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Studies of the symptom abdominal pain—a systematic review and meta-analysis

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Abstract

Background. Diagnostic reasoning in primary care patients with abdominal pain is a complex challenge for GPs. To ensure evidence-based decision making for this symptom, GPs need setting-specific knowledge about the prevalence, potential risks for diseases and chance of recovery or risk of undesirable courses of disease.

Aim. We conducted a systematic review of symptom-evaluating studies on prevalence, aetiology or prognosis of abdominal pain.

Methods. We included all studies evaluating the symptom 'abdominal pain' as a reason for consultation in primary care. We included all types of study designs except for qualitative studies. Studies focussed solely on children or settings other than primary care were also excluded.

Results. We identified 14 studies. Mean consultation prevalence is 2.8% for abdominal pain. In about one-third of patients the underlying cause of abdominal pain cannot be specified. The most common aetiologies are gastroenteritis (7.2–18.7%), irritable bowel disease (2.6–13.2%), urological cause (5.3%) and gastritis (5.2%). About 1 in 10 abdominal pain patients suffers from an acute disease like appendicitis (1.9%), diverticulitis (3.0%), biliary/pancreatic (4.0%) or neoplastic (1.0%) diseases needing immediate therapy.

Conclusion. There is a high prevalence of patients consulting GPs for abdominal pain. The review identified a comparably high rate of acute underlying diseases in need of further investigation or therapy. At the same time, the underlying cause of the complaints often remains unexplained. Further symptom-evaluating studies are necessary, ideally using standardized methodology in order to gain sufficient evidence for developing much-needed guidelines and decision support tools.

Key words: Abdominal pain, aetiology, prevalence, primary care, symptom evaluating study, systematic review.

Introduction

Abdominal pain is supposed to be a common complaint and reason for consultation in primary care (1). It affects nearly every person once in their lifetime independent from age, gender and social background (2,3). Abdominal pain can be caused by a broad spectrum of diseases from primarily trivial and self-limited (e.g. gastroenteritis) to acute and life-threatening conditions (e.g. abdominal aortic aneurysm) (4).

For most abdominal pain patients, the GP is the main contact person and the gate keeper to the health care system. GPs coordinate health care by triaging uncomplicated abdominal pain (self-limiting, needing only symptomatic relief) and potentially serious diseases which need further investigation and intensified therapy. Decisions are based on history and clinical examination by balancing risks and disease probabilities. For rational

judgment and counselling, GPs need setting-specific knowledge about the prevalence (pre-test probability), the suspected underlying aetiology (work-up probability) and the prognosis of abdominal pain. However, the respective evidence about these information, is scarce, and findings from single studies are not necessarily transferable to general practice setting. To date, there are no systematic reviews summarizing current evidence concerning the risks and probabilities in abdominal pain.

We conducted a systematic review of symptom-evaluating studies on the prevalence, aetiology, frequencies and prognosis of abdominal pain (as main or secondary complaint) as presented to GPs in a primary care setting.

Methods

Types of studies

We performed a systematic review which includes symptom-evaluating studies about abdominal pain.

Inclusion and exclusion criteria

We included all studies evaluating the symptom 'abdominal pain' as a primary or secondary consulting reason in the primary care setting. Results of the studies had to yield one of the following estimates: prevalence or incidence of abdominal pain, information about underlying diagnoses and/or prognoses of abdominal pain. We included various study designs, excepting qualitative studies. There was no restriction regarding the type of data assessment, outcome measurement or the study quality. We excluded studies which that only included children (0–18 years) or evaluated settings other than primary care (e.g. hospital care, emergency centres, secondary care). We also excluded studies where patients were selected before recruitment, e.g. because they had an increased probability for a certain diagnosis.

Search strategy

In November 2010 we did a computer-based search of the PUBMED and EMBASE databases. In addition, we searched through the conference abstracts volumes of the European General Practice Research Network and the North American Primary Care Research Group for relevant studies. The authors also screened the reference list of all relevant studies. Studies published in English, German, Dutch, Italian and Spanish were included.

We used the following search syntax for electronic searches:

The term 'abdominal pain' in various notations (in title or abstract) OR the MESH term 'abdominal pain' AND the term 'general practice' in various notations (in title or abstract) OR a journal representing our research area OR the term 'general practice' in various notations (in affiliation of authors) OR the MESH terms 'family practice', 'physicians, family' and 'primary health care'. The entire syntax is available on request from the authors.

Selection of publications

All identified studies went through a two-step selection process. In the first step, we screened titles and abstracts. Studies meeting all three criteria, 'original research article', 'inclusion of patients because of abdominal pain' and 'primary care setting', were classified as potentially appropriate. In the next step, we analysed the full texts of the selected articles regarding inclusion and exclusion criteria. Reasons for exclusion were documented.

Two independent review authors (CK, TB) performed a parallel selection process. Disagreements were resolved by discussion between the two review authors (CK, TB). A third review author (AV) was consulted if disagreement persisted.

