



# Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies

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## Summary

**Background** Substantial uncertainty exists about prevalence of mood disorders in patients with cancer, including those in oncological, haematological, and palliative-care settings. We aimed to quantitatively summarise the prevalence of depression, anxiety, and adjustment disorders in these settings.

**Methods** We searched Medline, PsycINFO, Embase, and Web of Knowledge for studies that examined well-defined depression, anxiety, and adjustment disorder in adults with cancer in oncological, haematological, and palliative-care settings. We restricted studies to those using psychiatric interviews. Studies were reviewed in accordance with PRISMA guidelines and a proportion meta-analysis was done.

**Findings** We identified 24 studies with 4007 individuals across seven countries in palliative-care settings. Meta-analytical pooled prevalence of depression defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM) or International Classification of Diseases (ICD) criteria was 16.5% (95% CI 13.1–20.3), 14.3% (11.1–17.9) for DSM-defined major depression, and 9.6% (3.6–18.1) for DSM-defined minor depression. Prevalence of adjustment disorder alone was 15.4% (10.1–21.6) and of anxiety disorders 9.8% (6.8–13.2). Prevalence of all types of depression combined was 24.6% (17.5–32.4), depression or adjustment disorder 24.7% (20.8–28.8), and all types of mood disorder 29.0% (10.1–52.9). We identified 70 studies with 10 071 individuals across 14 countries in oncological and haematological settings. Prevalence of depression by DSM or ICD criteria was 16.3% (13.4–19.5); for DSM-defined major depression it was 14.9% (12.2–17.7) and for DSM-defined minor depression 19.2% (9.1–31.9). Prevalence of adjustment disorder was 19.4% (14.5–24.8), anxiety 10.3% (5.1–17.0), and dysthymia 2.7% (1.7–4.0). Combination diagnoses were common; all types of depression occurred in 20.7% (12.9–29.8) of patients, depression or adjustment disorder in 31.6% (25.0–38.7), and any mood disorder in 38.2% (28.4–48.6). There were few consistent correlates of depression: there was no effect of age, sex, or clinical setting and inadequate data to examine cancer type and illness duration.

**Interpretation** Interview-defined depression and anxiety is less common in patients with cancer than previously thought, although some combination of mood disorders occurs in 30–40% of patients in hospital settings without a significant difference between palliative-care and non-palliative-care settings. Clinicians should remain vigilant for mood complications, not just depression.

**Funding** None.

## Introduction

Of all the possible mood complications associated with cancer, depression has been most extensively investigated. Depression is one of the most common mental health problems worldwide; its 30-day prevalence in the community is about 5% with an incidence of about 9% over 12 months.<sup>1</sup> Depression is known to be a substantial complication in patients with cancer, and its prevalence is higher in these patients than in the general population.<sup>2–4</sup> In two studies,<sup>5,6</sup> the relative risk of depression in patients with cancer exceeded that of patients who had stroke, diabetes, and heart disease. In cancer settings, evidence shows that depression causes serious suffering and distress, reduces participation with medical care, and potentially prolongs duration of stay in hospital.<sup>7,8</sup> Depression is also a significant determinant of quality of life and

survival.<sup>9,10</sup> Yet depression is often overlooked by busy cancer professionals in palliative-care and non-palliative-care settings.<sup>11</sup>

Although low rates of depression recognition and treatment are concerning, there might be several mitigating explanations. First, those making the diagnosis are most often cancer specialists who are not trained in mental health, and find operational (syndromal) diagnoses and formal screening questionnaires cumbersome.<sup>12</sup> Second, symptoms of depression suggested by the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV)<sup>13</sup> and International Classification of Diseases 10 (ICD10)<sup>14</sup> are generic and might not be appropriate in cancer settings. Third, depression is only one, albeit important, mood disorder that clinicians have to be aware of. Fourth, prevalence of depression seems to be modest, and its onset often

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unpredictable. Despite many years of research, prevalence of depression in patients with cancer is still subject to much debate.<sup>15</sup> The picture is especially unclear because most published work has relied on depression symptom-screening methods rather than diagnostic instruments.<sup>16</sup> Diagnostic instruments are the criterion (gold) standard and include a diagnostic algorithm, clinical significance criteria, and minimum duration to support a robust diagnosis (webappendix p 1). Although depression in patients with advanced cancer has been researched, the actual rate of depression is still not clear. Reviews of depression in palliative-care settings show a prevalence of between 1% and 69%.<sup>17</sup> Many investigators have stated that depression is a more common problem in palliative-care settings than in others and propose demographic (age, sex) and disease-based (tumour stage, tumour type) risk factors.<sup>18,19</sup> Only one previous meta-analysis has examined predictors of prevalence, although no pooled rate was reported. Van't Spijker and colleagues<sup>20</sup> identified 50 studies of psychological and psychiatric problems using various self-report scales, but only eight with formal interviews. They reported low rates of psychological and psychiatric problems in patients with breast cancer and in studies of women only, and noted that studies with young patients (mean age <50 years) reported significantly more depression, as did older studies published before 1988.

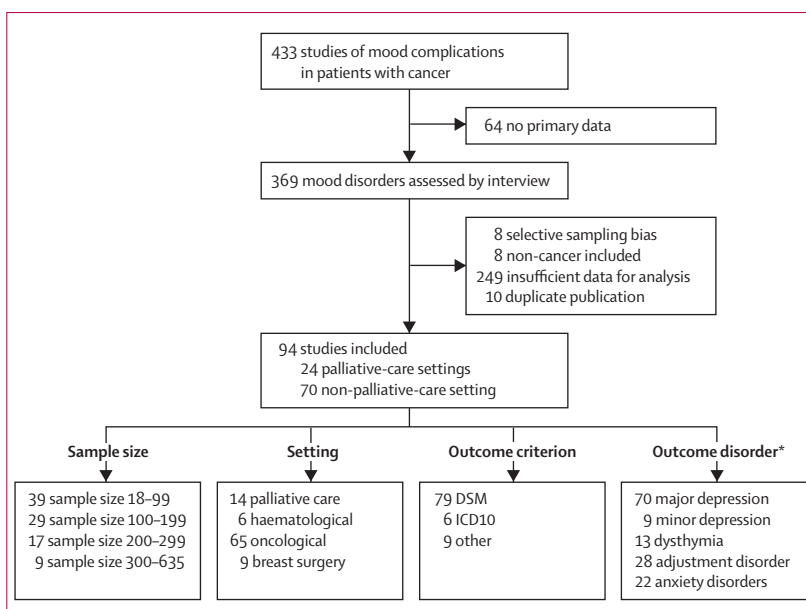
In view of uncertainties about the prevalence of depression and related mood disorders in patients with cancer, we aimed to quantitatively summarise the prevalence of robustly defined depression, anxiety, and adjustment disorders in oncological, haematological, and palliative-care settings. Our secondary aim was to examine the main correlates of depression in these settings.

## Methods

### Search strategy and selection criteria

AJM and NM designed the review protocol and extraction forms in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines.<sup>21</sup> A systematic search of Medline, PsycINFO, and Embase abstract databases was done by AJM and NM, from inception to November, 2010. Four full text collections were also searched and when necessary, authors of the publications were contacted directly for primary data. Sample searches are shown in webappendix p 2.

