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Alcohol use disorder and the gut

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ABSTRACT

Acute and chronic gastrointestinal problems are common in the setting of excessive alcohol use, and excessive alcohol use is associated with injury to all parts of the gastrointestinal tract. There is mounting evidence of gastrointestinal injury and increased cancer risk even from moderate alcohol consumption. The major causes of alcohol-related morbidity and mortality within the gastrointestinal system are liver disease, pancreatitis and gastrointestinal cancer. Other alcohol-related intestinal dysfunction is common but not life-threatening, leading to diarrhoea, malabsorption and nutritional deficiencies. This review describes non-neoplastic and neoplastic alcohol-related disorders of the gastrointestinal tract, omitting the liver, which has been reviewed elsewhere.

Keywords Alcohol, cancer, gastrointestinal tract, gastro-oesophageal reflux, pancreatitis, pathogenesis.

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INTRODUCTION

Excessive alcohol use is associated with injury to all parts of the gastrointestinal (GI) tract, and several detailed reviews have been published [1,2]. The major causes of alcohol-related morbidity and mortality within the GI system are liver disease, pancreatitis and GI cancer. Other alcohol-related intestinal dysfunction is common, but not life-threatening, leading to diarrhoea, malabsorption and nutritional deficiencies. The relative risk of alcohol-related GI toxicity appears to differ between affected tissues and between benign and neoplastic disorders. Similarly, the pattern and type of beverage have not been consistently shown to predispose to any specific GI effects of alcohol. This narrative review describes these disorders site by site, omitting the liver, which has been reviewed elsewhere [3,4].

NON-NEOPLASTIC DISEASE

Parotid glands and oral cavity

Painless symmetrical enlargement of the salivary glands (termed sialosis or sialadenosis) has been associated with alcohol-related liver cirrhosis and is characterized by the triad of acinar cell hypertrophy, myoepithelial degeneration and neural degeneration [5]. Abelson *et al.* [6] found that 61% of patients with alcohol-related cirrhosis had sialosis. More recently, the contribution of alcohol to sialosis has been questioned, and nutritional deficiencies in the setting of liver disease are now thought to contribute to this condition. Guggenheimer *et al.* [7] identified sialosis in 9.3% of patients with cirrhosis on a transplant waiting-list, but only 39.3% of those had alcohol-related liver disease. The effect of alcohol use on salivary function in humans is controversial, with reports of increased, unaltered [8] and decreased salivary flow [5].

Oesophagus

Both acute and chronic alcohol consumption are associated with symptomatic gastroesophageal reflux disease (GORD). Reflux episodes were increased by 60 g of ethanol given with a meal to healthy subjects without alcohol dependence [9]. Upper GI symptoms are a classic accompaniment of hangover [10]. A recent meta-analysis of observational studies [11] showed increased risk of symptomatic GORD comparing alcohol drinkers versus non-drinkers with an odds ratio (OR) = 1.48, 95% confidence interval (CI) = 1.31–1.67, with a linear dose–response association. A number of mechanisms have been identified that may contribute to these effects of alcohol. Direct application of 40% ethanol, but not lower concentrations, causes injury to the oesophageal mucosa [12]. An acute dose of alcohol reduces lower oesophageal sphincter pressure (LOSP) [13] and maximal LOSP stimulated by a

meal [14]. Alcohol inhibits gastric and gallbladder emptying with greater effect related to increased alcohol concentration [15]. Chronic excessive alcohol use is associated with manometric abnormalities of increased LOSP [8] and increased oesophageal contraction amplitude, which suggests a compensatory mechanism in response to chronic alcohol exposure [16].

Upper GI bleeding (UGIB) is more frequent in patients with alcohol use disorder, especially those with liver cirrhosis. In a 2007 UK audit of 6750 patients with acute UGIB, 9% had known cirrhosis and 26% a history of alcohol excess [17]. A common alcohol-related cause for non-variceal UGIB is Mallory–Weiss syndrome. This condition is characterized by massive bleeding caused by tears in the mucosa at the cardio–oesophageal junction after vomiting. In one series, almost 50% of patients with Mallory–Weiss syndrome were associated with repeated retching and vomiting following excessive acute alcohol consumption [18].

