Management of acute pancreatitis: a practical guide

Acute pancreatitis is a surgical emergency that is common, poorly understood and carries a significant risk of death. It is an inflammatory process of the pancreas that is caused most commonly by gallstones or alcohol, and ranges from mild to severe disease (approximately 20% of cases). Acute pancreatitis is a common cause of emergency hospital admission, with an incidence of approximately 13–45 per 100 000 population per year (Yadav and Lowenfels, 2013). Severe acute pancreatitis is associated with a significant systemic inflammatory response, multiorgan failure and serious local complications. It is a challenging condition to treat, with substantial morbidity and mortality.

The revised Atlanta classification provides clear definitions to classify acute pancreatitis, using easily identified clinical and radiological criteria (Banks et al, 2013). The most up-to-date guidance on the clinical management of acute pancreatitis was published in 2013 by the Working Party International Association of Pancreatology and the American Pancreatic Association (IAP/APA) (Working Group IAP/APA Acute Pancreatitis Guidelines, 2013) and should serve as a reference standard for current management. In the UK, a report by the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) (2016) identified that the management of acute pancreatitis was suboptimal in more than half the patients reviewed. This article is an up-to-date practical guide for the management of acute pancreatitis, consistent with the latest evidence-based guidelines, which builds upon the key findings and recommendations of the NCEPOD report.

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Table 1. Differential diagnosis in acute pancreatitis

Perforated peptic ulcer
Peptic ulcer disease or gastritis
Cholecystitis, cholangitis or choledocholithiasis
Intestinal obstruction
Gastroenteritis
Mesenteric ischaemia
Ruptured abdominal aortic aneurysm
Pneumonia
Myocardial infarction

Make an initial assessment and establish a diagnosis

Initial assessment and investigation should focus on early diagnosis and exclusion of differential diagnoses (*Table 1*), allowing prompt initial management, and should involve a full patient assessment to establish aetiology (*Table 2*) and severity.

The commonest presenting symptoms of acute pancreatitis are abdominal pain (>90%) and vomiting (up to 45%). Characteristic abdominal pain is of sudden onset, severe, epigastric and sometimes radiates to the back (Banks et al, 2013). Other presentations include back pain (15%) and shock (4.7%). Examination of the abdomen reveals epigastric tenderness, often with guarding. Skin signs such as Grey Turner's, Cullen's or Fox's signs (flank, peri-umbilical and upper anterior thigh ecchymosis respectively) are uncommon, occur in up to 3% and are associated with severe acute pancreatitis and significant mortality (Lankisch et al, 2009). They result from the spread of retroperitoneal haemorrhagic fluid: from the posterior pararenal space to the lateral edge of quadratus lumborum in Grey Turner's sign, to the umbilicus via the falciform and round ligaments in Cullen's sign, and along the iliopsoas fascia to the upper thigh in Fox's sign.

Table 2. Aetiology of pancreatitis

Gallstones (50%)	
Alcohol (25%)	
Drugs	Immunosuppressants (steroids, azathioprine)
	Statins (simvastatin)
	Diuretics (furosemide, hydrocholorothiazide)
	Disease-modifying drugs (sulphasalazine)
	5-aminosalicyclic acid
	Paracetamol
	Cancer therapies (e.g. capecitabine, cisplatin, tamoxifen)
	Angiotensin-converting enzyme inhibitors (enalapril)
	Antimicrobials (erythromycin, metronidazole, tetracycline, septrin, itraconazole)
	Oestrogens
	Anti-epileptics (carbamazepine, valproic acid)
	Antipsychotics (olanzapine)
Post-intervention (endoscopic retrograde cholangiopancreatography, endoscopic ultrasound and fine needle aspiration)	
Hypertriglyceridaemia	
Hypercalcaemia	
Morphological abnormalities (pancreas divisum)	
Viral infections (mumps, coxsackie B4)	
Autoimmune	
Idiopathic	

The diagnosis of pancreatitis per the revised Atlanta definitions (Banks et al, 2013) requires two of the following:

Table 3. Initial investigations in the management of acute pancreatitis

Haematology: full blood count, coagulation screen
Serum biochemistry: liver function tests, urea and electrolytes, amylase or lipase levels, corrected calcium, glucose, C-reactive protein, lactate dehydrogenase, troponin levels (where required)
Arterial blood gas
Electrocardiography
Chest X-ray

From National Confidential Enquiry into Patient Outcome and Death (2016)

1. Abdominal pain consistent with acute pancreatitis
2. Elevated serum amylase (or lipase) levels more than three times the upper limit of normal
3. Characteristic findings on contrast-enhanced computed tomography, magnetic resonance or ultrasonography.

