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Abbreviations

CD	Crohn's disease
CT	Computed tomography
ERCP	Endoscopic retrograde cholangiopancreatography
FAPS	Functional abdominal pain syndrome
GI	Gastrointestinal
IBD	Inflammatory bowel disease
IBS	Irritable bowel syndrome
UC	Ulcerative colitis
US	Ultrasound

Introduction

Chronic abdominal pain is a commonly seen complaint by primary care physicians, gastroenterologists, and pain physicians. Generally, it is defined as continuous or intermittent abdominal discomfort for at least 6 months, and can be caused by a wide variety of etiologies ranging from organic to functional. Organic causes can be anatomical, physiological, metabolic, or can arise from the abdominal wall musculature, fascia, or nerves. Functional abdominal pain is a more challenging problem and can be difficult to diagnose and manage. In patients with functional abdominal pain, frequently, there is no clear organic cause that can explain the underlying symptoms.

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Epidemiology

The prevalence of unspecified chronic abdominal pain is suggested by the epidemiological data to be around 22.9 per 1,000 person-years. Abdominal pain is a common complaint with cross-sectional data suggesting that up to 25 % of adult populations have abdominal pain at any one time [1–3]. The prevalence is equal across different age groups, ethnicities, and geographic regions [4–9]. In a national, cross-sectional, telephone survey of US households, Sandler et al. [3] suggest that the prevalence of abdominal pain and discomfort was 22 % overall, and 16 % in individuals of age 60 and older. The same study suggests that women are more likely to report abdominal pain than men. Other studies found that the overall frequency of abdominal pain and discomfort of more than six times per year was 21 % in healthy individuals [10] and 24 % in people of age 65 and older [11]. There is a wide range of variation in the reported prevalence of upper abdominal symptoms (mostly upper abdominal pain or discomfort) ranging from 8 to 54 % [4]. The most likely explanation of the broad range in reported prevalence is variation in the definition of symptoms.

Visceral Chronic Abdominal Pain

A. Inflammatory Bowel Disease: Of the chronic abdominal pain etiologies which are of a primarily visceral origin, the most common and most costly to our healthcare resources is that of inflammatory bowel disease (IBD), specifically Ulcerative Colitis (UC) and Crohn's Disease (CD). Unfortunately, very limited data exist on tools that could help identify those patients with IBD that may go on to develop a chronic pain syndrome. Therefore, it is of particular importance to understand the current epidemiologic trends of the disease process itself, using a wealth of data currently available to researchers... IBD is an ongoing area of needed research as the past several decades

have seen a rapid rise in incidence and shift in susceptible populations. Large disparities are seen globally as changing worldwide demographics have seen a rise in areas previously believed to be resistant to disease.

The incidence of IBD worldwide is generally thought to be in the range of 0.6–20.3/100,000 for Crohn's disease and 0.1–15.6/100,000 for Ulcerative colitis [12]. Such wide incidence range and high variability are due to a large disparity between geographical areas. Historically, believed to be a “westernized disease” or “urbanized disease,” the highest IBD incidence rates are seen in North America, the United Kingdom, and northern Europe as compared to southern Europe, Asia, and Africa. In North America, incidence rates for IBD ranges from 2.2 to 14.3/100,000 with 3.1–14.6/100,000 cases of CD and 2.2–14.3 cases of UC diagnosed annually [12–17]. Similar incidence data are recorded in Europe with ranges of 1.5–20.3/100,000 for UC and 0.7–9.8/100,000 for CD. A large scale study out of Europe in the 1990s found the mean annual incidence to be in the range of 7.6–13.1 for UC and 2.8–8.3 for CD. Of particular interest is that this study showed a predominant north hemisphere versus south distribution with rates in northern Europe to be 40 % higher for UC and 80 % higher for CD [14]. This trend appears to be shifting slightly, however, with data suggesting a disproportionate rise in incidence in areas such as Japan, Korea, and northern India [18–20]. IBD is generally considered to be a disease of younger adults and adolescents. Peak incidence for CD is from 15 to 25 years of age, and for UC 25–35 years of age with about 10 % of cases diagnosed before the age of 18. A second and rather modest peak in incidence for both diseases is seen between the ages of 50–60 [16, 17, 21]. Recent data suggested a rise in the incidence of pediatric IBD with a greater proportion of these cases being CD. A recent statewide epidemiologic survey from Wisconsin demonstrated the highest rate of pediatric IBD in the world to date, with an overall incidence of 7.05/100,000 in children <18 years of age with 4.56/100,000 newly diagnosed cases of CD and 2.14/100,000 cases of UC [21]. Similar studies out of Europe, including Sweden and Finland have seen incidence rates of pediatric IBD almost double, with the majority of this being in cases of CD while UC has remained relatively stable [22, 23] (Fig. 2.1). In regards to gender prevalence, in UC, there is a male predominance; while in CD female, those gender differences appear to be decreasing [12, 14]. Breakdowns of racial and ethnic predispositions are another area that is continually changing. Historically, IBD was thought to be more common in Caucasians and people of Jewish descent, with lower rates in African-Americans and Asian-Americans were documented. A recent data suggested that this gap is closing [16, 17, 24, 25]. Data from urbanized

