

Prevalence of pain in patients with cancer: a systematic review of the past 40 years

M. H. J. van den Beuken-van Everdingen^{1*}, J. M. de Rijke¹, A. G. Kessels², H. C. Schouten³, M. van Kleef⁴ & J. Patijn¹

¹Pain Management and Research Centre, University Hospital Maastricht; ²Department of Clinical Epidemiology and Medical Technology Assessment, University Hospital Maastricht; ³Department of Internal Medicine, University Hospital Maastricht; ⁴Department of Anaesthesiology, University Hospital Maastricht, PO Box 5800, 6202 AZ Maastricht, The Netherlands

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Background: Despite the abundant literature on this topic, accurate prevalence estimates of pain in cancer patients are not available. We investigated the prevalence of pain in cancer patients according to the different disease stages and types of cancer.

Patients and methods: A systematic review of the literature was conducted. An instrument especially designed for judging prevalence studies on their methodological quality was used. Methodologically acceptable articles were used in the meta-analyses.

Results: Fifty-two studies were used in the meta-analysis. Pooled prevalence rates of pain were calculated for four subgroups: (i) studies including patients after curative treatment, 33% [95% confidence interval (CI) 21% to 46%]; (ii) studies including patients under anticancer treatment: 59% (CI 44% to 73%); (iii) studies including patients characterised as advanced/metastatic/terminal disease, 64% (CI 58% to 69%) and (iii) studies including patients at all disease stages, 53% (CI 43% to 63%). Of the patients with pain more than one-third graded their pain as moderate or severe. Pooled prevalence of pain was >50% in all cancer types with the highest prevalence in head/neck cancer patients (70%; 95% CI 51% to 88%).

Conclusion: Despite the clear World Health Organisation recommendations, cancer pain still is a major problem.

Key words: cancer pain, prevalence, systematic review

introduction

In cancer patients, pain is one of the most feared and burdensome symptoms. Early reports on the prevalence of pain in cancer patients draw attention to high figures that ranged from 52% to 77% [1–5]. More recent studies on the prevalence of pain in patients with cancer showed figures that ranged from 24% to 60% in patients on active anticancer treatment [6–9] and 62%–86% in patients with advanced cancer [10–15], which illustrates that this problem has not been solved.

These high prevalence figures contrast sharply with the rapidly increasing interest in pain and pain relief in the past decade. Apparently, greater insight into the pathophysiological mechanisms of pain and the wider availability of antinociceptive therapies, such as opioids, coanalgesics and NMDA-receptor-antagonists, have not influenced the prevalence of pain in cancer patients. Moreover, the World Health Organisation (WHO) introduced a pain ladder [16] in 1986 that has been accepted worldwide. Combined with appropriate dosage guidelines, it

should be able to provide tools for adequate pain relief in 70%–90% of the patients [17–22].

In 1985, Bonica [23] attempted to evaluate the prevalence of cancer pain worldwide by extrapolating the prevalence rates retrieved from 47 selected reports published in 15 countries. The mean pain prevalence in patients with various stages of cancer was 50%. In patients with advanced/metastatic/terminal cancer, the percentage was 71%. However, these prevalence figures have to be interpreted with caution, because sample size differences were not taken into account in the calculation of the mean prevalence and no information was given about the search methods used to select the articles or about differences between patient groups other than type and stage of cancer.

It took almost two decades before another systematic review was carried out to estimate the prevalence of cancer pain [24]. The authors included the review by Bonica and made an additional literature search (period 1980–2000), which resulted in 54 more studies. Although the search method was described, it was not clear how these articles had been selected, because the total number of articles retrieved in the search was not mentioned. Furthermore, the methodological quality of the studies that reported pain prevalence rates was not taken into account [25].

*Correspondence to: Dr M. H. J. van den Beuken-van Everdingen, University Hospital Maastricht, Pain Management and Research Centre, PO Box 5800, 6202 AZ Maastricht, The Netherlands. Tel: +31-433875384; Fax: +31-433875457; E-mail: mvdb@adcc.azm.nl

The end result was a very heterogeneous sample of articles, for example, with respect to the methods of data collection, six studies had surveyed medical records and five studies had used retrospective data collected from proxies (bereaved care providers or other informants). It is well known that these two methods can result in prevalence figures that differ from data obtained directly from the patient [26–32]. Although the authors stated that it was not possible to carry out a meta-analysis owing to the variation in measurements, they reported combined weighted mean prevalences of pain in patients with all/various stages versus patients with metastatic or terminal disease. No description was given of how the weighted mean average had been calculated. Prevalence rates were 40% (range 18%–100%) and 74% (range 53%–100%), respectively.