We included studies with data for prevalence of depression and related mood disorders in adults with cancer in hospital settings. Studies that were included were stratified into those undertaken in palliative-care settings (including late stage or advanced cancers) and those in oncological or haematological settings (ie, those cancers diagnosed at mixed or early stages). We restricted studies to those using psychiatric interviews (ie, a structured, semi-structured, or clinical interview applied by a trained researcher or health professional). We



**Figure 1: Study selection**

DSM=Diagnostic and Statistical Manual of Mental Disorders. ICD=International Classification of Diseases.

\*Not mutually exclusive.

excluded studies with epidemiologically selective samples (eg, intervention trials), those with people under the age of 18 years, and those with prevalence of depression reported before diagnosis of cancer. We also excluded duplicate publications (ie, two or more studies investigating the same sample) and community surveys of depression, even when cancer was reported, because we considered this sample to be too small and clinically distinct.<sup>2-4</sup>

See Online for webappendix

### Data extraction and classification

MC, HB, and MH extracted the primary data independently, which were reviewed systematically. A four-point quality rating and a five-point bias risk was applied to each study. Quality-rating score was used to assess the study sample size, design, attrition, criterion method, and method of dealing with possible confounders with the following scale: 1=low quality; 2=low-to-medium quality; 3=medium-to-high quality; and 4=high quality. Bias-rating score was used to assess possible bias in assessments of age, sex, clinical setting, and cancer type and stage with the following score: 0=no appreciable bias risk; 1=low bias risk; 2=low-to-medium bias risk; 3=medium-to-high bias risk; and 4=high bias risk. Finally, the sampling method was assessed for each study, because this could affect the interpretation of prevalence data. Any area of disagreement was resolved by AJM and NM.

### Outcome measures

We defined the main outcomes of interest as: syndromal (clinical) depression defined by formal interview; major and minor depressions defined by interview against DSM research criteria (minor depression is listed in DSM-IV

text revision under depressive disorder not otherwise specified); dysthymia; adjustment disorder (either alone or in combination with depression); anxiety disorders; and combined mood disorders. We defined point estimate of prevalence as the rate of depression (or disorder of interest) assessed in a consecutive, random, or convenience sample at least once (cross-sectionally or longitudinally), and subject to definitions of duration according to ICD or DSM, typically 2 weeks. This point estimate of period prevalence we henceforth refer to simply as prevalence.

**Statistical analysis**

We pooled individual study data with DerSimonian-Laird meta-analysis. Heterogeneity was invariably moderate to

high, therefore a random effects meta-analysis was done with StatsDirect (version 2.77). For comparative and subanalyses we needed a minimum of three independent studies to justify analysis according to convention. We used the *I*<sup>2</sup> test to assess heterogeneity (thresholds were ≥80%=moderate and ≥90%=high), and also assessed publication bias with Begg-Mazumdar and Egger tests. We used Spearman correlation with adjusted *r*<sup>2</sup> to assess the association between linear variables.

**Role of the funding source**

There was no funding source for this study. AJM and NM had access to the raw data. The corresponding author had full access to all the data and had final responsibility for the decision to submit for publication.

	Sampling method*	Quality†	Bias risk‡	Number with cancer	Mean age (years)	Setting	Criteria for definition of depression	Cancer duration	Cancer type	Women (%)	Country
<b>Palliative-care or advanced-cancer settings</b>											
Akechi et al (2004) <sup>22</sup>	0	3	2	209	61	Palliative, outpatients	SCID for DSM-III-R	NR	Mixed, palliative	34	Japan
Breitbart et al (2000) <sup>23</sup>	0	1	1	92	66.5	Palliative, inpatients	SCID for DSM-IV	NR	Mixed, palliative	60	USA
Chochinov et al (1994) <sup>24</sup>	0	2	2	130	71.5	Palliative, inpatients	SADS (RDC and Endicott criteria)	Palliative	Mixed	49	USA
Chochinov et al (1997) <sup>25</sup>	1	2	2	197	70.9	Palliative, inpatients	SADS (RDC criteria)	Palliative	Mixed	51	USA
Desai et al (1999) <sup>26</sup>	0	1	1	24	68	Mixed	DIS (DSM-III criteria)	First primary tumour, late stage	Breast	100	USA
Hopwood et al (1991) <sup>27</sup>	1	1	1	81	NR	Outpatients	CIS (DSM-III criteria)	Advanced breast cancer	Breast	100	UK
Jen et al (2006) <sup>28</sup>	0	2	3	114	NR	Mixed, inpatients	DSM-IV SCID	Advanced metastatic	Mixed	67	Germany
Kadan-Lottich et al (2005) <sup>29</sup>	0	4	3	251	60	Mixed, palliative	DSM-IV SCID	NR	Mixed, palliative	NR	USA
Kelly et al (2004) <sup>30</sup>	0	1	2	56	67.1	Mixed, palliative	DSM-IV SCID	Palliative stages	Mixed	41	Australia
Le Fevre et al (1999) <sup>31</sup>	1	1	3	79	68.3	Hospice, inpatients	Revised Clinical Interview for Schedule (CIS-R18) ICD10 (moderate to severe depression)	NR	Mixed	56	UK
Lichtenthal et al (2009) <sup>32</sup>	0	3	1	272	58.7	Mixed, advanced cancer and palliative	SCID (DSM-IV criteria)	NR	Mixed	44	USA
Lloyd-Williams et al (2001) <sup>33</sup>	1	2	2	100	57.3	Palliative	PSE ICD10	NR	Mixed	56	UK
Lloyd-Williams et al (2003) <sup>34</sup>	1	1	2	74	68	Palliative	Clinical interview	NR	Mixed	NR	UK
Lloyd-Williams et al (2007) <sup>35</sup>	1	3	2	246	68	Palliative	Clinical interview	NR	Mixed	NR	UK
Love et al (2004) <sup>36</sup>	1	3	1	227	52	Mixed, advanced cancer	DSM-IV	Advanced breast cancer	Breast	100	Australia
Maguire et al (1999) <sup>37</sup>	0	1	2	59	69	Mixed, oncological unit	Psychiatric Assessment Schedule for DSM	Advanced cancers	Mixed	46	UK
McCaffrey et al (2007) <sup>38</sup>	0	1	2	23	73.9	Hospital, advanced cancer	SCID (DSM-IV)	Stage III or IV	Head and neck	17	USA
Meyer et al (2003) <sup>39</sup>	0	1	2	45	40% of patients 70-79	Palliative, outpatients	SCID mild to severe depression (DSM)	NR	Mixed	58	UK