Stomach

Alcohol-related gastritis and gastropathy

The term 'alcoholic gastritis' is non-specific, and used to describe a broad range of symptoms experienced by individuals who drink excessive alcohol. Despite extensive research there is limited evidence to support alcohol as a cause of gastritis. The term 'gastritis' is used to denote inflammation associated with mucosal injury. Epithelial cell damage and regeneration without associated inflammation are referred to as 'gastropathy' [19]. It is often difficult to establish with certainty that a particular agent, such as alcohol, has caused gastritis. In high concentrations, alcohol (80% volume/volume) has been shown to induce apoptosis in cells of the gastric mucosa in rats [20]. Lower alcohol concentrations that may be achieved during acute intoxication (1.0–4.0% volume/volume) have been shown to enhance neutrophil-mediated gastric endothelial cell injury in an *in-vitro* model [21]. Subepithelial haemorrhages of the gastric mucosa have been observed in chronic heavy drinkers but prominent inflammatory cells, which would be consistent with gastritis, were not identified [22]. Two separate prospective cohort studies found no link between alcohol consumption and *Helicobacter pylori(H.pylori)* negative gastritis in patients undergoing elective gastroscopy [23,24]. Moreover, there is no link between alcohol consumption and development of chronic atrophic gastritis (CAG) [25], and there has been evidence to suggest that moderate quantities of alcohol actually decrease the risk of CAG [26]. The reason for the reduced risk of CAG in alcohol drinkers is unclear, but it has been proposed that that it could be due to decreased risk of *H. pylori* infection. *H. pylori* is a common cause of CAG, but it has been observed that risk of infection is reduced with regular alcohol consumption [27,28].

Peptic ulcer disease

Despite multiple studies alcohol has not been identified as a risk factor for peptic ulcer disease (PUD) [29–31]. There are conflicting data on the role of alcohol and risk of peptic ulcer bleeding. A large population study in Denmark (n = 26518) showed moderate and heavy alcohol consumption to be associated with increased risk of ulcer bleeding [32], whereas smaller retrospective studies identified no such association [33,34].

Alcohol-related pancreatitis

Approximately 10% of patients with chronic alcohol use disorder develop attacks of clinical acute pancreatitis. Conversely, alcohol is responsible for approximately 30% of cases of acute pancreatitis in the United States [35]. In a large cohort study from the United States, alcohol was estimated to account for half the cases of chronic pancreatitis and the incidence has increased in the past 20 years [36], with a similar trend seen in Europe [37].

Definitions

The term 'acute pancreatitis' refers to an acute inflammatory process of the pancreas, with variable involvement of other regional tissues or remote organ systems. Chronic pancreatitis is characterized by chronic inflammation, glandular atrophy and fibrosis. Clinically, it manifests with pain and/or exocrine or endocrine insufficiency. The revised Atlanta classification of acute pancreatitis identified two phases of the disease: early, which can last for approximately 1 week, and a late phase that can run for weeks to months. Severity is classified as mild, moderate or severe (Table 1). Local complications of acute pancreatitis are peripancreatic fluid collections, pseudocyst, acute necrotic collection and walled-off necrosis (sterile or infected). The

Table 1 Revised Atlanta classification for acute pancreatitis severity.

Severity	*Criteria*
Mild	No organ failure No local complications (e.g. pancreatic necrosis, peripancreatic necrosis, peripancreatic fluid collection, splenic and portal vein thrombosis) No systemic complications Typically resolves in first week
Moderate	Transient organ failure < 48 hours and/or Local or systemic[a] complications
Severe	Persistent organ failure > 48 hours

[a]Systemic complications refers to exacerbation of pre-existing comorbidity precipitated by acute pancreatitis [38].

risk of death remains high in severe acute pancreatitis, with mortality rates of 36–50% reported [38].

Aetiology

The most common causes of acute pancreatitis in Western societies are gallstones and heavy alcohol use, which together account for approximately 75% of cases. Yadav *et al.* [36] found that while alcohol was the most common aetiology in men (59%), it was a less common aetiology in women (28%). Nonetheless, only a minority of heavy drinkers develop clinically evident pancreatic disease.

The association between alcohol and pancreatitis appears to be dose-related. Pancreatitis typically occurs in subjects who have consumed greater than 100 g alcohol per day for at least 5–10 years and rarely, if ever, follows an isolated large alcohol binge [39,40]. Once the disease is established, episodic heavy drinking often precipitates relapse. Relapses have been described after only 1 day of recurrent drinking. Many patients with acute alcoholic pancreatitis progress to chronic pancreatitis, with continued alcohol excess being a key prognostic factor [41].

