FCSEMS group and multiple PS group had similar improvement in pain after stent placement (88% [79%-93%] vs 89% [70%-96%], respectively; $P = .79$), recurrence of pain after stent removal, recurrence of stricture after stent removal (14% [8%-26%] vs 11.8% [7%-20%], $P = .48$), and rates

of reintervention (20.2% [13.1%-29.9%] vs 25.4% [17.1%-36%], $P = .31$). However, the FCSEMS group had significantly more adverse events (38.6% vs 14.3%, $P < .0001$) than the multiple PS group, with higher rates of stent migration, biliary obstruction, and pancreatitis.[45] Of note, of the 3 studies in the noncomparative multiple PS group, 1 was in abstract form and 1 (as mentioned above) compared 1 PS and multiple PSs and included persistent but not refractory strictures.[39] The third study in this group included an observational study of 48 patients from a single center followed for a median of 9.5 years after a median placement of 3 PSs.[46] In this study, 74.4% of patients remained asymptomatic after stent removal. A recent, multicenter, noncomparative study by Sherman et al[47] evaluated FCSEMSs in the treatment of a distal dominant PD stricture with upstream dilation. Approximately half of the patients had prior PS placement within 90 days of FCSEMS placement and the other half were undergoing initial treatment. Of the 67 enrolled patients, 46 patients were eligible for evaluation of the primary endpoint of pain relief. Pain reduction in these patients was seen in 12 of 46 patients (26.1%) and was much lower than the target goal performance of 53.3%. Also, significant adverse events occurred in 31.3% (21/67), with stent migration in 47.7% (n = 31) and secondary strictures in 8% (n = 5) of patients.[47]

Overall, data informing these clinical questions were scarce. Yet, the panel noted that clinicians often struggle with these important clinical questions and that guidance on these topics is important for the panel and the ASGE to consider. Based on the of low quality of evidence, the panel agreed that for the initial treatment of a main PD stricture, a single PS appears to perform better than multiple PSs, and whenever possible the largest diameter PS that can be safely deployed should be used without forceful placement. Currently, routine placement of FCSEMSs has no role in initial or secondary treatment of PD strictures given the high rates of adverse events and questionable efficacy. These recommendations are conditional with very low to low quality of evidence.

Question 5: In patients with CP complicated by benign biliary strictures (BBSs) with jaundice and/or elevated alkaline phosphatase for >4 weeks, how do multiple PSs compare with FCSEMSs?

Recommendation 5: The ASGE suggests FCSEMSs over multiple PSs for treatment of BBSs complicating CP.

(Conditional recommendation/low to moderate quality of evidence)

To address this clinical question, we performed a systematic review and meta-analysis of RCTs that compared multiple PSs with FCSEMSs in patients with BBSs with jaundice and/or elevated alkaline phosphatase >4 weeks. The search yielded 204 studies that were screened by 2 reviewers (S.G.S. and J.D.M.) (Appendix 1). After evaluating 10 full-text articles, 3 RCTS were identified that met inclusion criterion comparing 259 patients managed with multiple PSs versus FCSEMSs (Supplementary Table 1).[48-50] Patient characteristics and study outcomes are summarized in Supplementary Tables 2 and 3.[48-50]

Procedural outcomes

1. *Stricture resolution.* The odds (evaluated radiographically at ERCP) were not statistically different in patients undergoing ERCP with multiple PSs as compared with FCSEMSs (OR, .59; 95% CI, .19-1.81; $I^2 = 50.6\%$) (Fig. 4A).
2. *Adverse events.* No differences were found in procedural adverse events in patients undergoing ERCP with multiple PSs as compared with FCSEMSs (OR, .67; 95% CI, .35-1.3; $I^2 = 0\%$) (Fig. 4B).
3. *Mortality.* No difference in mortality occurred in the multiple PS group compared with the FCSEMS group (OR, .41; 95% CI, –.12 to 1.38; $I^2 = 0\%$) (Fig. 4C).[49,50]
4. *Time to resolution of stricture.* Coté et al[48] reported a similar time to resolution of stricture in patients with multiple PSs (median, 199.5 days [IQR, 95]) as compared with FCSEMSs (median, 184 days [IQR, 38]; $P = .146$). The study by Ramchandani et al[49] also showed no difference in the time to resolution between both groups (PS vs FCSEMS: 360 days vs 362 days, $P = .9$).

ERCP utilization

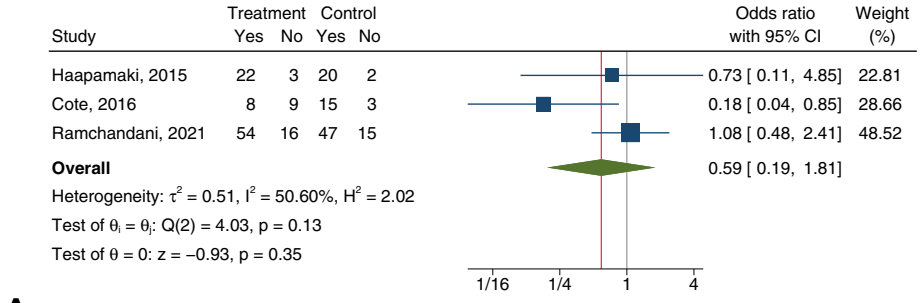
A significantly higher number of ERCP procedures occurred in patients undergoing multiple PS insertion as compared with FCSEMSs (mean difference, 1.42; 95% CI, 1.15-1.70; $I^2 = .00$, $P < .01$) (Fig. 4D).[48,49] No difference in procedural time was found for ERCP sessions between the multiple PS and FCSEMS groups (mean difference, 8.26; 95% CI, –6.24 to 22.76; $I^2 = 83\%$) (Fig. 4E).[49,50] Ramchandani et al[49] described a significantly higher number of PSs used compared with FCSEMSs (7.0 ± 4.4 vs 1.3 ± .6, respectively; $P < .001$).

Sensitivity analysis

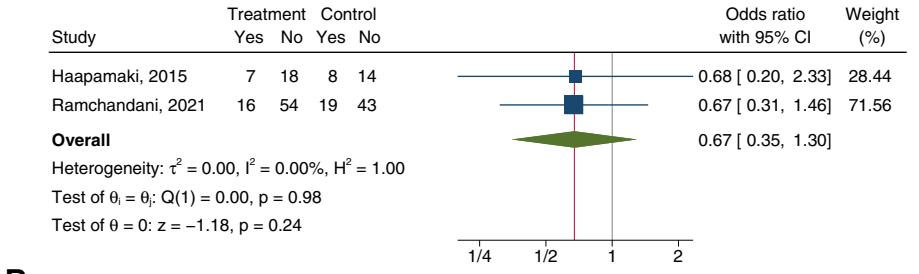
A sensitivity analysis evaluating the outcome of stricture resolution showed substantial alteration in the CI when the study by Coté et al[48] was removed (Supplementary Fig. 1D). The OR changed from .59 (95% CI, .19-1.81) to 1.02 (95% CI, .48-2.13), although the effect size did not change significantly ($P = .43$) (Supplementary Fig. 1E).

Certainty in the evidence

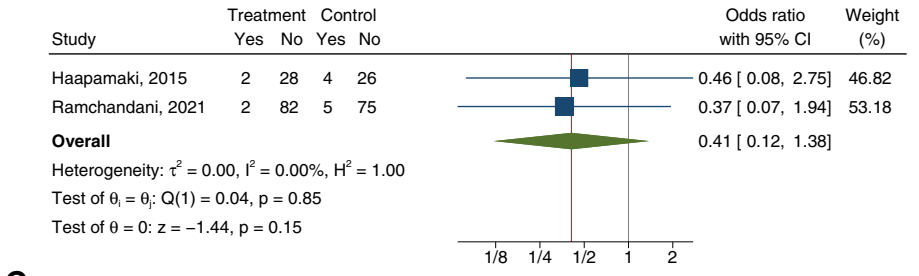
The risk of bias in the eligible studies was not serious, with only some concerns noted in the domain of deviation from intended interventions (Supplementary Fig. 2). The certainty of the evidence for mean difference in the number of ERCPs was downgraded to moderate because of the imprecision from a low sample size. For the remaining outcomes, low event rates and wide CIs caused very serious



A Random−effects REML model



B Random−effects REML model



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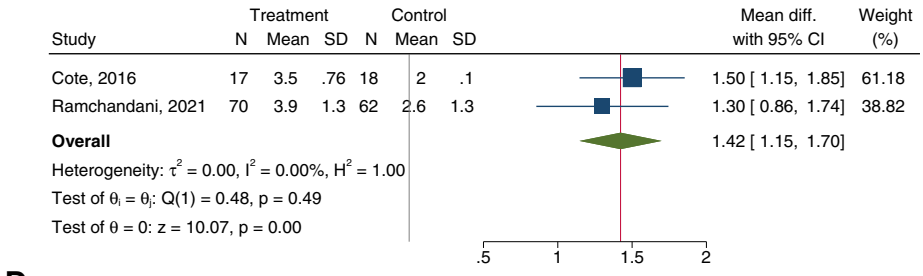
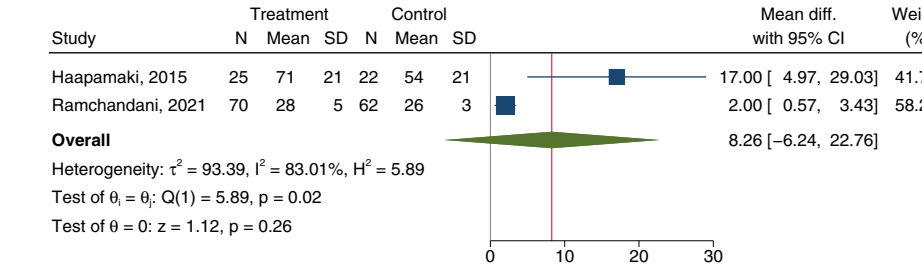


D Random−effects REML model



E Random−effects REML model

Figure 4. Among chronic pancreatitis patients with benign biliary strictures undergoing stent placement with multiple plastic stents as compared with fully covered self-expandable metal stents, the odds ratios of (**A**) stricture resolution, (**B**) adverse events, (**C**) mortality, (**D**) mean difference in the number of ERCPs, and (**E**) mean difference in ERCP times are shown. *CI*, Confidence interval; *SD*, standard deviation

imprecision and thus had a low certainty of evidence (Table 10).

Other considerations

No cost data were available in the included RCTs.[48-50]

Discussion

Up to 30% of patients with CP can develop BBSs that may result in biliary obstruction with associated jaundice, elevation of alkaline phosphatase, cholangitis, and high risk of secondary biliary cirrhosis.[51,52] Occasionally, the biliary obstruction may be caused by a self-limited compression of the common bile duct because of acute inflammation in the head of the pancreas or a fluid collection.[53] Hence, when the obstruction persists beyond 4 weeks, it should be treated to prevent secondary biliary cirrhosis. Biliary strictures in the setting of CP tend to be more fibrotic and have a higher chance of recurrence.[54] Endoscopic options are similar to other BBSs and include dilation of strictures with placement of multiple PSs or FCSEMSs.

Three RCTs comparing multiple PSs and FCSEMSs for the treatment of BBSs are discussed above.[48-50] Two of these studies were noninferiority trials,[48,49] whereas the study by Haapamaki et al[50] was a superiority trial. A systematic review and meta-analysis was performed and showed that rates of stricture resolution, time to resolution of stricture, ERCP procedural time, adverse events, and mortality were similar in both groups. In cases of the use of multiple PSs, patients underwent ERCPs every 3 months, and for FCSEMSs, ERCP was performed every 6 months. The duration of stent placement period ranged from 6 to 12 months, with a follow-up period of 1 to 2 years after stent placement. Coté et al[48] studied BBSs in a variety of diseases. Hence, a subgroup analysis was performed in 35 of 112 patients who had BBSs secondary to CP only. The rates of stricture resolution in all 3 studies ranged from 75% to 90% in follow-up. The major difference in the 2 groups was a significantly higher number of ERCPs in the multiple PS group compared with the FCSEMS group, with a higher number of stents used in the PS group. In most patients in the 3 studies, up to 3 PSs of 8.5F to 10F and FCSEMSs 8 to 10 mm in diameter were placed.

In summary, the studies show that FCSEMSs are as efficacious as multiple PSs in the treatment of BBSs in CP patients but require fewer ERCPs. The panel believed that in cases with concerns for noncompliance or difficulty in scheduling multiple procedures, FCSEMSs can be considered over multiple PSs because serious adverse events have been reported because of noncompliance when PSs are placed.[55] Multiple PS placement may be considered if the biliary stricture is indeterminate and when obstructing the cystic duct is a concern, as in cases with an intact gallbladder because of the potential risk of holecystitis.[48,49] These recommendations are conditional with a low to moderate quality of evidence.

Question 6: In patients with CP and symptomatic pseudocysts, how does endoscopic drainage compare with surgical drainage?

Recommendation 6: The ASGE suggests endoscopic drainage over surgical drainage of symptomatic pseudocysts in patients with CP.

(Conditional recommendation/low quality of evidence)

To address this clinical question, a literature search yielded 958 citations and abstracts, which were screened by 2 reviewers (S.G.S. and J.D.M.) (Appendix 1). After evaluating 31 full-text articles, only 1 comparative study (an RCT) was identified that met the inclusion criterion and included 20 adult patients in both endoscopic and surgical groups (Supplementary Table 1).[56] Pseudocysts were diagnosed based on CT criteria, measured ≥6 cm, and were located adjacent to the stomach with persistent pancreatic pain, symptomatic gastric outlet, or bile duct obstruction. The study excluded patients aged <18 years or >80 years, with contraindications to surgery and endoscopic drainage, who were pregnant, and had associated necrosis and pseudocyst with multilocularity, multiplicity, or distant from stomach. Patient characteristics and study outcomes are summarized in Supplementary Tables 2 and 3.

Procedural outcomes

1. *Treatment success.* Similar treatment success in the EUS-guided cystogastrostomy group (19 [95%]) was observed as compared with the surgical cystogastrostomy group (20 [100%], $P = .5$). Treatment success was defined as the clinical resolution of symptoms at 4 weeks for the surgical group compared with CT and clinical resolution at 8 weeks for the endoscopic group.[56]
2. *Recurrence.* The endoscopic and surgical interventions lacked significant difference in recurrence rates (0 vs 1 [5%], respectively).[56]
3. *Adverse events.* No difference was seen in procedural adverse events between the endoscopic and surgical groups (0 vs 2 [10%], respectively; $P = .24$).[56]
4. *Duration of hospital stay.* Patients who underwent endoscopic interventions had a significantly lower duration of hospital stay as compared with the surgery group (2 days [IQR, 1 -4] vs 6 days [IQR, 5-9], respectively; $P < .001$).[56]
5. *Quality of life.* The physical and mental quality of life improved in both endoscopic and surgical groups. Although both groups had an improvement in the score, the improvement in the physical component of the 36-item Short Form Survey score was significantly lower with surgery as compared with endoscopy (4.48 points; 95% CI, –8.23 to –.73; $P = .019$). The improvement in the mental component of the summary score was also

TABLE 10. Evidence profile on population, intervention, comparator, outcome question 5: ERCP with multiple PSs compared with FCSEMSs in patients with chronic pancreatitis complicated by benign biliary strictures and jaundice and/or elevated alkaline phosphatase >4 wk

Certainty assessment						
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**
Number of ERCP sessions to achieve resolution (follow-up: range, 14-21 mo)						
2	Randomized trials	Not serious	Not serious	Not serious	Serious*	None
Number of stents placed						
1	Randomized trials	Not serious	Not serious	Not serious	Very serious†	None
Stricture resolution (follow-up: range, 12-41 mo)						
3	Randomized trials	Not serious	Not serious	Not serious	Very serious†	None
ERCP time (follow-up: range, 12-41 mo)						
2	Randomized trials	Not serious	Serious‡	Not serious	Serious*	None
Time to resolution						
2	Randomized trials	Not serious	Serious‡	Not serious	Serious*	None
Adverse effects (follow-up: range, 12-41 mo)						
2	Randomized trials	Not serious	Not serious§	Not serious	Very serious†	None
Total deaths (follow-up: range, 12-41 mo)						
2	Randomized trials	Not serious	Not serious	Not serious	Very serious†	None

PS, Plastic stent; *FCSEMS*, fully covered self-expandable metal stent; *OR*, odds ratio; *CI*, confidence interval.
*Small sample size of the trial not meeting the optimal information size.
†Low number of events and sample size of included studies.
‡The results from 1 study showed a statistically important difference between interventions, whereas the other trial showed no difference.
§I^2 = .0%, and most studies point estimates and 95% CIs overlap considerably.

significantly lower in the surgical versus endoscopic groups (4.41 points; 95% CI, –8.26 to –.55; P = .025).[56]

6. *Reintervention.* No difference in reinterventions was observed in either the endoscopic (1 [5%]) or surgical (1 [5%]) groups (P = .76).[56]

Certainty in the evidence

The study was a RCT, and the risk of bias was not serious (Supplementary Fig. 2). The small sample size caused very serious imprecision. Thus, the certainty of evidence for all outcomes was low (Table 11).

Other considerations

The cost of endoscopic drainage of pseudocysts in CP patients was significantly lower compared with surgical drainage ($7011 vs $15,052, P = .003). No cost-effective analysis was performed.