Initial investigations are summarized in *Table 3*. The NCEPOD report (2016) demonstrated that these were not undertaken appropriately in up to 20% of cases.

Be clear on the goals of initial management

The aim of initial management is adequate resuscitation to restore tissue perfusion and oxygenation, including administration of oxygen followed by early optimal fluid therapy. Adequate pain control is essential to optimize respiratory function. Management of poorly controlled comorbidities is key in reducing further morbidity.

Provide adequate fluid therapy

Optimal fluid resuscitation within the first 24–48 hours is the most important treatment for patients with acute pancreatitis. The IAP/APA consensus guidelines (Working Group IAP/APA Acute Pancreatitis Guidelines, 2013) recommend initial fluid resuscitation with Hartmann's solution at an initial rate of 5–10 ml/kg/h. A total of 2.5–4 litres in 24 hours will usually suffice, although fluid resuscitation should be goal-directed – total volumes should be tailored to comorbidities and dictated by clinical response (heart rate <120 bpm, a mean arterial blood pressure 65–85 mmHg and a urine output of >0.5 ml/kg/hr) and haematological targets (haematocrit >35%). Failure to respond to resuscitation should prompt early critical care review.

Ensure relief of pain

It is well understood that uncontrolled pain restricts abdominal wall and diaphragmatic movements, thereby increasing the risk of respiratory complications. Effective analgesia is therefore essential in acute pancreatitis. Managing acute pain may require intravenous opioids or patient-controlled analgesia. Support from specialist acute pain services is often useful, particularly for those in whom adequate pain control is challenging (Banks et al, 2013; Stigliano et al, 2017).

Practice antimicrobial stewardship

Several meta-analyses, including a Cochrane review in 2010, have demonstrated no significant reduction of mortality or infected necrosis with prophylactic antibiotics (Villatoro et al, 2010; Lim et al, 2015). As such, antibiotic prophylaxis cannot be recommended in acute pancreatitis. Despite this, a global overview (Baltatzis et al, 2016) and the NCEPOD report (2016) revealed widespread antibiotic use; antibiotics were prescribed in 60% of cases in the UK and considered inappropriate in 20%. There are well-known risks of encouraging antimicrobial resistance with over-prescription of antibiotics and a programme of antimicrobial stewardship has been advocated through publication of a patient safety alert by Public Health England (NHS England et al, 2015). Indications for antibiotics in acute pancreatitis are suspected or confirmed infected pancreatic necrosis or other concomitant infective processes. The choice of agent should be guided by local policies and sensitivities of any positive cultures.

Identify those with severe disease

Prompt recognition of patients with early or established organ dysfunction is vital as these patients have, by definition, moderate or severe pancreatitis.

Definition of severity

The revised Atlanta classification (Banks et al, 2013) defines three levels of severity:

- Mild acute pancreatitis, with no organ failure, local or systemic complications
- Moderately severe acute pancreatitis, where organ failure resolves within 48 hours and/or local or systemic complications occur but without persistent organ failure
- Severe acute pancreatitis, when persistent organ failure (>48 hours) occurs.

The Atlanta classification also describes two peaks of mortality that occur in acute pancreatitis:

- An early phase – during which mortality is the result of the body reacting to the injury to the pancreas causing a systemic inflammatory response. When this persists there is an increased risk of developing organ failure
- A late phase – this is characterized by persistence of systemic signs of inflammation or by the presence of additional local complications.

Prediction of severity

Multiple scoring systems (e.g. modified Glasgow, Ranson and APACHE II scores) exist, in addition to single serum markers (e.g. C-reactive protein), but none directly alters management. A national early warning score (NEWS) has been introduced in the UK by the Royal College of Physicians (2012). NEWS has standardized the early identification of patients with critical illness and with the potential to deteriorate, and accordingly is an important adjunct in managing acute pancreatitis. Any patient 'triggering' should be assessed promptly, and persistently triggering or deteriorating NEWS scores should elicit early critical care involvement.