Data extraction

We extracted bibliographic data (author, publication year, title, journal), country, setting, study design, inclusion and exclusion criteria, type of recruitment, study population (age, gender distribution) and study duration. For prevalence data, we registered the number of abdominal pain cases, the number and type of the population from which the cases descended from (e.g. number of all practice consultations or all registered patients in a practice). Furthermore, we extracted all diagnostic categories and their absolute and relative frequencies. We documented every kind of prognostic outcome.

Quality assessment

For quality assessment, we developed a 13-point catalogue of criteria to query essential quality characteristics for studies of symptoms. Until now, no official quality or reporting guideline for studies of symptoms had been developed. All included studies underwent quality assessment regarding the criteria of Table 2, independent of the particular research question.

Data analysis

For meta-analysis, we used the random effects model and calculated confidence intervals (CIs) to show the precision of the mean. We chose this model because it allows a variation of the true effect from study to study (5).

Since our review includes studies with various study sizes, we used tau^2 for quantifying heterogeneity. Tau^2 is an estimate of the between study variance in a random effects meta-analysis (6). In contrast to the commonly used I^2, tau^2 is independent from the sizes of the included studies (7,8). We approximately estimated the 95% prediction interval using [expit (PE – 2 × tau); expit (PE +

2 × tau)], where prediction interval is the random effects pooled estimate of the proportion on the logit scale and expit is the inverse logit function. The prediction interval describes the distribution of the true effect size of the included studies and is an estimate of an interval in which the true effect size (e.g. prevalence of a symptom) of a future study will fall with a probability of 95% (6). While the CI quantifies the uncertainty in the estimation of the true effect size, the prediction interval reflects the between study heterogeneity. The fact that the values of the prediction intervals are equal to the scale of the original results simplifies the clinical interpretation and makes it more ostensive. We did no data pooling in cases where prediction intervals were broader than 10%.

Data analysis was done with the statistical program R 2.14.0 (R Foundation for statistical analysis, Vienna, Austria). We used the R package 'meta: Meta-Analysis with R' (9). CIs of frequencies were calculated as exact binomial CIs according to Clopper Peason.

Results

Search result and study selection

The computer-based search identified 1815 references in EMBASE and 716 in PUBMED. The manual search in the congress abstracts identified nine references. After extracting 529 duplicates, 2011 unique references remained. The title and abstract screening of these references detected 73 studies as potentially appropriate. Finally, the full text analysis of these trials produced 14 studies which met the inclusion criteria (10–23). Further details are given in a flowchart (Fig. 1).

Included studies

Data was accrued from Europe (five studies), the USA (four studies), the Near East (two studies) and Australia/New Zealand (three studies). The time of publication varied between 1982 and

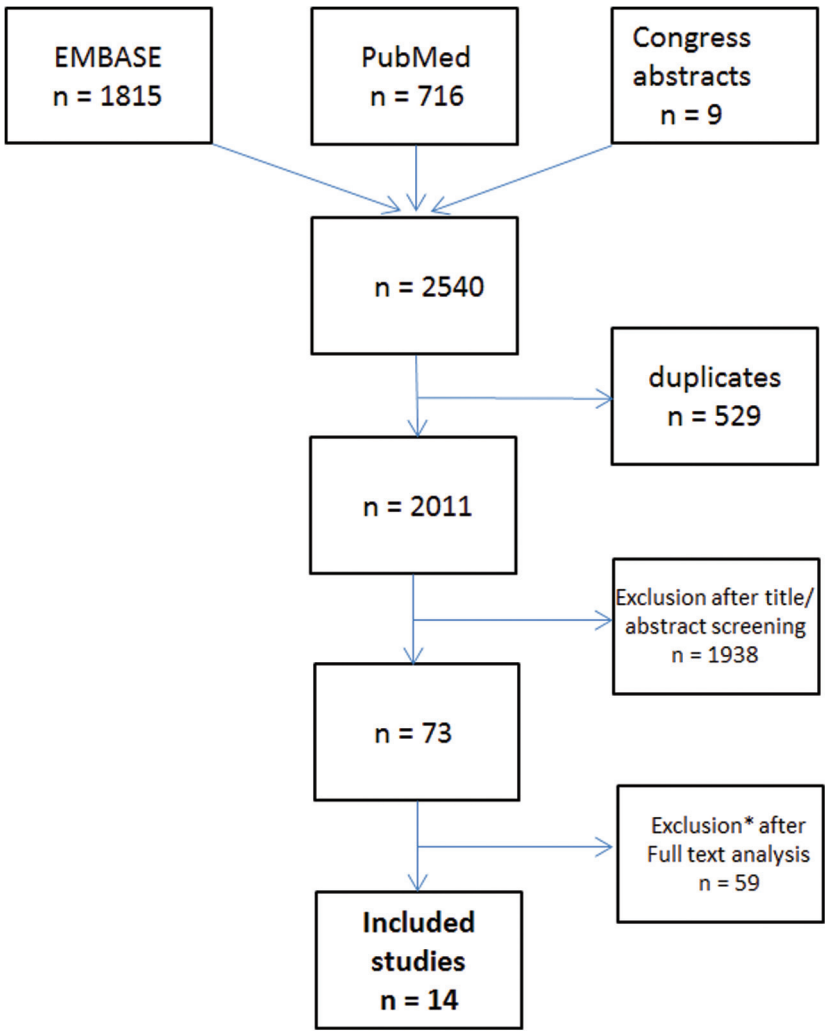

Figure 1. Flowchart of the selection process. *Reasons for exclusion (several exclusion reasons per study were possible): 22 publications: no primary care setting; 14 publications: no original research; 36 publications: preselected study population; 19 publications: abdominal pain was not the consultation reason; 32 publications: missing outcome.