TABLE 2. IBD in Children in Southern Finland, 1987–2003

Year	Incidence (95% CIs)*			
	IBD	CD	UC	IC
1987	3.9 (2.5–5.8)	1.7 (0.8–3.1)	2.2 (1.2–3.7)	0.0 (0.0–0.6)
1988	3.0 (1.8–4.8)	1.0 (0.4–2.2)	1.3 (0.6–2.7)	0.7 (0.2–1.7)
1989	3.4 (2.1–5.2)	0.8 (0.3–2.0)	2.0 (1.0–3.5)	0.5 (0.1–1.5)
1990	4.7 (3.1–6.7)	1.2 (0.5–2.4)	2.8 (1.6–4.5)	0.2 (0.2–1.7)
1991	6.4 (4.6–8.8)	2.0 (1.0–3.4)	3.9 (2.5–5.9)	0.5 (0.1–1.4)
1992	4.1 (2.6–6.0)	1.0 (0.4–2.1)	2.6 (1.5–4.2)	0.5 (0.1–1.4)
1993	5.0 (3.4–7.1)	1.8 (0.9–3.2)	2.9 (1.7–4.6)	0.3 (0.0–1.2)
1994	5.0 (3.4–7.1)	1.5 (0.7–2.8)	2.6 (1.5–4.2)	0.9 (0.4–2.1)
1995	4.7 (3.1–6.7)	1.3 (0.6–2.5)	1.9 (1.0–3.4)	1.4 (0.7–2.7)
1996	6.1 (4.3–8.4)	2.2 (1.2–3.8)	2.7 (1.6–4.4)	1.1 (0.5–2.3)
1997	4.6 (3.1–6.7)	1.8 (0.9–3.1)	2.2 (1.2–3.8)	0.6 (0.2–1.6)
1998	9.7 (7.5–12.5)	3.4 (2.1–5.1)	5.1 (3.5–7.2)	1.2 (0.6–2.5)
1999	7.4 (5.4–9.8)	2.7 (1.6–4.4)	3.4 (2.1–5.1)	1.2 (0.6–2.5)
2000	6.6 (4.7–8.9)	1.9 (1.0–3.4)	3.5 (2.2–5.3)	1.1 (0.5–2.3)
2001	7.7 (5.7–10.3)	2.6 (1.5–4.2)	4.0 (2.6–5.9)	1.1 (0.5–2.3)
2002	8.7 (6.6–11.4)	3.6 (2.2–5.4)	4.8 (3.3–6.9)	0.3 (0.0–1.2)
2003	7.0† (5.0–9.4)	2.6 (1.5–4.2)	3.2 (2.0–5.0)	1.0 (0.4–2.1)

*Expressed as n/100,000.

†In 1 case, diagnosis unsettled because of missing data and therefore included only in total incidence figure.

Fig. 2.1 Incidence of Pediatric IBD over 17-year period in southern Finland. The mean annual incidence rate increased from 3.9/100,000 (95 % confidence interval [CI] 2.5–5.8) in 1987 to 7.0/100,000 (CI 5.0–9.4) in 2003 ($P < 0.001$). Reprinted with permission from Elsevier - Askling J, Grahnquist L, Ekblom A, Finkel Y. Incidence of paediatric Crohn's disease in Stockholm, Sweden. *Lancet*. 1999 Oct 2;354(9185):1179

areas of the United States have shown that disease rates amongst African-Americans and Caucasian populations are similar. Studies of migrant populations suggest that the ethnic and racial differences may be more related to lifestyle and environmental influences than true genetic differences [12]. In regards to potential risk factors identified for IBD, a thorough review is outside the scope of this discussion, however, briefly those factors which have been identified, and are under current investigation include cigarette smoking/tobacco use, diet, high stress occupations, sanitation and exposure to infection, gut flora, and oral contraceptives [12, 15, 25].

With a better understanding of the scope and makeup of the IBD patient population, we can now shift our focus to a specific subset of this population, those patients who experience chronic abdominal pain. As IBD is a disease of chronic inflammation, it is not surprising that 50–70 % of patients cite pain as their initial symptom, or as a prevalent symptom during exacerbations of their disease. What is surprising, however, is that up to 20 % of IBD patients will report chronic pain, despite a clinical

Annual incidence	Crohn's disease (n=50)	Ulcerative colitis (n=27)	Unspecified colitis (n=14)
1990	0.0 (0.0-3.3)	0.9 (0.0-5.0)	0.9 (0.0-5.0)
1991	2.7 (0.6-7.8)	3.6 (1.0-9.1)	1.8 (0.2-6.4)
1992	4.4 (1.4-10)	4.4 (1.4-10.2)	0.0 (0.0-3.2)
1993	1.7 (0.2-6.2)	0.9 (0.0-4.8)	1.7 (0.2-6.2)
1994	4.2 (1.4-9.8)	2.5 (0.5-7.4)	1.7 (0.2-6.1)
1995	2.7 (0.9-6.3)	1.6 (0.3-4.8)	0.0 (0.0-2.0)
1996	4.3 (1.9-8.5)	2.7 (0.9-6.3)	1.6 (0.3-4.7)
1997	5.9 (2.9-11)	2.1 (0.6-5.5)	1.6 (0.3-4.7)
1998	5.9 (2.9-11)	0.5 (0.0-3.0)	0.5 (0.0-3.0)

Incidence (per 100 000, 95% CI) of inflammatory bowel disease among individuals below 17 years of age in northern Stockholm, Sweden, 1990-98

Fig. 2.2 In the TREAT registry, patients using narcotic analgesics had increased mortality rates (OR 1.84, $P=0.044$). Also the use of narcotic analgesics was an independent predictor of serious infection (OR 2.38, $P<0.001$). Reprinted with permission from Elsevier – Lichtenstein GR, Feagan BG, Cohen RD, Salzberg BA, Diamond RH, Chen DM, et al. Serious infections and mortality in association with therapies for Crohn's disease: TREAT registry. Clin Gastroenterol Hepatol. 2006 May;4(5):621-30

diagnosis of remission and negative endoscopic findings [26]. Up to 15 % of them continue with opioid use for treatment of their chronic abdominal pain [13, 26-29]. This is of particular importance, as studies have shown an increase in the morbidity and mortality of those patients which require chronic opioid use [28].