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	Sampling method*	Quality†	Bias risk‡	Number with cancer	Mean age (years)	Setting	Criteria for definition of depression	Cancer duration	Cancer type	Women (%)	Country
(Continued from previous page)											
Minagawa et al (1996) <sup>40</sup>	0	1	2	54	67.2	Palliative, inpatients	SCID (DSM-III-R)	Palliative	Mixed	41	Japan
Olden et al (2009) <sup>41</sup>	1	4	1	422	65.8±13.7	Hospital, inpatients	SCID (DSM-IV)	Terminally ill	Mixed	56	USA
Payne et al (2007) <sup>42</sup>	1	2	2	167	67	Palliative unit	SCID (DSM-IV)	NR	Mixed	47	Ireland
Spencer et al (2010) <sup>43</sup>	0	4	0	635	50.7	Multicentre cancer sites	SCID (DSM-IV)	Advanced with metastatic disease	Mixed, advanced	50	USA
Wilson et al (2004) <sup>44</sup>	0	1	3	69	64.5	Mixed, palliative	DSM-IV by PRIME-MD	NR	Mixed, palliative	64	Canada
Wilson et al (2007) <sup>45</sup>	0	3	3	381	67.2	Mixed, palliative	DSM-IV by PRIME-MD	NR	Mixed, palliative	NR	Canada
<b>Non-palliative-care settings</b>											
Akizuki et al (2005) <sup>46</sup>	1	3	3	295	51.5	Mixed, cancer	Clinical interview DSM-IV major depression alone	41% metastatic	Breast 28%, leukaemia 15%, lymphoma 10%	56	Japan
Alexander et al (1993) <sup>47</sup>	0	1	3	60	53.2	Mixed, inpatients	DSM-III-R criteria	3–7 days after hospital admission	Mixed cancer	57	India
Alexander et al (2010) <sup>48</sup>	1	3	0	200	58.1	Outpatients	SCID (DSM-IV)	Mean time since last treatment was 10.1 months (SD 5.7; range 3–23)	Breast	100	UK
Atesci et al (2004) <sup>49</sup>	0	2	1	117	53.7±14.2	Oncological inpatients	SCID (DSM-IV)	In first 12 months since diagnosis	Mixed	51	Turkey
Baile et al (1992) <sup>50</sup>	0	1	2	45	NR	Mixed, oncological	DSM-III criteria	Unknown	Head and neck	NR	USA
Berard et al (1998) <sup>51</sup>	0	2	3	100	50	Mixed cancer, radiotherapy outpatients	SCID (DSM-IV criteria)	Unknown	Mixed	87	South Africa
Bukberg et al (1984) <sup>52</sup>	0	1	2	62	51	Mixed, inpatients	DSM-III criteria interview	NR	Mixed	48	USA
Burgess et al (2005) <sup>53</sup>	0	3	1	202	48	Mixed	DSM-IV (SCID)	5 months after diagnosis	Breast	100	UK
Ciamarella and Poli (2001) <sup>54</sup>	0	2	2	100	64.15 (depressed), 63.05 (not depressed)	Mixed, outpatients	SCID (DSM-III-R) and Endicott criteria	67 patients had <1 year of cancer (31 depressed, 36 not depressed)	Mixed	50	Italy
Colon et al (1991) <sup>55</sup>	0	2	1	100	30	Haematological, pre-bone-marrow transplant	DSM-III criteria	NR	Acute leukaemia	35	USA
Costantini et al (1999) <sup>56</sup>	1	2	3	132	52.7	Mixed	SCID DSM-III major depression and adjustment disorder	NR	Breast	NR	Italy
Coyne et al (2004) <sup>57</sup>	0	2	1	113	56	Mixed	SCID (DSM-IV)	22% stage I, 28% stage IIa, 10% stage IIIa, 6% stage IIIb, 10% stage IV	Breast	100	USA
Derogatis et al (1983) <sup>58</sup>	0	3	2	215	50	Mixed	DSM-III criteria	NR	Breast (n=39), lung (n=43), lymphoma (n=24), other (n=109)	51	USA
Desai et al (1999) <sup>59</sup>	0	1	1	45	68	Mixed	DIS (DSM-III criteria)	First primary tumour	Breast	100	USA
Devlen et al (1987) <sup>60</sup>	0	1	2	90	44.4	Mixed, haematological	Shortened version of PSE*	Mean of 32 months after diagnosis (range 6–72, median 2.2)	Hodgkin's disease and non-Hodgkin lymphoma	48	UK

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	Sampling method*	Quality†	Bias risk‡	Number with cancer	Mean age (years)	Setting	Criteria for definition of depression	Cancer duration	Cancer type	Women (%)	Country
(Continued from previous page)											
Evans et al (1986) <sup>61</sup>	0	1	1	83	53	Mixed	DSM-III criteria	NR	Gynaecological (excluding ovarian)	100	USA
Fallowfield et al (1990) <sup>62</sup>	0	3	0	269	56	Breast	DSM-III (PSE)	Post-mastectomy (n=154), post-lumpectomy (n=115)	Breast	100	UK
Gandubert et al (2009) <sup>63</sup>	0	2	2	144	53	Mixed	MINI (DSM-IV criteria)	Mostly post-surgery in chemotherapy or radiotherapy	Breast	100	France
Ginsburg et al (1995) <sup>64</sup>	0	1	3	52	69% of patients 50-70 years	Oncological	DIS (DSM-III criteria)	45 days after diagnosis	Lung	25	Canada
Golden et al (1991) <sup>65</sup>	0	1	0	65	54	Gynecological	DSM-III criteria	Most patients (82%) had been recently diagnosed and were being assessed for cancer staging and initial cancer treatment; the remaining 18% were undergoing a recurrence assessment	Gynaecological	100	USA
Grandi et al (1987) <sup>66</sup>	0	1	0	18	53	Breast	DSM-III criteria	Stage II or III	Breast	100	Italy
Grassi et al (1993) <sup>67</sup>	0	2	3	157	52.3	Mixed, outpatients	DSM-III-R	NR	Mixed	NR	Italy
Grassi et al (2009) <sup>68</sup>	1	2	3	109	57.49	Mixed, outpatients	CIDI for ICD10 (any depression)	52% breast cancer	Mixed	76	Italy
Green et al (1998) <sup>69</sup>	0	2	0	160	53	Breast surgery unit	SCID (DSM IV)	Early-stage breast cancer	Breast	100	USA
Hall et al (1999) <sup>70</sup>	0	3	0	266	<75	Discharged from breast surgery unit	PSE depression (DSM-III)	Early-stage breast cancer	Breast	100	UK
Hardman et al (1989) <sup>71</sup>	0	2	3	126	46.1	Mixed, oncological; inpatients	ICD10 (clinical interview)	NR	Mixed	43	UK
Hosaka and Aoki (1996) <sup>72</sup>	0	1	2	50	Men 58.2, women 56.6	Mixed	DSM-IV criteria	Unknown (described as various stages except terminal stage)	Breast, gastric, prostatic, lung	50	Japan
Hosaka et al (1994) <sup>73</sup>	1	1	1	31	52.35±16.2	Haematological, inpatients	SCID (DSM-III-R)	NR	Haematological	26	Japan
Ibbotson et al (1994) <sup>74</sup>	1	2	2	161	NR	Mixed, outpatients	PAS (DSM-III criteria)	Cancer in remission	Mixed	100	UK
Iqbal (2004) <sup>75</sup>	0	3	1	365	NR	Hopsital	SCID (DSM IV)	Newly diagnosed	Mixed	49	Pakistan
Jenkins et al (1991) <sup>76</sup>	0	1	0	22	54.1 (SD 8.8) at time of diagnosis	Breast surgery unit	CIDI (DSM-III criteria)	Mean time elapsed between mastectomy and most recent local recurrence was 68.4 months. Mean time from recurrence to interview was 7.33 months	Breast	100	UK
Joffe et al (1986) <sup>77</sup>	0	1	1	21	55	Pancreatic and gastric	DSM-III (SADS)	Referred to hospital 2 years earlier	Pancreatic and gastric	29	USA
Kangas et al (2005) <sup>78</sup>	0	1	2	49	57.5	Oncological, outpatients	SCID (DSMIV)	1 year since diagnosis	Head and neck or lung	25	Australia
Kathol et al (1990) <sup>79</sup>	0	2	2	152	59	Mixed, minimal details	DSM-III-R	NR	Terminal at various stages	59	USA

