Quality in Practice Committee

The management of chronic pancreatitis in primary care

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Guidelines are not policy documents. Feedback from local faculty and individual members on ease of implementation of these guidelines is welcomed.

EVIDENCE-BASED MEDICINE
Evidence-based medicine is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.

In this document you will see that evidence and recommendations are graded according to levels of evidence (Level 1 – 5) and grades of recommendations (Grades A-C) respectively. This grading system is an adaptation of the revised Oxford Centre 2011 Levels of Evidence.

LEVELS OF EVIDENCE
Level 1: Evidence obtained from systematic review of randomised trials
Level 2: Evidence obtained from at least one randomised trial
Level 3: Evidence obtained from at least one non-randomised controlled cohort/follow-up study
Level 4: Evidence obtained from at least one case-series, case-control or historically controlled study
Level 5: Evidence obtained from mechanism-based reasoning

GRADES OF RECOMMENDATIONS
A. Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. (Evidence levels 1, 2)
B. Requires the availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendation. (Evidence levels 3, 4).
C. Requires evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level 5).

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1.0 Introduction

1.1 Background
Chronic pancreatitis (CP) is defined as a chronic, inflammatory disease, characterised by an irreversible change of the pancreas, causing pain and/or permanent loss of function\(^1\). Life altering consequences of CP include chronic pain, pancreatic insufficiency and diabetes mellitus, contributing to markedly reduced median survival of 15–20 years post-diagnosis\(^{2,3}\).

Prevalence of CP in Ireland is 11.6–13.0 per 100,000 population\(^4\) and 11–49.3 per 100,000 in Europe\(^5,6\). The incidence of chronic pancreatitis is unknown in Ireland, but estimated at 4.4–11.9 per 100,000 annually worldwide\(^6\), and is increasing\(^7,8\).

The predominant aetiology is alcohol. Other aetiologies include recurrent acute pancreatitis, hyperlipidaemia, ductal obstruction, cystic fibrosis, idiopathic, and hypercalcaemia. Features of CP include pancreatic atrophy, fibrosis, duct distortion, calcification, and dysplasia.

CP is best managed in primary care. Severely ill patients require inpatient care, otherwise, patients may be managed in the community setting with out-patient support\(^9,10\). General Practitioners (GPs) and Practice Teams have important roles in treating chronic pain, endocrine / exocrine impairment, determining the need for referral, and care-coordination between the hospital and home.

Aetiology
Recurrent episodes of acute pancreatitis can lead to CP. Relevant risk factors include ongoing alcohol abuse, smoking, genetic factors and autoimmune diseases.

Determining aetiology of CP is an important step in ensuring appropriate and focused treatment. Aetiology is defined through investigation, consideration of all risk factors (particularly smoking & alcohol), family history and laboratory findings. In western countries, alcohol is the most common aetiological factor, accounting for up to 80% of all cases\(^11\).

A recent Irish study\(^4\) showed hospital discharges for “other aetiology” chronic pancreatitis were double that of “alcohol aetiology” chronic pancreatitis, where “other aetiology” includes idiopathic and genetic causes, among others. Earlier work reported an increase in alcohol-related acute pancreatitis admissions in Ireland\(^12\).
AETIOLOGY | DESCRIPTION
--- | ---
Alcohol | • Estimated 80g alcohol per day (less in females) for 6–12 years required to produce symptomatic pancreatitis, disease risk increases with amount /duration of consumption. There is individual variability; some people develop CP with as low as 20g/day alcohol, others may drink >200g/day before disease develops.
• Alcohol-related CP is characterised by pain, exocrine insufficiency and diabetes.

Genetic factors | • Early onset idiopathic CP (<20 years of age) or patients with idiopathic CP should be referred for genetic testing for associated variants.
• Diagnosis of cystic fibrosis should be ruled out in all patients with onset of CP symptoms <20 years, as well as all patients with idiopathic CP, regardless of age of onset (Grade 1B – strong consensus).
• Genetic susceptibility gene variants include:
  - Cationic trypsinogen (PRSS1)
  - Serine Protease Inhibitor Kazal Type-1 (SPINK1)
  - Carboxypeptidase A1 (CPA1)
  - Cystic Fibrosis Transmembrane Conductance Regulator (CFTR)
  - Chymotrypsinogen C (CTRC)
  - Carboxyesterlipase (CEL)
• In suspected idiopathic CP, early onset of symptoms, or in the absence of aetiological cause, cystic fibrosis should be excluded using chloride iontophoresis if no other clinical signs. Check availability with local pathology services.

