BJPsych | The British Journal of Psychiatry (2020) 217, 427–433. doi: 10.1192/bjp.2019.211

Extent of disease at first cancer presentation and previous anxiety and depressive symptoms: the HUNT study

Robert Stewart, Sophie Dorothea Fosså, Matthew Hotopf and Arnstein Mykletun

Background

Depressive symptoms are associated with higher cancer mortality, whereas anxiety symptoms are associated with lower than expected risk.

Aims

This study aimed to investigate the prospective association between depressive/anxiety symptoms and the extent of disease (EOD) of first cancer at diagnosis.

Method

Prospective population-based study conducted from the second wave of the Nord-Trøndelag Health (HUNT) study. Of 65 000 residents comprehensively interviewed and examined for health status, 407 received first lifetime cancer diagnoses 1–3 years later, ascertained from the Cancer Registry of Norway, and had EOD recorded. Patients with localised disease or regional/distant spread at cancer diagnosis were analysed for earlier depressive/anxiety symptoms ascertained by the Hospital Anxiety and Depression Scale in HUNT.

Results

Beyond-local EOD was present in 59.8% of those with neither anxiety nor depression, in 76.6% of those with depression alone (odds ratio, 2.20; 1.08–4.49), in 39.3% of those with anxiety alone (odds ratio, 0.44; 0.20–0.96) and in 57.7% of those with both anxiety and depression (odds ratio, 0.92; 0.41–2.06). After adjustment for demographic and health status, and cancer type, these associations were marginally stronger, but no longer statistically significant (odds ratios, 2.26; 0.84–6.11; 0.43; 0.15–1.26; and 1.00; 0.98–1.03, respectively).

Conclusions

In people who develop cancer, beyond-local EOD at diagnosis was more common in people with previous depression and less common in people with previous anxiety; however, independence from confounding factors could not be concluded.

Keywords

Depressive disorders; anxiety disorders; comorbidity; mortality; first cancer presentation.

Mental disorders contribute substantially to all-cause mortality.[1] However, the mechanisms underlying these associations remain unclear. Historically, research has prioritised depression and cardiovascular mortality, although similar associations have been found for other disorders such as schizophrenia[2] and bipolar disorder.[3] Furthermore, depressive symptoms have been found to be associated with an increased risk of a range of causes of death, and strengths of association with cancer mortality are as strong as those with cardiovascular mortality.[4] Treating comorbid psychiatric conditions may improve the likelihood of cancer survival[5] because depression has been specifically associated with decreased overall survival after cancer diagnosis, although anxiety symptoms may be associated with increased survival.[6] These symptoms might modify help-seeking behaviours and other lifestyle factors that subsequently influence time to detection and diagnosis; this would account for mortality associations because cancer survival is strongly associated with extent of disease (EOD) at diagnosis.

Investigations of the association between mental disorder and cancer presentation present substantial logistic and methodological challenges primarily because obtaining sufficient numbers of people with both disorders requires a large source sample. Most studies have relied on retrospective evaluation of prior mental health in people who have received a cancer diagnosis,[7–11] with high potential for recall bias. The few studies with previously recorded data on mental health have relied on primary care records[12] or on relatively restrictive diagnostic criteria,[13] both of which may underestimate morbidity. We sought to overcome these difficulties through carrying out a record linkage between a large cross-sectional survey whose participants had been systematically screened for anxiety and depressive symptoms, and a national cancer registry with information on EOD at diagnosis. Our hypothesis, given earlier mortality findings, was that beyond-local EOD at cancer diagnosis would be associated positively with previous depression, would be negatively associated with previous anxiety and would show no elevation or reduction in people with both states.

Method

The Cancer Registry of Norway (CRN; www.kreftregisteret.no) was established in 1951 and, from that point onward, all hospitals, laboratories of pathology and general practitioners (GPs) have been legally required to report neoplasms to the CRN.[14] The CRN discriminates between pre-malignant and malignant tumours, classifying diagnoses according to the ICD-7[15] system as well as coding the EOD at diagnosis (as local, regional, distant or unknown). Beyond prevention efforts, these screening programmes gather data about incidence and mortality. The analysis described here was carried out by linking the CRN database with the second Health Study of Nord-Trøndelag County (HUNT-2). HUNT-2 has been described in detail previously;[16] however, in summary it was a cross-sectional survey carried out between 1995 and 1997 of adult residents in one of Norway's 19 counties, containing 3% of the national population. Based on updated population register lists, all inhabitants ($N = 93\,138$) in Nord-Trøndelag County aged ≥20 years received a mailed questionnaire and were invited to a clinical examination, resulting in 65 648 participants (71% response rate). The clinical examination was wide-ranging, including biometric measurements and blood assays, as well as the administration of the Hospital Anxiety and Depression Scale (HADS) described below. At the time of the survey, the population of Nord-Trøndelag County was relatively rural and stable with a net migration of 0.3% per year, and also relatively homogenous with less