2010. The age of included patients ranged from 0 to 99 years. Seven of the included studies recruited patients prospectively during the consultations, whereas seven studies retrieved data retrospectively from databases including medical records of all individuals registered at participating primary care physicians. Further details of the included studies are shown in Table 1.

Quality of included studies: Of the 14 studies included, prospective recruitment was used in seven studies, consistent recruitment of all abdominal pain cases was used in ten studies, and well-defined inclusion and exclusion criteria were used in eight studies. A multicentre approach was used in 10 studies and drop out follow-up was reported in five studies. A consistent definition of the prevalence rate was given in 7 out of 11 studies assessing symptom prevalence.

As for symptom aetiology, the categories of diagnoses were comprehensibly described in three cases. None of the respective studies described a reference standard deemed as appropriate by the study team. Workup bias was frequent: Only one study applied the same reference standard to all patients, and no study reported whether all patients received the same diagnostic procedures.

As for the prognosis of abdominal pain, we identified the two studies (12,23). The operationalization of the prognostic result was deemed appropriate in both studies. One study included a comparison group while investigating the prognosis.

In summary, 6 of the 14 included studies fulfilled at least 50% of our quality criteria; see Table 2.

Prevalence of the symptom 'abdominal pain' in general practice: Eleven studies commented on prevalence data for 'abdominal pain' (Fig. 2). Except for two outliers [studies from Abu-Mourada *et al.* (prevalence: 13.8%, CI: 11.2–16.6) and Martin *et al.* (prevalence: 11.6%, CI: 9.7–13.7) which took place in countries with military conflicts, the prevalence of abdominal pain was 2.8% (CI: 2.5–3.2). The results are shown as a forest plot in Fig. 2.

Aetiologies of the symptom 'abdominal pain' in general practice: We identified nine studies assessing data on the aetiology of abdominal pain cases. The authors described a variety of differential diagnoses which we summarized in 17 categories, see Table 3. The most common category referred to unexplained symptoms named no 'diagnosis' (prediction interval 12.7–63.8%, no data pooling). The authors described this category mostly as self-limited pain where doctors could not specify the underlying cause. Further diagnoses were gastroenteritis (minimum 7.2–maximum 18.7%, no data pooling), irritable bowel disease (minimum 2.6–maximum 13.2, no data pooling), urological diseases (5.3%, CI: 4.6–6.1) and gastritis (5.2%, CI: 3.3–8.2). In comparison, the frequency of potentially serious diseases such as appendicitis (1.9%, CI: 1.6–2.2), diverticulitis (3.0%, CI: 2.2–4.2) and acute diseases of gall/pancreas (4.0%, CI: 3.1–5.1) were relatively rare. The most uncommon causes were bowel cancer or neoplastic disorders (1.0%, CI: 0.5–1.7). Further details are given in Table 3.

Prognosis of the symptom 'abdominal pain' in general practice: Prognostic parameters were assessed in 3 of the 14 studies. Wallander *et al.* conducted a database-based 1 year follow-up cohort study (cases: patients with non-specific abdominal pain; controls: age- and sex-matched persons without abdominal pain). They measured the 1 year mortality. In comparison to the control group (proportion of mortality 1.8%), 3.4% of patients from the abdominal pain group died [relative risk (RR) = 2.8, 95% CI: 2.3–3.3] (23). Furthermore, they assessed patterns of newly prescribed drugs and the proportion of patients with a new gastrointestinal diagnosis 1 year after index date.

Muris *et al.* prospectively recruited patients with abdominal pain in 11 general practices. After 15 months all medical records from the included patients were examined regarding health care utilization. About 80% of patients were seen for their abdominal pain, some as many as three times (22).

Adelman *et al.* (12) investigated the aetiology and prognosis of adult patients who consulted their GP because of acute abdominal pain. The authors recruited the patients retrospectively by chart review in two family practice centres. Patients' pain status was assessed 6–8 weeks after the time of recruitment. In 65% of the patients pain had resolved.

Discussion

This systematic review identified 14 symptom-evaluating studies on abdominal pain in the primary care setting. Mean consultation prevalence is 2.8% for abdominal pain in general practices. In about one-third of patients the underlying cause of abdominal pain cannot be specified. The most common aetiologies are gastroenteritis (7.2–18.7%), irritable bowel disease (2.6–13.3%), urological cause (5.3%) and gastritis (5.2%). About 1 in 10 abdominal pain patients suffers from an acute disease (potentially life-threatening) like appendicitis (1.9%), diverticulitis (3.0%), biliary/pancreatic (4.0%) or neoplastic (1.0%) diseases needing immediate therapy (e.g. at hospital or other specialist).

The methodological quality of the included studies is limited. Only 6 out of 14 studies fulfil half of the required quality criteria.

