www.bjcancer.com

# Incidence and drug treatment of emotional distress after cancer diagnosis: a matched primary care case-control study

# F Desplenter\*,1,2, C Bond<sup>1</sup>, M Watson<sup>1</sup>, C Burton<sup>1</sup>, P Murchie<sup>1</sup>, AJ Lee<sup>3</sup>, K Lefevre<sup>1</sup>, S Simoens<sup>2</sup> and G Laekeman<sup>2</sup>

Academic Primary Care, University of Aberdeen, Foresterhill, Polwarth Building, Aberdeen AB25 2ZD, UK; <sup>2</sup>Department of Pharmaceutical and Pharmacological Sciences, ON 2, Herestraat 49, PO Box 521, 3000 Leuven, Belgium; <sup>3</sup>Medical Statistics Team, University of Aberdeen, Foresterhill, Polwarth Building, Aberdeen AB25 2ZD, UK

BACKGROUND: Emotional distress is common in cancer patients. This study aimed to describe, in the year after a cancer diagnosis: the incidence of anxiety, depression and excessive alcohol use; the pattern of these diagnoses and treatment over time; and the nature and duration of the prescribed treatment.

METHODS: A matched case-control study was conducted using routinely collected primary care data from 173 Scottish general practices. A presumptive diagnosis of emotional distress (anxiety, depression and/or excessive alcohol use) was based on prescription data or diagnostic code. Prescriptions for psychotropic drugs were described in terms of drug class, volume and treatment duration. RESULTS: In total, 7298 cancer cases and 14596 matched-controls were identified. Overall, 1135 (15.6%) cases and 201 (1.4%) controls met criteria for emotional distress (odds ratio 13.7, 95% confidence interval 11.6-16.1). Psychotropic drugs were prescribed in the 6 months following initial cancer diagnosis for 1066 (14.6%) cases and 161 (1.1%) controls. The volume and duration of anxiolytic and antipsychotic prescribing was significantly different between cases and controls.

CONCLUSION: This study quantified the higher incidence of new emotional distress in cancer patients in the first year post diagnosis. Clinicians should be aware of the possibility of emotional distress at any time in the year after cancer diagnosis.

British Journal of Cancer (2012) 107, 1644–1651. doi:10.1038/bjc.2012.364 www.bjcancer.com

Published online 11 October 2012

© 2012 Cancer Research UK

**Keywords:** cancer; anxiety; depression; incidence; primary care; case-control study

Depression and anxiety are common in patients with cancer (Massie, 2004; Sharpe et al, 2004; Vahdaninia et al, 2010), may occur and be diagnosed at any stage of the cancer journey (Miovic and Block, 2007; Hansen and Sawatzky, 2008) and are estimated to affect up to 40% of people with cancer. About 50% of patients with advanced cancer meet criteria for a psychiatric diagnosis if adjustment disorder is included (Massie, 2004). Newly diagnosed alcohol abuse after cancer diagnosis is a further indication of the emotional impact of the condition (Bringmann et al, 2008; Yung and Piccirillo, 2008). Both depression and anxiety are amenable to treatment, both pharmacologically and using cognitive behavioural approaches (Strong et al, 2008; Deshields and Nanna, 2010; Holland and Alici, 2010; Wein et al, 2010).

Although secondary care is largely responsible for cancer-specific treatment such as surgery or chemotherapy, most general and supportive care of cancer patients takes place in primary care (Lewis et al, 2009). This is also where the majority of treatment for depression and anxiety takes place (Munoz-Arroyo et al, 2006; Hodges et al, 2009). While consultation rates for coded depression or anxiety have been reported to be similar to those of the general population in long-term survivors of common cancers in the UK, there is an increase in the proportion receiving at least one prescription for an antidepressant, indicating increased mental health morbidity (Khan et al, 2010). However, it is not clear at which stage of the cancer journey this excess mental health morbidity occurs.

The aim of this study was to describe, in the first year following a cancer diagnosis in subjects without a pre-existing mental health condition: (a) the incidence of three common mental health problems: depression, anxiety and excessive alcohol use, using a combination of prescription data and diagnostic codes; (b) the pattern of these problems and treatment over time; and (c) the nature and duration of prescribed treatment. Throughout this paper, one or any combination of the above three problems is referred to as emotional distress.

# MATERIALS AND METHODS

# Design

A matched case-control study was conducted, using routinely collected primary care data (http://www.abdn.ac.uk/pcciu/ PCCIU.htm).

#### Subjects and setting

Data from 173 general practices in Scotland was obtained from the Primary Care Clinical Informatics Unit (PCCIU), University of

published online 11 October 2012



Aberdeen. The PCCIU data comprised anonymised extracts from 173 practices, which used the General Practice Administration System for Scotland (GPASS) software (NHS Scotland, Glasgow, UK). The data for this study was obtained by running specified queries against the Microsoft SQL server holding the extracted general practitioners (GP) data and transferring this into a SPSS database (version 18 for Windows, SPSS Inc., Chicago, IL, USA). The study period was 1 April 2005-1 April 2010, and data were available for 1026770 patients.