https://doi.org/10.1192/bjp.2019.211 Published online by Cambridge University Press

than 3% of the population identifying as non-White. Non-responders were younger and more likely to be male than participants.[16]

The linked database comprised first CRN registrations after the time of the HUNT-2 survey (i.e. those with prior registrations were not included). For solid (i.e. rather than haematological) malignant tumours the EOD at diagnosis is, at the CRN, categorised as local (within the organ), loco-regional (spread outside the organ limits or regional metastases) and distant metastases. For this analysis, EOD was defined as a binary dependent variable: local EOD and beyond-local EOD. After initial descriptive analyses, unknown or missing EOD at diagnosis was considered as an exclusion criterion; haematological cancers were not included because of EOD non-applicability. Basal cell skin carcinoma was also excluded in accordance with standard practice for CRN output, on the basis that beyond-local spread is not a feature of this condition.

The HADS is a self-report questionnaire comprising 14 four-point items (seven for anxiety symptoms (HADS-A) and seven for depressive symptoms (HADS-D)) enquiring about symptoms during the past week.[17] The scale has been widely used and was specifically developed to detect anxiety and depressive symptoms in the context of somatic illness (hence, omitting somatic items, sleeping difficulties or appetite disturbance), with good case-finding properties in primary care and hospital settings (a cut-off score of 8 on each subscale found to give an optimal balance between sensitivity and specificity, both at about 0.80, for depression and anxiety diagnoses).[18] For brevity, case-level anxiety symptoms and depressive symptoms are hereafter referred to as 'anxiety' and 'depression', respectively. As in previous analyses using this measure and these cut-off points, three groups were identified: anxiety only, depression only and comorbid anxiety and depression. All three were compared separately to a fourth reference group with no disorder.[19]

Specific covariates were chosen *a priori* from the source databases as potential confounders because they were known to be associated with common mental disorder symptoms and also had at least a potential influence on pathways to cancer presentation and diagnosis. These comprised the following: demographic factors of age, gender and education (categorised into three groups: compulsory only, college level and university level); smoking status (binary variable: current smoker or not), applied as a covariate as an indicator of health risk behaviour; living alone (binary variable), applied as a covariate assuming that participants with more social support might present at an earlier stage; level of physical health, quantified by number of self-reported conditions (angina pectoris, asthma, diabetes, epilepsy, hypertension, myocardial infarction, musculoskeletal disorder, respiratory disease, stroke and thyroid disease); type of first lifetime cancer (ICD-7 codes), as recorded by the CRN between 12–36 months after the HUNT-2 survey (type of cancer was considered as a covariate in this analysis on the basis that it is a strong determinant of EOD and that there is some evidence for associations between mental disorders and certain cancer types);[20,21] and finally, reported recent (during the past 12 months) physician contact before the HUNT-2 survey was available on a slightly smaller sample and was entered as a covariate in exploratory secondary analyses as it could potentially represent a factor lying on the causal pathway between mental state in HUNT-2 and cancer EOD at subsequent diagnosis (assuming that individuals in more regular physician contact may be more likely to receive an earlier diagnosis).

Statistical analysis

Statistical analyses were carried out using SPSS version 17.0 for Windows. The analysed sample was restricted *a priori* to HUNT-2 participants who had received a cancer diagnosis within 1–3 years of participation, having had no previous cancer diagnosis. Diagnoses within 1 year were excluded because of the possibility that some common mental disorder symptoms might be early manifestations of the cancer itself. Diagnoses beyond 3 years were excluded because of the diminishing likelihood that common mental disorder symptoms recorded at HUNT-2 participation would reflect symptoms around the time between first manifestations of cancer and diagnosis. Sample size was determined simply by the overlap between the two data-sets. After description of the sample, associations between case-level anxiety or depression and beyond-local EOD at cancer diagnosis (restricting to the subsample with data on EOD) were investigated in unadjusted analyses followed by logistic regression models to assess the influence of potential confounding factors. As stated above, adjustment for recent GP contact was treated as an exploratory secondary analysis. Statistical significance was set at $P < 0.05$.