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	Sampling method*	Quality†	Bias risk‡	Number with cancer	Mean age (years)	Setting	Criteria for definition of depression	Cancer duration	Cancer type	Women (%)	Country
(Continued from previous page)											
Katz et al (2004) <sup>30</sup>	1	1	2	60	60.5	Mixed	SADS (DSM-IV major and minor depression)	NR	Head and neck	NR	Canada
Kawase et al (2006) <sup>31</sup>	0	3	3	282	62.2	Mixed, radiotherapy	SCID (DSM-III-R) and Endicott criteria	NR	Mixed	NR	Japan
Kirsh et al (2004) <sup>32</sup>	1	1	1	95	45.76 (SD 11.72)	Oncological, outpatients	SCID (DSM-IV)	NR	Haematological (bone marrow transplant)	43	USA
Kugaya et al (1998) <sup>33</sup>	1	2	3	128	NR	Mixed, cancer patients	SCID DSM-III-R major depressive disorder	NR	Mixed	NR	Japan
Kugaya et al (2000) <sup>34</sup>	0	2	2	107	61.0 (SD 11.8)	Oncological inpatients	SCID (DSM-III-R)	61% advanced stage III or IV	Head and neck	24	Japan
Lansky et al (1985) <sup>35</sup>	0	3	1	505	48	Mixed	RDC (DSM-III criteria)	Median 3 years; range 2 weeks to 23 years	Mixed	100	USA
Lee et al (1992) <sup>36</sup>	0	2	1	183	NR	Breast surgery unit	DSM-III-R (PSE)	3 months after surgery	Breast	100	UK
Leopold et al (1998) <sup>37</sup>	0	1	3	53	NR	Mixed, radiotherapy	SCID DSM-III-R major depressive disorder	During radiotherapy	Mixed	48	USA
Levine et al (1978) <sup>38</sup>	0	2	2	100	43% of patients 60–69 years	Mixed	DSM-II criteria	NR	Mixed	51	USA
Love et al (2002) <sup>39</sup>	1	4	1	303	46	Mixed	Monash interview for liaison psychiatry DSM-IV major depression	Early stage	Breast	100	Australia
Matsuoka et al (2002) <sup>40</sup>	1	1	3	74	48 (SD 5.7)	Breast surgery unit (outpatients)	SCID (DSM-IV)	Mean 4.3 years after breast surgery	Breast	100	Japan
Maunsell et al (1992) <sup>41</sup>	0	3	1	205	NR	Mixed	DIS (DSM-III criteria)	Newly diagnosed	Breast	100	Canada
Mehner et al (2007) <sup>42</sup>	0	2	1	127	55	Mixed	SCID (DSM-IV)	After surgery	Breast	100	Germany
Morasso et al (1996) <sup>43</sup>	1	2	2	107	30 patients <50, 26 patients 50–59, 35 patients 60–69, and 16 patients >69	Mixed outpatients	ICD10 (data taken from second sample only)	Unknown	Head and neck (n=4), lung (n=16), breast (n=55), colorectal (6), others (n=26)	67	Italy
Morasso et al (2001) <sup>44</sup>	0	2	3	132	46 patients <50, 46 patients 51–60, and 37 patients >60	Oncological	DSM-III-R	During chemotherapy	Breast	100	Italy
Morton et al (1984) <sup>45</sup>	0	1	1	48	NR	Oncological	DSM-III criteria	Treated within the past 3 years	Oropharyngeal	0	UK
Murphy et al (1996) <sup>46</sup>	0	1	2	56	35.4	Haematological	CIDI (DSM-III-R criteria)	Post bone marrow transplant	Haematological (bone marrow transplant)	48	UK
Nakaya et al (2006) <sup>47</sup>	0	3	1	229	35% <59 and 30% >70	Oncological	SCID (DSM-III-R)	Resectable non-small-cell lung cancer; 51% stage 1A and 26% stage 1B; 3 months after surgery	Non-small-cell lung cancer	39	Japan
Okamura et al (2000) <sup>48</sup>	0	1	3	55	NR	Mixed, oncological	SCID (DSM-IV)	Recurrent breast cancer	Breast	100	Japan
Okamura et al (2005) <sup>49</sup>	0	1	3	50	53 (SD 10)	Oncological, outpatients	SCID (DSM-III-R)	First recurrence	Breast	100	Japan
Ozalp et al (2008) <sup>50</sup>	1	2	1	175	50.76	Mixed, breast cancer	SCID DSM-IV major depressive disorder	NR	Breast	100	Turkey

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	Sampling method*	Quality†	Bias risk‡	Number with cancer	Mean age (years)	Setting	Criteria for definition of depression	Cancer duration	Cancer type	Women (%)	Country
(Continued from previous page)											
Pasacreta et al (1997) <sup>101</sup>	0	1	1	79	54.9	Mixed, breast cancer	DIS (DSM-IV criteria)	79 women 3–7 months after breast cancer diagnosis	Breast	100	USA
Passik et al (2001) <sup>102</sup>	1	1	3	60	58	Mixed, outpatients	MINI (DSM-IV criteria)	Unknown	Mixed	53	USA
Payne et al (1999) <sup>103</sup>	1	1	1	31	NR	Outpatients	SCID (all versions)	NR	Breast	100	USA
Plumb and Holland (1981) <sup>104</sup>	0	1	2	80	50% <35, 50% >35 (range 15–70)	Mixed, haematological	CAPPS	Mixed	Acute leukaemia (n=40), Hodgkin's disease (n=11), multiple myeloma (n=7), other (n=22)	50	USA
Prieto et al (2002) <sup>8</sup>	0	3	1	220	38	Haematological, inpatients	DSM-IV	Median 13 months	Leukaemia (n=103), non-Hodgkin lymphoma (n=46), Hodgkin's disease (n=19), multiple myeloma (n=27), other (n=13)	59	Spain
Razavi et al (1990) <sup>105</sup>	1	3	2	210	55	Mixed, inpatients	DSM-III	4% at diagnostic phase, 24% at initial treatment phase, 59% recurrence phase, 13% pre-terminal/terminal	33% breast, 8% respiratory, 13% digestive, 19% genitourinary, 27% other	67	USA
Reuter and Harter (2001) <sup>106</sup>	1	2	4	184	NR	Mixed	CIDI for any depression	NR	Mixed	NR	Germany
Silberfarb et al (1980) <sup>107</sup>	0	2	1	146	NR (30–80)	Mixed	Psychiatric status schedule	Mixed	Breast	100	USA
Singer et al (2008) <sup>108</sup>	1	4	1	308	41% (60–69)	Ambulatory outpatients	SCID for DSM-IV (any Depression)	NR	Ambulatory laryngeal	9	Germany
Sneeuw et al (1994) <sup>109</sup>	1	4	1	556	NR	Mixed	DIS (DSM-III criteria)	Stage I and II	Breast	100	Netherlands
Spiegel et al (1984) <sup>110</sup>	0	1	2	96	53	Mixed	SCID (DSM-III criteria)	68% has metastatic disease	Breast (n=35), lung (n=10), colon (n=7), blood or lymphatic (n=13), other (n=31)	75	USA
Stark et al (2002) <sup>111</sup>	1	2	2	178	54.9	Oncological	SCAN or PSE for ICD10	39% with metastatic disease	Mixed	40	UK
Uchitomi et al (2000) <sup>112</sup>	0	3	1	223	62.6 (SD 10.8)	Thoracic surgery, outpatients	SCID (DSM-III-R)	71% stage I	Non-small-cell lung cancer	39	Japan
Walker et al (2007) <sup>113</sup>	1	3	3	361	61.7	Mixed	SCID DSMIV major depression	Mixed	Mixed, but 64% had breast cancer	77	UK
Wellisch et al (2002) <sup>114</sup>	0	1	2	89	43.2 (SD NR)	Oncological, outpatients	SCID (DSM-IV)	Mixed	Brain	45	USA

