Acute Pancreatitis Task Force on Quality: Development of Quality Indicators for Acute Pancreatitis Management

Elaina Vivian, MPH, CPHQ[1], Leslie Cler, MD, FACP, CPE[1], Darwin Conwell, MD, MS[2], Gregory A. Coté, MD, MSCI, MS[3], Richard Dickerman, MD, FACS[1], Martin Freeman, MD, FACG, FASGE[4], Timothy B. Gardner, MD, MS, FACG[5], Robert H. Hawes, MD, FACG[6], Prashant Kedia, MD, FASGE[1], Rajesh Krishnamoorthi, MD[7], Hellen Oduor, MBChB, MPH, CPHQ, LSSGB[1], Stephen J. Pandol, MD[8], Georgios I. Papachristou, MD, PhD, FACG, FASGE, AGAF[9], Andrew Ross, MD, FASGE[7], Amrita Sethi, MD, MSc, FASGE[10], Shyam Varadarajulu, MD[11], Santhi Swaroop Vege, MD, FACP, MACG, AGAF[12], Wahid Wassef, MD, MPH, FACG[13], C. Mel Wilcox, MD, MSPH, FACG[14], David C. Whitcomb, MD, PhD, FACG[9], Bechien U. Wu, MD, MPH[15], Dhiraj Yadav, MD, MPH[9], Ashton Ellison, MD[1], Samar Habash, MD[16], Sheila Rastegari, MD[16], Rathan Reddy, MD[1], Timothy Yen, MD[1], Mary Rachel Brooks, MCN, RDN, LD[1] and Paul Tarnasky, MD, FACG[1], on behalf of the American College of Gastroenterology and ACG Institute's Acute Pancreatitis Task Force on Quality

INTRODUCTION: **Detailed recommendations and guidelines for acute pancreatitis (AP) management currently exist. However, quality indicators (QIs) are required to measure performance in health care. The goal of the Acute Pancreatitis Task Force on Quality was to formally develop QIs for the management of patients with known or suspected AP using a modified version of the RAND/UCLA Appropriateness Methodology.**

METHODS: **A multidisciplinary expert panel composed of physicians (gastroenterologists, hospitalists, and surgeons) who are acknowledged leaders in their specialties and who represent geographic and practice setting diversity was convened. A literature review was conducted, and a list of proposed QIs was developed. In 3 rounds, panelists reviewed literature, modified QIs, and rated them on the basis of scientific evidence, bias, interpretability, validity, necessity, and proposed performance targets.**

RESULTS: **Supporting literature and a list of 71 proposed QIs across 10 AP domains (Diagnosis, Etiology, Initial Assessment and Risk Stratification, etc.) were sent to the expert panel to review and independently rate in round 1 (95% of panelists participated). Based on a round 2 face-to-face discussion of QIs (75% participation), 41 QIs were classified as valid. During round 3 (90% participation), panelists rated the 41 valid QIs for necessity and proposed performance thresholds. The final classification determined that 40 QIs were both valid and necessary.**

DISCUSSION: **Hospitals and providers managing patients with known or suspected AP should ensure that patients receive high-quality care and desired outcomes according to current evidence-based best practices. This physician-led initiative formally developed 40 QIs and performance threshold targets for AP management. Validated QIs provide a dependable quantitative framework for health systems to monitor the quality of care provided to patients with known or suspected AP.**

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/AJG/A182

Am J Gastroenterol 2019;114:1322–1342. https://doi.org/10.14309/ajg.0000000000000264

INTRODUCTION

The incidence and severity of acute pancreatitis (AP) has increased, and the burden of pancreatic disorders is expected to increase over time (1,2). AP is one of the leading gastrointestinal causes of hospitalization in the United States (3), with mortality ranging from 3% in patients with interstitial pancreatitis (4), 15%

[1]Methodist Dallas Medical Center, Dallas, Texas, USA; [2]The Ohio State University Wexner Medical Center, Columbus, Ohio, USA; [3]Medical University of South Carolina, Charleston, South Carolina, USA; [4]University of Minnesota, Minneapolis, Minnesota, USA; [5]Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, USA; [6]Institute for Minimally Invasive Therapy, Florida Hospital, Orlando, Florida, USA; [7]Virginia Mason Medical Center, Seattle, Washington, USA; [8]Cedars-Sinai Medical Center, Los Angeles, California, USA; [9]University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA; [10]Columbia University Medical Center, New York Presbyterian, New York, New York, USA; [11]Center for Interventional Endoscopy, Florida Hospital, Orlando, Florida, USA; [12]Mayo Clinic, Rochester, Minnesota, USA; [13]University of Massachusetts Memorial Medical Center, Worchester, Massachusetts, USA; [14]University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, USA; [15]Kaiser Permanente Los Angeles, Los Angeles, California, USA; [16]AtlantiCare Regional Medical Center, Atlantic City, New Jersey, USA; and [17]American College of Gastroenterology and ACG Institute's Acute Pancreatitis Task Force on Quality. **Correspondence**: Paul Tarnasky, MD, FACG. E-mail: PaulTarnasky@mhd.com.

Received November 15, 2018; accepted March 8, 2019; published online June 12, 2019

in those with necrotizing pancreatitis, and up to 35% if associated with persistent organ failure (5). Impaired physical health-related quality of life is experienced in patients with AP, particularly when associated with multisystem organ failure (6). In an effort to optimize outcomes and provide care of the highest value, health systems and providers managing patients with AP should adhere to current evidence-based best practices and routinely identify gaps and opportunities for improvement.

Validated quality indicators (QIs), which assess process, outcome, appropriateness, efficiency, and structure of care metrics, can provide a quantitative basis for quality improvement (7). Using such metrics makes it possible to "document the quality of care; make comparisons (benchmarking) over time between facilities (e.g., hospitals and providers); make judgments and set priorities (e.g., choosing a hospital or surgery or organizing medical care); support accountability, regulation and accreditation; support quality improvement; and support patient choice of providers (8)." QIs are developed using evidence-based standards of care and are determined by an expert panel of health professionals in a consensus process.

Clinical practice guidelines are recommendations derived from systemic appraisal of the best available evidence for the purposes of advising both caregivers and patients about certain disease-specific management issues (7). Although there are many guidelines for diagnosis and management of AP, it is important to recognize that quality of such guidelines can be variable (9). QIs serve a different purpose than clinical practice guidelines; they are intended to emphasize the importance of outcomes with the goal of measuring performance in health care (10).

The burden of pancreatic disorders is expected to rise over time, and the future of health care requires tracking quality. Validated AP QIs could be used by hospitals and clinicians to assess their performance, set priorities, and develop specific initiatives to improve the quality of patient care and outcomes. The objective of this research was to formally develop a set of validated AP QIs using a robust, rigorous, and widely used methodology.

METHODS

RAND/UCLA Appropriateness Methodology

AP QIs were developed using the RAND/UCLA Appropriateness Methodology (RAM), a well-defined and scientifically rigorous methodology that correlates with criteria set by national organizations, which specialize in the development and endorsement of clinical quality measurement (11–14). The RAM also reflects the approach of numerous studies across a spectrum of disease processes that have developed QIs (7,15–17). This methodology enables the combination of evidence-based recommendations with the collective judgment of clinical experts in their respective disease-specific specialties to determine the appropriateness of treatment options in clinical care. The modified Delphi methodology used in this study expounds on the original RAM by providing the experts the opportunity to discuss validity of QIs at a face-to-face meeting and rate the indicators in 3 rounds instead of 2, with the third round dedicated to establishing the necessity of indicators and establishing thresholds for adherence.

Operational definitions

Valid indicators are defined as those that measure the quality of care and have the potential to improve clinical practices (18). "Necessary" indicators are those that identify practices that must exist in every scenario. Not "Not necessary" means only that the indicator is not universally required across health care systems (11). Therefore, an indicator can be "valid" and "not necessary."

Establishment of the expert panel

The RAM recommended the use of multidisciplinary teams to reflect the variety of specialties involved in treatment decisions for patients with AP (11). The standards used to select the panel included having individuals who (i) are acknowledged leaders in their specialties, (ii) have an absence of conflicts of interest, and (iii) represent geographic and practice setting diversity (11). The nationally representative panel was made up of gastroenterologists, internists, and a surgeon. The study also recruited a panel moderator and established a research team made up of medical fellows and residents, a dietitian, a pancreatitis nurse navigator, a project manager/statistician, and a project coordinator.

Round 0: meeting

Round 0 was a face-to-face meeting (with an option for attendees to connect via webinar) held during the World Congress of Gastroenterology in Orlando, FL, on October 17, 2017. The purpose was to orient panelists to the study objectives, methodology, and project timeline. Panelists were also polled to gauge study-related preferences and needs.

Literature review and development of proposed quality indicators

The literature and proposed indicators were organized into 10 domains, outlining the plan of care for a patient with typical AP from diagnosis to disposition. These included Diagnosis, Etiology, Initial Assessment and Risk Stratification, Initial Management (baseline–72 hours), Endoscopic Retrograde Cholangiopancreatography (ERCP), Nutrition, Pharmacotherapy, Management of Early Complications (72 hours–4 weeks), Surgery, and Structure of Care. With some minor modifications, these domains were selected based on the established domains in the ACG Guidelines for Management of AP (19). The Structure of Care domain reflected the resources, infrastructure, and policies that a hospital or organization would need to have in place to have a quality program.

The literature review was extensive and a critical step to summarize and rate the available scientific evidence and provide a consistent body of evidence for expert panel members. This was the groundwork needed to resolve any potential disagreements, which may arise during expert panel ratings and/or during the face-to-face round 2 meeting (11).

A medical librarian and the study's research team were enlisted to access PubMed, Ovid, MEDLINE, Embase, and the Cochrane Database of Systematic Reviews/Cochrane Register of Controlled Trials for relevant articles. The literature review was restricted to original research and expert opinion manuscripts, a variety of medical subject headings (MeSH) and non-MeSH terms were used per AP domain, publication dates were limited from 1995 to present, and only English language articles were included. The 1995 cutoff year was elected by the expert panel during round 0 to focus the search on the most relevant clinical literature.

The research team developed proposed QIs based on the ongoing literature review.

For each proposed QI, the following descriptive information was documented:

1. Relevant article citation(s) and identification of the research methodology used (e.g., randomized control trial [RCT], prospective cohort, case series) (11,12).
2. Clinical recommendations/rationale, which lend support to the proposed QI (11,12).
3. Indicator characteristics (i.e., type: process, outcome, appropriateness, efficiency, and/or structure of care) and level of measurement (i.e., hospital or patient) (7,8,11,13).
4. Measure specifications (i.e., target population or exclusion criteria) (11,12).
5. Performance targets identified, if available (17,20,21).
6. Challenges in measurement or evidence gaps (11).

Expert panel members were divided into teams and assigned to 1 of the 10 AP domains. They were sent the literature review and proposed QIs and asked to reword/modify, delete, or suggest new indicators or literature for their assigned domain. Based on their feedback, a list of proposed QIs was revised and sent to the all panelists for round 1 rating.

Together, the literature review and descriptive information related to QIs identifies and organizes the quantity, quality, and consistency of the body of evidence and helps establish whether the evidence leads to desired health outcomes (13) (see Supplement I, Supplementary Digital Content 1, http://links.lww.com/AJG/A182).

Round 1: initial rating of proposed quality indicators

All panelists were sent *via* email a Qualtrics survey link with instructions on rating 71 proposed QIs for round 1. Based on guidance from the developers of RAM, panelists were given strict instructions stating (i) ratings should be based on their personal clinical judgments and available scientific evidence and not on what they think other panelists might say or believe; (ii) NOT to consider cost implications or feasibility of implementation; (iii) the indicators should be viewed from the perspective of an "average" patient who presents to an "average" physician at an "average" hospital; and (iv) indicators should not necessarily apply to any one specific patient, but rather should pertain to the overall care of patients with AP (11) (see Supplement II, Supplementary Digital Content 1, http://links.lww.com/AJG/A182).

For each proposed indicator, panelists were asked 4 required questions. The first 3 questions were "focusing questions." According to guidance from the Agency for Healthcare Research and Quality (AHRQ), RAM, and similar studies (11,12,18), these focusing questions help ensure that the panelists consider similar issues when assigning their overall ratings to indicators. The responses to these questions were primarily used to facilitate discussion of QIs during round 2. Focusing questions included the following:

1. Scientific evidence: Is the scientific evidence for the proposed QI sufficient? This was rated on a 9-point scale, where 1 = totally disagree and 9 = totally agree.
2. Interpretability: Is the proposed indicator written such that it can be interpreted by clinicians? This was rated on a 9-point scale, where 1 = totally disagree and 9 = totally agree.
3. Bias: To what extent is the indicator subject to bias? For example, some facilities/hospitals may be judged as poor performers on the indicator because they systematically differ from other hospitals in some aspect, such as severity of the case mix, which is not due to poor quality care. This was rated on a 9-point scale, where 1 = not at all biased and 9 = totally biased.