Discussion

Pancreatic pseudocysts can develop in up to one-third of patients with CP during the course of their disease and is usually the consequence of acute inflammation of the pancreas.[57] Pancreatic pseudocysts do not contain necrotic

TABLE 10. Continued

No. of patients		Effect			
ERCP with multiple PSs	FCSEMSs	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
87	80		Mean difference, 1.42 ERCPs more (1.15 more to 1.7 more)	⨁⨁⨁◯ Moderate	CRITICAL
Ramchandani et al (2022)[49] (non-inferiority trial) • Per-protocol analysis ie as treated o Multiple PS mean 7.0 ± 4.4 (69 patients) o FCSEMS mean 1.3 ± 0.6 (68 patients) o $P < .001$ • Intention-to-treat analysis o Multiple PS mean 6.7 ± 4.4 (81 patients) o FCSEMS mean 2.3 ± 3.3 (79 patients) o $P < .001$				⨁⨁◯◯ Low	IMPORTANT
84/112 (75.0%)	82/102 (80.4%)	OR .59 (.19-1.81)	96 fewer per 1000 (from 366 fewer to 77 more)	⨁⨁◯◯ Low	CRITICAL
95	84		Mean difference, 8.26 min more (6.24 fewer to 22.76 more)	⨁⨁◯◯ Low	IMPORTANT
• Not significant; also cannot meta-analyze as Ramchandani[49] did not provide interquartile rnage • Coté 2016[48] o PS: 233 days o FCSEMS: 187.3 days o $P = .1461$ • Ramchandani 2022[49] o PS: 360 o FCSEMS: 362 o $P = .9$				⨁⨁◯◯ Low	IMPORTANT
23/95 (24.2%)	27/84 (32.1%)	OR .67 (.35-1.30)	81 fewer per 1000 (from 179 fewer to 60 more)	⨁⨁◯◯ Low	CRITICAL
4/114 (3.5%)	9/110 (8.2%)	OR .41 (.12-1.38)	47 fewer per 1000 (from 71 fewer to 28 more)	⨁⨁◯◯ Low	CRITICAL

material and are distinct from walled-off necrosis, which is commonly encountered as a consequence of acute necrotizing pancreatitis.[58] When symptomatic (ie, pain, gastric outlet obstruction, or biliary obstruction), pseudocysts require drainage, which can be accomplished endoscopically, surgically, or percutaneously. A PC approach typically results in an external fistula and therefore is rarely performed.[59,60]

A single RCT compared endoscopic cystgastrostomy with surgical cystgastrostomy for the treatment of symptomatic pseudocysts in CP patients.[56] As noted above, there were 20 patients in each group, and endoscopic cystgastrostomy was performed by EUS and fluoroscopic guidance. The primary outcome in this study was pseudocyst recurrence during a follow-up period of 24 months. Treatment success was defined variably between the 2 groups. In the surgical group, treatment success was defined as the resolution of symptoms at 4 weeks. Alternatively, in the endoscopy group, treatment success was defined as cyst resolution on CT and symptom resolution in addition to symptoms at the 8-week follow-up. The difference in follow-up periods was because surgical and endoscopic practices differed at this institution. No statistical differences were found in treatment success, recurrence, adverse events, and reintervention rates in both groups. However, in the endoscopy group, the length of hospital stay was significantly shorter with lower costs and with significantly more improvement in physical and mental quality of life scores compared with the surgical group.

Farias et al[61] in a systematic review and meta-analysis of 6 studies of 342 patients compared endoscopic versus surgical drainage of pseudocysts of any etiology. Most patients (302/342) had pseudocysts in the setting of acute pancreatitis.

TABLE 11. Evidence profile on population, intervention, comparator, outcome question 6: endoscopic drainage compared with surgical drainage in patients with chronic pancreatitis and symptomatic pseudocysts

Certainty assessment									
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Impact	Certainty	Importance
Treatment success (clinical resolution of symptoms at 4 wk for surgery; CT and clinical resolution at 8 wk for endoscopy)									
1	Randomized trials	Not serious	Not serious	Not serious	Very serious*	None	• EUS/endoscopic cystogastrostomy: 19/20 (95%) • Surgical cystogastrostomy: 20/20 (100%), $P = .50$	⨁⨁◯◯ Low	CRITICAL
Recurrence									
1	Randomized trials	Not serious	Not serious	Not serious	Very serious*	None	• Endoscopy 0 • Surgery 1, $P =$ not significant	⨁⨁◯◯ Low	CRITICAL
Adverse events									
1	Randomized trials	Not serious	Not serious	Not serious	Very serious*	None	• Endoscopy 0 • Surgery 2 (wound infection and hematemesis), $P = .24$	⨁⨁◯◯ Low	CRITICAL
Duration of hospital stay (days)									
1	Randomized trials	Not serious	Not serious	Not serious	Very serious†	None	• Endoscopy 2 days (interquartile range, 1-4) • Surgery 6 days (interquartile range, 5-9), $P < .001$	⨁⨁◯◯ Low	IMPORTANT
Physical component summary score (assessed with 36-item Short Form Survey; higher score is better with a score of 100 being healthy)									
1	Randomized trials	Not serious	Not serious	Not serious	Very serious†	None	• Physical component summary score improved over time in both groups (1.9 points a mo; $P < .001$) • Surgery physical component score 4.48 points lower (95% confidence interval, −8.23 to −.73) lower than endoscopy; $P = .019$	⨁⨁◯◯ Low	IMPORTANT
Mental component summary score (assessed with 36-item Short Form Survey; higher score is better with a score of 100 being healthy)									
1	Randomized trials	Not serious	Not serious	Not serious	Very serious†	None	• Mental component summary score improved over time for both treatment groups (1.2 points a mo; $P < .001$ • Surgery mental component score 4.41 points lower 95% confidence interval, −8.26 to −.55) than endoscopy; $P = .025$	⨁⨁◯◯ Low	IMPORTANT

(*continued on the next page*)

TABLE 11. Continued

Certainty assessment									
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Impact	Certainty	Importance
Reintervention									
1	Randomized trials	Not serious	Not serious	Not serious	Very serious*	None	• Endoscopic: 1 (5%) • Surgical: 1 (5%); P = .76	⨁⨁◯◯ Low	IMPORTANT

*Low number of events and small sample size of included studies.
†Small sample size of the trial not meeting the optimal information size.

Similar to the RCT by Varadarajulu et al[56] in CP patients reported above, the endoscopy group had a significantly shorter length of stay and lower cost compared with the surgical group, with no significant differences between success rate, drainage-related adverse events, general adverse events, and recurrence in both groups. A cost-effectiveness analysis study by Quinn et al[62] showed that endoscopic management of pseudocysts resulted in an additional .22 more quality-adjusted life-years while also saving $23,976 compared with laparoscopic surgical treatment.

Although data on these outcomes in CP patients were scarce, many studies have assessed the efficacy of endoscopic versus surgical drainage of pseudocysts in non-CP (ie, acute pancreatitis) patients. The outcomes data on pseudocyst drainage in CP patients are similar to the more extensive evidence reported in acute pancreatitis patients. These data were used as indirect evidence. Hence, the panel suggested endoscopic drainage over surgical drainage for pseudocysts in CP patients. This recommendation is conditional with a low quality of evidence.

HEALTH DISPARITIES AND EQUITY

The panel addressed health equity and feasibility for each PICO question. They acknowledged that many patients have reduced access to high-quality medical care and specific therapies. Members of the panel addressed that in a number of countries, including the United States, ESWL is not readily available at many centers. Also, newer therapies such as pancreatoscopy and access to expert pancreatic surgeons may be limited to specialized centers. Additionally, the availability of technical expertise with placement of pancreatic stents and endoscopic cystgastrostomy may be greater at tertiary centers rather than community health centers. No racial- or gender-specific disparities were identified.

GUIDELINE UPDATE

ASGE guidelines are reviewed for updates approximately every 5 years or in the event that new data may influence a recommendation. Updates follow the same ASGE guideline development process.

DISCLOSURE

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REFERENCES

1. Singh VK, Yadav D, Garg PK. Diagnosis and management of chronic pancreatitis: a review. JAMA 2019;322:2422-34.
2. Vege SS, Chari ST. Chronic pancreatitis. N Engl J Med 2022;386:869-78.
3. Dominguez-Munoz JE, Drewes AM, Lindkvist B, et al. Recommendations from the United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis. Pancreatology 2018;18:847-54.
4. Wani S, Sultan S, Qumseya B, et al. The ASGE's vision for developing clinical practice guidelines: the path forward. Gastrointest Endosc 2018;87:932-3.
5. Jackson R, Feder G. Guidelines for clinical guidelines. BMJ 1998;317:427-8.
6. Bramer WM, Giustini D, de Jonge GB, et al. De-duplication of database search results for systematic reviews in EndNote. J Med Libr Assoc 2016;104:240-3.
7. Higgins JP, Thomas J, Chandler J, et al. Cochrane handbook for systematic reviews of interventions. Hoboken, NJ: John Wiley & Sons; 2019.
8. Sterne JA, Hernan MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016;355:i4919.
9. Sterne JAC, Savovic J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019;366:l4898.
10. Dite P, Ruzicka M, Zboril V, et al. A prospective, randomized trial comparing endoscopic and surgical therapy for chronic pancreatitis. Endoscopy 2003;35:553-8.
11. Cahen DL, Gouma DJ, Nio Y, et al. Endoscopic versus surgical drainage of the pancreatic duct in chronic pancreatitis. N Engl J Med 2007;356:676-84.
12. Cahen DL, Gouma DJ, Laramee P, et al. Long-term outcomes of endoscopic vs surgical drainage of the pancreatic duct in patients with chronic pancreatitis. Gastroenterology 2011;141:1690-5.
13. Hirota M, Asakura T, Kanno A, et al. Long-period pancreatic stenting for painful chronic calcified pancreatitis required higher medical costs and frequent hospitalizations compared with surgery. Pancreas 2011;40:946-50.
14. Kawashima Y, Kawaguchi Y, Kawanishi A, et al. Comparison between endoscopic treatment and surgical drainage of the pancreatic duct in chronic pancreatitis. Tokai J Exp Clin Med 2018;43:117-21.
15. Issa Y, Kempeneers MA, Bruno MJ, et al. Effect of early surgery vs endoscopy-first approach on pain in patients with chronic pancreatitis: the ESCAPE randomized clinical trial. JAMA 2020;323:237-47.
16. Bloechle C, Izbicki JR, Knoefel WT, et al. Quality of life in chronic pancreatitis—results after duodenum-preserving resection of the head of the pancreas. Pancreas 1995;11:77-85.
17. Melzack R. The short-form McGill Pain Questionnaire. Pain 1987;30:191-7.
18. Kempeneers MA, Issa Y, Bruno MJ, et al. Cost-effectiveness of early surgery versus endoscopy-first approach for painful chronic pancreatitis in the ESCAPE trial. Ann Surg 2023;277:e878-84.
19. Mullady DK, Yadav D, Amann ST, et al. Type of pain, pain-associated complications, quality of life, disability and resource utilisation in chronic pancreatitis: a prospective cohort study. Gut 2011;60:77-84.
20. Drewes AM, van Veldhuisen CL, Bellin MD, et al. Assessment of pain associated with chronic pancreatitis: an international consensus guideline. Pancreatology 2021;21:1256-84.
21. Hu LH, Ye B, Yang YG, et al. Extracorporeal shock wave lithotripsy for Chinese patients with pancreatic stones: a prospective study of 214 cases. Pancreas 2016;45:298-305.
22. Gress F, Schmitt C, Sherman S, et al. A prospective randomized comparison of endoscopic ultrasound- and computed tomography-guided celiac plexus block for managing chronic pancreatitis pain. Am J Gastroenterol 1999;94:900-5.
23. Santosh D, Lakhtakia S, Gupta R, et al. Clinical trial: a randomized trial comparing fluoroscopy guided percutaneous technique vs. endoscopic ultrasound guided technique of coeliac plexus block for treatment of pain in chronic pancreatitis. Aliment Pharmacol Ther 2009;29:979-84.
24. Sachdev AH, Gress FG. Celiac plexus block and neurolysis: a review. Gastrointest Endosc Clin North Am 2018;28:579-86.
25. Puli SR, Reddy JB, Bechtold ML, et al. EUS-guided celiac plexus neurolysis for pain due to chronic pancreatitis or pancreatic cancer pain: a meta-analysis and systematic review. Dig Dis Sci 2009;54:2330-7.
26. Sey MS, Schmaltz L, Al-Haddad MA, et al. Effectiveness and safety of serial endoscopic ultrasound-guided celiac plexus block for chronic pancreatitis. Endosc Int Open 2015;3:E56-9.
27. O'Toole TM, Schmulewitz N. Complication rates of EUS-guided celiac plexus blockade and neurolysis: results of a large case series. Endoscopy 2009;41:593-7.
28. Bick BL, Patel F, Easler JJ, et al. A comparative study between single-operator pancreatoscopy with intraductal lithotripsy and extracorporeal shock wave lithotripsy for the management of large main pancreatic duct stones. Surg Endosc 2022;36:3217-26.
29. Dumonceau JM, Costamagna G, Tringali A, et al. Treatment for painful calcified chronic pancreatitis: extracorporeal shock wave lithotripsy versus endoscopic treatment: a randomised controlled trial. Gut 2007;56:545-52.

30. Vaysse T, Boytchev I, Antoni G, et al. Efficacy and safety of extracorporeal shock wave lithotripsy for chronic pancreatitis. Scand J Gastroenterol 2016;51:1380-5.
31. Suzuki Y, Sugiyama M, Inui K, et al. Management for pancreatolithiasis: a Japanese multicenter study. Pancreas 2013;42:584-8.
32. Frulloni L, Gabbrielli A, Pezzilli R, et al. Chronic pancreatitis: report from a multicenter Italian survey (PanCroInfAISP) on 893 patients. Dig Liver Dis 2009;41:311-7.
33. Karanjia ND, Widdison AL, Reber HA. Pancreatic tissue and ductal pressures in chronic pancreatitis. Br J Surg 1992;79:469.
34. Rosch T, Daniel S, Scholz M, et al. Endoscopic treatment of chronic pancreatitis: a multicenter study of 1000 patients with long-term follow-up. Endoscopy 2002;34:765-71.
35. Dumonceau JM, Delhaye M, Tringali A, et al. Endoscopic treatment of chronic pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) guideline—updated August 2018. Endoscopy 2019;51:179-93.
36. Guzman-Calderon E, Martinez-Moreno B, Casellas JA, et al. Per-oral pancreatoscopy-guided lithotripsy for the endoscopic management of pancreatolithiasis: a systematic review and meta-analysis. J Dig Dis 2021;22:572-81.
37. Moole H, Jaeger A, Bechtold ML, et al. Success of extracorporeal shock wave lithotripsy in chronic calcific pancreatitis management: a meta-analysis and systematic review. Pancreas 2016;45:651-8.
38. Tandan M, Nageshwar Reddy D, Talukdar R, et al. ESWL for large pancreatic calculi: report of over 5000 patients. Pancreatology 2019;19:916-21.
39. Papalavrentios L, Musala C, Gkolfakis P, et al. Multiple stents are not superior to single stent insertion for pain relief in patients with chronic pancreatitis: a retrospective comparative study. Endosc Int Open 2019;7:E1595-604.
40. Sauer BG, Gurka MJ, Ellen K, et al. Effect of pancreatic duct stent diameter on hospitalization in chronic pancreatitis: Does size matter? Pancreas 2009;38:728-31.
41. Lee SH, Kim YS, Kim EJ, et al. Long-term outcomes of fully covered self-expandable metal stents versus plastic stents in chronic pancreatitis. Sci Rep 2021;11:15637.
42. Eleftherladis N, Dinu F, Delhaye M, et al. Long-term outcome after pancreatic stenting in severe chronic pancreatitis. Endoscopy 2005;37:223-30.
43. Seza K, Yamaguchi T, Ishihara T, et al. A long-term controlled trial of endoscopic pancreatic stenting for treatment of main pancreatic duct stricture in chronic pancreatitis. Hepatogastroenterology 2011;58:2128-31.
44. Delhaye M, Matos C, Deviere J. Endoscopic management of chronic pancreatitis. Gastrointest Endosc Clin North Am 2003;13:717-42.
45. Sofi AA, Khan MA, Ahmad S, et al. Comparison of clinical outcomes of multiple plastic stents and covered metal stent in refractory pancreatic ductal strictures in chronic pancreatitis—a systematic review and meta-analysis. Pancreatology 2021;21:854-61.
46. Tringali A, Bove V, Vadala di Prampero SF, et al. Long-term follow-up after multiple plastic stenting for refractory pancreatic duct strictures in chronic pancreatitis. Endoscopy 2019;51:930-5.
47. Sherman S, Kozarek RA, Costamagna G, et al. Soft self-expanding metal stent to treat painful pancreatic duct strictures secondary to chronic pancreatitis: a prospective multicenter trial. Gastrointest Endosc 2023;97:472-81.e3.
48. Coté GA, Slivka A, Tarnasky P, et al. Effect of covered metallic stents compared with plastic stents on benign biliary stricture resolution: a randomized clinical trial. JAMA 2016;315:1250-7.
49. Ramchandani M, Lakhtakia S, Costamagna G, et al. Fully covered self-expanding metal stent vs multiple plastic stents to treat benign biliary strictures secondary to chronic pancreatitis: a multicenter randomized trial. Gastroenterology 2021;161:185-95.
50. Haapamaki C, Kylanpaa L, Udd M, et al. Randomized multicenter study of multiple plastic stents vs. covered self-expandable metallic stent in the treatment of biliary stricture in chronic pancreatitis. Endoscopy 2015;47:605-10.
51. Costamagna G, Boskoski I. Current treatment of benign biliary strictures. Ann Gastroenterol 2013;26:37-40.
52. Familiari P, Boskoski I, Bove V, et al. ERCP for biliary strictures associated with chronic pancreatitis. Gastrointest Endosc Clin North Am 2013;23:833-45.
53. Abdallah AA, Krige JE, Bornman PC. Biliary tract obstruction in chronic pancreatitis. HPB 2007;9:421-8.
54. Siiki A, Helminen M, Sand J, et al. Covered self-expanding metal stents may be preferable to plastic stents in the treatment of chronic pancreatitis-related biliary strictures: a systematic review comparing 2 methods of stent therapy in benign biliary strictures. J Clin Gastroenterol 2014;48:635-43.
55. Kiehne K, Folsch UR, Nitsche R. High complication rate of bile duct stents in patients with chronic alcoholic pancreatitis due to noncompliance. Endoscopy 2000;32:377-80.
56. Varadarajulu S, Bang JY, Sutton BS, et al. Equal efficacy of endoscopic and surgical cystogastrostomy for pancreatic pseudocyst drainage in a randomized trial. Gastroenterology 2013;145:583-90.
57. Ammann RW, Akovbiantz A, Largiader F, et al. Course and outcome of chronic pancreatitis. longitudinal study of a mixed medical-surgical series of 245 patients. Gastroenterology 1984;86:820-8.
58. Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013;62:102-11.
59. Khan MA, Hammad T, Khan Z, et al. Endoscopic versus percutaneous management for symptomatic pancreatic fluid collections: a systematic review and meta-analysis. Endosc Int Open 2018;6:E474-83.
60. Nealon WH, Walser E. Main pancreatic ductal anatomy can direct choice of modality for treating pancreatic pseudocysts (surgery versus percutaneous drainage). Ann Surg 2002;235:751-8.
61. Farias GFA, Bernardo WM, De Moura DTH, et al. Endoscopic versus surgical treatment for pancreatic pseudocysts: aystematic review and meta-analysis. Medicine 2019;98:e14255.
62. Quinn PL, Bansal S, Gallagher A, et al. Endoscopic versus laparoscopic drainage of pancreatic pseudocysts: a cost-effectiveness analysis. J Gastrointest Surg 2022;26:1679-85.