#### Inclusion and exclusion criteria

Cases were defined as individuals aged 18 years and older with a diagnosis of one of eight cancer types, selected for their high incidence in the UK: breast, colorectal, lung, prostate, upper gastro-intestinal, melanoma (excluding non-melanoma skin cancers), gynaecological and urological cancers (Cancer Research UK, 2011). Controls were matched according to gender, age (5-year age bands) and general practice. Patients with any cancer diagnosis were excluded from the control group. Patients with a diagnosis of depression, anxiety or excessive alcohol use or who had used antidepressants, anxiolytics or medicines for alcohol dependence in the year before the index date, that is, the date of cancer diagnosis for each individual case, were excluded from both the cases and their matched controls.

#### Subject identification

The GPASS clinical system utilises the READ V2 clinical terminology for the recording of patient findings, diagnoses and procedures. READ codes are a coded thesaurus of clinical terms (http://www.connectingforhealth.nhs.uk/systemsandservices/data/ uktc/readcodes). READ codes have two versions: Version 2 (v2) and version 3 (CTV3 or v3), which are the basic means by which clinicians record patient findings and procedures in health and social care IT systems across primary and secondary care (e.g., general practice surgeries and pathology reporting of results). READ codes have been in use in the NHS since 1985 and are still widely used in the primary care sector. Scottish primary care exclusively uses Read V2. They are maintained by the UK Terminology Centre. Cross-maps are maintained from the Read codes to the UK-mandated classifications of OPCS-4 and ICD-10 Pathology Bounded Code List. Code sets to identify cancer cases and the diagnoses of depression, anxiety and excessive alcohol use were developed from the Scotland READ V2 browser released in Spring 2010. Prescription of antidepressants, anxiolytics or medicines for alcohol dependence was defined by the British National Formulary (BNF) 59 chapter sections 4.3.1-4.3.4 (antidepressants), 4.1.2 (anxiolytics) and 4.10 (subsection alcohol dependence) (2010).

A 1:2 case-control matching ratio was applied. Hence, each cluster comprised one case and two-matched control patients. The following criteria were then applied (Figure 1). First, cases without sufficient matching control patients were excluded. Second, clusters which included patients with multiple cancer diagnoses at first date of diagnosis were excluded if no clinical evidence was available to identify the first diagnosed cancer thus preventing stratification according to index cancer site. Third, only clusters with an index date earlier than 1 October 2008 were included to allow for 18 months of follow-up data for the outcome assessment. Finally, clusters which included at least one patient who had died before the index date were excluded.

#### Outcome

The primary outcome was the composite measure of emotional distress (i.e., anxiety, depression and/or excessive alcohol use).

The secondary outcome was the prescription of psychotropic drugs in the first 6 months after the diagnosis of emotional distress. For this secondary outcome we included drugs listed as indicating emotional distress plus those in BNF chapter sections 4.1.1 (hypnotics), 4.2.1 (antipsychotics) and 4.2.3 (anti-manics). For each patient we recorded the type of drug, the total quantity prescribed (expressed as total DDDs (defined daily dose) (WHO, 2010)) and treatment duration.

#### Data specification

For each patient we extracted data on gender, age, socioeconomic deprivation (seven categories of the Carstairs index (Morris and Carstairs, 1991)), urban/rural status (six-fold classification of the Scottish Index of Multiple Deprivation 2006 at practice level (Office of the Chief Statistician, 2006)), smoking (never smoked, ex-smoker and current smoker according to the latest registration of READ codes) and date of death (if relevant). For cases, data on registration in the Palliative Care Register (an indicator for the cancer stage) was also extracted.

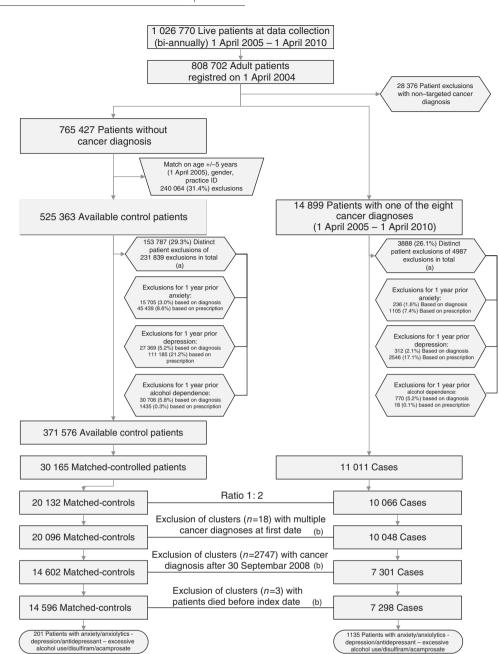
For each prescription in the 6-month follow-up period, we extracted the generic drug name, the date of issue, the strength, the dose and the frequency. Estimated daily doses were translated into DDDs (Burton et al, 2012), using the WHO standard values (WHO, 2010). Total duration of treatment in days was calculated by subtracting the date of the last prescription from the date of the first prescription and adding the actual duration of the last prescription. Total DDDs prescribed and duration was calculated per patient for drug groups and subgroups of interest. Liquid preparations (about 1% of the psychotropic drug prescriptions) were excluded from the database as calculations for volume and treatment duration were unreliable. In reporting medication use in patients who met our criteria for emotional distress, we did not attempt to distinguish between use for a primary psychiatric condition or for other indications such as pain (tricyclic antidepressants) or nausea (typical antipsychotics) as this information is not available in the database.