The fourth question asked panelists to rate the validity of the proposed QI:

1. Validity: What is your overall validity rating of the indicator's ability to measure the quality of care and its potential to improve clinical practices (18)? This was rated on a 9-point scale, where 1 = definitely not valid and 9 = definitely valid. Indicators with median ratings between 7 and 9 that meet all criteria for agreement are considered valid (see the Statistical analysis section).

Panelists also had the opportunity to suggest wording changes to improve clarity or increase the potential validity of the QIs and propose new indicators and/or supporting literature.

Round 2: face-to-face meeting of the expert panel

Data from round 1 were analyzed. Panelists met on March 8–9, 2018, in Dallas, TX, for a face-to-face meeting. Each panel member was provided a summary book of their individual ratings and the aggregated round 1 ratings and comments. Panelists were oriented to the meeting objectives and given a brief methodology review, which included how agreement was determined. The panel moderator (R.H.H.) then led the group in discussions of each indicator (by domain) reviewing the aggregated data for scientific evidence, interpretability, bias, and validity. The panel discussed proposed wording changes and options to modify, combine, or eliminate indicators. There was a ≥80% vote required to eliminate an indicator, ultimately classifying it as "not valid." New QIs were also proposed. After each domain was discussed, the panel rated the revised indicators again for validity based on a 9-point scale, where 1 = definitely not valid and 9 = definitely valid.

All panelists in attendance completed an after-meeting evaluation (17) (see Supplement III, Supplementary Digital Content 1, http://links.lww.com/AJG/A182).

Round 3: necessity rating and proposed performance thresholds

Data from round 2 were analyzed, and indicators were categorized as valid or not valid. All panelists were sent *via* email the round 2 results and a Qualtrics survey link with instructions on round 3, rating valid QIs for necessity and proposing performance thresholds.

Necessary indicators are those that identify practices that must exist in every scenario. Not necessary means only that the indicator is not universally required across health care systems (11). Panelists were informed that necessary indicators may be used to detect the underuse or overuse of a procedure or treatment; by hospitals and clinicians to quickly evaluate the quality of their AP programs and focus specifically on interventions or changes needed to fill critical gaps in care; and/or inform which indicators

will be the focus of future research endeavors to develop quality measures from QIs (11). Panelists rated valid indicators for necessity based on a 9-point scale, where 1 = definitely not necessary and 9 = definitely necessary. The final classification of indicators could be (i) valid and necessary, (ii) valid and not necessary, or (iii) not valid.

Performance thresholds reflect the rate at which panelists recommend providers or health care systems (depending on the context of the QI) should fulfill the QIs in clinical practice (17). Most QIs can be applied to individual providers and/or systems. Performance thresholds represented a rate between 0 and 100. Indicators that recommend against a practice have a low median threshold and range, which suggests that the practice be avoided. A low median threshold is considered any rate between 0% and 40%. The suggested performance targets were determined by calculating the median and range (i.e., minimum target to maximum target) proposed by the expert panel.

Evidence summaries and GRADE classification

Expert panel members were informed of the final results and indicator classifications after round 3. They then drafted evidence summaries for their assigned domains and used the Grades of Recommendation Assessment, Development and Evaluation (GRADE) framework to evaluate supporting literature and identify the quality of evidence and strength of recommendation for each indicator (22). The evidence summaries are not exhaustive reviews of the literature. Instead, they are meant to represent an overview of the key concepts related to each care domain and may identify areas that deserve further clarification and/or the need for future research.

Statistical analysis

Validity was classified (i.e., valid or not valid) based on (i) the median rating and (ii) whether panelists agreed, as measured by the amount of dispersion of the ratings. Valid indicators had to have a median rating between 7 and 9 (on a scale of 1–9, where 1 = definitely not valid and 9 = definitely valid) and meet all 3 criteria for statistical agreement (which measure the dispersion of ratings). During round 2, there was a ≥80% vote required to eliminate an indicator, ultimately classifying it as "not valid." Necessary indicators also had to have a median rating between 7 and 9 (on a scale of 1–9, where 1 = definitely not necessary and 9 = definitely necessary) and meet all 3 criteria for statistical agreement.

There is no consensus on the best statistical approach to measure dispersion, and different approaches may lead to different conclusions. To mitigate this issue/minimize variation and increase robustness, we used 3 versions (11): BIOMED classical, *P* value, and interpercentile range (IPR) adjusted for symmetry. The BIOMED classical definition of agreement sets the maximum number of responses that are allowed to fall outside the 3-point region (1–3, 4–6, and 7–9) containing the median to conclude agreement. For our panel sizes in rounds 1 and 3, this was ≤5 responses; for round 2, this was ≤4. The *P* value definition of agreement is simply the result of a binomial hypothesis test that 80% of the ratings are within the 3-point region containing the median. Finally, the interpercentile range adjusted for symmetry (IPRAS), a measure developed by the Carlos III Health Initiative (11), is based on the nonparametric measure of spread, which is the difference between the 70th and 30th percentiles (i.e., IPR). After adjusting for the lack of symmetry in responses, if the resulting IPR is less than the IPRAS, then the conclusion is that there is agreement.

Results of all questions from round 1 through 3 were provided to panelists. After round 1, panelists were provided a summary book of their individual and the aggregated round 1 rating responses and comments. For the focusing questions (scientific evidence, interpretability, and bias), this included (i) the median response, (ii) histogram of ratings, and (iii) the BIOMED classical measure of agreement. For the question of validity, this included (i) the median response, (ii) histogram of ratings, and (iii) 3 measures of agreement (i.e., IPRAS, BIOMED classical, and *P* value). After round 2, panelists were provided (i) median validity response, (ii) the count of responses in each 3-point region, (iii) 3 measures of agreement (i.e., IPRAS, BIOMED classical, and *P* value), and (iv) the classification of indicators (i.e., valid or not valid). After round 3, panelists were provided the (i) median necessity response, (ii) the count of responses in each 3-point region, (iii) 3 measures of agreement (i.e., IPRAS, BIOMED classical, and *P* value), (iv) the final classification of indicators (i.e., valid and necessary, valid and not necessary, or not valid), and (v) the median proposed performance threshold and range.

RESULTS

A 20-member nationally representative expert panel was convened. Nineteen (95%) participated in round 1, 15 (75%) participated in round 2, and 18 (90%) participated in round 3. At the end of round 1, 37 indicators were rated as valid, and 34 were rated as not valid. All indicators (valid and not valid) were discussed during round 2 and left as is or revised (n = 37), combined (resulting in n = 4), or eliminated (n = 25). After round 2, 41 indicators were rated as valid. After round 3, 40 valid indicators were all found to be necessary, and 1 indicator was eliminated from consideration, deeming it not valid. Table 1 shows the results following round 3. See Supplement IV (Supplementary Digital Content 1, http://links.lww.com/AJG/A182) for the list of 26 indicators deemed not valid.

The 40 final QIs were categorized by domain: Diagnosis (3 indicators), Etiology (6 indicators), Initial Assessment and Risk Stratification (3 indicators), Initial Management (3 indicators), ERCP (5 indicators), Nutrition (3 indicators), Pharmacotherapy (4 indicators), Management of Early Complications (5 indicators), Surgery (4 indicators), and Structure of Care (4 indicators) (Table 1).

Tables 2–11 list the QIs per domain including details about the type of QI, median performance target, and the quality of evidence and strength of recommendation of the indicator based on the GRADE classification criteria (22). An evidence summary follows for each AP care domain.

Diagnosis domain—evidence summary

Although severe upper abdominal pain is a principle component of AP, confirmation by objective data is required to ensure an accurate and specific diagnosis. Most commonly, the diagnosis of AP is supported by a 3-fold elevation in serum pancreatic enzymes (amylase and/or lipase) in the setting of characteristic epigastric pain. It is imperative that serum pancreatic enzymes be checked within 24 hours of pain onset; lipase levels tend to remain elevated for a longer period. Serum pancreatic enzymes may even be normal in some cases of AP (e.g., alcohol or hyperlipidemia) (23,24) or abnormal in some patients (e.g., type II diabetes) who are asymptomatic and do not have AP (25). Serum amylase and lipase may be elevated in cases of

Table 1. Valid and necessary AP QIs[a]

No.	QI	Validity and necessity median rating	Suggested performance threshold (range)	Type(s) of measure
Diagnosis domain				
1	IF a patient presents with acute-onset severe upper abdominal pain with epigastric tenderness, THEN AP should be suspected, and serum lipase and/or amylase levels obtained.	9, 9	98 (80–100)	Process
2	IF a patient is suspected to have AP and the serum amylase and/or lipase levels are not diagnostic, THEN cross-sectional imaging (CT or MRI) should be performed to confirm AP and/or exclude an alternate diagnosis.	8, 8	98 (70–100)	Process and appropriateness
3	IF a patient presents with at least 2 of the following 3 conditions, THEN a diagnosis of AP should be made: a. Acute-onset upper abdominal pain with epigastric tenderness b. Serum pancreatic enzymes elevated greater than 3 times the upper limit of normal c. Findings consistent with AP on cross-sectional imaging (CT or MRI)	9, 9	98 (90–100)	Process
Etiology domain				
4	IF a patient is diagnosed with AP, THEN a thorough history including (a) alcohol intake, (b) smoking, and (c) medications should be obtained and documented on presentation.	9, 8.5	(a) 98.5 (75–100) (b) 96.5 (50–100) (c) 98 (75–100)	Process
5	IF a patient is diagnosed with AP, THEN a medical history should be obtained and documented to include (a) previous attacks of acute or chronic pancreatitis and (b) family history of pancreatic disease.	9, 8	(a) 96.5 (80–100) (b) 95 (75–100)	Process
6	IF a patient is diagnosed with AP, THEN (a) serum liver chemistry, (b) triglyceride levels, and (c) serum calcium levels should be obtained on presentation.	9, 8	(a) 98 (90–100) (b) 90 (50–100) (c) 90 (50–100)	Process and efficiency
7	IF a patient is diagnosed with AP and no clear etiology is evident after history, biochemical testing, and transabdominal ultrasound, THEN an elective CECT, EUS, and/or MRI with MRCP should be performed after the acute phase of pancreatitis has resolved.	9, 8	96.5 (75–100)	Process and appropriateness
8	IF a patient is diagnosed with AP, THEN ERCP is not recommended purely for determination of etiology.	9, 9	2 (0–20)	Process and appropriateness

Table 1. (*continued*)

No.	QI	Validity and necessity median rating	Suggested performance threshold (range)	Type(s) of measure
9	IF a patient has recovered from either recurrent mild AP or any AP of more than mild severity and the etiology remains unknown after history, biochemical testing, and cross-sectional imaging, THEN the patient should be referred for an elective outpatient evaluation at a pancreatic center of excellence.	9, 7	77.5 (10–99)	Process
Initial Assessment and Risk Stratification domain				
10	IF a patient is diagnosed with AP, THEN intravascular volume depletion/hemoconcentration (orthostatic vital signs, hematocrit, BUN, and creatinine) should be assessed and documented.	9, 9	98.5 (90–100)	Process
11	IF a patient is diagnosed with AP, THEN indicators for severity (organ failure, SIRS, age, impaired mental status, and pleural effusion) should be assessed and documented on presentation.	9, 9	98 (80–100)	Process
12	IF a patient is diagnosed with AP and has SIRS and/or organ failure, THEN they should be documented to be at risk for severe AP.	9, 8	90 (70–100)	Process
Initial Management domain (baseline–72 hr)				
13	IF a patient is diagnosed with AP, THEN fluid resuscitation should be initiated (with bolus and maintenance) within 2 hr of the time of diagnosis as directed by assessment of intravascular volume/hemoconcentration.	9, 9	96.5 (75–100)	Process and efficiency
14	IF a patient is diagnosed with AP, THEN lactated Ringer solution should be the preferred crystalloid replacement fluid unless contraindicated.	9, 7	80 (50–99)	Process
15	IF a patient is diagnosed with AP, THEN fluid resuscitation should be titrated according to interval assessment of vital signs, urine output, BUN, and hematocrit during the first 48 hr.	8, 8	96.5 (75–100)	Process
ERCP domain				
16	IF a patient has AP with cholangitis, THEN they should undergo ERCP with appropriate endotherapy within 24 hr of diagnosis.	9, 9	95 (50–100)	Process and efficiency

