In patients with acute alcohol-related pancreatitis, what is the safety and efficacy of prophylactic antibiotics vs placebo?								
Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Dellinger EP, Tellado JM, Soto NE et al. Early antibiotic treatment for severe acute necrotizing pancreatitis: a randomized, double-blind, placebo-controlled study. *Annals of Surgery.* 2007; 245(5):674-683.	RCT 1++ Multicentre, randomized, double-blind, powered, ITT	N=100	Inclusion criteria: male or female patients' ≥18 years of age with a confirmed diagnosis of necrotizing pancreatitis within 120 hours of the onset of symptoms. Patients with ≥30% necrosis of the pancreas confirmed by contrast-enhanced CT, if this was not possible then noncontrast scans with extensive or multiple peripancreatic fluid collections and pancreatic oedema (Balthazar grade E) and either CRP >120mg/l or a multiple organ dysfunction score >2. Exclusion criteria: patients diagnosed with concurrent pancreatic or peripancreatic infection, patients who had received an investigational drug <30 days prior to enrolment, antimicrobial therapy for	Meropenum 1g reconstituted in infusion fluid or dose administered over 15-30 minutes every 8 hrs. (recommended 14 days (ranged 7-21)) N=50	Placebo N=50	At least 35 days		AstraZeneca Pharmaceuticals

			>48 hrs prior to randomization or who had an allergy to beta-lactam antimicrobial agents. Patients who received or were likely to require probenicid or who had progressing underlying disease, neutropenia, or cirrhosis (Child-Pugh class C) and pregnant or lactating females. Patient characteristics: Meropenum group: male/female: 32/18; age: 18-64: 34 (68%); 65-74: 9 (18%); >75: 7 (14%); alcohol use: 29 (58%); alcohol aetiology: 18 (36%); % necrosis: <30%: 15 (30%); ≥30%: 26 (52%); Ranson score (mean/median): 4.5/4 (1-8) Placebo group: male/female: 38/12; age: 18-64: 34 (68%); 65-74: 9(18%); >75: 7 (14%); Alcohol use: 33 (66%); Alcohol aetiology: 26 (52%); % necrosis: <30%: 10 (20%); ≥30%: 31 (62%); Ranson score (mean/median): 3.8/3.8 (0-					

			8)					
Effect Antibiotics vs placebo Pancreatic infection 9/50 vs 6/50 Mortality 10/50 vs 9/50 Non-pancreatic infection 16/50 vs 24.50 Surgical intervention 13/50 vs 10/50 Length of stay Not reported								
Isenmann R, Runzi M, Kron M et al. Prophylactic antibiotic treatment in patients with predicted severe acute pancreatitis: a placebo-controlled,	RCT 1++ Multi-centre, double-blind, randomized	N=119 (5 drop outs) N=114 included in ITT analysis	Inclusion criteria: patients with predicted severe attack of acute pancreatitis; defined as abdominal pain in combination with 3 fold elevation of serum amylase and/or lipase, serum CRP exceeding 150mg/L and/or presence of pancreatic necrosis on contrast-enhanced CT. Upper abdominal pain had	Ciprofloxacin 2 x 400 mg/day iv in combination with metronidazole 2 x 500mg/day iv N= 58 (n=41 with necrotizing pancreatitis)	Placebo N=56 (n=35 with necrotizing pancreatitis)	21 days		Bayer Vital and Ratiopharm

double-blind trial. *Gastroenterology.* 2004; 126(4):997-1004.			to start within 72 hrs of inclusion. Patient characteristics: Ciprofloxacin/metronidazole group: Male/female: 43/15; age: 47.9 (25.1-72.5); Alcohol aetiology: 32 (55%); Ranson 48h points: 2.5 (0-6) Placebo group: Male/female: 44/12; age: 45.6 (21.9-78.4); alcohol aetiology: 34 (60%); Ranson 48h points: 2 (0-7) Necrotizing subgroup: Ciprofloxacin/metronidazole group: Male/female: 31/10; Age: 46.4 (27.5-72.5); alcohol aetiology: 24 (59%); Ranson 48 h points: 3 (0-7) Placebo: male/female: 25/10; age: 46.5 (21.9-78.4); alcohol aetiology: 20 (57%); Ranson 48 h points: 2 (0-7)					