Standard methods of data cleaning and validation were applied. The internal reliability of the data was checked by searching and checking the type of data received and the outliers for each variable.

The North of Scotland Research Ethics Committee was contacted to determine whether formal ethical approval was required for this study. As the data used was anonymous at every stage of the research process full formal ethical approval was not required.

# Statistical analysis

Descriptive analyses (frequencies for categorical variables, mean and s.d. for normally distributed continuous data, and median and inter quartile range for non-normally distributed continuous data) were conducted. Demographic characteristics and incidence rates were compared between cases and controls using conditional logistic regression. Odds ratios (OR) and the 95% confidence intervals (CI) were reported. Matched survival analysis (using a stratified COX model) (Cox, 1972) was used to produce Kaplan-Meier graphs to illustrate the timeline of incident emotional distress. The assumption of proportionality was tested and met. Analysis was completed for the time from index date up to 1 year, using death as a censoring variable. The  $\chi^2$  test was used to compare the proportions of drugs (and drug groups) and to compare the frequencies of users of psychotropic drugs between cases and controls. When numbers were small, Fisher's Exact test was used instead of the  $\chi^2$  test. The Mann-Whitney *U*-test was used to compare the quantity and the duration of prescriptions between cases and controls.



- (a) The sum of the numbers in the exclusion boxes below do not add up owing to duplicate patients.
- (b) Exclusion made at case level.

161 Patients with prescriptions for psychotropic drugs

Figure I Flow chart of sample.

Data handling and analyses were performed using PASW Statistics 19.0 (Predictive Analytics SoftWare) for Windows (2010, SPSS Inc.). STATA 11 (2009, STATA, TX, USA) was used for the conditional logistic regression and the stratified COX model.

#### **RESULTS**

#### Sample

Based on the inclusion and exclusion criteria and the subject identification process, 7298 cancer cases and 14596 matchedcontrols were identified (Figure 1). Sample characteristics are summarised in Table 1. Half of the sample was female (50.7%). The mean age was 67.4 years. No statistically significant differences between cases and controls were observed for deprivation. The proportion of ex-smokers (OR 1.57 (95% CI 1.48-1.68)) and smokers (OR 1.35 (95% CI 1.24-1.46)) was significantly higher among cases. A higher proportion of cases died within 12 months (OR 99.5 (95% CI 47.1-210.3)) and within 18 months (OR 52.1 (95% CI 31.6-85.9)) of index date.

alcohol use/disulfiram/acamprosate

1066 Patients with prescriptions for psychotropic drugs

#### Incidence of emotional distress

Overall, 1135 (15.6%) cases and 201 (1.4%) controls were identified with emotional distress within 1 year following the index date

**Table I** Demographic and clinical characteristics of the cases<sup>a</sup> and controls

	Cases (n = 7298) % (n)	Controls (n = 14596) % (n)	Total (n = 21 894) % (n)	OR (95% CI)
Age (mean (s.d.))	68.2 (12.8)	67.0 (13.4)	67.4 (13.2)	Ь
Female gender	50.7 (3703)	50.7 (7406)	50.7 (11109)	Ь
Deprivation				
DepCat1 (least deprived)	6.4 (464)	6.1 (887)	6.2 (1351)	Reference
DepCat2	11.1 (812)	11.6 (1696)	11.5 (2508)	0.88 (0.74-1.04)
DepCat3	20.0 (1462)	20.6 (3004)	20.4 (4466)	0.90 (0.77-1.05)
DepCat4	31.6 (2303)	31.0 (4522)	31.2 (6825)	0.98 (0.84-1.14)
DepCat5	15.5 (1128)	15.6 (2283)	15.6 (3411)	0.94 (0.79-1.11)
DepCat6	11.7 (853)	11.5 (1677)	11.6 (2530)	0.99 (0.82-1.18)
DepCat7 (most deprived)	3.8 (276)	3.6 (527)	3.7 (803)	1.04 (0.81–1.34)
Urban/Rural status				
Large urban	35.6 (2595)	35.6 (5190)	35.6 (7785)	Ь
Other urban	37.2 (2716)	37.2 (5432)	37.2 (8148)	Ь
Accessible small town	12.7 (925)	12.7 (1850)	12.7 (2775)	Ь
Remote small town	7.7 (560)	7.7 (1120)	7.7 (1680)	Ь
Accessible rural	4.0 (292)	4.0 (584)	4.0 (876)	Ь
Remote rural	2.9 (210)	2.9 (420)	2.9 (630)	Ь
Smoking status				
Non-smoker	37.8 (2759)	47.0 (6863)	43.9 (9622)	Reference
Ex-smoker	44.8 (3268)	36.6 (5336)	39.3 (8604)	1.57 (1.48-1.68)
Smoker	17.4 (1271)	16.4 (2397)	16.8 (3668)	1.35 (1.24–1.46)
Died within 12 months of index date	4.9 (358)	0.1 (20)	1.7 (378)	99.5 (47.1–210.3)
Died within 18 months of index date	5.9 (429)	0.2 (32)	2.1 (461)	52.1 (31.6–85.9)
Palliative care register	7.0 (510)	0 (0)		
Cancer site				
Breast	21.2 (1548)	0 (0)	_	_
Colorectal	17.4 (1271)	0 (0)	_	_
Lung	17.8 (1296)	0 (0)	_	_
Prostate	14.5 (1061)	0 (0)	_	_
Upper gastro-intestinal	7.4 (537)	0 (0)	_	_
Melanoma	5.5 (402)	0 (0)	_	_
Gynaecological	6.1 (447)	0 (0)	_	_
Urological	10.1 (736)	0 (0)	_	_

