

Prevalence, associations, and adequacy of treatment of major depression in patients with cancer: a cross-sectional analysis of routinely collected clinical data

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Summary

Background Major depression is an important complication of cancer. However, reliable data are lacking for the prevalence of depression in patients with cancer in different primary sites, the association of depression with demographic and clinical variables within cancer groupings, and the proportion of depressed patients with cancer receiving potentially effective treatment for depression. We investigated these questions with data from a large representative clinical sample.

Methods We analysed data from patients with breast, lung, colorectal, genitourinary, or gynaecological cancer who had participated in routine screening for depression in cancer clinics in Scotland, UK between May 12, 2008, and Aug 24, 2011. Depression screening was done in two stages (first, Hospital Anxiety and Depression Scale; then, major depression section of the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition). Data for depression status were linked with demographic and clinical data obtained from the Scottish National Cancer Registry.

Findings We analysed data for 21151 patients. The prevalence of major depression was highest in patients with lung cancer (13.1%, 95% CI 11.9–14.2%), followed by gynaecological cancer (10.9%, 9.8–12.1), breast cancer (9.3%, 8.7–10.0), colorectal cancer (7.0%, 6.1–8.0), and genitourinary cancer (5.6%, 4.5–6.7). Within these cancer groupings, a diagnosis of major depression was more likely in patients who were younger, had worse social deprivation scores, and, for lung cancer and colorectal cancer, female patients. 1130 (73%) of 1538 patients with depression and complete patient-reported treatment data were not receiving potentially effective treatment.

Interpretation Major depression is common in patients attending cancer clinics and most goes untreated. A pressing need exists to improve the management of major depression for patients attending specialist cancer services.

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Introduction

Major depression is a leading cause of disability worldwide and when comorbid with a chronic disease it is associated with reduced quality of life and increased health-care costs.^{1–3} Cancer is becoming a chronic disease for a rapidly increasing number of people; in the UK alone more than 3 million people are expected to have a diagnosis of cancer by 2030.⁴ Patients with cancer and comorbid depression have worse anxiety, pain, fatigue, and functioning than do other patients with cancer.^{5–7} They are also more likely to have suicidal thoughts, and to have more difficulties with adherence to cancer treatments.^{8,9}

Consequently, better methods of identification and treatment of depression in patients attending cancer services are needed: the English Department of Health, the UK National Institute for Health and Care Excellence, and the US Institute of Medicine have all called for effective management of depression that is integrated into patients' cancer care.^{10–13} The American College of Surgeons' Commission on Cancer¹⁴ requires that, from 2015, cancer centres in the USA must screen patients for psychosocial distress (which includes depression).

To improve care, we need to know how many patients attending cancer services have major depression, which

patients are most likely to be depressed, and what proportion of patients receive adequate treatment for their depression. However, we lack robust data to answer all of these basic questions. Two recent meta-analyses have reported pooled prevalence (for patients with all types of cancer) of interview-diagnosed depression of 16% and 13%.^{15,16} However, these findings are substantially limited by (1) the questionable assumption that the prevalence of major depression is similar across different patient subgroups and consequently that a pooled estimate is clinically meaningful, (2) the use of various diagnostic criteria, interview types, and interviewer expertise for defining and identifying depression, and (3) the typically small, non-representative samples and generally poor methodological quality of the primary studies. These limitations are shown by the wide range (1–77%)¹⁵ of prevalence reported in the individual studies. A systematic review¹⁷ that addressed study quality found that only 15 publications met basic methodological standards; even these higher quality studies did not provide reliable data for the prevalence of depression in patients with different primary cancer sites or useful estimates of the proportion of patients with cancer and comorbid depression receiving potentially effective treatment.

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See Online for podcast interview with Michael Sharpe and Jane Walker

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We assessed in a large representative sample (1) the prevalence of major depression in patients with common cancers (breast, lung, colorectal, genitourinary, and gynaecological), (2) the association of major depression with demographic and clinical variables within each of these cancer groupings, and (3) the proportion of patients with major depression who were receiving potentially effective treatment.

Methods

Study design

We did a cross-sectional analysis of routine clinical data provided by a large-scale outpatient depression screening service linked with demographic and clinical data. The data relate to patients who attended outpatient clinics of the Edinburgh, Glasgow, and Dundee National Health Service cancer centres in Scotland, UK. Each centre provides a full range of diagnostic and treatment services in large urban teaching hospitals and has outreach clinics in the smaller hospitals of surrounding towns. The centres together serve a geographically defined area of roughly 4 million people and provide specialist care for the vast majority of patients in this region diagnosed with cancer.

We included a patient's data if they had attended an outpatient oncology consultation (in a central or outreach cancer clinic) between May 12, 2008 and Aug 24, 2011; if they had participated in the routine screening service for depression that operated in the three centres; if we could obtain matched demographic and clinical data from the Scottish National Cancer Registry; if they had given consent for their relevant clinical data to be used for research; and if they had a primary breast, lung, colorectal, genitourinary, or gynaecological cancer. We chose these cancer groupings because they are the most common, they often form the basis for multidisciplinary cancer care (therefore the

prevalence of depression in each group is clinically useful), and the number of patients within each grouping was sufficient to estimate prevalence with acceptable accuracy.