Effect Antibiotics vs placebo Pancreatic infection 7/41 vs 5/35 Mortality 3/41 vs 4/35 Non-pancreatic infection 12/41 vs 12/34 Surgical intervention 7/30 vs 14/30 Length of stay Not reported								
Craig RM, Dordal E, Myles L. Letter: The use of ampicillin in acute pancreatitis. *Annals of Internal Medicine.* 1975; 83(6):831-832.	RCT 1+	N=39 (47 episodes) Blinding unclear	Patients with acute pancreatitis. Diagnosed clinically and with elevated serum amylase Patient population – Antibiotic: mean age 41 yrs, mean serum amylase 325 U/dl Placebo: mean age 40 yrs, mean serum amylase 340 U/dl Alcohol aetiology 43/46 episodes	Antibiotic 1 g every 6 hrs intravenously. When ng tube removed and clear fluids begun 2 x 500 mg every 6hrs to complete a seven day course N=23 (episodes) NG suction and i.v fluids until asymptomatic for	Placebo N=23 (episodes)	Length of hospitalisation	Leukocytosis Pain or tenerness Serum amylase Fever	Bristol lab. Syracuse, New York

<table>
<tr><td></td><td></td><td></td><td></td><td>48 hrs</td><td></td><td></td><td></td><td></td></tr>
<tr><td colspan="9">Effect

<table>
<tr><td></td><td>Antibiotic
(mean no. of days with findings*)</td><td>Placebo
(mean no. of days with findings*)</td><td>P value</td></tr>
<tr><td>Leukocytosis (absolute counter greater than 10 000)
Subjects with 8 or more days findings</td><td>1.8

3</td><td>2.3

3</td><td>0.2</td></tr>
<tr><td>Pain or tenderness
Subjects with 8 or more days findings</td><td>3.0
1</td><td>3.0
2</td><td>0.5</td></tr>
<tr><td>Elevated serum amylase
Subjects with 8 or more days findings</td><td>6.0
10</td><td>5.0
9</td><td>0.3</td></tr>
<tr><td>Fever
Subjects with 8 or more days findings</td><td>3.0
1</td><td>3.0
0</td><td>0.6</td></tr>
<tr><td>Death (no.)
Complications (no.)</td><td>0
0</td><td>0
0</td><td>ns
ns</td></tr>
</table></td></tr>
<tr><td>Finch WT, Sawyers JL, Schenker S. A prospective study to determine the efficacy of antibiotics in acute pancreatitis. Annals of Surgery. 1976;</td><td>Double blind
Randomised by card 1+</td><td>N=58</td><td>Patients with acute pancreatitis. Diagnosed clinically and confirmed by serum amylase value greater than 160 Somogyi units per 100 ml

Exclusion criteria included: Blunt abdominal trauma, previous history compatible with cholelithiasis or choledocholithiasis, medications: steroids,</td><td>Antibiotics

N=31

Ampicillin 500 mg every 6 hrs 19/31 1 g every 6 hrs 11/31

(or Keflin 1 g every 6 hrs for 7 days if penicillin sensitivity, 1/31)</td><td>No antibiotics

N=27</td><td>24 mth study period</td><td>Length of hospitalisation, serum amylase, afebrile by day, recurrent pancreatitis, complications</td><td>None reported</td></tr>
</table>