To our knowledge, there are only a few publications describing quality criteria for prevalence studies (24–26). Hoy *et al.* (24) developed a 10-item risk of bias tool for prevalence studies and tested its interrater reliability. The Evidence-Based Medicine Working Group from Richardson *et al.* defined criteria to evaluate articles on disease probability for differential diagnosis (25). Since these published quality criteria only cover the prevalence studies, we developed a more comprehensive catalogue of criteria based on an extensive literature review and the Standards for the Reporting of Diagnostic Accuracy (STARD) statement

Table 1. Brief description of the included studies

Studies	Recruitment duration (month)	Region	Setting	Age distribution of study sample	Female (%)	Data assessment	Inclusion criteria	Exclusion criteria	Answered research questions
Abu-Mourada, 2010 (10)	–	Gaza Strip	10 govermental primary health care centres + 5 clinics	18–44 years: 69.1% ≥45 years: 30.9%	51.5	Prospective	–	- Severely ill patients - <18 years old	1#
Adelman, 1987 (11)	28	USA	Charts from three family practice centres	18–44 years: 74.8% 45–64 years: 16.0% ≥65 years: 9.2%	69.4	Retrospective	All documented patients with abdominal pain	- <18 years	2##
Adelman, 1988 (12)	6	USA	Charts from two family practice centres	18–44 years: 84% 45–64 years: 11% >64 years: 5%	84.0	Prospective	(1) patient age > 17 years, (2) primary or major complaint of abdominal pain and (3) initial visit for this episode of pain	Patient with abdominal pain in the last 3 months	2## + 3###
BEACH Programme, 2004	72	Australia	Primary care database of 6021 GPs	<5 years: 3.3% 5–14 years: 10.2% 15–24 years: 14.2% 25–44 years: 30.2% 45–64 years: 24.9% 65–74 years: 8.7% 75+ years: 8.5%	66.3	Retrospective	All documented patients with abdominal pain	–	1# + 2##
Britt, 1994 (14)	12	Australia	Primary care database of 495 GPs	–	55.4	Retrospective	All documented patients with abdominal pain	–	1# + 2##
Edwards, 1985 (15)	8	UK	One general practice with five physicians	0–4 years: 10% 5–14 years: 22% 15–24 years: 19% 25–34 years: 13% 35–44 years: 12% 45–54 years: 6% 55–64 years: 9% 65–74 years: 7% 75–84 years: 2%	58.7	Prospective	All ages, all patients who present abdominal pain as a primary symptom	–	2##
Frear, 1997 (16)	12	New Zealand	Record database of 12 general practices	–	–	Retrospective	All patients with abdominal pain	–	1# + 2##
Gold, 1982 (17)	24	USA	Database of six primary care clinics, including 36 practitioners	Mean age: 44.5 years	63.6	Retrospective	All patients with abdominal pain	–	1#

Table 1. Continued

Studies	Recruitment duration (month)	Region	Setting	Age distribution of study sample	Female (%)	Data assessment	Inclusion criteria	Exclusion criteria	Answered research questions
Halder, 2010 (18)	15	UK	Three general practices	25–40 years: 26.4% 41–55 years: 44.3% 56–65 years: 29.3%	–	Prospective	All documented patients with gastrointestinal symptoms	Patients with the following diseases: gastrointestinal malignancy, Crohn's disease, ulcerative colitis, chronic pancreatitis, peptic ulcer disease, alcohol-related disorders and liver disease	1#
Kroenke, 1989 (19)	36	USA	Database of one military primary care centre	Mean age: 59.5 years	–	Retrospective	All patients with abdominal pain	–	1# + 2##
Mäntyselkä, 2001 (20)	1	Finland	25 primary health centres, including 28 primary care physicians	Mean age: 46 years ± 21 SD	–	Prospective	Aged 1–99 years, all documented patients with pain	–	1# + 2##
Martin, 1984 (21)	–	Saudi Arabia	One primary care department in a hospital serving a military community	0–14 years: 28.1% 15–24 years: 26.7% 25–44 years: 35.3% +45 years: 9.9%	–	Prospective	Presenting the problem for the first time at a general practice	–	1#
Muris, 1993 (21)	3	Netherlands	11 general practices	18–39 years: 53% 40–49 years: 14% 50–59 years: 16% 60–75 years: 16%	61.7	Prospective	–	- <18 years - Patients with a referral	1# + 2## + 3###
Wallander, 2007 (23)	24	UK	Primary care database* which contains information entered by 1500 GPs	2–19 years: 29.4% 20–39 years: 23.2% 40–59 years: 26.6% 60–79 years: 20.7%	61.8	Retrospective	Aged 2–79 years, all documented patients with abdominal pain	- Patients with history of cancer - Pregnant women—visit because of past abdominal pain	1# + 3###

*The database includes the complete medical records of all individuals registered with participating primary care doctors, including demographics, diagnoses [recorded using Oxford Medical Information System and Read codes that map to codes in the eighth edition of the International Classification of Diseases (ICD-8)], prescriptions (generated automatically from the system) and referrals.

#First research question: Prevalence of the consulting reason abdominal pain at general practice.