Analysis from the Therapy Resource, Evaluation and Assessment Tool (TREAT) registry showed that chronic use of opioids increased the risk of serious infections, possibly by decreasing gut transit, increasing bacterial growth within the gut, or masking early symptoms. Also, of concern with regards to chronic opioid use is the risk of narcotic bowel syndrome (NBS), risk of toxic megacolon, narcotic dependence, and masking of more serious complications, such as bowel perforation [27, 28] (Fig. 2.2). There is a limited data to identify those risk factors, or patients at a proportionally higher risk for chronic pain, or with need for ongoing opioid therapy. Edwards et al. found a high rate of preexisting psychiatric illness amongst IBD patients on chronic opiates (up to 67 %) [27]. In a retrospective study of 291 CD patients over a 5-year period, Cross et al. found that patients using chronic opioids were more likely to be female, at the higher rates of disability, a longer duration of disease, and were more likely to be active smokers [29]. Finally, in a case-control study of 100 IBD patients, Hanson et al. found significant associations between chronic opioid use and female gender, two or more previous surgeries, higher rates of depression/anxiety, and a history of sexual, emotional, or physical abuse [13]. Again, as limited epidemiologic data are available it is difficult to make generalizations or truly make cause-effect relationships but it does identify a growing need for more data in this patient population.

Key Points

- There is a rapid rise in IBD incidence over the past several decades, with CD becoming as equally apparent as UC.
 - Up to 1.8-fold increase in incidence in pediatric IBD with the majority of cases being CD.
 - Racial/ethnic disparities are becoming less evident, as population differences appear to be more geographically versus genetically dependent.
 - Up to 20 % of IBD patients report chronic abdominal pain despite clinical remission and the majority of these patients require chronic opioid use.
 - Limited epidemiologic data in IBD patients that report chronic pain, however, associations that have been drawn include preexisting psychiatric illness, female gender, smoking, and longer duration of disease.
- B. *Chronic Pancreatitis*: While not as common as IBD, chronic pancreatitis is an inflammatory condition that leads to progressive and irreversible destruction of tissue and has a significant impact on the quality of life of patients with ever increasing healthcare costs everywhere in the world.

Epidemiologic studies regarding prevalence of chronic pancreatitis over the past several decades are few and not consistent. Given the natural history of the disease process, and constantly changing disease classification, clear comparison amongst patient groups is very difficult. In regards to the incidence and prevalence of the disease, we do know that it is rising [30-32]. Most studies suggest the incidence of chronic pancreatitis to be around 3-14/100,000 in Europe, 6-7/100,000 [31] in the United States [30, 33], and 5-6/100,000 in Japan [32, 34]. The overall prevalence of the disease has been on the rise, with an increased incidence worldwide at 13-35 cases per 100,000 [30-34]. There is a great variability in peak age of onset of disease amongst the studies, but in general the mean age range when diagnosis is established is between 39.7 and 57 years of age [31]. There is a marked disparity in disease prevalence between men and women, mostly related to a higher incidence of chronic alcoholism in men, with male to female ratios of 3:1. That may be direct consequence of majority, 68.5-91 % of patients with chronic pancreatitis being men [31, 32, 34]. In regards to etiology of disease, chronic alcohol use is the most common cause as 60-90 % of cases can be related to alcohol [35, 36]. This number, however, appears to be declining, with a higher incidence of idiopathic cases recently mostly in women [32, 34, 35]. A more recent study by Cote et al. suggested that only 44.5 % of causative etiology could be attributed to alcohol, and only 59.4 % occurred in men. Smoking in particular has been identified as a potential major risk factor for developing chronic pancreatitis, as well as advancing the rate of progression [35]. Such increased incidence may be also related to use

