

## Chapter 2

### Symptom prevalence in patients with incurable cancer: a systematic review

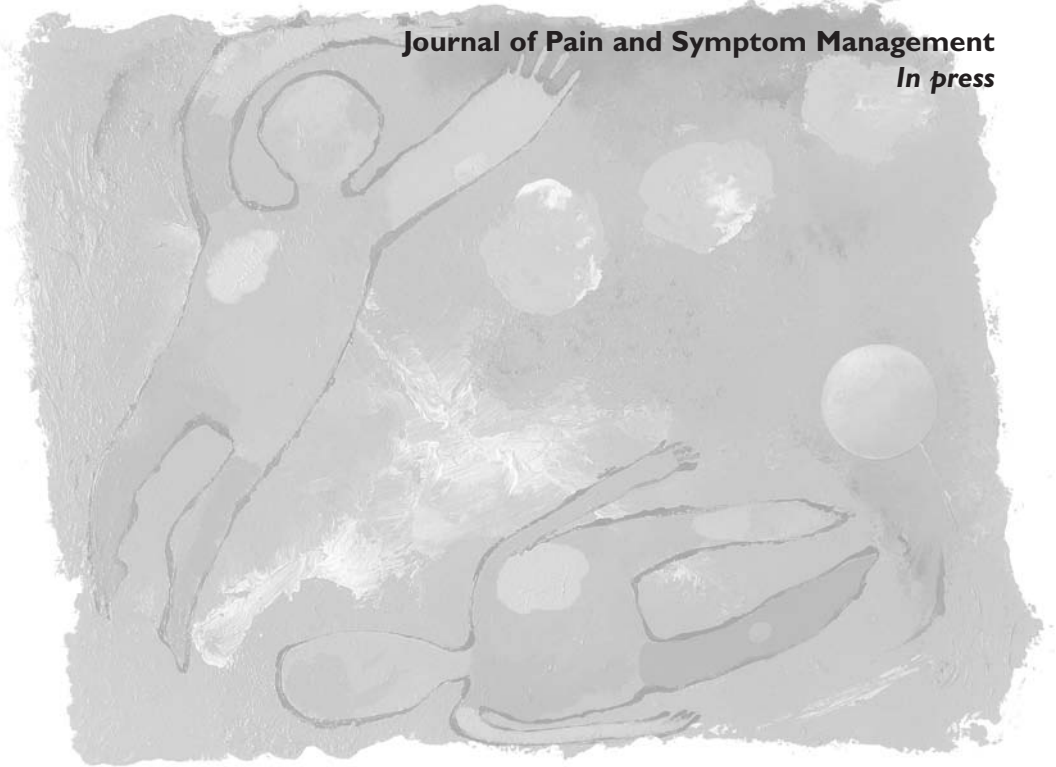
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*In palliative cancer care symptoms mean everything*

## **Abstract**

### **Purpose**

The suffering of patients with incurable cancer is determined to a large degree by the presence and intensity of the symptoms of their disease. Knowledge of symptom prevalence is important for clinical practice. The main aim of this study was to obtain a reliable estimation of symptom prevalence in patients with incurable cancer by performing a systematic review of studies assessing this topic.

### **Patients and methods**

We included 44 studies (including 25074 patients) on overall symptom prevalence (Group 1) and 6 studies (including 2219 patients) on symptom prevalence during the last 1-2 weeks of life (Group 2). In these studies symptom prevalence was assessed by a questionnaire, a standardized interview or the medical record.

### **Results**

We identified 37 symptoms assessed in at least 5 studies. Almost all symptoms occurred in >10% of the patients. Five symptoms, fatigue, pain, lack of energy, weakness and appetite loss, occurred in more than 50% of the patients of Group 1. Weight loss occurred significantly more often in Group 2 compared to Group 1, and pain, nausea and urinary symptoms significantly less often. Generally, symptom prevalence was highest if assessed by a questionnaire.

### **Conclusion**

The results of this study should be used to guide doctors and nurses in symptom management. Proper attention to symptom burden and suffering should be the basis for individually tailored treatment aimed at improving or maintaining quality of life of patients in their last period of life.

## **Introduction**

Palliation implies a shift from cure and control of the disease to improvement or maintenance of quality of life. This shift in focus is an essential event for cancer patients and their loved ones, but also for doctors and nurses. Physical symptoms, functional deficits and feelings of loss of control become the focus of care<sup>1,2</sup>.