Idiopathic | CP in the absence of any other known clinical cause

Smoking | Smoking is an independent factor in the development of CP. Smoking accelerates disease progression, and patients perception of pain.

Autoimmune disease | Autoimmune pancreatitis (AIP) includes recurrent attacks of abdominal pain, jaundice, and morphological change of the pancreas, ductal stenosis and this disease is often mistaken for pancreatic cancer. AIP should be ruled out in the absence of other causes of CP. Two subtypes: AIP type 1 and AIP type 2. Both respond well to steroids, and in many steroids dramatically improve the condition.

Other | • Hereditary pancreatitis
• Hyperthyroidism
• Hypertriglyceridemia
• Ductal obstruction
• Pancreas divisum
• Trauma
• Tropical pancreatitis

**TABLE 1: Aetiology of chronic pancreatitis**
1.2 Aims of the Document
The aim of this document is to provide general practitioners and practice nurses with an up-to-date, easy-to-follow, evidence-based guidance document on the care of people with CP in the community.

It may be especially helpful for designing a care plan for people who are newly diagnosed, and in planning clinical audits.

1.3 Summary of key points / recommendations
At diagnosis, ensure appropriate coding for CP, and for tobacco and alcohol use, using relevant ICPC2 codes, noting the date of diagnosis and main care details are reflected clearly in the summary or problem-orientated medical record.

1. Multidisciplinary management is important
2. Pain should be measured using validated pain scale; adequate pain management is important
3. Refractory continuous pain is an indication for interventional or surgical treatment
4. Pancreatic enzyme replacement therapy (PERT) is important for management of pancreatic exocrine insufficiency (PEI)
5. Endocrine function should be assessed annually by checking HbA1C
6. Patients should undergo regular, structured nutritional assessment
7. Patients intolerant of diet and oral supplementation should be referred for enteral nutrition (EN)
8. Patients should undergo periodic bone mineral density (BMD) testing by DXA and educated regarding bone health. People with osteopenia should have a follow-up DXA at 2 years.
9. Patients with progressive osteoporosis or history of fragility fracture should commence treatment, be screened for associated causes, and consider referral to bone specialist
10. Patients should be counselled on alcohol avoidance and smoking cessation
11. Each patient should have a self-management plan which includes advice on comorbidities, lifestyle, and detailed / listed actions in case of exacerbation
12. Psychological co-morbidities require consideration at reviews (e.g. depression, anxiety, opiate abuse)
13. Where necessary, referral to addiction services is important
2.0 Subtopics

2.1 Clinical presentation and diagnosis
Clinical symptoms are non-specific and varied (Table 1). There is no accepted diagnostic gold standard for CP. Diagnostic tests of pancreatic structure and function are required, which fall into four broad categories: histology, radiological studies, endoscopic studies, and pancreatic function tests.

<table>
<thead>
<tr>
<th>SYMPTOM</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>Abdominal pain, upper or middle abdomen, typically radiating to the back, may be intractable and difficult to manage</td>
</tr>
<tr>
<td>Gastrointestinal symptoms</td>
<td>Steatorrhoea, diarrhoea, constipation, nausea, vomiting, bloating and distention, excessive flatulence, borborygmi, dyspepsia, heartburn</td>
</tr>
<tr>
<td>Nutrition-related</td>
<td>Anorexia and food aversion (due to abdominal pain, gastrointestinal symptoms, nausea, vomiting, alcohol abuse, heavy smoking)</td>
</tr>
<tr>
<td></td>
<td>Weight loss, muscle depletion, fat-soluble vitamin deficiencies (ADEK) due to malabsorption, B12, Thiamine and Folate deficiencies secondary to alcohol use</td>
</tr>
<tr>
<td></td>
<td>Impaired glycaemia (fasting glucose, symptoms of diabetes)</td>
</tr>
</tbody>
</table>