Abbreviations: ASGE, American Society for Gastrointestinal Endoscopy; BBS, benign biliary stricture; CI, confidence interval; CP, chronic pancreatitis; CPB, celiac plexus block; ESWL, extracorporeal shock wave lithotripsy; EUS-CPB, EUS-guided celiac plexus block; FCSEMS, fully covered self-expandable metal stent; GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; IQR, interquartile range; OR, odds ratio; PC, percutaneous; PICO, population, intervention, comparator, outcome; PD, pancreatic duct; PS, plastic stent; RCT, randomized controlled trial.

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APPENDIX 1

PICO 1: Endoscopy vs Surgery for obstructed chronic pancreatitis

Database: Ovid MEDLINE

Search Date: 12 November 2021

Limits: English language; RCTs, meta-analyses, systematic reviews, prospective or retrospective comparative studies; published after January 1, 2001

Number of Results: 87

1	(exp Pancreatitis, Chronic/ or exp Pancreatitis, Alcoholic/ or (Pancreatitis/ and Chronic Diseases/) or (chronic adj2 pancreatitis).tw,kf. or ((autoimmun$ or auto-immun$ or Tropical or hereditar$ or familiar$) and pancreatitis).tw,kf. or (Hypertriglyceridemia/ or Hypercalcemia/ or alcohol intoxicat$.tw,kf. or (autoimmun$ or auto-immun$).tw,kf.)) and (Pancreas/ or pancrea*.tw,kf.)	28519
2	(exp Pancreatic Ducts/ and obstruct*.tw,kf.) or (pancrea$ adj2 duct$ adj2 obstruct$).tw,kf. or ((main adj2 duct$ adj2 obstruct*) and pancrea*).tw,kf. or (pancrea* duct*.tw,kf. and (pain or painful).ti.)	1884
3	1 and 2	511
4	exp Cholangiopancreatography, Endoscopic Retrograde/ or Drainage/ or Endoscopy/ or Endoscopy, Digestive System/	123244
5	(ERCP or (endoscop* adj2 retrograd* adj2 (cholangiopancreatograph* or cholangio-pancreatograph*))).tw,kf.	15195
6	exp Sphincterotomy, Endoscopic/ or exp papillotomy/ or ((endoscop* adj3 sphincterotom*) or EST).tw,kf. or papillotom*.tw,kf. or rendezvous.tw,kf. or (drain* and duct*).tw,kf. or (endoscop* or endotherap*).ti,ab.	252989
7	exp Decompression/ or decompress*.tw,kf.	51696
8	exp Dilatation/ or (dilate* or dilation*).tw,kf.	102805
9	or/4-8	457960
10	(exp Pancreatitis, Chronic/ or exp Pancreas/ or Pancreatic Diseases/ or Pancreatitis/ or (chronic pancreatitis or pancrea*).tw,kf.) and (General Surgery/ or Surgical Procedures, Operative/ or (resect* or surger* or surgical or operat* or recis* or duodenectom* or PPPD or pylorus-reserving).tw,kf.)	67360
11	exp Pancreaticojejunostomy/ or exp Pancreatectomy/ or exp Pancreaticoduodenectomy/ or (pancreatojejunostom* or pancreaticojejunostom* or (pancrea* adj5 (duodenectom* or jejunostom*))).tw,kf. or (duodenopancreatectom* or pancreatoduodenectom* or pancreaticoduodenectom* or pancreaticogastrostom* or hemipancreatectom*).tw,kf. or (anastomos* adj5 (pancreatojejunal or jejunopancreatic)).tw,kw. or whipple.tw,kf. or pancreatectom*.tw,kf. or (Beger or Frey or puestow or Partington-Rochelle).tw,kf. or ((left or tail or distal or caudal) and (resection or pancreatectomy)).tw,kf. or (dilation adj2 pancrea$).tw,kf.	72304
12	10 or 11	116974
13	3 and (9 or 12)	430
14	exp "sensitivity and specificity"/	622845
15	false negative reactions/ or false positive reactions/	39725
16	(sensitivity or specificity).ti,ab.	1125314
17	(predicitve adj value$1).ti,ab.	14
18	(likelihood adj ratio$1).ti,ab.	17307
19	(false adj (negative$1 or positive$1)).ti,ab.	82680
20	(randomized controlled trial or controlled clinical trial).pt.	639777
21	double blind method/ or single blind method/	198435
22	practice guideline.pt.	29250
23	consensus development conference.pt.	12186
24	random$.ti,ab.	1266585
25	random allocation/	106169
26	(single blind$3 or double blind$3 or triple blind$3).ti,ab.	180051
27	(review or review academic).pt.	2891079
28	meta analysis.pt.	146383
29	(systematic adj review$).ti,ab. or (systematic* adj3 search*).ab.	242702
30	or/14-27	5731309
31	30 and (28 or 29)	221099
32	Randomized controlled trials as Topic/	150114
33	Randomized controlled trial/	550109
34	Random allocation/	106169
35	Double blind method/	168250
36	Single blind method/	31173
37	Clinical trial/	532194
38	exp Clinical Trials as Topic/	366362
39	or/32-38	1250772
40	(clinic$ adj trial$1).tw.	415775
41	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	184125
42	Placebos/	35755
43	Placebo$.tw.	230184
44	Randomly allocated.tw.	32219
45	(allocated adj2 random).tw.	806
46	or/40-45	699526
47	39 or 46	1560994
48	Case report.tw.	347685
49	Letter/	1158573
50	Historical article/	366448
51	Review of reported cases.pt.	0
52	Review, multicase.pt.	0
53	or/48-52	1855402
54	47 not 53	1523918
55	Epidemiologic studies/	8885
56	exp case control studies/	1248691
57	exp cohort studies/	2245588
58	Case control.tw.	138272
59	(cohort adj (study or studies)).tw.	252680
60	Cohort analy$.tw.	9632
61	(Follow up adj (study or studies)).tw.	52302
62	(observational adj (study or studies)).tw.	130453
63	Longitudinal.tw.	278366
64	Retrospective.tw.	624109
65	Cross sectional.tw.	421170
66	Cross-sectional studies/	397938
67	or/55-66	3378229
68	31 or 54 or 67	4686898
69	13 and 68	152
70	limit 69 to english language	135
71	limit 70 to dt=20010101-20211231	87

Database: Embase.com (Elsevier)

Search Date: 12 November 2021

Limits: English language; RCTs, meta-analyses, systematic reviews, prospective or retrospective comparative studies; published after January 1, 2001

Number of Results: 109

1	('chronic pancreatitis'/exp OR 'alcoholic pancreatitis'/exp OR ('pancreatitis'/de AND 'chronic disease'/de) OR (chronic NEAR/2 pancreatitis):ti,ab,kw OR ((autoimmune* OR auto-immun* OR Tropical OR hereditary* OR familiar*) AND pancreatitis):ti,ab,kw OR ('hypertriglyceridemia'/de OR 'hypercalcemia'/de OR alcohol intoxicat*:ti,ab,kw OR (autoimmune* OR auto-immun*):ti,ab,kw)) AND ('pancreas'/de OR pancrea*:ti,ab,kw)

2	('pancreatic duct'/exp AND obstruct*:ti,ab,kw) OR (pancreas* NEAR/2 duct* NEAR/2 obstruct*):ti,ab,kw OR ((main NEAR/2 duct* NEAR/2 obstruct*) AND pancrea*):ti,ab,kw OR (pancrea* duct*:ti,ab,kw AND (pain OR painful):ti)
3	#1 AND #2
4	'endoscopic retrograde cholangiopancreatography'/exp OR 'drainage'/exp OR 'endoscopy'/de OR 'digestive tract endoscopy'/de
5	(ERCP OR (endoscop* NEAR/2 retrograd* NEAR/2 (cholangiopancreatograph* OR cholangio-pancreatograph*))):ti,ab,kw
6	'endoscopic sphincterotomy'/exp OR 'Vater papillotomy'/exp OR ((endoscop* NEAR/3 sphincterotom*) OR EST):ti,ab,kw OR papillotom*:ti,ab,kw OR rendezvous:ti,ab,kw OR (drain* AND duct*):ti,ab,kw OR (endoscop* OR endotherap*):ti,ab
7	'decompression'/exp OR decompress*:ti,ab,kw
8	'balloon dilatation'/exp OR (dilate* OR dilation*):ti,ab,kw
9	#4 OR #5 OR #6 OR #7 OR #8
10	('chronic pancreatitis'/exp OR 'pancreas'/exp OR 'pancreas disease'/exp OR 'pancreatitis'/de OR (chronic pancreatitis OR pancrea*):ti,ab,kw) AND ('general surgery'/de OR 'surgery'/de OR (resect* OR surger* OR surgical OR operat* OR recis* OR duodenectom* OR PPPD OR pylorus-reserving):ti,ab,kw)
11	'pancreaticojejunostomy'/exp OR 'pancreatectomy'/exp OR 'pancreaticoduodenectomy'/de OR (pancreatojejunostom* OR pancreaticojejunostom* OR (pancrea* NEAR/5 (duodenectom* OR jejunostom*))):ti,ab,kw OR (duodenopancreatectom* OR pancreatoduodenectom* OR pancreaticoduodenectom* OR pancreaticogastrostom* OR hemipancreatectom*):ti,ab,kw OR (anastomos* NEAR/5 (pancreatojejunal OR jejunopancreatic)):ti,ab,kw OR whipple:ti,ab,kw OR pancreatectom*:ti,ab,kw OR (Beger OR Frey OR puestow OR Partington-Rochelle):ti,ab,kw OR ((left OR tail OR distal OR caudal) AND (resection OR pancreatectomy)):ti,ab,kw OR (dilation NEAR/2 pancrea*):ti,ab,kw
12	#10 OR #11
13	#3 AND (#9 OR #12)
14	('Clinical trial'/de OR 'Randomized controlled trial'/de OR 'Randomization'/de OR 'Single blind procedure'/de OR 'Double blind procedure'/de OR 'Crossover procedure'/de OR 'Placebo'/de OR Randomi?ed controlled trial*:ti,ab,kw OR Rct:ti,ab,kw OR Random allocation:ti,ab,kw OR Randomly allocated:ti,ab,kw OR Allocated randomly:ti,ab,kw OR (allocated NEAR/2 random):ti,ab,kw OR Single blind*:ti,ab,kw OR Double blind*:ti,ab,kw OR ((treble OR triple) NEAR (blind*)):ti,ab,kw OR Placebo*:ti,ab,kw OR 'Prospective study'/de) NOT ('Case study'/de OR Case report:ti,ab,kw OR 'Abstract report'/de or 'letter'/de) OR 'Clinical study'/de OR 'Case control study'/de OR 'Family study'/de OR 'Longitudinal study'/de OR 'Retrospective study'/de OR ('Prospective study'/de NOT 'Randomized controlled trials'/de) OR 'Cohort analysis'/de OR (Cohort NEAR (study OR studies)):ti,ab,kw OR ("Case control" NEAR (study OR studies)):ti,ab,kw OR ("follow up" NEAR (study OR studies)):ti,ab,kw OR (observational NEAR (study OR studies)):ti,ab,kw OR (epidemiologic* NEAR (study OR studies)):ti,ab,kw OR ("cross sectional" NEAR (study OR studies)):ti,ab,kw OR ('Meta Analysis'/exp OR ((meta NEAR analy*) OR metaanalys*):ti,ab,kw OR (systematic NEAR (review*1 OR overview*1)):ti,ab,kw OR cancerlit:ab OR Cochrane:ab OR Embase:ab OR (psychlit OR psyclit):ab OR (psychinfo OR psycinfo):ab OR (cinahl OR cinhal):ab OR science citation index:ab OR bids:ab OR reference lists:ab OR bibliograph*:ab OR hand-search*:ab OR manual search*:ab OR relevant journals:ab OR ((data extraction:ab OR selection criteria:ab) AND review:it)) NOT (letter:it OR editorial:it OR ('animal'/de NOT ('animal'/de AND 'human'/de)))
15	#13 AND #14
16	#15 AND [01/01/2001]/sd
17	#16 AND English:LA

Database: Cochrane Library (Wiley)
Search Date: 12 November 2021
Limits: Published after January 1, 2001
Number of Results: 20

1	([mh "Pancreatitis, Chronic"] OR [mh "Pancreatitis, Alcoholic"] OR ([mh ^"Pancreatitis"] AND [mh ^"Chronic Diseases"]) OR (chronic NEAR/2 pancreatitis):ti,ab,kw OR ((autoimmune* OR auto-immun* OR Tropical OR hereditary* OR familiar*) AND pancreatitis):ti,ab,kw OR ([mh ^"Hypertriglyceridemia"] OR [mh ^"Hypercalcemia"] OR alcohol intoxicat*:ti,ab,kw OR (autoimmune* OR auto-immun*):ti,ab,kw)) AND ([mh ^"Pancreas"] OR pancrea*:ti,ab,kw)
2	([mh "Pancreatic Ducts"] AND obstruct*:ti,ab,kw) OR (pancreas* NEAR/2 duct* NEAR/2 obstruct*):ti,ab,kw OR ((main NEAR/2 duct* NEAR/2 obstruct*) AND pancrea*):ti,ab,kw OR (pancrea* duct*:ti,ab,kw AND (pain OR painful):ti)
3	#1 AND #2
4	[mh "Cholangiopancreatography, Endoscopic Retrograde"] OR [mh Drainage] OR [mh ^"Endoscopy"] OR [mh ^"Endoscopy, Digestive System"]
5	(ERCP OR (endoscop* NEAR/2 retrograd* NEAR/2 (cholangiopancreatograph* OR cholangio-pancreatograph*))):ti,ab,kw
6	[mh "Sphincterotomy, Endoscopic"] OR [mh "papillotomy"] OR ((endoscop* NEAR/3 sphincterotom*) OR EST):ti,ab,kw OR papillotom*:ti,ab,kw OR rendezvous:ti,ab,kw OR (drain* AND duct*):ti,ab,kw OR (endoscop* OR endotherap*):ti,ab
7	[mh Decompression] OR decompress*:ti,ab,kw
8	[mh Dilatation] OR (dilate* OR dilation*):ti,ab,kw
9	#4 OR #5 OR #6 OR #7 OR #8
10	([mh "Pancreatitis, Chronic"] OR [mh Pancreas] OR [mh ^"Pancreatic Diseases"] OR [mh ^"Pancreatitis"] OR (chronic pancreatitis OR pancrea*):ti,ab,kw) AND ([mh ^"General Surgery"] OR [mh ^"Surgical Procedures, Operative"] OR (resect* OR surger* OR surgical OR operat* OR recis* OR duodenectom* OR PPPD OR pylorus-reserving):ti,ab,kw)
11	[mh Pancreaticojejunostomy] OR [mh Pancreatectomy] OR [mh Pancreaticoduodenectomy] OR (pancreatojejunostom* OR pancreaticojejunostom* OR (pancrea* NEAR/5 (duodenectom* OR jejunostom*))):ti,ab,kw OR (duodenopancreatectom* OR pancreatoduodenectom* OR pancreaticoduodenectom* OR pancreaticogastrostom* OR hemipancreatectom*):ti,ab,kw OR (anastomos* NEAR/5 (pancreatojejunal OR jejunopancreatic)):ti,ab,kw OR whipple:ti,ab,kw OR pancreatectom*:ti,ab,kw OR (Beger OR Frey OR puestow OR Partington-Rochelle):ti,ab,kw OR ((left OR tail OR distal OR caudal) AND (resection OR pancreatectomy)):ti,ab,kw OR (dilation NEAR/2 pancrea*):ti,ab,kw
12	#10 OR #11
13	#3 AND (#9 OR #12)