In 2005, Goudas et al. [33] aimed to present a literature overview of epidemiological data on cancer-related pain during the period 1982–2001. They restricted their search to the field of epidemiology and found 464 studies. Only surveys that explicitly targeted the prevalence of cancer pain were included, which left 28 studies. The authors argued that it was not possible to combine these surveys because of differences in settings, study populations, primary cancer sites and the methods employed. The only classification they could make was by sample size: <1000 patients ($n = 20$), 1000–10 000 ($n = 4$) and >10 000 ($n = 2$). In this way, a comprehensive but fairly unstructured enumeration of prevalence figures was presented [33].

Despite the large body of literature on pain in cancer patients, none of the previous reviews provided accurate prevalence estimates. We carried out a systematic review that included statistical pooling of the study results in an attempt to obtain accurate figures on the prevalence of cancer pain during the period 1966–2005.

patients and methods

A systematic literature search was carried out using the following databases: Medline 1966–September 2005, Embase 1989–September 2005, Pubmed 1975–September 2005, Cinahl 1982–September 2005, Cochrane Systematic reviews, Cochrane Central, the Cancer Library 2002.

Our keywords comprised ‘pain’ and ‘prevalence’, or ‘symptom’ and ‘prevalence’ in combination with each of the following terms: ‘cancer’, ‘neoplasm’, ‘terminal’, ‘end stage’, ‘advanced’, ‘hospice’ or ‘palliative’ in the title, abstract or keywords. Reference lists of the retrieved articles were inspected manually to identify any papers that had been missed.

inclusion/exclusion criteria

Studies were included if they reported on the prevalence, irrespectively of the type of prevalence used, of cancer pain in an adult cancer population and were written in the languages English or Dutch. Publications were excluded if they comprised case studies, letters, prevalence studies carried out at pain clinics (institute bias) or had only selected patients with pain.

study characteristics

subgroups. A consistent finding in earlier reviews on cancer pain was that pain was more prevalent in the more advanced stages [23, 24, 34]. In anticipation of this difference, we a priori subdivided the studies into four groups on the basis of the disease characteristics described in the methods/results sections: (i) studies that included patients after finishing curative treatment, (ii) studies that included patients receiving anticancer treatment,

with curative or palliative intention, (iii) studies that included patients with advanced, metastatic and/or with terminal disease and (iv) studies that included all disease stages (1 to 3).

pain prevalence. Data were documented on pain prevalence, pain severity, recall periods for pain (point prevalence, pain in the past week/months/year) and the scale or instrument used to measure pain: VAS (visual analogue scale), numerical rating scale, verbal rating scale, pain ‘yes’/‘no’. When pain was reported as VAS scores or numeric scores, the rating of Serlin et al. [35] was used to convert severity into none (0), mild (1–4), moderate (5–6) or severe (≥ 7).

general study characteristics

General characteristics were recorded from each study: authors, year of publication, aim of the study (prevalence or other), sample size, setting (inpatient, outpatient, home, hospice or palliative care unit, referred to palliative care service), method of data collection (questionnaire patient or proxy, interview patient or proxy, medical record), type of prevalence (point, week, month, year), use of validated or nonvalidated instruments, distribution of gender, distribution of age and type of cancer (head and neck, gastrointestinal, lung/bronchus, breast, urogenital, gynaecological, all types of cancer).

methodological quality and pooling of data

In addition to documenting the general characteristics mentioned above, a more detailed analysis was conducted on the quality of the articles. The studies were evaluated using methodological criteria based on Leboeuf-Yde and Lauritsen [36] (Table 1), which were the first to be especially constructed for prevalence studies. Walker [37] improved the criteria by adding a criterion to identify proxy reporting and suggested that some weighting should be given to the different criteria. In our paper, the criteria specifically for lower back pain were substituted by an adequate description of the disease stage and/or condition of the cancer patients and a weighting factor was introduced for each criterion (Table 1). This resulted in a quality score that ranged from 0 to 19 points. The cut-off level for methodological acceptability was set at 14 points, which was 75% of the total points that could be achieved [36]. All the studies were reviewed independently by two researchers (MHJBE, JMR). Differences between interpretations were resolved using a discussion and consensus approach. The quality score was used to determine whether the data were suitable for inclusion in the meta-analysis. Only articles with a quality score of ≥ 14 were selected and subsequently divided into the four groups described above. To obtain pooled prevalence rates related to the type of cancer, a separate meta-analysis was carried out on the studies that reported pain prevalence in patients with specific types of cancer. We were able to identify 41 datasets that reported on head and neck, gastrointestinal, lung, breast, urogenital or gynaecological cancer. In the meta-analysis, we used the reciprocal of the variance from individual studies as a weighting factor, which relates closely to sample size. This weighting factor was chosen to reflect the amount of information that each study contains [25]. Then, the pooled prevalence was calculated for each group and the precision [95% confidence interval (CI)] and statistical significance of the overall estimate were determined. To investigate whether the variation in prevalence rates between the studies was more than could be attributed to chance alone, a test for homogeneity was carried out, which turned out to be statistically significant. The extra variation was incorporated into the analysis using a random effects model. Bivariate analyses were carried out to explore whether the study period (before 1990, 1990–1999, 2000 and later), location of the study (continent of origin), average age of the population (<65 years, ≥ 65 years), type of prevalence (point, week, month) and type of cancer were associated with the outcome. All the analyses were carried out using STATA SE 8 (meta, metareg).