Abbreviations: CI = confidence interval; OR = odds ratio; s.d. = standard deviation. <sup>a</sup>Cases: patients diagnosed with cancer during the period 1 April 2005–30 September 2008 with no history of mental health problems in the year before cancer diagnosis; controls were age, gender and practice-matched patients with no cancer diagnosis in their medical history. <sup>b</sup>No statistics reported as age, gender and practice (urban/rural data is on practice level, not on patient level) were used for matching.

(Table 2). The overall OR for emotional distress between cases and controls was 13.66 (95% CI 11.59–16.11). When comparing cases with controls, the OR for the incidence of anxiety and/or anxiolytics was 14.32 (95% CI 11.23–18.26) (537 (7.4%) cases vs 84 (0.6%) controls); for depression and/or antidepressants 13.84 (95% CI 11.24–17.03) (713 (9.8%) cases vs 112 (0.8%) cases); and for excessive alcohol use and/or disulfiram/acamprosate 4.07 (95% CI 2.57–6.46) (55 (0.8%) cases vs 27 (0.2%) controls).

The Kaplan–Meier graphs (Figure 2) illustrate the time from the index date to identification of emotional distress. The figures show that during the 1-year period post index cancer diagnosis there was no specific time point at which indicators of emotional distress, as previously defined, were recorded.

# Psychotropic drug prescriptions in the 6 months after the diagnosis of emotional distress

Psychotropic drugs were prescribed for 1066 (14.6%) cases and 161 (1.1%) controls in the 6-month period after initial diagnosis (Table 3). Cases were prescribed more psychotropic drugs (P < 0.001) and more psychotropic drug groups (P < 0.001). The majority of the controls used one psychotropic drug (80.7%) or drug group (85.1%) compared with 61.8% and 64.1%, respectively, among cases. Of the individuals prescribed psychotropic drugs,

prescriptions for antidepressants were issued in 64.9% (n=692) vs 62.7% (n=101) controls (P=0.589), anxiolytics in 46.5% (n=496) of cases vs 37.9% (n=61) of controls (P=0.040), hypnotics in 22.7% (n=242) vs 7.5% (n=12) (P<0.001), antipsychotics in 8.8% (n=94) vs 6.2% (n=10) (P=0.268) and anti-manic drugs in 0.9% (n=14) vs 1.1% (n=2) (P=1.000).

The total prescribing volume and duration of psychotropic drug prescriptions in the 6-month follow-up period is listed in Table 4. These values were significantly different between the cohorts for anxiolytic and antipsychotic drugs. Anxiolytics were prescribed in greater volume ( $P\!=\!0.017$ ) and for a longer time ( $P\!=\!0.003$ ) in cases. The opposite was observed for antipsychotic drugs, which were prescribed in smaller volumes ( $P\!=\!0.041$ ) and for shorter periods ( $P\!=\!0.002$ ) in cases. Hypnotic, antidepressant and antimanic prescriptions were comparable between cases and controls.

## DISCUSSION

### Summary of findings

Patients diagnosed with cancer were at least 10 times more likely than matched controls to be diagnosed with emotional distress in the year following a cancer diagnosis. The first coded diagnosis or

**Table 2** I year incidence (and proportion of affected individuals identified by diagnostic code, prescription or both) of diagnosis of emotional distress with ORs and the number of emotional distress categories per patient

	Cases (n = 7298) % (n)	Controls (n = 14596) % (n)	Total (n = 21 894) % (n)	OR (95% CI)
Anxiety/Anxiolytics	7.4 (537)	0.6 (84)	2.8 (621)	14.32 (11.23–18.26)
READ code only	6.7 (37)	26.2 (22)	9.5 (59)	
Anxiolytic drug use only	89.2 (479)	69.0 (58)	86.5 (537)	
Both	3.9 (21)	4.8 (4)	4.0 (25)	
Depression/Antidepressants <sup>a</sup>	9.8 (713)	0.8 (112)	3.8 (825)	13.84 (11.24–17.03)
READ code only	2.0 (14)	9.8 (11)	3.4 (25)	,
Antidepressant use only	84.3 (601)	72.3 (81)	82.7 (682)	
Both	13.7 (98)	17.9 (20)	14.3 (118)	
Alcohol/Acamprosate/Disulfiram	0.8 (55)	0.2 (27)	0.4 (82)	4.07 (2.57–6.46)
READ code only	100.0 (55)	96.3 (26)	98.8 (81)	, ,
Acamprosate/Disulfiram	0 (0)	0 (0)	0 (0)	
Both	0 (0)	3.7 (1)	1.2 (1)	
Total number of persons with emotional distress	15.6 (1135)	1.4 (201)	6.1 (1336)	13.66 (11.59–16.11)
Number of emotional distress categories				
1	85.1 (966)	89.1 (179)	85.7 (1145)	
2	14.8 (168)	10.9 (22)	14.2 (190)	
2 3	0.1 (1)	0 (0)	0.1 (1)	