SCID=Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders. SADS=Schedule for Affective Disorders and Schizophrenia-Lifetime. RDC=Research Diagnostic Criteria. DSM-III-R=diagnostic and statistical manual of mental disorder, revised third edition. NR=not reported. DSM-IV=diagnostic and statistical manual of mental disorder, fourth edition. DIS=diagnostic interview schedule. CIS=Clinical Interview Schedule. DSM-III=diagnostic and statistical manual of mental disorder, third edition. CIS-R18= Revised Clinical Interview for Schedule 18. ICD10=international classification of disease 10. PSE=Present State Examination. PAS=Psychiatric Assessment Schedule. PRIME-MD=Primary Care Evaluation of Mental Health Disorders. MINI=Mini-International Neuropsychiatric Interview. CAPPS=Current and Past Psychopathology Scales. CIDI=Composite International Diagnostic Interview. SCAN=Schedules for Clinical Assessment in Neuropsychiatry. \*1=convenience sample and a score of 0=consecutive or random sample. †1=low quality, 2=low-to-medium quality, 3=medium-to-high quality, and 4=high quality. ‡0=no appreciable bias risk, 1=low bias risk, 2=low-to-medium bias risk, 3=medium-to-high bias risk, and 4=high bias risk.

**Table 1: Overview of interview-based prevalence studies of mood in patients with cancer**

**Results**

We identified 433 relevant articles; 369 included patients with cancer who were assessed with an interview-based diagnostic method (figure 1). Ten potentially valid studies were excluded because they contained duplicate data

presented elsewhere (webappendix p 3). Several others were excluded because of issues with the criterion standard (webappendix p 3); most studies that were excluded provided insufficient data for analysis. 94 studies were eligible for quantitative review: 24 in

palliative settings<sup>22–45</sup> and 70 studies in non-palliative-care settings (table 1).<sup>8,22,46–114</sup> Data extraction is shown in figure 1 in accordance with Quality of Reporting of Meta-analyses guidelines.<sup>115</sup>

We identified 24 studies of mood disorders in palliative-care settings that were done in seven countries, with 4007 individuals (mean 166·7, SD 147·6). Investigators of five studies recruited patients with advanced breast cancer from oncological or surgical settings, but the remainder were from palliative-care settings. Prevalence of depression ranged from 5·1% to 30·1% in individual studies. Meta-analytical pooled prevalence of syndromal (clinical) depression was 16·5% (95% CI 13·1–20·3) with moderate heterogeneity (table 2 and figure 2). Infrequent reports of low prevalence in small studies suggests possible publication bias (Begg-Mazumdar  $p=0\cdot04$ , webappendix p 4). After exclusion of nine studies that used convenience sampling to measure prevalence of depression, our best estimate for prevalence of major depressive disorder was 14·1% (10·3–18·4).

A subanalysis of studies of advanced cancer that used a DSM definition of major depression showed a prevalence of 14·3% (95% CI 11·1–17·9), with moderate heterogeneity (table 2). Although the sample size was small, prevalence of minor depression was 9·6% (3·6–18·1; table 2). Prevalence of adjustment disorder was 15·4% (10·1–21·6) and anxiety disorders 9·8% (6·8–13·2; table 2). There were also seven studies that reported prevalence of depression and adjustment disorder combined, with a prevalence of 24·7 (20·8–28·8) with low heterogeneity (table 2). Finally, prevalence of any mood disorder was 29·0% (10·1–52·9; table 2).

We noted no association between age or sex and prevalence of major or minor depression or anxiety in palliative-care settings, but there was a small but significant association between adjustment disorder and women (adjusted  $r^2$  0·06;  $p=0\cdot02$ ). We identified an

association between low prevalence of depression and recent publication year (adjusted  $r^2$  0·09;  $p=0\cdot01$ ) and studies of high quality (adjusted  $r^2$  0·05;  $p=0\cdot04$ ).

Only studies from the USA and the UK could be analysed for correlation between country and mood disorder because of insufficient samples. Prevalence of depression in palliative-care settings in the USA was 14·1% (95% CI 9·4–19·5;  $n=8$ ), whereas the rate in the UK was 21·1% (15·1–28·0;  $n=7$ ). Prevalence in outpatients was 16·2% (5·3–31·6;  $n=3$ ) and in inpatients 19·8% (15·4–24·5;  $n=7$ ). We had insufficient data to analyse prevalence of mood disorders in palliative-care settings and its association with individual cancer types and cancer duration.