The study was approved by the South East Scotland Research Ethics Committee, the NHS Scotland Caldicott Guardian Forum, and the NHS Scotland Privacy Advisory Committee.

Procedures

The screening service for depression was offered to everyone who attended the clinics and used a conventional two-stage procedure.¹⁸ In the first stage, patients rated their symptoms over the preceding week on the Hospital Anxiety and Depression Scale (HADS), which has 14 items, each of which is scored from zero to three.¹⁹ This was done with the help of a screening assistant, using touchscreen computers or paper questionnaires, while the patient was waiting in the cancer clinic to see their oncologist (if the patient did not complete the HADS, the reason was recorded). The screening database automatically calculated each patient's total HADS score and highlighted those patients who needed a second stage assessment.

In the second stage, patients with a high HADS score (total score ≥ 15 ; a cut-off which has been reported to offer good sensitivity and specificity for major depression in patients with cancer with a misclassification rate of only 0.01)²⁰ were telephoned at home (usually within several days of clinic attendance) and given a brief semi-structured clinical interview (reasons for non-completion of this interview were recorded). The interview consisted of the depression section of the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (SCID)²¹ to establish whether the patient met criteria for major depression.²² Telephone SCID interviews have good agreement with face-to-face interviews.²³ Patients diagnosed with major depression were asked additional questions about the treatments that they were receiving for depression. The patient's primary care physician and oncologist were then told that their patient had depression.

The timing of screening for depression varied by cancer clinic (some oncologists preferred that screening was only offered to patients attending return appointments). The screening service was delivered by a team of screening assistants (psychology graduates and general nurses), trained and supervised by consultation-liaison psychiatrists. All clinical and administrative data, including telephone interviews (which were digitally recorded with patients' permission), were stored on a secure database.

A diagnosis of major depression was made using the standard inclusive approach (all relevant symptoms counted towards the diagnosis of depression without attempting to establish whether they should be attributed to depression or to cancer); this is the most reliable method and does not significantly overestimate

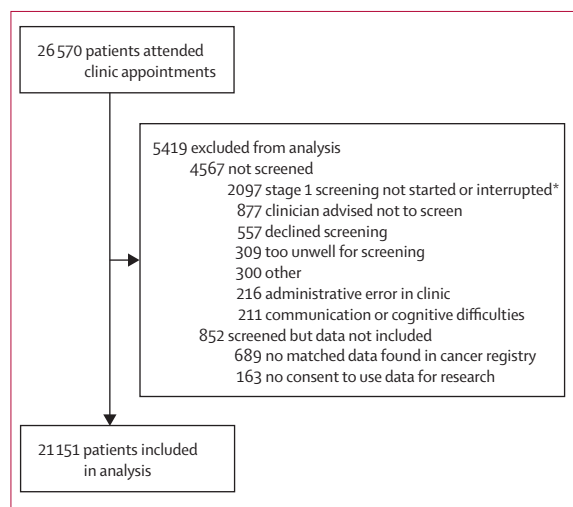


Figure 1: Study profile

*The patient was taken into their oncology appointment before they were able to complete the Hospital Anxiety and Depression Scale.

Patients (N=21 151)	
Sex	
Women	15 112 (71%)
Men	6039 (29%)
Age (years)	
Mean (SD)	64.4 (11.9)
Range	19–100
Age groups (years)	
<50	2521 (12%)
50–59	4104 (19%)
60–69	6820 (32%)
≥70	7706 (36%)
Area of residence	
Urban	16 689 (79%)
Small town	2001 (9%)
Rural	2461 (12%)
SIMD quintile score*	
1	4572 (22%)
2	4259 (20%)
3	3781 (18%)
4	3731 (18%)
5	4808 (23%)
Primary cancer	
Breast	8461 (40%)
Lung	4316 (20%)
Colorectal	3355 (16%)
Gynaecological	3010 (14%)
Genitourinary	2009 (9%)
Clinic appointment type	
First appointment	3117 (15%)
Return appointment	17760 (84%)
Missing data	274 (1%)
Time since cancer diagnosis (years)	
Median (IQR)	1.0 (0.3–3.2)
Recently started initial cancer treatment†	
No	13 325 (63%)
Yes	7462 (35%)
Missing data	364 (2%)
First treatment objective	
Curative	13 127 (62%)
Palliative	5413 (26%)
Missing data	2611 (12%)

Data are number (%) unless otherwise stated. SIMD=Scottish Index of Multiple Deprivation. *1=most deprived, 5=least deprived. †Any of chemotherapy, radiotherapy, or surgery started in the preceding 6 months.