Table 1. (*continued*)

No.	QI	Validity and necessity median rating	Suggested performance threshold (range)	Type(s) of measure
17	IF a patient has biliary pancreatitis and a low probability* of CDL, THEN ERCP is not indicated. *Low probability of CDL: normal LFTs and common bile duct diameter ≤7 mm	9, 9	5 (0–20)	Process and appropriateness
18	IF a patient has biliary pancreatitis and has an intermediate probability* of CDL, THEN adjunctive imaging (EUS/MRCP) or intraoperative cholangiography during cholecystectomy should be performed before discharge. *Intermediate probability of CDL: increased LFTs or CBDS > 7 mm	8.5, 8	90 (50–99)	Process
19	IF a patient has biliary pancreatitis but is not a surgical candidate, THEN ERCP with biliary sphincterotomy and stone extraction (if applicable) should be performed before discharge.	9, 8	90 (30–99)	Process and efficiency
20	IF a patient is diagnosed with biliary pancreatitis and CDL is confirmed, THEN ductal clearance should be achieved before discharge.	9, 9	98 (75–100)	Process and efficiency
Nutrition domain				
21	IF a patient is diagnosed with AP (regardless of severity), THEN enteral feeding is the preferred route of nutrition (over parenteral feeding) unless it is not tolerated or is contraindicated (i.e., bowel obstruction or paralytic ileus).	9, 9	98 (90–100)	Process and appropriateness
22	IF a patient is diagnosed with AP, THEN the preferred choice of enteral feeding is a low-fat solid diet as tolerated.	9, 8	90 (70–99)	Process and appropriateness
23	IF a patient with AP cannot tolerate oral feeding within 72 hr, THEN either NG- or NJ-assisted enteral feeding should be initiated.	9, 8	90 (50–99)	Process and appropriateness
Pharmacotherapy domain				
24	IF a patient is diagnosed with AP, THEN severity of pain should be assessed and managed according to institutional guidelines.	9, 9	95 (70–100)	Process and appropriateness
25	IF a patient is diagnosed with biliary pancreatitis and has evidence of cholangitis, THEN they should be started on appropriate antibiotics.	9, 9	99 (75–100)	Process
26		9, 9	10 (0–50)	Process and appropriateness

Table 1. (*continued*)

No.	QI	Validity and necessity median rating	Suggested performance threshold (range)	Type(s) of measure
	IF a patient is diagnosed with AP, THEN prophylactic antibiotics should not be prescribed.			
27	IF a patient is predicted to have severe AP, THEN probiotic agents should not be prescribed.	9, 8.5	2 (0–40)	Process and appropriateness
Management of Early Complications (72 hr–4 wk)				
28	IF a patient diagnosed with AP fails to improve clinically within 72 hr of hospital admission, THEN CECT or MRI with contrast should be performed unless contraindicated.	9, 8	92.5 (75–100)	Process and efficiency
29	IF a patient has worsening or persistent abdominal distension in association with severe AP, THEN they should be evaluated for possible abdominal compartment syndrome and if confirmed, managed appropriately.	8.5, 8	90 (25–100)	Process
30	IF a patient with necrotizing pancreatitis has characteristic findings of infection on imaging, or clinically deteriorates, THEN infected necrosis should be suspected and appropriate antibiotics prescribed.	9, 9	98 (75–100)	Process
31	IF a patient with necrotizing pancreatitis has suspected infection on appropriate intravenous antibiotics and clinically deteriorates, THEN minimally invasive drainage should be performed.	9, 8.5	95 (75–100)	Process
32	IF a patient with severe AP demonstrates signs of clinically significant hemorrhage, THEN appropriate workup for potential vascular complications (e.g., pseudoaneurysm and/or thrombosis) should be documented.	9, 9	97 (80–100)	Process
Surgery domain				
33	IF a patient has acute biliary pancreatitis, THEN surgery should be consulted to consider cholecystectomy before discharge.	9, 9	98 (79–100)	Process
34	IF a patient has acute biliary pancreatitis complicated by necrosis or peripancreatic fluid collection, THEN cholecystectomy should be	9, 8.5	7.5 (0–40)	Process

Table 1. (*continued*)

No.	QI	Validity and necessity median rating	Suggested performance threshold (range)	Type(s) of measure
	deferred until active inflammation subsides and fluid collection(s) resolve or stabilize.			
35	IF a patient has an asymptomatic pseudocyst(s) and pancreatic and/or extrapancreatic necrosis, THEN drainage interventions should not be performed.	9, 9	5 (0–30)	Process
36	IF a patient has symptomatic necrotizing pancreatitis, THEN open necrosectomy should not be performed as a first-line treatment.	9, 9	5 (0–20)	Process
Structure of Care domain				
37	IF a patient is diagnosed with AP and has the following, THEN the severity should be classified and documented as moderately severe AP: a. Organ failure that resolves within 48 hr (transient organ failure) and/or b. Local or systemic complications without persistent organ failure.	9, 8	92.5 (40–99)	Outcome
38	IF a patient is diagnosed with AP, and has persistent organ failure (>48 hr), THEN the severity should be classified and documented as severe AP.	9, 8.5	98 (40–100)	Outcome
39	IF a patient is diagnosed with severe AP, THEN the patient should be managed in a center with expertise in surgery, pancreaticobiliary endoscopy, interventional radiology, intensive care, and nutrition or transferred to a center that does.	9, 8	90 (70–100)	Structure of care
40	IF an institution manages patients with AP, THEN the hospital should have EUS/ERCP services available, or a transfer agreement with a facility that has those capabilities.	9, 9	98 (70–100)	Structure of care

[a]Valid indicators are defined as those that have the ability to measure the quality of care provided and potential to improve clinical practice. Necessary indicators are those that identify practices that must exist in every scenario, every time. Not necessary means only that the indicator is not absolutely necessary for a quality program or system to exist. Validity and necessity were determined by having a median rating between 7 and 9 and meeting statistical criteria for expert panel agreement (i.e., BIOMED classical, *P* value, and IPRAS).

AP, acute pancreatitis; BUN, blood urea nitrogen; CBDS, common bile duct stones; CDL, choledocholithiasis; CECT, contrast-enhanced computed tomography; CT, computed tomography; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; LFT, liver function test; MRCP, magnetic resonance cholangiopancreatography; NG, nasogastric; NJ, nasojejunal; SIRS, systemic inflammatory response syndrome; QI, quality indicator.

non–pancreatitis-related abdominal pain, particularly in the setting of renal insufficiency (26).

In the presence of abdominal pain and normal serum pancreatic enzymes or elevated enzymes in the absence of abdominal pain, imaging is necessary for the diagnosis of AP. For example, cross-sectional imaging with computed tomography (CT) has been shown to be quite sensitive for both the diagnosis and staging of AP (27). The most widely accepted definition for the diagnosis of AP is the requirement of 2 of 3 of the following criteria (19,28–32):

Table 2. Details of Diagnosis domain QIs

1.1	QI:	IF a patient presents with acute-onset severe upper abdominal pain with epigastric tenderness, THEN AP should be suspected, and serum lipase and/or amylase levels obtained.
	Type of measure:	Process
	Performance target:	98%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong
1.2	QI:	IF a patient is suspected to have AP and the serum amylase and/or lipase levels are not diagnostic, THEN cross-sectional imaging (CT or MRI) should be performed to confirm AP and/or exclude alternate diagnosis.
	Type of measure:	Process
	Performance target:	98%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong
1.3	QI:	IF a patient presents with at least 2 of the following 3 conditions, THEN a diagnosis of AP should be made: a) Acute-onset abdominal pain with epigastric tenderness b) Serum pancreatic enzymes elevated greater than 3 times the upper limit of normal c) Findings consistent with AP on cross-sectional imaging (CT or MRI)
	Type of measure:	Process
	Performance target:	98%
	Quality of evidence:	Moderate
	Strength of recommendation:	Weak

AP, acute pancreatitis; CT, computed tomography; QI, quality indicator.

1. Acute, severe spontaneous pain in the upper abdomen
2. Three-fold elevation of serum pancreatic enzymes (amylase and/or lipase)
3. Cross-sectional imaging (e.g., CT) that reveals signs of AP

See Table 2 for details of QIs in this domain.

Etiology domain—evidence summary

A comprehensive assessment for potential etiology(-ies), including a careful history, physical examination, laboratory testing (liver chemistries, serum calcium, and serum triglycerides), and transabdominal ultrasound, is of paramount importance to guide immediate therapy and/or minimize recurrence. Etiologies that may require immediate etiology-based management include hypertriglyceridemia, biliary pancreatitis with ascending cholangitis, diabetic ketoacidosis, and hypercalcemic AP. Patients with AP are more likely to have recurrent attacks if the underlying etiology is not addressed including (i) counseling for smoking and alcohol cessation; (ii) discontinuation of high-risk medications that may be associated with AP (33); (iii) cholecystectomy or biliary sphincterotomy for gallstone-induced pancreatitis; and (iv) diet and medical intervention for hypertriglyceridemia (34) and management of genetic disorders. Because nearly 20% of individuals presenting with AP will develop 2 or more episodes in follow-up, recognition and intervention on etiologic factors is of utmost importance (35).

A contrast-enhanced cross-sectional imaging study with thin (approximately 1 mm) slice cuts obtained through the pancreas and surrounding structures and/or endoscopic ultrasonography is recommended in patients with AP without obvious etiologic factors. This is especially important in adults older than 40 years presenting with their first episode of AP because the prevalence of occult pancreatic ductal adenocarcinoma or other tumors is relatively higher (36). Diagnostic ERCP is not recommended because the yield is low (<10%) when high-quality cross-sectional imaging does not suggest a periampullary process or other obstructive lesions (e.g., main duct intraductal papillary mucinous neoplasm) and because there is risk of iatrogenic pancreatitis and other adverse events specific to ERCP.

An expanding number of pathogenic genetic susceptibility factors are believed to be common in patients with idiopathic AP and in those with recurrent AP with progression to chronic pancreatitis (37,38). Genetic testing is indicated in cases of idiopathic acute and acute recurrent pancreatitis; this should be coordinated by providers with experience in genetic counseling for pancreatitis risk genes and interpretation of the results. Pretest face-to-face counseling with a genetic counselor should be considered in proportion to the significance of test results, especially if the patient is younger (<35 years old), a family history of cystic fibrosis (39), hereditary pancreatitis (40), or in all patients being tested for pancreatic cancer risk (41). Posttest discussions are directed at helping the patient understand the test results and risk perception and developing a disease management plan with the treating physician.

The management of patients with idiopathic AP remains in evolution. However, because the risk of recurrence is substantial, especially after 2 or more episodes, treating physicians should have a low threshold for referral to a pancreatic center of excellence where advanced imaging, genetic testing, and state-of-the-art management approaches are available (42). See Table 3 for details of QIs in this domain.

Initial Assessment and Risk Stratification domain—evidence summary

Baseline intravascular volume status, assessment for evidence of hemoconcentration, and response to fluid resuscitation may influence both risk stratification and initial medical management (0–72 hours.) in patients with AP. Initial and then interval evaluation of hemodynamics, urine output, and renal function may be helpful to guide appropriate (goal-directed) early volume resuscitation (43) (see Initial Management domain). Volume depletion can be attributed to the attack of pancreatitis as a result of fluid loss (e.g., vomiting) and/or third-space losses. Ongoing volume depletion may promote further organ failure due to systemic hypoperfusion, renal insufficiency, hypoxia, and necrotizing pancreatitis. Persistent elevations of blood urea nitrogen (BUN) during the first 48 hours were reported to be associated with increased mortality (44). Clinical evidence of volume depletion (hemoconcentration) at baseline and during the first 24 hours

Table 3. Details of Etiology domain QIs

2.1	QI:	IF a patient is diagnosed with AP, THEN a thorough history including (a) alcohol intake, (b) smoking, and (c) medications should be obtained and documented on presentation.
	Type of measure:	Process
	Performance target:	(a) 98.5% (b) 96.5% (c) 98%
	Quality of evidence:	High
	Strength of recommendation:	Strong
2.2	QI:	IF a patient is diagnosed with AP, THEN a medical history should be obtained and documented to include (a) previous attacks of acute or chronic pancreatitis and (b) family history of pancreatic disease.
	Type of measure:	Process
	Performance target:	(a) 96.5% (b) 95%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong
2.3	QI:	IF a patient is diagnosed with AP, THEN (a) serum liver chemistry, (b) triglyceride levels, and (c) serum calcium levels should be obtained on presentation.
	Type of measure:	Process and efficiency
	Performance target:	(a) 98% (b) 90% (c) 90%
	Quality of evidence:	Moderate
	Strength of recommendation:	Weak
2.4	QI:	IF a patient is diagnosed with AP and no clear etiology is evident after history, biochemical testing, and transabdominal ultrasound, THEN an elective CECT, EUS, and/or MRI with MRCP should be performed after the acute phase of pancreatitis has resolved.
	Type of measure:	Process and appropriateness
	Performance target:	96.5%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong
2.5	QI:	IF a patient is diagnosed with AP, THEN ERCP is not recommended purely for determination of etiology.
	Type of measure:	Process and appropriateness
	Performance target:	2%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong
2.6	QI:	IF a patient has recovered from either recurrent mild AP or any AP of more than mild severity and the etiology remains unknown after history, biochemical testing, and cross-sectional imaging, THEN the patient should be referred for an elective outpatient evaluation at a pancreatic center of excellence.
	Type of measure:	Process
	Performance target:	77.5%
	Quality of evidence:	Low
	Strength of recommendation:	Weak

AP, acute pancreatitis; CECT, contrast-enhanced computed tomography; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; MRCP, magnetic resonance cholangiopancreatography; QI, quality indicator.