##Second research question: Aetiology of the consulting reason abdominal pain at general practice.

###Third research question: Prognosis of the consulting reason abdominal pain at general practice.

Table 2. Study quality

+ Yes
- No
? Unclear
O not relevant[#]

	Was the recruitment of patients prospective?	Were all patients with symptoms included (consecutive recruitment or random sample)?	Are inclusion and exclusion criteria clearly defined?	Was the study design multicentred?	Were the reasons for drop outs clearly defined and documented?	Was the denominator of the prevalence's result size of the clearly defined?	Were categories of diagnoses described clearly?	Was the reference standard used appropriate?	Did every patient require the reference standard?	Did every patient have the same diagnostic procedures?	Were the definitions of the prognostic outcomes and their items clearly defined?	Was the operationalization of the prognostic result sizes appropriate?	Was there an appropriate comparison group?	Number of reached quality criteria/ number of all potential quality criteria
Abu-Mourada, 2010 (10)	+	+	+	+	+	+	O	O	O	O	O	O	O	6/6
Adelman, 1987 (11)	-	?	+	+	+	O	+	?	?	?	O	O	O	4/9
Adelman, 1988 (12)	+	-	+	+	+	O	-	?	?	?	+	+	-	6/12
BEACH Programme, 1994	-	+	-	+	?	+	+	?	?	?	O	O	O	4/10
Britt, 1994 (14)	-	?	-	+	?	-	-	?	?	?	O	O	O	1/10
Edwards, 1985 (15)	+	+	-	-	?	O	+	-	-	-	O	O	O	3/9
Frear, 1997 (16)	-	+	-	+	?	+	-	?	?	-	O	O	O	3/10
Gold, 1982 (17)	-	+	+	+	-	-	O	O	O	O	O	O	O	3/6
Halder, 2010 (18)	+	+	-	+	+	+	O	O	O	O	O	O	O	5/6
Kroenke, 1989 (19)	-	+	-	-	-	+	-	-	?	?	O	O	O	2/10
Mäntyselkä, 2001 (20)	+	+	+	+	+	+	-	?	?	?	O	O	O	6/10
Martin, 1984 (21)	+	?	+	-	?	-	O	O	O	O	O	O	O	2/6
Muris, 1993 (22)	+	+	+	-	?	-	-	-	+	-	+	?	-	5/13
Wallander, 2007 (23)	-	+	+	+	?	+	O	O	O	O	+	+	+	7/10

O: not relevant (quality criteria should not be used because it belongs to a research question which did not appear in the study).