Ethical approval

HUNT and the current project were approved by the National Data Inspectorate and the Board of Research Ethics in Health Region Midt-Norge of Norway (reference number 4.2008.2489). All individuals gave their written informed consent upon HUNT participation.

Results

In total, 681 first lifetime cancer diagnoses were made in HUNT-2 participants between 1–3 years after the time of participation. EOD at diagnosis was recorded in 459; of these, 407 (59.8% of the 681) had data on HADS subscales, comprising the analysed sample. Participants with missing HADS data were older (mean difference, 9.1 years; 95% CI 5.2–13.0 years) and had lower education (odds ratio across three education groups, 0.16; 0.06–0.43). However, they did not differ substantially with respect to gender (odds ratio for female gender, 1.60; 0.90–2.88), living alone (odds ratio, 0.67; 0.40–1.11), current smoking at the time of HUNT-2 participation (odds ratio, 0.68; 0.34–1.37), number of non-malignant disorders (odds ratio across four groups, 1.05; 0.80–1.37) or recent GP contact at HUNT-2 participation (odds ratio, 0.71; 0.37–1.36). They were also not significantly different with respect to beyond-local EOD of cancer at diagnosis (odds ratio, 1.15; 0.63–2.09). Proportions with missing data on EOD are summarised for the most common cancer types in the first column of Table 1. Missing EOD was associated with younger age (mean difference, −2.1 years; −3.5 to −0.6) and marginally with female gender (odds ratio, 1.17; 0.98–1.38), higher education (odds ratio across three groups, 1.11; 0.99–1.24) and negatively with living alone (odds ratio, 0.84; 0.70–1.00), but was not associated with smoking (odds ratio, 1.02; 0.86–1.24), number of non-malignant disorders (odds ratio across four groups, 1.04; 0.96–1.14) or recent GP contact (odds ratio, 1.03; 0.82–1.28). There were no associations between case-level anxiety or depression on the HADS and missing information on EOD (odds ratios compared with those with no disorder: 0.73 (95% CI 0.41–1.31) for depression alone, 1.22 (0.65–2.30) for anxiety alone and 1.00 (0.50–2.01) for both anxiety and depression).

Characteristics of the 407 participants in the analysed sample are summarised in Table 1 with respect to cancer diagnosis and EOD. Beyond-local EOD of cancer at diagnosis was present in 245 participants (60.2%) and was only significantly associated with current smoking (Table 2). Descriptive data on covariates are summarised for HADS case categories in Table 3.

Of the 407 participants analysed, 306 (75.2%) had no case-level anxiety or depression at HUNT-2 participation, 47 (11.5%) had depression alone, 28 (6.9%) had anxiety alone and 26 (6.4%) had both. Beyond-local EOD at cancer diagnosis was present in 59.8%, 76.6%, 39.3% and 57.7% of these four groups, respectively (Fig. 1). Associations between these groups and EOD were

https://doi.org/10.1192/bjp.2019.211 Published online by Cambridge University Press

Table 1 EOD at diagnosis in new cancer cases within 1–3 years after HUNT-2 participation[a]

ICD-7 diagnosis	Unknown EOD (%)	Number with known EOD (% of the total)	EOD (%)		
			Localised	Locally advanced/regional metastasis	Distant metastasis
151.00 gastric	34.8	15 (3.7)	20.0	46.7	33.3
153.00 colon	11.1	64 (15.7)	10.9	50.0	39.1
154.00 rectal	8.0	23 (5.7)	30.4	56.5	13.0
157.00 pancreas	61.5	5 (1.2)	0.0	20.0	80.0
162.00 lung	28.6	40 (9.8)	17.5	35.0	47.5
170.00 breast	26.3	59 (14.5)	49.2	47.5	3.4
172.00 endometrial	0.0	13 (3.2)	61.5	23.1	15.4
175.00 ovarian	5.6	17 (4.2)	35.3	0.0	64.7
177.00 prostatic	44.9	59 (14.5)	54.2	3.4	42.4
180.00 renal	33.3	8 (2.0)	37.5	12.5	50.0
181.00 bladder	48.0	13 (3.2)	92.3	7.7	0.0
190.00 skin (melanoma)	23.5	13 (3.2)	92.3	0.0	7.7
191.00 skin (squamous cell)	26.7	11 (2.7)	100.0	0.0	0.0
199.00 unknown primary	6.3	15 (3.7)	0.0	6.7	93.3
Other	54.4	52 (12.8)	48.1	34.6	17.3
Total	32.8	407 (100)	39.8	29.7	30.5