Table 1. Quality criteria for prevalence studies

A. The final sample should be representative of the target population	1. At least one of the following should apply for the study: an entire target population, randomly selected sample or sample stated to represent the target population (2 points). 2. At least one of the following: reasons for nonresponse described, nonresponders described, comparison of responders and nonresponders or comparison of sample and target population (2 points). 3. Response rate $\geq 90\%$ (2 points); 70%–90% (1 point); $<70\%$ (0 point).
B. Quality of data	4. Were the data primary from a prevalence study (2 points) or was it taken from a survey not specifically designed for that purpose (1 point)? 5. The same mode of data collection should be used for all subjects (2 points) if not (1 point). 6. The data have been collected directly from the patient by means of a validated questionnaire/interview (3 points); no validated questionnaire/interview (2 points); data have been collected from proxies or retrospectively from medical record (1 point).
C. General description of the method and results should include definitions of pain prevalence	7. Description of the target population and setting where patients were found (2 points). 8. Description of stage of disease, type of cancer, sex, age. All: 2 points, 2 or 3: 1 point. 9. Final sample size (1 point). 10. Prevalence recall periods should be stated (1 point).

A test for homogeneity revealed that the variation in prevalence rates between the studies was more than could be attributed to chance alone. Therefore, a random effects model was used to incorporate the extra variation into the analyses.

results

selected articles

On the basis of the keywords, we found 4737 articles. After removing double hits, the abstracts were screened for figures on the prevalence of cancer pain and the inclusion and exclusion criteria were applied. This left 356 articles, of which another 196 had to be excluded. Reasons for exclusion were no study had been carried out ($n = 36$), no pain prevalence was mentioned ($n = 68$), all the patients had pain ($n = 45$), the pain prevalence was indistinguishable between cancer and noncancer patients ($n = 21$), a secondary analysis had been conducted on combined articles ($n = 3$), the publication comprised an overview article ($n = 14$), the same population had been reported on twice ($n = 5$) and others ($n = 4$).

The quality score of 34% ($n = 54$) of the remaining 160 articles was 14 points or more (Figure 1). A combination of shortcomings in representativeness and data collection method (the two criteria with the heaviest weighting) was the main reason for not reaching the required score of 14 points: response rate of $<70\%$, response rate not mentioned, data retrieved from medical records prospectively, or retrospectively, lack of description of the nonresponders, sample not representative and/or data collected by proxy or from medical record. A more detailed description of the excluded articles is given in the Appendix. All included studies were published in English.

general characteristics

General characteristics of the 54 articles are listed in Tables 2–5. In 46 studies, (part of) the aim of the study had been to determine the prevalence of pain in cancer patients. This had not been a primary goal in the other eight studies [11, 13, 49, 65, 71, 73, 75, 82, 84]. One study looked at unmet needs, one described the experiences of a palliative care programme, two

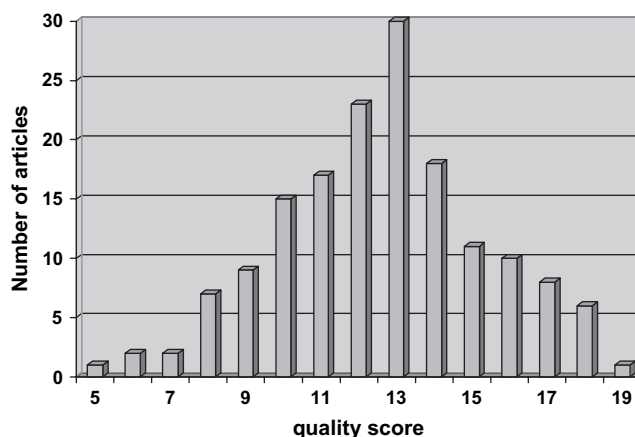


Figure 1. Distribution of the methodological quality scores.

compared usual care with intensive care, one was on the influence of demographic and disease specific variables on pain and one compared differences in symptoms between cancer and noncancer patients.

prevalence of pain

A total of 54 articles reached the cut-off level of 14 points, but two articles [54, 85] reported the prevalence of moderate to severe pain alone and were therefore excluded from the meta-analyses.