Further management considerations

Identify the cause

Identification of aetiology (*Table 2*) is vital, enabling effective treatment of the cause and prevention of recurrence. The NCEPOD report (2016) found no cause identified in up to 17.5% of patients, but recommended that the rate of true idiopathic pancreatitis should be <10%. A thorough search for the aetiology of acute pancreatitis should be undertaken and must include detailed clinical assessment, serum blood tests and ultrasonography.

Imaging

Imaging is essential for establishing aetiology. It may also be required to confirm a diagnosis of severe acute pancreatitis or to assess for complications.

Ultrasonography

Ultrasonography is the first-line investigation to assess for gallstones, and should be performed in all patients within 24 hours of admission. Patients with a negative

ultrasonography and no obvious aetiology should later undergo a repeat ultrasonography of the biliary system (Working Group IAP/APA Acute Pancreatitis Guidelines, 2013).

Computed tomography

Contrast-enhanced computed tomography is indicated where there is diagnostic uncertainty, persisting systemic disturbance or clinical deterioration at any time, to assess for complications and/or confirm severity. For the latter, a minimum of 72–96 hours should be allowed where possible, as early computed tomography may not show pancreatic necrosis, fluid collections or their extent (Working Group IAP/APA Acute Pancreatitis Guidelines, 2013).

Magnetic resonance cholangiopancreatography

Magnetic resonance cholangiopancreatography should be considered in patients with biliary pancreatitis and suspected choledocholithiasis, in the absence of cholangitis and/or abnormal liver function tests, rather than endoscopic retrograde cholangiopancreatography, which should be reserved for therapeutic intervention. Magnetic resonance cholangiopancreatography can also diagnose rare anatomical abnormalities (Working Group IAP/APA Acute Pancreatitis Guidelines, 2013).

Endoscopic ultrasound

Endoscopic ultrasound detects the presence of previously undetected small stones and microlithiasis, important causes of acute pancreatitis, in addition to rarer causes (e.g. occult neoplasms and anatomical abnormalities) and features of chronic pancreatitis. In recurrent apparently idiopathic acute pancreatitis, an underlying cause can be identified on endoscopic ultrasound in up to 88% of cases (Wilcox et al, 2006). Endoscopic ultrasound should thus be considered following negative ultrasonography in the absence of other aetiology, and particularly in recurrent idiopathic acute pancreatitis. Further investigation after a negative endoscopic ultrasound should be directed at identifying rarer causes (Working Group IAP/APA Acute Pancreatitis Guidelines, 2013).

Assess nutritional status and provide supplementation where indicated

All patients admitted to hospital with acute pancreatitis should be assessed for their overall risk of malnutrition. The Malnutrition Universal Screening Tool (MUST) provides a basis for appropriate referral to a dietitian or nutritional support team and subsequent timely and adequate nutritional support (British Association for Parenteral and Enteral Nutrition, 2011).

Currently, in patients with predicted mild acute pancreatitis early oral nutrition is safe, does not increase complications and should be allowed as soon as tolerated (Working Group IAP/APA Acute Pancreatitis Guidelines, 2013). Nasogastric or nasojejunal tube feeding may be required in patients with severe acute pancreatitis where nutritional needs are not met orally. A Cochrane review of eight randomized controlled trials demonstrated that enteral feeding reduced mortality, multiorgan failure, systemic infections and operative interventions when compared with parenteral nutrition. Additionally, in severe acute pancreatitis a reduction of infective complications and mortality was found (Al-Omran et al, 2010). Thus, parenteral nutrition should be considered only where oral or enteral nutrition is not tolerated or not possible.

Venous thromboembolism prophylaxis

As with all conditions resulting in reduced mobility and intra-abdominal inflammation, there is a substantial risk of venous thromboembolism in patients with acute pancreatitis. Appropriate chemical and/or mechanical prophylaxis should be instituted according to National Institute for Health and Care (2010) guidelines.