The World Health Organization has defined palliative care as 'an approach to care which improves quality of life of patients and their families facing life threatening illness through the prevention and relief of suffering by means of identification and impeccable assessment of pain and other problems, physical, psychosocial and spiritual'<sup>3</sup>. The palliative phase has different dynamics in every patient. However, the suffering of these patients is determined to a large degree by the presence and intensity of the symptoms of their disease. Knowledge of symptom prevalence is important for clinical practice as it enables doctors and nurses to focus on the more prevalent symptoms and may help to anticipate problems and plan care for patients, to educate clinical staff, to direct assessments of health care need and for planning services<sup>4</sup>.

Many studies have addressed this issue in patients with incurable diseases, most often in those with cancer. However, these studies are heterogeneous with regard to patients and assessment method and the numbers of patients included are often relatively low.

The main aim of this study was to obtain a reliable estimation of symptom prevalence in patients with incurable cancer by performing a systematic review of studies assessing this topic. Secondary aims were 1) to study differences in symptom prevalence during the last 1-2 weeks of life and 2) to assess the influence of assessment method, gender and age on symptom prevalence.

## **Methods**

### **Literature review**

We performed a systematic literature review using the following databases: MEDLINE, EMBASE and CINAHL. When papers were found, they were hand searched for cross-references. In order to avoid problems concerning the meaning and categorization of symptoms, we included only papers in the English language. The data were primarily extracted by one of the authors (W.W.) and checked by two other authors (ST and AdG). These 3 authors decided how to categorize the symptoms (see Results). Papers were excluded if they:

- were not describing original studies
- focused on only one specific symptom (e.g. fatigue, depression) without prevalence data on other symptoms
- assessed symptoms by proxy

- gave only data on symptom intensity (without specifying the number or percentage of patients with or without the symptom)
  - included more than 10% of patients without cancer and did not supply data on symptom prevalence by diagnosis
  - included patients with cancer before, during or after curative treatment.
- Symptoms were included in the analysis only if they were assessed in at least 10% of the studies.

## **Analysis**

We separated studies assessing symptom prevalence in the last 1-2 weeks of life (Group 2) from other studies (Group 1). If symptoms were assessed at different time points in the same study, only the baseline data were used for Group 1. If the last assessment was done in the last 1-2 weeks of life, these data were also used for Group 2.

Obviously, the prevalence of a symptom could be determined only for those studies assessing that specific symptom. Each prevalence was first transformed to log odds to better conform to a normal distribution. The Q test was used to determine whether there was heterogeneity in the log odds of the various studies. Pooled log odds were then estimated using the random effects model<sup>5</sup>, and consequently back transformed, resulting in pooled prevalence estimates with 95% confidence intervals.

Non-parametric tests (Mann-Whitney, Kruskal-Wallis) were used to detect differences in mean percentages between groups.

For statistical analysis, the Statistical Package for the Social Sciences, version 12.0 (SPSS Inc., Chicago, IL) was used, and the statistical package R (R version 2.2.0, The R Development Core Team) with library "meta". Statistical significance was assumed if  $p < 0.05$ .

## **Results**

We identified 46 studies that met the inclusion criteria,<sup>6-55</sup> including a total of 26223 patients. Some papers referred to the same patient population<sup>6</sup>, and <sup>7,20</sup> and <sup>21,32</sup> and <sup>33,43</sup> and <sup>44</sup>. Data of 40 of these studies<sup>6-53</sup> were included for Group 1, data of 4 studies were included for both groups,<sup>26,32</sup> and <sup>33,34,46</sup> and data of 2 studies were included for Group 2 only<sup>54,55</sup>. Patient characteristics are summarized in Table 1.

Group 1 included 25074 patients and Group 2 2219 patients. Ten studies gave data on median or mean survival, which varied from 3 to 12 weeks<sup>16,23,31,32,33,35,37,41,43,44,48,52</sup>.

