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A comprehensive pain assessment tool (COMPAT) for chronic pancreatitis: Development, face validation and pilot evaluation

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ABSTRACT

Background/objectives: Chronic pancreatitis (CP) pain is challenging to treat. Treatment selection is hampered by there being no validated pain assessment tool that accounts for the complexity of CP pain and its underlying mechanisms.
This study aims to develop a comprehensive pain assessment tool (COMPAT) specific for CP, evaluate its face validity with experts and patients and test it with a pilot cohort of patients.
Methods: COMPAT was developed from existing pain assessment tools and a literature review. Face validity was conducted by pancreatologists and CP patients using an item-content validity index for importance, relevance and clarity. Subsequent revisions were made to COMPAT. A pilot cohort of CP patients tested COMPAT.
Results: COMPAT was developed and covered all important aspects of CP pain. Experts and CP patients reported that 70% of questions were important and relevant to CP pain. Most experts were willing to use COMPAT in clinic, ward/hospital and research settings. The most common location of pain was the epigastrium and food was the most important trigger. Pain Pattern C (constant background pain with pain attacks), had significantly higher frequency of pain attacks, higher opioid use, and affective descriptors of pain than Pattern A (pain attacks with no background pain).
Conclusions: COMPAT has high face validity and met with high acceptance. CP patients successfully self-reported their pain with COMPAT. The results reveal many differences in the CP pain within the pilot cohort, which may reflect different mechanisms of pain. A larger prospective cohort study is planned to further validate COMPAT.

Introduction

Chronic pancreatitis (CP) is a complex disease characterised by progressive inflammation and fibrosis of the pancreas. The cardinal clinical feature of CP is abdominal pain, which is difficult to treat and impacts quality of life (QOL) [1,2]. Many patients develop refractory abdominal pain despite many different interventions over time [3]. Not only is pain the most common presenting symptom, it is also the most important endpoint for trials aimed at evaluating interventions [1,4–6]. In contrast to pain, there are effective treatments for the other important consequences of CP such as exocrine and endocrine insufficiency [7]. (see Tables 5 and 6)

There is no universally accepted, comprehensive and validated pain assessment tool for CP pain [8]. Historically pain assessment for CP has used general tools developed for other painful conditions. Where CP-specific tools have been developed, they do not cover all the relevant aspects of CP pain [8]. Further, none of the CP-specific tools attempt to address the different mechanisms of pain in CP, including mechanical, inflammatory, maladaptive and neurogenic [1,9]. This hampers the ability to identify the mechanism(s) of the pain to better select treatment options. Current treatment decisions for CP are usually based on clinical assessment and imaging of pancreatic morphology, although the latter is not related to pain Pattern or severity [10,11]. Increasing evidence points to CP pain having nociceptive, neuropathic and central

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sensitisation components, which vary from case to case, similar to other visceral pain syndromes [12]. This complex pain condition requires a pain assessment tool that can account for these variables. When combined with clinical assessment, imaging, genetics and central modulation techniques like quantitative sensory testing [12,13], a comprehensive pain assessment tool might elucidate "the pain phenotype" for individual patients, indicating which mechanism(s) are important, and assisting in the selection of appropriate treatments for more effective pain relief and a reduction in unhelpful interventions.

The aims of this study are to describe the development of a comprehensive pain assessment tool (COMPAT) specific for CP, to report the results of face validity studies with experts and patients and to present the results of a pilot evaluation by CP patients.

Methods

Development of the comprehensive pain assessment tool (COMPAT)

A comprehensive pain assessment tool (COMPAT) (Appendix 1) was developed by comparing all published pain assessment tools used in the management of CP patients [8], and revised on the basis of face validity studies with two sets of expert reviewers and by CP patients. The aspects of pain included in the assessment were identified by a review of the literature and from recommendations of the American Gastroenterological Association [14] (Table 1). Questions were formulated or extracted from existing questionnaires and incorporated in COMPAT. These questions were reframed to make it easier for patients to independently answer the questions.

The Short-Form McGill Pain Questionnaire 2 (SF-MPQ-2) [15] was included in COMPAT in its entirety (question 14). This was chosen as the preferred way to assess neuropathic and non-neuropathic pain because it has been well validated in other studies on chronic pain [15,16]. The additional questions (1–6) following the SF-MPQ-2 relate to aspects of pain that are clinically apparent in patients with central sensitisation [17–19].

Expert review of COMPAT

Australasian and European pancreatic experts were invited to critique COMPAT through a questionnaire distributed and collated by SurveyMonkey (San Mateo, California). The experts were selected on the basis that they were active clinical pancreatologists who currently manage patients with CP. Australian and New Zealand consultant gastroenterologists and surgeons were identified through membership of three organizations: (1) Australian and New Zealand Hepatic, Pancreatic and Biliary Association (ANZHPBA), (2) Pancreas Club of Australasia, and (3) Pancreas Network of New Zealand. Clinical expert pancreatologists from the Scandinavian-Baltic Pancreatic Club were invited to critique the second version of COMPAT in English using the SurveyMonkey questionairre.

The experts were asked to give specific feedback on the 1) importance, 2) relevance and 3) clarity (ease of understanding) for each question in COMPAT using a 5-point rating scale (Table 2). This was analysed for content validity with an item-content validity index (I-CVI) (see below). In addition to the rating scale, the experts were asked to make specific recommendations on how to improve the framing of each COMPAT question. They were also asked to rate the ease of use of COMPAT, usability in different settings (outpatient clinic, inpatient hospital and clinical research) and assign an overall rating of COMPAT.

Patient review of COMPAT

Ethics approval was obtained from the Health and Disability Ethics Committees, New Zealand (Ref: 16/NTA/27) for the study of eligible patients with CP. Patients discharged from Auckland City Hospital, New Zealand, with CP as a diagnosis from 1 March 2010 to 29 February 2016 were identified from medical records. Other patients who were admitted as inpatients during the study period or attended Pancreas Clinic appointments were also identified.

These patients with CP were subsequently recruited based on pre-determined inclusion and exclusion criteria as follows:

- Inclusion criteria
  a. Diagnosis of chronic pancreatitis will be based on Mayo criteria [20,21] with a score of >4 indicating a high probability of chronic pancreatitis; and
  b. Recurrent acute pancreatitis – defined as more than one episode of acute pancreatitis, symptom-free in-between and with no evidence of underlying chronic pancreatitis [22–24].
- Exclusion criteria:
  a. Under 18 years of age;
  b. Co-morbidities, including end-stage cancer, HIV, end-stage congestive heart failure, end-stage chronic obstructive pulmonary disease, cirrhosis and renal failure;
  c. Acute pancreatitis (single episode);
  d. Autoimmune pancreatitis;
  e. Chronic pancreatitis secondary to malignancy; and
  f. Non-English speaking.

Table 1
Criteria for the evaluation of pain in chronic pancreatitis as proposed by the American Gastroenterological Association (AGA) [1] and 8 additional aspects of pain from the literature [2].

Evaluation of pain proposed by AGA	Duration of pain dating back to the first episode Character of pain: intermittent vs. daily; frequency if intermittent Subjective estimation of intensity of pain: mild, moderate, or severe Objective measurement of pain: visual analogue or descriptor (e.g.,1–5; 1–10) Use of narcotics and other medications to treat pain Evaluation of addiction to narcotics Documentation that other diseases have been excluded that could be causing abdominal pain Measurement of quality of life including work performance, social interaction, and family interaction
Eight additional aspects of pain from the literature	Location of pain Radiation of pain Triggers/exacerbators of pain Description of pain Associated symptoms of pain Postprandial pain Relieving factors of pain Effect on mental health

Table 2
Rating scale of weighting for importance, relevance and clarity of questions in the Comprehensive Pain Assessment Tool (COMPAT) for chronic pancreatitis.