Treat the underlying cause

Definitive eradication of gallstones is necessary unless unfit

Cholecystectomy

Cholecystectomy and/or endoscopic retrograde cholangiopancreatography with endoscopic sphincterotomy are definitive treatments for biliary pancreatitis. The PONCHO randomized controlled trial showed that same-admission cholecystectomy reduced the rate of recurrent gallstone-related complications in patients with mild gallstone pancreatitis, with a very low risk of cholecystectomy-related complications (da Costa et al, 2015). All patients with mild biliary pancreatitis should undergo laparoscopic cholecystectomy during the index admission or within 2 weeks of discharge. In severe acute pancreatitis, cholecystectomy should be performed after the resolution of peripancreatic fluid collections, or after 6 weeks.

In those not fit for surgery, endoscopic retrograde cholangiopancreatography and endoscopic sphincterotomy is considered definitive treatment to prevent recurrent pancreatitis (Working Group IAP/APA Acute Pancreatitis Guidelines, 2013). The NCEPOD report (2016) showed that only 20% of patients with biliary pancreatitis underwent definitive management for gallstones during their admission. Additionally, 30% of recurrent admissions were the result of gallstones, highlighting the importance of definitive treatment on the index admission.

Early endoscopic retrograde cholangiopancreatography

A Cochrane review of five randomized controlled trials identified a reduction in mortality and local and systemic complications with early endoscopic retrograde cholangiopancreatography in acute pancreatitis with cholangitis. Additionally, there was a trend towards a benefit in acute pancreatitis with biliary obstruction (Tse and Yuan, 2012). Routine early endoscopic retrograde cholangiopancreatography in biliary pancreatitis without cholangitis is not recommended, rather magnetic resonance cholangiopancreatography or endoscopic ultrasound should be considered, and may identify patients in whom endoscopic retrograde cholangiopancreatography is required (Working Group IAP/APA Acute Pancreatitis Guidelines, 2013).

Address alcohol dependence in alcohol-related pancreatitis

Apte et al (2009) describe the 'extraordinary situation…[where] the major factor responsible for the illness, namely excessive alcohol intake, receives little attention in its routine medical management.' Recurrent acute pancreatitis will occur in up to half of patients with alcohol-related pancreatitis. A randomized controlled trial has shown that structured repeated interventions delivered at 6-monthly intervals (discussing how and why patients should remain abstinent) significantly lowers the rate of recurrence (Nordback et al, 2009). It is vital that these patients are given alcohol cessation advice and are referred to hospital alcohol liaison services.

Table 4. Definitions of the morphological features of acute pancreatitis, modified from the revised Atlanta classifications and definitions

Morphological feature	Definition	Contrast-enhanced computed tomography criteria
Interstitial oedematous pancreatitis	Acute inflammation of the pancreatic parenchyma and peripancreatic tissues, without tissue necrosis	■ Pancreatic parenchyma enhancement by intravenous contrast ■ No peripancreatic necrosis
Pancreatic necrosis	Inflammation associated with pancreatic parenchymal necrosis and/or peripancreatic necrosis	■ Lack of pancreatic parenchymal enhancement by intravenous contrast and/or ■ Presence of peripancreatic necrosis (including acute necrotic collection and walled-off necrosis, see below)
Acute peri-pancreatic fluid collection, (<4 weeks, without features of pseudocyst)	Peripancreatic fluid associated with interstitial oedematous pancreatitis with no associated peripancreatic necrosis	■ Occurs in the setting of interstitial oedematous pancreatitis ■ Homogenous collection with fluid density ■ Confined by normal peripancreatic fascial planes ■ No definable encapsulating wall ■ Adjacent to pancreas (no intrapancreatic extension)
Pancreatic pseudocyst (>4 weeks)	An encapsulated collection of fluid with a well-defined inflammatory wall usually outside the pancreas with minimal or no necrosis	■ Well circumscribed, usually round or oval ■ Homogenous fluid density ■ No non-liquid component ■ Well-defined wall that completely encapsulates ■ Maturation usually requires >4 weeks after interstitial oedematous pancreatitis
Acute necrotic collection	A collection containing variable amounts of both fluid and necrosis associated with necrotizing pancreatitis. The necrosis can involve pancreatic parenchyma and/or peripancreatic tissues	■ Only in the setting of acute necrotizing pancreatitis ■ Heterogeneous, non-liquid density of varying degrees in different locations ■ No definable wall encapsulating the collection ■ Intrapancreatic and/or extrapancreatic
Walled-off necrosis (>4 weeks)	A mature, encapsulated collection of pancreatic and/or peripancreatic necrosis which has developed a well-defined inflammatory wall. Usually occurring >4 weeks after the onset of necrotizing pancreatitis	■ Heterogeneous with liquid and non-liquid density with varying degrees of loculations (some may appear homogenous) ■ Well-defined wall that completely encapsulates ■ Intra- and/or extra-pancreatic ■ Maturation usually requires 4 weeks after onset of acute necrotizing pancreatitis