EOD, extent of disease; HUNT-2, second Health Study of Nord-Trøndelag County.
a. All analyses restricted to participants with Hospital Anxiety and Depression Scale data recorded in HUNT-2 and with a first cancer registration 1–3 years later ($N = 606$, when including participants with unknown EOD).

investigated through logistic regression models, the results of which are displayed in Table 4. In summary, adjustment for covariates made little difference to odds ratios for the associations of interest, slightly strengthening those for depression alone and weakening slightly those for anxiety alone. Negative associations with anxiety alone fell below statistical significance in most adjusted models, whereas those for depression alone retained significance in most models; however, confidence intervals for the latter overlapped the null value in the final *a priori* model, which included cancer type as a covariate. Associations for both anxiety and depression (compared with neither) were close to null values in all models. Further addition of recent GP contact to model 6 in 373 participants with data on this variable gave rise to odds ratios of 2.43 (CI 1.13–5.23) for depression only, 0.50 (0.21–1.20) for anxiety only and 0.86 (0.34–2.15) for anxiety and depression.

Discussion

Linking data from a large cross-sectional survey and a national cancer registry, we investigated the association between EOD at first cancer diagnosis and previous symptoms of anxiety and depression. In summary, beyond-local EOD at diagnosis was more likely in participants with previous depressive symptoms and less likely in those with previous anxiety symptoms, supporting our hypothesis. Both associations were marginally stronger in fully adjusted models than in unadjusted, but confidence intervals also widened, and associations were no longer statistically significant according to conventional norms. Where depressive and anxiety symptoms were both present, there was no significant difference in EOD at cancer diagnosis compared with those with no case-level symptoms.

The influence of mental health on mortality and morbidity from other disorders is increasingly recognised,[1] and there is a growing awareness that the public health effect of mental disorders may be underestimated. Effects of depression on diagnosis and treatment are potential pathways underlying associations with risk of death from cancer. However, associations with EOD at diagnosis have received relatively little research. Prasad *et al* found that men with depression and an intermediate- or high-risk prostate cancer were less likely to undergo treatment.[22] This also appears to be the case where depression is pre-existing before receiving a cancer diagnosis.[23] Timing of diagnosis is an important factor predicting cancer

Table 2 Characteristics of the analysed sample[a] and associations with beyond-local EOD at cancer diagnosis

Characteristic recorded at HUNT-2	Total ($n = 407$)	Beyond-local EOD at diagnosis 1–3 years later		Odds ratio or mean difference
		No ($n = 162$)	Yes ($n = 245$)	
Mean (s.d.) age, years	64.0 (13.9)	62.4 (15.0)	65.0 (13.0)	2.58 (–1.67 to 5.33)
Gender, % female	45.9	46.3	45.7	0.98 (0.66–1.46)
Education, %				
Compulsory only	60.7	54.3	64.9	1.00 (reference)
College level	28.3	32.1	25.7	0.67 (0.43–1.05)
University level	11..1	13.6	9.4	0.36 (0.31–1.10)
Current smoker, %	28.3	21.0	33.1	1.86 (1.17–2.95)
Living alone, %	19.7	22.2	18.2	0.77 (0.47–1.26)
Number of non-malignant disorders, %[b]				
0	50..4	50.0	50.6	1.00 (reference)
1	28..3	28.4	28.2	0.98 (0.62–1.56)
2	12..0	12.3	11.8	0.95 (0.50–1.79)
3+	9..3	9.3	9.4	1.00 (0.49–2.03)
Recent prior-survey contact with GP, %[c]	69.8	74.0	77.5	1.21 (0.75–1.97)

EOD, extent of disease; HUNT-2, second Health Study of Nord-Trøndelag County.
a. Restricted to participants with Hospital Anxiety and Depression Scale data present at HUNT-2 and a first cancer registration 1–3 years later.
b. Angina pectoris, asthma, diabetes, epilepsy, hypertension, myocardial infarction, musculoskeletal disorder, respiratory disease, stroke and thyroid disease.
c. N=373 with data on this item.