Table 1: Characteristics of patients

depression in the medically ill.²⁴ To minimise the misdiagnosis of major depression in patients who might have been more properly diagnosed with an adjustment disorder, major depression was only diagnosed if the patient described relevant symptoms of at least 4 weeks' duration. If they reported symptoms between 2 weeks (the usual minimum duration required for a diagnosis

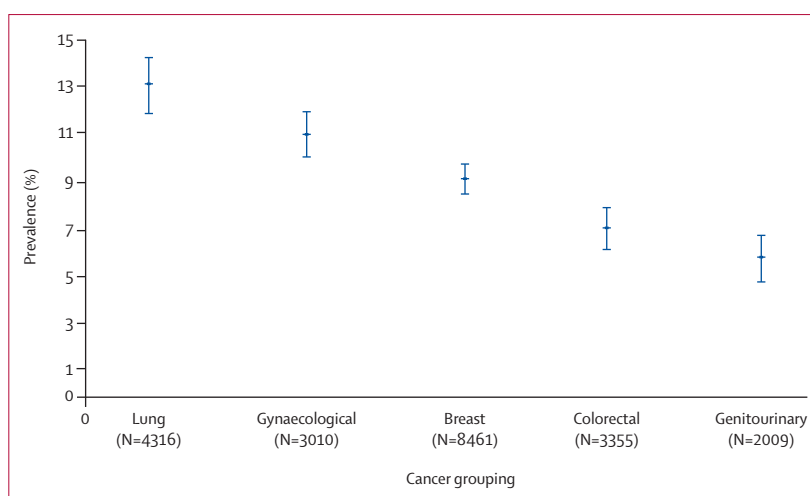


Figure 2: Prevalence of major depression in patients with cancer
Error bars show 95% CIs.

of major depression) and 4 weeks, the patient was re-interviewed 2 weeks later. The screening service used the following procedures to ensure the validity of the diagnosis of major depression: (1) screening assistants were trained for 4 weeks by consultation-liaison psychiatrists with expertise in SCID interviewing; (2) they were then required to show competence by completion of 20 well done interviews resulting in accurate diagnoses; and (3) their ongoing competence was ensured by weekly supervision by a psychiatrist informed by review of recordings of at least 10% of their telephone interviews.

Patients with major depression at interview were asked whether they were receiving any drug treatment for depression and whether they were visiting a mental health professional (psychiatrist or psychologist). The screening team used additional questions to clarify patients' responses where necessary and noted anti-depressant drug names and doses.

We obtained data for the patients' demographic and clinical characteristics from the NHS Scotland Cancer Registry. The Registry systematically collects information from hospitals throughout Scotland for all recorded cases of cancer. The demographic data obtained included data for sex, age, area of residence (urban, small town, rural) and social deprivation score (calculated with the Scottish Index of Multiple Deprivation, based on area of residence; appendix p 2). The clinical data included primary cancer grouping (appendix pp 3–5), time since diagnosis, whether initial cancer treatment had been started in the preceding 6 months, and initial treatment objective (curative or palliative), as supplied to the Registry by the relevant hospital.

The data manager for the screening service identified a single depression screening episode for each patient and extracted the relevant data from the screening database. If patients were screened for depression more than once