Table 4. Details of Initial Assessment and Risk Stratification domain QIs

3.1	QI:	IF a patient is diagnosed with AP, THEN intravascular volume depletion/ hemoconcentration (orthostatic vital signs, hematocrit, BUN, and creatinine) should be assessed and documented.
	Type of measure:	Process
	Performance target:	98.5%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong
3.2	QI:	IF a patient is diagnosed with AP, THEN indicators for severity (organ failure, SIRS, age, impaired mental status, and pleural effusion) should be assessed and documented on presentation.
	Type of measure:	Process
	Performance target:	98%
	Quality of evidence:	Moderate
	Strength of recommendation:	Weak
3.3	QI:	IF a patient is diagnosed with AP and has SIRS and/or organ failure, THEN they should be documented to be at risk of severe AP.
	Type of measure:	Process
	Performance target:	90%
	Quality of evidence:	Moderate
	Strength of recommendation:	Weak

AP, acute pancreatitis; BUN, blood urea nitrogen; SIRS, systemic inflammatory response syndrome; QI, quality indicator.

might suggest risk of necrotizing pancreatitis (45,46), whereas the lack of hemoconcentration portends a low risk of necrosis (47,48).

Fortunately, most attacks of AP are self-limited and uncomplicated. Meeting criteria (absence of rebound tenderness/ guarding and normal creatinine and hematocrit) for the Harmless Acute Pancreatitis Score is predictive (98%) for having a mild attack (49). Such low-risk patients might be candidates for brief observation and early discharge. Risk stratification is helpful to determine strategies related to early resuscitation and guide triage (intensive care unit [ICU] or ward) decisions. The ability to predict the severity of AP remains challenging, in part because most cases will be mild in severity. Studies comparing the many clinical scoring systems concluded that ability to predict severe AP is limited (50,51). Recognition of patient baseline intrinsic risk factors (e.g., age and comorbidities) and early evidence of clinical deterioration (organ failure and systemic inflammatory response syndrome [SIRS]) despite initial fluid resuscitation seem to be most important (19,52,53). The Bedside Index of Severity in Acute Pancreatitis (BISAP) score (BUN, impaired mental status, SIRS, age >60 years, and pleural effusion) (54) is simple and considered to be an accurate predictor for severe AP (55–57). Organ failure and meeting SIRS criteria are the principle factors associated with severe AP (58,59). It is recommended that patients with hemodynamic instability and/or SIRS (>2 criteria) be admitted to the ICU (19). See Table 4 for details of QIs in this domain.

Initial Management (baseline–72 hours) domain—evidence summary

Early fluid resuscitation with crystalloid solutions remains the cornerstone of initial management for AP, while recognizing that currently available data lack clarity to support a specific strategy (43,60). Intravascular volume depletion in AP occurs for multiple reasons including reduced oral intake, vomiting, insensible losses, and third-space fluid sequestration. The primary goals of initial management are to replete intravascular volume depletion and maintain end-organ perfusion with fluid resuscitation regardless of the clinical setting, severity of the attack, or patient comorbidities.

Adding to the complexity, there is risk of fluid overload due to overly aggressive fluid resuscitation resulting in end-organ damage (e.g., pulmonary edema, hemodilution/tissue hypoxia, and abdominal compartment syndrome). For example, fluid sequestration is associated with worse outcomes (necrosis, fluid collections, and organ failure) in AP (61). However, fluid sequestration may indicate the need for aggressive intravascular fluid resuscitation and is associated with an increased risk of adverse outcomes (e.g., abdominal compartment syndrome). As such, studies regarding fluid resuscitation and AP are potentially subject to reverse causation bias whereby the outcome (fluid sequestration) precedes the intervention (intravenous fluids [IVFs]) (62).

Table 5. Details of Initial Management (baseline–72 hours) domain QIs

4.1	QI:	IF a patient is diagnosed with AP, THEN fluid resuscitation should be initiated (with bolus and maintenance) within 2 hr of the time of diagnosis as directed by assessment of intravascular volume/ hemoconcentration.
	Type of measure:	Process and efficiency
	Performance target:	96.5%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong
4.2	QI:	IF a patient is diagnosed with AP, THEN lactated Ringer solution should be the preferred crystalloid replacement fluid unless contraindicated.
	Type of measure:	Process
	Performance target:	80%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong
4.3	QI:	IF a patient is diagnosed with AP, THEN fluid resuscitation should be titrated according to interval assessment of vital signs, urine output, BUN, and hematocrit during the first 48 hr.
	Type of measure:	Process
	Performance target:	96.5%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong

AP, acute pancreatitis; BUN, blood urea nitrogen; QI, quality indicator.

Table 6. Details of ERCP domain QIs

5.1	QI:	IF a patient has AP with cholangitis, THEN they should undergo ERCP with appropriate endotherapy within 24 hr of diagnosis.
	Type of measure:	Process and efficiency
	Performance target:	95%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong
5.2	QI:	IF a patient has biliary pancreatitis and a low probability* of CDL, THEN ERCP is not indicated. *Low probability of CDL: normal LFTs and common bile duct diameter ≤7 mm
	Type of measure:	Process and appropriateness
	Performance target:	5%
	Quality of evidence:	High
	Strength of recommendation:	Strong
5.3	QI:	IF a patient has biliary pancreatitis and has an intermediate probability* of CDL, THEN adjunctive imaging (EUS/MRCP) or intraoperative cholangiography during cholecystectomy should be performed before discharge. *Intermediate probability of CDL: increased LFTs or CBDS >7 mm
	Type of measure:	Process
	Performance target:	90%
	Quality of evidence:	High
	Strength of recommendation:	Strong
5.4	QI:	IF a patient has biliary pancreatitis but is not a surgical candidate, THEN ERCP with biliary sphincterotomy and stone extraction (if applicable) should be performed before discharge.
	Type of measure:	Process and efficiency
	Performance target:	90%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong
5.5	QI:	IF a patient is diagnosed with biliary pancreatitis and CDL is confirmed, THEN ductal clearance should be achieved before discharge.
	Type of measure:	Process and efficiency
	Performance target:	98%
	Quality of evidence:	High
	Strength of recommendation:	Strong

AP, acute pancreatitis; CBDS, common bile duct stones; CDL, choledocholithiasis; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; MRCP, magnetic resonance cholangiopancreatography; LFT, liver function test; QI, quality indicator.

Table 7. Details of Nutrition domain QIs

6.1	QI:	IF a patient is diagnosed with AP [regardless of severity], THEN enteral feeding is the preferred route of nutrition (over parenteral feeding) unless it is not tolerated or is contraindicated (i.e., bowel obstruction or paralytic ileus).
	Type of measure:	Process and appropriateness
	Performance target:	98%
	Quality of evidence:	High
	Strength of recommendation:	Strong
6.2	QI:	IF a patient is diagnosed with AP, THEN the preferred choice of enteral feeding is a low-fat solid diet as tolerated.
	Type of measure:	Process and appropriateness
	Performance target:	90%
	Quality of evidence:	High
	Strength of recommendation:	Strong
6.3	QI:	IF a patient with AP cannot tolerate oral feeding within 72 hr, THEN either NG- or NJ-assisted enteral feeding should be initiated.
	Type of measure:	Process and appropriateness
	Performance target:	90%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong

AP, acute pancreatitis; NG, nasogastric; NJ, nasojejunal; QI, quality indicator.

It is challenging to draw firm conclusions from studies of fluid resuscitation in patients with AP because results are often divergent. For example, 1 retrospective cohort study reported that early aggressive fluid resuscitation was associated with improved clinical outcomes (63), whereas another concluded that increased IVFs were associated with adverse outcomes (64). Two prospective studies have also suggested worse outcomes with early aggressive IVF resuscitation (65,66). However, another prospective study reported that early aggressive fluid resuscitation was beneficial even in patients predicted to have mild AP (67).

Although most practitioners and experts can agree that IVF resuscitation is important, several important questions are relevant: (i) What is the optimal initial strategy for resuscitation in terms of bolus and rate of fluid? (ii) How should the response to resuscitation efforts in terms of markers, frequency, and duration be monitored? and (iii) What type of IVFs should be administered?

Limited data suggest that there is an early therapeutic window in AP during which aggressive fluid resuscitation in the emergency department (62) and/or within the first 24 hours of presentation (68–70) can result in meaningfully improved clinical outcomes. Thereafter, a reactive (goal-directed) rather than dogmatic strategy to manage ongoing resuscitation efforts should be adopted based on patient responsiveness to hydration and especially in severe AP (43). It is recommended that monitoring physiologic (mean arterial

Table 8. Details of Pharmacotherapy domain QIs

7.1	QI:	IF a patient is diagnosed with AP, THEN severity of pain should be assessed and managed according to institutional guidelines.
	Type of measure:	Process and appropriateness
	Performance target:	95%
	Quality of evidence:	Low
	Strength of recommendation:	Weak
7.2	QI:	IF a patient is diagnosed with biliary pancreatitis and has evidence of cholangitis, THEN they should be started on appropriate antibiotics.
	Type of measure:	Process
	Performance target:	99%
	Quality of evidence:	Low
	Strength of recommendation:	Weak
7.3	QI:	IF a patient is diagnosed with AP, THEN prophylactic antibiotics should not be prescribed.
	Type of measure:	Process and appropriateness
	Performance target:	10%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong
7.4	QI:	IF a patient is predicted to have severe AP, THEN probiotic agents should not be prescribed.
	Type of measure:	Process and appropriateness
	Performance target:	2%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong

AP, acute pancreatitis; QI, quality indicator.

pressure and urine output) and laboratory parameters (BUN and HCT) over the first 48 hours should guide decisions regarding fluid resuscitation (71). Lactated Ringer solution is the preferred fluid for resuscitation in AP. Compared with normal saline, the anti-inflammatory effect of lactated Ringer solution has been associated with reduced SIRS and CRP levels (72–74).

Current recommendations for fluid resuscitation are based on the sparse body of evidence derived from expert opinion, translational trials, and inconsistent retrospective and prospective clinical studies. Thus, further high-quality prospective trials are needed to further clarify the best strategy for initial hydration, type of fluid, and methods for monitoring resuscitation efforts. See Table 5 for details of QIs in this domain.

ERCP domain—evidence summary

Cholangitis is an uncommon but potentially life-threatening complication of biliary pancreatitis. In most patients, intravenous antibiotics alone will be effective, and thus, ERCP for definitive endoscopic therapy can be deferred for at least 24 hours (75,76). However, for patients with severe disease manifested by hypotension and/or altered mental status, urgent ERCP is recommended following optimization of medical status (77).