Other than gallstones, relatively common causes for pancreatitis include hypercalcaemia of any cause and severe hypertriglyceridaemia [42], while in most series approximately 10% of cases are idiopathic.

Predisposing factors

Numerous investigators have attempted to account for this individual susceptibility by studying associations between alcoholic pancreatitis and potential risk factors. These studies have been previously reviewed and have focused on the amount, type and pattern of alcohol consumption, genetic markers, diet, hypertriglyceridaemia, tobacco consumption and pancreatic ischaemia. There is insufficient evidence to consider that any of the above factors are well established [43].

Two important genetic mutations are linked to acute and chronic pancreatitis, but not the alcoholic form. Mutations in the serine protease 1 gene (PRSS1), which encodes cationic trypsinogen and results in an autosomal dominantly inherited form of hereditary pancreatitis and mutations in the cystic fibrosis gene (CFTR) which are associated with an autosomal recessive form of pancreatitis [44]. Other mutations such as in chymotrypsin C (CTRC) have been identified as risk factors for non-alcoholic chronic pancreatitis alone [45]. In alcoholic pancreatitis, a mutation of the gene coding for pancreatic secretory trypsin inhibitor (SPINK1) has been described in 5.8% of patients compared with 1% of alcoholic controls [46]. Multiple single nucleotide polymorphisms have recently been identified in genes, including PRSS1, that are associated with acute and chronic alcohol related pancreatitis [47,48]. These studies support the concept that genetic factors influence susceptibility to alcohol-related pancreatitis, but given the small proportion of subjects that carry these mutations, other unidentified factors contribute to this disease.

Pathogenesis

Two important factors leading to tissue injury in pancreatitis are autodigestion and oxidant stress secondary to the inflammatory response. Several lines of evidence indicate that activated digestive enzymes play an important role in pancreatitis [49]. The inflammatory response triggered by autodigestion leads to production of reactive oxygen species, or free radicals. Free radicals are highly reactive and bind to lipids, proteins and nucleic acids, leading to cellular injury [50].

Several mechanisms have been proposed to explain why alcohol-related pancreatitis occurs only after many years of alcohol abuse. These include the role of progressive pancreatic fibrosis related to activation of pancreatic stellate cells by acetaldehyde and oxidative stress [51] and the potential for bacterial endotoxin to precipitate pancreatitis in the alcohol-exposed gland [52,53].

Diagnosis

Diagnosis of pancreatitis can be made if at least two of the following three criteria are met: an attack of severe abdominal pain and tenderness; serum amylase; and/or lipase more than three times the upper limit of normal or imaging studies, suggestive of inflammation in and around the pancreas [38]. Gallstones should be excluded by ultrasound examination, as this is the most common cause of pancreatitis other than alcohol [54].

Treatment

Despite improvements in treatment, approximately 20% of patients with acute pancreatitis have a severe course and 10–30% of these will die [55]. Treatment in an intensive care unit is generally required for severe cases, particularly those associated with respiratory or renal failure.

Initially, patients are treated with bed rest, analgesics, intravenous fluids and fasting. Despite evidence from randomized controlled trials there remains uncertainty concerning the type of analgesia and method of administration. All patients with acute pancreatitis require some form of analgesia, and there is no evidence to withhold opioids. Intravenous opiates may be required in cases of severe pain, and patient-controlled analgesia should be considered [56].

Early feeding (<48 hours) is probably beneficial, with a systematic review comparing delayed versus early feeding showing reduced length of hospital admission in mild and moderate cases [57]. In moderate to severe cases, delayed feeding is associated with higher rates of infected

peripancreatic necrosis, multiple organ failure and necrotizing pancreatitis [58,59]. Patients who cannot tolerate an oral diet may require enteral feeding for nutritional support, which is preferred over total parenteral nutrition (TPN) due to increased risk of infection and death [60,61].

Infection secondary to acute pancreatitis is common and can occur in up to 20% of patients. Despite the risk of infection, prophylactic antibiotics are not recommended regardless of the type or disease severity but should be started promptly in the setting of suspected or established infection [62].