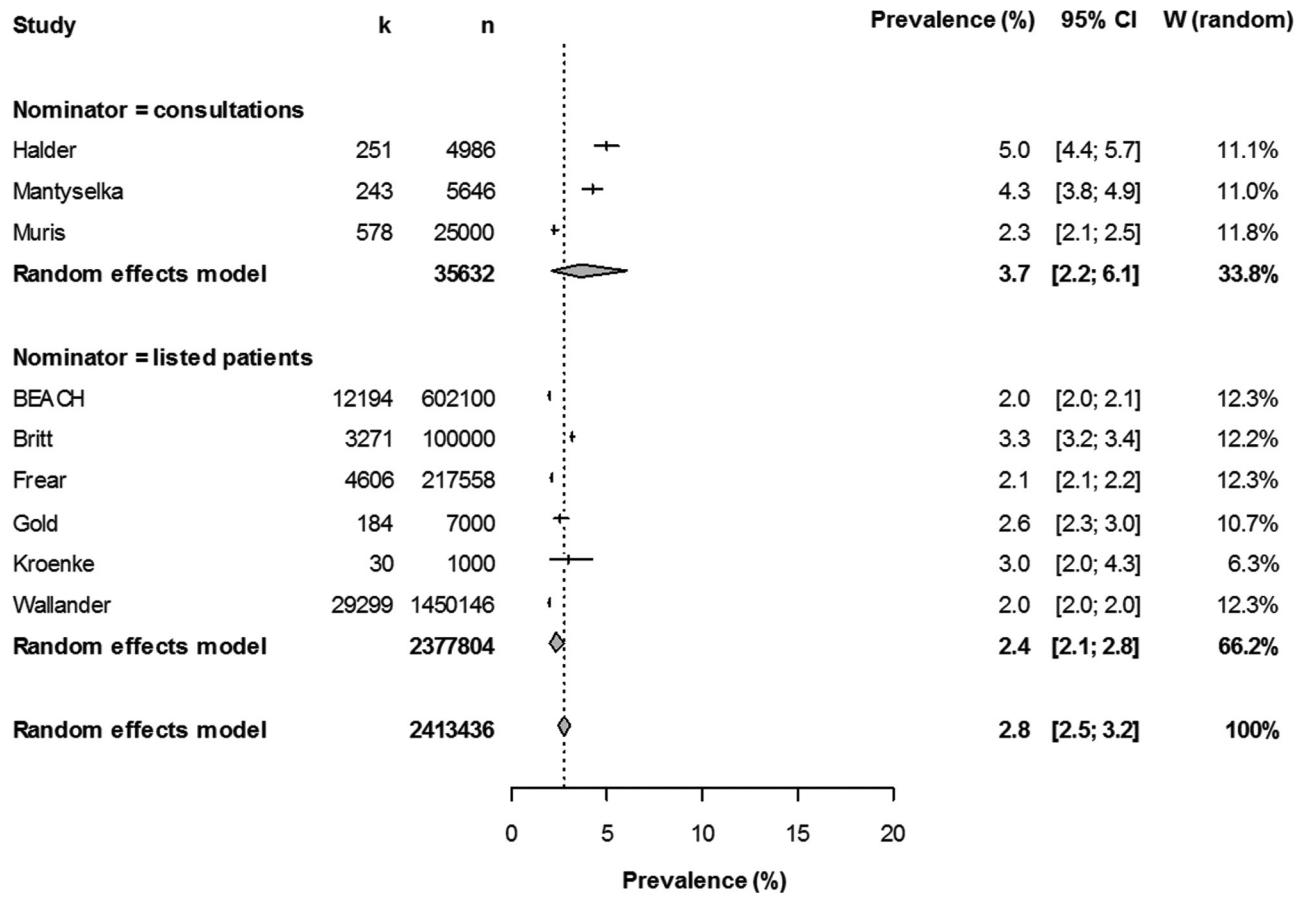

Figure 2. Forest plot of the prevalences of abdominal pain.

on diagnostic accuracy studies (27). The validation of our quality assessment tool will be published elsewhere. According to our quality criteria, only 6 out of 14 studies fulfilled half of the required quality criteria. This might be associated with the absence of standardized quality assessments or reporting guidelines for symptom-evaluating studies.

The consultation prevalence of abdominal pain varies from study to study. There are two kinds of studies evaluating the prevalence of abdominal pain (database studies + non-database studies). In comparison to non-database studies, database studies usually measure lower prevalence values. This could be because disease frequencies in database studies refer to all registered patients rather than only those presenting for abdominal pain, as in non-database studies. Furthermore, database studies have more human subjects. This systematic review comprises various types of studies. We found an overall consultation prevalence of 2.8% for abdominal pain in the primary care setting. In comparison to other symptoms, abdominal pain ranks ninth among the most frequent reasons for consultation in general practice (1).

A low prevalence for potentially serious causes of diseases is a well-known characteristic of primary health care (28). However, we identified a high rate of acute diseases requiring immediate therapy or referral for patients with abdominal pain in the primary care setting. Summarizing the identified diagnostic categories, we introduced the category 'acute abdominal pain'. However, the resulting prevalences are likely more than were found since all other categories also likely contain acutely ill patients. Diagnosis of abdominal pain is clearly an ambitious challenge for GPs. As we know from qualitative studies, the management of abdominal pain is accompanied by a high diagnostic uncertainty, especially considering the limited diagnostic possibilities in general practices (29). Furthermore, Ely *et al.* (30) showed that the complaint of abdominal pain is most often associated with diagnostic errors at general practices. There are presently no diagnostic guidelines for abdominal pain. Further research seems to be necessary.

In comparison to other symptoms (like dyspnoea or chest pain), the proportion of unexplained complaints (category 'no diagnosis') is more frequent among patients with abdominal pain (31,32). Even though most of these unexplained complaints resolve spontaneously, the high proportion of patients with unexplained symptoms underlines the uncertainty GPs face when dealing with abdominal pain. At the same time, patients experience health care as dissatisfying when left without

Table 3. Aetiologies of the symptom 'abdominal pain' in general practice

N	Adelman, 1987 (11) 551	Adelman, 1988 (12) 91	BEACH, 2004; 18267	Britt, 1994 (14) 3271	Edwards, 1985 (15) 150	Frear, 1997 (16) 2511	Kroenke, 1989 (19) 30	Mäntyselkä, 2001 (20) 243	Muris, 1993 (22) 578	Prediction interval (%)	Tau^2	Random effects model
Appendicitis	6 1.1% 0.4–2.3	–	384 2.1% 1.9–2.3	52 1.6% 1.2–2.1	2 1.3% 0.2–4.7	50 2.0% 1.5–2.6	–	–	–	1.5–2.4	0.0133	1.9 (1.6–2.2)
Biliary or pancreas disease	9 1.6% 0.7–3.1	6 6.6% 2.5–13.8	785 4.3% 4.0–4.6	157 4.8% 4.1–5.6	1 0.7% 0.0–3.7	155 6.2% 5.3–7.2	–	–	11 1.9% 1.0–3.4	2.4–6.6	0.0705	4.0 (3.1–5.1)
Diverticulitis	12 2.2% 1.1–3.7	–	822 4.5% 4.2–4.8	131 4.0% 3.4–4.7	2 1.3% 0.2–4.7	52 2.1% 1.6–2.7	–	–	–	1.6–5.7	0.1101	3.0 (2.2–4.2)
Gastritis	–	–	–	193 5.9% 5.1–6.8	5 3.3% 1.1–7.6	–	–	–	–	3.1–8.6	0.0726	5.2 (3.3–8.2)
Gastroenteritis	51 9.2% 6.9–11.9	–	2064 11.3% 10.3–11.8	373 11.4% 10.3–12.5	31 20.7% 14.5–28.0	422 16.8% 15.4–18.3	–	–	34 5.9% 4.1–8.1	7.2–18.7	0.0744	–
Gynaecological cause	21 3.8%, 2.4–5.7	3 3.3%, 0.7–9.3	18 0.1%, 0.1–0.2	7 0.2%, 0.1–0.4	10 6.7%, 3.2–11.9	257 10.3%, 9.1–11.5	–	–	17 2.9%, 1.7–4.7	0.0–47.6	3.8014	–
Inflammatory bowel disease	5 0.9% 0.3–2.1	–	–	–	–	9 0.4% 0.2–0.7	–	–	–	0.2–1.5	0.2714	0.5 (0.2–1.3)
Irritable bowel disease	32 5.8% 4.0–8.0	4 4.4% 1.2–10.9	968 5.3% 5.0–5.6	206 6.3% 5.5–7.2	18 12.0% 7.3–18.3	50 2.0% 1.5–2.6	-	-	69 11.9% 9.4–14.9	2.6–13.2	0.1903	–
Musculoskeletal cause	5 0.9% 0.3–2.1	2 2.2% 0.3–7.7	–	–	3 2.0% 0.4–5.7	51 2.0% 1.5–2.7	–	–	–	1.6–2.2	0.0075	1.9 (1.4–2.5)
Neoplasia	–	–	110 0.6% 0.5–0.7	52 1.6% 1.2–2.1	–	32 1.3% 0.9–1.8	–	–	3 0.5% 0.1–1.5	0.3–2.9	0.3174	1.0 (0.5–1.7)