Rating scale	Not at all	Slightly	Moderately	Very	Extremely
	1	2	3	4	5
How **important** is this question to the assessment of pancreatic pain in general?	☐	☐	☐	☐	☐
How **relevant** is this question to the assessment of pain to chronic pancreatitis patients?	☐	☐	☐	☐	☐
Is this question clear and **easy to understand (clarity)** for a layperson?	☐	☐	☐	☐	☐

The Mayo criteria for the diagnosis of CP was chosen for this study, which is comparable to Ammann's (Zurich Workshop) [25,26] criteria and the Japanese Pancreas Society (JPS) criteria [27,28]. Demographic and clinical data were extracted from the medical records of the patients who met the eligibility criteria. Reports of pancreatic imaging, including computed tomography (CT), magnetic resonance imaging (MRI), magnetic resonance cholangiopancreatography (MRCP), endoscopic ultrasound (EUS), abdominal ultrasound (US) and endoscopy retrograde cholangiopancreatography (ERCP) for eligible patients were extracted from medical records. The morphological criteria used were based mainly on the Cambridge classification of pancreatic morphology for CP and the M-ANNHEIM pancreatic imaging criteria [2,29–31]. The data collected included the presence of pancreatic calcifications (ductal and parenchymal), fibrosis, atrophy, divisum, cysts/pseudocysts, masses, main pancreatic duct (MPD) dilation (defined as greater than 4 mm diameter) and strictures (localised narrowing of MPD).

Eligible patients were approached and consented for the study. The patients initially completed two tasks. The first was to provide detailed feedback on the first version of COMPAT using the same rating scale used by the expert reviewers (Table 2). The second was to comment on each question, to suggest other aspects of pain not covered by COMPAT, provide general comments related to face validity and comments about how the questionnaire might be improved. In contrast to the expert review, patients only gave feedback on pain Patterns (COMPAT question 10–13) that were relevant to themselves. The rationale for this was that the patient would not be able to give a fair review of a pain Pattern they had not experienced.

The analysis of the data from the patient review was for content validity using the I-CVI (see below), similar to the expert review. The data obtained from expert and patient review were compared and analysed for trends and associations.

Based on the I-CVI scores and detailed feedback from the Australasian experts and patient reviews of COMPAT, revisions were made and a second version of COMPAT compiled. This updated version was then reviewed by the European experts using the same method used by Australasian experts.

Pilot study of CP patients

The eligible patients with CP were also invited to complete the first version of COMPAT in relation to their own pain. This self-reporting of pain was completed in hospital, in clinic, or off-site. Patients were contacted by phone to clarify any issues and ensure that all questions were answered.

Statistical analysis

Descriptive statistics were used for demographic and clinical characteristics of patients. Where continuous variables were present, they were expressed as mean ± SD. A percentage was used for dichotomous variables. Group differences between patients were compared using the Fisher's exact test or Pearson chi-square test for categorical variables and the student's *t*-test for continuous variables. A p value of <0.05 was considered statistically significant. SPSS Statistics version 23 (IBM Corporation, New York) was utilised for statistical analysis.

Content validity

The importance, relevance and clarity of each question were estimated using level of consensus among the experts and patients independently. This was calculated using an I-CVI [32] with the following scoring method: The number of experts who selected 4 or 5 on the scale were divided by the total number of experts. Each question was considered important, relevant and easy to understand if I-CVI was >0.78 by more than three experts [32].

Comparison of experts and patients

The level of consensus was compared between Australasian experts and patients for the first version of COMPAT. The total number of questions in COMPAT considered important, based on I-CVI > 0.78, was compared using the Fisher's Exact test. This was also performed for the other two domains: relevance and ease of understanding. A similar comparison was performed between the European experts for the second version of COMPAT and the Australasian experts and patients.

Self-reported pain via COMPAT

The pilot study of patients using COMPAT to report their own pain was analysed. Frequencies of pain aspects from COMPAT questions were calculated. Where applicable, comparisons between pain aspects and patients' demographics and clinical characteristics were made. In addition, pain aspects in COMPAT were compared with each other, as indicated. Calculations for these comparisons were performed with Student's *t*-test for continuous variables and Pearson chi-square or Fisher's Exact test for categorical variables. For SF-MPQ-2 in COMPAT (question 14), total scores and subscale scores were calculated based on the analysis proposed by the authors of SF-MPQ-2 [15].

Results

Details of the experts and patients

Of the 40 Australasian experts invited to participate, 21 (52.5%) completed the online survey on the first version of COMPAT. There were more Australian pancreatic experts ($n = 14$) than New Zealand experts ($n = 7$) but a similar number of gastroenterologists ($n = 10$) and pancreatic surgeons ($n = 11$). Of the 23 Scandanavian-Baltic experts invited to participate, 8 (35%) completed the online survey on the second version of COMPAT.

Of the 41 patients who agreed to participate in the study, 16 (39%) provided detailed feedback on COMPAT and 18 (44%) completed COMPAT for themselves. Nineteen (46.3%) patients did not complete the study despite repeated reminders while 3 (7.3%)

patients submitted incomplete questionnaires. One (2.4%) patient did not have pain currently and did not complete COMPAT.

Table 3 compares the demographic and clinical characteristics of the patients who completed ($n = 18$) and did not complete the study ($n = 23$). None of the demographics, aetiology, or clinical characteristics were significantly different between these two groups. Those who completed the questionnaire tended to have less severe pancreatic morphology – significantly less parenchymal calcifications ($p = 0.02$) and cysts/pseudocysts ($p = 0.001$), and a trend towards less calcification ($p = 0.054$).

Review of COMPAT by Australasian experts and patients with CP

Table 4 shows the aspects of pain (first version of COMPAT) and the I-CVI scores for each domain for both experts and patients. Most aspects of pain were considered important, relevant and easy to

Table 3
Demographic and clinical characteristics of the chronic pancreatitis patients in the study cohort. Values expressed in number of patients and percentages (%) unless specified otherwise.

Variable	Completed (n=18)	Did not complete (n=23)	*p*-value[b]
Age, mean±SD (years)	42.8±14.2	46.7±15.6	0.40
Gender			
Male	10 (56%)	16 (70%)	0.52
Female	8 (44%)	7 (30%)	
Ethnicity			
European	13 (72%)	17 (74%)	0.70
Fijian Indian	1 (6%)	0 (0%)	
Indian	3 (16%)	4 (17%)	
Maori	1 (6%)	2 (9%)	
Aetiology			
Alcohol	8 (44%)	11 (48%)	0.36
Idiopathic	7 (39%)	8 (35%)	
Divisum	2 (11%)	1 (4%)	
Genetic[a]	1 (6%)	0 (0%)	
Others	0 (0%)	3 (13%)	
Clinical			
History of recurrent acute pancreatitis	15 (83%)	19 (83%)	1.0
Number of acute pancreatitis episodes, mean±SD	5.9±3.6	4.8±3.2	0.37
Insulin dependent diabetes mellitus	1 (6%)	4 (17%)	0.36
Pancreatic insufficiency on enzyme replacement	6 (33%)	6 (26%)	0.73
Morphology			
MPD dilation	9 (53%)	13 (57%)	1.0
MPD stricture(s)	6 (35%)	6 (26%)	0.73
Calcification	5 (29%)	15 (65%)	0.054
Ductal	3 (18%)	5 (22%)	1.0
Parenchymal	3 (18%)	13 (57%)	0.02
Calcification and MPD dilation	5 (29%)	11 (48%)	0.33
Pancreatic fibrosis	2 (12%)	3 (13%)	1.0
Pancreatic atrophy	6 (35%)	6 (26%)	0.73
Pancreatic divisum	3 (18%)	2 (9%)	0.63
Pancreatic mass	1 (6%)	2 (9%)	1.0
Cysts/Pseudocysts	0 (0%)	11 (48%)	0.001
Normal imaging overall	3 (18%)	3 (13%)	1.0
Overall duration of pancreatic pain[#]			
1 – 6 months	1 (6%)	-	-
7 – 11 months	1 (6%)	-	-
1 – 5 years	7 (39%)	-	-
6 – 10 years	4 (22%)	-	-
11 – 15 years	4 (22%)	-	-
16 – 20 years	1 (6%)	-	-
More than 20 years	0 (0%)	-	-
Medications[#]			
Non-opioid analgesics	8 (44%)	-	-
Opioid analgesics	10 (56%)	-	-
Gabanoids	4 (22%)	-	-
TCAs/SSRIs	7 (39%)	-	-
Benzodiazepines	2 (11%)	-	-
Current lifestyle factors[#]			
Smoking cigarettes	5 (29%)	-	-
Alcohol use	11 (61%)	-	-
Interventions for pain[#]			
Endoscopy	10 (56%)	-	-
Clear duct	1 (6%)	-	-
Dilate duct	1 (6%)	-	-
Stent duct	7 (39%)	-	-
Other endoscopy	1 (6%)	-	-
Nerve procedures	4 (22%)	-	-
Coeliac plexus block	2 (11%)	-	-
Spinal cord stimulation	1 (6%)	-	-
Skin stimulation (TENS)	1 (6%)	-	-
Surgery	8 (44%)	-	-
Remove part of pancreas	3 (18%)	-	-
Puestow procedure	2 (11%)	-	-
Frey procedure	2 (11%)	-	-
Cholecystectomy	1 (6%)	-	-