TABLE 2: Clinical presentation and symptoms of chronic pancreatitis

2.2 General Practitioner role in chronic pancreatitis management
The management priorities for chronic pancreatitis in general practice include the following:

1. Education and modification of lifestyle (smoking cessation, alcohol cessation, counselling)
2. Appropriate, early, and adequate use of PERT
3. Arranging and reinforcing dietary intervention
4. Effective stepwise approach to analgesia
5. Annual practice review, to include influenza and pneumonia vaccination, and co-ordination of multidisciplinary care
6. Consultation with patients regarding goals and objectives
7. Provision of appropriate and high quality information, including a written care plan
8. Ensuring good care coordination, particularly during transitions of care
9. End of Life Planning in progressive advanced illness
FIGURE 1: Algorithm for the management of chronic pancreatitis in primary care

Managing chronic pain

Pain may be the first presentation of chronic pancreatitis in most patients. It is the most difficult to manage and dominant symptom in most patients. It may be intermittent or constant and associated with reduced quality of life.

Adequate pain therapy is important (Evidence level: 2. Grade of recommendation: A).

Refractory pain should be considered an indication for interventional or surgical treatment.
Cessation of alcohol, and possibly smoking, improves pain in chronic pancreatitis \[(Evidence\ level: 1. Grade\ of\ recommendation: B)\]. There is insufficient evidence that PERT or antioxidant supplements help to reduce pain\[22\].

The HaPanEU guidelines\[16\] recommend a step-wise approach to pain relief in chronic pancreatitis:

- **Level 1 analgesia**: Paracetamol (avoid non-steroidal anti-inflammatory drugs (NSAIDS), due to their gastrointestinal toxicity)
- **Level 2 analgesia**: Tramadol (shown to be superior to morphine with fewer side-effects)
- **Level 3 analgesia**: Opiates, including morphine (high risk for addiction and side-effects including constipation and other gastrointestinal symptoms)

**Evidence level 4, Grade C.** This approach should be reflected in the written care plan for each individual.

**Managing pancreatic exocrine insufficiency (PEI)**

PEI is caused by pancreatic duct blockage, inadequate stimulation of pancreatic secretions, insufficient production of digestive enzymes, and inadequate mixing of pancreatic juice with ingested foods. PEI may occur without pain, resulting in steatorrhea, weight loss, undernutrition, and related consequences, such as vitamin deficiency and osteoporosis.

**Symptoms and diagnosis**

In chronic pancreatitis stools are bulky, pale (white, cream, grey), floating, offensive, requiring several flushing attempts to remove. The appearance of oil in stools is pathognomonic of chronic pancreatitis and represents gross fat malabsorption of \(>40g/day\).

There are several methods for diagnosing PEI (quantification of coefficient fat absorption (CFA), C-triglyceride (CMTG) breath tests, and faecal-elastase-1 (FE-1))

FE-1 is the most commonly performed test in Ireland to diagnose PEI. It requires the collection of a sample of formed stool, but does not require fasting, a special diet, nor does PERT need to be halted prior to measuring. Availability of testing varies, and it is advised to liaise with local Pathology Services. FE-1 is less accurate for mild-moderate PEI. Result parameters are detailed below; check with local pathology services regarding availability.

<table>
<thead>
<tr>
<th>CATEGORY OF PEI</th>
<th>FE-1 RESULT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>(&gt;200ug/g)</td>
</tr>
<tr>
<td>Mild</td>
<td>(&lt;200ug/g)</td>
</tr>
<tr>
<td>Severe</td>
<td>(&lt;100ug/g)</td>
</tr>
</tbody>
</table>

**TABLE 3**: Category of pancreatic exocrine insufficiency (PEI), faecal elastase-1 reference values
**Treatment**

The gold standard treatment of PEI is PERT, which reduces fat malabsorption, and helps restore normal nutrition. Evidence: Level 1, Grade A