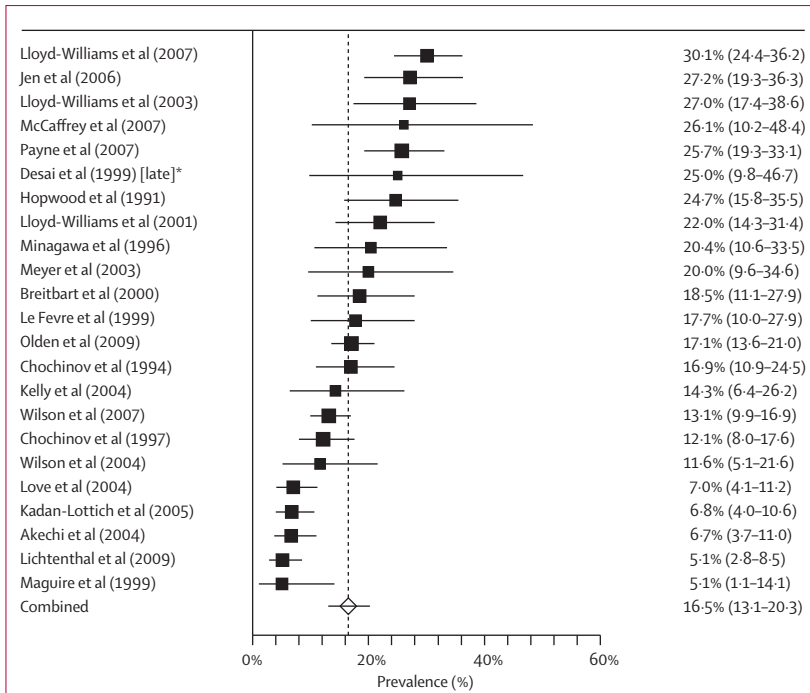
We identified 70 studies of mood disorder in oncological and haematological settings with 10071 individuals (mean 143·9, SD 107·7) across 14 countries. Patients were recruited from outpatient settings in 16 studies and from inpatient settings in eight, breast surgery units in nine studies, haematological settings in six studies; the remainder were from mixed oncological settings. Patients with breast cancer alone were recruited in 24 studies, head and neck cancer in three studies, and lung cancer in three studies, but no other cancer group was individually represented. Heterogeneity was moderate to high in all but one analysis (table 2). We had insufficient data to analyse prevalence of mood disorder in oncological and haematological settings associated with individual cancer types and cancer duration, although there were data from four studies ( $n=497$ ) with patients who were undergoing or had completed radiotherapy.

From 66 studies of syndromal depression the meta-analytical pooled prevalence of syndromal depression was 16·3% (95% CI 13·4–19·5; figure 3). There was strong evidence of publication bias—namely, infrequent reports of small studies showing low prevalence (Begg-Mazumdar  $p<0\cdot0001$ ; webappendix p 5).

	Palliative-care settings			Oncological and haematological settings		
	Number of studies	Prevalence (95% CI)	Heterogeneity $I^2$ (95% CI)	Number of studies	Prevalence (95% CI)	Heterogeneity $I^2$ (95% CI)
<b>Unitary diagnoses</b>						
Depression (DSM major depression or ICD major depressive episode)	23	16·5% (13·1–20·3)	86·8% (81·7–89·9)	66	16·3% (13·4–19·5)	93·5% (92·6–94·2)
Depression (DSM major depression only)	18	14·3% (11·1–17·9)	83·9% (75·7–88·4)	52	14·9% (12·2–17·7)	89·8% (87·8–91·4)
Depression (DSM minor depression only)	6	9·6% (3·6–18·1)	92·8% (87·6–95·2)	4	19·2% (9·1–31·9)	89·4% (72·6–94·1)
Adjustment disorder	5	15·4% (10·1–21·6)	70·6% (0–86·4)	23	19·4% (14·5–24·8)	92·3% (90·2–93·8)
Anxiety disorders	6	9·8% (6·8–13·2)	75·3% (25·2–87·3)	16	10·3% (5·1–17·0)	96·4% (95·5–97)
Dysthymia	2	Insufficient sample	Insufficient sample	11	2·7% (1·7–4·0)	51·1% (0–73·8)
<b>Combination diagnoses*</b>						
Any depression (Major or minor or dysthymia)	7	24·6% (17·5–32·4)	89·2% (80·1–93·1)	12	20·7% (12·9–29·8)	95·5% (94·1–96·4)
Depression (DSM or ICD) or adjustment disorder	5	24·7% (20·8–28·8)	20·4% (0–70·9)	22	31·6% (25·0–38·7)	93·3% (91·5–94·5)
Depression (DSM or ICD) or adjustment disorder or anxiety	4	29·0% (10·1–52·9)	97·4% (96·2–98·2)	17	38·2% (28·4–48·6)	97·4% (96·8–97·8)

Heterogeneity interpretation  $I^2$  greater than 80%=moderate,  $I^2$  greater than 90%=high. DSM=diagnostic and statistical manual of mental health. ICD=international classification of diseases. \*Primary studies where combination diagnoses were measured.

**Table 2: Summary of depression prevalence and heterogeneity findings**



**Figure 2: Prevalence of depression in palliative-care advanced-cancer settings**  
 Pooled prevalence of syndromal depression in palliative-care and advanced-cancer settings by random effects meta-analysis. \*Sample of patients with late stage of cancer.

Prevalence of depression ranged from 1.0% to 77.5% in individual studies. After exclusion of 20 studies that used convenience sampling, prevalence of depression was corrected to 18.5% (14.3–23.2).

52 studies used the DSM criterion of major depression, from which prevalence of major depressive disorder was 14.9% (95% CI 12.2–17.7) and minor depression 19.2% (9.1–31.9). Prevalence for adjustment disorder alone was 19.4% (14.5–24.8), anxiety disorders 10.3% (5.1–17.0), and 2.7% (1.7–4.0) for dysthymia. Prevalence of a combination of any type of depression (major or minor or dysthymia) was 20.7% (12.9–29.8), depression or adjustment disorder 31.6% (25.0–38.7), and any mood disorder, including anxiety, 38.2% (28.4–48.6).

We noted no association between mean age or sex and prevalence of depression or anxiety. Findings from meta-regression showed no significant difference in prevalence of depression in women at the study level, and a non-significant association between adjustment disorder and female sex (adjusted  $r^2$  0.06;  $p=0.15$ ). In studies published up to 1990, the reported prevalence of depression was 23.3% (95% CI 13.8–34.5), in those published from 1991 to 2000 it was 15.5% (11.0–20.7), and in those published since 2001 it was 13.4% (9.1–18.4; adjusted  $r^2$  0.136  $p=0.003$ ). We identified a small but significant association between high study quality and low prevalence (adjusted  $r^2$  0.05;  $p=0.003$ ). No significant difference was reported in studies of breast cancer alone (14.1%; 95% CI 10.0–18.7;  $n=19$ ). In studies of

radiotherapy, prevalence of major depression was 15.1% (10.1–21.0). In nine studies rated as medium-to-high quality and with a low bias risk, the prevalence of major depressive disorder was 8.4% (4.8–12.9).

In oncological and haematological settings, prevalence of depression was 21.6% (95% CI 14.4–29.7;  $n=23$ ) in the USA and 17.4% (7.8–29.8;  $n=13$ ) in the UK. On the basis of the DSM criteria, prevalence of depression was 18.3% (12.5–24.8) in the USA versus 11.6% (7.4–16.8) in the UK. Prevalence in outpatients was 15.8% (10.7–21.7) and in inpatients 12.3% (6.6–19.4).

### Discussion

Although several informative systematic reviews have been published, no previous studies have quantitatively analysed such a robust dataset of mood disorder in cancer settings.<sup>15–17,20,116</sup> Massie and colleagues<sup>15</sup> estimated that the prevalence of depression in patients with cancer was 0–38%, and Hotopf and colleagues<sup>17</sup> estimated 5–26%. Findings from two small meta-analyses of methods to diagnose mood disorders showed a prevalence of 13.2%<sup>16</sup> and 12.7%<sup>116</sup> in studies with convenience sampling, which is lower than that typically noted when using severity scales are used. Our study incorporates and extensively updates these results, and clarifies the difference between major and minor depression, dysthymia, adjustment disorder, and anxiety disorder. Subtypes of anxiety, which consist of roughly equal rates of post-traumatic stress disorder, panic disorder, and generalised anxiety disorder, could not be analysed because of insufficient data.