MPD: main pancreatic duct (MPD)
[b]Fisher's exact test or Pearson chi-square test were utilised to compute group differences for categorical variables. Student's *t* test was utilised to compute group differences for continuous variables.
SD: standard deviation..
Cells highlighted in grey represent significant differences ($p < 0.05$)
[#]Obtained from COMPAT responses
Non-opioid analgesics: paracetamol, non-steroidal anti-inflammatories and tramadol
Opioid analgesics: morphine, methadone, codeine, oxycodone
TCAs: tricyclic antidepressants, SSRIs: serotonin-selective reuptake inhibitors
TENS: transcutaneous electrical nerve stimulation

Table 4
Summary of the Item-Content Validity Index (I-CVI) scores for pain aspects assessed in COMPAT for the 3 domains – important, relevant and easy to understand, by Australasian experts and patients (version 1 of COMPAT) and European experts (version 2 of COMPAT). A score for I-CVI > 0.78 was considered valid, and these are highlighted.

Pain aspects assessed in COMPAT (question number)	I-CVI domains	I-CVI score by Australasian experts (v 1)	I-CVI score by patients (v 1)	I-CVI score by European experts (v 2)
Duration (1)	Important	0.90	0.88	0.88
	Relevant	0.95	0.93	1
	Easy to understand	0.76	1	0.63
Location (2)	Important	0.86	1	0.88
	Relevant	0.81	1	0.75
	Easy to understand	0.81	1	0.75
Radiation (3)	Important	0.57	0.94	0.63
	Relevant	0.67	0.93	0.63
	Easy to understand	0.57	0.88	0.25
Triggers and onset time (4, 5)	Important	0.85	0.75	0.75
	Relevant	0.81	0.73	0.88
	Easy to understand	0.71	0.88	0.88
Exacerbators and onset time (6, 7)	Important	0.81	0.88	0.63
	Relevant	0.81	0.87	0.63
	Easy to understand	0.71	0.81	0.75
Other pain conditions (8)	Important	0.65	0.6	0.75
	Relevant	0.7	0.5	0.75
	Easy to understand	0.7	0.8	0.75
Pain Pattern (9)	Important	1	0.94	1
	Relevant	1	0.93	1
	Easy to understand	0.84	1	0.88
Pain Pattern A (10)	Important	0.95	0.78	1
	Relevant	0.9	0.75	1
	Easy to understand	0.7	1	1
Pain Pattern B[a] (11)	Important	0.89	-	1
	Relevant	0.89	-	1
	Easy to understand	0.61	-	1
Pain Pattern C (12)	Important	0.89	1	1
	Relevant	0.89	1	1
	Easy to understand	0.5	0.75	0.75
Pain Pattern D[b] (13)	Important	0.84	-	1
	Relevant	0.84	-	1
	Easy to understand	0.58	-	0.75
Description of pain (14)	Important	0.68	0.88	0.75
	Relevant	0.68	0.87	0.88
	Easy to understand	0.58	0.75	0.38
Admissions for pancreatitis (15)	Important	-	-	1
	Relevant	-	-	1
	Easy to understand	-	-	1
Medications (16)	Important	1	0.93	1
	Relevant	1	0.92	1
	Easy to understand	0.65	0.79	0.43
Physical relief of pain (17)	Important	0.74	0.88	1
	Relevant	0.74	0.8	1
	Easy to understand	0.79	0.94	0.88
Mental relief of pain (18)	Important	0.88	0.81	0.75
	Relevant	0.88	0.8	0.63
	Easy to understand	0.88	1	0.88
Coping with pain (19)	Important	0.8	0.88	0.75
	Relevant	0.75	0.87	0.88
	Easy to understand	0.9	0.94	0.88
Interventions for pain (20)	Important	1	0.87	0.88
	Relevant	0.95	0.86	0.75
	Easy to understand	0.7	0.93	0.13
PANQOLI (21)	Important	-	-	1
	Relevant	-	-	1
	Easy to understand	-	-	0.5
Alcohol use (22)	Important	0.95	0.93	1
	Relevant	0.9	0.77	1
	Easy to understand	0.85	0.86	0.88
Cigarette use (23)	Important	0.94	0.75	1
	Relevant	0.88	0.7	1
	Easy to understand	0.88	0.92	0.88

[a, b] None of the CP patients reported pain Patterns B and D in the study.
Numbers in brackets reference the question number in COMPAT found in Appendix 1.
Questions 15, Admissions for pancreatitis, and question 21, the Pancreas Quality of Life Instrument (PANQOLI) were added to the second version of COMPAT.
Cells highlighted in grey represent I-CVI scores > 0.78.

understand as they had I-CVI scores of >0.78.

Interestingly, patients found more questions about aspects of pain in COMPAT easy to understand than experts. Overall the patients liked the question on pain Patterns (question 9–13) because it tended to describe their pain course appropriately. None of the patients self-reported pain Patterns B and D (questions 11 and 13), which meant that patients' I-CVI could not be calculated for these two questions. In contrast, experts gave feedback on all pain Patterns (questions 10–13) because they manage patients with all pain Patterns. Several patients commented that triggers of pain (question 4) were difficult to ascertain due to their random Pattern and lack of consistency.

Fig. 1A shows the percentages of pain aspects assessed in the first version of COMPAT that had I-CVI scores >0.78 in all 3 domains (important, relevant and easy to understand) for both experts and patients. The differences were not statistically significant for the domains "important" (82% vs 79%, $p = 1.0$) and "relevant" (71% vs 74%, $p = 1.0$). For the domain "easy to understand", the difference was highly significant (88% vs 37%, $p = 0.001$) (as above). It was noted that the I-CVI scores for radiation of pain (question 3) and description of pain (question 14) were significantly different between Australasian experts and patients for all 3 domains (Table 4).

The overall ease of use of COMPAT (version 1) showed that 85% of Australasian experts rated the questionnaire as acceptable, easy or very easy to use (Fig. 1B). This response was consistent with the findings that experts would be willing to use COMPAT in the clinic (84%), ward/hospital (74%) and research (95%) settings (Fig. 1C). The median overall assessment of COMPAT by the Australasian experts was 7.44/10.

Revision of first version of COMPAT

Based on the I-CVI scores and comments from experts and patients, revisions were made to the first version of COMPAT. In particular, modifications were made to how questions were phrased and word choices within questions to make them simpler and easier to understand. For example, the "most important item that brings on the pain" (question 4) was changed to the "one item that brings on your pancreatic pain most often". Another example was pain Pattern C (question 12), where "the trend in the severity of your pain attacks" was changed to "is the severity of your pain attacks" increasing, same or decreasing. This simplified the question for patients. Many questions were also modified to be personalised, (e.g. "the pancreatic pain" became "your pancreatic pain").