Given the role of oxidative stress in the pathogenesis of theses diseases a number of anti-oxidant therapies have been evaluated for both acute and chronic pancreatitis with encouraging results from early small trials. However, a well-conducted trial in acute pancreatitis found no benefit [63]. Peritoneal lavage might improve the outcome by removing toxic inflammatory products from the peritoneum, but the results of controlled studies have been conflicting [64,65].

Surgery is not commonly required, the main indication being necrotizing pancreatitis. Observational data support delaying surgical debridement of necrotic tissue for at 3–4 weeks if possible while the patient's medical condition is optimized [66]. Pancreatic abscess carries a very high mortality and is an absolute indication for drainage by open surgery or percutaneous techniques [67]. Small pseudocysts may resolve spontaneously, but large or symptomatic ones usually require drainage via endoscopic, percutaneous or operative techniques [68].

Chronic pancreatitis

Recurrent episodes of acute pancreatitis, clinical or subclinical, may lead to chronic pancreatitis. Chronic excessive consumption of alcohol is the most common cause and accounts for approximately 50% of cases in western societies [42]. Interestingly, idiopathic pancreatitis is the most common type in India (tropical pancreatitis) and China, accounting for approximately 70% of all cases of chronic pancreatitis [69].

Clinical features

The main clinical feature is usually pain, and this may be very challenging. Like that of acute pancreatitis, the pain of chronic pancreatitis is typically diffusely located in the upper abdomen and may radiate to the back when severe. Pain tends to increase with meals and decreases both appetite and food consumption, often resulting in weight loss. A minority present without pain. The other manifestations are endocrine (diabetes mellitus) and exocrine failure (steatorrhoea). Weight loss is common but typically mild, and vitamin deficiency is generally subclinical. Investigations may reveal malabsorption of fat-soluble vitamins and osteopenia. Other complications include pseudocyst formation, bile duct or duodenal obstruction, pancreatic ascites or pleural effusion, splenic vein thrombosis, pseudoaneurysms and pancreatic cancer [42].

Treatment

Complete abstinence from alcohol is essential to minimize progression of the disease. Reassurance that the disorder is benign with a tendency to slowly remit may be helpful. Non-narcotic analgesia may suffice, but opioids are often required and should not be unreasonably withheld. A Danish randomized double-blind clinical trial of 64 patients found that pregabalin compared with placebo resulted in a 36% versus 24% decrease in average daily pain score after 3 weeks of treatment [70]. Coeliac plexus neurolysis or coeliac ganglia neurolysis improves pain in approximately 60% of chronic pancreatitis patients, but symptoms often recur and the procedure caries a significant risk of complications [71,72]. Pancreatic enzyme supplements have been evaluated for the treatment of pain, but the evidence is mixed [73]. A trial of 1 month is sufficient to determine whether or not this works in practice.

There is mixed evidence concerning anti-oxidant therapy in chronic pancreatitis. One study, using a combination preparation that contained selenium, beta-carotene, vitamin C, vitamin E and l-methionine, found reduced pain and improved quality of life [74]. No benefit was identified in a larger double-blind randomized controlled trial despite achieving sustained elevated serum levels of anti-oxidants [75].

The relationship between pancreatic duct obstruction and pain is not clear, but relief of obstruction is frequently clinically associated with relief of pain. Endoscopic approaches to dilate pancreatic duct strictures and remove calculi are preferred when medical management fails to adequately control symptoms, and surgery is typically reserved for refractory cases [76]. Two small randomized trials comparing endoscopic and surgical treatment for pancreatic duct obstruction in chronic pancreatitis showed that surgery was associated with better long-term analgesia and quality of life [77,78]. An emerging treatment option for resistant cases of pain is total pancreatectomy with islet auto-transplantation (IAT). This procedure has shown favourable outcomes with regard to pain reduction and enables a significant proportion of patients to remain independent of insulin supplementation [79].

Exocrine failure is treated by dietary modification, vitamin supplementation and pancreatic enzyme replacement [80]. Diabetes associated with chronic pancreatitis is known as Type 3c (pancreatogenic) diabetes mellitus. It is treated with dietary modification, treatment of malabsorption and diabetes-specific therapy, with most requiring insulin. Long-term surviving patients with this form of diabetes are prone to diabetic complications and

should be monitored accordingly [81]. Patients with substantial steatorrhoea may develop deficiency in fat-soluble vitamins A, D, E and K. Serum levels of these vitamins should be regularly monitored with supplementation as appropriate [80].