See Online for appendix

	Lung cancer (n=4316)			Breast cancer (n=8461)*			Genitourinary cancer (n=2009)			Gynaecological cancer (n=3010)*			Colorectal cancer (n=3355)		
	Major depression	Adjusted odds ratio (95% CI)	p value	Major depression	Adjusted odds ratio (95% CI)	p value	Major depression	Adjusted odds ratio (95% CI)	p value	Major depression	Adjusted odds ratio (95% CI)	p value	Major depression	Adjusted odds ratio (95% CI)	p value
Total	564 (13%)			788 (9%)			113 (6%)			329 (11%)			236 (7%)		
Sex			<0.0001			..			0.252		..				0.031
Men	238 (11%)	1			105 (5%)	1			112 (6%)	1	
Women	327 (16%)	1.52 (1.24-1.87)			8 (10%)	1.68 (0.69-4.07)			124 (8%)	1.38 (1.03-1.86)	
Age (years)			<0.0001			<0.0001			0.0038		<0.0001				<0.0001
<50	39 (26%)	1		205 (14%)	1		15 (9%)	1		105 (19%)	1		37 (15%)	1	
50-59	119 (20%)	0.76 (0.48-1.21)		277 (13%)	0.90 (0.73-1.11)		18 (9%)	0.97 (0.43-2.22)		98 (16%)	0.88 (0.64-1.21)		75 (14%)	0.97 (0.61-1.53)	
60-69	212 (14%)	0.51 (0.33-0.79)		223 (8%)	0.54 (0.44-0.67)		47 (7%)	0.77 (0.38-1.55)		74 (8%)	0.41 (0.29-0.57)		70 (6%)	0.43 (0.27-0.68)	
≥70	194 (9%)	0.31 (0.20-0.48)		84 (4%)	0.23 (0.18-0.31)		34 (3%)	0.36 (0.17-0.77)		51 (5%)	0.25 (0.17-0.36)		54 (4%)	0.24 (0.14-0.39)	
Time since diagnosis			0.599			0.151			0.672		0.036				0.395
<1 year	447 (13%)	1.08 (0.81-1.43)		317 (9%)	0.78 (0.55-1.10)		44 (7%)	1.12 (0.66-1.92)		179 (12%)	1.47 (1.03-2.11)		124 (7%)	1.19 (0.80-1.76)	
≥1 year	117 (12%)	1		472 (9%)	1		69 (5%)	1		151 (10%)	1		112 (7%)	1	
Recently started initial treatment†			0.740			0.623			0.701		0.052				0.241
No	327 (13%)	1		491 (9%)	1		92 (5%)	1		204 (11%)	1		158 (7%)	1	
Yes	237 (14%)	1.04 (0.83-1.30)		297 (9%)	1.09 (0.77-1.56)		21 (7%)	1.14 (0.59-2.20)		126 (11%)	0.70 (0.48-1.00)		78 (7%)	0.78 (0.52-1.18)	
Initial treatment objective			0.430			0.216			0.687		0.984				0.645
Palliative	401 (13%)	1		60 (11%)	1		46 (6%)	1		66 (10%)	1		58 (7%)	1	
Curative	163 (13%)	1.10 (0.87-1.37)		728 (9%)	0.80 (0.57-1.14)		67 (6%)	0.90 (0.54-1.51)		263 (11%)	1.00 (0.72-1.41)		178 (7%)	0.92 (0.64-1.32)	
Area of residence			0.627			0.225			0.150		0.180				0.163
Urban	481 (13%)	1		648 (10%)	1		98 (6%)	1		265 (12%)	1		196 (7%)	1	
Small town	50 (13%)	1.13 (0.78-1.64)		63 (8%)	0.84 (0.63-1.12)		8 (4%)	0.75 (0.31-1.78)		24 (7%)	0.64 (0.39-1.05)		24 (9%)	1.45 (0.89-2.35)	
Rural	33 (10%)	0.87 (0.57-1.34)		78 (7%)	0.82 (0.62-1.08)		7 (2%)	0.43 (0.18-1.00)		40 (10%)	0.99 (0.68-1.46)		16 (4%)	0.74 (0.41-1.34)	
SIMD score quintile‡			<0.0001			<0.0001			<0.0001		<0.0001				<0.0001
1	243 (16%)	2.20 (1.50-3.21)		218 (15%)	2.88 (2.25-3.67)		43 (12%)	11.0 (3.89-31.1)		115 (18%)	2.63 (1.77-3.92)		82 (13%)	3.21 (2.02-5.08)	
2	154 (15%)	1.95 (1.31-2.91)		176 (11%)	2.18 (1.69-2.80)		30 (9%)	7.69 (2.69-22.0)		71 (11%)	1.44 (0.94-2.20)		51 (8%)	1.90 (1.17-3.10)	
3	81 (12%)	1.50 (0.97-2.33)		152 (10%)	1.83 (1.41-2.39)		16 (4%)	4.18 (1.37-12.8)		50 (9%)	1.19 (0.76-1.87)		43 (7%)	1.82 (1.08-3.05)	
4	43 (8%)	0.98 (0.59-1.62)		116 (7%)	1.34 (1.00-1.78)		18 (4%)	4.33 (1.45-12.9)		52 (9%)	1.20 (0.76-1.90)		26 (4%)	1.09 (0.61-1.95)	
5	44 (8%)	1		127 (6%)	1		7 (1%)	1		42 (7%)	1		33 (4%)	1	

We imputed missing data for the depression diagnosis, recent treatment, and treatment objective with multiple imputation with the reported frequencies averaged over the imputed datasets. SIMD=Scottish Index of Multiple Deprivation. *Analyses not adjusted for sex; one of 28 men with breast cancer had depression. †Any of chemotherapy, radiotherapy, or surgery started in the preceding 6 months. ‡1=most deprived, 5=least deprived.

Table 2: Prevalence and associations of major depression in cancer outpatients

during the study period, the data extracted were those relating to the earliest of their clinic appointments. These data were then linked with corresponding data in the cancer registry. To ensure data security and confidentiality the screening dataset was sent to the Information Services Division of NHS Scotland for linking using unique patient identification numbers (Community Health Index numbers) and dates of birth. All identifying data were then removed in a one-way linkage to produce the anonymised dataset that was used for analysis.

Statistical analysis

We estimated the point prevalence of major depression for patients in each of the primary cancer groupings (breast, lung, colorectal, genitourinary, and gynaecological). 1145 (21%) of 5510 patients who had scored high on the HADS had missing data for depression diagnosis because of non-completion of the clinical interview; to assume that such patients were not depressed or to simply omit them from the analysis could have resulted in biased estimates. We therefore handled these incomplete data with multiple imputation techniques (for full details of the imputation, see appendix p 2) to estimate the number (and therefore proportion) of screened patients who had major depression in each cancer grouping. We did sensitivity analyses to assess the robustness of our findings under alternative scenarios for missing data.