Other key changes based on the recommendations were as follows: time periods for questions 10–13 extended to 3–6 months as patients preferred longer time periods to describe their pain; items added for physical relief of pain (question 17): drinking and stopping alcohol and cigarettes, and work; modified question 22 to include resumed alcohol use after stopping; and reformatted question 23 on cigarette use to separate patients who quit and are currently smoking.

Several experts commented on the lack of QOL assessment in the version of COMPAT used in the study. The Pancreas Quality of Life Instrument (PANQOLI) [33] could not be included until published, and has since been added as Question 21 in the second version of COMPAT.

Table 5 compares the criteria for evaluation of pain in CP (Table 1) with aspects of pain assessed in COMPAT. This indicates that most criteria have been met by COMPAT. The 'subjective' estimate of intensity of pain was included, but the 'objective' estimation of intensity of pain was omitted because a questionnaire cannot achieve this. Evaluation of narcotic addiction can be inferred from medications (question 16). Documentation of other diseases

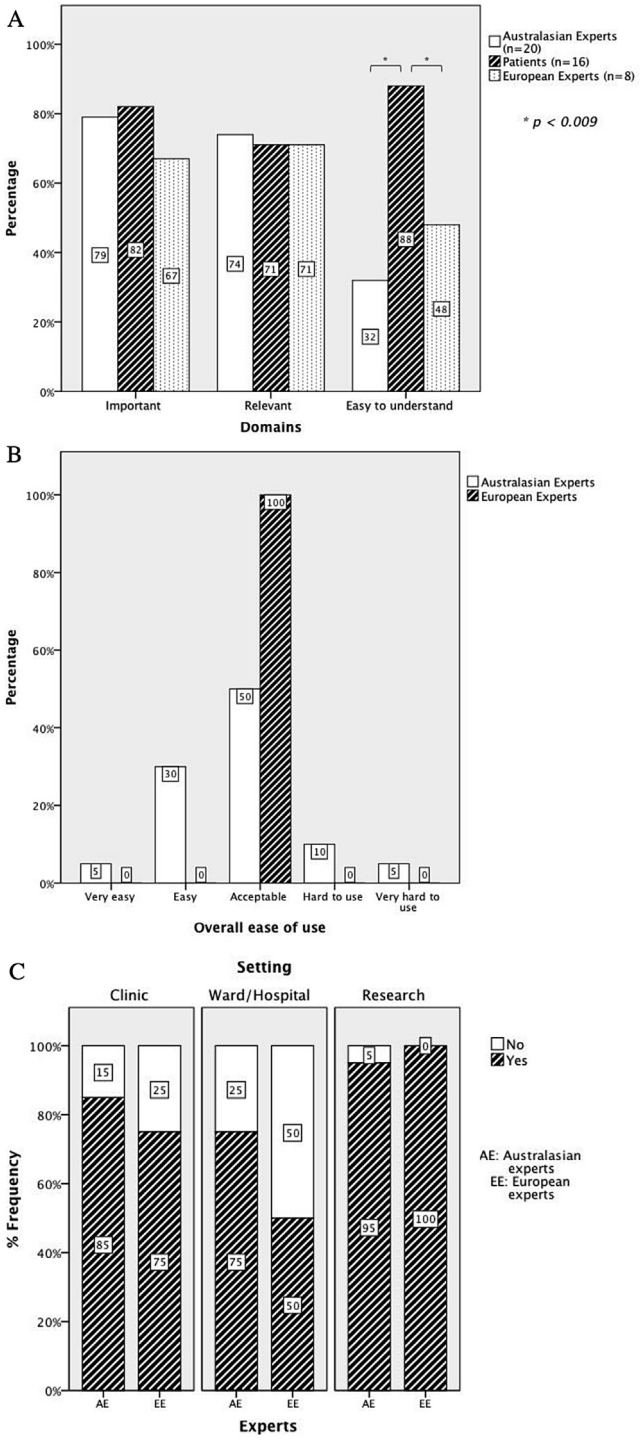

Fig. 1. The results of the expert and patient reviews of COMPAT. (A): Percentages of pain aspects assessed in COMPAT with Item-content validity index (I-CVI) > 0.78. European experts reviewed COMPAT version 2. (B): Expert opinions on patients' overall ease of use of COMPAT; and (C): Expert review of COMPAT's use in the clinic, ward/hospital and research settings.

causing abdominal pain was not needed specifically in COMPAT.

Additional questions in Table 5 were formulated from the literature review: other painful conditions (question 8) – suggested an element of central sensitisation; admissions to hospital for pain relief (question 15) - reflected intensity of pain and how disruptive it was to a patient's QOL; levels of avoidance and catastrophizing

Table 5
Criteria for evaluation of pain in chronic pancreatitis from Table 1, compared with aspects of pain assessed in the Comprehensive Pain Assessment Tool (COMPAT) for chronic pancreatitis.

Criteria for evaluation of pain in chronic pancreatitis from Table 1	Aspects of Pain assessed in COMPAT
Duration of pain dating back to the first episode	Duration of pain dating back to the first episode
Character of pain: intermittent vs. daily; frequency if intermittent	• Pain Patterns: pain attacks, constant pain, constant background pain with pain attacks and severe constant background pain with reduced pain periods in-between • Frequency of pain attacks/reduced pain periods and frequency trend • Duration of pain attacks/reduced pain periods and duration trend
Subjective estimation of intensity of pain: mild, moderate, or severe	Subjective pain intensity using visual analogue scale and intensity trend
Objective measurement of pain: visual analogue or descriptor	
Use of narcotics and other medications to treat pain	Current medications including analgesics, antioxidants, vitamins and enzymes
Evaluation of addiction to narcotics	
Documentation that other diseases have been excluded that could be causing abdominal pain	
Measurement of quality of life including work performance, social interaction, and family interaction	Pancreas Quality of Life Instrument (PANQOLI)
Location of pain	Location of pain and worst spots of pain
Radiation of pain	Radiation of pain
Triggers/exacerbators of pain	Triggers/exacerbators of pain and onset time
Description of pain Associated symptoms of pain	Description of pain using Short-form McGill Pain Questionnaire[1] with additional questions
Postprandial pain	Any food and fatty food under triggers/exacerbators of pain
Relieving factors of pain	Physical and mental relieving factors
Effect on mental health	PANQOLI[2]
Additional aspects of pain included in COMPAT	Other pain conditions Admissions to hospital for pain relief Avoidance and catastrophizing (significant questions from Pain Catastrophizing scale) Interventions for pain Lifestyle factors influencing pain (CAGE questionnaire for alcohol use and smoking history)

CAGE: Concern/cut-down, anger, guilt and eye-opener

(question 19) in patients from the Pain Catastrophizing Scale (PCS) – well characterised as a predictor of poorer treatment responses and has associations with increased pain severity, depression and disability [34–37]; and effects of interventions on pain and lifestyle factors (alcohol and smoking) that might contribute to pain (questions 22 and 23).

Review of second version of COMPAT by European experts

Table 4 shows the results of the review of the second version of COMPAT by the 8 European experts. The results are broadly similar to those obtained from the Australasian experts. Both groups of experts did not consider radiation of pain (question 3) and other pain conditions (question 8) as valid in all 3 domains. The following pain aspects were considered easier to understand by European experts compared with Australasian experts: triggers and onset time (questions 4 and 5) and pain Patterns A and B (questions 10 and 11).

Similar to their Australasian counterparts, European experts were concerned about patients accurately distinguishing pancreatic pain from other pain, self-reporting complex questions (questions 14 and 20) and they considered the length of the questionnaire may be a barrier to completion. Compared with Australasian experts, European experts made few suggestions regarding phrasing of questions and word choices and did not recommend additional questions for COMPAT.

Comparing the two groups of experts, it was found that there were no significant differences in the percentage of those pain aspects that scored >0.78 for I-CVI in all 3 domains (Fig. 1A): "important" (79% vs 67%, $p = 0.49$), "relevant" (74% vs 71%, $p = 1.0$) and "easy to understand" (32% vs 48%, $p = 0.35$) for Australasian and European experts, respectively.