Prisma Flow Chart (PICO 1)

185 references imported for screening as 185 studies
9 duplicates removed
176 studies screened against title and abstract
168 studies excluded
8 studies assessed for full-text eligibility
2 studies excluded
2 Wrong study design
0 studies ongoing
0 studies awaiting classification
6 studies included

PICO 2: EUS vs Percutaneous Celiac Plexus Block

Database: Ovid MEDLINE

Search Date: 12 November 2021

Limits: English language; RCTs, meta-analyses, systematic reviews, prospective or retrospective comparative studies; published after January 1, 2001

Number of Results: 28

1	(exp Pancreatitis, Chronic/ or exp Pancreatitis, Alcoholic/ or (Pancreatitis/ and Chronic Diseases/) or (chronic adj2 pancreatitis).tw,kf. or ((autoimmun$ or auto-immun$ or Tropical or hereditar$ or familiar$) and pancreatitis).tw,kf. or (Hypertriglyceridemia/ or Hypercalcemia/ or alcohol intoxicat$.tw,kf. or (autoimmun$ or auto-immun$).tw,kf.)) and (Pancreas/ or pancrea*.tw,kf.)	28519
2	Pain/ or Abdominal Pain/ or Chronic Pain/ or Pain, Postoperative/ or exp Pain Management/ or pain*.ti,ab,kw.	817309
3	1 and 2	4055
4	celiac plexus/ or ("celiac plexus" or "coeliac plexus").tw,kf.	1478
5	(neurolysis or "nerve block$" or block?).tw,kf.	355515
6	4 and 5	771
7	(("celiac plexus" adj5 block$) or ("coeliac plexus" adj5 block$)).tw,kf.	538
8	NCPB.ti,ab.	56
9	("neurolytic sympathetic plexus" adj5 block$).tw,kf.	2
10	or/6-9	822
11	3 and 10	117
12	exp "sensitivity and specificity"/	622845
13	false negative reactions/ or false positive reactions/	39725
14	(sensitivity or specificity).ti,ab.	1125314
15	(predicitve adj value$1).ti,ab.	14
16	(likelihood adj ratio$1).ti,ab.	17307
17	(false adj (negative$1 or positive$1)).ti,ab.	82680
18	(randomized controlled trial or controlled clinical trial).pt.	639777
19	double blind method/ or single blind method/	198435
20	practice guideline.pt.	29250
21	consensus development conference.pt.	12186
22	random$.ti,ab.	1266585
23	random allocation/	106169
24	(single blind$3 or double blind$3 or triple blind$3).ti,ab.	180051
25	(review or review academic).pt.	2891079
26	meta analysis.pt.	146383
27	(systematic adj review$).ti,ab. or (systematic* adj3 search*).ab.	242702
28	or/12-25	5731309
29	28 and (26 or 27)	221099
30	Randomized controlled trials as Topic/	150114
31	Randomized controlled trial/	550109
32	Random allocation/	106169
33	Double blind method/	168250
34	Single blind method/	31173
35	Clinical trial/	532194
36	exp Clinical Trials as Topic/	366362
37	or/30-36	1250772
38	(clinic$ adj trial$1).tw.	415775
39	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	184125
40	Placebos/	35755
41	Placebo$.tw.	230184
42	Randomly allocated.tw.	32219
43	(allocated adj2 random).tw.	806
44	or/38-43	699526
45	37 or 44	1560994
46	Case report.tw.	347685
47	Letter/	1158573
48	Historical article/	366448
49	Review of reported cases.pt.	0
50	Review, multicase.pt.	0
51	or/46-50	1855402
52	45 not 51	1523918
53	Epidemiologic studies/	8885
54	exp case control studies/	1248691
55	exp cohort studies/	2245588
56	Case control.tw.	138272
57	(cohort adj (study or studies)).tw.	252680
58	Cohort analy$.tw.	9632
59	(Follow up adj (study or studies)).tw.	52302
60	(observational adj (study or studies)).tw.	130453
61	Longitudinal.tw.	278366
62	Retrospective.tw.	624109
63	Cross sectional.tw.	421170
64	Cross-sectional studies/	397938
65	or/53-64	3378229
66	29 or 52 or 65	4686898
67	11 and 66	33
68	limit 67 to english language	31
69	limit 68 to dt=20010101-20211231	28

Database: Embase.com (Elsevier)

Search Date: 12 November 2021

Limits: English language; RCTs, meta-analyses, systematic reviews, prospective or retrospective comparative studies; published after January 1, 2001

Number of Results: 31

1	('chronic pancreatitis'/exp OR 'alcoholic pancreatitis'/exp OR ('pancreatitis'/de AND 'chronic disease'/de) OR (chronic NEAR/2 pancreatitis):ti,ab,kw OR ((autoimmune* OR auto-immun* OR Tropical OR hereditary* OR familiar*) AND pancreatitis):ti,ab,kw OR ('hypertriglyceridemia'/de OR 'hypercalcemia'/de OR alcohol intoxicat*:ti,ab,kw OR (autoimmune* OR auto-immun*):ti,ab,kw)) AND ('pancreas'/de OR pancrea*:ti,ab,kw)
2	Pain/de OR 'abdominal pain'/exp OR 'chronic pain'/de OR 'postoperative pain'/de OR 'analgesia'/de OR pain*:ti,ab,kw
3	#1 AND #2
4	'celiac plexus'/exp OR ("celiac plexus" OR "coeliac plexus"):ti,ab,kw
5	(neurolysis OR "nerve block*" OR block?):ti,ab,kw
6	#4 AND #5
7	(("celiac plexus" NEAR/5 block*) OR ("coeliac plexus" NEAR/5 block*)):ti,ab,kw
8	NCPB:ti,ab
9	("neurolytic sympathetic plexus" NEAR/5 block*):ti,ab,kw
10	#6 OR #7 OR #8 OR #9
11	#3 AND #10
12	('Clinical trial'/de OR 'Randomized controlled trial'/de OR 'Randomization'/de OR 'Single blind procedure'/de OR 'Double blind procedure'/de OR 'Crossover procedure'/de OR 'Placebo'/de OR Randomi?ed controlled trial*:ti,ab,kw OR Rct:ti,ab,kw OR Random allocation:ti,ab,kw OR Randomly allocated:ti,ab,kw OR Allocated randomly:ti,ab,kw OR (allocated NEAR/2 random):ti,ab,kw OR Single blind*:ti,ab,kw OR Double blind*:ti,ab,kw OR ((treble OR triple) NEAR (blind*)):ti,ab,kw OR Placebo*:ti,ab,kw OR 'Prospective study'/de) NOT ('Case study'/de OR Case report:ti,ab,kw OR 'Abstract report'/de or 'letter'/de) OR 'Clinical study'/de OR 'Case control study'/de OR 'Family study'/de OR 'Longitudinal study'/de OR 'Retrospective study'/de OR ('Prospective study'/de NOT 'Randomized controlled trials'/de) OR 'Cohort analysis'/de OR (Cohort NEAR (study OR studies)):ti,ab,kw OR

	("Case control" NEAR (study OR studies)):ti,ab,kw OR ("follow up" NEAR (study OR studies)):ti,ab,kw OR (observational NEAR (study OR studies)):ti,ab,kw OR (epidemiologic* NEAR (study OR studies)):ti,ab,kw OR ("cross sectional" NEAR (study OR studies)):ti,ab,kw OR ('Meta Analysis'/exp OR ((meta NEAR analy*) OR metaanalys*):ti,ab,kw OR (systematic NEAR (review*1 OR overview*1)):ti,ab,kw OR cancerlit:ab OR Cochrane:ab OR Embase:ab OR (psychlit OR psyclit):ab OR (psychinfo OR psycinfo):ab OR (cinahl OR cinhal):ab OR science citation index:ab OR bids:ab OR reference lists:ab OR bibliograph*:ab OR hand-search*:ab OR manual search*:ab OR relevant journals:ab OR ((data extraction:ab OR selection criteria:ab) AND review:it)) NOT (letter:it OR editorial:it OR ('animal'/de NOT ('animal'/de AND 'human'/de)))
13	#11 AND #12
14	#13 AND [01/01/2001]/sd
15	#14 AND English:LA

Database: Cochrane Library (Wiley)
Search Date: 12 November 2021
Limits: Published after January 1, 2001
Number of Results: 21

1	([mh "Pancreatitis, Chronic"] OR [mh "Pancreatitis, Alcoholic"] OR ([mh ^"Pancreatitis"] AND [mh ^"Chronic Diseases"]) OR (chronic NEAR/2 pancreatitis):ti,ab,kw OR ((autoimmune* OR auto-immun* OR Tropical OR hereditary* OR familiar*) AND pancreatitis):ti,ab,kw OR ([mh ^"Hypertriglyceridemia"] OR [mh ^"Hypercalcemia"] OR alcohol intoxicat*:ti,ab,kw OR (autoimmune* OR auto-immun*):ti,ab,kw)) AND ([mh ^"Pancreas"] OR pancrea*:ti,ab,kw)
2	[mh ^"Pain"] OR [mh ^"Abdominal Pain"] OR [mh ^"Chronic Pain"] OR [mh ^"Pain, Postoperative"] OR [mh "Pain Management"] OR pain*:ti,ab,kw
3	#1 AND #2
4	[mh "celiac plexus"] OR ("celiac plexus" OR "coeliac plexus"):ti,ab,kw
5	(neurolysis OR "nerve block*" OR block?):ti,ab,kw
6	#4 AND #5
7	(("celiac plexus" NEAR/5 block$) OR ("coeliac plexus" NEAR/5 block*)):ti,ab,kw
8	NCPB:ti,ab
9	("neurolytic sympathetic plexus" NEAR/5 block*):ti,ab,kw
10	#6 OR #7 OR #8 OR #9
11	#3 AND #10

Prisma Flow Chart (PICO 2)

62 references imported for screening as 62 studies
1 duplicate removed
61 studies screened against title and abstract
49 studies excluded
12 studies assessed for full-text eligibility
11 studies excluded
5 Wrong comparator
4 Abstract Only
1 Wrong patient population
1 Wrong study design
0 studies ongoing
0 studies awaiting classification
1 study included + 1 study (from cross referencing/snow balling)

PICO 3: Pancreatic duct stones

Database: Ovid MEDLINE
Search Date: 12 November 2021

Limits: English language; RCTs, meta-analyses, systematic reviews, prospective or retrospective comparative studies; published after January 1, 2001
Number of Results: 102

1	((exp Pancreatitis, Chronic/ or exp Pancreatitis, Alcoholic/ or (Pancreatitis/ and Chronic Diseases/) or (chronic adj2 pancreatitis).tw,kf. or ((autoimmun$ or auto-immun$ or Tropical or hereditar$ or familiar$) and pancreatitis).tw,kf. or (Hypertriglyceridemia/ or Hypercalcemia/ or alcohol intoxicat$.tw,kf. or (autoimmun$ or auto-immun$).tw,kf.)) and (Pancreas/ or pancrea*.tw,kf.)) or pancreatolithiasis.tw,kf.	28559
2	((exp Pancreatic Ducts/ or exp Pancreatitis, Chronic/) and (exp Calculi/ or exp Calcinosis/)) or (pancrea* adj3 (stone* or calculi or calculus)).tw,kf. or (pancrea$ adj2 duct$ adj2 (stone* or calculi or calculus)).tw,kf. or ((main adj2 duct$ adj2 (stone* or calculi or calculus)) and pancrea*).tw,kf.	2739
3	1 and 2	885
4	exp Cholangiopancreatography, Endoscopic Retrograde/ or ERCP.tw,kf. or (endoscop* adj2 retrograd* adj2 (cholangiopancreatograph* or cholangio-pancreatograph*)).tw,kf.	23771
5	exp Lithotripsy/ or (lithotrips* or eswl or swl).tw,kf.	15218
6	3 and (4 or 5)	379
7	exp "sensitivity and specificity"/	622845
8	false negative reactions/ or false positive reactions/	39725
9	(sensitivity or specificity).ti,ab.	1125314
10	(predicitve adj value$1).ti,ab.	14
11	(likelihood adj ratio$1).ti,ab.	17307
12	(false adj (negative$1 or positive$1)).ti,ab.	82680
13	(randomized controlled trial or controlled clinical trial).pt.	639777
14	double blind method/ or single blind method/	198435
15	practice guideline.pt.	29250
16	consensus development conference.pt.	12186
17	random$.ti,ab.	1266585
18	random allocation/	106169
19	(single blind$3 or double blind$3 or triple blind$3).ti,ab.	180051
20	(review or review academic).pt.	2891079
21	meta analysis.pt.	146383
22	(systematic adj review$).ti,ab. or (systematic* adj3 search*).ab.	242702
23	or/7-20	5731309
24	23 and (21 or 22)	221099
25	Randomized controlled trials as Topic/	150114
26	Randomized controlled trial/	550109
27	Random allocation/	106169
28	Double blind method/	168250
29	Single blind method/	31173
30	Clinical trial/	532194
31	exp Clinical Trials as Topic/	366362
32	or/25-31	1250772
33	(clinic$ adj trial$1).tw.	415775
34	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	184125
35	Placebos/	35755
36	Placebo$.tw.	230184
37	Randomly allocated.tw.	32219
38	(allocated adj2 random).tw.	806
39	or/33-38	699526
40	32 or 39	1560994
41	Case report.tw.	347685
42	Letter/	1158573
43	Historical article/	366448
44	Review of reported cases.pt.	0
45	Review, multicase.pt.	0

46	or/41-45	1855402
47	40 not 46	1523918
48	Epidemiologic studies/	8885
49	exp case control studies/	1248691
50	exp cohort studies/	2245588
51	Case control.tw.	138272
52	(cohort adj (study or studies)).tw.	252680
53	Cohort analy$.tw.	9632
54	(Follow up adj (study or studies)).tw.	52302
55	(observational adj (study or studies)).tw.	130453
56	Longitudinal.tw.	278366
57	Retrospective.tw.	624109
58	Cross sectional.tw.	421170
59	Cross-sectional studies/	397938
60	or/48-59	3378229
61	24 or 47 or 60	4686898
62	6 and 61	148
63	limit 62 to english language	131
64	limit 63 to dt=20010101-20211231	102

Database: Embase.com (Elsevier)
Search Date: 12 November 2021
Limits: English language; RCTs, meta-analyses, systematic reviews, prospective or retrospective comparative studies; published after January 1, 2001
Number of Results: 286

1	('chronic pancreatitis'/exp OR 'alcoholic pancreatitis'/exp OR ('pancreatitis'/de AND 'chronic disease'/de) OR (chronic NEAR/2 pancreatitis):ti,ab,kw OR ((autoimmune* OR auto-immun* OR Tropical OR hereditary* OR familiar*) AND pancreatitis):ti,ab,kw OR ('hypertriglyceridemia'/de OR 'hypercalcemia'/de OR alcohol intoxicat*:ti,ab,kw OR (autoimmune* OR auto-immun*):ti,ab,kw)) AND ('pancreas'/de OR pancrea*:ti,ab,kw)
2	(('pancreatic duct'/exp OR 'chronic pancreatitis'/exp) AND ('stone formation'/exp OR 'calcinosis'/exp)) OR (pancrea* NEAR/3 (stone* OR calculi OR calculus)):ti,ab,kw OR (pancreas* NEAR/2 duct* NEAR/2 (stone* OR calculi OR calculus)):ti,ab,kw OR ((main NEAR/2 duct* NEAR/2 (stone* OR calculi OR calculus)) AND pancrea*):ti,ab,kw
3	#1 AND #2
4	'endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ti,ab,kw OR (endoscop* NEAR/2 retrograd* NEAR/2 (cholangiopancreatograph* OR cholangio-pancreatograph*)):ti,ab,kw
5	'lithotripsy'/exp OR (lithotrips* OR eswl OR swl):ti,ab,kw
6	#3 AND (#4 OR #5)
7	('Clinical trial'/de OR 'Randomized controlled trial'/de OR 'Randomization'/de OR 'Single blind procedure'/de OR 'Double blind procedure'/de OR 'Crossover procedure'/de OR 'Placebo'/de OR Randomi?ed controlled trial*:ti,ab,kw OR Rct:ti,ab,kw OR Random allocation:ti,ab,kw OR Randomly allocated:ti,ab,kw OR Allocated randomly:ti,ab,kw OR (allocated NEAR/2 random):ti,ab,kw OR Single blind*:ti,ab,kw OR Double blind*:ti,ab,kw OR ((treble OR triple) NEAR (blind*)):ti,ab,kw OR Placebo*:ti,ab,kw OR 'Prospective study'/de) NOT ('Case study'/de OR Case report:ti,ab,kw OR 'Abstract report'/de or 'letter'/de) OR 'Clinical study'/de OR 'Case control study'/de OR 'Family study'/de OR 'Longitudinal study'/de OR 'Retrospective study'/de OR ('Prospective study'/de NOT 'Randomized controlled trials'/de) OR 'Cohort analysis'/de OR (Cohort NEAR (study OR studies)):ti,ab,kw OR ("Case control" NEAR (study OR studies)):ti,ab,kw OR ("follow up" NEAR (study OR studies)):ti,ab,kw OR (observational NEAR (study OR studies)):ti,ab,kw OR (epidemiologic* NEAR (study OR studies)):ti,ab,kw OR ("cross sectional" NEAR (study OR studies)):ti,ab,kw OR ('Meta Analysis'/exp OR ((meta NEAR analy*) OR metaanalys*):ti,ab,kw OR (systematic NEAR (review*1 OR overview*1)):ti,ab,kw OR cancerlit:ab OR Cochrane:ab OR Embase:ab OR (psychlit OR psyclit):ab OR (psychinfo OR psycinfo):ab OR (cinahl OR cinhal):ab OR science citation index:ab OR bids:ab OR reference lists:ab OR bibliograph*:ab OR hand-search*:ab OR manual search*:ab OR relevant journals:ab OR ((data extraction:ab OR selection criteria:ab) AND review:it)) NOT (letter:it OR editorial:it OR ('animal'/de NOT ('animal'/de AND 'human'/de)))
8	#6 AND #7
9	#8 AND [01/01/2001]/sd
10	#9 AND English:LA