https://doi.org/10.1192/bjp.2019.211 Published online by Cambridge University Press

Table 3 Characteristics of the analysed sample[a] according to previous anxiety and depression status

Characteristic recorded at HUNT-2	Depression/anxiety caseness according to HADS scores at HUNT-2			
	Neither (*n* = 306)	Depression only (*n* = 47)	Anxiety only (*n* = 28)	Both (*n* = 26)
Mean (s.d.) age, years	63.3 (13.8)	70.1 (10.7)	59.1 (15.3)	66.0 (15.3)
Gender, % female	48.0	25.5	50.0	53.8
Education, %				
Compulsory only	57.5	72.3	57.1	80.8
College level	30.1	25.5	25.0	15.4
University level	12.4	2.1	17.9	3.8
Current smoker, %	30.4	17.0	25.0	26.9
Living alone, %	80.4	87.2	75.0	73.1
Number of non-malignant disorders[b]				
0	55.2	38.3	42.9	23.1
1	27.5	42.6	21.4	23.1
2	10.8	6.4	17.9	30.8
3+	6.5	12.8	17.9	26.9
Recent contact with GP[c]	75.4	77.8	87.5	69.6

EOD, extent of disease; HUNT-2, second Health Study of Nord-Trøndelag County; HADS, Hospital Anxiety and Depression Scale.
a. Restricted to participants with HADS data present at HUNT-2 and a first cancer registration 1–3 years later.
b. Angina pectoris, asthma, diabetes, epilepsy, hypertension, myocardial infarction, musculoskeletal disorder, respiratory disease, stroke and thyroid disease.
c. *N* = 373 with data on this item.

survival and is determined by both characteristics of the person with cancer (in terms of help-seeking behaviour and time taken to presentation) and characteristics of the healthcare provider (in terms of promptness of investigation, diagnosis and treatment after presentation).[24] In a review of studies of breast cancer specifically, characteristics of the symptoms and personal attributions of these were found to influence delay in presentation, as well as some demographic predictors.[25] The role of mental disorders in predicting delay in presentation has received relatively little attention. Low trait anxiety was found to be associated with delayed presentation of rectal cancer,[7] particularly in men.[8] In contrast, other studies have found no association between delayed presentation of breast cancer and previous mood disorders, adverse life events[9] or previous psychological treatment.[11] However, all these studies have relied on retrospective evaluation of mental health, which is likely to be biased in people who have received a cancer diagnosis.

As far as we are aware, only two previous studies have used data on mental health collected before cancer diagnosis. One of these found associations with both previous anxiety/depressive symptoms/disorders recorded on primary care records and longer time from presentation to treatment in people with colorectal cancer.[12] The other study investigated a small sample women with breast cancer who had previously been screened for mental disorder in a large community survey and found that major depression was associated with a higher risk of late-stage diagnosis, whereas phobia was associated with a lower risk of late-stage diagnosis.[13] In our study, case-level anxiety was, if anything, associated with an earlier stage of cancer presentation, although it was not statistically significant in some of the adjusted model and there was no evidence in any model of a risk association; however, comparability with previous findings is limited because we were not able to examine colorectal cancer specifically with adequate power (unlike the primary care