Comparing the I-CVIs between patients and European experts, there were no significant differences for the domains "important" (82% VS 67%, $p = 0.29$) and "relevant" (71% VS 71%, $p = 0.96$), respectively. Similar to Australasian experts, patients reported that COMPAT questions were significantly easier to understand than European experts (88% VS 48%, $p = 0.008$).

All of the European experts rated the overall ease of use of COMPAT from a patient's perspective as acceptable (Fig. 1B), which is comparable to the Australasian experts. Fig. 1C shows that European experts were willing to use COMPAT in the clinic (75%), ward/hospital (50%) and research (100%) settings, which was similar to the Australasian experts. Lastly, the European experts rated the median overall assessment of COMPAT 8/10 – similar to Australasian experts.

Pilot cohort of CP patients

Eighteen patients completed COMPAT, and 14 (78%) did this independently. Fig. 2 shows the distribution of the locations of pain and radiating pain (question 2 and 3). The most frequent location of

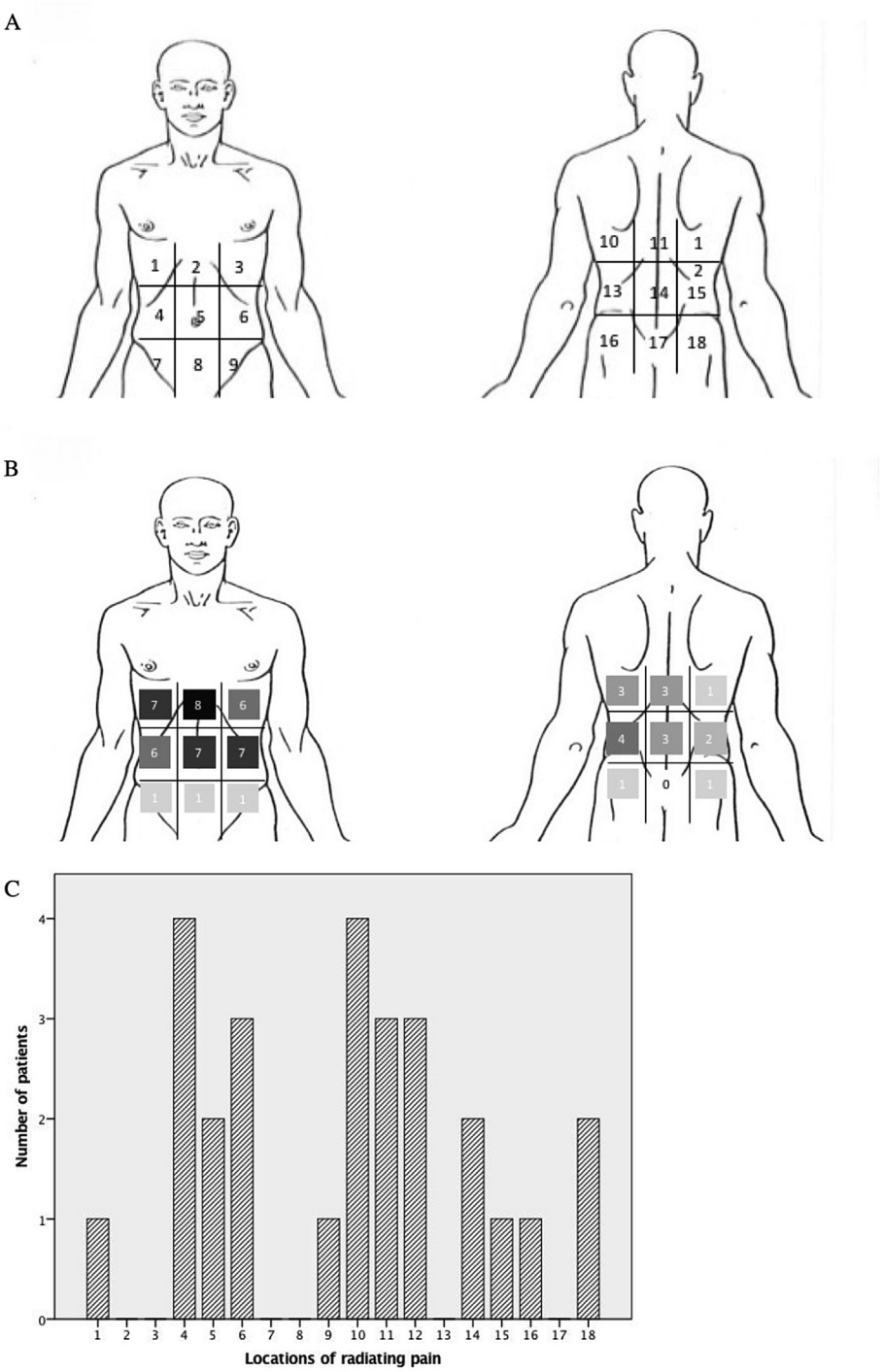

Fig. 2. The responses for location and radiation of pain reported in COMPAT (questions 2 and 3). (A): An anatomical diagram divided into different areas; (B): The distribution of locations of pain – numbers represent number of patients and darker shades correspond to more patients reporting pain in that area; (C) Radiation of pain, reported in COMPAT (questions 2 and 3).

pain (area 2) reported by 8 patients (44%) occurred in the epigastrium. Radiating pain occurred in 11 (61%) patients, and most commonly in the right lumbar region and upper left of the posterior abdomen. Table 3 gives results for the duration of CP pain (question 1), medications (question 16), current lifestyle factors (question 22 and 23) and types of interventions for pain (question 21). There were no significant differences between the overall duration of CP pain and taking opioid analgesics ($p = 0.554$), current alcohol use ($p = 0.483$) and current cigarette use ($p = 0.415$). Items that triggered and exacerbated pain (question 4–7) and pain onset time are outlined in Fig. 3A. Most common triggers of pain were fatty food, drinking alcohol and stress. Any food was the most common exacerbator of pain. Items that triggered or exacerbated pain most often were fatty food and any food respectively (Fig. 3B). This finding validates the results in Fig. 3A. The most frequent pain onset time of the items that triggered or exacerbated pain most often were between 10 and 30 min and under 10 min respectively (Fig. 3C).