The results of the stratified meta-analyses on the prevalence of pain, yes or no, in the four patient groups are presented in Figure 2. In group 1, seven studies included patients after curative treatment ($N = 726$), in group 2, seven studies included patients on anticancer treatment ($N = 1408$), in group 3, 22 studies included patients with advanced, metastatic or terminal disease ($N = 9763$) and in group 4, 16 studies included cancer patients with all stages ($N = 8088$). The prevalence rates of pain were 33% (95% CI 21% to 46%), 59% (CI 44% to 73%), 64% (CI 58% to 69%) and 53% (CI 43% to 63%), respectively.

Pooled prevalence of pain was significantly higher in groups 2, 3 and 4 than in group 1 ($P = 0.004$, $P < 0.004$, $P = 0.009$),

Table 2. Articles that reported prevalence of pain in all cancer stages

Author, year of publication	Quality points	Continent ^a	Setting ^b	Mean age (years)	Type of cancer ^c	Sample size	% no pain	% mild pain	% moderate pain	% severe pain	% total pain	Response rate ^d	Recall ^e
Beck 2001 [38]	17	4	1, 2	55	1	263					36	2	2
Chang 1999 [39]	18	1	1, 2	68	1	240			18	22	59	2	2
Daut 1982 [40]	15	1	1, 2	58	1	667					41	0	3
Dorrepal 1989 [41]	18	2	1		1	240					45	2	1
Ger 1998 [42]	18	3	1	57	1	296					38	1	2
Greenwald 1987 [43]	18	1	6		3, 4, 6, 7	536	35	20	26	19	72, 72, 57, 60	2	2
Lidstone 2003 [44]	15	2	2	61	4, 5, 6, 7	480	45	31	(22) ^f		68, 62, 40, 50	2	2
Menzies 2000 [45]	15	2	1		1	186					28	1	2
Portenoy 1994-1 [46]	16	1	1, 2	55	7	151					42	1	2
Portenoy 1994-2 [47]	14	1	1, 2	56	3, 5, 6, 7	243					62, 60, 68, 67	1	1
Ripamonti 2000 [48]	14	1	1		1	258					51	1	1
Rustoen 2003 [49]	17	2	2	57	1	1392	39	32	22	7	61	1	2
Sandblom 2001 [50]	17	2	6	77	8	1243	58	16	14	12	42	1	2
Strohbuecker 2005 [51]	18	2	1	54	1	167					58	1	1
Wells 2000 [52]	15	1	1	59	1	176					79	0	2
Zhimin 2001 [53]	14	3	6	54	1	60	13	54	27	6	87	0	99
Zhukovski 1995 [54]	14	1	1	56	1	101			(44) ^f			0	2

^a1, North America; 2, Europe; 3, Asia; 4, other.

^b1, inpatient; 2, outpatient; 3, at home; 4, hospice; 5, referred to palliative care service; 6, all.

^c1, all; 2, head and neck; 3, gastrointestinal; 4, bronchus/lung; 5, breast; 6, urogenital; 7, gynaecological.

^d0, <70% or not mentioned; 1, 70%–90%; 3, ≥90%.

^e1, point prevalence; 2, prevalence past week; 3, prevalence past months; 99, unknown.

^fModerate to severe.

Table 3. Articles that reported the prevalence of pain after curative treatment

Author, year of publication	Quality points	Continent ^a	Setting ^b	Mean age (years)	Type of cancer ^c	Sample size	% no pain	% mild pain	% moderate pain	% severe pain	% total pain	Response rate ^d	Recall ^e
Chaplin 1999 [55]	19	4	2	61	2	93					48	2	1
Harrison 1997 [56]	15	1	2	58	2	29					43	2	2
Henningssohn 2001 [57]	15	2	3	70	6	224					13	1	3
Henningssohn 2002 [58]	16	2	2	79	6	58					22	1	3
Rietman 2004 [8]	15	2	2	57	5	55					60	0	99
Taylor 2004 [9]	14	4	2	59	5	170					45	1	99
Yan 2004 [59]	18	3	2	55	1	107					42	1	2

^a1, North America; 2, Europe; 3, Asia; 4, other.