Variable	Pain pattern			Pain pattern		
	Intermittent	Constant	p Value	Mild to moderate	Severe	p Value
Number (%)	186 (44.9)	228 (55.1)		96 (23.2)	318 (76.8)	
Gender						
Male	98 (52.7)	107 (46.9)	0.28	52 (54.2)	153 (48.1)	0.35
Age at enrolment (mean±SD)	50.6±17.1	47.6±13.8	0.05	50.1±14.6	48.6±15.7	0.38
Race (%) (n=413)						
White	160 (86.5)	184 (80.7)	0.26	76 (80.0)	268 (84.3)	0.22
Black	19 (10.3)	31 (13.6)		16 (16.8)	34 (10.7)	
Others or mixed	6 (3.2)	13 (5.7)		3 (3.2)	16 (5.0)	
Body mass index (n=406)						
Normal or low	109 (59.6)	130 (58.3)	0.95	50 (53.2)	189 (60.6)	0.45
Overweight	52 (28.4)	68 (30.5)		34 (36.2)	86 (27.6)	
Obese	22 (12.0)	25 (11.2)		10 (10.6)	37 (11.9)	
Drinking category (%) (n = 413)						
Abstainer	48 (25.9)	47 (20.6)	0.01	16 (16.7)	79 (24.9)	0.50
Light	38 (20.5)	41 (18.0)		24 (25.0)	55 (17.4)	
Moderate	43 (23.2)	41 (18.0)		20 (20.8)	64 (20.2)	
Heavy	20 (10.8)	28 (12.3)		9 (9.4)	39 (12.3)	
Very heavy	36 (19.5)	71 (31.1)		27 (28.1)	80 (25.2)	
Smoking (%) (n = 412)						
Never	65 (35.3)	55 (24.1)	0.02	24 (25.3)	96 (30.3)	0.25
Past	44 (23.9)	52 (22.8)		28 (29.5)	68 (21.5)	
Current	75 (40.8)	121 (53.1)		43 (45.3)	153 (48.3)	
Amount of smoking (%) (n=401)						
Never	65 (36.3)	55 (24.8)	0.05	24 (25.8)	96 (31.2)	0.52
<1 packs/day	45 (25.1)	71 (32.0)		30 (32.3)	86 (27.9)	
≥1 packs/day	69 (38.5)	96 (43.2)		39 (41.9)	126 (40.9)	
Acute pancreatitis ever (%) (n=411)						
Yes	122 (66.3)	146 (64.3)	0.62	58 (61.7)	210 (66.2)	0.62
No	29 (15.8)	44 (19.4)		17 (18.1)	56 (17.7)	
Unclear	33 (17.9)	37 (16.3)		19 (20.2)	51 (16.1)	
Regular use of pain medication (%) (n=330)						
Yes	37 (22.3)	119 (72.6)	<0.001	36 (45.0)	120 (48.0)	0.73
No	129 (77.7)	45 (27.4)		44 (55.0)	130 (52.0)	
Disability (%) (n=399)						
Yes	32 (17.5)	91 (42.1)	<0.001	23 (25.0)	100 (32.6)	0.21
No	151 (82.5)	125 (57.9)		69 (75.0)	207 (67.4)	

Fig. 2.3 Survey of 540 patients with chronic pancreatitis. Fifty-five percent of patients identified a chronic (versus intermittent) pain pattern and in this subgroup, 72.6 % required the use of daily analgesics, 75.9 % were current or ex-smokers, and 42.1 % identified themselves as currently disabled. Reprinted with permission from BMJ Publishing

Group Ltd.—Mullady DK, Yadav D, Amann ST, O'Connell MR, Barmada MM, Elta GH, et al. Type of pain, pain-associated complications, quality of life, disability and resource utilisation in chronic pancreatitis: A prospective cohort study. *Gut*. 2011 Jan;60(1):77–84

of more sensitive diagnostic modalities such as US, CT, and ERCP [32, 34].

The socioeconomic impact of chronic pancreatitis is of obvious concern. These patients who have a significantly poorer quality of life, require extended hospitalizations, and typically require chronic analgesia. According to current literature, 27–67 % of patients with chronic alcoholic pancreatitis experience chronic pain, and as high as 80–90 % of those patients report either chronic, or recurrent pain during the course of their illness [37, 38]. In some of these cases the source of their pain is apparent,

such as bile duct or duodenal stenosis, pancreatic fibrosis/inflammation, or intra-pancreatic causes, however, in the majority of the cases a definitive source of pain cannot be identified [38]. There is a limited data on the epidemiology of chronic pain in the setting of chronic pancreatitis. Probably the largest study comes from Mullady et al. [39] in which 540 chronic pancreatitis patients were identified of which 414 self-identified a particular pain pattern A-E which were defined by the temporal nature (intermittent/chronic) and pain severity (mild, moderate, severe) (Fig. 2.3). This study revealed that 55 % of patients

identified a chronic pain pattern as opposed to intermittent. Of particular importance, 72.6 % of patients that identified a chronic pain pattern required the use of daily pain medications. This is in comparison to those patients which identified as intermittent in which only 22.3 % required chronic pain medications. Of this specific patient population, 46.9 % of these patients were men, 75.9 % of patients were either current or ex-smokers, and a much higher percentage, 42.1 % versus 17.5 %, reported themselves as disabled. There was no difference in frequency of intermittent or constant pain based on race, BMI, family history of pancreatic cancer, or personal history of acute pancreatitis [39]. Somewhat higher proportion (63 %) of patients with ongoing alcohol use were also reporting constant pain patterns.

Key Points

- Incidence/prevalence of chronic pancreatitis is on the rise worldwide, and potential causes include increased use of alcohol, but also use of more sensitive diagnostic modalities.
 - There is a subset of rising CP cases in which alcohol is not identified as the primary cause, and it appears to be higher in women.
 - As high as 80–90 % of patients identify either chronic or intermittent, recurrent pain during the course of their illness and a large majority of these patients require chronic pain medications.
 - Limited epidemiologic data are available regarding prevalence of pain from chronic pancreatitis; however there appears to be association between ongoing alcohol use, smoking, and patients with chronic pain syndrome.
- C. *Adhesions/Postsurgical*: Intra-abdominal adhesion-related diseases include postsurgical chronic abdominal pain syndromes, most common of which are post-cholecystectomy, herniorrhaphy, and lysis of adhesions. Very limited epidemiological data exist on this subset of patients, as the operative management remains controversial, and true causal relationships have been difficult to prove.