- PERT should be started at a minimum dose of 40,000–50,000 u with meals, and 20,000–25,000 u with snacks (prescription of a variety of doses e.g. 10,000, 25,000, 40,000 u is helpful for flexibility)
- Take with a cold drink at the start of a meal, or dispersed through the meal
- Dose may need to be titrated up, depending on symptoms, food eaten, cooking methods etc. The patient should be educated regarding adjusting the dose. (Online resources are available [here](#) and [here](#).)
- No need to avoid dietary fat (low-moderate fat intake acceptable). Very low fat, or ‘fat-free’ diets not recommended
- Increase dose where there is insufficient response (increase initially by 100%)
- Maximum dose: 10,000 units lipase / Kg body weight (e.g. for 70Kg man, max 700,000 units lipase per day)
- Acid-suppression medication may be needed due to reduced pancreatic secretion of bicarbonate
- Monitor and sense check patient understanding and compliance
- If ongoing insufficient response to PERT, reconsider PEI diagnosis, consider alternative causes of malabsorption (coeliac disease, small intestinal bacterial overgrowth, giardiasis, biliary obstruction), reduce dietary fat (last resort)
- Monitoring by a specialist dietitian is required

**Managing endocrine impairment**

Diabetes develops in chronic pancreatitis due to the destruction of islet cells. Diabetes associated with diseases of the pancreas (including chronic pancreatitis) is known as type 3c (pancreatogenic) diabetes. Hypoglycaemia is a key clinical risk for these individuals. Type 3c diabetes has features of both type 1 and type 2 diabetes, but is distinct from both. Like type 2 diabetes, ketoacidosis is rare and hyperglycaemia is usually mild. As in type 1 diabetes, hypoglycaemia is frequent and insulin levels are low. Type 3c diabetes is characterised by swings between hyperglycaemia and hypoglycaemia (brittle diabetes), and management is complicated by poor dietary intake, alcohol consumption, malabsorption, and undernutrition. Specialist endocrinology and dietetic intervention is usually required to ensure or maintain optimal control.

Endocrine function should be assessed annually (Glycated haemoglobin, HbA1c), and where results are equivocal, consider oral glucose tolerance testing.

**Evidence: Level 5, Grade C**
FIGURE 2: Type 3c Pancreatogenic diabetes mellitus and suggested management strategies: adapted from Duggan et al\textsuperscript{3}, Duggan and Conlon\textsuperscript{4}
Nutritional status and bone health

People with CP are at a high risk of undernutrition. Evidence Level 3 Serial clinical reviews should include measurement of weight and BMI. They should undergo structured nutritional assessment and should receive advice from a specialist pancreatic dietitian. Grade C

People with chronic pancreatitis are at increased risk of osteoporosis, osteopenia and low-trauma (fragility) fracture. Evidence Level 3. Irish research shows 1 in 4 patients with chronic pancreatitis have osteoporosis and almost two-thirds of patients have either osteoporosis or osteopenia25,26

- All patients with chronic pancreatitis should have bone density scanning (DXA), and be counselled on preventative measures (adequate calcium/vitamin D, and smoking/alcohol avoidance). Grade B
- Patients with osteopenia should undergo repeat DXA at 2 years. Grade B
- Patients with osteoporosis should receive appropriate medication, screening for associated causes, and consider a referral to a bone specialist for evaluation. Grade B

Alcohol abstinence/addiction advice

If a patient has a history of alcohol abuse then full alcohol abstinence is a key objective in their management. If the aetiology is not alcohol, full abstinence remains important, due to the toxic effect of alcohol on the pancreas. Continued alcohol consumption and smoking increase the risk of recurrent attacks of pancreatitis and disease progression27,28. In a large Cochrane meta-analysis, including 21 randomised controlled trials, brief cognitive-behavioural interventions in primary care have consistently been shown to produce reductions in alcohol consumption29.

All patients (and particularly those with alcohol aetiology) should be counselled regarding full alcohol avoidance30. Evidence level: 2/3, Grade A. Even if complete abstinence is not achieved, it is probable that reductions in alcohol consumption are useful.