Abbreviations: CI = confidence interval; odds radio = OR. <sup>a</sup>Antidepressant treatment may be used to treat anxiety disorders without depression: categories relate to diagnosis or treatment class rather than accurate diagnosis.

prescription occurred evenly throughout the year after diagnosis, with no discernible peak to indicate a time of particular vulnerability or recognition. Treatment was mainly of brief duration indicating that it might have been more symptomatic (e.g., hypnotic or antipsychotic prescription) rather than diagnosis-specific (e.g., sufficient dose and long duration of anti-depressant prescription).

#### Strengths and limitations

This study quantifies the primary care recorded incidence and pattern of emotional distress in the year following a cancer diagnosis. The data were derived from a large database of routine general practice data capturing comprehensive information on prescriptions. Matching by age, gender and location removed the effects of these confounders. We were able to study newly incident emotional distress by excluding, from case and control groups, patients with a relevant diagnostic code or treatment in the year before their index date. We used detailed prescribing data to estimate treatment dose and duration and this included two measures of treatment duration - one based on actual dates of issue and one based on the sum of the durations of actual regimens. We found no meaningful difference in duration by these two methods (results available from the authors on request). Our matched control group had an incidence of 0.6% for anxiety/ anxiolytics and 0.8% for depression/antidepressants, which is consistent with other studies (Rait et al, 2009; Martin-Merino et al, 2010). These figures support the validity of our methods and representativeness of the GPs and patients included in the data set.

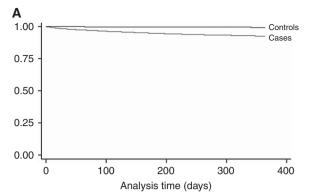
There are several limitations with this study. Firstly, GPs do not record diagnostic codes for all patients they see or treat for common mental disorders. It is possible that GPs saw more patients with emotional distress than were identified by diagnostic codes, particularly patients who did not receive drug treatment. Also, some individuals may have received psychological support from non-general practice providers or organisations. Moreover, in mental health research, diagnoses should be supported by structured clinical interviews, such as the Structured Clinical Interview for DSM-IV (First et al, 1996). Such interviews were

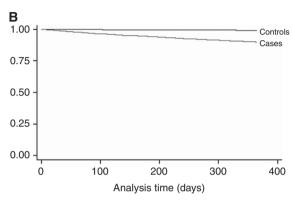
unlikely to have been conducted by GPs. Secondly, while GPs in Scotland issue prescriptions through practice computer systems and the volume of prescribing is reliable, the indication for treatment is not available and can only be inferred. Our data included tricyclic antidepressants, which are commonly (up to 70%) prescribed for non-psychiatric problems such as pain management (Patten et al, 2007; Lockhart and Guthrie, 2011). Some antipsychotics (e.g., prochlorperazine) might also be prescribed for nausea (Roffman and Pirl, 2003). As such, it is likely that our figures overestimate the incidence of drug treatment for emotional distress. Thirdly, we excluded patients with preexisting emotional distress. Therefore, our results may underplay the burden of emotional distress in people with cancer, as a cancer diagnosis may exacerbate underlying psychological morbidity. However, our rates indicate the considerable burden of 'new' emotional distress following a diagnosis of cancer.

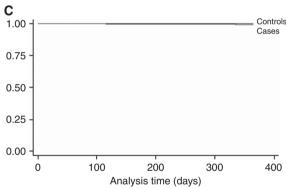
Only very small numbers of newly incident cases or treatment for alcohol-related disorders were identified and no meaningful interpretation could be made of these. Although this study described the cases identified or treated by their GP, it does not include those who were not. Finally, a higher case:control matching ratio (for example, up to 1:5) may have given us slightly higher statistical power compared with the 1:2 ratio achieved. The size of the database population did not permit this.

#### Relationship to other research

Prevalence rates of depression in cancer patients previously reported from cross-sectional studies have been estimated to be up to 40% (Massie, 2004). These increased rates in cancer patients were found irrespective of cancer site (Miovic and Block, 2007). Similar prevalence rates for anxiety have been described in cancer patients. Our findings showed an overall incidence rate of emotional distress of 15.6% (9.8% for depression and 7.4% for anxiety) within 1 year following cancer diagnosis, which was much greater than in the non-cancer population. It appears that GPs are identifying and addressing emotional distress in people with cancer, but no conclusions can be drawn from our data on whether all incident cases were identified. Our results differ from the







**Figure 2** Kaplan–Meier graphs illustrating the proportion of patients at each time in I year after the index date with a first diagnosis and/or prescription for (**A**) anxiety/anxiolytics, for (**B**) depression/antidepressants and for (**C**) alcohol/acamprosate/disulfiram; the time to diagnosis and/or prescription is expressed in days.

case-control study by Khan *et al* (2010), which showed no significant increase of depression and anxiety in those surviving for 5 years after a cancer diagnosis. The longer time since diagnosis used in Khan's study may have obscured rises in emotional distress in the immediate post-diagnostic period which subsequently resolved at the time of data collection. Furthermore, the current study included patients who did not have such a good prognosis (study period covers up to 1 year after cancer diagnosis) as all cancer cases in the study of Khan (survival for at least 5 years).