We used multivariable logistic regressions to assess the independent associations of major depression with patients' demographic and clinical characteristics, within each cancer grouping.

We also calculated the proportion of patients with depression in the whole sample who were receiving potentially effective treatment for depression. We defined potentially effective treatment as presently receiving an antidepressant drug at a minimal effective or higher dose (appendix p 6)²⁵ or presently visiting a mental health professional (psychiatrist or psychologist). These data were from patients who had been diagnosed with major depression in the clinical interview and had given information about the treatment that they were receiving (ie, we did not impute missing data for this part of the analysis). We also analysed the associations of treatment receipt with sex, age, social deprivation, and cancer grouping in a multivariable logistic regression.

Role of the funding source

The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report. JW, CHH, PM, GM and MS had full access to data collected for the study and all authors had final responsibility for the decision to submit the report for publication.

Results

26 570 patients had attended cancer clinic appointments during the time period for which screening data were obtained. We analysed data for 21 151 (80%) of these

patients. The main reason that patients were excluded from the analysis was failure to participate in depression screening; most commonly because the patient's oncology appointment had begun before they could complete the HADS (figure 1).

Most participants were women and their mean age was 64 years (table 1). Most were attending return (rather than first) appointments at the oncology clinic. Median time from cancer diagnosis to screening for depression was 1 year. 5510 (26%) of 21 151 screened patients had a HADS score of 15 or more. Of these patients, 4365 (79%) completed a SCID depression interview (the main reason for non-completion of an interview was that the patient declined or could not be contacted; n=701); we imputed data for depression diagnosis for the remainder.

The prevalence of major depression was highest in patients with lung cancer (13.1%, 95% CI 11.9–14.2) followed by gynaecological cancer (10.9%, 9.8–12.1), breast cancer (9.3%, 8.7–10.0), colorectal cancer (7.0%, 6.1–8.0), and genitourinary cancer (5.6%, 4.5–6.7; figure 2). In sensitivity analyses to assess the robustness of our findings under alternative scenarios for missing data, prevalence estimates differed from those of the main analysis by less than 2 percentage points, there was little variation in the absolute differences between the five prevalence estimates, and the order of estimates remained unchanged (data not shown).

In all five cancer groupings, depression was significantly more common in younger patients than in older patients and in those with worse than in those with better social deprivation scores (table 2). In the cancer groupings for which we were able to analyse the independent associations of sex (lung, genitourinary, and colorectal), depression was significantly more common in female patients than in male patients for lung cancer and colorectal cancer, with a non-significant trend in this direction for patients with genitourinary cancer. Depression was not independently associated with urban or rural residence. Time since cancer diagnosis was not associated with depression except for patients with gynaecological cancer (table 2). Nor was depression associated with whether the patient had started initial cancer treatment (chemotherapy, radiotherapy, or surgery) in the 6 months preceding screening, or with stated initial treatment objective (palliative or curative) in any of the five groupings. Estimates of these associations with major depression differed negligibly across our sensitivity analyses (data not shown).

Of the 1599 patients diagnosed with major depression at interview, we had complete patient-reported treatment data for 1538 (96%). Most (n=1130, 73%) of these patients were not receiving any potentially effective treatment for depression; less than a quarter were receiving an antidepressant drug at a minimal effective dose or higher and very few were visiting a mental health professional (figure 3). Patients with depression were more likely to be receiving treatment if they were younger and if they were female (table 3). Patients with breast cancer were most likely to

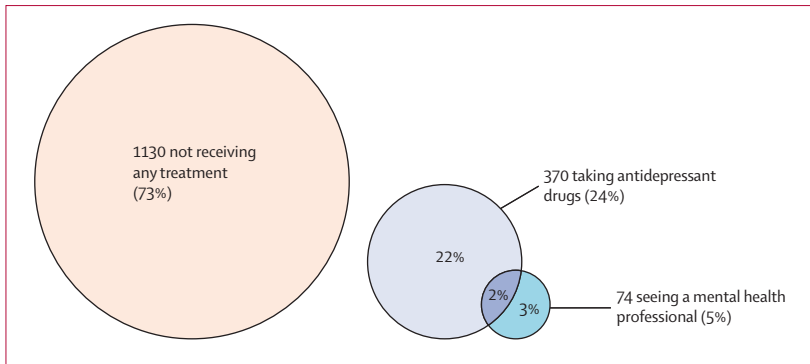


Figure 3: Treatments received by outpatients with cancer and major depression
 Proportions based on 1538 patients diagnosed with major depression at clinical interview and with complete treatment data. Antidepressant drugs were amitriptyline, citalopram, clomipramine, dosulepin, doxepin, duloxetine, escitalopram, fluoxetine, flupentixol, fluvoxamine, imipramine, lofepramine, mirtazapine, nortriptyline, paroxetine, phenelzine, reboxetine, sertraline, trazodone, trimipramine, venlafaxine.