Small intestine

Diarrhoea is common among those who drink alcohol excessively, both acutely and chronically. Multiple factors contribute to this problem, including altered motility, permeability, blood flow and nutritional disorders. Small intestinal mucosal injury can occur after acute or chronic administration of alcohol [82]. Gut microbiome research has shown that alcohol may lead to quantitative and qualitative dysbiotic changes, leading to inflammation and hyperpermeability [83].

Ethanol inhibits absorption of actively transported sugars, dipeptides and amino acids. Many defects in absorption have been reported in patients with alcohol use disorder, including water [84,85], carbohydrate, lipid, vitamins (notably thiamine and folate) and minerals (calcium, iron, zinc and selenium) [82].

Thiamine and/or folate deficiencies are common and clinically relevant for patients with alcohol use disorder. Thiamine deficiency is due to a combination of decreased intake, decreased intestinal absorption and impaired utilization by cells [86]. Thiamine deficiency can result in Wernicke's encephalopathy (WE), which can progress to irreversible Korsakoff's syndrome if left untreated. Treatment of suspected WE requires administration of repeated high doses of parenteral thiamine. Oral thiamine is ineffective in treatment of severe deficiency due to very limited intestinal absorption [87]. Folate deficiency is secondary to decreased intake, reduced intestinal absorption, impaired hepatic storage and decreased renal tubular re-absorption [88]. Folate deficiency can lead to macrocytic anaemia, and may promote the progression of alcohol-related liver disease [89,90]. Treatment is generally with oral folic acid, but parenteral folic acid is often preferred in the setting of severe symptomatic anaemia [91].

Colon

Portal hypertension from alcohol-related liver disease may manifest uncommonly with haemorrhoids and rarely with colonic varices. Colonic varices appear as filling defects on barium enema and may occur in any part of the colon, most commonly in the rectum [12]. Alcohol has been shown to promote bacterial overgrowth and dysbiosis in the colon [92] which may promote alcohol-related liver disease secondary to increased bacterial endotoxin in the portal circulation [93].

Alcohol consumption has been correlated with increased GI symptoms in inflammatory bowel disease. A retrospective study found that documented alcohol use resulted in increased intestinal infections, parenteral antibiotics, computerized tomography (CT) abdomen scans and large intestine biopsies [94]. This study also used a mouse model of ulcerative colitis to show that binge drinking after an induced colitis flare resulted in increased weight loss, colonic shortening, inflammation and infection.

NEOPLASTIC DISEASE

Alcohol and GI cancer

Alcohol use is a well-recognized risk factor for neoplasms in most parts of the GI tract, including tumours of the tongue, mouth, pharynx, larynx, oesophagus, stomach, pancreas, colon and liver [95,96]. The effect of alcohol on cancer risk appears to be dose-related. A large meta-analysis of alcohol consumption and site-specific cancer risk reported that even relatively modest alcohol consumption of 12.5 g or less a day, well within the guidelines for many countries, is associated with an increased relative risk (RR) for some gastrointestinal cancers, including oropharyngeal (RR = 1.13) and oesophageal SCC (RR = 1.26). At moderate and high levels of alcohol consumption there is increased risk of cancer in other regions of the gastrointestinal tract, including pancreas, liver, colon and stomach [97].

The pathophysiology of alcohol-associated gastrointestinal malignancy is varied. Current understanding suggests that alcohol and its metabolite acetaldehyde have direct mutagenic and carcinogenic affects. Acetaldehyde has the ability to produce aberrant methylation of DNA. Chronic alcohol consumption induces CYP2E1, which increases reactive oxygen species which, in turn, generate aberrant DNA products. Alcohol causes hypomethylation of DNA and has the direct effect of increasing vascular endothelial growth factor and polyamines, which promote cell growth and tumorigenesis [98]. Interestingly, racial differences appear to affect the risk of carcinogenesis. In Asia, a large proportion of individuals carry a mutation of acetaldehyde dehydrogenase (ALDH) 2, which has very low activity leading to an accumulation of acetaldehyde after alcohol consumption. Homozygotes of the ALDH2 mutation develop severe side effects with small amounts of alcohol and hence reduction of their drinking protects against alcohol-related disorders [99].