As to be expected, symptoms were labeled differently in different studies. We categorized these symptoms (in order of decreasing prevalence) as follows: fatigue (including tiredness), pain, lack of energy, weakness (asthenia), appetite loss (anorexia), nervousness, weight loss, dry mouth (xerostomia), depressed mood (depression, mood changes, feeling low, miserable or sad), constipation, worrying, insomnia

**Table 1. Patient characteristics**

	<u>Group 1</u>	<u>Group 2</u>
<b>Number of patients</b>	25074	2219
<b>Mean age</b>	65 years	64 years
<b>Gender:</b>		
- Male	28%	53%
- Female	25%	47%
- Unspecified	47%	
<b>Setting:</b>		
- Hospice inpatient	45%	51%
- Hospital inpatient	25%	19%
- Outpatient	16%	8%
- Home	4%	14%
- Unspecified	10%	8%
<b>Tumor type:</b>		
- Brain	1%	2%
- Head and neck	5%	6%
- Lung	13%	25%
- Breast	9%	11%
- Gastro-intestinal	17%	26%
- Gynecological	4%	4%
- Prostate	3%	3%
- Other genito-urinary	5%	9%
- Skin/melanoma/sarcoma	1%	1%
- Hematological	2%	2%
- Other types of cancer	10%	11%
- Unspecified cancer	29%	-
No cancer	1%	-

(inability to sleep, difficulty or problems sleeping, sleeping problems or disturbances, sleeplessness, poor sleeping), dyspnea (breathlessness, shortness of breath, trouble with breathing), nausea, anxiety (fearfulness), irritability, bloating, cough, cognitive symptoms (memory or concentrating problems, difficulty concentrating), early satiety, taste changes (unpleasant taste), sore mouth/stomatitis (mouth sores or lesions, oral candida, oral or mouth discomfort, mucositis), vomiting (emesis), drowsiness (sleepiness, sedation), edema (swollen limb, lymph edema), urinary symptoms (dysuria, incontinence, problems with urination, loss of bladder control, bladder disturbances), dizziness, dysphagia (difficulty swallowing), confusion (disorientation), bleeding (haemorrhage), neurological symptoms (hemiplegia, paralysis, paresis, numbing/tingling, paresthesias), hoarseness, dyspepsia (gastric discomfort), skin symptoms (pressure, wound or bed sores, dermatological problems), diarrhea (loose stool), pruritis (itching) and hiccup.

For both groups, virtually all Q tests for statistical heterogeneity were (very) significant, indicating a very high level of heterogeneity of the studies included in this review.

### **Symptom prevalence in Group 1 (Table 2 and Appendix 1)**

In total, we identified 37 symptoms which were assessed in at least 5 (>10%) studies (range: 5-40) for Group 1. Almost all symptoms occurred in >10% of the patients.

For Group 1, seventeen studies used a questionnaire (the Memorial Symptom

**Table 2. Sympton prevalence in Group I**

	Number of studies	Number of patients	Pooled prevalence %	95% confidence interval %
N.		25,074		
Fatigue	17	6727	74%	(63% ; 83%)
Pain	37	21917	71%	(67% ; 74%)
Lack of energy	6	1827	69%	(57% ; 79%)
Weakness	18	14910	60%	(51% ; 68%)
Appetite loss	37	23112	53%	(48% ; 59%)
Nervousness	5	727	48%	(39% ; 57%)
Weight loss	17	13167	46%	(34% ; 59%)
Dry mouth	20	6359	40%	(29% ; 52%)
Depressed mood	19	8678	39%	(33% ; 45%)
Constipation	34	22437	37%	(33% ; 40%)
Worrying	6	1378	36%	(21% ; 55%)
Insomnia	28	18597	36%	(30% ; 43%)
Dyspnea	40	24490	35%	(30% ; 39%)
Nausea	39	24263	31%	(27% ; 35%)
Anxiety	12	7270	30%	(17% ; 46%)
Irritability	6	1009	30%	(22% ; 40%)
Bloating	5	626	29%	(20% ; 40%)
Cough	24	11939	28%	(23% ; 35%)
Cognitive symptoms	9	1696	28%	(20% ; 38%)
Early satiety	5	1639	23%	( 8% ; 52%)
Taste changes	11	3045	22%	(15% ; 31%)
Sore mouth/ stomatitis	8	2172	20%	( 8% ; 39%)
Vomiting	24	9598	20%	(17% ; 22%)
Drowsiness	16	11634	20%	(12% ; 32%)
Edema	13	3486	19%	(15% ; 24%)
Urinary symptoms	15	12011	18%	(15% ; 21%)
Dizziness	12	3322	17%	(11% ; 25%)
Dysphagia	25	16161	17%	(14% ; 20%)
Confusion	17	11728	16%	(12% ; 21%)
Bleeding	5	8883	15%	(11% ; 20%)
Neurological symptoms	11	10004	15%	(10% ; 23%)
Hoarseness	5	1410	14%	( 7% ; 26%)
Dyspepsia	7	3028	12%	( 9% ; 15%)
Skin symptoms	7	9177	11%	( 6% ; 20%)
Diarrhea	22	16592	11%	( 7% ; 16%)
Pruritis	14	6676	10%	( 7% ; 15%)
Hiccup	7	3991	7%	( 3% ; 15%)