From Banks et al (2013)

Identify complications of acute pancreatitis

Local complications have been defined by the Atlanta classification (*Table 4*). Within the first 4 weeks pancreatic necrosis, acute peri-pancreatic fluid collections and acute necrotic collections can occur. After 4 weeks these may develop into pancreatic pseudocyst and walled-off necrosis (Banks et al, 2013). Other less common complications include gastric dysfunction or obstruction, obstructive jaundice from enlargement of the pancreatic head, acute colonic necrosis, portal vein thrombosis, pseudo-aneurysms, pancreaticopleural fistula and pancreatic ascites.

Necrotizing pancreatitis

Necrosis of the pancreatic parenchyma and/or peri-pancreatic tissue is seen in 5–10% and results from impaired pancreatic perfusion. Sterile necrosis carries a mortality of 9–12%, whereas this rises to 20–30% in infected necrosis (Banks et al, 2006).

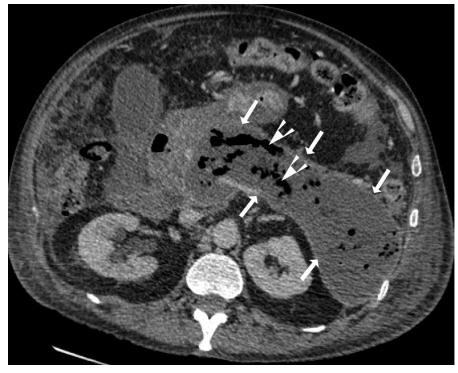


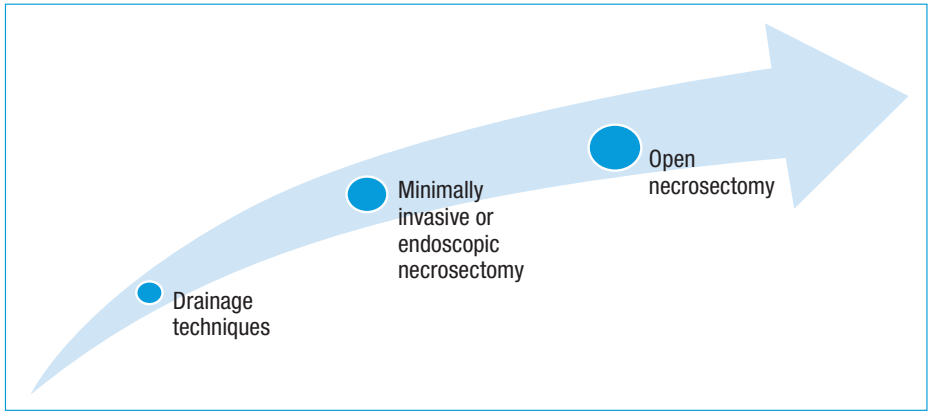
Figure 1. Acute necrotizing pancreatitis complicated by infected pancreatic necrosis. There is an acute necrotic collection in the pancreatic and peripancreatic area (white arrows pointing at the borders of the acute necrotic collection) with presence of gas bubbles (white arrowheads), usually a pathognomonic sign of infection of the necrosis (infected necrosis).