^b1, inpatient; 2, outpatient; 3, at home; 4, hospice; 5, referred to palliative care service; 6, all.

^c1, all; 2, head and neck; 3, gastrointestinal; 4, bronchus/lung; 5, breast; 6, urogenital; 7, gynaecological.

^d0, <70% or not mentioned; 1, 70%–90%; 3, ≥90%.

^e1, point prevalence; 2, prevalence past week; 3, prevalence past months; 99, unknown.

respectively. No significant differences were found between patients on treatment and patients with advanced or metastatic disease ($P = 0.51$).

Assessment of pain severity was described in 17 studies. None of the articles in group 1 (patients after curative treatment) mentioned the severity of pain. One study [56] reported moderate to severe distress in 89% of the patients because of pain.

In group 2, the severity of pain was measured in four studies; 36% of the patients ($N = 743$) rated their pain as moderate to severe (VAS >4). In group 3, the severity of pain was measured in six studies and the pain was rated as moderate to severe by 45% of the patients ($N = 3405$).

In group 4, the severity of pain was described in seven studies; 31% ($N = 5441$) of the patients rated their pain as moderate to severe.

In the bivariate regression analyses, none of the covariates (type of cancer, period of publication, continent of origin, mean age of the study population, type of prevalence, use of validated or nonvalidated questionnaires or interviews) were significantly associated with the pain prevalence rates.

type of cancer

A total of 36 datasets (11 studies) were made of pain prevalence in six specific types of cancer (Table 6). Prevalence rates in groups 2–4 were pooled (3300 patients). In all the cancer types, prevalence of pain was >50%; the highest prevalence was found in the head and neck cancer patients (70%). Bivariate regression analysis did not reveal any significant associations between the pain prevalence rate and type of cancer.

discussion

This systematic review on prevalence of pain in cancer patients was the first to pool only articles that met the quality criteria formulated specifically to review prevalence studies.

A total of 54 articles met the predefined quality standards and the data from 52 could be pooled. Pain prevalence in patients with cancer was high: 64% (CI 58% to 69%) in patients with

metastatic, advanced or terminal disease, 59% (CI 44% to 73%) in patients on anticancer treatment and 33% (CI 21% to 46%) in patients who had been cured of cancer.

Pain prevalence in patients with advanced/metastatic disease was lower (64%) than that previously reported [23, 24, 33, 86]. The higher prevalence rates (71%–74%) found in earlier reviews [23, 24] were probably due to the inclusion of studies on data obtained by proxy. Ratings of pain control given by the family were significantly poorer than those given by the patients [29, 30]; 75% of the care providers overestimated the patient's pain intensity by an average of 35 mm (11–97 mm) on a 100-mm scale [31].

The prevalence of pain found in studies including patients with all stages was higher than previously reported [24]. This result has to be interpreted with caution: There may have been too much difference in the condition of the patients included in these studies to allow pooling of the data.

The prevalence of pain in patients during anticancer treatment and in patients after finishing curative anticancer treatment was not earlier published in a review. The prevalence of pain in patients during anticancer treatment (59%) was not significantly different from that in patients with advanced/metastatic disease (64%). It is likely that there was considerable overlap in the condition of the patients in these two groups, because only two studies [6, 61] on anticancer treatment patients included patients on curative/radical treatment alone. The other studies included more patients who were on palliative treatment than on curative treatment, so patients with and without metastases were combined.

A total of 18 studies reported, at least some, information about pain severity. More than one-third of the patients with pain rated their pain as moderate to severe (VAS >4). Although distinction between the presence or absence of pain in a population will enable the calculation of pain prevalence, it cannot provide information about the severity, duration, frequency or amount of interference. To facilitate the comparison of studies and coordinate the planning of needs from pain services, multidimensional tools can be used in research. Most patients will accept mild pain, whereas moderate and severe pain will require attention [35].

Table 4. Articles that reported the prevalence of pain in patients on anticancer treatment

Author, year of publication	Quality points	Continent ^a	Setting ^b	Mean age (years)	Type of cancer ^c	Sample size	% no pain	% mild pain	% moderate pain	% severe pain	% total pain	Response rate ^d	Recall ^e
Degner 1995 [60]	17	4	2	59	1	434	(77) ^f		(23) ^g			2	99
Kelsen 1995 [61]	14	1	1, 2	63	3	130					78	0	2
Pignon 2004 [6]	14	2	2	60	2, 3, 4, 5	28, 13, 8, 15			19	9	71, 85, 38, 47	1	99
Portenoy 1992 [62]	16	1	2		3, 4	181, 145					29, 39	1	2
Rummans 1998 [63]	14	1	2	59, 60	5, 7	63, 51					70, 63	1	3
Stevens 1995 [64]	15	1	2	51	5	95	65				35	0	2
Wang 1999 [65]	14	1	1, 2	48	1	216	20	17	18	45	80	0	2