	In receipt of treatment* (n=408)	Not in receipt of treatment (n=1130)	Adjusted odds ratio (95% CI)	p value
Sex				0.0004
Men	54 (18%)	251 (82%)	1	
Women	354 (29%)	879 (71%)	2.22 (1.43-3.45)	
Age (years)				<0.0001
<50	105 (35%)	199 (65%)	1	
51-59	146 (31%)	318 (69%)	0.91 (0.67-1.25)	
60-69	120 (25%)	369 (75%)	0.68 (0.49-0.94)	
≥70	37 (13%)	244 (87%)	0.33 (0.22-0.51)	
SIMD score				0.489
1	153 (29%)	372 (71%)	1.37 (0.92-2.03)	
2	92 (25%)	269 (75%)	1.14 (0.75-1.72)	
3	68 (26%)	196 (74%)	1.13 (0.73-1.76)	
4	49 (26%)	142 (74%)	1.10 (0.69-1.77)	
5	46 (23%)	151 (77%)	1	
Primary cancer grouping†				0.0048
Colorectal	44 (25%)	133 (75%)	1	
Breast	198 (32%)	429 (68%)	0.93 (0.61-1.42)	
Genitourinary	25 (30%)	57 (70%)	2.16 (1.13-4.13)	
Gynaecological	66 (25%)	195 (75%)	0.68 (0.42-1.10)	
Lung	75 (19%)	316 (81%)	0.75 (0.48-1.17)	

Data are n (%). Of 1599 patients diagnosed with major depression at interview, 61 had incomplete treatment data. *Presently receiving an antidepressant drug at a minimal effective dose or higher (according to dose guidance) or seeing a mental health professional (psychiatrist or psychologist). †The associations of sex and cancer site were heavily confounded (eg, treatment receipt was highest among patients with breast cancer despite the moderate adjusted effect size). Odds ratios are fully adjusted and estimate independent effects (eg, among participants with otherwise similar characteristics, there was no evidence that patients with breast cancer are more likely to receive treatment).

Table 3: Independent associations of receipt of potentially effective treatment for major depression

receive treatment for depression (32%) and those with lung cancer were least likely to receive treatment (19%).

Discussion

The prevalence of major depression was highest in patients with lung cancer and lowest in those with genitourinary cancer. The variation between cancer

groupings shows the limitations of prevalence estimates based on pooled samples. Within the cancer groupings, patients who were younger, had worse social deprivation scores, and (for cancers that affected both sexes) those who were female were more likely to have major depression; consistent with findings in the general population.²⁶ Of the patients diagnosed with major depression, most were not in receipt of any potentially effective treatment.

It was notable that patients who had been living with a cancer diagnosis for more than a year were just as likely to have depression as were those diagnosed more recently, and that patients who had received initial curative treatment were just as likely to have depression as were those who had been treated with palliative intent.

Our findings suggest that major depression is substantially more common in people with cancer than in the general population. Direct comparisons between these findings and those from the general population are made difficult by the varying diagnostic criteria, time periods, and interview methods that have been used in published population surveys. However, the prevalence of depression we recorded in all cancer groupings was more than twice the estimated point prevalence reported in the general population (2%)²⁷ and higher than the estimated 12 month prevalence in the general population (4-5%).^{26,28}

Perhaps our most important finding was that most cancer outpatients with depression were not in receipt of potentially effective treatment for their depression. Although under-treatment of major depression has previously been reported for the general population, and for those who self-reported a diagnosis of cancer when asked in a survey, the under-treatment of patients attending specialist cancer services is especially concerning.^{27,29-32}

This study is the first to report the prevalence of major depression in patients with cancer with data from large-scale screening (panel). It has several strengths. First, the size of the sample was more than twice that of the total number of patients included in each of two meta-analyses (8747 and 10 071 patients);^{15,16} second, the use of screening to obtain a representative sample; third, the use of rigorous interview-based diagnoses of depression (rather than questionnaires, which are likely to have a high false-positive rate) made according to standard diagnostic criteria by trained interviewers; fourth, cancer diagnoses made by specialist clinicians; fifth, the use of interviews to establish the treatments for depression actually received by patients.

The study also had limitations. First, patients had attended publicly funded specialist cancer clinics in Scotland. Our findings might not therefore generalise to other populations (such as for patients who were diagnosed many years ago and who no longer attend clinics) or to cancer patients in all health-care settings. However, they are likely to have relevance to all cancer centres that treat common cancers. Second, not all

Panel: Research in context**Systematic review**

We did a systematic review of studies that met pre-defined basic quality criteria to obtain the best estimate of the prevalence of depression in clinically meaningful subgroups of patients with cancer.¹⁰ We searched Medline (from 1950), PsycINFO (from 1806), Embase Classic and Embase (from 1947), Web of Science, and BIOSIS, up to January 2012, for the combination of "prevalence", "cancer", and "depression", using both standardised subject terms and free text terms, including synonyms and alternative spellings. Of 66 relevant studies, only 15 (23%) met quality criteria. These 15 studies had used interviewers with a range of expertise to diagnose depression (studies that used expert interviewers reported lower prevalence). Prevalence estimates differed widely (5–16% for outpatients, 4–14% for inpatients, 4–11% for mixed outpatient and inpatient samples, and 7–49% for palliative care), and did not provide reliable comparisons of prevalence between patients with different primary cancer sites and did not offer useful estimates of the proportion of depressed patients who were receiving potentially effective treatment.