In many patients who initially present with chronic abdominal pain, no immediate source of intra-abdominal adhesions can be identified [40]. Postsurgical adhesions incidence varied in the literature, from 45 to 90–100 % [40–45]. Post-mortem studies done out of the UK, suggested that in as high as 28 % of autopsies in patients without prior abdominal surgery, found intra-abdominal adhesive disease believed to be related to intra-abdominal infections. Indeed, a true causal relationship between presence of abdominal adhesions and chronic abdominal pain could not be consistently found in the literature [40, 43, 44]. Despite the fact that the link between presence of adhesions and chronic abdominal pain is difficult to make, several studies provided evidence that diagnostic laparoscopy benefits this patient population, providing postsurgi-

cal pain relief rates as high as 80 %, even regardless of whether adhesiolysis was performed [40, 43]. Risk factors for development of adhesions post-surgery predominantly revolve around surgical approach, patient age, type of procedure, use of foreign bodies such as peritoneal mesh, and presence or absence of a contaminated field (i.e., gallbladder debris) [40–45].

Other risk factors for development of chronic postsurgical pain included type of surgery, duration, open versus minimally invasive, intraoperative nerve damage and gender [46–52]. Of these, most striking association is type of surgery, specifically cholecystectomy, herniorrhaphy, pelvic procedures, and adhesiolysis. Rates for post-cholecystectomy chronic abdominal pain have been reported to be in the range of 3–56 % [46, 47, 49, 53]. More specifically, risk factors include preexisting psychiatric illness, female gender, long duration of symptom prior to surgery, and pain at 6 weeks post-surgery [53]. Post-herniorrhaphy chronic pain incidence rate was also high, from 0 to 63 % [46–49, 51, 53]. Conclusions from these studies suggest that recurrent disease, presence of preoperative pain, severity acute postoperative pain, higher body mass index, and younger age correlate with higher rates of chronic pain development. On the other hand it seems to be consistent throughout the studies that older patients have a reduced risk for the development of chronic pain.

Key Points

- Rate of painful post abdominal surgery adhesion development is between 45 and 90 %. Risk of adhesion formation is higher in open procedures (versus minimally invasive), use of foreign bodies (i.e., mesh), and presence of a contaminated surgical field (i.e., gallbladder/bowel contamination).
- Most common surgical procedures linked to chronic abdominal pain include cholecystectomy, herniorrhaphy, and adhesiolysis.
- Postsurgical chronic pain risk factors identified include type and duration of surgical procedure, preexisting psychiatric illness, female gender, and younger age at operation.

Chronic Somatosensory Pain of the Abdomen

Abdominal pain is one of the frequent patient complaints in the United States. Acute abdominal pain differential diagnosis is extensive, with predominance of abdominal organ functional disorders. Possible defined sources of chronic abdominal pain (defined as an interval between 3 and 12 months) may remain elusive for the treating clinician. Chronic abdominal pain can be roughly divided into visceral, somatosensory, and functional. While visceral pain typically

originates from deep, internal abdominal structures, somatic pain originates from nociceptors in superficial tissues (i.e., skin), or the musculoskeletal system (i.e., bones, ligaments, muscles, etc.). In addition, the nerves that innervate these superficial structures can incur injury leading to neuropathic causalgia. The most common causes of chronic abdominal pain in these superficial structures will be the focus of the next several sections.

A. Postsurgical Pain: It is common to experience pain immediately after major abdominal surgery. However, chronic pain (defined as pain >6 months following surgery) varies in incidence from 3 to 80 %, depending on the type of surgery performed [53]. Chronic postsurgical pain can be associated with limb amputation (i.e., phantom limb pain), or post-thoracotomy [54, 55]. Chronic abdominal pain after major abdominal surgery incidence varies from 3 to 50 % [56–58]. Various peri-operative risk factors in patients undergoing specific surgery have been linked to chronic abdominal pain. For example, psychological vulnerability, male gender, and long-standing symptoms before cholecystectomy were preoperative risk factors for chronic postoperative pain [59]. Interestingly, surgical approach (laparoscopic versus open cholecystectomy) made no difference in the incidence of abdominal pain 1 year after the surgery [60]. One of the strongest predictors of persistent pain at 1 year is presence of the pain at 6 weeks after procedure [61]. Incidence of chronic pain after inguinal hernia repair varies from 0 to 37 %, on average, around 11 % [53]. Patients with recurrent hernias and those with occupation-related injuries had a higher incidence of pain at 1 year [62]. Various studies that compared open versus laparoscopic inguinal hernia repair and, mesh versus non-mesh repair showed no statistically significant difference in the incidence of chronic pain between those surgical approaches [53]. Again, the incidence of pain at 4 weeks postoperatively was a strong predictor of future chronic abdominal pain [63]. For abdominal surgery, patients with psychological vulnerability, preexisting chronic pain, and persistent pain at 4–6 weeks after surgery seem to have highest likelihood for developing chronic abdominal pain.

Organic causes such as nerve damage, adhesions, or continued bowel dysfunction have been suggested as possible etiologies for continued pain at these postoperative intervals (3–12 months). Laparoscopic adhesiolysis has been attempted in chronic abdominal pain patients who have had previous abdominal surgery. Of the patients who underwent laparoscopic adhesiolysis, 47 % became pain free, 36 % reported relief, and 16 % had no change in symptoms [64]. Similar results have been found in patients female patients reporting chronic pelvic pain [65]. These studies suggest that non-obstructive adhesions, which are a common postoperative complication,

could significantly contribute to the development of chronic abdominal pain. Perhaps, further studies looking at quality rather than severity of pain would help differentiate the origin (visceral versus somatic) of pain. Hyperalgesia after nociceptors activation (i.e., surgery) has been suggested as another mechanism for chronic pain [66, 67]. One study looked at the effect of systemic lidocaine in blunting the sensitization of nociceptive afferents. Peri-operative lidocaine was shown to decrease total peri-operative morphine consumption [66]. In addition, patients in the lidocaine treatment group reported less pain with movement (i.e., walking, deep inspiration, etc.). It has been suggested that lidocaine may inhibit peripheral neuropeptides which activate nociceptors and produce a central hyperalgesic effect.