Table 3. Continued

N	Adelman, 1987 (11) 551	Adelman, 1988 (12) 91	BEACH, 2004; 18267	Britt, 1994 (14) 3271	Edwards, 1985 (15) 150	Frear, 1997 (16) 2511	Kroenke, 1989 (19) 30	Mäntyselkä, 2001 (20) 243	Muris, 1993 (22) 578	Prediction interval (%)	Tau^2	Random effects model
No diagnosis	280 50.4% 46.1–54.6	65 71.4% 61.0–80.4	4366 23.9% 23.3–24.5	507 15.5% 14.3–16.8	21 14.0% 8.9–20.6	–	24 80.0% 61.4–92.3	37 15.2% 11.0–20.4	–	12.7–63.8	0.3884	–
Oesophageal disease	–	–	822 4.5% 4.2–4.8	–	–	–	–	–	–	–	–	–
Constipation	–	–	895, 4.9% 4.6–5.2	114, 3.5% 2.9–4.2	10, 6.7% 3.2–11.9	103, 4.1% 3.4–5.0	–	–	–	3.1–6.2	0.0338	4.4 (3.5–5.4)
Psychosomatic cause	–	–	–	–	9 6.0% 3.0–11.4	–	–	–	–	–	–	–
Reflux/dyspepsia/ hiatal Hernia	13 2.3% 1.3–4.0	–	–	–	3 2.0% 0.4–5.7	677 27.0% 25.2–28.7	–	–	–	0.1–73.7	3.7422	–
Ulcer	8 1.4%, 0.6–2.8	2 2.2%, 0.3–7.7	457 2.5%, 2.3–2.7	242 7.4%, 6.5–8.3	6 4.0%, 1.5–8.5	94 3.7%, 3.0–4.6	–	–	33 5.7%, 4.0–7.9	1.0–11.9	0.4128	–
Urological cause	44 7.9%, 5.8–10.5	3 3.3%, 0.7–9.3	932 5.1%, 4.8–5.4	180 5.5%, 4.7–6.3	5 3.3%, 1.1–7.6	141 5.6%, 4.7–6.6	–	–	18 3.1%, 1.9–4.9	4.1–6.9	0.0180	5.3 (4.6–6.1)
Other	**a**	**b**	**c**	**d**	**e**	**f**	**g**	**h**	**i**			
a	-Diarrhoea, cause undetermined 9 (1.6%, CI: 0.7–3.1) -Tumor benign 8 (1.4%, CI: 0.6–2.8) -Other (includes pyelonephritis, endometriosis, malignant tumours, oesophagitis, gastritis, gastric ulcer, hepatitis, spontaneous abortion, anxiety, depression) 53 (9.5%, CI: 7.2–12.3)											
b	-Other 6 (7.0%, CI: 2.5–13.8)											
c	-Diagnoses in 5644 cases (30.9%, CI: 30.2–31.6) are not listed at original article.											
d	-Other gastrointestinal diseases (including: volvulus, pancreatitis, peritonitis): 111 (3.4%, CI: 2.8–4.1) -Renal colic 49 (1.5%, CI: 1.1–2) -Benign neoplasm 7 (0.2%, CI: 0.1–0.4) -Diagnoses in 890 cases (27.2%, CI: 25.7–28.8) are not listed at original article.											