Table 2 shows a small overlap between diagnostic codes and psychotropic drug prescriptions. The majority of individuals identified with emotional distress received a psychotropic drug prescription without a diagnostic code. This might be due to under-coding of mental health disorders in patients' medical records. Contextual and psychosocial circumstances might

**Table 3** Number of different psychotropic drugs per patient, different psychotropic drug groups taken per patient and users within each drug group taken by patients identified with a diagnosis of emotional distress and with a psychotropic drug prescription in the 6 months after initial diagnosis and/or prescription (n = 1227)

	Cases (n = 1066) % (n)	Controls (n = 161) % (n)	Р
Number of psychotrog	bic drugs		
1	61.8 (659)	80.7 (130)	< 0.001
2	25.1 (268)	17.4 (28)	
3	9.8 (104)	1.9 (3)	
4	26 (2.4)	0 (0)	
5	0.8 (8)	0 (0)	
О	0.1 (1)	0 (0)	
Number of psychotrop	bic drug groups		
1	64.1 (683)	85.1 (137)	< 0.001
2	28.2 (301)	13.7 (22)	
3	7.0 (75)	1.2 (2)	
4	0.7 (7)	0 (0)	
Users within each dru	ig group		
Anxiolytics	46.5 (496)	37.9 (61)	0.040
Hypnotics	22.7 (242)	7.5 (12)	< 0.001
Antidepressants	64.9 (692)	62.7 (101)	0.589
Tricyclic	35.1 (374)	28.6 (46)	0.104
antidepressants	22.5 (257)	2( ( (50)	0.420
Other	33.5 (357)	36.6 (59)	0.430
antidepressants	0.0 (0.4)	(2 (10)	0.268
Antipsychotics Typical	8.8 (94) 8.3 (89)	6.2 (10) 3.1 (5)	0.266
antipsychotics	0.5 (07)	5.1 (5)	0.020
Atypical	0.6 (6)	3.1 (5)	0.009 <sup>a</sup>
antipsychotics	(0)	(0)	-1007
Anti-manic	0.9 (14)	1.1 (2)	1.000°
Anti-alcohol	0 (0)	0.5 (1)	0.131ª

<sup>a</sup>Fisher's Exact test was used instead of  $\chi^2$  due to low numbers in one or more cells. Statistically significant results (P < 0.05) are indicated in bold.

influence a GP's decision to prescribe an antidepressant but not record a diagnostic code for depression. For example, GPs might omit these codes believing significant distress in the face of a cancer diagnosis to be 'normal' despite warranting treatment. Alternatively, codes may be omitted to avoid stigmatising patients or avoid a further diagnostic burden (Rait et al, 2009; Burton et al, 2012). The present data provide evidence that GPs are identifying and managing emotional distress but not always recording it as a diagnosis. In a time of increasing performance review, audit, and guideline-driven care, there is a need for universal diagnostic coding of all encounters. Our data suggests that the fixed terms available within the READ V2 hierarchy may not always fit the requirements of GPs in recording details of a consultation. Clinicians may prefer free text (not assessed during this study) or perhaps new codes appropriate to the cancer context should be created?

Patients at later stages of cancer, who have more physical symptoms or at specific times during their trajectory (such as diagnosis, suspicious symptoms and beginning and starting treatment) are at increased risk of distress (Madden, 2006). The steady development of emotional distress throughout the first year following diagnosis described in our study might be explained by our heterogeneous sample with respect to cancer site, disease stage and treatment.

The duration of anxiolytic prescriptions followed the clinical guideline to use benzodiazepines for short term relief (2-4 weeks only) (NICE, 2011). The drug group 'hypnotics' are not licensed for long-term use but the median of 55 days (8 weeks) of use among cases tended to exceed guideline recommendations of a

**Epidemiology** 



 Table 4
 Volume of prescribing (expressed as total DDD of all prescriptions) and duration of treatment by drug class in the 6-month follow-up period