B. Chronic Abdominal Wall Pain: Chronic abdominal wall pain is a common, yet elusive, clinical entity that may account for up to 10 % of patients seen in gastroenterologists' practice [68]. The difficulty in identifying chronic abdominal wall pain is that clinicians often search for etiologies affecting visceral organs. The clinical work-up for the organic causes has huge economic implications (roughly \$1,300 dollars per patient in 1993). The incidence of chronic abdominal wall pain varies greatly depending on the study with ranges from 11 to 74 %. However, most notably Rubio et al. [69] reported an 11 % incidence of abdominal wall pain in patients with abdominal pain of obscure etiology over a 2-year interval. Multiple etiologies have been suggested as the cause of chronic abdominal wall pain. Commonly this is related to nerve injuries of the anterior abdominal wall such as entrapment of the anterior abdominal cutaneous nerve [70] caused by increased abdominal pressure, impingement by a surgical scar, or perhaps a painful rib. Other less commonly suggested etiologies include rectus sheath hematomas, incisional hernia, or radicular pain (T7–T12). Various studies have investigated the utility of anesthetic injections as a therapeutic and diagnostic maneuver for these patients. Abdominal wall pain was defined as superficial tenderness localized to a distinct point with abdominal wall tensing (positive Carnett test). Roughly 60–90 % percent of patients reported pain relief with anesthetic (local anesthetics and/or steroids) injections to the anterior cutaneous nerve block [70].

C. Radiculopathy: The abdominal wall is innervated by spinal nerves exiting T7–T12. Irritation of a nerve root due to disc herniation or degeneration will produce neurogenic pain in a radicular pattern. The patient may also have associated sensory deficits or decrease in elicited reflexes. Although L5–S1 and C5–C7 are the most commonly involved roots for radiculopathy, thoracic nerves can also produce radicular symptoms due to spinal pathology. The difficulty of specifically isolating abdominal pain in the

setting of radiculopathy has perhaps contributed to the difficulty in the studying the prevalence of this clinical entity. Despite radiculopathy being a relatively common occurrence, there is a paucity of literature regarding the epidemiology of radicular chronic abdominal pain.

- D. *Diabetic Neuropathy*: Patients with long-standing diabetes mellitus can experience pain and/or weakness in the distal aspects of their extremities. Less frequently described is an abdominal radiculopathy originating from the thoracic nerves. Although no prospective clinical or epidemiological studies have investigated abdominal diabetic neuropathy, a case series from the Mayo Clinic [71] illustrated four patients, which after extensive clinical investigation for other etiologies ultimately were found to have diffuse neuropathy in the abdomen by electromyography. This was presumed to be related to diabetic neuropathy. Fortunately, all patients in this case series had spontaneous resolution with conservative medical management. Again, due to lack of epidemiologic data in this area, the extent of this disease process is unclear.
- E. *Post herpetic Neuralgia*: Acute herpes zoster (shingles) is the reactivation of dormant varicella-zoster virus in ganglionic neurons. The incidence has been shown to be in the range of 0.4–1.6 cases per 1,000 in patients under the age of 20 years old. The incidence in patients over the age of 80 is much higher at 4.5–11 cases per 1,000 [72]. Immunocompromised patients (leukemia and transplant recipients) also experience a much higher incidence with rates as high as 45 per 1,000 in this susceptible population. [73]. Thoracic nerves (T7–12) are most commonly affected followed by trigeminal, cervical, and sacral spinal roots. Pain typically follows a unilateral dermatome progression with a rash that spontaneously resolves over the course of several weeks. Of the patients with acute herpes zoster 10–70 % progress to post herpetic neuralgia [73, 74].

Functional Abdominal Pain

Abdominal pain of unknown origin represents a frustrating topic among gastroenterologists and pain physicians due to difficulties in diagnoses and management. Extensive gastrointestinal evaluations often fail to show any correctable pathology. This is due to the complexities of visceral innervation and the fact that some chronic abdominal pain may not be visceral in origin. Epidemiological studies suggest many patients with chronic abdominal pain have a functional GI disorder such as irritable bowel syndrome (IBS) or functional dyspepsia [1–9, 75]. Often the pain associated with functional GI disorders coexists with other organic disorders. Psychological risk factors such as fatigue, psychological distress, health anxiety, and illness behavior are predictors of the development of new onset abdominal pain [8].

The results of this latter study suggest that functional abdominal pain is consistent with other non-organic pain syndromes. Many patients with abdominal pain have no obvious cause of their symptoms and receive an inconclusive diagnosis or no diagnosis at all. One study [1] suggests that patients consulting for the first time with a diagnosis of unspecified abdominal pain were 16–27 times more likely than controls to receive a new diagnosis of gallbladder disease, diverticular disease, pancreatitis, or appendicitis. US Householder Survey of Functional Gastrointestinal Disorders by Drossman et al. [6] suggests that females reported a higher incidence of IBS, functional abdominal pain, and functional biliary pain than males. Symptoms reported tended to decline with age. The survey also showed that patients in lower socioeconomic categories had an increased incidence. The rate of school / work absenteeism and physician visits is increased for those having a functional gastrointestinal disorder.