Table 9. Details of Management of Early Complications domain QIs

8.1	QI:	IF a patient diagnosed with AP fails to improve clinically within 72 hr of hospital admission, THEN CECT or MRI with contrast should be performed unless contraindicated.
	Type of measure:	Process and efficiency
	Performance target:	92.5%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong
8.2	QI:	IF a patient has worsening or persistent abdominal distension in association with severe AP, THEN they should be evaluated for possible abdominal compartment syndrome and if confirmed, managed appropriately.
	Type of measure:	Process
	Performance target:	90%
	Quality of evidence:	Low
	Strength of recommendation:	Strong
8.3	QI:	IF a patient with necrotizing pancreatitis has characteristic findings of infection on imaging, or clinically deteriorates, THEN infected necrosis should be suspected and appropriate antibiotics prescribed.
	Type of measure:	Process
	Performance target:	98%
	Quality of evidence:	Low
	Strength of recommendation:	Strong
8.4	QI:	IF a patient with necrotizing pancreatitis has suspected infection on appropriate intravenous antibiotics and clinically deteriorates, THEN minimally invasive drainage should be performed.
	Type of measure:	Process
	Performance target:	95%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong
8.5	QI:	IF a patient with severe AP demonstrates signs of clinically significant hemorrhage, THEN appropriate workup for potential vascular complications (e.g., pseudoaneurysm and/or thrombosis) should be documented.
	Type of measure:	Process
	Performance target:	97%
	Quality of evidence:	Low
	Strength of recommendation:	Weak

AP, acute pancreatitis; CECT, contrast-enhanced computed tomography; QI, quality indicator.

Biliary pancreatitis is typically caused as a result of small stones or sludge passing through the ampulla spontaneously; therefore, persistent common bile duct stones are infrequent and

Table 10. Details of Surgery domain QIs

9.1	QI:	IF a patient has acute biliary pancreatitis, THEN surgery should be consulted to consider cholecystectomy before discharge.
	Type of measure:	Process
	Performance target:	98%
	Quality of evidence:	High
	Strength of recommendation:	Strong
9.2	QI:	IF a patient has acute biliary pancreatitis complicated by necrosis or peripancreatic fluid collection, THEN cholecystectomy should be deferred until active inflammation subsides and fluid collection(s) resolve or stabilize.
	Type of measure:	Process
	Performance target:	7.5%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong
9.3	QI:	IF a patient has an asymptomatic pseudocyst(s) and pancreatic and/or extrapancreatic necrosis, THEN drainage interventions should not be performed.
	Type of measure:	Process
	Performance target:	5%
	Quality of evidence:	Moderate
	Strength of recommendation:	Strong
9.4	QI:	IF a patient has symptomatic necrotizing pancreatitis, THEN open necrosectomy should not be performed as a first-line treatment.
	Type of measure:	Process
	Performance target:	5%
	Quality of evidence:	High
	Strength of recommendation:	Strong

QI, quality indicator.

Table 11. Details of Structure of Care domain QIs

10.1	QI:	IF a patient is diagnosed with AP and has the following, THEN the severity should be classified and documented as moderately severe AP: a. Organ failure that resolves within 48 hr (transient organ failure) and/or b. Local or systemic complications without persistent organ failure.
	Type of measure:	Outcome
	Performance target:	92.5%
	Quality of evidence:	Moderate
	Strength of recommendation:	Weak
10.2	QI:	IF a patient is diagnosed with AP, and has persistent organ failure (>48 hr), THEN the severity should be classified and documented as severe AP.
	Type of measure:	Outcome
	Performance target:	98%
	Quality of evidence:	Moderate
	Strength of recommendation:	Weak
10.3	QI:	IF a patient is diagnosed with severe AP, THEN the patient should be managed in a center with expertise in surgery, pancreaticobiliary endoscopy, interventional radiology, intensive care, and nutrition or transferred to a center that does.
	Type of measure:	Structure of care
	Performance target:	90%
	Quality of evidence:	Low
	Strength of recommendation:	Weak
10.4	QI:	IF an institution manages patients with AP, THEN the hospital should have EUS/ERCP services available, or a transfer agreement with a facility that has those capabilities.
	Type of measure:	Structure of care
	Performance target:	98%
	Quality of evidence:	Moderate
	Strength of recommendation:	Weak

AP, acute pancreatitis; EUS, endoscopic ultrasound; ERCP, endoscopic retrograde cholangiopancreatography; QI, quality indicator.

routine ERCP not indicated (78,79). Elective ERCP in the setting of biliary pancreatitis may be indicated, however, based on the likelihood of common bile duct stones as assessed by liver test abnormalities, bile duct dilation, and the presence or absence of an intact gallbladder. ERCP should be performed for patients with biliary pancreatitis in whom common bile duct stones are identified on transabdominal ultrasound, cross-sectional imaging, and/or on intraoperative cholangiography. The need and timing for ERCP in patients with an intermediate probability of common bile duct stones as suggested by liver test abnormalities or by bile duct dilation alone depend on preoperative ancillary imaging and/or intraoperative cholangiography. If intraoperative cholangiography is unavailable or the diagnosis is still uncertain before surgery, preoperative endoscopic ultrasonography or magnetic resonance cholangiopancreatography is appropriate in centers with low ERCP expertise (80). Ancillary imaging is not required in patients with a low probability of bile duct stones (minimal liver test abnormalities and absence of bile duct dilation) before cholecystectomy.

Elective ERCP in the setting of biliary pancreatitis may also be required for the management of complications and/or to prevent further attacks (81). For patients with bile duct stones in whom laparoscopic cholecystectomy is contraindicated based on comorbidity, ERCP and biliary sphincterotomy should be performed preferably during the hospitalization to decrease the subsequent risks of symptomatic common bile duct stones. See Table 6 for details of QIs in this domain.

Nutrition domain—evidence summary

Nutrition support *via* oral or enteric (either with nasogastric [NG] or nasojejunal [NJ]) route is recommended as early as possible in patients with AP (19). Enteral nutritional within 48–72 hours is preferred over the parenteral route as long as there are no contraindications for oral feeding (tolerance, abdominal pain, and ileus) or tube placement (bowel obstruction or other complications). Total parenteral nutrition should be considered only if enteral feeding is not tolerated or cannot be administered. Both oral and enteral feeding have been shown to be more cost-effective and superior to total parenteral nutrition in preventing pancreatic infectious complications and sepsis-related sequelae in AP (82). Oral and enteral nutrition prevents intestinal mucosal atrophy and preserves the gut mucosal barrier, preventing bacterial translocation across the gut.

In mild AP, a diet should be started immediately once the patient's symptoms have improved to the point where they can tolerate oral intake. With initiation of a low fat, a solid diet is as safe and effective as starting clear liquids (83–86). Oral feeding with a low-fat solid diet may accelerate recovery without increased risk of adverse gastrointestinal events (e.g., pain with refeeding) and may result in shorter inpatient length of stay (87).

In severe AP, early (within 48 hours of admit) enteral nutrition has been associated with decreased rates of pancreatic infectious complications, organ failure, mortality, and length of stay (88–90). Contrast-enhanced CT in these patients may be helpful to confirm diagnosis, guide management of complications, and rule out contraindications for tube placement. Enteral feeding *via* NG route has been shown to be as safe and effective as NJ feeding in patients with AP. Meta-analyses suggest that there are no significant differences in mortality, infectious-related complications, diarrhea, and pain associated with feeding, or length of stay between the NG or NJ routes of enteral nutrition (91,92). See Table 7 for details of QIs in this domain.

Pharmacotherapy domain—evidence summary

Severe abdominal pain is the cardinal symptom of AP and pain relief should be a clinical priority. A critical step to providing adequate pain control is pain assessment (93). This may require focused training of medical personnel in pain assessment and implementation of an institutional policy on pain management. Parenteral analgesics are usually required for adequate pain control in patients with AP. Inadequate pain management can cause adverse physical and psychological effects on individual patients and their family members.

Extrapancreatic infections are a major cause of morbidity and mortality in patients with AP. If there is clinical evidence of cholangitis or an alternate source of infection, appropriate antibiotics should be promptly initiated. However, routine prophylactic use of antibiotics in severe AP is not recommended (94). There is concern that the use of prophylactic broad-spectrum antibiotics could lead to fungal superinfections. Prophylactic use of antibiotics failed to reduce risk of infection in 2 double-blind prospective controlled trials (95,96). Meta-analyses concluded that prophylactic antibiotics do not reduce infected necrosis and/or mortality (97,98). Prophylactic antibiotics should be considered, however, in the management of severe AP in specific patients, such as those with suspected infected necrosis and associated clinical deterioration.

Infection of pancreatic/peripancreatic necrosis is believed to occur from translocation of intestinal bacterial flora. In an effort to prevent the bacterial translocation, probiotics have been considered but are not recommended. A randomized double-blind placebo-controlled trial reported increased mortality associated with the use of probiotics in severe AP (99). A meta-analysis of 4 studies concluded that probiotics do not reduce the risk of infected necrosis (100). See Table 8 for details of QIs in this domain.

Management of Early Complications (72 hours–4 weeks) domain—evidence summary

Early complications of AP cause significant morbidity and potential mortality if not recognized quickly and managed appropriately. If patients are hospitalized for >72 hours, CT scan or MRI should be performed to evaluate for complications in those who fail to improve clinically (e.g., increased pain requirements, inability to tolerate oral intake, and persistence of SIRS) and/or in those who develop signs of worsening severity such as organ failure (19,101). Necrotizing pancreatitis, thrombosis, or pseudoaneurysms can be assessed with CT, and this modality is preferred over the use of MRI (102). In patients with contraindications to CT, such as contrast allergy or elevated creatinine, MRI should be performed.

For patients with AP and persistent severe abdominal distension, often in association with hypotension, abdominal compartment syndrome should be considered, and appropriate diagnostic evaluation and treatment should be initiated (103,104). Initial therapy for suspected abdominal compartment syndrome should be conservative. There are limited data suggesting benefit of continuous veno-venous hemofiltration (105,106).

Infected necrosis can be one of the most devastating early complications of AP and must be recognized and treated appropriately (94). Empiric broad-spectrum antibiotics should be initiated in febrile patients in whom infected necrosis is suspected (necrotizing pancreatitis documented on cross-sectional imaging without another source of infection). If a patient with suspected infected necrosis has been treated with appropriate antibiotics for 48–72 hours and has persistence of fever and/or sign of clinical deterioration, then minimally invasive drainage should be initiated (107,108). The choice of drainage modality (e.g., percutaneous, endoscopic and/or laparoscopic) should be guided by local expertise.

Vascular complications of AP such as pseudoaneurysm or thrombosis can lead to serious consequences including bleeding and intestinal ischemia (109). In patients who develop signs of hemorrhage, contrast-enhanced CT should be performed immediately to rule out vascular complications. Patients with evidence of bleeding should be considered for evaluation and therapy by interventional radiology. Anticoagulation for thrombosis (i.e., of the splenic or portal vein) is controversial; the general consensus is to consider anticoagulation for portal or mesenteric vein, but not splenic vein thrombosis, if acute (no collaterals), and there are clinically significant effects such as development of portal hypertension and/or intestinal ischemia. See Table 9 for details of QIs in this domain.

Surgery domain—evidence summary

Surgical interventions for AP and early complications include cholecystectomy, drainage of fluid collections/necrosectomy, and decompressive procedures for abdominal compartment syndrome. Decisions regarding timings for these interventions should take into account etiology and severity of AP and patient comorbidities. Other than elective cholecystectomy, surgical intervention should only be undertaken when all other measures

have failed or the patient has a rapidly declining clinical course associated with abdominal compartment syndrome or overwhelming sepsis.

In patients with uncomplicated, mild to moderate acute gallstone pancreatitis, outcomes are improved when cholecystectomy is performed during the index admission (110–114). Readmissions are decreased when cholecystectomy is performed within 4 weeks from the index episode of acute gallstone pancreatitis (115). Delayed cholecystectomy should be reserved for patients with severe pancreatitis associated with fluid collections/necrosis (116). Cholecystectomy may also be considered in hopes of decreasing recurrent attacks in patients with idiopathic pancreatitis (117,118).

Asymptomatic pseudocysts and pancreatic collections can resolve spontaneously and should not undergo operative intervention due to potential complications. For management of complicated necrotizing pancreatitis, minimally invasive percutaneous, endoscopic, and/or laparoscopic procedures are preferred (108,119–121).

Patients with suspected abdominal compartment syndrome should be managed in a multidisciplinary fashion that includes nephrology, interventional radiology, and surgical consultation. Firm conclusions regarding the need and timing for interventional therapy remain unclear (104). When indicated, there are a variety of surgical approaches that can be implemented (122). See Table 10 for details of QIs in this domain.