Database: Cochrane Library (Wiley)
Search Date: 12 November 2021
Limits: Published after January 1, 2001
Number of Results: 22

1	([mh "Pancreatitis, Chronic"] OR [mh "Pancreatitis, Alcoholic"] OR ([mh ^"Pancreatitis"] AND [mh ^"Chronic Diseases"]) OR (chronic NEAR/2 pancreatitis):ti,ab,kw OR ((autoimmune* OR auto-immun* OR Tropical OR hereditary* OR familiar*) AND pancreatitis):ti,ab,kw OR ([mh ^"Hypertriglyceridemia"] OR [mh ^"Hypercalcemia"] OR alcohol intoxicat*:ti,ab,kw OR (autoimmune* OR auto-immun*):ti,ab,kw)) AND ([mh ^"Pancreas"] OR pancrea*:ti,ab,kw)
2	(([mh "Pancreatic Ducts"] OR [mh "Pancreatitis, Chronic"]) AND ([mh Calculi] OR [mh Calcinosis])) OR (pancrea* NEAR/3 (stone* OR calculi OR calculus)):ti,ab,kw OR (pancreas* NEAR/2 duct* NEAR/2 (stone* OR calculi OR calculus)):ti,ab,kw OR ((main NEAR/2 duct* NEAR/2 (stone* OR calculi OR calculus)) AND pancrea*):ti,ab,kw
3	#1 AND #2
4	[mh "Cholangiopancreatography, Endoscopic Retrograde"] OR ERCP:ti,ab,kw OR (endoscop* NEAR/2 retrograd* NEAR/2 (cholangiopancreatograph* OR cholangio-pancreatograph*)):ti,ab,kw
5	[mh Lithotripsy] OR (lithotrips* OR eswl OR swl):ti,ab,kw
6	#3 AND (#4 OR #5)

Prisma Flow Chart (PICO 3)

360 references imported for screening as 360 studies
5 duplicates removed
355 studies screened against title and abstract
338 studies excluded
17 studies assessed for full-text eligibility
13 studies excluded
10 Wrong study design
2 Wrong comparator
1 Wrong intervention
0 studies ongoing
0 studies awaiting classification
4 studies included

PICO 4: Pancreatic duct stricture

Database: Ovid MEDLINE
Search Date: 12 November 2021
Limits: English language; RCTs, meta-analyses, systematic reviews, prospective or retrospective comparative studies; published after January 1, 2001
Number of Results: 74

1	(exp Pancreatitis, Chronic/ or exp Pancreatitis, Alcoholic/ or (Pancreatitis/ and Chronic Diseases/) or (chronic adj2 pancreatitis).tw,kf. or ((autoimmun$ or auto-immun$ or Tropical or hereditar$ or familiar$) and pancreatitis).tw,kf. or	28519

	(Hypertriglyceridemia/ or Hypercalcemia/ or alcohol intoxicat$.tw,kf. or (autoimmun$ or auto-immun$).tw,kf.)) and (Pancreas/ or pancrea*.tw,kf.)	
2	((exp Pancreatic Ducts/ or exp Pancreatitis, Chronic/) and exp Constriction, Pathologic/) or (pancrea* adj5 (strictur* or stenos*)).tw,kf. or (pancrea$ adj2 duct$ adj2 (strictur* or stenos*)).tw,kf. or ((main adj2 duct$ adj2 (strictur* or stenos*)) and pancrea*).tw,kf. or (pancrea* adj2 duct* adj5 (size* or sizing or diameter*)).tw,kf.	2928
3	1 and 2	1045
4	(exp Cholangiopancreatography, Endoscopic Retrograde/ or ERCP.tw,kf. or (endoscop* adj2 retrograd* adj2 (cholangiopancreatograph* or cholangio-pancreatograph*)).tw,kf.) and (exp stents/ or stent*.tw,kf.)	4437
5	(exp stents/ or stent*.tw,kf. or (SEM or SEMTs or SEM or SEMs).tw,kf.) and (exp plastics/ or (plastic or 10F or "10 F" or 10Fr or "10 Fr" or "10-F" or "10-Fr" or 7F or "7 F" or 7Fr or "7 Fr" or "7-F" or "7-Fr" or "mm" or millimeter* or length or size*).tw,kf.)	56866
6	3 and (4 or 5)	229
7	exp "sensitivity and specificity"/	622845
8	false negative reactions/ or false positive reactions/	39725
9	(sensitivity or specificity).ti,ab.	1125314
10	(predicitve adj value$1).ti,ab.	14
11	(likelihood adj ratio$1).ti,ab.	17307
12	(false adj (negative$1 or positive$1)).ti,ab.	82680
13	(randomized controlled trial or controlled clinical trial).pt.	639777
14	double blind method/ or single blind method/	198435
15	practice guideline.pt.	29250
16	consensus development conference.pt.	12186
17	random$.ti,ab.	1266585
18	random allocation/	106169
19	(single blind$3 or double blind$3 or triple blind$3).ti,ab.	180051
20	(review or review academic).pt.	2891079
21	meta analysis.pt.	146383
22	(systematic adj review$).ti,ab. or (systematic* adj3 search*).ab.	242702
23	or/7-20	5731309
24	23 and (21 or 22)	221099
25	Randomized controlled trials as Topic/	150114
26	Randomized controlled trial/	550109
27	Random allocation/	106169
28	Double blind method/	168250
29	Single blind method/	31173
30	Clinical trial/	532194
31	exp Clinical Trials as Topic/	366362
32	or/25-31	1250772
33	(clinic$ adj trial$1).tw.	415775
34	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	184125
35	Placebos/	35755
36	Placebo$.tw.	230184
37	Randomly allocated.tw.	32219
38	(allocated adj2 random).tw.	806
39	or/33-38	699526
40	32 or 39	1560994
41	Case report.tw.	347685
42	Letter/	1158573
43	Historical article/	366448
44	Review of reported cases.pt.	0
45	Review, multicase.pt.	0
46	or/41-45	1855402
47	40 not 46	1523918
48	Epidemiologic studies/	8885
49	exp case control studies/	1248691
50	exp cohort studies/	2245588
51	Case control.tw.	138272
52	(cohort adj (study or studies)).tw.	252680
53	Cohort analy$.tw.	9632
54	(Follow up adj (study or studies)).tw.	52302
55	(observational adj (study or studies)).tw.	130453
56	Longitudinal.tw.	278366
57	Retrospective.tw.	624109
58	Cross sectional.tw.	421170
59	Cross-sectional studies/	397938
60	or/48-59	3378229
61	24 or 47 or 60	4686898
62	6 and 61	100
63	limit 62 to english language	93
64	limit 63 to dt=20010101-20211231	74

Database: Embase.com (Elsevier)

Search Date: 12 November 2021

Limits: English language; RCTs, meta-analyses, systematic reviews, prospective or retrospective comparative studies; published after January 1, 2001

Number of Results: 172

1	('chronic pancreatitis'/exp OR 'alcoholic pancreatitis'/exp OR ('pancreatitis'/de AND 'chronic disease'/de) OR (chronic NEAR/2 pancreatitis):ti,ab,kw OR ((autoimmune* OR auto-immun* OR Tropical OR hereditary* OR familiar*) AND pancreatitis):ti,ab,kw OR ('hypertriglyceridemia'/de OR 'hypercalcemia'/de OR alcohol intoxicat*:ti,ab,kw OR (autoimmune* OR auto-immun*):ti,ab,kw)) AND ('pancreas'/de OR pancrea*:ti,ab,kw)
2	(('pancreatic duct'/exp OR 'chronic pancreatitis'/exp) AND 'stenosis, occlusion and obstruction'/exp) OR (pancrea* NEAR/5 (strictur* OR stenos*)):ti,ab,kw OR (pancreas* NEAR/2 duct* NEAR/2 (strictur* OR stenos*)):ti,ab,kw OR ((main NEAR/2 duct* NEAR/2 (strictur* OR stenos*)) AND pancrea*):ti,ab,kw OR (pancrea* NEAR/2 duct* NEAR/5 (size* OR sizing OR diameter*)):ti,ab,kw
3	#1 AND #2
4	('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ti,ab,kw OR (endoscop* NEAR/2 retrograd* NEAR/2 (cholangiopancreatograph* OR cholangio-pancreatograph*)):ti,ab,kw) AND ('stent'/exp OR stent*:ti,ab,kw)
5	('stent'/exp OR stent*:ti,ab,kw OR (SEM OR SEMTs OR SEM OR SEMs):ti,ab,kw) AND ('plastic'/exp OR 'prosthesis design'/de OR (plastic OR 10F OR "10 F" OR 10Fr OR "10 Fr" OR "10-F" OR "10-Fr" OR 7F OR "7 F" OR 7Fr OR "7 Fr" OR "7-F" OR "7-Fr" OR "mm" OR millimeter* OR length OR size*):ti,ab,kw)
6	#3 AND (#4 OR #5)
7	('Clinical trial'/de OR 'Randomized controlled trial'/de OR 'Randomization'/de OR 'Single blind procedure'/de OR 'Double blind procedure'/de OR 'Crossover procedure'/de OR 'Placebo'/de OR Randomi?ed controlled trial*:ti,ab,kw OR Rct:ti,ab,kw OR Random allocation:ti,ab,kw OR Randomly allocated:ti,ab,kw OR Allocated randomly:ti,ab,kw OR (allocated NEAR/2 random):ti,ab,kw OR Single blind*:ti,ab,kw OR Double blind*:ti,ab,kw OR ((treble OR triple) NEAR (blind*)):ti,ab,kw OR Placebo*:ti,ab,kw OR 'Prospective study'/de) NOT ('Case study'/de OR Case report:ti,ab,kw OR 'Abstract report'/de or 'letter'/de) OR 'Clinical study'/de OR 'Case control study'/de OR 'Family study'/de OR 'Longitudinal study'/de OR 'Retrospective study'/de OR ('Prospective study'/de NOT 'Randomized controlled trials'/de) OR 'Cohort analysis'/de OR (Cohort NEAR (study OR studies)):ti,ab,kw OR ("Case control" NEAR (study OR studies)):ti,ab,kw OR ("follow up" NEAR (study OR studies)):ti,ab,kw OR (observational NEAR (study OR studies)):ti,ab,kw OR (epidemiologic* NEAR (study OR studies)):ti,ab,kw OR ("cross sectional" NEAR (study OR studies)):ti,ab,kw OR ('Meta Analysis'/exp OR ((meta NEAR analy*) OR metaanalys*):ti,ab,kw OR

	(systematic NEAR (review*1 OR overview*1)):ti,ab,kw OR cancerlit:ab OR Cochrane:ab OR Embase:ab OR (psychlit OR psyclit):ab OR (psychinfo OR psycinfo):ab OR (cinahl OR cinhal):ab OR science citation index:ab OR bids:ab OR reference lists:ab OR bibliograph*:ab OR hand-search*:ab OR manual search*:ab OR relevant journals:ab OR ((data extraction:ab OR selection criteria:ab) AND review:it)) NOT (letter:it OR editorial:it OR ('animal'/de NOT ('animal'/de AND 'human'/de)))
8	#6 AND #7
9	#8 AND [01/01/2001]/sd
10	#9 AND English:LA

Database: Cochrane Library (Wiley)
Search Date: 12 November 2021
Limits: Published after January 1, 2001
Number of Results: 32

1	([mh "Pancreatitis, Chronic"] OR [mh "Pancreatitis, Alcoholic"] OR ([mh "Pancreatitis"] AND [mh "Chronic Diseases"]) OR (chronic NEAR/2 pancreatitis):ti,ab,kw OR ((autoimmune* OR auto-immun* OR Tropical OR hereditary* OR familiar*) AND pancreatitis):ti,ab,kw OR ([mh "Hypertriglyceridemia"] OR [mh "Hypercalcemia"] OR alcohol intoxicat*:ti,ab,kw OR (autoimmune* OR auto-immun*):ti,ab,kw)) AND ([mh "Pancreas"] OR pancrea*:ti,ab,kw)
2	(([mh "Pancreatic Ducts"] OR [mh "Pancreatitis, Chronic"]) AND [mh "Constriction, Pathologic"]) OR (pancrea* NEAR/5 (strictur* OR stenos*)):ti,ab,kw OR (pancreas* NEAR/2 duct* NEAR/2 (strictur* OR stenos*)):ti,ab,kw OR ((main NEAR/2 duct* NEAR/2 (strictur* OR stenos*)) AND pancrea*):ti,ab,kw OR (pancrea* NEAR/2 duct* NEAR/5 (size* OR sizing OR diameter*)):ti,ab,kw
3	#1 AND #2
4	([mh "Cholangiopancreatography, Endoscopic Retrograde"] OR ERCP:ti,ab,kw OR (endoscop* NEAR/2 retrograd* NEAR/2 (cholangiopancreatograph* OR cholangio-pancreatograph*)):ti,ab,kw) AND ([mh stents] OR stent*:ti,ab,kw)
5	[mh stents] OR stent*:ti,ab,kw OR (SEM OR SEMTs OR SEM OR SEMs):ti,ab,kw
6	#3 AND (#4 OR #5)

Prisma Flow Chart (PICO 4)

239 references imported for screening as 239 studies
3 duplicates removed
236 studies screened against title and abstract
221 studies excluded
15 studies assessed for full-text eligibility
12 studies excluded
5 Wrong intervention
4 abstract form
2 Wrong study design
1 Wrong comparator
0 studies ongoing
0 studies awaiting classification
3 studies included

PICO 5: Plastic vs FC-SEMS for Biliary Strictures

Database: Ovid MEDLINE
Search Date: 12 November 2021
Limits: English language; RCTs, meta-analyses, systematic reviews, prospective or retrospective comparative studies; published after January 1, 2001

Number of Results: 57

1	(exp Pancreatitis, Chronic/ or exp Pancreatitis, Alcoholic/ or (Pancreatitis/ and Chronic Diseases/) or (chronic adj2 pancreatitis).tw,kf. or ((autoimmun$ or auto-immun$ or Tropical or hereditar$ or familiar$) and pancreatitis).tw,kf. or (Hypertriglyceridemia/ or Hypercalcemia/ or alcohol intoxicat$.tw,kf. or (autoimmun$ or auto-immun$).tw,kf.)) and (Pancreas/ or pancrea*.tw,kf.)	28519
2	exp bile ducts/ or exp biliary tract diseases/ or (bile duct* or biliary or hilar or peri?hilar or hilum or hilus).tw,kf.	216664
3	exp constriction, pathologic/ or (constriction or stricture* or stenos?s or obstruction or occlusion or blockage).tw,kf.	535528
4	2 and 3	23776
5	exp cholestasis/ or cholestasis.tw,kf. or ((bile duct* or biliary or hilar or peri?hilar or hilum or hilus or anastomotic or non-anastomic or nonanastomic) adj2 (stricture* or obstruction or occlusion or stenos?s or blockage)).tw,kf.	51840
6	4 or 5	60844
7	exp Cholangiopancreatography, Endoscopic Retrograde/ or ERCP.tw,kf. or (endoscop* adj2 retrograd* adj2 (cholangiopancreatograph* or cholangio-pancreatograph*)).tw,kf.	23771
8	exp stents/ or stent*.tw,kf. or (SEM or SEMTs or SEM or SEMs or FC-SEMS).tw,kf.	248307
9	7 and 8	4456
10	1 and 6 and 9	170
11	exp "sensitivity and specificity"/	622845
12	false negative reactions/ or false positive reactions/	39725
13	(sensitivity or specificity).ti,ab.	1125314
14	(predicitve adj value$1).ti,ab.	14
15	(likelihood adj ratio$1).ti,ab.	17307
16	(false adj (negative$1 or positive$1)).ti,ab.	82680
17	(randomized controlled trial or controlled clinical trial).pt.	639777
18	double blind method/ or single blind method/	198435
19	practice guideline.pt.	29250
20	consensus development conference.pt.	12186
21	random$.ti,ab.	1266585
22	random allocation/	106169
23	(single blind$3 or double blind$3 or triple blind$3).ti,ab.	180051
24	(review or review academic).pt.	2891079
25	meta analysis.pt.	146383
26	(systematic adj review$).ti,ab. or (systematic* adj3 search*).ab.	242702
27	or/11-24	5731309
28	27 and (25 or 26)	221099
29	Randomized controlled trials as Topic/	150114
30	Randomized controlled trial/	550109
31	Random allocation/	106169
32	Double blind method/	168250
33	Single blind method/	31173
34	Clinical trial/	532194
35	exp Clinical Trials as Topic/	366362
36	or/29-35	1250772
37	(clinic$ adj trial$1).tw.	415775
38	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	184125
39	Placebos/	35755
40	Placebo$.tw.	230184
41	Randomly allocated.tw.	32219
42	(allocated adj2 random).tw.	806
43	or/37-42	699526
44	36 or 43	1560994
45	Case report.tw.	347685
46	Letter/	1158573
47	Historical article/	366448