Table 3. Continued

N	Adelman, 1987 (11) 551	Adelman, 1988 (12) 91	BEACH, 2004; 18267	Britt, 1994 (14) 3271	Edwards, 1985 (15) 150	Frear, 1997 (16) 2511	Kroenke, 1989 (19) 30	Mäntyselkä, 2001 (20) 243	Muris, 1993 (22) 578	Prediction interval (%)	Tau^2	Random effects model
e	-Possible appendicitis 2 (1.3%, CI: 0.2–4.7) -Food poisoning 1 (0.7%, CI: 0.0–3.7) -Milk intolerance 1 (0.7%, CI: 0.0–3.7) -Intussusception 1(0.7%, CI: 0.0–3.7) -Infectious hepatitis 1 (0.7%, CI: 0.0–3.7) -Non-specific viral 9 (6.0%, CI: 2.8–11.1) -Ear, nose and throat 6 (4.0%, CI: 1.5–8.5) -Periodic syndrome 2 (1.3%, CI: 0.2–4.7) -Mesenteric adenitis 1 (0.7%, CI: 0.0–3.7)											
f	-Other 127 (5.1%, CI: 4.2–6.0) -Renal pathology 88 (3.5%, CI: 2.8–4.3) -Drug reaction 71 (2.8%, CI: 2.2–3.6) -Non-gastrointestinal infection 64 (2.5%, CI: 2.0–3.2) -Trauma 51 (2.0%, CI: 1.5–2.7) -Abdominal aortic aneurysm 8 (0.3%, CI: 0.1–0.6) -Hernia 7 (0.3%, CI: 0.1–0.6) -Perforation 2 (0.1%, CI: 0.0–0.3)											
g	-This study exclusively illustrated the portion of undiagnosed abdominal pain cases. A differentiation in other diagnostic categories was not done.											
h	-This study exclusively illustrated the portion of undiagnosed abdominal pain cases. A differentiation in other diagnostic categories was not done.											
i	-Generalized abdominal pain/cramps 105 (18.2%, CI: 15.1–21.6) -Other localized abdominal pain 86 (14.9%, CI: 12.1–18.0) -Stomach pain 71 (12.3%, CI: 9.7–15.2) -Disorders of stomach function 40 (6.9%, CI: 5.0–9.3) -Diarrhoea 7 (1.2%, CI: 0.5–2.5) -Other gastrointestinal complaints 25 (4.3%, CI: 2.8–6.3) -Other gastrointestinal diagnoses 22 (3.8%, CI: 2.4–5.7) -Miscellaneous 37 (6.4%, CI: 4.5–8.7)											

explanation for their painful condition (29). Both primary care-specific decision rules and educational support on how to communicate uncertainty seem crucial when dealing with abdominal pain in primary care.

In 2001, Donner-Banzhoff *et al.* (26) suggested a prognostic research question in symptom-evaluating studies aiming to gain knowledge on risk of deterioration or recovery. Knowledge about the setting-specific prognosis of abdominal pain helps enable the emotional realisation of regret, which is important for medical decision making (33). Regret is defined as the difference between the utility of the outcome of the action taken and the utility of the outcome of the action that, in retrospect, should have been taken (34).

The study from Wallander *et al.* (23) found an increased RR for death in patients with non-specific abdominal pain (in comparison to age- and sex-matched persons without abdominal pain). Further studies evaluating the setting-specific mortality for abdominal pain are needed. In fact, few studies evaluated prognostic outcomes, showing great variation in methodologies. In the future, standardization of symptom-evaluating studies might be necessary with respect to the most relevant clinical parameters (e.g. mortality percentage per year or experiencing symptoms after 4 weeks).

There are limitations to our study; these were governed by four factors which could bias the effect size of our systematic review from the real effect size:
(i) Factors which influence the internal validity of the included studies, like incomplete recruitment or imprecise inclusion criteria; (ii) Factors which might influence the external validity of the included studies, like setting or recruitment characteristics which impede transferability to the local health care system; (iii) Factors which influence the internal validity of our systematic review based on our own methodology; (iv) Factors influencing the external validity of the review.

To confront these problems, we decided on a transparent and standardized procedure for the quality assessment of the included studies. We defined clear inclusion criteria for the included studies, the screening process was done by two independent reviewers, and outliers were excluded from calculation of effect sizes if necessary.

Generally, study results depend on cultural variances between the countries (different health care systems, patient's health traditions and the threshold of consulting a doctor). Therefore, summarizing studies and interpreting study results may vary according the reviewer's perspective. Researchers must be aware of this when drawing parallels from the presented studies to their own health care system.

The methodical inhomogeneity of the studies might cause difficulties regarding data analysis (6). We considered this problem and refrained from data pooling in cases where the inhomogeneity of the included studies likely had a significant influence on the results, or when the prediction interval was too broad (5). In cases where a meta-analysis could be performed, we chose the random effects model instead of the fixed effect model because the random effects model allows the true effect to vary from study to study.

Conclusion and implications for future research

In conclusion, we have shown that abdominal pain is a common reason for consultation in general practice. The review identified a comparably high rate of acute underlying diseases in need of further investigation or therapy. At the same time, the underlying cause of the complaints often remains unexplained. Our review thereby emphasizes the high diagnostic challenge of abdominal pain in general practice. Further studies on the aetiology and prognosis of abdominal pain in primary care are necessary, ideally using standardized methodology in order to gain sufficient evidence for developing much-needed guidelines and decision support tools.

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