^a1, North America; 2, Europe; 3, Asia; 4, other.^b1, inpatient; 2, outpatient; 3, at home; 4, hospice; 5, referred to palliative care service; 6, all.^c1, all; 2, head and neck; 3, gastrointestinal; 4, bronchus/lung; 5, breast; 6, urogenital; 7, gynaecological.^d0, <70% or not mentioned; 1, 70%–90%; 3, ≥90%.^e1, point prevalence; 2, prevalence past week; 3, prevalence past months; 99, unknown.^fNone or mild.^gModerate to severe.

In our meta-analyses, the variation in prevalence rates between the studies was more than could be attributed to chance alone. The hypothesis was that factors such as type of cancer studied, study period, continent of origin, mean age of the study population, type of prevalence or the use of validated or nonvalidated questionnaires would be associated with the prevalence of cancer pain. No significant relationship was found between pain prevalence and type of cancer. However, we used fairly broad categories due to the limited number of studies. For example, the gastrointestinal cancer group included colon, oesophagus and pancreas tumours, while the urogenital cancer group included prostate and bladder cancer. Although many books refer to malignancies with a high risk of pain (bone, pancreas, oesophagus) or a low risk of pain (lymphoma, leukaemia, soft tissue)[87, 88] it is not clear which studies provided arguments for these statements.

Contrary to our expectations, period of publication and/or continent of origin were not responsible for the heterogeneity. There has been growing attention to pain and pain management over the past 50 years and our knowledge is increasing. The gap between what is possible in pain control and what is achieved is caused by many different patient-centred, care provider centred and government-centred factors. Fear of medication in general and opioids in particular, patients wanting to be 'good' patients, lack of knowledge, lack of interest and requests from care providers are well-known barriers against adequate pain control [26, 89–97].

Since 1984, the global consumption of morphine has more than tripled [98]. Although an increase in opioid consumption in cancer patients is considered to reflect an increased awareness towards pain treatment [99], the effect on the prevalence of pain is yet unknown. Unfortunately, from this systematic review, it did not become clear whether the increased opioid consumption is associated with the prevalence of pain. Studies conducted in the 10 countries responsible for 90% of the increase showed the same prevalence rates as studies from Africa and Asia where the availability of essential drugs for medical purposes is insufficient. However, the Asian studies were probably nonrepresentative of the continent due to the adequate use of the WHO ladder at the special palliative care units [80]. Only one study that was included in the meta-analyses originated from Africa.

Age is another study characteristic that might explain the heterogeneity. However, it is not necessarily associated with a larger number of symptoms in patients with cancer [100] and the literature on age and cancer pain is scarce and conflicting. In this review, no differences were found in prevalence of pain between elderly and younger patients. Less pain was reported by 903 cancer patients in the SUPPORT study [101] on 3571 older subjects. The adjusted odds ratio for higher levels of pain was 0.85 per increasing decade of age. Compared with the age group 65–74 years in a retrospective study on 13 625 elderly cancer patients [102], the odds ratios in the age group 75–84 years and the age group ≥85 years were 0.68 and 0.52, respectively. In contrast, other studies found a relation between more advanced age and undermedication [26, 102].

Type of prevalence (point, week or month) did not influence the prevalence of pain. The difference between a period prevalence and a point prevalence is the number of new cases

Table 5. Articles that reported the prevalence of pain in patients with advanced, metastatic or terminal disease