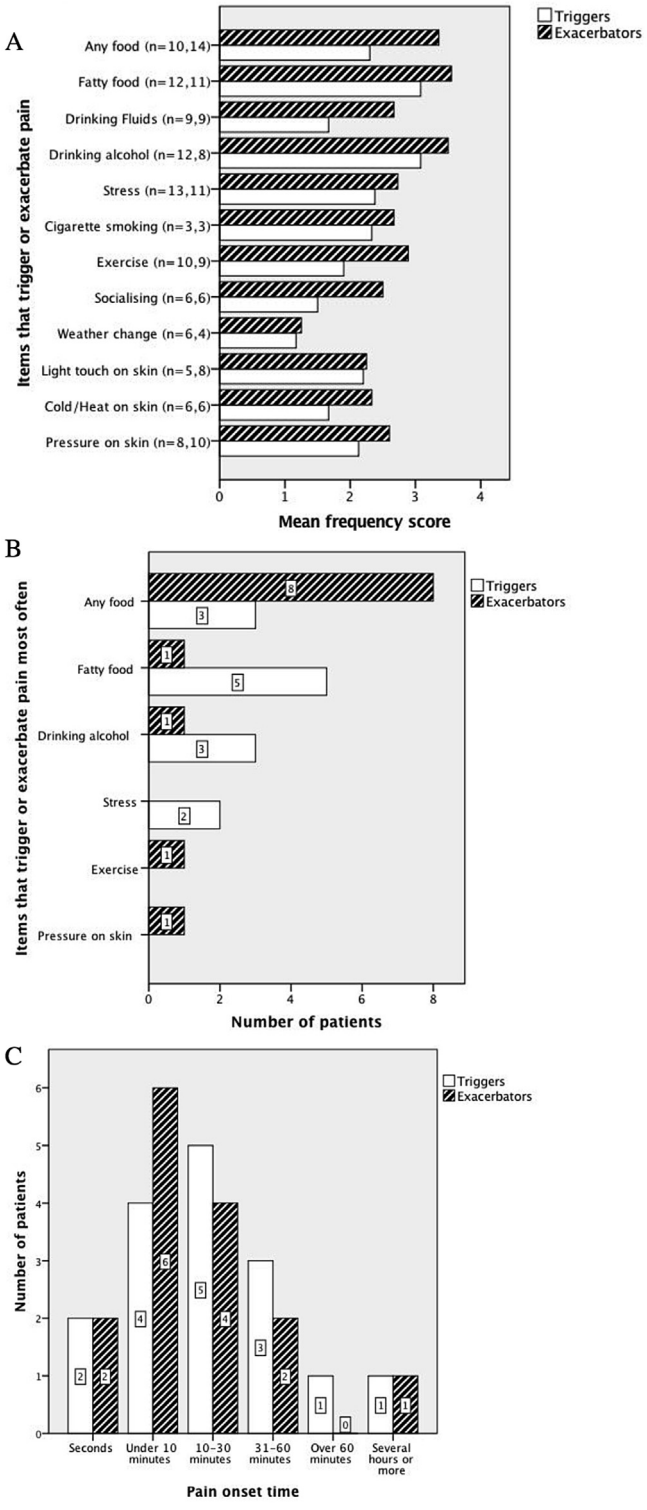

Fig. 3. The responses for triggers and exacerbators of pain reported in COMPAT (questions 4 – 7). (A): The mean frequency scores for triggers and exacerbators of pain according to the scale: 1 – rarely, 2 – sometimes, 3 – very often, 4 – always. 0 – never and not applicable were excluded (n = triggers sample size, exacerbators sample size); (B): The items that trigger and exacerbate pain most often; and (C): The pain onset time by items that trigger and exacerbate pain most often.

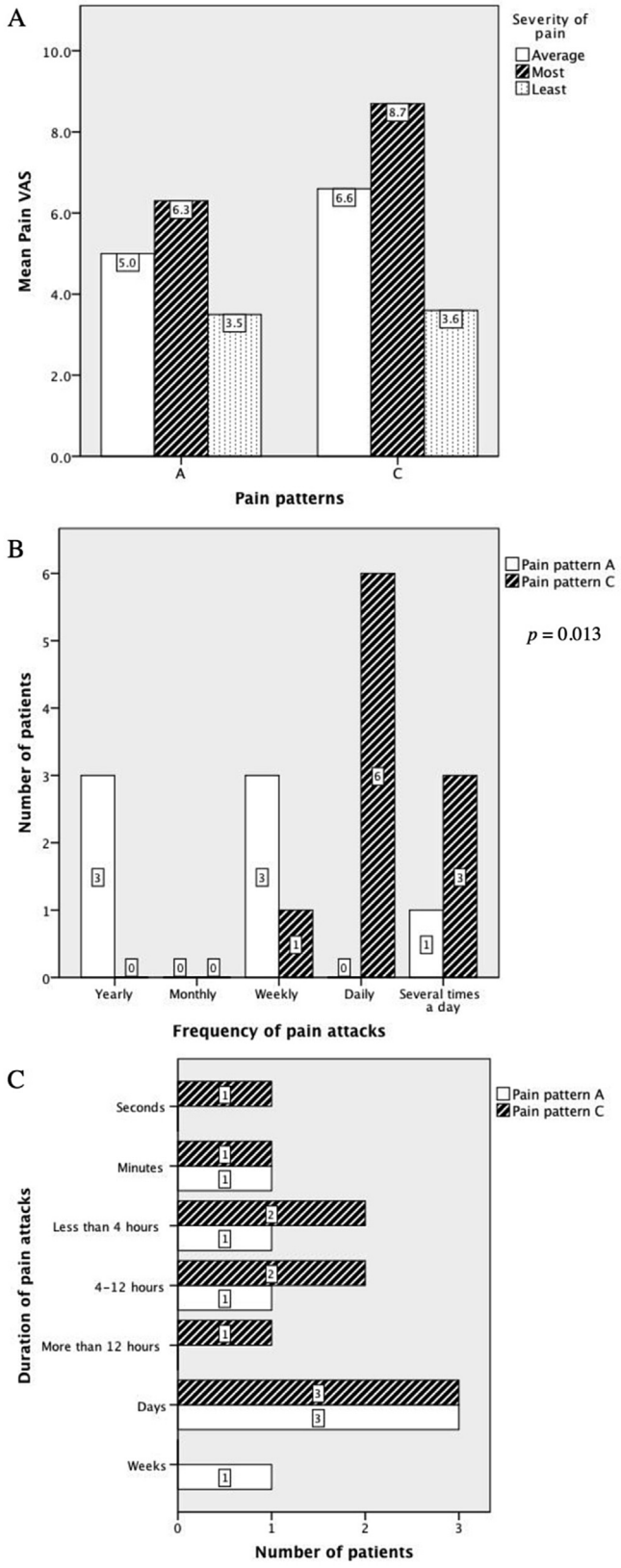

Fig. 4. The responses for pain Patterns A and C reported in COMPAT (questions 10 and 12). (A): The mean pain visual analogue scores (VAS) for the average, most and least severity of pain attacks; (B): The frequency of pain attacks; and (C): The duration of pain attacks.

Of the 18 patients, 7 (41%) reported pain Pattern A and 10 (59%) reported pain Pattern C. One patient did not indicate the pain Pattern. None of the patients reported pain Patterns B and D. Fig. 4A

shows the mean pain severity for the average, most and least severe of pain attacks. Scores for pain Patterns C appeared higher than A but did not reach significance. Pain Pattern C had significantly higher frequency of pain attacks compared with A ($p = 0.013$) (Fig. 4B). The durations of pain attacks for pain Pattern A and C (Fig. 4C) were similar ($p = 0.778$). There were no significant differences between pain Patterns A and C with gender ($p = 0.335$), patient age ($p = 0.155$), overall duration of pain ($p = 0.327$), current alcohol use ($p = 0.622$) and current cigarette use ($p = 0.603$). Significantly more patients with pain Pattern C than pain Pattern A reported opioid use ($p = 0.05$).

Table 6 shows the scores from the SF-MPQ-2 and additional questions reported in COMPAT (question 14). The total scores showed a trend towards a statistically significant difference for pain Pattern C having a higher mean score than pain Pattern A (mean 4.19 versus 2.28, $p = 0.066$). Continuous pain ($p = 0.014$), affective descriptors ($p = 0.016$) and night pain score ($p = 0.04$) were higher for Pattern C compared with A.

Fig. 5 shows rest, starvation, sleep and the hot water bottle were physical factors that provided the most pain relief and support from family and friends was the psychological factor providing the most pain relief. Fig. 6 shows that avoidance was the most endorsed pain coping strategy for patients with a mean score of 3.25.

Discussion

This study is the first attempt to develop a comprehensive pain assessment tool, that includes all of the aspects of pain that are evaluated in published tools and from recommendations in the literature. As such it addresses the gap highlighted in the recent publication [8]. The key findings of this study are that COMPAT addresses all the key aspects of pain, has high face validity and was easy to use by patients. A cohort of patients with CP used COMPAT to self-report their pain provided a range of responses in a detailed description of the pain phenotype of CP.

As reported in the comparative review, international consensus guidelines lacked unanimity regarding the recommended methods for pain assessment in CP patients [8]. COMPAT includes complete questionnaires (e.g. SF-MPQ-2 and PANQOLI) which have been independently validated in CP [33,38–42] as well as portions of questionnaires (e.g. PCS for pain catastrophizing and Concern/cut-down, anger, guilt and eye-opener (CAGE) questions for alcohol use) that have been used in chronic pain assessment [34–37] and alcohol screening [43,44], respectively. These tools were included because they covered some of the key aspects in CP pain.

Overall, the experts and patients reported that COMPAT questions were important and relevant with no significant differences between their I-CVIs. In contrast, patients reported that COMPAT questions were easier to understand compared with both expert groups. The majority of experts supported the use of COMPAT in the clinic and research settings, although the European experts were less supportive of its use in hospitals.