Common causes of functional abdominal pain include: IBS, functional dyspepsia, and functional abdominal pain syndrome (FAPS).

- A. *Irritable bowel syndrome*: IBS is a symptom-based condition in which affected individuals report recurrent episodes of abdominal pain or discomfort associated with altered bowel habits [10]. Population-based studies report that the IBS prevalence is 7–15 % and that IBS occurs more commonly in women than men [76–78] (Fig. 2.4). Most healthcare providers consider IBS a diagnosis of exclusion after first ruling out organic causes and other functional causes of abdominal pain. Patients with IBS often undergo an extensive work up to rule out organic causes such as IBD or colorectal cancer. Community based surveys indicate that half of IBS patients undergo colonoscopy as part of an evaluation of their symptoms [79]. One national database analysis found that up to 25 % of all colonoscopies performed in the United States are for symptoms related to IBS [80]. One prospective controlled US trial by Chey et al. [81] demonstrates the yield of colonoscopy in patients with non-constipated IBS. The study showed the prevalence of structural abnormalities of the colon is equal between suspected IBS patients as opposed to healthy controls. Microscopic colitis was identified in a small portion (1.5 %) of patients with IBS symptoms. Recent research on the pathophysiology of painful functional gastrointestinal disorders, including IBS, has focused on visceral hypersensitivity and dysregulation of brain-gut interaction [82, 83]. One prospective controlled study [84] shows that women undergoing gynecological surgeries for non-pain indications may develop abdominal pain (17 %), and that IBS might be a consequence as well, although the previous observation did not reach statistical significance. Psychological factors and adverse life events are often implicated in the etiology of IBS [85, 86]. There is also evidence for the overlap

Demographic characteristics	Demographic composition (%) within IBS subtype				Prevalence (%) within each demographic stratum			
	Diarrhoea (n = 901)	Alternator (n = 453)	Constipation (n = 333)	Overall (n = 1713)	Diarrhoea (n = 901)	Alternating (n = 453)	Constipation (n = 333)	Overall (n = 1713)
Overall	NA	NA	NA	NA	3.5	1.7	1.3	6.6 (6.3–6.9)
Gender								
Male	39.0	32.9	29.1	34.9	2.8	1.2	0.8	4.7 (4.4–5.1)
Female	61.0	67.1	70.9	63.6	4.1	2.3	1.8	8.2 (7.7–8.7)
Education level								
Less than HS	5.0	7.9	9.3	6.5	3.0	2.4	2.1	7.4 (6.2–8.9)
HS	23.9	25.6	29.4	25.0	3.3	1.8	1.5	6.7 (6.1–7.3)
Some college	46.4	42.8	39.6	43.4	4.0	1.9	1.3	7.2 (6.7–7.7)
Bachelor or higher	24.8	23.6	21.6	23.5	2.9	1.4	0.9	5.2 (4.7–5.8)
Race/ethnicity								
White	85.5	78.8	79.9	81.3	3.6	1.6	1.2	6.4 (6.1–6.8)
Black/African-American	8.1	13.2	13.2	10.3	2.8	2.3	1.7	6.8 (5.9–7.9)
Other combined	6.2	6.2	6.0	6.1	3.5	1.8	1.3	6.6 (5.4–7.9)
Latino/Hispanic	5.4	7.5	9.6	6.7	2.6	1.8	1.7	6.2 (5.2–7.4)
Age								
<35	21.8	24.7	23.4	22.5	3.1	1.8	1.2	6.2 (5.6–6.8)
35–44	31.1	29.6	30.3	30.1	3.7	1.8	1.4	6.9 (6.3–7.5)
45–54	28.6	29.4	26.4	28.0	3.6	1.8	1.2	6.6 (6.0–7.2)
55+	18.5	16.3	19.8	17.9	3.4	1.5	1.3	6.2 (5.5–6.9)
Income								
<\$20 000	14.7	23.2	21.0	17.9	3.9	3.1	2.0	9.0 (8.1–10.0)
\$20 000–\$34 999	18.6	17.0	18.9	18.0	4.0	1.8	1.5	7.4 (6.6–8.2)
\$35 000–\$49 999	22.2	19.9	21.3	21.1	3.7	1.6	1.3	6.6 (6.0–7.3)
\$50 000–\$74 999	23.6	20.5	24.0	22.5	3.2	1.4	1.2	5.8 (5.2–6.4)
\$75 000+	20.5	19.2	14.7	18.7	3.0	1.4	0.8	5.2 (4.7–5.8)
Marital status								
Not married	37.8	44.4	37.8	39.0	3.9	2.3	1.4	7.7 (7.2–8.3)
Married	62.0	55.4	62.2	59.4	3.24	1.4	1.2	5.9 (5.6–6.2)
Employment status								
Working	81.5	78.6	64.0	76.1	3.4	1.2	1.0	5.9 (5.6–6.3)
Not working	15.5	18.1	21.3	17.1	4.8	2.8	2.4	10.0 (8.9–11.1)
Disabled	–	–	14.7	2.9	0.0	0.0	4.5	4.5 (3.4–5.9)
Head of household								
No	15.9	20.3	15.6	16.8	3.8	2.5	1.4	7.7 (6.9–8.6)
Yes	83.6	79.2	84.4	81.3	3.4	1.6	1.3	6.3 (6.0–6.6)