Author, year of publication	Quality points	Continent ^a	Setting ^b	Mean age (years)	Type of cancer ^c	Sample size	% no pain	% mild pain	% moderate pain	% severe pain	% total pain	Response rate ^d	Recall ^e
Bradley 2005 [10]	15	4	2	69	1	1296	22	28	32	17	78	0	1
Cleeland 1994 [66]	16	1	2	62	1	1308	41	23	(36) ^f		59	2	2
Conill 1997 [67]	14	2	1, 3, 4	68	1	176					52	0	1
Cowan 2003 [68]	14	1	5	73	1	98					85	1	1
Di Maio 2004 [11]	14	2	2	70	4	1021	26	42	24	7	74	1	1
Esnaola 2002 [69]	16	1		62	3	45					40	1	2
Higginson 1989 [70]	14	2	5		3, 4, 6	21, 33, 12					48, 30, 42	0	2
Hwang 2004 [13]	17	1	1, 2	68	1	296					86	2	2
Kane 1985 [71]	14	1	2	64	1	110					38	0	2
Lo 1999 [72]	15	3	4	64	1	133					50	0	1
McKegney 1981 [73]	17	1	3	55	1	199					80	2	1
Mercadante 2000 [74]	14	2	5	66	1	370					66	2	1
Morris 1986 [30]	17	1	6	54	1	1754					71	1	1
Peruselli 1999 [75]	16	2	6	70	1	401	38	24	19	19	62	0	2
Schuit 1998 [76]	16	2	2	61	1	151			(20) ^f		68	0	1
Soebadi 1996 [77]	14	3				578	11	24	39	26	89	0	2
Spiegel 1983 [78]	15	1	2, 3	55	5	109	44	21	32	3	56	1	1
Swanwick 2001 [79]	17	2	4	71	1	242					75	2	1
Sze 1998 [80]	17	3	4	62	1	203					44	1	1
Tay 1994 [81]	15	3	5	62	2, 3, 4, 5, 7	7, 29, 23, 8, 10			(43) ^f		86, 58, 65, 50, 80	2	99
Tranmer 2003 [82]	14	4	1	64	1	66					78	0	2
Vuorinen 1993 [83]	16	2	6	64	1	240					35	2	2

^a1, North America; 2, Europe; 3, Asia; 4, other.^b1, inpatient; 2, outpatient; 3, at home; 4, hospice; 5, referred to palliative care service; 6, all.^c1, all; 2, head and neck; 3, gastrointestinal; 4, bronchus/lung; 5, breast; 6, urogenital; 7, gynaecological.^d0, <70% or not mentioned; 1, 70%–90%; 3, ≥90%.^e1, point prevalence; 2, prevalence past week; 3, prevalence past months; 99, unknown.^fModerate to severe.

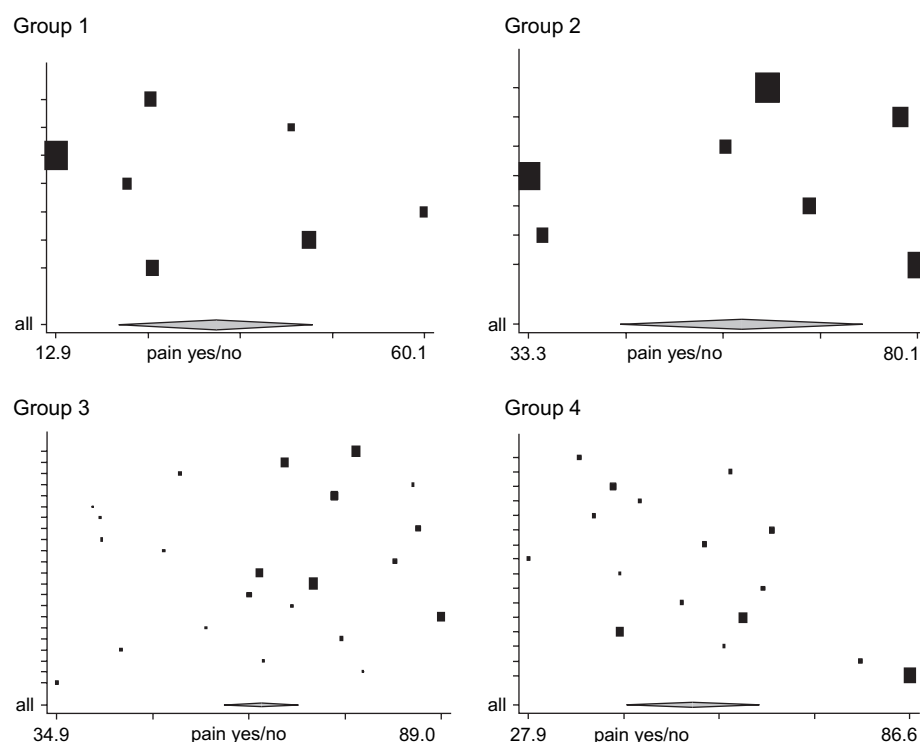


Figure 2. The prevalence of pain per disease group (group 1, patients after curative treatment; group 2, patients during anticancer treatment; group 3, patients with advanced, metastatic or terminal disease; group 4, all disease stages). Forest plots (the number of boxes indicates the number of studies included. The area of the boxes indicates the number of patients in this study. The diamonds at the bottom show the results of the meta-analyses with the 95% confidence intervals) indicating the number of studies included, the number of patients per study, the prevalence rate of pain per study and the overall prevalence found in the meta-analyses (diamond).