48	Review of reported cases.pt.	0
49	Review, multicase.pt.	0
50	or/45-49	1855402
51	44 not 50	1523918
52	Epidemiologic studies/	8885
53	exp case control studies/	1248691
54	exp cohort studies/	2245588
55	Case control.tw.	138272
56	(cohort adj (study or studies)).tw.	252680
57	Cohort analy$.tw.	9632
58	(Follow up adj (study or studies)).tw.	52302
59	(observational adj (study or studies)).tw.	130453
60	Longitudinal.tw.	278366
61	Retrospective.tw.	624109
62	Cross sectional.tw.	421170
63	Cross-sectional studies/	397938
64	or/52-63	3378229
65	28 or 51 or 64	4686898
66	10 and 65	77
67	limit 66 to english language	75
68	limit 67 to dt=20010101-20211231	57

Database: Embase.com (Elsevier)
Search Date: 12 November 2021
Limits: English language; RCTs, meta-analyses, systematic reviews, prospective or retrospective comparative studies; published after January 1, 2001
Number of Results: 150

1	('chronic pancreatitis'/exp OR 'alcoholic pancreatitis'/exp OR ('pancreatitis'/de AND 'chronic disease'/de) OR (chronic NEAR/2 pancreatitis):ti,ab,kw OR ((autoimmune* OR auto-immun* OR Tropical OR hereditary* OR familiar*) AND pancreatitis):ti,ab,kw OR ('hypertriglyceridemia'/de OR 'hypercalcemia'/de OR alcohol intoxicat*:ti,ab,kw OR (autoimmune* OR auto-immun*):ti,ab,kw)) AND ('pancreas'/de OR pancrea*:ti,ab,kw)
2	'bile duct'/exp OR 'biliary tract disease'/exp OR (bile duct* OR biliary OR hilar OR peri?hilar OR hilum OR hilus):ti,ab,kw
3	'stenosis, occlusion and obstruction'/exp OR (constriction OR stricture* OR stenos?s OR obstruction OR occlusion OR blockage):ti,ab,kw
4	#2 AND #3
5	'cholestasis'/exp OR cholestasis:ti,ab,kw OR (("bile duct*" OR biliary OR hilar OR peri?hilar OR hilum OR hilus OR anastomotic OR non-anastomic OR nonanastomic) NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
6	#4 OR #5
7	'endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ti,ab,kw OR (endoscop* NEAR/2 retrograd* NEAR/2 (cholangiopancreatograph* OR cholangio-pancreatograph*)):ti,ab,kw
8	'stent'/exp OR stent*:ti,ab,kw OR (SEM OR SEMTs OR SEM OR SEMs OR FC-SEMS):ti,ab,kw
9	#7 AND #8
10	#1 AND #6 AND #9
11	('Clinical trial'/de OR 'Randomized controlled trial'/de OR 'Randomization'/de OR 'Single blind procedure'/de OR 'Double blind procedure'/de OR 'Crossover procedure'/de OR 'Placebo'/de OR Randomi?ed controlled trial*:ti,ab,kw OR Rct:ti,ab,kw OR Random allocation:ti,ab,kw OR Randomly allocated:ti,ab,kw OR Allocated randomly:ti,ab,kw OR (allocated NEAR/2 random):ti,ab,kw OR Single blind*:ti,ab,kw OR Double blind*:ti,ab,kw OR ((treble OR triple) NEAR (blind*)):ti,ab,kw OR Placebo*:ti,ab,kw OR 'Prospective study'/de) NOT ('Case study'/de OR Case report:ti,ab,kw OR 'Abstract report'/de or 'letter'/de) OR 'Clinical study'/de OR 'Case control study'/de OR 'Family study'/de OR 'Longitudinal study'/de OR 'Retrospective study'/de OR 'Prospective study'/de NOT 'Randomized controlled trials'/de) OR 'Cohort analysis'/de OR (Cohort NEAR (study OR studies)):ti,ab,kw OR ("Case control" NEAR (study OR studies)):ti,ab,kw OR ("follow up" NEAR (study OR studies)):ti,ab,kw OR (observational NEAR (study OR studies)):ti,ab,kw OR (epidemiologic* NEAR (study OR studies)):ti,ab,kw OR ("cross sectional" NEAR (study OR studies)):ti,ab,kw OR ('Meta Analysis'/exp OR ((meta NEAR analy*) OR metaanalys*):ti,ab,kw OR (systematic NEAR (review*1 OR overview*1)):ti,ab,kw OR cancerlit:ab OR Cochrane:ab OR Embase:ab OR (psychlit OR psyclit):ab OR (psychinfo OR psycinfo):ab OR (cinahl OR cinhal):ab OR science citation index:ab OR bids:ab OR reference lists:ab OR bibliograph*:ab OR hand-search*:ab OR manual search*:ab OR relevant journals:ab OR ((data extraction:ab OR selection criteria:ab) AND review:it)) NOT (letter:it OR editorial:it OR ('animal'/de NOT ('animal'/de AND 'human'/de)))
12	#10 AND #11
13	#12 AND [01/01/2001]/sd
14	#13 AND English:LA

Database: Cochrane Library (Wiley)
Search Date: 12 November 2021
Limits: N/A
Number of Results: 0

Prisma Flow Chart (PICO 5)

204 references imported for screening as 204 studies
2 duplicates removed
202 studies screened against title and abstract
192 studies excluded
10 studies assessed for full-text eligibility
7 studies excluded
2 Abstract Only
2 Wrong comparator
2 Wrong study design
1 Wrong patient population
0 studies ongoing
0 studies awaiting classification
3 studies included

PICO 6: Endoscopy vs Surgery for Pseudocyst

Database: Ovid MEDLINE
Search Date: 12 November 2021
Limits: English language; RCTs, meta-analyses, systematic reviews, prospective or retrospective comparative studies; published after January 1, 2001
Number of Results: 483

1	exp Pancreatic Pseudocyst/ or (pancrea* adj3 pseudocyst*).tw,kf. or ($pancrea* adj2 fluid adj2 collection*).tw,kf. or (pfc or pfcs).tw,kf.	19305
2	exp Stents/ or exp Catheters/ or exp Catheterization/ or exp Drainage/ or exp Suction/	332906
3	stent*.tw,kf. or (catheter* or cannula* or tube* or pipe* or "SEMS").tw,kw. or (pancreatic duct* adj5 holder*).tw,kw. or drainag*.tw,kw. or (suction* or aspirate* or aspiration*).tw,kw.	1106617
4	2 or 3	1239817
5	Endoscopy/ or Endoscopy, Digestive System/ or exp endosonography/ or (endoscop* adj3 ultrasound*).tw,kf. or EUS.tw,kf. or endosonograph*.tw,kf. or (endoscop* or endotherap*).tw,kf.	256702

6	General Surgery/ or Surgical Procedures, Operative/ or percutaneous.tw,kf. or (cystogastrostom*or cystjejunostom* or cystduodenostom*).tw,kf. or (surgical or surger* operat*).tw,kf. or su.fs.	2789359
7	4 and (5 or 6)	359537
8	1 and 7	2483
9	exp "sensitivity and specificity"/	622845
10	false negative reactions/ or false positive reactions/	39725
11	(sensitivity or specificity).ti,ab.	1125314
12	(predicitve adj value$1).ti,ab.	14
13	(likelihood adj ratio$1).ti,ab.	17307
14	(false adj (negative$1 or positive$1)).ti,ab.	82680
15	(randomized controlled trial or controlled clinical trial).pt.	639777
16	double blind method/ or single blind method/	198435
17	practice guideline.pt.	29250
18	consensus development conference.pt.	12186
19	random$.ti,ab.	1266585
20	random allocation/	106169
21	(single blind$3 or double blind$3 or triple blind$3).ti,ab.	180051
22	(review or review academic).pt.	2891079
23	meta analysis.pt.	146383
24	(systematic adj review$).ti,ab. or (systematic* adj3 search*).ab.	242702
25	or/9-22	5731309
26	25 and (23 or 24)	221099
27	Randomized controlled trials as Topic/	150114
28	Randomized controlled trial/	550109
29	Random allocation/	106169
30	Double blind method/	168250
31	Single blind method/	31173
32	Clinical trial/	532194
33	exp Clinical Trials as Topic/	366362
34	or/27-33	1250772
35	(clinic$ adj trial$1).tw.	415775
36	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	184125
37	Placebos/	35755
38	Placebo$.tw.	230184
39	Randomly allocated.tw.	32219
40	(allocated adj2 random).tw.	806
41	or/35-40	699526
42	34 or 41	1560994
43	Case report.tw.	347685
44	Letter/	1158573
45	Historical article/	366448
46	Review of reported cases.pt.	0
47	Review, multicase.pt.	0
48	or/43-47	1855402
49	42 not 48	1523918
50	Epidemiologic studies/	8885
51	exp case control studies/	1248691
52	exp cohort studies/	2245588
53	Case control.tw.	138272
54	(cohort adj (study or studies)).tw.	252680
55	Cohort analy$.tw.	9632
56	(Follow up adj (study or studies)).tw.	52302
57	(observational adj (study or studies)).tw.	130453
58	Longitudinal.tw.	278366
59	Retrospective.tw.	624109
60	Cross sectional.tw.	421170
61	Cross-sectional studies/	397938
62	or/50-61	3378229
63	26 or 49 or 62	4686898
64	8 and 63	737
65	limit 64 to dt=20010101-20211231	535
66	limit 65 to english language	483

Database: Embase.com (Elsevier)
Search Date: 12 November 2021
Limits: English language; RCTs, meta-analyses, systematic reviews, prospective or retrospective comparative studies; published after January 1, 2001
Number of Results: 652

1	'pancreas pseudocyst'/exp OR (pancrea* NEAR/3 pseudocyst*):ti,ab,kw OR ($pancrea* NEAR/2 fluid NEAR/2 collection*):ti,ab,kw OR (pfc OR pfcs):ti,ab,kw
2	'stent'/exp OR 'catheter'/exp OR 'catheterization'/exp OR 'drainage'/exp OR 'suction'/exp
3	stent*:ti,ab,kw OR (catheter* OR cannula* OR tube* OR pipe* OR "SEMS"):ti,ab,kw OR (pancreatic duct* NEAR/5 holder*):ti,ab,kw OR drainag*:ti,ab,kw OR (suction* OR aspirate* OR aspiration*):ti,ab,kw
4	#2 OR #3
5	'Endoscopy'/de OR 'digestive tract endoscopy'/de OR 'endoscopic ultrasonography'/exp OR (endoscop* NEAR/3 ultrasound*):ti,ab,kw OR EUS:ti,ab,kw OR endosonograph*:ti,ab,kw OR (endoscop* OR endotherap*):ti,ab,kw
6	'general surgery'/de OR 'surgery'/de OR percutaneous:ti,ab,kw OR (cystogastrostom*OR cystjejunostom* OR cystduodenostom*):ti,ab,kw OR (surgical OR surger* operat*):ti,ab,kw
7	#4 AND (#5 OR #6)
8	#1 AND #7
9	('Clinical trial'/de OR 'Randomized controlled trial'/de OR 'Randomization'/de OR 'Single blind procedure'/de OR 'Double blind procedure'/de OR 'Crossover procedure'/de OR 'Placebo'/de OR Randomi?ed controlled trial*:ti,ab,kw OR Rct:ti,ab,kw OR Random allocation:ti,ab,kw OR Randomly allocated:ti,ab,kw OR Allocated randomly:ti,ab,kw OR (allocated NEAR/2 random):ti,ab,kw OR Single blind*:ti,ab,kw OR Double blind*:ti,ab,kw OR ((treble OR triple) NEAR (blind*)):ti,ab,kw OR Placebo*:ti,ab,kw OR 'Prospective study'/de) NOT ('Case study'/de OR Case report:ti,ab,kw OR 'Abstract report'/de or 'letter'/de) OR 'Clinical study'/de OR 'Case control study'/de OR 'Family study'/de OR 'Longitudinal study'/de OR 'Retrospective study'/de OR ('Prospective study'/de NOT 'Randomized controlled trials'/de) OR 'Cohort analysis'/de OR (Cohort NEAR (study OR studies)):ti,ab,kw OR ("Case control" NEAR (study OR studies)):ti,ab,kw OR ("follow up" NEAR (study OR studies)):ti,ab,kw OR (observational NEAR (study OR studies)):ti,ab,kw OR (epidemiologic* NEAR (study OR studies)):ti,ab,kw OR ("cross sectional" NEAR (study OR studies)):ti,ab,kw OR ('Meta Analysis'/exp OR ((meta NEAR analy*) OR metaanalys*):ti,ab,kw OR (systematic NEAR (review*1 OR overview*1)):ti,ab,kw OR cancerlit:ab OR Cochrane:ab OR Embase:ab OR (psychlit OR psyclit):ab OR (psychinfo OR psycinfo):ab OR (cinahl OR cinhal):ab OR science citation index:ab OR bids:ab OR reference lists:ab OR bibliograph*:ab OR hand-search*:ab OR manual search*:ab OR relevant journals:ab OR ((data extraction:ab OR selection criteria:ab) AND review:it)) NOT (letter:it OR editorial:it OR ('animal'/de NOT ('animal'/de AND 'human'/de)))
10	#8 AND #9
11	#10 AND [01/01/2001]/sd
12	#11 AND English:LA

Database: Cochrane Library (Wiley)
Search Date: 12 November 2021
Limits: Published after January 1, 2001
Number of Results:

1	[mh "Pancreatic Pseudocyst"] OR (pancrea* NEAR/3 pseudocyst*):ti,ab,kw OR ($pancrea* NEAR/2 fluid NEAR/2 collection*):ti,ab,kw OR (pfc OR pfcs):ti,ab,kw

2	[mh Stents] OR [mh Catheters] OR [mh Catheterization] OR [mh Drainage] OR [mh Suction]
3	stent*:ti,ab,kw OR (catheter* OR cannula* OR tube* OR pipe* OR "SEMS"):ti,ab,kw OR (pancreatic duct* NEAR/5 holder*):ti,ab,kw OR drainag*:ti,ab,kw OR (suction* OR aspirate* OR aspiration*):ti,ab,kw
4	#2 OR #3
5	[mh "Endoscopy"] OR [mh "Endoscopy, Digestive System"] OR [mh endosonography] OR (endoscop* NEAR/3 ultrasound*):ti,ab,kw OR EUS:ti,ab,kw OR endosonograph*:ti,ab,kw OR (endoscop* OR endotherap*):ti,ab,kw
6	[mh "General Surgery"] OR [mh "Surgical Procedures, Operative"] OR percutaneous:ti,ab,kw OR (cystogastrostom*OR cystjejunostom* OR cystduodenostom*):ti,ab,kw OR (surgical OR surger* operat*):ti,ab,kw
7	#4 AND (#5 OR #6)
8	#1 AND #7

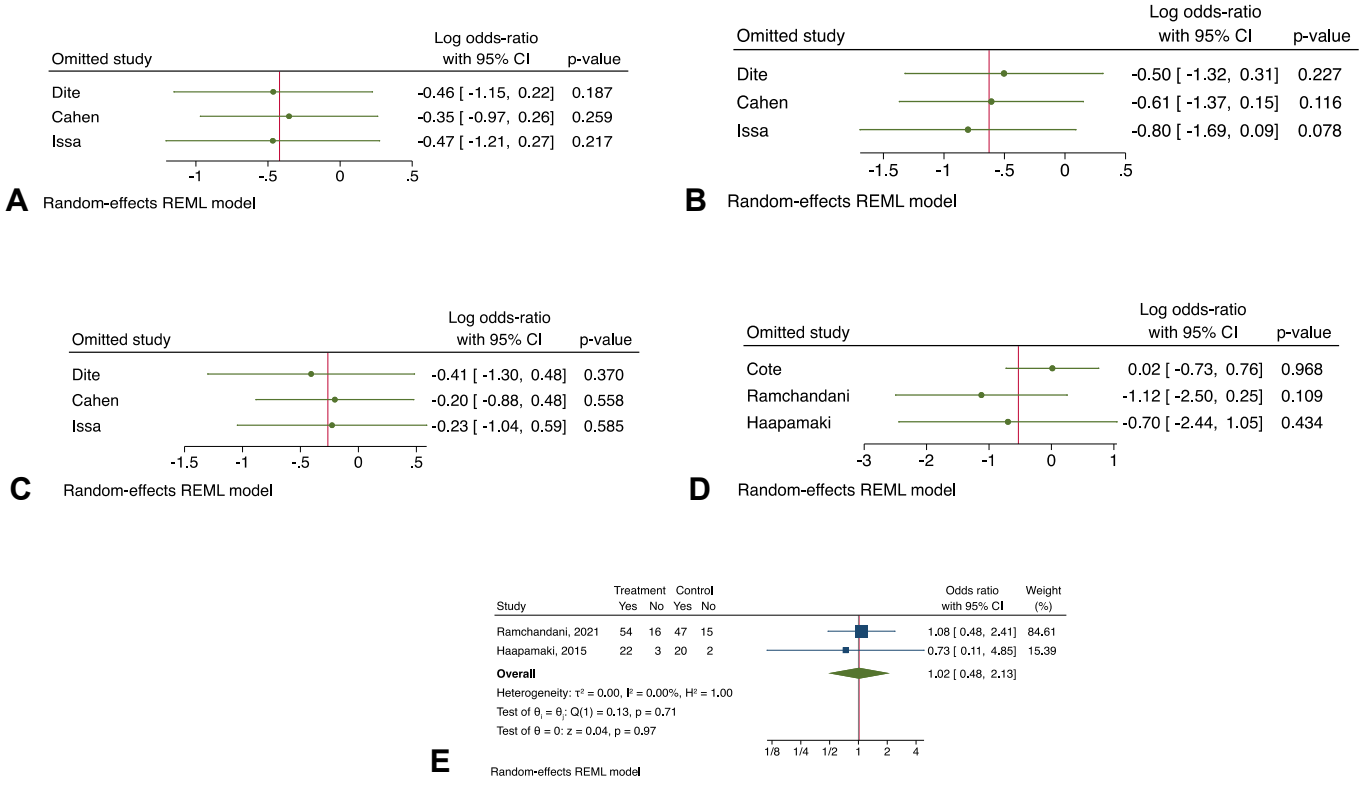
Prisma Flow Chart (PICO 6)