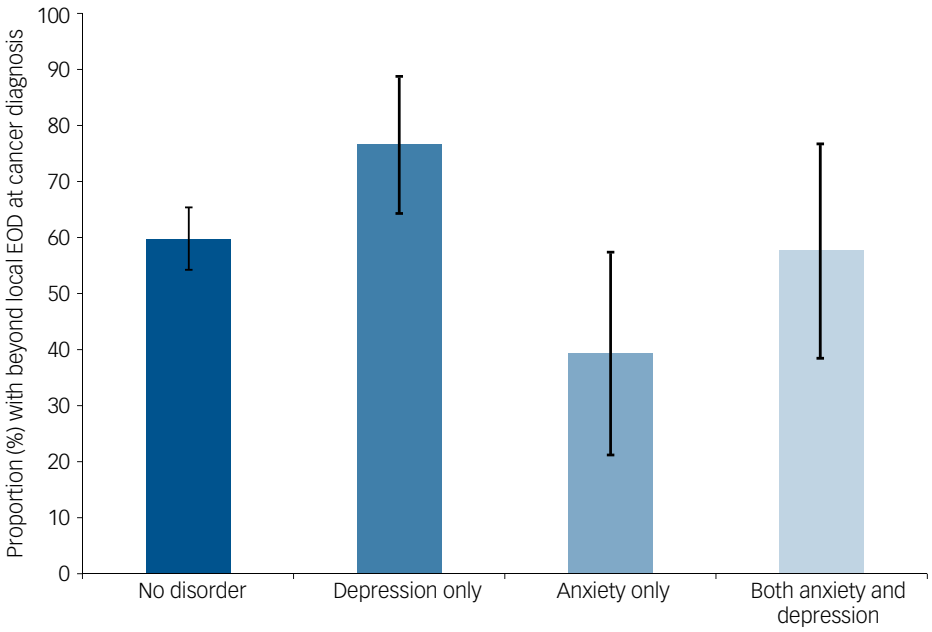

Fig. 1 Proportion (%) of sample with beyond-local extent of disease (EOD) at first cancer diagnosis according to anxiety and/or depression caseness 1–3 years previously.

https://doi.org/10.1192/bjp.2019.211 Published online by Cambridge University Press

Table 4 Logistic regression analysis of associations between HADS case category and EOD at subsequent cancer diagnosis[a]

Covariates included	Association with beyond-local EOD at presentation (odds ratio, adjusted for age)		
	Depression only	Anxiety only	Both
All incident cancer ($n = 407$)			
Unadjusted	2.20 (1.08–4.49)	0.44 (0.20–0.96)	0.92 (0.41–2.06)
1. Age	2.06 (1.00–4.23)	0.45 (0.20–1.00)	0.89 (0.40–2.01)
2. Model 1 + gender	2.09 (1.01–4.32)	0.45 (0.20–1.00)	0.89 (0.39–2.00)
3. Model 2 + education[b]	2.01 (0.97–4.17)	0.44 (0.20–0.99)	0.83 (0.36–1.88)
4. Model 3 + current smoking status[c]	2.21 (1.06–4.62)	0.46 (0.20–1.03)	0.84 (0.36–1.92)
5. Model 4 + living alone	2.21 (1.06–4.61)	0.46 (0.20–1.04)	0.84 (0.37–1.94)
6. Model 5 + number of disorders[b]	2.22 (1.06–4.64)	0.48 (0.21–1.08)	0.90 (0.38–2.12)
7. Model 6 + cancer type[d]	2.26 (0.84–6.11)	0.43 (0.15–1.26)	1.00 (0.98–1.03)

EOD, extent of disease; HADS, Hospital Anxiety and Depression Scale; HUNT-2, second Health Study of Nord-Trøndelag County.
a. Restricting analysis to a lag time of 1–3 years between HUNT-2 and first cancer diagnosis.
b. Entered as ordinal variables, using the categories described in Table 2.
c. Entered as a binary variable (current smoking or not at the time of HUNT-2 participation).
d. As categorised in Table 1.

study[12]), and anxiety symptoms measured on the HADS instrument tend toward those of generalised anxiety and panic disorder, rather than phobia (unlike the community survey[13]). Case-level depressive symptoms were associated with a higher likelihood of beyond-local EOD to a significant extent in most adjustment models and are thus more consistent with both previous studies, although this could not be demonstrated at statistical significance in the final model, potentially because of insufficient statistical power and/or overfitted covariates. Our conclusion is therefore that it lends support to the study hypothesis, but not to a conclusive extent.