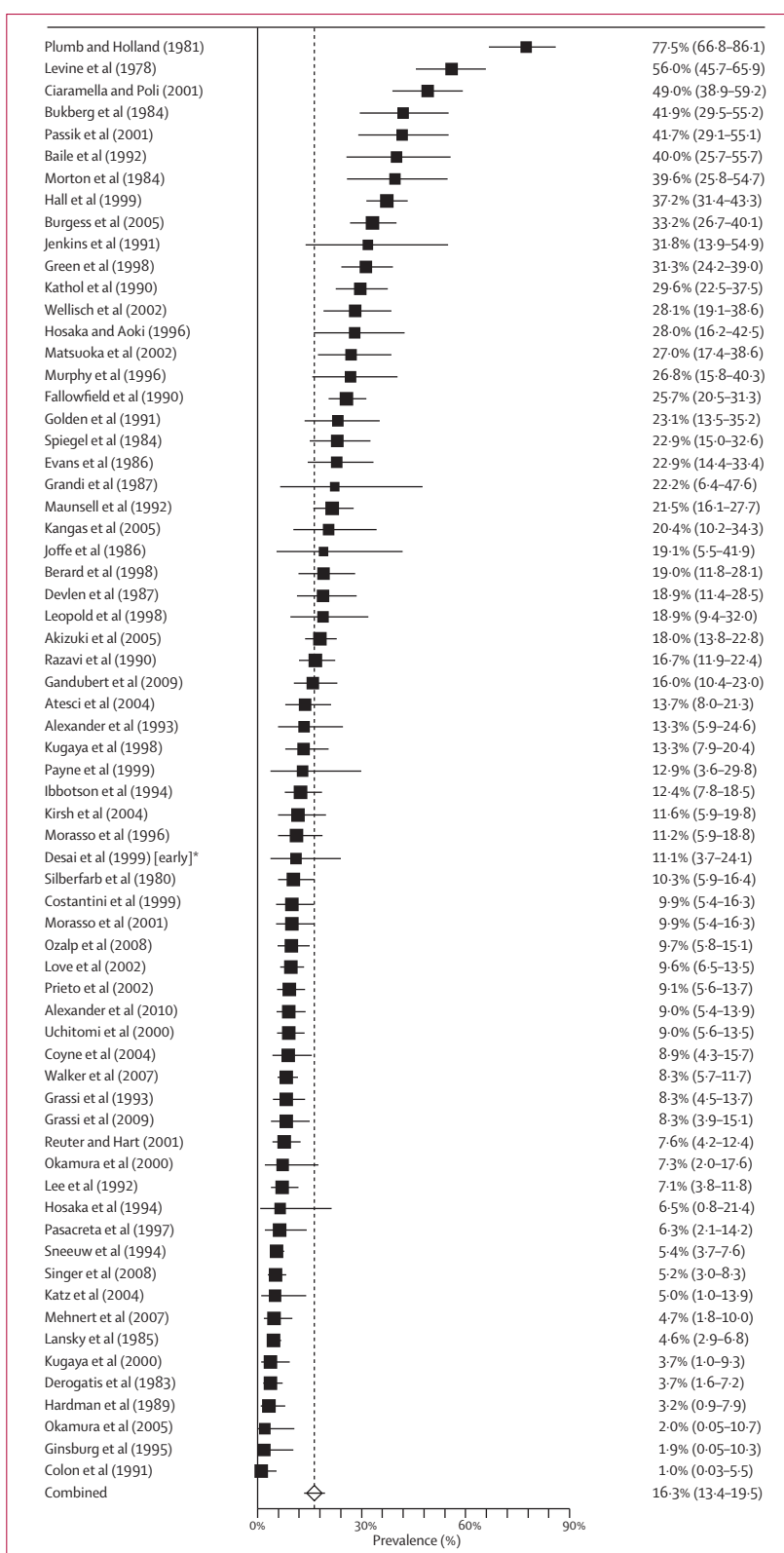
After exclusion of 25 studies for methodological reasons, we extracted data from 94 valid independent studies of 14078 patients interviewed for mood disorders, with use of a criterion method and sampled without selection bias. Although interview methods are the gold standard, they do not produce identical results.<sup>117</sup> Across all studies we found modest rates of syndromal depression in patients with cancer. This finding reinforces the suggestion that, when judged cross-sectionally, depression is not an invariable complication of cancer, and is common only when all subtypes and related mood disorders are combined. No clear pattern emerges from the rare studies investigating the rate of depression at several points during cancer treatments.<sup>8,53,86</sup> Furthermore, the prevalence of major depression in hospital settings reported in our study is nearly identical to the long-term 12-month rate of major depression in patients diagnosed with cancer living in the community.<sup>118</sup>

Depression is not an invariable consequence of advanced cancer in palliative settings. Indeed we noted no difference between palliative and non-palliative settings for depression or anxiety (table 1). Even after restriction of depression analysis to the same DSM standard we recorded no difference, suggesting that differences in cancer setting and perhaps cancer stage

might have been overstated previously. The only notable difference according to setting (stage) was detected in patients with minor depression; however, this analysis was underpowered. One interview study<sup>119</sup> and several large-scale symptom studies have shown no difference or modest differences in prevalence of depression or distress according to disease stage.<sup>120</sup>

There was also no appreciable difference in prevalence of adjustment disorders or anxiety disorders in palliative versus non-palliative settings, indeed combination mood disorders appeared slightly more common in non-palliative patients. A 30–40% prevalence of any mood complication measured by interview is close to that measured by self-report.<sup>16,116</sup> However, one should note that adjustment disorder is poorly studied and imprecisely defined relative to other mood disorders, especially in medically ill patients.<sup>121</sup> Adjustment disorder can occur with and without features of depression. Scarcity of data for adjustment disorder probably relates to its absence from the Clinical Interview Schedule-Revised (CIS-R)<sup>122</sup> or the Composite International Diagnostic Interview (CIDI).<sup>123</sup> Less common forms of mood disorder were difficult to study. For example, dysthymia was examined in only nine studies (two originated from palliative-care settings). We suggest that more work should examine the relation between cancer and dysthymic disorder.

The association between year of publication and prevalence might suggest that rates of depression have been falling with time; however, this theory is not entirely consistent with population-based research. An alternative explanation is that recent studies tend to be of higher quality than older studies and report more realistic rates. Findings of publication bias and trends according to quality rating could lend further support to this hypothesis. Other predictors such as age or cancer type<sup>18</sup> were not supported by findings from our study. The question of whether or not existing diagnostic criteria are ideal in cancer settings remains unanswered. Modified diagnostic criteria have been proposed for use in palliative-care and non-palliative-care settings,<sup>124,125</sup> but as yet there is no consensus about the optimum diagnostic approach, and little attention is given to ICD criteria. Endicott<sup>124</sup> proposed that four groups of somatic symptoms should be substituted (poor appetite or weight gain could be replaced by fearfulness or depressed appearance; insomnia or hypersomnia could be substituted for social withdrawal or decreased talkativeness; loss of energy or fatigue could be replaced by brooding, self pity, pessimism; and diminished concentration or slowed thinking could be substituted for loss of interest). Only three studies provided direct data for this comparison of diagnoses with versus without the Endicott symptoms, and results are inconsistent. Kathol and colleagues<sup>79</sup> reported that 30% of patients with cancer were depressed according to DSM-III-R, 38% according to DSM-III, 25% according to research diagnostic criteria, and 36% according to modified



**Figure 3: Prevalence of depression in oncological and haematological settings**

Pooled prevalence of syndromal depression in oncological and haematological settings by random effects meta-analysis.