Structure of Care domain—evidence summary

To objectively measure the quality of care of AP and to assist in accuracy of patient recruitment into clinical trials, a scheme for risk adjustment of outcomes is warranted (123). Early and persistent organ failure is a reliable predictor of poor outcome and mortality (26). Mortality differs significantly between patients classified as having moderately severe AP and severe AP (52). Even local or systemic complications without persistent organ failure can impact outcomes, so they should be routinely considered in classifying patients with AP into risk categories (19,26). Standard classification and documentation can assist in assessing expectations of outcomes and gaps in meeting expectations.

Patients admitted to medical centers with high-volume admissions for AP have better outcomes (e.g., length of stay) compared with low-volume centers (124,125). For those patients with severe AP, an experienced multidisciplinary team plays a role in development and execution of a therapeutic plan. For example, >90% of patients with severe AP will require intensive care stay and nutritional support (126). Patients with necrotizing pancreatitis may require all components of a team consisting of surgery, pancreaticobiliary endoscopy, interventional radiology, intensive care, and appropriate nutritional support (127).

Regarding specialized care, patients with AP should have readily available access to EUS and ERCP expertise. For example, a decrease in mortality of patients with biliary pancreatitis was associated with centers having higher volume ERCP, less diagnostic ERCP, and less unsuccessful ERCP (128). For this reason, hospitals treating AP should be able to provide these services without encountering delays in obtaining care from such specialists. See Table 11 for details of QIs in this domain.

DISCUSSION

Clinical practice guidelines are developed with the intention to summarize standards of care and inform treating providers in an effort to improve patient safety and quality of care (129). The notion of having too many guidelines for AP was raised 10 years ago (130). Since then, at least 10 additional AP consensus statements/guidelines have been published (19,29,43,94,131–136). Having multiple guidelines is likely to generate confusion and reduce adherence to guideline-based practice (137). There are also a number of limitations associated with guidelines (138) including variable quality according to endorsements and multidisciplinary influence (9), being derived without a clear grading of quality of evidence (139), and being subject to risk of expert bias (140).

A literature search in 2016 revealed that the groundwork for identification and development of QIs for AP management had been initiated (141), yet the formal evaluation and validation of indicators had not been performed. Validated QIs are developed with scientific rigor in a transparent process. A modified version of the RAM was used, a highly used and scientifically rigorous statistical methodology. This was a Delphi process designed to combine scientific evidence and expert opinion to achieve group consensus (convergence of opinion). In reiterative rounds, the proposed QIs were rephrased for clarity or eliminated from consideration. This resulted in a set of QIs with face, construct, and predictive validity (7), for which the panelists set adherence thresholds. Caregivers, patients, payors, regulators, and administrators can use QIs to provide trusted data for determining priorities, making judgments, and benchmarking for accountability and quality improvement (142). Validated QIs are not recommendations (i.e., Clinical Practice Guidelines); instead, they represent desired standards of care. To identify the potentially most impactful indicators, clinicians and organizations may find it useful to focus on QIs that have GRADE classifications with moderate to high quality of evidence corresponding with a strong strength of recommendation. Implementation and monitoring of clinical care pathways in patients with AP have been associated with improved clinical outcomes (143,144).

Quality medical care is difficult to define, particularly for complex conditions such as AP that has a variety of causes, variable course, and potential for devastating outcomes that may require a multidisciplinary approach. High-quality management has been defined as the degree to which health care services both (i) increase the likelihood of desired health outcomes and (ii) are consistent with current professional knowledge (145). A model for the integration of quality into the cycle of therapeutic development has been described to define the development of professional knowledge (146). It starts with concepts that evolve from clinical observations, then to clinical research, from which that with the highest-level evidence, clinical practice guidelines are developed. QIs are specific recommendations that are to be applied in defined clinical circumstances.

The work described herein is part of a project that builds on itself. The next step would involve identifying QIs, which are measurable, and developing those into "performance/quality measures." Performance measures can be further specified (with inclusion/exclusion criteria) and evaluated using risk adjustment to understand their relationships to patient perspectives (e.g., satisfaction) and patient outcomes (e.g., mortality) (12). Linking measured performance with better outcomes closes the circle. A registry study would be required to retrospectively or prospectively obtain clinical data related to performance measures. After statistical analyses, those found to be significant with strong supporting evidence could be submitted to national benchmark organizations such as the National Quality Forum for endorsement. Organizations like the National Quality Forum require the

information obtained in the first phase (i.e., expert panel ratings, performance thresholds, literature, and GRADE classifications) combined with statistical evidence to gauge the suitability of quality measures for endorsement (13). For more than 50 years, clinical outcomes have remained the principle validation of the effectiveness and quality of medical care (147).

The principle weakness of this initiative pertains to the fact that results of this study are time limited and lack firm recommendations in some clinical domains. It is important to recognize that validated QIs are based on currently available evidence, some of which is expert opinion only. There is potential for expert bias if experts are using their own opinions as the basis of their recommendations. We minimized this risk by grading expert opinion sources as weak recommendations (20). Furthermore, each indicator was evaluated using the GRADE classification (22).

Evaluation of clinical practice guidelines for AP has shown areas of clear agreement but also aspects that reflect knowledge gaps (148). Randomized controlled trials in AP have yielded a number of important answers to clinical questions (94). The process of validating QIs in AP has exposed the areas of pancreatitis care (e.g., fluid resuscitation) that need further high-quality studies.

The strengths of this quality initiative are several, mostly related to the rigorous methodology as outlined above. To minimize expert bias, a qualified library and research staff conducted the literature search and initial grading of strength of evidence. Furthermore, our multidisciplinary expert panel achieved group consensus. The Institute of Medicine declared that effective medical care is one of the 6 aims of quality. Requisites of effective medical care include (i) avoidance of overuse, underuse, and misuse; (ii) evidence-based practice; and (iii) required monitoring to assess performance (149). The development of the set of validated QIs from this study will enable hospitals and providers to monitor and achieve effective medical care for the management of AP.

ACKNOWLEDGMENTS

The American College of Gastroenterology endorses this document and the quality indicators contained therein.

CONFLICTS OF INTEREST

Guarantor of the article: Paul Tarnasky, MD, FACG, Chair, American College of Gastroenterology and ACG Institute's Acute Pancreatitis Task Force on Quality, accepts full responsibility for the conduct of the study.

Specific author contributions: E.V., P.K., H.O., and P.T. planned and conducted the study, collected and interpreted data, and drafted the manuscript. L.C., D.C., G.A.C., R.D., M.F., T.B.G., R.H.H., R.K., S.J.P., G.I.P., A.R., A.S., S.V., S.S.V., W.W., C.M.W., D.C.W., B.U.W., D.Y., A.E., S.H., S.R., R.R., T.Y., and M.R.B. participated in the study and/or drafted the manuscript. All authors have approved the final draft submitted.

Financial support: The ACG Institute for Clinical Research & Education provided funding for this study, but the work was conducted independently. No writing assistance was provided for this manuscript.

Potential competing interests: D.C.W. serves as a consultant for AbbVie, Regeneron, and Ariel Precision Medicine; received research support from Regeneron and Shire; cofounded and may have equity in Ariel Precision Medicine; is a board member of the National Pancreas Foundation and Ariel Precision Medicine; and is Editor-in-Chief, *Clinical and Translational Gastroenterology* and Pancreas Section Editor, *UpToDate*. All other authors disclosed no financial relationships relevant to this publication. This work was presented in abstract form (oral presentation) at the 2018 Annual ACG Meeting in Philadelphia, PA.

Study Highlights

WHAT IS KNOWN

- ✓ Detailed recommendations and guidelines for AP management currently exist. However, QIs serve a different purpose: to measure performance in health care.
- ✓ Hospitals and providers managing patients with known or suspected AP should ensure that patients receive high-quality care and desired outcomes according to current evidence-based best practices.
- ✓ The burden of pancreatic disorders is expected to rise over time, and the future of health care requires tracking quality.

WHAT IS NEW HERE

- ✓ A multidisciplinary expert panel composed of physicians (gastroenterologists, hospitalists, and surgeons) who are acknowledged leaders in their specialty and who represent geographic and practice setting diversity was convened.
- ✓ This physician-led initiative formally developed 40 QIs and performance threshold targets for AP management across 10 different domains outlining the plan of care for a patient with typical AP from diagnosis to disposition.
- ✓ These domains included Diagnosis, Etiology, Initial Assessment and Risk Stratification, Initial Management (baseline–72 hours.), ERCP, Nutrition, Pharmacotherapy, Management of Early Complications (72 hours–4 weeks), Surgery, and Structure of Care. The Structure of Care domain reflected the resources, infrastructure, and policies that a hospital or organization would need to have in place to have a quality program.
- ✓ The development of the set of validated QIs from this study will enable hospitals and providers to monitor and achieve effective medical care for the management of AP.

REFERENCES

1. Yadav D, Lowenfels AB. The epidemiology of pancreatitis and pancreatic cancer. Gastroenterology 2013;144:1252–61.
2. Munigala S, Yadav D. Case-fatality from acute pancreatitis is decreasing but its population mortality shows little change. Pancreatology 2016;16:542–50.
3. Peery AF, Crockett SD, Murphy C, et al. Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: Update 2018. Gastroenterology 2019;156:254–272.
4. Singh VK, Bollen TL, Wu BU, et al. An assessment of the severity of interstitial pancreatitis. Clin Gastroenterol Hepatol 2011;9:1098–103.
5. van Santvoort HC, Bakker OJ, Bollen TL, et al. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. Gastroenterology 2011;141:1254–63.
6. Machicado JD, Gougol A, Stello K, et al. Acute pancreatitis has a long-term deleterious effect on physical health related quality of life. Clin Gastroenterol Hepatol 2017;15:1435–43 e2.
7. Bilimoria KY, Bentrem DJ, Lillemoe KD, et al. Assessment of pancreatic cancer care in the United States based on formally developed quality indicators. J Natl Cancer Inst 2009;101:848–59.
8. Mainz J. Defining and classifying clinical indicators for quality improvement. Int J Qual Health Care 2003;15:523–30.
9. Loveday BP, Srinivasa S, Vather R, et al. High quantity and variable quality of guidelines for acute pancreatitis: A systematic review. Am J Gastroenterol 2010;105:1466–76.