Assessment Scale,<sup>7,13,18,20,21,24</sup> Edmonton Symptom Assessment Scale<sup>6,19</sup> Support Team Assessment Schedule,<sup>10,15</sup> Patient Disease Symptom/Sign Assessment Scale,<sup>8</sup>

## Appendix I. Symptom prevalence of the individual studies (Group I)

Reference	6,7	8	9	10	11	12	13	14	15	16	17	18	19	20,21	22	23	24	25	26	27	28	29	
Assessment	Questionnaire																					Standardized interview	
N.	240	121	50	352	1635	146	192	480	133	278	60	178	162	243	151	100	66	952	176	125	254	39	
Fatigue		40				83		79	52	100	81		88			89							
Pain	59	62	46	59		61	88	53	50	83		83	67	64		77	78			52	72	82	
Lack of energy	62											89		74			83						
Weakness			82													86				77		41	
Appetite loss		47	58	73	48	49			20	75	65	57	70	44	38	64	61	68	68	50		64	
Nervousness	37							56				45				61							
Weight loss	33															27						51	
Dry mouth	54		68									78		54		80	82			61		41	
Depressed mood	40		52	40	31			51				42	71	65			55			53		39	
Constipation			36	36	33	27	48	33	18	54					25	40		48	59	49	33	41	
Worrying	40							27						44		71				61			
Insomnia	45	67	46		59	36		49	10	64		37		52		50	55			35	40	54	
Dyspnea	50	14	30	32	24	47		45	32	77	73	70	47	24	29		38	43	40	21		21	
Nausea	27	24	42	24	27	29	32	23	11	66		38	29	44	42	30	61	78	26	28	39	41	
Anxiety	63				9									74						51			
Irritability	28						40					35				47				29			
Bloating												39				37						23	
Cough	33		28			38			24		75	57		29	34		52	42	28			18	
Cognitive symptoms							45	49					34		41		50						
Early satiety																						62	
Taste changes							28	50							35		50					46	
Sore mouth/ Stomatitis				59														68					
Vomiting			32	13	20	9			7			21		21	20	24	41			19	17	27	
Drowsiness	44		4		2							44	79	60			74	23					
Edema		8	46						11								32					21	
Urinary symptoms				14				25				21		17	22			26	8				
Dizziness			2									37		24		39	29					21	
Dysphagia				22			16	6			23			11			24			28		24	
Confusion			30													50		18		30			
Bleeding																						16	
Neurological sympt				10								39			37							21	
Hoarseness																							
Dyspepsia			2		11																		
Skin symptoms		17			3																		
Diarrhea			4		6	25		17	3	44		18		24			24			9		15	
Pruritis			8		6		8					30		27	27		24						
Hiccup																10	28						

Symptom Monitor,<sup>12</sup> Symptoms and Concerns checklist,<sup>14</sup> EORTC Core Questionnaire,<sup>16</sup> Lung Cancer Symptom Scale,<sup>17</sup> Symptom Distress Scale,<sup>22</sup> Therapy Impact Questionnaire<sup>23</sup> or other questionnaires<sup>9,11</sup>). Eighteen studies used a self-developed standardized interview by the doctor or nurse,<sup>25-44</sup> 8 studies used the medical record<sup>45-52</sup> and in one study the method was unclear<sup>53</sup>.

Five symptoms, fatigue, pain, lack of energy, weakness and appetite loss, occurred in more than 50% of the patients of Group I. Large 95% confidence intervals (>20%) were seen for lack of energy, weight loss, dry mouth, worrying, anxiety, early satiety and sore mouth/stomatitis.