Infected necrotizing pancreatitis is diagnosed clinically (systemic disturbance and/or increasing inflammatory markers in pancreatic necrosis), radiologically (computed tomography evidence of gas in pancreatic collections (*Figure 1*)), or on fine needle aspiration (not routinely required). Current consensus recommends intervention be avoided until necrosis has walled off (usually 4 weeks from onset). Where required, a 'step-up' approach to intervention should be adopted, involving initial image-guided percutaneous catheter drainage or endoscopic transgastric drainage, followed by endoscopic or minimally invasive surgical necrosectomy. Open necrosectomy is then reserved for those occasions when these interventions fail to control sepsis (*Figure 2*) (van Santvoort et al, 2010).

When to involve other specialties

Acute pancreatitis is a systemic disorder and can result in complex complications. Moreover, patient comorbidities may complicate or be exacerbated by acute pancreatitis. The management of acute pancreatitis therefore requires a multidisciplinary approach, including general surgeons, gastroenterologists, dietitians, critical care physicians, interventional radiologists and other specialists (e.g. respiratory physicians). Referral to, or discussion with a specialist hepatopancreatobiliary centre should

Figure 2. The step-up approach to the management of acute necrotizing pancreatitis. Initial image-guided percutaneous catheter drainage or endoscopic trans-gastric drainage is performed with the aim of controlling sepsis. If this is not achieved, endoscopic, minimally invasive, surgical or even open necrosectomy are used to achieve this goal in a stepwise manner.



be undertaken in cases of severe acute pancreatitis, particularly where complications develop in the context of organ failure, and where there is a requirement for radiological, specialist endoscopic or surgical intervention (Working Group IAP/APA Acute Pancreatitis Guidelines, 2013; NCEPOD, 2016). **BJHM**

Figure 1 *is reproduced courtesy of Dr Rafik Filobbos. Conflict of interest: Ms CGV Slawinski: none; Mr DA O'Reilly is author of the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report on acute pancreatitis and has received honoraria from Mylan.*

KEY POINTS

- Prompt initial assessment and investigation should focus on establishing the diagnosis of acute pancreatitis and excluding other surgical diagnoses requiring an immediate operation.
- Initial management of acute pancreatitis is goal-directed fluid resuscitation tailored to clinical response, administration of oxygen and effective analgesia.
- Early warning scores should be calculated, as these help guide which patients require early critical care involvement.
- Concerted efforts to establish and treat aetiology should be made. Ultrasound should be performed to assess for gallstones within 24 hours of admission. A careful alcohol history should be taken.
- Patients can and should be fed early where tolerated.
- Antibiotics are not indicated in the absence of infection.
- Where gallstone pancreatitis is identified, cholecystectomy should be undertaken during the index admission or within 2 weeks of discharge in mild acute pancreatitis, and after resolution of peri-pancreatic fluid collections in severe acute pancreatitis.
- All patients with alcohol-related pancreatitis must be given alcohol cessation advice and referred to hospital alcohol liaison services.
- Refer to a specialist centre when complications develop and where radiological, specialist endoscopic or surgical intervention is required.

Al-Omran M, Albalawi ZH, Tashkandi MF, Al-Ansary LA (2010) Enteral versus parenteral nutrition for acute pancreatitis. *Cochrane Database Syst Rev* **1**(1): CD002837. https://doi.org/10.1002/14651858.CD002837.pub2

Apte MV, Pirola RC, Wilson JS (2009) Pancreas: alcoholic pancreatitis—its the alcohol, stupid. *Nat Rev Gastroenterol Hepatol* **6**(6): 321–322. https://doi.org/10.1038/nrgastro.2009.84

Baltatzis M, Jegatheeswaran S, O'Reilly DA, Siriwardena AK (2016) Antibiotic use in acute pancreatitis: global overview of compliance with international guidelines. *Pancreatology* **16**(2): 189–193. https://doi.org/10.1016/j.pan.2015.12.179

Banks PA, Freeman ML; Practice Parameters Committee of the American College of Gastroenterology (2006) Practice guidelines in acute pancreatitis. *Am J Gastroenterol* **101**(10): 2379–2400. https://doi.org/10.1111/j.1572-0241.2006.00856.x

Banks PA, Bollen TL, Dervenis C et al; Acute Pancreatitis Classification Working Group (2013) Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. *Gut* **62**(1): 102–111. https://doi.org/10.1136/gutjnl-2012-302779