10. Medicine Io. Clinical Practice Guidelines. National Academy Press: Washington, DC, 1990.
11. Fitch K, Bernstein SJ, Aguilar MD, et al. The RAND/UCLA Appropriateness Method User's Manual. RAND: Santa Monica, CA, 2001.
12. Agency for Healthcare, Research, and Quality. Center for Health Policy/Center for Primary Care and Outcomes Research & Battelle Memorial Institute. Quality Indicator Measure Development, Implementation, Maintenance, and Retirement. Battelle: Rockville, MD, May 2011.
13. NQF Measure Evaluation Criteria and Guidance for Evaluating Measures for Endorsement. (http://www.qualityforum.org/Measuring_Performance/Submitting_Standards/2015_Measure_Evaluation_Criteria.aspx) (2015). Accessed on December 12, 2016.
14. PCPI. American Medical Association Physician Consortium for Performance Improvement. (https://www.thepcpi.org/default.aspx) (2018). Accessed on July 9, 2018.
15. Yadlapati R, Gawron AJ, Bilimoria K, et al. Development of quality measures for the care of patients with gastroesophageal reflux disease. Clin Gastroenterol Hepatol 2015;13:874–83.e2.
16. Yadlapati R, Gawron AJ, Keswani RN, et al. Identification of quality measures for performance of and interpretation of data from esophageal manometry. Clin Gastroenterol Hepatol 2016;14:526–34.e1.
17. Wani S, Muthusamy VR, Shaheen NJ, et al. Development of quality indicators for endoscopic eradication therapies in Barrett's esophagus: The TREAT-BE (treatment with resection and endoscopic Ablation techniques for Barrett's esophagus) consortium. Gastrointest Endosc 2017;86:1–17.e3.
18. Wang X, Su S, Li S, et al. Development of quality indicators for non-small cell lung cancer care: A first step toward assessing and improving quality of cancer care in China. BMC Cancer 2017;17:603.
19. Tenner S, Baillie J, DeWitt J, et al. American College of Gastroenterology guideline: Management of acute pancreatitis. Am J Gastroenterol 2013;108:1400–15.
20. Rizk MK, Sawhney MS, Cohen J, et al. Quality indicators common to all GI endoscopic procedures. Am J Gastroenterol 2015;110:48–59.
21. Adler DG, Lieb JG II, Cohen J, et al. Quality indicators for ERCP. Am J Gastroenterol 2015;110:91–101.
22. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924–6.
23. Clavien PA, Robert J, Meyer P, et al. Acute pancreatitis and normoamylasemia. Not an uncommon combination. Ann Surg 1989;210:614–20.
24. Shah AM, Eddi R, Kothari ST, et al. Acute pancreatitis with normal serum lipase: A case series. JOP 2010;11:369–72.
25. Steinberg WM, Nauck MA, Zinman B, et al. LEADER 3–lipase and amylase activity in subjects with type 2 diabetes: Baseline data from over 9000 subjects in the LEADER trial. Pancreas 2014;43:1223–31.
26. Forsmark CE, Baillie J; AGA Institute Clinical Practice and Economics Committee; et al. AGA Institute technical review on acute pancreatitis. Gastroenterology 2007;132:2022–44.
27. Chatzicostas C, Roussomoustakaki M, Vardas E, et al. Balthazar computed tomography severity index is superior to Ranson criteria and APACHE II and III scoring systems in predicting acute pancreatitis outcome. J Clin Gastroenterol 2003;36:253–60.
28. Sunamura M, Lozonschi L, Takeda K, et al. Criteria for diagnosis of acute pancreatitis in Japan and clinical implications. Pancreas 1998;16:243–9.
29. Working Group IAPAPAAPG. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology 2013;13:e1–15.
30. Mayumi T, Takada T, Kawarada Y, et al. Management strategy for acute pancreatitis in the JPN Guidelines. J Hepatobiliary Pancreat Surg 2006;13:61–7.
31. Banks PA, Freeman ML. Practice guidelines in acute pancreatitis. Am J Gastroenterol 2006;101:2379–400.
32. Working Party of the British Society of Gastroenterology; Association of Surgeons of Great Britain and Ireland; Pancreatic Society of Great Britain and Ireland; Association of Upper GI Surgeons of Great Britain and Ireland. UK guidelines for the management of acute pancreatitis. Gut 2005;54(Suppl 3):iii1–9.
33. Badalov N, Baradarian R, Iswara K, et al. Drug-induced acute pancreatitis: An evidence-based review. Clin Gastroenterol Hepatol 2007;5:648–4; quiz 644.
34. Pedersen SB, Langsted A, Nordestgaard BG. Nonfasting mild-to-moderate hypertriglyceridemia and risk of acute pancreatitis. JAMA Intern Med 2016;176:1834–42.
35. Ahmed Ali U, Issa Y, Hagenaars JC, et al. Risk of recurrent pancreatitis and progression to chronic pancreatitis after a first episode of acute pancreatitis. Clin Gastroenterol Hepatol 2016;14:738–46.
36. Cote GA, Xu H, Easler JJ, et al. Informative patterns of health-care utilization prior to the diagnosis of pancreatic ductal adenocarcinoma. Am J Epidemiol 2017;186:944–51.
37. Giefer MJ, Lowe ME, Werlin SL, et al. Early-onset acute recurrent and chronic pancreatitis is associated with PRSS1 or CTRC gene mutations. J Pediatr 2017;186:95–100.
38. Jalaly NY, Moran RA, Fargahi F, et al. An evaluation of factors associated with pathogenic PRSS1, SPINK1, CTFR, and/or CTRC genetic variants in patients with idiopathic pancreatitis. Am J Gastroenterol 2017;112:1320–9.
39. Dequeker E, Stuhrmann M, Morris MA, et al. Best practice guidelines for molecular genetic diagnosis of cystic fibrosis and CFTR-related disorders–updated European recommendations. Eur J Hum Genet 2009;17:51–65.
40. LaRusch J, Solomon S, Whitcomb DC. Pancreatitis overview. In: Adam MP, Ardinger HH, Pagon RA, et al. (eds). GeneReviews((R)). University of Washington, Seattle University of Washington, Seattle. GeneReviews is a registered trademark of the University of Washington, Seattle. All rights reserved: Seattle, WA, 1993.
41. Whitcomb DC, Shelton CA, Brand RE. Genetics and genetic testing in pancreatic cancer. Gastroenterology 2015;149:1252–e4.
42. Sheth SG, Conwell DL, Whitcomb DC, et al. Academic pancreas centers of excellence: Guidance from a multidisciplinary chronic pancreatitis working group at PancreasFest. Pancreatology 2017;17:419–30.
43. Crockett SD, Wani S, Gardner TB, et al. American Gastroenterological Association Institute guideline on initial management of acute pancreatitis. Gastroenterology 2018;154:1096–101.
44. Wu BU, Johannes RS, Sun X, et al. Early changes in blood urea nitrogen predict mortality in acute pancreatitis. Gastroenterology 2009;137:129–35.
45. Brown A, Orav J, Banks PA. Hemoconcentration is an early marker for organ failure and necrotizing pancreatitis. Pancreas 2000;20:367–72.
46. Baillargeon JD, Orav J, Ramagopal V, et al. Hemoconcentration as an early risk factor for necrotizing pancreatitis. Am J Gastroenterol 1998;93:2130–4.
47. Gardner TB, Olenec CA, Chertoff JD, et al. Hemoconcentration and pancreatic necrosis: Further defining the relationship. Pancreas 2006;33:169–73.
48. Lankisch PG, Mahlke R, Blum T, et al. Hemoconcentration: An early marker of severe and/or necrotizing pancreatitis? A critical appraisal. Am J Gastroenterol 2001;96:2081–5.
49. Lankisch PG, Weber-Dany B, Hebel K, et al. The harmless acute pancreatitis score: A clinical algorithm for rapid initial stratification of nonsevere disease. Clin Gastroenterol Hepatol 2009;7:702–5; quiz 607.
50. Papachristou GI, Muddana V, Yadav D, et al. Comparison of BISAP, Ranson's, APACHE-II, and CTSI scores in predicting organ failure, complications, and mortality in acute pancreatitis. Am J Gastroenterol 2010;105:435–41; quiz 442.
51. Mounzer R, Langmead CJ, Wu BU, et al. Comparison of existing clinical scoring systems to predict persistent organ failure in patients with acute pancreatitis. Gastroenterology 2012;142:1476–82.
52. 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.
53. Forsmark CE, Yadav D. Predicting the prognosis of acute pancreatitis. Ann Intern Med 2016;165:523–4.
54. Wu BU, Johannes RS, Sun X, et al. The early prediction of mortality in acute pancreatitis: A large population-based study. Gut 2008;57:1698–703.
55. Park JY, Jeon TJ, Ha TH, et al. Bedside index for severity in acute pancreatitis: Comparison with other scoring systems in predicting severity and organ failure. Hepatobiliary Pancreat Dis Int 2013;12:645–50.
56. Senapati D, Debata PK, Jenasamant SS, et al. A prospective study of the Bedside Index for Severity in Acute Pancreatitis (BISAP) score in acute pancreatitis: An Indian perspective. Pancreatology 2014;14:335–9.
57. Gao W, Yang HX, Ma CE. The value of BISAP score for predicting mortality and severity in acute pancreatitis: A systematic review and meta-analysis. PLoS One 2015;10:e0130412.

58. Buxbaum J, Quezada M, Chong B, et al. The pancreatitis activity scoring system predicts clinical outcomes in acute pancreatitis: Findings from a prospective cohort study. Am J Gastroenterol 2018;113:755–64.
59. Zubia-Olaskoaga F, Maravi-Poma E, Urreta-Barallobre I, et al. Development and validation of a multivariate prediction model for patients with acute pancreatitis in intensive care medicine. Pancreatology 2018;18:161–7.
60. Solanki NS, Barreto SG. Fluid therapy in acute pancreatitis. A systematic review of literature. JOP 2011;12:205–8.
61. de-Madaria E, Banks PA, Moya-Hoyo N, et al. Early factors associated with fluid sequestration and outcomes of patients with acute pancreatitis. Clin Gastroenterol Hepatol 2014;12:997–1002.
62. Singh VK, Gardner TB, Papachristou GI, et al. An international multicenter study of early intravenous fluid administration and outcome in acute pancreatitis. United Eur Gastroenterol J 2017;5:491–8.
63. Gardner TB, Vege SS, Chari ST, et al. Faster rate of initial fluid resuscitation in severe acute pancreatitis diminishes in-hospital mortality. Pancreatology 2009;9:770–6.
64. Weitz G, Woitalla J, Wellhoner P, et al. Detrimental effect of high volume fluid administration in acute pancreatitis: A retrospective analysis of 391 patients. Pancreatology 2014;14:478–83.
65. Mao EQ, Fei J, Peng YB, et al. Rapid hemodilution is associated with increased sepsis and mortality among patients with severe acute pancreatitis. Chin Med J 2010;123:1639–44.
66. de-Madaria E, Soler-Sala G, Sanchez-Paya J, et al. Influence of fluid therapy on the prognosis of acute pancreatitis: A prospective cohort study. Am J Gastroenterol 2011;106:1843–50.
67. Buxbaum JL, Quezada M, Da B, et al. Early aggressive hydration hastens clinical improvement in mild acute pancreatitis. Am J Gastroenterol 2017;112:797–803.
68. Warndorf MG, Kurtzman JT, Barten MJ, et al. Early fluid resuscitation reduces morbidity among patients with acute pancreatitis. 2011;9:705–9.
69. Wall I, Badalov N, Baradarian R, et al. Decreased mortality in acute pancreatitis related to early aggressive hydration. Pancreas 2011;40: 547–50.
70. Yamashita T, Horibe M, Sanui M, et al. Large volume fluid resuscitation for severe acute pancreatitis is associated with reduced mortality: A multicenter retrospective study. J Clin Gastroenterol 2019;53:385–91.
71. Aggarwal A, Manrai M, Kochhar R. Fluid resuscitation in acute pancreatitis. World J Gastroenterol 2014;20:18092–103.
72. Wu BU, Hwang JQ, Gardner TH, et al. Lactated ringer's solution reduces systemic inflammation compared with saline in patients with acute pancreatitis. Clin Gastroenterol Hepatol 2011;9:710–7.e1.
73. de-Madaria E, Herrera-Marante I, Gonzalez-Camacho V, et al. Fluid resuscitation with lactated ringer's solution vs normal saline in acute pancreatitis: A triple-blind, randomized, controlled trial. United Eur Gastroenterol J 2018;6:63–72.
74. Iqbal U, Anwar H, Scribani M. Ringer's lactate versus normal saline in acute pancreatitis: A systematic review and meta-analysis. J Dig Dis 2018;19:335–41.
75. Lee HS, Chung MJ, Park JY, et al. Urgent endoscopic retrograde cholangiopancreatography is not superior to early ERCP in acute biliary pancreatitis with biliary obstruction without cholangitis. PLoS One 2018;13:e0190835.
76. Hakuta R, Hamada T, Nakai Y, et al. No association of timing of endoscopic biliary drainage with clinical outcomes in patients with non-severe acute cholangitis. Dig Dis Sci 2018;63:1937–45.
77. Tse F, Yuan Y. Early routine endoscopic retrograde cholangiopancreatography strategy versus early conservative management strategy in acute gallstone pancreatitis. Cochrane Database Syst Rev 2012;5:CD009779.
78. Williams E, Beckingham I, El Sayed G, et al. Updated guideline on the management of common bile duct stones (CBDS). Gut 2017;66:765–82.
79. Besselink M, van Santvoort H, Freeman M, et al. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology 2013;13:e1–15.
80. Tarnasky PR. ERCP pericholecystectomy. In: Cotton PB, Leung J (eds). ERCP: The Fundamentals. 2nd edn, John Wiley & Sons, Ltd, Chichester, UK, 2015, pp 228–49.
81. Kuo VC, Tarnasky PR. Endoscopic management of acute biliary pancreatitis. Gastrointest Endosc Clin N Am 2013;23:749–68.
82. Yi F, Ge L, Zhao J, et al. Meta-analysis: Total parenteral nutrition versus total enteral nutrition in predicted severe acute pancreatitis. Intern Med 2012;51:523–30.
83. Eckerwall GE, Tingstedt BB, Bergenzaun PE, et al. Immediate oral feeding in patients with mild acute pancreatitis is safe and may accelerate recovery: A randomized clinical study. Clin Nutr 2007;26:758–63.
84. Jacobson BC, Vander Vliet MB, Hughes MD, et al. A prospective, randomized trial of clear liquids versus low-fat solid diet as the initial meal in mild acute pancreatitis. Clin Gastroenterol Hepatol 2007;5: 946–51; quiz 886.
85. Sathiaraj E, Murthy S, Mansard MJ, et al. Clinical trial: Oral feeding with a soft diet compared with clear liquid diet as initial meal in mild acute pancreatitis. Aliment Pharmacol Ther 2008;28:777–81.
86. Larino-Noia J, Lindkvist B, Iglesias-Garcia J, et al. Early and/or immediately full caloric diet versus standard refeeding in mild acute pancreatitis: A randomized open-label trial. Pancreatology 2014;14: 167–73.
87. Moraes JM, Felga GE, Chebli LA, et al. A full solid diet as the initial meal in mild acute pancreatitis is safe and result in a shorter length of hospitalization: Results from a prospective, randomized, controlled, double-blind clinical trial. J Clin Gastroenterol 2010;44:517–22.
88. Petrov MS, McIlroy K, Grayson L, et al. Early nasogastric tube feeding versus nil per os in mild to moderate acute pancreatitis: A randomized controlled trial. Clin Nutr 2013;32:697–703.
89. Louie BE, Noseworthy T, Hailey D, et al. 2004 MacLean-Mueller prize enteral or parenteral nutrition for severe pancreatitis: A randomized controlled trial and health technology assessment. Can J Surg 2005;48: 298–306.
90. Wu XM, Liao YW, Wang HY, et al. When to initialize enteral nutrition in patients with severe acute pancreatitis? A retrospective review in a single institution experience (2003-2013). Pancreas 2015;44:507–11.
91. Chang YS, Fu HQ, Xiao YM, et al. Nasogastric or nasojejunal feeding in predicted severe acute pancreatitis: A meta-analysis. Crit Care 2013;17: R118.
92. Zhu Y, Yin H, Zhang R, et al. Nasogastric nutrition versus nasojejunal nutrition in patients with severe acute pancreatitis: A meta-analysis of randomized controlled trials. Gastroenterol Res Pract 2016;2016: 6430632.
93. Wells N, Pasero C, McCaffery M. Advances in patient safety improving the quality of care through pain assessment and management. In: Hughes RG (ed). Patient Safety and Quality: An Evidence-Based Handbook for Nurses. Agency for Healthcare Research and Quality (US): Rockville, MD, 2008.
94. van Dijk SM, Hallensleben NDL, van Santvoort HC, et al. Acute pancreatitis: Recent advances through randomised trials. Gut 2017;66: 2024–32.
95. Isenmann R, Rünzi M, Kron M, et al. Prophylactic antibiotic treatment in patients with predicted severe acute pancreatitis: A placebo-controlled, double-blind trial. Gastroenterology 2004;126:997–1004.
96. Garcia-Barrasa A, Borobia FG, Pallares R, et al. A double-blind, placebo-controlled trial of ciprofloxacin prophylaxis in patients with acute necrotizing pancreatitis. J Gastrointest Surg 2009;13:768–74.
97. Jafri NS, Mahid SS, Idstein SR, et al. Antibiotic prophylaxis is not protective in severe acute pancreatitis: A systematic review and meta-analysis. Am J Surg 2009;197:806–13.
98. Villatoro E, Mulla M, Larvin M. Antibiotic therapy for prophylaxis against infection of pancreatic necrosis in acute pancreatitis. Cochrane Database Syst Rev 2010:CD002941.
99. Besselink MG, van Santvoort HC, Buskens E, et al. Probiotic prophylaxis in predicted severe acute pancreatitis: A randomised, double-blind, placebo-controlled trial. Lancet 2008;371:651–9.
100. Sun S, Yang K, He X, et al. Probiotics in patients with severe acute pancreatitis: A meta-analysis. Langenbecks Arch Surg 2009;394:171–7.
101. Balthazar EJ. Acute pancreatitis: Assessment of severity with clinical and CT evaluation. Radiology 2002;223:603–13.
102. Bollen TL, Singh VK, Maurer R, et al. Comparative evaluation of the modified CT severity index and CT severity index in assessing severity of acute pancreatitis. AJR Am J Roentgenol 2011;197:386–92.
103. Kirkpatrick AW, Roberts DJ, De Waele J, et al. Intra-abdominal hypertension and the abdominal compartment syndrome: Updated consensus definitions and clinical practice guidelines from the World Society of the abdominal compartment syndrome. Intensive Care Med 2013;39:1190–206.
104. van Brunschot S, Schut AJ, Bouwense SA, et al. Abdominal compartment syndrome in acute pancreatitis: A systematic review. Pancreas 2014;43:665–74.