30	31	32,33	34	35	36	37	38	39	40	41	42	43,44	45	46	47	48	49	50	51	52	53	
Standardized interview												Medical record				Unknown						
100	530	211	593	150	108	1592	312	78	100	166	1840	1000	1103	90	105	547	38	3030	400	171	6677	
52							98					67		58	85			84	23	43		
86	76	80		65	72	62	90	71	64	88	57	82	73	54		42	79	69	64	92	71	
38												59										
47		63			70				62	60	51	64		43	79	40		83	32	31	47	
68	64		37	57	44	79	53	42	48	56	30	64	31	8	76			57	34	36	67	
39						75	93	23	56	17	39	60			73		79			18	6	77
40	29	14	7	25		74			13	23		55								16	2	
34									7	27		40		8					48	16	32	
52		25	27	33	21	54	42	27	33	39	23	51		4		37		46	32	24	47	
																					3	
43			31		26		69		20	36	9	47		7					43	12	5	29
70	34	16	21	33	29	53	27	17	27	30	19	51	27	17	43	21		35	31	19	51	
24		11	27	29	36	44	21		13	38	21	36	19	12		19		30	29	35	40	
27									3	58		23		21				60	13	11		
														6								
10																						
47			5	29	13			6	18			37		6			66		15	7	50	
6									6	14											29	
46									3			50								4		
32									3			28								2	1	
5				7						17							47				2	
15			16				11	49	12	24		23						16	16	16		
5		9	5						10	27				24						11	10	
16				27	8				23			28		4						12		
			14	23	10			24	21					3					14		23	
16			10				38		6					1							10	
9	24	10	21		16	43		12	7	12		18	22	3			74		7	4	23	
13		6	2			12		15	3	17	8	20	33	24		15		21				
						13																
				23	10				14	14							47		6		14	
																			8	6	8	
33									6			24									1	
13		8	12																		8	
								9	12	12										14		19
		4	5	7		25		6	3	16								9	10	7	4	
			7	3				6	4									8		2		
12																		4	2	1		

### Symptom prevalence in Group 2 (Table 3 and Appendix 2)

One study used a questionnaire,<sup>54</sup> four studies used a standardized interview<sup>26,32,33,34,55</sup> and one study used the medical record<sup>46</sup>.

Twenty-six of the 37 symptoms from Group 1 were assessed in at least one study for Group 2 (range 1-6). Four symptoms, fatigue, weight loss, weakness, and appetite loss, occurred in >50% of patients. Large 95% confidence intervals (>20%) were seen for most of the symptoms.

Weight loss occurred significantly more often in Group 2 compared to Group 1, and pain, nausea and urinary symptoms significantly less often.

**Table 3. Symptom prevalence in Group 2: patients in the last 1-2 weeks of life**

	Number of studies	Number of patients	Pooled prevalence %	95% confidence interval %	p <sup>1</sup>
N		2219			
Fatigue	2	120	88%	(12% ; 100%)	.506
Weight loss	2	1149	86%	(77% ; 92%)	.023
Weakness	3	477	74%	(50% ; 89%)	.262
Appetite loss	5	2008	56%	(13% ; 92%)	.460
Pain	5	1626	45%	(32% ; 59%)	.004
Dyspnea	6	2219	39%	(20% ; 62%)	.695
Drowsiness	3	894	38%	(14% ; 70%)	.303
Dry mouth	4	1010	34%	(10% ; 70%)	.794
Neurological symptoms	1	176	32%	(26% ; 40%)	.500
Anxiety	2	266	30%	(11% ; 62%)	.923
Constipation	6	2219	29%	(16% ; 48%)	.747
Confusion	4	1070	24%	( 6% ; 61%)	.410
Depressed mood	3	859	19%	( 9% ; 36%)	.104
Nausea	6	2219	17%	( 8% ; 31%)	.047
Skin symptoms	1	593	16%	(14% ; 20%)	.750
Dysphagia	4	1070	16%	( 6% ; 37%)	.825
Insomnia	4	889	14%	( 3% ; 44%)	.094
Cough	4	889	14%	( 3% ; 43%)	.291
Vomiting	3	799	13%	( 9% ; 18%)	.313
Bleeding	1	176	12%	( 8% ; 18%)	.667
Edema	1	90	8%	( 4% ; 16%)	.286
Dizziness	2	683	7%	( 5% ; 9%)	.264
Irritability	1	90	7%	( 3% ; 14%)	.571
Diarrhea	5	2129	6%	( 2% ; 19%)	.258
Urinary symptoms	3	859	6%	( 5% ; 8%)	.017
Dyspepsia	2	804	2%	( 1% ; 4%)	.111