Fig. 2.4 Web-based survey sent to 31,829 individuals of which 25,986 responded. Prevalence of IBS was similar across all race/ethnicity groups, was the highest in persons without a high school education, and increased as income decreased. Higher rates were also seen in unemployed or unmarried individuals. Reprinted with permission from John

Wiley and Sons—Andrews EB, Eaton SC, Hollis KA, Hopkins JS, Ameen V, Hamm LR, et al. Prevalence and demographics of irritable bowel syndrome: Results from a large web-based survey. *Aliment Pharmacol Ther.* 2005 Nov 15;22(10):935–42

of symptoms in different functional disorders. In one study of patients with chronic fatigue, there was a point prevalence of IBS symptoms of 63 % [87]. It is difficult to prove whether these factors are a predictor of onset, or merely a consequence, of symptoms. Furthermore, research into IBS has mainly taken place in primary or secondary care settings. The findings, therefore, cannot be easily extrapolated to other populations as consultation and referral behavior as well as recall bias of adverse events render the subjects highly selected and unrepresentative of the general population [88, 89].

B. Functional dyspepsia: Dyspepsia refers to a constellation of upper gastrointestinal symptoms that commonly occurs in adults. Dyspepsia can occur as a result of organic causes;

however the majority of patients suffer from non-ulcer or functional dyspepsia. Functional dyspepsia is defined as the presence of recurrent pain or discomfort centered in the upper abdomen in the absence of any known structural cause and without any features of IBS [90]. Mahadeva and Goh [91] have reviewed epidemiological data from population-based studies of various geographical locations. The summary of the data collected supports the notion that dyspepsia is common in most populations in the world. The varying prevalence of uninvestigated dyspepsia in different populations appears to be related to the different definitions of dyspepsia used by investigators of different surveys. The true prevalence of functional dyspepsia amongst the general population has not been

evaluated, due to the difficulties in excluding organic disease in large cohorts. However, several studies [91–94] have been able to examine this in some detail. The estimated prevalence of functional dyspepsia globally is between 11.5 and 29.2 %. Epidemiologically, according to the Mahadeva and Goh review [95], it appears that risk factors for functional dyspepsia are different than that of organic dyspepsia or uninvestigated dyspepsia. Female gender and underlying psychological disturbances have been shown to be the important factors in functional dyspepsia [82, 92, 94, 96, 97]. In contrast, environmental and life style habits such as poor socioeconomic status, smoking, increased caffeine intake, and NSAID ingestion appear to be more relevant to uninvestigated dyspepsia. That might be the result of a greater rate of organic disease in these populations. Dyspepsia has a peak prevalence between the ages of 40–50 years [93, 98]. There does not appear to be a significant difference in the incidence amongst varying ethnic groups [91].

- C. *Functional abdominal pain syndrome*: FAPS represents a pain syndrome attributed to the abdomen that is poorly related to gut function, is associated with some loss of daily activities, and has been present for at least 6 months. The pain is constant or very frequent. The principal criterion differentiating FAPS from other functional gastrointestinal disorders, such as IBS and functional dyspepsia, is the lack of symptom relationship to food intake or defecation. The epidemiology of FAPS is limited due to a lack of available data as well as difficulties in establishing a diagnosis that can be differentiated from other more common functional gastrointestinal disorders, such as IBS and functional dyspepsia. Reported prevalence figures in North America range from 0.5 to 2 % and do not differ from those reported in other countries [97, 99, 100]. The disorder is more common in women, with a female to male ratio of 3:2 [6]. The prevalence peaks in the fourth decade of life [6, 101]. Patients with FAPS have a high rate of work absenteeism and healthcare utilization and impose a significant economic burden [6, 99, 101]. FAPS shows a close relationship with a variety of psychiatric and psychological conditions. Clinical evidence suggests that there is strong association of adverse life events and psychological stressors with increased pain reports in functional gastrointestinal disorders [102, 103]. The combination of genetic factors, vulnerabilities factors, and adult stress may determine in part the effectiveness of endogenous pain modulation systems and thereby influence the development of FAPS [75]. Studies have confirmed a significant association between chronic abdominal pain and affective disorders, most notably anxiety and depression [104]. FAPS may be seen with other somatoform disorders such as somatization disorder, conversion disorder, and hypochondriasis [105]. Patients with FAPS may

exhibit ineffective coping strategies or have poor social and family support [106–110]. Histories of sexual and physical abuse are common [111, 112].

- D. *Opioid bowel dysfunction and NBS*: NBS is a recognized subset of opioid bowel dysfunction that is characterized by chronic or frequently recurring abdominal pain that worsens with continued or escalating dosages of narcotics [113, 114]. This syndrome is thought to be under-recognized, but probably is becoming more prevalent due to an increase in the use of opiate analgesia. Opioid bowel dysfunction is manifested by symptoms of constipation, nausea, bloating, ileus, and sometimes worsening abdominal pain [115, 116]. The effects of opioids on bowel function have been best studied in patients with cancer pain [117]. A population-based study by Choung et al. [118] demonstrated that NBS is a relatively rare disorder with a prevalence of 0.17 %. Those patients using prescription narcotics, however, were much more likely to report increased gastrointestinal symptoms and use more laxatives. In a case series, four patients with NBS were identified over a 20-year period. The authors [119] suggested that NBS may now become more prevalent because of the use of narcotics for chronic nonmalignant painful disorders.

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