\*Sample of patients with late stage of cancer.

Endicott criteria. Chochinov and colleagues<sup>24</sup> reported that differences between research diagnostic criteria and Endicott criteria had an effect only in mild cases of depression. Ciaramella and Poli<sup>54</sup> showed that the prevalence of depression was 49% with DSM-III-R criteria but only 29% with Endicott criteria. Indirect evidence for other physical disorders suggests that no substitution of somatic symptoms is needed, and that under-recognition would be helped by a simplification of criteria.<sup>126</sup> Consideration of the assessment of shared features of depression, adjustment disorder, and dysthymia (namely distress and impaired function) would be useful.

Combination of all types of depression and adjustment disorder showed a prevalence of emotional disorders of up to 38.2%. This finding is similar to that reported in a meta-analysis of ten studies that used a criterion standard, in which the prevalence of distress was 47.8%.<sup>116</sup> These results lend support to the notion that screening for distress is conceptually similar to screening for all emotional disorders but distinct from screening for depression alone. Sufficient data for specific cancers were available only for an assessment of mood disorders in patients with breast cancer in postoperative non-palliative-care settings, in which prevalence of clinical depression was 14.1%. In view of the scarcity of large comparable data, it is possible that the prevalence of depression could vary by cancer type. Such variation has been shown in relation to distress with self-report methods,<sup>120,127</sup> but needs to be replicated in interview-based studies.

Our findings indicate that about a sixth of patients with cancer have depression alone and around a quarter have any type of depression. Although these rates are modest, this group of patients should not be overlooked. Improvements in survival and high prevalence of most cancers actually increase rates of depression, amounting to what we estimate to be 340 000 people in the UK and 2 million in the USA with major depression and cancer at any time (calculated as prevalence of cancer × prevalence of depression). Most people with depression acknowledge that they have unmet needs (eg, social, interpersonal, or therapeutic)<sup>128</sup> and at least half with cancer who have moderate-to-severe depression are willing to accept professional help or referral.<sup>129</sup> A study has shown that 40% of patients with depression have suicidal thoughts on direct questioning;<sup>130</sup> however, most people with depression are either not detected or not treated.<sup>11</sup>

An examination of how the prevalence of major depression in patients with cancer compares with that in other settings is noteworthy. Findings from a meta-analysis<sup>131</sup> showed that the rate of interview-defined depression in primary care was 17% in the most robust studies; one should note that most cases of depression in primary care are also comorbid with miscellaneous physical illnesses. To assess whether depression is more common in cancer settings than in non-cancer settings,

population surveys are informative. Honda and colleagues<sup>3</sup> undertook a large study in the USA of 45 patients with cancer and 5826 people without cancer, and reported an increased rate of major depression in patients with cancer, with a WHO Composite International Diagnostic Interview (CIDI) score of 3.6 (adjusted odds ratio 95% CI 1.4–8.8) within 12 months of the diagnosis. In the Health and Retirement Study,<sup>6</sup> also done in the USA, risk of significant depressive symptoms, as measured by the Center for Epidemiologic Studies Depression Scale, was more than three times higher in 583 patients with cancer within 2 years of diagnosis than in 7804 people without cancer.<sup>6</sup> In the Canadian Community Health Survey of 36 984 people, interviewed with the CIDI, Rasic and colleagues<sup>118</sup> reported that a diagnosis of cancer was significantly associated with a higher 12-month prevalence of major depression (15.5% vs 5.4%;  $p=0.01$ ) in patients aged 15–54 years than the rate of depression in those without cancer. Dalton and colleagues<sup>4</sup> examined linked data from 608 591 adults diagnosed with cancer in the Danish Cancer Registry and identified a relative risk of depression (in the first year after a cancer diagnosis) of 1.16–3.08. The risk remained increased, albeit modestly so, throughout 10 years of follow-up.

We note several limitations to this analysis. Studies that were reviewed were of variable quality, and although only one was rated with a high risk of bias,<sup>106</sup> 29 received a low methodological quality score. We acknowledge that definitions of prevalence could vary slightly across studies, typically relying on cross-sectional assessment at different cancer stages and different times during the cancer trajectory, and occasionally used convenience sampling. In view of the paucity of long-term data, our results might only be representative during the first 5 years after diagnosis. Furthermore, interview methods commonly underestimate prevalence of psychiatric disorders compared with self-report scales. From the nine most robust studies, prevalence of major depressive disorder in non-palliative-care settings was 8.4% (95% CI 4.8–12.9), which suggests that prevalence of depression in patients with cancer could be overestimated in many small studies. Indeed the main factors that affected prevalence of depression were publication year and study quality, and this finding was mirrored by publication bias favouring large effects in smaller studies (Egger bias  $p=0.04$  in palliative settings and  $p<0.0001$  in non-palliative settings).

We were unable to extract many correlates of depression or anxiety because of limitations in the underlying dataset. Small, non-significant effects were identified for care setting, country, and patient age. Individual studies have noted other predictors of depression or adjustment disorder that include low performance status, high burden of symptoms such as pain and fatigue, previous depression, and low levels of support.<sup>22,52,85,112,119</sup> A further limitation is the scarcity of

data for non-DSM defined depression. For example, only six studies used explicit ICD criteria. Another limitation is the paucity of longitudinal data, available in only three studies, and the scarcity of studies with a defined period of prevalence.<sup>8,53,86</sup> One excluded study documented rates of major depression in 200 patients with cancer in hospital at 1 month (1.5%), 12 months (4.5%), and lifetime rates (9.0%).<sup>119</sup> Ideally we would have liked to examine whether stage of treatment or disease duration affected prevalence of depression. Sufficient data were available only for subgroup assessment of patients in non-palliative-care settings, who were receiving radiotherapy, and the rate of major depression suggested no significant differences by treatment stage (or treatment intent).

Our results suggest that in the first 5 years after diagnosis about a sixth of people with cancer have syndromal depression, rising to about a third with either depression or adjustment disorder. Standardised criteria and semistructured interviews cannot easily be adopted into routine cancer care and should probably be simplified or broadened to focus on core components such as distress, activities of daily living, quality of life, unmet needs, and desire for help. Although a focus on depression alone is not recommended, depression remains an important and overlooked complication of cancer, which, in view of the exponential rise in survivors, calls for a more systematic approach in clinical assessment and follow-up.

#### Contributors

AJM designed the study and analysed the data. AJM and NM supervised the data extraction. AJM, LG, CJ, and NM wrote and revised subsequent drafts of the report. AJM, MC, HB, MH, and NM contributed to the search of published works and data extraction.

#### Conflicts of interest

The authors declared no conflicts of interest.

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