	n		DDD <sup>a</sup> (median (IQR))		Duration <sup>b</sup> (median (IQR))			
	Cases	Controls	Cases	Controls	P	Cases	Controls	P
Anxiolytics	496	61	11.2(5.6–21.8)	6.0 (3.1–14.0)	0.017	28.0 (14.0–64.8)	18.7 (9.2–30.3)	0.002
Hypnotics	242	12	28.0 (14.0–84.0)	49.0 (16.8–80.5)	0.777	55.5 (28.0–131.8)	64.5 (28.0–159.3)	0.773
Antidepressants	692	101	30.0 (14.0–86.0)	28.0 (14.0–87.0)	0.695	64.5 (30.0–168.0)	60.0 (28.0–155.5)	0.361
Tricyclic antidepressants	374	46	14.0 (7.5–35.5)	12.7 (4.7–26.1)	0.230	60.0 (30–145.3)	58.00 (29.5-129.8)	0.905
Other antidepressants	357	59	56.0 (28.0–168.0)	56.0 (28.0–135.0)	0.487	77.0 (30.0–181.5)	78.0 (28.0–167.0)	0.527
Antipsychotics	94	10	4.7 (2.0–10.5)	15.8 (4.1–80.9)	0.041	28.0 (15.0–56.0)	82.5 (52.0–162.8)	0.003
Typical antipsychotics	89	5	4.7 (1.9–10.0)	5.3 (2.8–95.3)	0.404	42.0 (28.0-84.0)	111.0 (56.0–211.0)	0.062
Atypical antipsychotics	6	5	50.0 (3.5–325.5)	42.0 (6.4–149.1)	0.784	69.5 (49.0–215.3)	141.0 (80.5–196.0)	0.314
Anti-manic	14	2	11.6 (5.6–59.5)	56.0 (22.4)	0.426	56.0 (42.3–137.5)	97.0 (56.0)	0.628
Anti-alcohol	0	1	_	28.0	_	_	98.0	-

Abbreviations: IQR = inter quartile range; DDD = defined daily dose. <sup>a</sup>For each prescription the strength, the dosing and the frequency were used to estimate the daily dose. Estimated daily doses were translated into DDD using the WHO standard doses (WHO, 2010). <sup>b</sup>Duration was based on the calculation of the number of days between issue date of first and last prescription, and added with the duration of the last prescription, in days. Statistically significant results (P < 0.05) are indicated in bold.

few (2-4) weeks (2010). Clinical guidelines recommend the use of antidepressants for 6 months after remission of depression (NICE, 2009). The median duration of antidepressant prescribing in this study was 2 months. The number of patients with anti-manic and anti-alcohol medicines was too low to draw any conclusions.

#### Implications for practice, policy and research

The small overlap of diagnostic coding with psychotropic prescribing and the shorter antidepressant treatment duration than that recommended in clinical guidelines might possibly point towards under-recognition and/or under-treatment of major depressive disorders in this patient population. The absence of a clear temporal pattern of incident emotional distress in the cancer trajectory indicates a need for clinician vigilance throughout the first year from diagnosis. All health professionals, in primary and secondary care, should be alert to emotional distress in patients with cancer and ensure psychological health is discussed and treated. Specific reference to the management of emotional distress should be incorporated into follow-up guidelines for cancer management.

Policy makers should address the need for improved coding of diagnosis and management of emotional distress in newly diagnosed cancer patients. While retaining an option for free text for clinical purposes, GPs might be encouraged to use a flexible coding system in which symptom codes for distress, such as low mood, are used until patients clearly meet criteria for a major depressive disorder. Another alternative would be to include a code such as 'distress related to cancer diagnosis'.

Further research is needed to explain the small overlap between mental health diagnostic codes and psychotropic prescriptions and the lower use of mental health diagnostic codes in general. Data linkage with secondary care systems would provide more comprehensive information about mental health service use by cancer patients. Moreover, studying the patient perspective in identifying and managing emotional distress after cancer diagnosis would enable these current results to be put in context. Finally, larger numbers of patients would be needed to study the extent of excessive alcohol use in this population.

#### CONCLUSIONS

Cancer patients are at substantially higher risk of emotional distress in the year following their cancer diagnosis. The pharmacological treatment of emotional distress in primary care tends to involve low doses of short duration. Incidence of emotional distress was evenly spread throughout the year after diagnosis with no time of particular vulnerability. Clinicians should be vigilant for emotional distress in patients during the first year following cancer diagnosis.

# **ACKNOWLEDGEMENTS**

We would like to thank Fiona Chaloner and Katie Wilde for extracting the database. The data contained herein were provided by the Primary Care Clinical Informatics Unit (http://www.abdn. ac.uk/pcciu/PCCIU.htm) at the University of Aberdeen. The views in this publication are not necessarily the views of the University of Aberdeen, its agents, or employees. Dr Amalraj Raja is thanked for the statistical support. Franciska Desplenter received a travel grant from the KU Leuven 'Fonds Apotheker en Mevrouw Ysebaert-Devos' for the period January–March 2011 and from FWO Vlaanderen (Reference V4.248.11N) for the period April-December 2011.

#### **REFERENCES**

Bringmann H, Singer S, Hockel M, Stolzenburg JU, Krauss O, Schwarz R (2008) Long-term course of psychiatric disorders in cancer patients: a pilot study. *Psychosoc Med* 5: Doc03

Burton C, Anderson N, Wilde K, Simpson C (2012) Factors associated with duration of new antidepressant treatment: a large database study. Br J Gen Pract 62: e104-e112 Cancer Research UK (CRUK) Cancer incidence for common cancers: UK statistics. http://info.cancerresearchuk.org/cancerstats/incidence/commoncancers/. Last updated on 21 April 2011. Last accessed on 4 January 2012

Cox DR (1972) Regression models and life-tables. J Roy Statist Soc Ser B (Methodological) 34(2): 187-220