<sup>1</sup> Comparison of median percentages, Group 2 versus Group 1, Mann-Whitney test

### Symptom prevalence by assessment method, gender, age and diagnosis

For 26 symptoms, different assessment methods could be compared (Table 4). Significant differences in mean percentages were found for dry mouth, insomnia, depressed mood, taste changes, confusion and pruritis. For all these symptoms, the highest mean percentages were found if the symptom was assessed by means of a questionnaire.

Six studies looked at gender differences in symptom prevalence<sup>9,11,14,15,30,44</sup>. Only one study corrected for diagnosis<sup>44</sup>. A clear indication for gender differences, occurring in most or all studies looking at that particular symptom, was found for dysphagia and insomnia (both more prevalent in men) and for nausea and vomiting

**Appendix 2. Symptom prevalence of the individual studies (Group 2)**

<b>Reference</b>	26	46	32,33	34	54	55
N	176	90	211	593	30	1119
Fatigue		52			100	
Weight loss					93	84
Weakness	82	49	85			
Appetite loss	80	6		12	93	90
Pain	30	34	47		57	60
Dyspnea	47	28	23	17	70	64
Drowsiness		57	51	15		
Dry mouth	70		10	16	60	
Neurological symptoms	32					
Anxiety	46	18				
Constipation	55	7	18	18	47	52
Confusion	68	28	29	3		
Depressed mood	39	4		21		
Nausea	13	13	4	20	23	44
Skin symptoms				16		
Dysphagia	46	7	14	10		
Insomnia	28	6		3	47	
Cough	18	7		3	60	
Vomiting	10			12	23	
Bleeding	12					
Edema		8				
Dizziness		6		7		
Irritability		7				
Diarrhea	7		1	4	3	27
Urinary symptoms	7	6		6		
Dyspepsia			1	3		

(more prevalent in women).

The relation between age and symptom prevalence was investigated in 4 studies<sup>11,16,44,45</sup>. No study corrected for diagnosis. An indication for age differences, occurring in at least two of the studies, was found for pain and dysphagia, both decreasing with age.

## Discussion

Many studies have addressed symptom prevalence in advanced cancer patients. However, almost all studies are heavily biased due to patient selection. Moreover, several studies included relatively low numbers of patients. This is the first systema-

**Table 4. Symptom prevalence by assessment method**

Assessment method	Questionnaire			Standardized interview			Medical record			p <sup>1</sup>
	No. of studies	Median %	Mean %	No. of studies	Median %	Mean %	No. of studies	Median %	Mean %	
N	4587			8326			5484			
Total number of studies	17			18			8			
Fatigue	8	83	77	4	60	66	5	58	59	.510
Pain	14	63	66	15	72	73	7	69	68	.370
Weakness	2	84	84	9	62	59	6	42	51	.084
Appetite loss	14	58	55	16	57	56	6	35	40	.236
Weight loss	3	29	30	9	51	50	4	46	44	.518
Dry mouth	6	73	69	12	35	36	2	9	9	.008
Depressed mood	9	51	50	6	37	33	4	24	26	.044
Constipation	11	36	36	17	39	38	5	32	29	.442
Insomnia	12	50	48	11	36	37	4	10	17	.018
Dyspnea	15	38	42	17	29	32	7	27	28	.124
Nausea	16	30	34	16	29	32	6	24	24	.294
Anxiety	3	63	49	4	25	26	4	17	26	.591
Cough	9	34	41	10	23	24	4	11	24	.095
Taste changes	4	43	41	5	28	26	2	2	2	.043
Sore mouth/stomatitis	2	36	36	4	12	24	2	25	25	.717
Vomiting	10	21	21	11	19	22	3	16	16	.574
Drowsiness	7	44	44	6	10	13	2	18	18	.327
Edema	4	19	23	7	23	22	2	8	8	.272
Urinary symptoms	5	21	20	7	21	18	2	9	9	.243
Dizziness	5	29	26	5	16	18	2	6	6	.192
Dysphagia	6	19	17	13	16	18	5	7	22	.692
Confusion	2	40	40	11	13	13	4	23	23	.023
Neurological symptoms	3	37	29	5	14	16	2	7	7	.084
Diarrhea	9	18	18	9	7	10	3	9	9	.383
Pruritis	7	24	19	5	6	7	2	5	5	.035
Hiccups	2	19	19	2	14	14	3	2	2	.105