958 references imported for screening as 958 studies
- **6 duplicates removed**

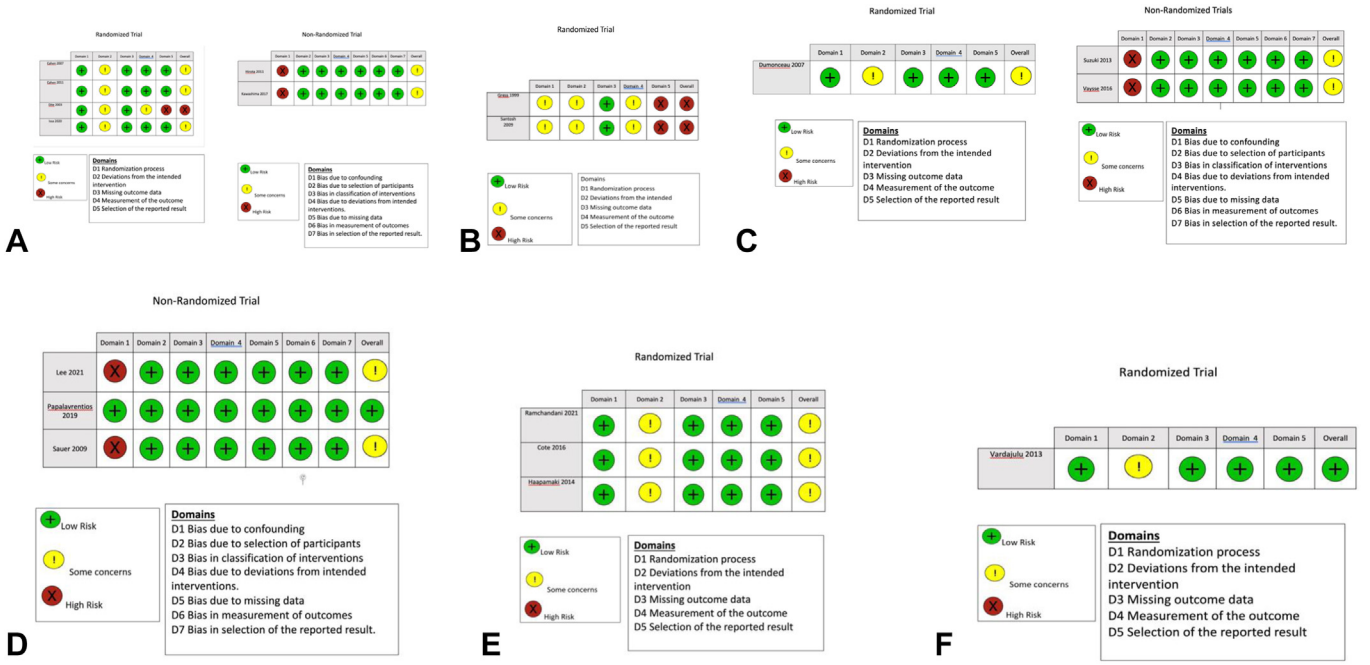
952 studies screened against title and abstract
- **921 studies excluded**

31 studies assessed for full-text eligibility
- **30 studies excluded**
  - **14 Wrong patient population**
  - **9 Wrong study design**
  - **7 Abstract Only**
- **0 studies ongoing**
- **0 studies awaiting classification**

1 study included



Supplementary Figure 1. Sensitivity analysis of various meta-analyses by removing 1 study for PICO question 1: (**A**) any pain relief, (**B**) complete pain relief, and (**C**) partial pain relief. For PICO 5: (**D**) stricture resolution and (**E**) forest plot after exclusion of Coté et al (2016).[48] *CI*, Confidence interval; *PICO*, population, intervention, comparator, outcome.



Supplementary Figure 2. Quality assessment of randomized and nonrandomized studies included in (**A**) PICO question 1, (**B**) PICO question 2, (**C**) PICO question 3, (**D**) PICO question 4, (**E**) PICO question 5, and (**F**) PICO question 6. *PICO*, Population, intervention, comparator, outcome.

SUPPLEMENTARY TABLE 1. Study design, setting, and inclusion and exclusion criteria for all included studies

Authors	Year	Country	Study design	Study setting	Inclusion criteria	Exclusion criteria
PICO question 1						
Cahen[12]	2011	Netherlands	RCT	Single center	1. CP diagnosis, based on clinical symptoms and morphologic changes detected by imaging studies, pancreatic functional insufficiency, or both 2. PD obstruction because of stenosis, intraductal stones, or both located left of the spine, with dilatation of the duct by ≥5 mm proximal to the obstruction, as determined by MRCP, CT, or both 3. Severe, recurrent pancreatic pain insufficiently relieved by non-narcotic analgesics or requiring opiates	1. Age <18 or >80 y 2. Enlargement of the pancreatic head >4 cm 3. Contraindications to surgery 3. American Society of Anesthesiologists class IV 4. Severe portal hypertension 5. Contraindications to endoscopic treatment 6. Gastrectomy with Billroth II reconstruction 7. Other pancreatitis-related adverse events requiring surgery 8. Previous pancreatic surgery 9. Suspected pancreatic cancer 10. Life expectancy <2 y 11. Pregnancy
Cahen[11]	2007	Netherlands	RCT	Single center	1. CP diagnosis, based on clinical symptoms and morphologic changes detected by imaging studies, pancreatic functional insufficiency, or both 2. PD obstruction because of stenosis, intraductal stones, or both located left of the spine, with dilatation of the duct by ≥5 mm proximal to the obstruction, as determined by MRCP, CT, or both 3. Severe, recurrent pancreatic pain insufficiently relieved by non-narcotic analgesics or requiring opiates	1. Age <18 or >80 y 2. Enlargement of the pancreatic head >4 cm 3. Contraindications to surgery 3. American Society of Anesthesiologists class IV 4. Severe portal hypertension 5. Contraindications to endoscopic treatment 6. Gastrectomy with Billroth II reconstruction 7. Other pancreatitis-related adverse events requiring surgery 8. Previous pancreatic surgery 9. Suspected pancreatic cancer 10. Life expectancy <2 y 11. Pregnancy
Dite[10]	2003	Czech Republic	RCT	Single center	1. Age 18-70 y 2. CP diagnosed with ERCP, CT, or EUS 3. Obstructive CP demonstrated on imaging, showing dilated duct structures and/or stones predominantly in the pancreatic head or body 4. Painful CP 5. Failure of conservative management during the previous 3 y 6. Duration of disease over 5 y 7. Indication of interventional treatment	1. Age < 18 or >70 y 2. Pregnancy 3. Previous interventional therapy celiac plexus, pancreatic endotherapy, pancreatic surgery for CP 4. Suspected pancreatic malignancy 5. Refusal of consent to the study therapies and/or noncompliance with follow-up examinations
Issa[15]	2020	Netherlands	RCT	Multicenter	1. Adult patients with severe pain because of obstructive CP with a dilated PD who recently started opioids because of progressive pain	1. History of prolonged need of opioids 2. Previous pancreatic surgery, endoscopic dilatation, or stent placement of the PD 3. Episode of biliary obstruction in the last 2 mo or the presence of a stent in the common bile duct 4. Proven autoimmune pancreatitis, stones, and strictures exclusively located in the tail of the pancreas with relatively normal pancreatic head and body

(*continued on the next page*)

SUPPLEMENTARY TABLE 1. Continued

Authors	Year	Country	Study design	Study setting	Inclusion criteria	Exclusion criteria
						5. Fully impacted stones casting the entire main PD (from head to tail) and side branches 6. Suspected or established pancreatic malignancies 7. Life expectancy of <1 y for any reason 8. Presence of duodenal obstruction necessitating surgery, as judged by the expert panel 9. Presence of a pseudocyst >6 cm necessitating intervention, as judged by the expert panel. 10. Contraindications for surgery 11. Pregnancy
Hirota[13]	2011	Japan	Retrospective chart review	Single center	NR	NR
Kawashima[14]	2018	Japan	Retrospective chart review	Single center	PS is indicated for 1. Symptomatic or asymptomatic patients requiring preservation of pancreatic function 2. Patients with alcoholic pancreatitis who are capable of abstaining from drinking	Surgical drainage is indicated for cases where EPS is difficult for severe stenosis of the PD or is associated with duodenal stenosis as a comorbidity
PICO question 2						
Santosh[23]	2009	India	RCT	Single center	CP patients with abdominal pain requiring daily analgesics for >4 wk	Patients having associated adverse events of CP such as pseudocysts, biliary strictures, or pancreatic abscess were excluded
Gress[22]	1999	US	RCT	Single center	CP patients with constant unremitting and intractable abdominal pain that was attributed to CP and was not controlled by currently used therapies	NR
PICO question 3						
Dumonceau[29]	2007	Switzerland	RCT	Multicenter	Painful CP with ≥1 calcification >4 mm in the pancreatic head or body with upstream MPD dilation and no prior intervention(s)	Presence of a pancreatic fluid collection >2 cm, serum alkaline phosphatases greater than twice the normal value or cholangitis, age <18 y, pregnancy or lactation, and unwillingness to participate
Suzuki[31]	2013	Japan	Retrospective study	Multicenter	Pancreatolithiasis managed during a 5-y period (January 2001 to December 2005) from 36 working units of key members of JSGPBL	NR
Vaysse[30]	2016	France	Retrospective study	Single	Painful CP or recurrent acute pancreatitis	NR
Bick[28]	2022	USA	Retrospective study	Single	Patients age >18 y, who had symptomatic large MPD stones (≥5 mm in greatest dimension); presence of abdominal pain and relative indications included symptomatic exocrine pancreatic insufficiency	Excluded patients included those without clear symptomatic indications for treatment
PICO question 4						
Lee[41]	2021	Korea	Retrospective study	Single center	1. Dominant MPD stricture located in pancreatic head and neck 2. Initially treated with single PS insertion	1. Obstructive PD stones without dominant MPD stricture 2. Concomitant tumor of pancreas and biliary tract

(*continued on the next page*)

SUPPLEMENTARY TABLE 1. Continued

Authors	Year	Country	Study design	Study setting	Inclusion criteria	Exclusion criteria
					3. Persistent MPD stricture with upstream PD dilatation after initial PS removal	3. Multiple MPD or body/tail strictures 4. Fully covered self-expandable metal stent inserted initially 5. Failure of selective MPD cannulation 6. History of PD stent placement at another hospital 7. Improved MPD stricture or follow-up loss after initial PD stent placement
Papalavrentios[39]	2019	Belgium	Retrospective	Single center	1. Painful CP defined as continuous or recurrent pain with >3 painful episodes a year 2. MPD stricture in the head of the pancreas	1. Previous pancreatic surgery, presence of a pancreatic pseudocyst ≥2 cm, or a biliary stricture 2. Total duration of follow-up <24 mo since stent insertion 3. Pancreatic cancer diagnosed during follow up
Sauer[40]	2009	USA	Retrospective	Single Center	1. Patients diagnosed with CP who had a PD stent placed	NR
PICO question 5						
Coté[48]	2016	USA	RCT	Multicenter	1. Bismuth type I benign bile duct stricture (common bile duct or common hepatic duct stricture whose proximal margin is ≥2 cm from the hepatic bifurcation) 2. Objective signs and symptoms related to the stricture	Suspected malignant etiology for the stricture 1. Prior endotherapy within 1 y of presentation except in the following 2 scenarios: early (<30 days) stent placement after liver transplant and in patients with CP, single PS placed during presenting ERCP while evaluating for malignancy 2. Bismuth type II-IV stricture 3. Proximal common hepatic duct diameter <6 mm 4. Intact gallbladder 5. Except in cases where a stent can be deployed >1 cm below the cystic duct insertion 6. Age <18 y, pregnancy, incarceration, inability to provide informed consent 7. Karnofsky score ≤40 8. Inability to pass a guidewire proximal to the stricture 9. Stricture >8 cm in length 10. Life expectancy <1 y 11. Concomitant nonanastomotic biliary strictures (eg, biliary cast syndrome
Ramchandani[49]	2021	Worldwide centers	RCT	Multicenter	1. Age ≥1.18 y with documented CP, symptomatic bile duct stricture (defined by cholangitis or persistent jaundice for ≥1 mo or cholestasis associated with ≥3 times normal alkaline phosphatase levels) 2. Documented at time of enrollment for naïve stricture or at the time of prior PS placement in strictures that had 1 prior PS inserted and common bile duct stricture based on imaging assessment of dilatation of the common and/or intrahepatic bile ducts	1. Non-CP etiology of stricture or malignant bile duct stricture 2. A prior biliary metal stent or >1 PS size ≤10F for >6 mo 3. Developing obstructive biliary symptoms associated with onset of acute pancreatitis 4. Stricture within 2 cm of common bile duct bifurcation, known bile duct fistula or leak, symptomatic duodenal stenosis with gastric stasis 5. Contraindication to endoscopic techniques or devices

(*continued on the next page*)

SUPPLEMENTARY TABLE 1. Continued

Authors	Year	Country	Study design	Study setting	Inclusion criteria	Exclusion criteria
						6. Participation in another investigational study within 90 days before consent 7. Investigator discretion
Haapamaki[50]	2015	Finland	RCT	Single center	1. At initial presentation, clinical and laboratory findings including bilirubin and alkaline phosphate levels, abdominal pain, jaundice, and cholangitis were recorded 2. Indication for the initial ERCP was suspected biliary obstruction caused by CP	1. Patients with malignancies 2. Known liver cirrhosis, acute or chronic hepatitis, or abnormal hepatic imaging studies 3. Patients with their first attack of acute pancreatitis
PICO question 6						
Vardarajulu[56]	2013	USA	RCT	Single center	1. Pseudocyst diagnosed based on CT criteria 2. Measuring $\geq$6 cm and located adjacent to the stomach with documented history of acute or CP 3. Persistent pancreatic pain requiring narcotics or analgesics 4. Symptomatic gastric outlet or bile duct obstruction induced by the pseudocyst	1. Age <18 or >80 y 2. Contraindications to surgery: American Society of Anesthesiologists class IV, severe portal hypertension 3. Contraindication to endoscopic drainage: gastrectomy with Billroth II reconstruction, gastric bypass surgery, prior surgery for pancreas-related adverse events 4. Pregnancy 5. Associated pancreatic necrosis on CT 6. Pseudocyst not adjacent to the stomach 7. Multiloculated pseudocyst or multiple pseudocysts

NR, Not reported; *RCT*, randomized controlled trial; *PS*, plastic stent; *PD*, pancreatic duct; *MPD*, main pancreatic duct; *CP*, chronic pancreatitis; *PICO*, population, intervention, comparator, outcome; *JSGPBL*, The Japanese Study Group for Pancreato-Biliary Lithiasis; *EPS*, exocrine pancreatic sufficiency.