105. Xu J, Tian X, Zhang C, et al. Management of abdominal compartment syndrome in severe acute pancreatitis patients with early continuous veno-venous hemofiltration. Hepatogastroenterology 2013;60:1749–52.
106. Xu J, Cui Y, Tian X. Early continuous veno-venous hemofiltration is effective in decreasing intra-abdominal pressure and serum interleukin-8 level in severe acute pancreatitis patients with abdominal compartment syndrome. Blood Purif 2017;44:276–82.
107. Gurusamy KS, Belgaumkar AP, Haswell A, et al. Interventions for necrotising pancreatitis. Cochrane Database Syst Rev 2016;4:CD011383.
108. Boumitri C, Brown E, Kahaleh M. Necrotizing pancreatitis: Current management and therapies. Clin Endosc 2017;50:357–65.
109. Nadkarni NA, Khanna S, Vege SS. Splanchnic venous thrombosis and pancreatitis. Pancreas 2013;42:924–31.
110. Aboulian A, Chan T, Yaghoubian A, et al. Early cholecystectomy safely decreases hospital stay in patients with mild gallstone pancreatitis: A randomized prospective study. Ann Surg 2010;251:615–9.
111. Nguyen GC, Rosenberg M, Chong RY, et al. Early cholecystectomy and ERCP are associated with reduced readmissions for acute biliary pancreatitis: A nationwide, population-based study. Gastrointest Endosc 2012;75:47–55.
112. van Baal MC, Besselink MG, Bakker OJ, et al. Timing of cholecystectomy after mild biliary pancreatitis: A systematic review. Ann Surg 2012;255:860–6.
113. da Costa DW, Bouwense SA, Schepers NJ, et al. Same-admission versus interval cholecystectomy for mild gallstone pancreatitis (PONCHO): A multicentre randomised controlled trial. Lancet 2015;386:1261–8.
114. Krishna SG, Kruger AJ, Patel N, et al. Cholecystectomy during index admission for acute biliary pancreatitis lowers 30-day readmission rates. Pancreas 2018;47:996–1002.
115. Kamal A, Akhuemonkhan E, Akshintala VS, et al. Effectiveness of guideline-recommended cholecystectomy to prevent recurrent pancreatitis. Am J Gastroenterol 2017;112:503–10.
116. Nealon WH, Bawduniak J, Walser EM. Appropriate timing of cholecystectomy in patients who present with moderate to severe gallstone-associated acute pancreatitis with peripancreatic fluid collections. Ann Surg 2004;239:741–9; discussion 749–51.
117. Raty S, Pulkkinen J, Nordback I, et al. Can laparoscopic cholecystectomy prevent recurrent idiopathic acute pancreatitis?: A prospective randomized multicenter trial. Ann Surg 2015;262:736–41.
118. Stevens CL, Abbas SM, Watters DA. How does cholecystectomy influence recurrence of idiopathic acute pancreatitis? J Gastrointest Surg 2016;20:1997–2001.
119. Freeman ML, Werner J, van Santvoort HC, et al. Interventions for necrotizing pancreatitis: Summary of a multidisciplinary consensus conference. Pancreas 2012;41:1176–94.
120. van Brunschot S, Bakker OJ, Besselink MG, et al. Treatment of necrotizing pancreatitis. Clin Gastroenterol Hepatol 2012;10:1190–201.
121. Arvanitakis M, Dumonceau JM, Albert J, et al. Endoscopic management of acute necrotizing pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) evidence-based multidisciplinary guidelines. Endoscopy 2018;50:524–46.
122. Leppaniemi A. Surgical management of abdominal compartment syndrome; indications and techniques. Scand J Trauma Resusc Emerg Med 2009;17:17.
123. Dellinger EP, Forsmark CE, Layer P, et al. Determinant-based classification of acute pancreatitis severity: An international multidisciplinary consultation. Ann Surg 2012;256:875–80.
124. Singla A, Simons J, Li Y, et al. Admission volume determines outcome for patients with acute pancreatitis. Gastroenterology 2009;137:1995–2001.
125. Hamada T, Yasunaga H, Nakai Y, et al. Impact of hospital volume on outcomes in acute pancreatitis: A study using a nationwide administrative database. J Gastroenterol 2014;49:148–55.
126. Koutroumpakis E, Slivka A, Furlan A, et al. Management and outcomes of acute pancreatitis patients over the last decade: A US tertiary-center experience. Pancreatology 2017;17:32–40.
127. da Costa DW, Boerma D, van Santvoort HC, et al. Staged multidisciplinary step-up management for necrotizing pancreatitis. Br J Surg 2014;101:e65–79.
128. James PD, Kaplan GG, Myers RP, et al. Decreasing mortality from acute biliary diseases that require endoscopic retrograde cholangiopancreatography: A nationwide cohort study. Clin Gastroenterol Hepatol 2014;12:1151–9 e6.
129. Field MJ, Lohr N; Medicine Io. Guidelines for Clinical Practice: From Development to Use. National Academy Press: Washington, DC, 1992.
130. Forsmark CE. Are there too many practice guidelines for acute pancreatitis? Curr Gastroenterol Rep 2008;10:347–8.
131. Wu BU, Conwell DL. Acute pancreatitis part I: Approach to early management. Clin Gastroenterol Hepatol 2010;8:410–8, quiz e56–8.
132. Isaji S, Takada T, Mayumi T, et al. Revised Japanese guidelines for the management of acute pancreatitis 2015: Revised concepts and updated points. J Hepatobiliary Pancreat Sci 2015;22:433–45.
133. Italian Association for the Study of the Pancreas (AISP); Pezzilli R, Zerbi A, Campra D, et al. Consensus guidelines on severe acute pancreatitis. Dig Liver Dis 2015;47:532–43.
134. Yokoe M, Takada T, Mayumi T, et al. Japanese guidelines for the management of acute pancreatitis: Japanese guidelines 2015. J Hepatobiliary Pancreat Sci 2015;22:405–32.
135. Guda NM, Muddana V, Whitcomb DC, et al. Recurrent acute pancreatitis: International state-of-the-Science conference with recommendations. Pancreas 2018;47:653–66.
136. Vege SS, DiMagno MJ, Forsmark CE, et al. Initial medical treatment of acute pancreatitis: American Gastroenterological Association Institute technical review. Gastroenterology 2018;154:1103–39.
137. Hayward RS, Wilson MC, Tunis SR, et al. Users' guides to the medical literature. VIII. How to use clinical practice guidelines. A. Are the recommendations valid? The evidence-based medicine working group. JAMA 1995;274:570–4.
138. Woolf SH, Grol R, Hutchinson A, et al. Clinical guidelines: Potential benefits, limitations, and harms of clinical guidelines. BMJ 1999;318:527–30.
139. Feuerstein JD, Akbari M, Gifford AE, et al. Systematic analysis underlying the quality of the scientific evidence and conflicts of interest in interventional medicine subspecialty guidelines. Mayo Clin Proc 2014;89:16–24.
140. Hirsh J, Guyatt G. Clinical experts or methodologists to write clinical guidelines? Lancet 2009;374:273–5.
141. Afghani E, Pandol SJ, Shimosegawa T, et al. Acute pancreatitis-progress and challenges: A report on an international Symposium. Pancreas 2015;44:1195–210.
142. Mainz J. Developing evidence-based clinical indicators: A state of the art methods primer. Int J Qual Health Care 2003;15(Suppl 1):i5–11.
143. Dimagno MJ, Wamsteker EJ, Rizk RS, et al. A combined paging alert and web-based instrument alters clinician behaviour and shortens hospital length of stay in acute pancreatitis. Am J Gastroenterol 2014;109:306–15.
144. Connor SJ, Lienert AR, Brown LA, et al. Closing the audit loop is necessary to achieve compliance with evidence-based guidelines in the management of acute pancreatitis. N Z Med J 2008;121:19–25.
145. Lohr KN, Schroeder SA. A strategy for quality assurance in Medicare. N Engl J Med 1990;322:707–12.
146. Califf RM, Peterson ED, Gibbons RJ, et al. Integrating quality into the cycle of therapeutic development. J Am Coll Cardiol 2002;40:1895–901.
147. Donabedian A. Evaluating the quality of medical care. Milbank Mem Fund Q 1966;44(Suppl):166–206.
148. Loveday BP, Windsor JA. How to introduce clinical practice guidelines. N Z Med J 2008;121:7–10.
149. IOM. Crossing the Quality Chasm: A New Health System for the 21st Century. National Academy Press: Washington, DC, 2001.