- Deshields TL, Nanna SK (2010) Providing care for the 'whole patient' in the cancer setting: the psycho-oncology consultation model of patient care. J Clin Psychol Med Settings 17(3): 249-257
- First MB, Spitzer RL, Gibbon M, Williams JBW (1996) Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version (SCID-CV). American Psychiatric Press, Inc: Washington D.C.
- Hansen F, Sawatzky JA (2008) Stress in patients with lung cancer: a human response to illness. Oncol Nurs Forum 35(2): 217-223
- Hodges L, Butcher I, Kleiboer A, McHugh G, Murray G, Walker J, Wilson R, Sharpe M (2009) Patient and general practitioner preferences for the treatment of depression in patients with cancer: how, who, and where? J Psychosom Res 67(5): 399-402
- Holland JC, Alici Y (2010) Management of distress in cancer patients. J Support Oncol 8(1): 4-12
- Khan NF, Ward AM, Watson E, Rose PW (2010) Consulting and prescribing behaviour for anxiety and depression in long-term survivors of cancer in the UK. Eur J Cancer 46(18): 3339-3344
- Lewis RA, Neal RD, Williams NH, France B, Hendry M, Russell D, Hughes DA, Russell I, Stuart NS, Weller D, Wilkinson C (2009) Follow-up of cancer in primary care versus secondary care: systematic review. Br I Gen Pract 59(564): e234-e247
- Lockhart P, Guthrie B (2011) Trends in primary care antidepressant prescribing 1995-2007: a longitudinal population database analysis. Br J Gen Pract 61(590): e565-e572
- Madden J (2006) The problem of distress in patients with cancer: more effective assessment. Clin J Oncol Nurs 10(5): 615-619
- Martin-Merino E, Ruigomez A, Wallander MA, Johansson S, Garcia-Rodriguez LA (2010) Prevalence, incidence, morbidity and treatment patterns in a cohort of patients diagnosed with anxiety in UK primary care. Fam Pract 27(1): 9-16
- Massie MJ (2004) Prevalence of depression in patients with cancer. J Natl Cancer Inst Monogr 32: 57-71
- Miovic M, Block S (2007) Psychiatric disorders in advanced cancer. Cancer 110(8): 1665-1676
- Morris R, Carstairs V (1991) Which deprivation? A comparison of selected deprivation indexes. J Public Health Med 13(4): 318-326
- Munoz-Arroyo R, Sutton M, Morrison J (2006) Exploring potential explanations for the increase in antidepressant prescribing in Scotland using secondary analyses of routine data. Br J Gen Pract 56(527): 423-428

- NICE (2009) National Clinical Practice Guideline 91: Depression in adults with a chronic physical health problem: treatment and management
- NICE (2011) National Clinical Guideline 113: Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults
- Office of the Chief Statistician (2006) Scottish Index of Multiple Deprivation 2006: General Report. Scottish Executive: Edinburgh
- Patten SB, Esposito E, Carter B (2007) Reasons for antidepressant prescriptions in Canada. Pharmacoepidemiol Drug Saf 16(7): 746-752
- Rait G, Walters K, Griffin M, Buszewicz M, Petersen I, Nazareth I (2009) Recent trends in the incidence of recorded depression in primary care. Br J Psychiatry 195(6): 520-524
- Roffman JL, Pirl WF (2003) Use of antipsychotic medication in chemotherapy-induced nausea and vomiting. Expert Rev Neurother 3(1): 77-84
- Roy-Byrne PP, Davidson KW, Kessler RC, Asmundson GJ, Goodwin RD, Kubzansky L, Lydiard RB, Massie MJ, Katon W, Laden SK, Stein MB (2008) Anxiety disorders and comorbid medical illness. Gen Hosp Psychiatry 30(3): 208
- Sharpe M, Strong V, Allen K, Rush R, Postma K, Tulloh A, Maguire P, House A, Ramirez A, Cull A (2004) Major depression in outpatients attending a regional cancer centre: screening and unmet treatment needs. Br J Cancer 90(2): 314-320
- Strong V, Waters R, Hibberd C, Murray G, Wall L, Walker J, McHugh G, Walker A, Sharpe M (2008) Management of depression for people with cancer (SMaRT oncology 1): a randomised trial. Lancet 372(9632): 40-48
- The British Medical Association and the Royal Pharmaceutical Society (2010) British National Formulary (BNF) 59. Pharmaceutical Press: London
- Vahdaninia M, Omidvari S, Montazeri A (2010) What do predict anxiety and depression in breast cancer patients? A follow-up study. Soc Psychiatry Psychiatr Epidemiol 45(3): 355-361
- Wein S, Sulkes A, Stemmer S (2010) The oncologist's role in managing depression, anxiety, and demoralization with advanced cancer. Cancer J 16(5): 493-499
- WHO (2010) Anatomical Therapeutic Chemical classification -Defined Daily Doses Index 2011. http://www.whocc.no/atc\_ddd\_index/ (last accessed on 25 May 2011)
- Yung KC, Piccirillo JF (2008) The incidence and impact of comorbidity diagnosed after the onset of head and neck cancer. Arch Otolaryngol Head Neck Surg 134(10): 1045-1049

This work is published under the standard license to publish agreement. After 12 months the work will become freely available and the license terms will switch to a Creative Commons Attribution-NonCommercial-Share Alike 3.0 Unported License.