SUPPLEMENTARY TABLE 2. Population features of patients and description of interventions performed in the studies

Authors	Patient distribution	Mean age (standard deviation) (y)	No. of women	Follow-up (mo)	Intervention groups	Comparison groups
PICO question 1						
Cahen[12]	Endotherapy: 19 Surgery: 19	Endotherapy: 52 (9) Surgery: 46 (12)	Endotherapy: 8 (42%) Surgery: 5 (25%)	Endotherapy: 85 (14) Surgery: 92 (11)	ERCP was performed every 3 mo, and stents were removed in case of stricture resolution.	17 patients underwent a pancreatojejunostomy, 1 Whipple procedure, 1 Frey procedure.
Cahen[11]	Endotherapy: 19 Surgery: 20	Endotherapy: 52 (9) Surgery: 46 (12)	Endotherapy: 8 (42%) Surgery: 5 (25%)	24	ERCP was performed every 3 mo, and stents were removed in case of stricture resolution.	18 underwent pancreatojejunostomy, 1 Whipple procedure, 1 Frey procedure.
Dite[10]	Endotherapy: 36 Surgery: 36	41.7	21 (32.8%)	60	Pancreatic sphincterotomy, dilation, or bougienage of strictures; stent placement in case of strictures that could not be resolved by sphincterotomy; and/or stone extraction, after mechanical lithotripsy as appropriate.	Duodenectomy, Whipple's procedure Partington-Rochelle pancreaticojejunal anastomosis.
Issa[15]	Endotherapy: 44 Surgery: 44	Endotherapy: 56 (9) Surgery: 49 (10)	Endotherapy: 10 (22.7) Surgery: 11 (25)	18	22 patients underwent ESWL, 32 endoscopic dilatations, 29 endoscopy (≥1) stents were inserted.	24 patients underwent lateral pancreatojejunostomy, 15 duodenum-preserving pancreatic head resection, 1 distal pancreatectomy, 1 pylorus-preserving pancreatoduodenectomy, endoscopic treatment, 1 medical treatment.
Hirota[13]	Endotherapy: 34 Surgery: 34	Endotherapy: 54.8 Surgery: 46.4	Endotherapy: 9 (26.5) Surgery: 8 (23.5)	Endotherapy: 40.7 Surgery: 40.1	Endoscopic treatment including endoscopic sphincterotomy, stone removal, and stent placement with or without ESWL.	Frey operation, resection
Kawashima[14]	Endotherapy: 41 Surgery: 10	Endotherapy: 59 (14) Surgery: 49 (16)	Endotherapy: 6 (15%) Surgery: 5 (50%)	48	NR	NR
PICO question 2						
Santosh[23]	EUS-guided CPB: 27 Percutaneous fluoroscopy-guided CPB: 29	EUS-guided CPB: 48.9 (11.5) Percutaneous fluoroscopy-	EUS-guided CPB: 6 (22.22) Percutaneous fluoroscopy-	Chronic pancreatitis patients with abdominal pain requiring	EUS-guided CPB was performed under the guidance of linear array echoendoscope	Percutaneous fluoroscopy-guided CPB was performed in the radiology department using a posterior

(*continued on the next page*)

SUPPLEMENTARY TABLE 2. Continued

Authors	Patient distribution	Mean age (standard deviation) (y)	No. of women	Follow-up (mo)	Intervention groups	Comparison groups
		guided CPB: 44.7 (13.8)	guided CPB: 9 (31.03)	daily analgesics for >4 wk	using a 20-gauge needle.	approach. A 22-gauge, 17-cm-long spinal needle was inserted and advanced using the "walking off" the vertebra technique and positioned 2 cm anterior to the upper border of the first lumbar vertebra in the antecrural space.
Gress[22]	EUS-guided CPB: 10 Percutaneous fluoroscopy-guided CPB: 8	NR	NR	Chronic pancreatitis patients with constant unremitting and intractable abdominal pain that was attributed to chronic pancreatitis and was not controlled by currently used therapies.	EUS-guided CPB was performed under the guidance of linear array endosonography using a sterile 22-gauge FNA needle.	CT-guided CPB was performed in the radiology department using a transposterior approach and a sterile 22-gauge, 15-cm-long spinal needle inserted anterior to the aorta under CT guidance, followed by the administration of bupivacaine and triamcinolone.
PICO question 3						
Dumonceau[29]	ESWL: 26 ESWL+ERCP: 29	ESWL: 51.8 (12.3) ESWL+ERCP: 49 (10.1)	ESWL: 4 (15%) ESWL+ERCP: 8 (28%)	ESWL: 52 (19.3) ESWL+ERCP: 50.7 (23.6); $P = .460$	One or more sessions of ESWL were performed in all patients using the Lithostar Plus (Siemens, Ehrlangen, Germany) until the obstructive stones were broken into <2-mm fragments.	ESWL combined with endoscopy group underwent ERCP immediately after the last ESWL session with attempted extraction of stone fragments and insertion of 10F plastic pancreatic stents if pancreatic strictures were identified.
Suzuki[31]	ESWL: 202 ESWL+ERCP: 255	NR	All population: 125 (13.64%)	NR	NR	NR
Vaysse[30]	ESWL: 41 ESWL+ERCP: 91	ESWL: 51.2 (13.4) ESWL+ERCP: 50.9 (13.0)	ESWL: 50 (34%) ESWL+ERCP: 44 (33%)	ESWL: 23 ESWL+ERCP: 23	ESWL was performed using a third-generation electromagnetic lithotripter and stones were targeted in line using fluoroscopy. Power and number of shocks delivered per session were decided by the physician who performed the procedure.	NR
Bick[28]	ESWL: 240 SOPIL: 18	ESWL: 57.8 (12.7) SOPIL: 61.3 (11.7)	ESWL: 79 (32.9%) SOPIL: 9 (50%)	NR	ESWL was performed using an electrohydraulic spark gap	SOPIL was performed using the SpyGlass (Boston Scientific Corporation, Marlborough,

(*continued on the next page*)

SUPPLEMENTARY TABLE 2. Continued

Authors	Patient distribution	Mean age (standard deviation) (y)	No. of women	Follow-up (mo)	Intervention groups	Comparison groups
					lithotripter. Intravenous secretin was administered 5-10 min after the initial shock wave and given via slow injection over 1 min. Shock waves were then continued until the stone was adequately fragmented per physician discretion based on serial fluoroscopic images or until a maximum of 11,000 shock waves were achieved. Patients typically underwent ERCP either on the same day or 14 days later.	Mass, USA) Direct Visualization System before 2015 and the SpyGlassDS Direct Visualization System after 2015. Lithotripsy was performed with electrohydraulic lithotripsy using the Autolith generator. Pancreatic sphincterotomy was performed before the advancement of the pancreatoscope catheter. Intraductal lithotripsy was then performed in an aqueous environment until the stone was adequately fragmented based on direct visualization. If partial but incomplete stone fragmentation was achieved, a pancreatic stent was placed and patients returned for additional treatment sessions.
PICO question 4						
Lee[41]	1. FCSEMS: 26 (32.5%) 2. PS: 54 (67.5%)	FCSEMS: 47.0 PS: 57.0	FCSEMS: 7 (26.9%) PS: 15 (27.8%)	FCSEMS: 24.9 (11.4-57.7) PS: 36.2 (12.7-85.6); $P = .237$	FCSEMS: 8 mm: 12 (46.2) 10 mm: 14 (53.8)	PS: 5F: 12 (22.2) 7F: 26 (48.1) 8.5F: 2 (3.7) 10F: 14 (25.9)
Papalavrentios[39]	1. (1 PS): 18 (21.2%), 2. (1 or 2 PSs): 35 (41.2%), 3. (2 PSs): 32 (37.6%)	1: 50 2: 48 3: 54	1: 4 (22%) 2: 11 (31%) 3: 9 (28%)	1: 81.5 2: 89.0 3: 79.0	8.5F to 10F straight polyethylene Amsterdam-type design PS with both an internal and external flap. Multiple stent placement consisted of deployment of 2 side-by-side plastic stents, after dilation with a hydrostatic balloon.	—
Sauer[40]	1. ≤8.5F: 129 (79) 2. 10F: 34 (21)	8.5F: 51.5 (13.9) 10F: 53.9 (12.8)	8.5F: 42 (33%) 10F: 14 (41%)	36.0 (31.2)	Each patient was placed into 1 of 2 groups based on the PD stent diameter used: 1. ≤8.5F stents and 2. 10F stents	—

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SUPPLEMENTARY TABLE 2. Continued

Authors	Patient distribution	Mean age (standard deviation) (y)	No. of women	Follow-up (mo)	Intervention groups	Comparison groups
PICO question 5						
Coté[48]	35 (PS: 17 FCSEMS: 18)	PS: 56.7 (11) FCSEMS: 54.5 (10.4)	PS: 17 (30.9) FCSEMS: 19 (33.3)	12	The stricture was dilated to the maximum safest diameter according to endoscopist judgment.	8-mm FCSEMS: 6- to 7-mm bile ducts 10-mm FCSEMS: bile ducts >8 mm
Ramchandani[49]	164 (PS: 84 FCSEMS: 80)	PS: 53.0 FCSEMS: 51.0	PS: 12 (14.3) FCSEMS: 10 (12.5)	24	≥2 stents 8.5F or 10F	Single 8-mm or 10-mm-diameter FCSEMS
Haapamaki[50]	PS: 30 FCSEMS: 30	PS: 49.5 FCSEMS: 54.5	6 (10%) PS: 1 (3) FCSEMS: 5 (17)	PS: 37 FCSEMS: 41	Dilation + stent exchange to 3F-10F PS	Dilation + stent exchange to 10-mm FCSEMS
PICO question 6						
Vardarajulu[56]	Endoscopic cystogastrostomy: 20 Surgical cystogastrostomy: 20	Endoscopic cystogastrostomy: 48 (14) Surgical cystogastrostomy: 51 (17)	Endoscopic cystogastrostomy: 8 (40%) Surgical cystogastrostomy: 4 (20%)	24	All patients who underwent outpatient endoscopic cystogastrostomy were discharged on the same day unless they had adverse events. Transmural stents were removed if the pseudocyst had resolved on the CT performed routinely in all patients.	After localizing the pseudocyst where it was adhered to the posterior wall of the stomach, it was aspirated and entered with cautery. Once entry was obtained, an endovascular stapler was used to create at least a 6-cm cystogastrostomy. A nasogastric tube then was left in the stomach and passed into the pseudocyst cavity to allow for intermittent irrigation until postoperative day 1. The anterior gastrostomy was closed and the patient was transferred to the surgical floor after postoperative monitoring.

NR, Not reported; *CPB*, celiac plexus block; *FCSEMS*, fully covered self-expandable metal stent; *PS*, plastic stent; *ESWL*, extracorporeal shock wave lithotripsy; *SOPIL*, single-operator pancreatoscopy and intraductal lithotripsy; *PICO*, population, intervention, comparator, outcome.

SUPPLEMENTARY TABLE 3. Outcome measures in studies

Author	Success	Impact on pancreatic exocrine insufficiency	Pain relief	Impact on diabetes	Quality of life physical	Quality of life mental	Cost	Adverse effects	Hospital stay	Intervention-related deaths
PICO question 1										
Cahen[12]	NR	Endotherapy: 0 Surgery: 2 (10.5%)	Endotherapy: 6 (31.6%) Surgery: 12 (63.1%) $P = .042$	Endotherapy: 7 (36.84%) Surgery: 3 (15.8%) $P = .32$	Endotherapy: 43 (11) Surgery: 48 (10) $P = .23$	Endotherapy: 46 (9) Surgery:48 (9) $P = .46$	Endotherapy: $31,048 Surgery:$25,042 $P = .29$	Endotherapy: 4 (2 PD occlusion; 2 PD rupture) Surgery: 0	Endotherapy: 0 Surgery: 0	Endotherapy: 0 Surgery: 0
Cahen[11]	Endotherapy: 10 (52.6%) Surgery: 20 (100%) $P < .001$	Endotherapy: 1 (5.3%) Surgery: 3 (15%) $P = .05$	Endotherapy: 6 (31.6%) Surgery: 15 (75%) $P = .007$	Endotherapy: 3 (31.6%) Surgery: 1 (10.5%) $P = .48$	Endotherapy: 38 (9) Surgery: 47 (7) $P = .003$	Endotherapy: 40 (9) Surgery:45 (9) $P = .15$	NR	Endotherapy: 11 Surgery: 7	Endotherapy: 8 Surgery :11 $P = .13$	Endotherapy: 0 Surgery: 0
Dite[10]	NR	NR	Endotherapy: 22 (61.1%) Surgery: 31 (86.1%)	Endotherapy: 12 Surgery: 14 $P =$ not significant	NR	NR	NR	Endotherapy: 3 Surgery: 6	NR	NR
Issa[15]	NR	NR	Endotherapy: 16 (36.4%) Surgery: 23 (52.3%) $P = .10$	NR	Endotherapy: 31 (8) Surgery: 38 (13) $P = .21$	Endotherapy: 36 (11) Surgery:35 (7) $P = .21$	Difference endotherapy vs surgery: $6673 vs $5207 ($P = .25$; Kempeneers et al.[18])	Endotherapy: 11 Surgery: 12	Endotherapy: 10 Surgery: 11 $P = .57$	Endotherapy: 0 Surgery: 0
Hirota[13]	NR	NR	NR	NR	NR	NR	Endotherapy: $15,400 Surgery: $10,800 $P = .11$	NR	Endotherapy: 29.3 Surgery: 18.6 $P = .055$	NR
Kawashima[14]	Endotherapy: 41 (100%) Surgery: 10 (100%) $P =$ not significant	Endotherapy: 3 (7.3%) Surgery: 1 (10%)	Endotherapy: 37 (90.2%) Surgery: 9 (90%) $P = .75$	Endotherapy: 4 Surgery: 1 $P = .54$	NR	NR	Endotherapy: $19,023 Surgery: $20,033; $P = .58$	Endotherapy: 11 Surgery: 2	Endotherapy: 18 Surgery: 23 $P = .38$	NR
PICO question 2										
Santosh[23]	EUS-guided CPB: 26 (96.3%) Percutaneous fluoroscopy-guided CPB: 28 (96.6%)	NR	EUS-guided CPB: 1 Percutaneous fluoroscopy-guided CPB: 7, $P = .04$	NR	NR	NR	NR	EUS-guided CPB: 2 Percutaneous fluoroscopy-guided CPB: 1	NR	NR
Gress[22]	EUS-guided CPB: 8 (96.3%) Percutaneous fluoroscopy-guided CPB: 2 (25%)	NR	EUS-guided CPB: 1 Percutaneous fluoroscopy-guided CPB: 9, $P = .02$	NR	NR	NR	EUS-guided CPB costs U.S.$1100 vs U.S.$1400 for CT-guided CPB. Average EUS block lasts for 15 wk vs 4 wk for the CT technique.	EUS guided CPB: 1 Percutaneous fluoroscopy-guided CPB: 3	NR	NR
PICO question 3										
Dumonceau[29]	ESWL: 26 (100%) ESWL+ERCP: 29 (100%): all obstructive calcifications were broken into fragments 2 mm in thickness	NR	Frequency NR: mean reduction in pain episodes: ESWL alone: 3.8 (95% CI, 2-5.6), ESWL +ERCP: 3.7 (95% CI, 2.1-5.2; $P <$ .001) $P = .759$	NR	NR	NR	ESWL: 4092.66 ESWL+ERCP: 12,939.3: $P < .001$	ESWL: 0 ESWL+ERCP: 1	ESWL: 3.1 ESWL+ERCP: 8.6: $P = .099$	ESWL: 0 ESWL+ERCP: 0
Suzuki[31]	NR	NR	Overall ESWL: 81 (17.6%)	NR	NR	NR	NR	Overall ESWL: 29 (6.1%)	NR	NR
Vaysse[30]	NR	NR	ESWL: 29 (71%) ESWL+ERCP: 71 (78%) $P = .37$	NR	NR	NR	NR	Overall ESWL: 6 (hematuria:1 acute pancreatitis :5)	NR	NR

(*continued on the next page*)

SUPPLEMENTARY TABLE 3. Continued

Author	Success	Impact on pancreatic exocrine insufficiency	Pain relief	Impact on diabetes	Quality of life physical	Quality of life mental	Cost	Adverse effects	Hospital stay	Intervention-related deaths
Bick	ESWL: 208 (86.7%) SOPIL: 16 (88.9%)	NR	ESWL: 182 (82.7%) SOPIL: 15 (93.8%)	NR	NR	NR	NR	ESWL: 16 (6.7%) SOPIL: 1 (5.6%)	NR	NR
PICO question 4										
Lee[41]	FCSEMS: 26 (100%) PS: 54 (100%); P = .99 FCSEMS: 26 (100%) PS: 52 (100%); P = .320	NR	FCSEMS: 20 (76.9%) PS: 29 (53.7%); P = .046	NR	NR	NR	FCSEMS: 1455.6 (333.1. PS: 1596.9 (1000.8); P = .486	FCSEMS: 10 PS: 20	NR	NR
Papalavrentios[39]	A: 15 (88.2%) B: 23 (74.2%) C: 15 (50%)	A: 1 (5%) B:3 (9%) C: 9 (28%) P = .89	Median Izbicki score: A: 0 (0) B: 0 (5) C: 6 (15) P = .03	A: 2 (11%) B: 3 (9%) C: 8 (25%) P = .56	NR	NR	NR	A: 3 Stent migration B: 9 Stent migration C: 6 Stent migration P = .87	NR	A: 0 B: 0 C: 0
Sauer[40]	NR	NR	NR	NR	NR	NR	NR	NR	8.5F: 63 (49%) 10F: 8 (24%) P < .001	NR
PICO question 5										
Coté[48]	PS: 8 (47.05%) FCSEMS: 15 (83.33%); P< .001	NR	NR	NR	NR	NR	NR	PS: 8 FCSEMS: 9	NR	PS: 0 FCSEMS: 0
Ramchandani[49]	PS: 54 (77.1%) FCSEMS: 47 (75.8%); P = .008	NR	NR	NR	NR	NR	NR	PS: 16 FCSEMS: 19; P = .568	NR	PS: 0 FCSEMS: 0
Haapamaki[50]	PS: 22 (88.0%) FCSEMS: 20 (91.0%); P = 1	NR	NR	NR	NR	NR	NR	PS: 7 FCSEMS: 8 P = .767	NR	PS: 0 FCSEMS: 0
PICO question 6										
Vardarajulu[56]	Endoscopic cystogastrostomy: 19 (95) Surgical cystogastrostomy: 20 (100); P = .50	NR	NR	NR	Odds ratio: −4.48 (95% CI, −8.23 to −.73); P = .019	Odds ratio: −4.41 (95% CI, −8.26 to −.55); P = .025	EUS cystogastrostomy: $7011 (4171) Surgical cystogastrostomy: $15,052 (10,670); P = .003	Endoscopic cystgastrostomy: 0 Surgical cystogastrostomy: 2	NR	NR

NR, Not reported; *FCSEMS*, fully covered self-expandable metallic stent; *PS*, plastic stent; *ESWL*, extracorporeal shock wave lithotripsy; *SOPIL*, single-operator pancreatoscopy and intraductal lithotripsy; *PS*, plastic stent; *PD*, pancreatic duct; *PICO*, population, intervention, comparator, outcome; *CI*, confidence interval; *CPB*, celiac plexus block.