183(6):667-671.			thorazine, thiazole diuretics, parathyroid disease, peptic ulcer, non-pancreas related fever Patient population – antibiotics: mean age 35 yrs, male:female 19:12, 14/71 black and 17/31 white, febrile on admission 15/31 (48%), average serum amylase 770 Somogyi units, average white blood count 10.4 1000/cc. Aetiology alcohol 22/31 Oral cholecystogram: normal study 8/19, non-visualisation on first dose 1/19, non-visualisation on double dose 6/19, normal on double dose 3/19, stones 1/19 Upper GI series: normal 15/19, C-loop deformity 3/19, retrogastric mass-pseudocyst 1/19 No antibiotics: mean age 37 yrs, male:female 15:12, 17/27 black and 10/27 white, febrile on admission	Nothing by mouth, NG suction until return of intestinal peristalsis and return of serum amylase to normal, intravenous fluids: maintenance 1500 cc 5% Dextrose with ¼ normal saline per square metre per 24 hr Replacement: gastric output to be replaced cc per cc with 5% Dextrose with ½ normal saline with supplemental KCL included. Anticholinergics: atropine 0.4 mg i.m every 6 hrs, Meperidine for pain, Librium 25 to 50 mg i.m four times daily, thiamine 100 mg				

			15/31 (44%), average serum amylase 780 Somogyi units, average white blood count 10.6 1000/cc. Alcohol aetiology 16/27 Oral cholecystogram: normal study 12/20, non-visualisation on first dose 1/20, non-visualisation on double dose 2/20, normal on double dose 3/20, stones 2/20 Upper GI series: normal 13/16, C-loop deformity 3/16, retrogastric mass-pseudocyst 0/16	i.m once on admission, no aspirin, Tylenol or other antipyrectics				

	Antibiotic N=31	No antibiotic N=27	P value
Total days hospitalised, mean (range)	10.4 (3 to 8)	11.3 (3 to 29)	ns
Normal Serum Amylase by day (range)	5.0 (2 to 11)	4.5 (2 to 13)	ns
Afebrile by day (range)	7.2 (3 to 14)	5.7 (1 to 11)	ns
Recurrent pancreatitis	6 (19.4%)	2 (7.4%)	P<0.05
Complications Alcoholic gastritis Delirium tremens Pseudocyst Deaths	 1 3 1 1	 1 4 0 0	 ns ns ns ns

Howes R, Zuidema GD, Cameron JL. Evaluation of	RCT 1+ Odd/even number allocation	N=95	Patients with a clinical diagnosis of acute pancreatitis with a serum amylase of 160 Caraway	Ampicillin N=44 1 g every 6 hrs for 5	No antibiotics N=47	Length of hospitalisation	Deaths, length of hospitalisation, amylase elevation, fever, septic	None reported

prophylactic antibiotics in acute pancreatitis. *Journal of Surgical Research.* 1975; 18(2):197-200.			units per 100 ml or greater	days Iv and then orally when patient eating History of penicillin allergy or if one developed then lincomycin 600 mg i.v every 8 hr and then 500 mg orally every 6 hrs for 5 days N=4 In addition i.v fluids, nasogastric suction, Demerol administration and intramuscular atropine			complications	

Effect

	Antibiotic	No antibiotic	P value
Deaths	0	0	ns
Hospitalisation (days)	9	12	ns
Amylase elevation (days)	2	2	ns
Fever (days)	3	3	ns
Septic complications (No. of patients)	5	6	ns

Pederzoli P, Bassi C, Vesentini S et al. A randomized multicenter	RCT 1+ Randomized multicentre	N=74	Inclusion criteria: no previous pancreatic disaease, admission within 48hrs of onset, no clinical evidence of sepsis, no previous antibiotic therapy,	Imipenem 0.5 g iv every 8 hrs + standard therapy (see control)- for 14 days	Control group: standard therapy: NG suction, H2 blockers, antiprotease drugs TPN and analgesics. N=33	14 days (until discharge)		Not reported