Interpretation

Our study is the first report of the prevalence of depression in patients with cancer to be based on a large-scale screening service that used rigorous interviews and expert cancer diagnoses. The prevalence of major depression varied by cancer grouping: prevalence was highest in patients with lung cancer (13.1%) and lowest in those with genitourinary cancer (5.6%). Within cancer groupings, patients who were younger, had worse social deprivation scores, and those who were female were more likely to have major depression. Of 1538 patients diagnosed with major depression, 1130 (73%) reported that they were not in receipt of any potentially effective treatment for depression.

clinic patients were screened for depression and we could not characterise those who were not (because they had not had the opportunity to give consent for their data to be used). However, most patients did participate, and the main reason for not doing so was simply insufficient time to complete the HADS screening before seeing the oncologist, which is unlikely to be substantially affected by depression. Third, because data for depression diagnosis were only available for patients who scored highly on the initial screening questionnaire, some cases might have been missed at this first stage. However, the misclassification rate of the HADS cutoff score used by the screening service is very low.²⁰ Fourth, we did not have diagnostic interview data for all patients who scored high on the HADS at stage one of screening. We did, however, use multiple imputation and sensitivity analyses to handle these missing data to reduce and assess the potential bias in estimates and these results were robust. Fifth, the number of demographic and clinical variables that we assessed for an association

with depression was limited by the data collected routinely by the screening service and by the cancer registry. Our findings should therefore be qualified by the possibility of unmeasured confounding variables. Finally, our assessment of treatment receipt relied on questions asked by the screening team. Although the interviewers were trained to interpret and probe answers to these questions and the accuracy of self-reported use of mental health services has been reported to be good,³³ some patients might not have reported their treatment accurately, might have been offered but declined treatment, or might have been receiving psychological treatment from other professionals.

These findings have several implications for clinical services. Major depression, although not ubiquitous among cancer outpatients, is common and therefore merits greater attention. Furthermore, its greater prevalence in patients with some cancer groupings, notably lung cancer, suggests where screening for depression will find the most cases. Finally, despite its adverse effects on quality of life and adherence to treatment, depression in patients attending cancer clinics is inadequately managed at present. Systematic approaches to improving depression care for patients with cancer are urgently needed; we have described and evaluated one such approach.^{34,35}

Contributors

JW, MS, CHH, PM, and GM had the idea for and designed the study. MS and GM obtained funding. JW managed the study and CHH led the study analysis under the supervision of MS and GM. PM managed the data. SS advised on study conduct, analysis, and data interpretation. RR searched the published work. JW wrote the draft with critical revision from all other authors. All authors have seen and approved the final version.

Declaration of interests

We declare no competing interests.

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References

- 1 Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; **380**: 2163–96.
- 2 Moussavi S, Chatterji S, Verdes E, Tandon A, Patel V, Ustun B. Depression, chronic diseases, and decrements in health: results from the World Health Surveys. *Lancet* 2007; **370**: 851–58.
- 3 Egede LE. Major depression in individuals with chronic medical disorders: prevalence, correlates and association with health resource utilization, lost productivity and functional disability. *Gen Hosp Psychiatry* 2007; **29**: 409–16.
- 4 Department of Health England. Living With and Beyond Cancer: Taking Action to Improve Outcomes. London; 2013.
- 5 Brown LF, Kroenke K, Theobald DE, Wu J, Tu W. The association of depression and anxiety with health-related quality of life in cancer patients with depression and/or pain. *Psychooncology* 2010; **19**: 734–41.