The pilot cohort of patients who self-reported their pain in COMPAT provided considerable data on pain aspects relevant to CP, and aspects that would not be available with CP-specific pain assessment tools in current use, including the Izbicki method [8,45]. While little of the findings from this pilot study were novel, the range of responses was notable and the detail allows for a more detail description of the pain phenotype for CP. There were important differences in the aspects of pain for those with pain Patterns A and C (e.g. higher frequency of pain attacks, opioid use, continuous pain and affective descriptors of pain). The question remains whether differences reflect different pain mechanisms or different stages in the pain diathesis. Longitudinal studies will be required to address this.

There was no readily apparent reason why some patients agreed to complete COMPAT and others did not. It was not possible to determine what clinical characteristics were associated with completion of COMPAT. It was noted that those who did not complete COMPAT tended to have more advanced disease, at least on morphological criteria, as they tended to have more parenchymal calcifications and cysts/pseudocysts [46].

The review by experts and patients confirmed that the questions in COMPAT were important and relevant. In addition, having experts from two distinct geographical regions providing similar feedback provided additional strength to the validity of COMPAT. The differences between the experts and patients regarding the ease of understanding of COMPAT questions were not anticipated. Either patients could easily understand the questions because the language used in COMPAT was accessible, or they wanted to appear health literate in order to receive better care and build stronger doctor-patient relationships even though they did not readily understand the questions. Ascertaining the reasons for their responses will require individual in-depth interviews with patients. However, the fact that patients' overall responses to understanding COMPAT questions were positive and 78% completed COMPAT independently suggests that self-reporting of COMPAT is feasible. The remaining patients did not require much additional assistance to complete COMPAT, although many noted that the questionnaire was long, taking more than 30 min to complete.

It was notable that several patients commented that specific triggers of pain were difficult to ascertain. The majority of patients indicated that fatty food triggered their pain most often. Perhaps random triggers only applied to a smaller subset of patients that had become more sensitised to CP pain.

There were a series of improvements from the first to second

Table 6
The mean and standard deviation (SD) of the total score and subscale scores in the Short form-McGill Pain Questionnaire 2 (SF-MPQ-2) and additional questions reported in COMPAT (question 14). The scores are divided in pain Patterns A and C for SF-MPQ-2. SD: standard deviation.*p < 0.05.

SF-MPQ-2 Total score/subscale scores	Mean	SD	*P* value
Total score	3.26	2.09	
Pain Pattern A	2.28	2.00	0.066
Pain Pattern C	4.19	1.80	
Continuous pain	3.97	2.60	
Pain Pattern A	2.33	1.19	0.014*
Pain Pattern C	5.18	2.84	
Intermittent pain	3.49	2.76	
Pain Pattern A	2.48	2.86	0.141
Pain Pattern C	4.55	2.36	
Neuropathic pain	1.41	1.50	
Pain Pattern A	1.88	2.08	0.453
Pain Pattern C	1.22	0.95	
Affective descriptors	4.19	3.10	
Pain Pattern A	2.39	2.57	0.016*
Pain Pattern C	5.88	2.47	
Additional questions scores	**Mean**	**SD**	***P* value**
Stretching pain	0.94	2.44	
Squeezing pain	3.06	3.81	
Night pain	4.82	3.34	
Pain Pattern A	2.71	3.20	0.041*
Pain Pattern C	6.22	2.82	
Night sweats	4.71	3.74	
Pain Pattern A	4.14	4.06	0.715
Pain Pattern C	4.89	3.82	
Widespread pain	1.76	2.54	
Pain Pattern A	1.14	2.03	0.312
Pain Pattern C	2.44	2.92	
Skin colour change at location of pain	1.65	2.76	
Pain Pattern A	1.43	2.70	0.697
Pain Pattern C	2.00	3.04	

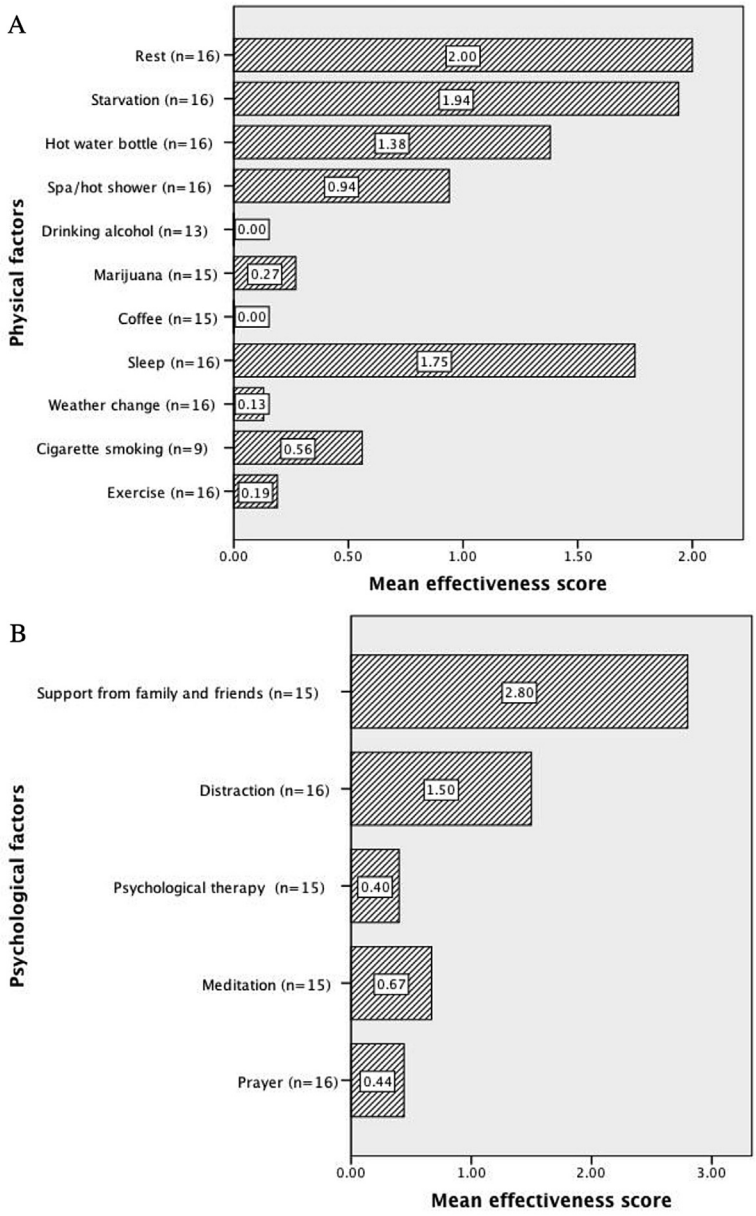

Fig. 5. The physical and psychological factors that contribute to pain relief reporting in COMPAT (questions 17 and 18). (A): Physical factors according to the scale: 0 – not at all effective, 1 – slightly effective, 2 – moderately effective, 3 – very effective, 4 – extremely effective. Not applicable excluded (n = sample size); and (B): Psychological factors according to the scale: 0 – not at all effective, 1 – slightly effective, 2 – moderately effective, 3 – very effective, 4 – extremely effective. Not applicable excluded (n= sample size).

versions of COMPAT. The European experts found several pain aspects easier to understand and suggested fewer changes compared with the Australasian experts, providing support for the revision process. Both experts' opinion of patient's ease of use, usability in different settings and median overall assessment of COMPAT were similar and affirmed that COMPAT could potentially be used clinically for better pain assessment of CP.

Pilot evaluation of cohort of CP patients

Overall the responses by CP patients produced a familiar and detailed description of pain, although as noted with quite a wide range of responses. The site and radiation of pain was as expected [7]. One of the omissions from previous published pain assessment tools was the presence of post-prandial pain [8]. We found that food commonly triggers and exacerbates pain, strengthening the view that this is an important and overlooked aspect of CP pain assessment [47,48].