<sup>1</sup> Comparison of mean percentages, Kruskal-Wallis test

tic review on symptom prevalence in patients with incurable cancer. As 46 different studies and 26223 patients were included, the estimations of symptom prevalence are likely to be as reliable as possible as the influence of sample size and selection bias is reduced as much as possible. Contrary to many systematic reviews on other topics, publication bias is unlikely to have influenced the results. There is no reason to presume that studies on symptom prevalence have not been published because of uninteresting or 'negative' results.

Thirty-seven symptoms (assessed in at least 5 studies) were identified, almost always occurring in >10% of patients. Overall, fatigue, pain, lack of energy, weakness and appetite loss were the most frequent symptoms, occurring in >50% of patients. During the last 1-2 weeks of life, fatigue, weight loss, weakness and appetite loss occurred in more than 50% of patients.

Several aspects of this study deserve further discussion.

The 95% confidence intervals of the symptom prevalence are quite large due to the heterogeneity of the studies included and probably also due to different interpretations of these symptoms in different studies. When combining the results from dif-

ferent studies, we had to make choices for categorizing symptoms which were labeled differently. Although most of these choices were relatively straightforward, one may argue about some of them, in particular: differences between fatigue, lack of energy and weakness; the various terms included for anxiety and depressed mood, respectively; grouping of symptoms as in mouth pain/stomatitis, cognitive, voiding, skin and neurological symptoms. Obviously, this has an impact on the symptom prevalence figures detected in our review.

Another factor that may influence symptom prevalence (and may also explain the large 95% confidence intervals) is the assessment method. We found clear differences in the prevalence of several symptoms between studies using different methods. Although this is an indirect comparison (no study compared different methods directly) and differences are probably partly due to patient selection, there seem to be patterns in prevalence differences for certain symptoms due to the assessment method used. For many symptoms, the lowest prevalence was seen in studies using the medical record. This finding emphasizes the importance of standardized comprehensive assessment of symptoms in palliative care<sup>56,57</sup>. However, this was not (clearly) the case for all symptoms, e.g. for pain, dyspnoea, nausea and vomiting, constipation and skin problems. This probably reflects the fact that these symptoms are usually spontaneously mentioned by patients and/or are explicitly and routinely addressed by doctors and nurses. For other symptoms, studies using a questionnaire showed higher prevalence figures than studies using a standardized interview. Apparently, when completing a questionnaire, patients have more time and/or feel freer to indicate the presence of some symptoms that are less often mentioned during a standardized interview. Questionnaires may pick up symptoms that are not considered to be important and/or treatable by patients, doctors and nurses and thus are not addressed by standardized interviews or a routine history<sup>56,57</sup>.

As there is some evidence of a final common clinical pathway in patients nearing death,<sup>55</sup> we looked separately at symptom prevalence in patients during the last 1-2 weeks of life. As only 6 such studies were included and these studies varied greatly with regard to the number of patients included and symptoms assessed, the estimations are less reliable and comparison with the overall population of incurable cancer patients is difficult. A significant increase was found for weight loss and a significant decrease for pain, nausea and urinary symptoms. Longitudinal studies are needed to test the hypothesis that symptoms change and are less dependent on diagnosis as the end approaches.

A limitation of our study is the lack of availability of individual patient data. Therefore, we were unable to assess reliably the influence of gender and age on symptom prevalence. In the limited amount of studies addressing those issues, there

seemed to be limited relations between gender and age on the one hand and symptoms on the other hand. No definite conclusions about the presence or absence of these relationships can be drawn and more study is necessary in this area.

In conclusion, we performed a systematic review giving the most reliable estimates possible of symptom prevalence in patients with incurable cancer. Focus on the more prevalent symptoms in these patients should guide symptom management by doctors and nurses. However, it must be emphasized that treatment should be based on symptom intensity, symptom burden and the impact of symptoms on quality of life. This should be the subject of further studies, in order to help doctors and nurses to provide individually tailored treatment aimed at improving or maintaining quality of life of cancer patients in their last period of their life.

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