Smoking

Patients who smoke should be strongly advised and supported to stop smoking and referred for community support/addiction services to assist. Smoking cessation can delay disease progression and can have a substantial effect on the subsequent mortality31. All patients with chronic pancreatitis should be consistently engaged with and counselled on smoking cessation. Evidence level: 2/3 Grade A

Patient education, support and self-management

CP is a chronic disease, with personal implications and socioeconomic consequences including disability, divorce and depression32. Sustained education
and support over time can play an integral role in improving skills and abilities to cope with illness and health status.

Educational aspects should be incorporated into all aspects of care in all settings. Patients will benefit from being consistently educated about optimising risk, recognising symptoms, and improving their own coping skills including treatment options and factors which worsen symptoms and increase disease severity. Each individual should have a written management plan, including advice on exacerbations, comorbidities, and lifestyle changes. Patients should be assessed for psychological co-morbidities (e.g. anxiety depression, opiate abuse)\(^2^0\). Evidence level: 5, Grade of recommendation: D

<table>
<thead>
<tr>
<th>SUGGESTED FOLLOW-UP</th>
<th>GP MANAGEMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical evaluation</td>
<td>History, symptoms, family history, weight, BMI, diet, muscle / fat stores</td>
</tr>
<tr>
<td>Pain management</td>
<td>Stepwise approach to analgesia (avoid NSAIDS)</td>
</tr>
<tr>
<td></td>
<td>(1) Paracetamol</td>
</tr>
<tr>
<td></td>
<td>(2) Tramadol</td>
</tr>
<tr>
<td></td>
<td>(3) Opiates (morphine)</td>
</tr>
<tr>
<td>Pancreatic exocrine insufficiency and enzyme therapy</td>
<td>Adequate symptomatic response – review and titrate dose</td>
</tr>
<tr>
<td></td>
<td>Consider acid suppression medication</td>
</tr>
<tr>
<td>Endocrine management (Type 1, 2, 3C Pancreatogenic DM)</td>
<td>Glycated haemoglobin, HbA1c, and consider oral glucose tolerance test</td>
</tr>
<tr>
<td></td>
<td>Dietary advice, establish diabetic care, insulin</td>
</tr>
<tr>
<td>Nutrition / bone health</td>
<td>Referral, monitoring clinical symptoms, treating malnutrition, biochemistry evaluation, fat soluble vitamins, vitamin B12, 25OHD (vitamin D), PTH, arrange initial and monitoring DEXA scans (if available)</td>
</tr>
<tr>
<td>Alcohol / smoking cessation, addiction advice</td>
<td>Screen, manage, referral, review, reinforcement</td>
</tr>
<tr>
<td></td>
<td>Community services, AA, counselling, support groups. Code in the EMR.</td>
</tr>
<tr>
<td>Patient education, support and self-management</td>
<td>Physical activity, mental health awareness, quality of life, social issues</td>
</tr>
<tr>
<td></td>
<td>Periodically update sources of patient education information</td>
</tr>
</tbody>
</table>

**TABLE 4: Multimodal follow-up of chronic pancreatitis patients**
National Referral Centres for Chronic Pancreatitis

Secondary and Tertiary Care services in Ireland are evolving in relation to CP. At time of writing, the following services can provide general practice teams with advice and guidance.

1. **Centre for Pancreatico-biliary Disease**, Tallaght Hospital, Dublin 24
   
   **Professor Kevin Conlon**, Professor of Surgery  
   Secretary: **Carol Cullen** (01-414 3363) Email: [carol.cullen@amnch.ie](mailto:carol.cullen@amnch.ie)  
   
   **Marie Egan**, Clinical Nurse Specialist (Pancreatico-biliary diseases)  
   (01-414 3361) Email: [suzanne.egan@amnch.ie](mailto:suzanne.egan@amnch.ie)

2. **St Vincent’s University Hospital**, Elm Park, Dublin 4
   
   **Professor Kevin Conlon**, Professor of Surgery  
   Surgical secretary: **Fiona McGee** (01-221 5031) Email: [fmcgee@svhg.ie](mailto:fmcgee@svhg.ie)

   **Anne McGuire**, Clinical Nurse Specialist  
   (01-221 3537) Email: [a.mcguire@st-vincents.ie](mailto:a.mcguire@st-vincents.ie)
3.0 References