- 6 O'Connor M, Weir J, Butcher I, et al. Pain in patients attending a specialist cancer service: Prevalence and association with emotional distress. *J Pain Symptom Manage* 2012; **43**: 29–38.
- 7 Storey DJ, Waters RA, Hibberd CJ, et al. Clinically relevant fatigue in cancer outpatients: the Edinburgh Cancer Centre symptom study. *Ann Oncol* 2007; **18**: 1861–69.
- 8 Walker J, Waters RA, Murray G, et al. 'Better off dead': suicidal thoughts in cancer patients. *J Clin Oncol* 2008; **26**: 4725–30.
- 9 Colleoni M, Mandala M, Peruzzotti G, Robertson C, Bredart A, Goldhirsch A. Depression and degree of acceptance of adjuvant cytotoxic drugs. *Lancet* 2000; **356**: 1326–27.
- 10 NICE. Depression in adults with a chronic physical health problem: treatment and management. London: National Institute for Clinical Excellence; 2009.
- 11 Department of Health England. Living with and beyond cancer: taking action to improve outcomes. London; 2013.
- 12 Institute of Medicine. From cancer patient to cancer survivor: lost in transition. Washington, DC: National Academies Press; 2006.
- 13 Institute of Medicine. Cancer care for the whole patient: meeting psychosocial health needs. Washington, DC: National Academies Press; 2008.
- 14 American College of Surgeons. Cancer program standards; 2012. <https://www.facs.org/quality%20programs/cancer/coc/standards> (accessed Aug 21, 2014).
- 15 Mitchell AJ, Chan M, Bhatti H, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *Lancet Oncol* 2011; **12**: 160–74.
- 16 Krebber AM, Buffart LM, Kleijn G, et al. Prevalence of depression in cancer patients: a meta-analysis of diagnostic interviews and self-report instruments. *Psychooncology* 2013; **23**: 121–30.
- 17 Walker J, Holm Hansen C, Martin P, et al. Prevalence of depression in adults with cancer: a systematic review. *Ann Oncol* 2013; **24**: 895–900.
- 18 Eastwood MR. Screening for psychiatric disorder. *Psychol Med* 1971; **1**: 197–208.
- 19 Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; **67**: 361–70.
- 20 Walker J, Postma K, McHugh GS, et al. Performance of the Hospital Anxiety and Depression Scale (HADS) as a screening tool for major depressive disorder in cancer patients. *J Psychosom Res* 2007; **63**: 83–91.
- 21 First MB, Gibbon M, Spitzer RL, Williams JBW. User's guide for the SCID-I, structured clinical interview for DSM-IV axis I disorders, research version. New York State Psychiatric Institute: New York; 1996.
- 22 American Psychiatric Association. Diagnostic and statistical manual of mental disorders 4th edition. Washington DC: American Psychiatric Association; 1994.
- 23 Simon GE, Revicki D, VonKorff M. Telephone assessment of depression severity. *J Psychiatric Res* 1993; **27**: 247–52.
- 24 Simon GE, von Korff M. Medical co-morbidity and validity of DSM-IV depression criteria. *Psychol Med* 2006; **36**: 27–36.
- 25 Taylor D, Paton C, Kapur S. The Maudsley prescribing guidelines. 10th edn. Informa Healthcare; 2011.
- 26 Hasin DS, Goodwin RD, Stinson FS, Grant BF. Epidemiology of major depressive disorder: results from the National Epidemiologic Survey on Alcoholism and Related Conditions. *Arch Gen Psychiatry* 2005; **62**: 1097–106.
- 27 McManus S. Adult psychiatric morbidity in England, 2007. NHS Information Centre; 2009. <http://www.hscic.gov.uk/pubs/psychiatricmorbidity07> (accessed Aug 21, 2014).
- 28 Waraich P, Goldner EM, Somers JM, Hsu L. Prevalence and incidence studies of mood disorders: a systematic review of the literature. *Can J Psychiatry* 2004; **49**: 124–38.
- 29 Wang PS, Aguilar-Gaxiola S, Alonso J, et al. Use of mental health services for anxiety, mood, and substance disorders in 17 countries in the WHO world mental health surveys. *Lancet* 2007; **370**: 841–50.
- 30 Wang PS, Demler O, Kessler RC. Adequacy of treatment for serious mental illness in the United States. *Am J Public Health* 2002; **92**: 92–98.
- 31 Nakash O, Levav I, Aguilar-Gaxiola S, et al. Comorbidity of common mental disorders with cancer and their treatment gap: findings from the World Mental Health Surveys. *Psychooncology* 2013; **23**: 40–51.
- 32 Findley PA, Shen C, Sambamoorthi U. Depression treatment patterns among elderly with cancer. *Depress Res Treat* 2012; **2012**: 676784.
- 33 Golding J, Gongga P. Feasibility of validating survey self-reports of mental health service use. *Am J Comm Psych* 1988; **16**: 39–51.
- 34 Sharpe M, Walker J, Holm Hansen C, et al. Integrated collaborative care for comorbid major depression in patients with cancer (SMaRT Oncology-2): a multicentre randomised controlled effectiveness trial. *Lancet* 2014; published online Aug 28. [http://dx.doi.org/10.1016/S0140-6736\(14\)61231-9](http://dx.doi.org/10.1016/S0140-6736(14)61231-9).
- 35 Walker J, Holm Hansen C, Martin P, et al. Integrated collaborative care for major depression comorbid with a poor prognosis cancer (SMaRT Oncology-3): a multicentre randomised controlled trial in patients with lung cancer. *Lancet Oncol* 2014; published online Aug 28. [http://dx.doi.org/10.1016/S1470-2045\(14\)70343-2](http://dx.doi.org/10.1016/S1470-2045(14)70343-2).