Oropharynx and oesophagus

Alcohol use is associated with an increased incidence of oesophageal and oropharyngeal cancer, especially in

those who also smoke. A Chinese population-based case–control study of oesophageal cancer with 902 cases and 1552 controls showed the combined effect of heavy smoking and drinking among men was pronounced: the OR was 12.0 for those who smoked more than one pack per day and drank more than 750 g of ethanol per week [100]. Blot *et al.* [101] reported a 5.8-fold increased risk of oesophageal cancer among those who drink alcohol, a 7.4-fold increased risk among smokers and a 38-fold increased risk among those who both drank and smoked. A large meta-analysis showed an increased RR of oropharyngeal cancer and oesophageal squamous cell carcinoma (ESCC) with any consumption of alcohol, but no association with oesophageal adenocarcinoma, even at higher levels of consumption >50 g/day [97]. Light alcohol intake appears to be associated with ESCC mainly in studies in Asia, which suggests a possible role of genetic susceptibility factors [102].

Stomach

The association between gastric cancer and alcohol consumption appears to be modest. Meta-analysis of 34 557 patients provided definitive evidence of a lack of association between moderate alcohol drinking and gastric cancer risk [103]. There was, however, a positive association with heavy alcohol drinking (RR = 1.14, 95% CI = 1.08–1.21) above 50 g/day. Gastric non-cardia adenocarcinomas were more common than gastric cardia cancers. Similar findings were found in a meta-analysis by Bagnardi *et al.* [97] and in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study [104]. This study also showed beer, but not wine or spirits, to be positively associated with gastric cancer.

Colonic

Alcohol has been shown to increase risk of colorectal cancer in moderate and heavy drinkers, but there is less robust evidence of increased risk in light drinkers, often defined by studies as less than 12.5 g/day. A large meta-analysis of 27 cohort and 34 case–control studies showed no increase in risk for light drinkers (RR = 1.00, 95% CI = 0.95–1.05) but increased risk in moderate drinkers (12.6–49.9 g/day) and heavy drinkers (>50 g/day), with RR = 1.21, 95% CI = 1.13–1.28 and RR = 1.52, 95% CI = 1.27–1.81, respectively [105]. Moskal *et al.* identified a modest but increased risk of colon cancer even in light drinkers, with RR = 1.03, 95% CI = 1.02–1.05 and RR = 1.15, 95% CI = 1.07–1.25 for alcohol consumption of 25 g/week and 100 g/week, respectively [106]. The RRs for men are slightly higher than for women, and the risk was seen to increase from proximal colon to rectum [105].

Pancreatic

Chronic pancreatitis is a well-recognized risk factor for pancreatic cancer. The role of alcohol in pancreatic cancer pathogenesis in the absence of pancreatitis is uncertain, but current evidence suggests a link. Within the European Prospective Investigation into Cancer and Nutrition study a positive association between alcohol intake, particularly with heavy intake (>60 g/day), and pancreatic cancer in men was established with a hazard ratio (HR) = 1.77, 95% CI = 1.06–2.95. The association did not meet statistical significance for the cohort of women [107]. This study found that smoking did not alter the association between alcohol and pancreatic cancer, which has previously been considered a potential confounder [108].

KEY POINTS

- Excessive alcohol use is associated with injury to all parts of the gastrointestinal tract, particularly the pancreas.
- Alcohol increases the risk of cancer in all regions of the gastrointestinal tract, even at low levels of consumption.

CONCLUSION

The gastrointestinal consequences of alcohol are very common but often neglected, and there are many areas where further research would be valuable. For example, the link between even regular moderate alcohol use and colorectal cancer supports international guidelines to limit alcohol use even in the absence of an alcohol use disorder. Alcoholic pancreatitis is a life-threatening disorder that is becoming more common, but the pathogenesis and genetic factors contributing to the disease are poorly understood. Diagnosis and research into the cause of these gastrointestinal disturbances allows for better management of their symptoms and, by linking these to the underlying alcohol use disorder, sets the foundation for comprehensive treatment and prevention of recurrences. This requires screening for alcohol use, appropriate intervention in medical and surgical gastrointestinal clinical services and access to specialist support where alcohol use disorders are identified.

Declaration of interests

None.

Author Contributions

Paul Haber: Conceptualization; data curation. **Nicholas Kortt:** Data curation.

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