Patients only reported pain Patterns A and C, which suggests that Patterns B and D may be uncommon and may have a low yield. This finding may reflect that the patients who were approached had all been referred to a Pancreas Clinic and had well established disease. Patterns B and D might be more relevant to patients with early and late disease, but this will be clarified with a larger prospective study that spans a wider spectrum of CP patients.

Of note, more frequent pain attacks and opioid use in patients with pain Pattern C was not surprising because constant pain with pain attacks often result in frequent hospitalisations for pain relief and opioids to relieve pain [49]. More continuous pain in SF-MPQ-2 for pain Pattern C affirmed the presence of constant pain in these group of patients. In addition, the increased score for affective descriptors of pain for pain Pattern C confirmed the negative effects

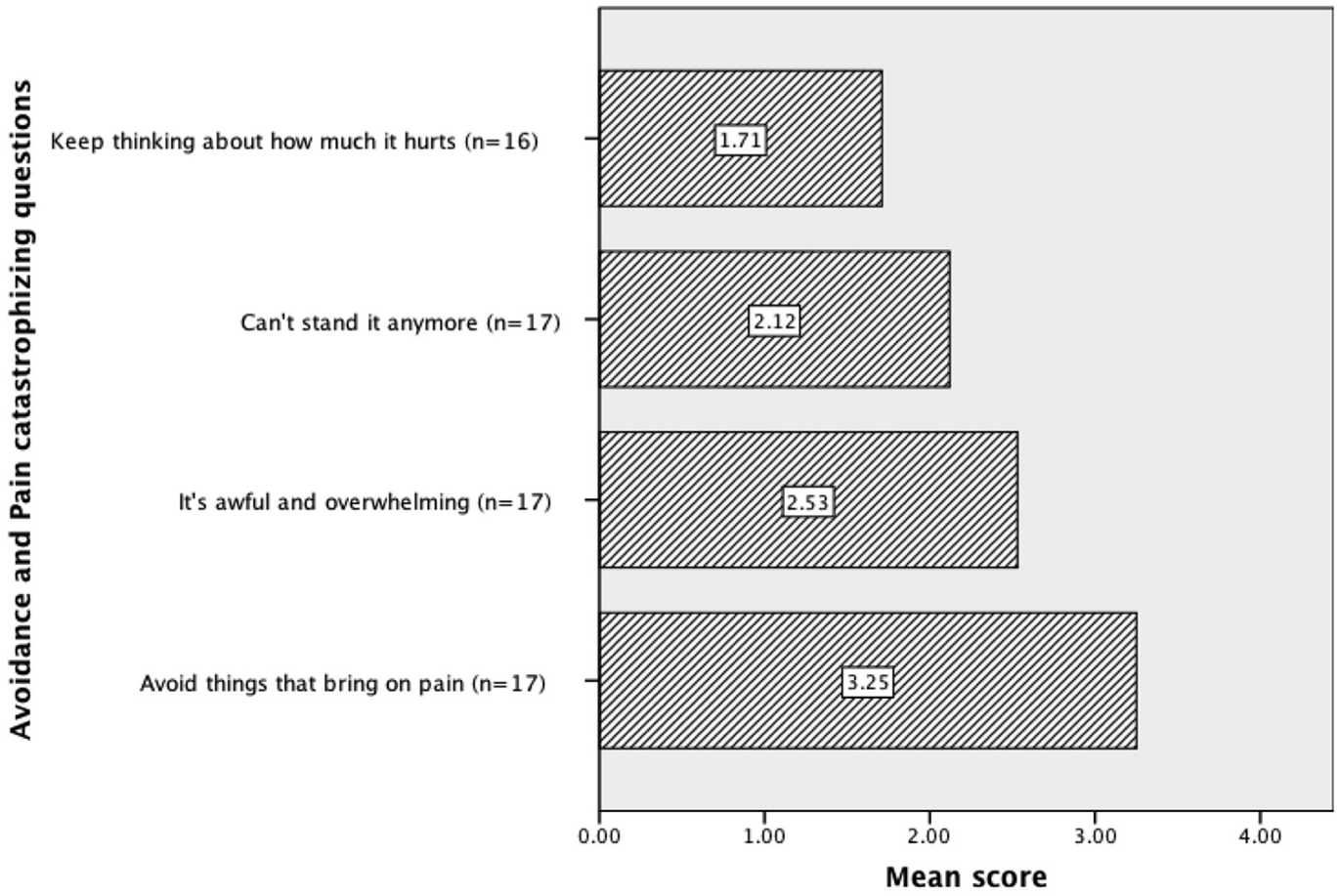

Fig. 6. The responses to avoidance and pain catastrophizing questions reported in COMPAT (question 19) according to the scale: 0 – not at all, 1 – to a slight degree, 2 – to a moderate degree, 3 – to great degree, 4 – all the time (n = sample size).

on patients' psychological state and QOL with constant background pain coupled with pain attacks [50–52]. The mean scores in SF-MPQ-2 were comparable to patients with chronic pain diagnoses [16] and clinical trial data in patients with chronic diabetic peripheral neuropathy [15], and slightly lower than patients with acute lower back pain [53]. This suggested that the responses by CP patients to the SF-MPQ-2 were in accord with patients that had other types of chronic pain.

Although deliberately included in the design of COMPAT, no formal attempt has been made in this study to determine whether it is able to discriminate between different pain mechanisms with this tool. This will require a larger sample and the use of cluster analysis methodology. However, some of the results from the pilot cohort were encouraging in this regard. For instance, post-prandial pain triggered by food intake suggested an obstructive-type pain that may benefit from endoscopic or surgical decompression of the main pancreatic duct [48,54–56]. In addition, reporting pain Pattern C might pre-dispose patients to more frequent pain attacks, continuous pain, risk of opioid use and reduced QOL. Identifying these patients early in the disease course might influence intervention strategies as early intervention may be associated with an improved success rate [57,58].

This study has a number of limitations. Most patients in the pilot cohort were retrospectively identified from medical records with only 22% being prospective patients admitted to hospital or seen in clinic. This provided a foundation for assessing the feasibility of COMPAT from an available pool of patients but introduced bias with a retrospective study. In addition, the sample size was small and only forty-four percent of eligible patients who agreed to participate completed the study despite repeated reminders. This has implications for compliance with future studies using COMPAT. In this study, with the majority of patient who completed COMPAT not being under active treatment, there was little incentive to participate. The majority of patients who completed the study were European (72%), which limits the generalizability of the results to other ethnic groups. Issues of language and culture were not addressed in the initial design of COMPAT. As with most questionnaires, patients may not fully understand the questions asked and responses may not be accurate. This potential limitation was managed by contacting them to clarify specific responses that were unclear after submission. This adds to the cost of using COMPAT. If COMPAT is to be used longitudinally and with independent self-reporting, compliance may be an issue that will need to be addressed.

COMPAT is a new tool for pain assessment in CP and it has been well received by experts and patients. To better validate COMPAT as a reliable pain assessment tool, larger studies of patient responses in COMPAT across geographical locations are key next steps. The findings must be correlated with clinical and diagnostic characteristics of patients to identify possible associations between aspects of pain and underlying mechanisms of pain. Determining the important pain mechanism(s) in CP, is important in selecting the most appropriate sequence and type of treatment. Thus, better assessment could lead to better management strategies. Currently,

the second version of COMPAT is being evaluated in larger cohorts of CP patients in New Zealand and Denmark (in Danish). The long-term goal is to create an abbreviated COMPAT smartphone application that will allow patients and pancreatologists to track pain remotely over time to allow early intervention and to monitor the response to interventions.

In conclusion, this study presents the development, validation and evaluation of the first comprehensive pain assessment tool for patients with CP. It has been shown to have high face validity by experts and patients, indicating that it covers important and relevant pain aspects and that it is easy to use. The pilot evaluation demonstrates that majority patients can successfully complete it on their own. The pilot evaluation suggests that different pain Patterns might be distinguished and that these may well reflect different pain mechanisms, opening the possibility of more tailored treatment decisions.

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Appendix 1. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.pan.2017.07.004.

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