clinical trial of antibiotic prophylaxis of septic complications in acute necrotizing pancreatitis with imipenem. *Surgery, Gynecology & Obstetrics.* 1993; 176(5):480-483.			availability of contrast CT within 72 hrs of onset and presence of detectable pancreatic necrosis (graded on degree of enhancement- >30%=mildly necrotic; <30 but more than 50%=moderately necrotic; <50% extensively necrotic) Patient characteristics: Control group: Age (mean): 50; Male/female: 20/13; Alcohol aetiology: 11; Mean Ranson score: 3.6; Necrosis: mild: 20; moderate: 11; severe:2 Treatment group: Age (mean): 54; Male/female: 24/17; Alcohol aetiology: 13; Mean Ranson score: 3.7; Necrosis: mild: 15, moderate: 12; severe 14	N=41				
Effect Antibiotics vs placebo Pancreatic infection 5/41 vs 10/23 Mortality 3/41 vs 4/33 Non-pancreatic infection 6/41 vs 16/33 Surgical intervention 12/41 vs 11/33								

Length of stay Not reported								
Sainio V, Kemppainen E, Puolakkainen P et al. Early antibiotic treatment in acute necrotising pancreatitis. *Lancet.* 1995; 346(8976):663-667. Ref ID: 2564	RCT 1+ Numbered envelopes	N=60	Patients with severe necrotising alcohol-induced pancreatitis Inclusion criteria: CRP above 120 mg/L within 48 hrs of admission and low contrast enhancement of the pancreas	Efuroxime 3 doses of 1.5 p i.v N=30 Continued until clinical recovery and fall to normal CRP concentrations	Control N= No antibiotics were given before infection verified or CRP of more than 20% in the acute phase	Mortality Pancreatic infection Non-pancreatic infection Surgical intervention Length of stay	Until clinical recovery	
Antibiotics vs placebo Pancreatic infection 9/30 vs 12.30 Mortality 1/30 vs 7/30 Non-pancreatic infection Not reported Surgical intervention 7/30 vs 14/30 Length of stay Mean 33.2 (SD22.1) vs 43.8 (43.1)								

Schwarz M, Isenmann R, Meyer H et al. Antibiotic use in necrotizing pancreatitis. Results of a controlled study (English Abstract). *Deutsche Medizinische Wochenschrift.* 1997; 122(12):356-361. Ref ID: 2565	RCT 1+	N=26	Patients with sever acute pancreatitis and sterile necrosis	Oxfloxacin 200 mg bd i.v and metronidazole 500 mg bd iv for ten day	Control	Mortality Pancreatic infection Non-pancreatic infection Surgical infection	10 days	Not reported
Effect Antibiotics vs placebo Pancreatic infection 8/13 vs 7/13 Mortality 0/13 vs 2/13 Non-pancreatic infection 4/13 vs 6/13 Surgical infection Not reported Length of stay Not reported								

Nordback I, Sand J, Saaristo R et al. Early treatment with antibiotics reduces the need for surgery in acute necrotizing pancreatitis--a single-center randomized study. *Journal of Gastrointestinal Surgery.* 2001; 5(2):113-118. Ref ID: 2566	RCT 1- No details of allocation concealment, randomisation, blinding >50% patients excluded post-randomisation	N=92 (randomised) N=32 included	Patients with acute pancreatitis based on clinical criteria, raised serum amylase and CT verified pancreatitits. The diagnosis of necrotising pancreatitis was based on CRP > 150 mg/L during first 48 hrs after admission and necrotic areas in the pancreas on the CT Patient population: Imipenem male:female 23:2, mean age 47 yrs, alcohol aetiology 20/25, C-reactive protein mean 211, pancreatic necrosis on CT < 30% 8/25 Control: male:female 28:5, mean age 46 yrs, alchol aetiology 25/33, CRP mean 214, pancreatic necrosis on CT < 30% 13/33 There were no significant differences reported at baseline	Imipenem 1.0 g plus cilastatin i.v three times a day	Control	Mortality Pancreatic infection Non-pancreatic infection Surgical infection	5 days or more	Not reported

Antibiotics vs placebo Pancreatic infection 1/25 vs 6/33 Mortality 2/25 vs 5/33 Non-pancreatic infection 4/25 vs 1/33 Surgical intervention 2/25 vs 5/33 Length of stay