Table 6. Results of the meta-analyses: pooled pain prevalence in six types of cancer (cured patients were excluded)

Type of cancer	Groups 2–4		
	% pain (95% CI)	No. of reports	No. of patients
Head/neck	70% (51% to 88%)	3	95
Gastrointestinal	59% (44% to 74%)	9	564
Lung/bronchus	55% (44% to 67%)	7	1546
Breast	54% (44% to 64%)	7	420
Urogenital	52% (40% to 60%)	4	336
Gynaecological	60% (50% to 71%)	6	372

CI, confidence interval.

that occur within the defined period [103]. Although cancer pain can fluctuate in severity, it does not tend to disappear for a few weeks or even months, in contrast with headaches for example that occur more episodically.

The use of validated or nonvalidated questionnaires or interviews did not appear to be responsible for the heterogeneity in prevalence rates. This implies that in daily practice, simply asking ‘the pain question’ without the use of extensive and time-consuming questionnaires will detect any patients with pain. Symptom detection relies on three types of data collection method: documented, elicited and volunteered [104]. All the studies included in our meta-analyses used questionnaires or interviews. Pain questionnaires may amplify true morbidity due

to overendorsement bias, i.e. the tendency for patients to answer questions concerning symptoms written on a checklist in a particularly enthusiastic manner [104]. Nevertheless, the results of questionnaires are probably more reliable than those of documented symptoms, because 57%–76% of medical oncologists do not ask about pain [26]. In addition, pain was only mentioned in 10% of the medical records kept by oncologists [26]. Therefore, reliance on data noted in medical records underestimates the prevalence and severity of pain. Also, volunteered symptoms will underestimate symptom prevalence because of the patient barriers mentioned above.

Other explanations for the heterogeneity could be differences in patient characteristics caused by variation in the selection processes between the studies or the absence or ill-defined description of the pain severity or level that caused systematic discrepancies. Furthermore, differences in response rate might still have influenced the prevalence of pain.

Our systematic review had some flaws. It should be taken into consideration that the instrument used to judge methodological quality (Table 1) was devised subjectively to review the prevalence of lower back pain [36, 37]. The 75% threshold for acceptability was set arbitrarily [36, 37]. To make the instrument suitable to review the prevalence of cancer pain, we substituted the criteria for the definition of lower back pain for the criteria on disease stage in cancer. These may be points for further improvement. Proxy reporting and retrospective studies on medical records probably deserve even less weighting. The adequate description of disease stage probably deserves

more weighting, but subdivision of the use of validated or nonvalidated questionnaires does not seem to be necessary.

All included studies dealt with period prevalences and not with point prevalences. However, considering the long duration of the disease the difference of the two prevalence measures is small. Another limitation is that we did not know to what extent other pain conditions influenced the reported prevalence of pain.

Future studies on the prevalence of pain in cancer patients should take representativeness, response rates and the description of nonresponders into full consideration and provide information on the severity, duration, frequency and amount of interference. The use of multidimensional tools in research will facilitate the comparison of studies and the planning of needs from pain services.

Studies on the prevalence of pain in cancer survivors are scarce. This topic should be addressed in future studies.

conclusion

The pooled data from 52 articles showed that pain was prevalent in cancer patients: 64% in patients with metastatic or advanced stage disease, 59% in patients on anticancer treatment and 33% in patients after curative treatment. More than one-third of the patients with pain in the reviewed articles graded their pain as moderate or severe. Despite the clear WHO recommendations, cancer pain still is a major problem. The increasing number of cancer survivors who live to an advanced age means that it is of paramount importance to reduce the prevalence of pain at all stages of the disease process.

appendix. Reasons for not reaching the quality score of 14 points

Response rate of >70% [14, 105–114].

Response rate not mentioned [1, 12, 102, 115–135].

Data retrieved from medical records prospectively [22, 136–150].

Data retrieved from medical records retrospectively [2–5, 15, 114, 151–173].

Lack of description of the nonresponders [1–4, 7, 12, 14, 15, 22, 52, 75, 102, 105–109, 112, 113, 115–129, 132–149, 151–192].

Sample not representative [1, 7, 12, 14, 15, 89, 106, 109–113, 117, 119, 122, 123, 125, 127, 130, 131, 133–135, 144–146, 148, 151, 153–155, 158, 165–168, 171, 175, 177, 179–182, 184, 188, 189, 192–194].

Data collected by proxy or from medical record [1–5, 15, 102, 105, 108, 118, 120, 129, 136, 137, 139–142, 145, 147, 148, 151, 152, 154, 155, 157–168, 171, 172, 174, 178, 185, 187, 191, 194–197].

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