British Association for Parenteral and Enteral Nutrition (2011) Malnutrition Universal Screening Tool. www.bapen.org.uk/pdfs/must/must_full.pdf (accessed 1 April 2017)

da Costa DW, Bouwense SA, Schepers NJ et al; Dutch Pancreatitis Study Group (2015) Same-admission versus interval cholecystectomy for mild gallstone pancreatitis (PONCHO): a multicentre randomised controlled trial. *Lancet* **386**(10000): 1261–1268. https://doi.org/10.1016/S0140-6736(15)00274-3

Lankisch PG, Weber-Dany B, Maisonneuve P, Lowenfels AB (2009) Skin signs in acute pancreatitis: frequency and implications for prognosis. *J Intern Med* **265**(2): 299–301. https://doi.org/10.1111/j.1365-2796.2008.02004.x

Lim C, Lee W, Liew Y, Tang S, Chlebicki M, Kwa A (2015) Role of antibiotic prophylaxis in necrotizing pancreatitis: A meta-analysis. *J Gastrointest Surg* **19**(3): 480–491. https://doi.org/10.1007/s11605-014-2662-6

National Confidential Enquiry into Patient Outcome and Death (2016) Treat the cause: A review of the quality of care provided to patients treated for acute pancreatitis. www.ncepod.org.uk/2016report1/downloads/TreatTheCause_fullReport.pdf (accessed 18 February 2017)

National Institute for Health and Clinical Excellence (2010) Venous thromboembolism: Reducing the risk for patients in hospital. CG92. www.nice.org.uk/guidance/cg92/chapter/1-recommendations (accessed 4 March 2017)

NHS England, Health Education England, Public Health England (2015) Patient Safety Alert: Addressing antimicrobial resistance through implementation of an antimicrobial stewardship programme. www.england.nhs.uk/wp-content/uploads/2015/08/psa-amr-stewardship-prog.pdf (accessed 4 March 2017)

Nordback I, Pelli H, Lappalainen-Lehto R, Järvinen S, Räty S, Sand J (2009) The recurrence of acute alcohol-associated pancreatitis can be reduced: a randomized controlled trial. *Gastroenterology* **136**(3): 848–855. https://doi.org/10.1053/j.gastro.2008.11.044

Royal College of Physicians (2012) National Early Warning Score (NEWS): Standardising the assessment of acute-illness severity in the NHS. www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news (accessed 4 March 2017)

Stigliano S, Sternby H, de Madaria E, Capurso G, Petrov MS (2017) Early management of acute pancreatitis: A review of the best evidence. *Dig Liver Dis* **49**(6): 585–594. https://doi.org/10.1016/j.dld.2017.01.168

Tse F, Yuan Y (2012) Early routine endoscopic retrograde cholangiopancreatography strategy versus early conservative management strategy in acute gallstone pancreatitis. *Cochrane Database Syst Rev* **5**(5): CD009779. https://doi.org/10.1002/14651858.CD009779.pub2

van Santvoort HC, Besselink MG, Bakker OJ et al; Dutch Pancreatitis Study Group (2010) A step-up approach or open necrosectomy for necrotizing pancreatitis. *N Engl J Med* **362**(16): 1491–1502. https://doi.org/10.1056/NEJMoa0908821

Villatoro E, Mulla M, Larvin M (2010) Antibiotic therapy for prophylaxis against infection of pancreatic necrosis in acute pancreatitis. *Cochrane Database Syst Rev* **5**(5): CD002941. https://doi.org/10.1002/14651858.CD002941.pub3

Wilcox CM, Varadarajulu S, Eloubeidi M (2006) Role of endoscopic evaluation in idiopathic pancreatitis: a systematic review. *Gastrointest Endosc* **63**(7): 1037–1045. https://doi.org/10.1016/j.gie.2006.02.024

Working Group IAP/APA Acute Pancreatitis Guidelines (2013) IAP/APA evidence-based guidelines for the management of acute pancreatitis. *Pancreatology* **13**(4) Suppl 2: e1–e15. https://doi.org/10.1016/j.pan.2013.07.063

Yadav D, Lowenfels AB (2013) The epidemiology of pancreatitis and pancreatic cancer. *Gastroenterology* **144**(6): 1252–1261. https://doi.org/10.1053/j.gastro.2013.01.068