The mechanisms underlying our findings may be complex and multiple. Delay in time of cancer diagnosis (for which EOD was used in our study as a proxy measure) has been divided conceptually into 'patient' and 'provider' sources, with further subdivision of the former into 'appraisal', 'illness' and 'behavioural' delay, and the latter into 'scheduling' and 'treatment' delays.[24] Considering 'patient' sources, it is possible that depressive syndromes reduce the likelihood or help-seeking (or attendance at a screening programme) for a known early symptom of cancer and that anxiety syndromes increase this. It has been proposed that there is a 'normal' response of minimisation during the period of symptom self-appraisal, which may be attenuated in high-anxiety states[7] and could conceivably be exaggerated in depression (or alternatively the normal help-seeking response to a concerning symptom could be inhibited by depressed mood, compounded by accompanying symptoms of poor motivation, guilt, feelings of not being worthy of care and/or nihilism about the future). Consistent with this, a study of presentations to a breast clinic regardless of diagnosis found that higher psychological morbidity was associated with delayed presentation, and that individuals who were least anxious about their symptoms also delayed seeking help.[10] It is also possible that an individual's symptom profile may influence physician behaviour; for example, a higher likelihood of referral for further investigation in people who report a given symptom in the context of co-occurring anxiety symptoms and a lower likelihood in those with depressive symptoms. However, our analysis was not designed to investigate these processes in depth and further research is required to identify the most appropriate point of intervention. Of note, an analysis of a large mental healthcare database linked to a cancer registry in south London found no differences in EOD at presentation in people with a range of mental disorders, including depressive and anxiety disorders and those not known to mental healthcare at the time of cancer diagnosis; however, post-diagnosis mortality remained raised in many disorder groups, including depressive disorder, and these associations were independent of EOD at presentation.[26] This suggests that inequalities in care persist after diagnosis, although the extent to which these are accounted for by patient or provider sources remains to be determined. Although no association was found between depressive disorder and EOD at cancer diagnosis in that study, the findings are not necessarily comparable with our own because a diagnosis of depression implies a level of service access that is unlikely to be attained by a community sample screening positive for depressive symptoms.

The negative age-adjusted association between anxiety symptoms in our analysis and EOD at cancer diagnosis is interesting in that the effect, if present, appears to be opposite to that of depression. It is also consistent with previous analyses of mortality data from HUNT-2, where anxiety (identically defined) was found to have a relatively protective effect compared with the risk effect associated with depression.[27] As mentioned, one possible explanation is that people with anxiety who experience early symptoms of cancer are more likely to seek medical help/investigation and/or that GPs are more likely to investigate these symptoms in someone with anxiety. Supporting this, people with case-level anxiety in HUNT-2 reported higher levels of recent GP contact; however, there was no marked association observed between that level of contact and EOD at cancer presentation 1–3 years later. On the other hand, the association was weakened and fell below statistical significance levels following adjustments for other risk factors such as smoking and comorbidity, so at least part of the explanation may lie in healthier lifestyles adopted by people with anxiety, which themselves might correlate with higher likelihood of help-seeking.

Our analysis had the advantage of a very large survey data-set in which anxiety and depressive symptoms were systematically obtained before cancer diagnosis, using a standard and widely applied screening instrument. This rendered the analysis in question at least feasible, although the overlap with cancer registrations was still small. A further advantage of the HADS is that it was specifically developed to ascertain symptoms of anxiety and depression in samples with somatic disorders, focusing primarily on cognitive symptoms. The HADS is therefore less likely than other screening scales (or indeed diagnostic instruments) to misclassify somatic symptoms, an important advantage for the analysis in question. Furthermore, the analysis specifically excluded cancer diagnoses within a year of HUNT-2 participation, reducing the likelihood that HADS caseness was influenced by early cancer manifestations. There is therefore little chance that information bias could explain the results, although we accept in retrospect that the restriction may have been overly conservative and limiting with respect to the sample size. In terms of the analysed sample, both the HUNT-2 survey and CRN are comprehensive and inclusive with respect to the population concerned and we do not believe that selection is likely to have influenced findings apart from

https://doi.org/10.1192/bjp.2019.211 Published online by Cambridge University Press

non-differential bias owing to missing data. None of covariates had any substantial influence on the associations of interest. However, as with any observational study, residual confounding cannot be ruled out entirely. For example, unmeasured personality characteristics might influence both risk of depression and cancer presentation, as might a family history of either/both mental disorders and cancer.

The principal limitation of the study was in the size of the analysed sample, which did not allow associations with specific cancers to be investigated and in which groups defined by the presence of case-level anxiety and depression were relatively small, despite the large size of the survey sample followed in this respect. Non-significant associations should therefore be treated with caution because of lack of statistical power. Furthermore, there was a high proportion of missing information about EOD in the national register, although we found no evidence that missing data were differential by gender or exposure status, only that those with missing staging were older ($P < 0.001$); no attempts were made at multiple imputation because of the likelihood that missing data were not at random. Considering measurement accuracy, it should be borne in mind that the HADS is a brief screening instrument designed for ascertaining symptoms rather than disorders, and it was only administered on a single occasion, which may have underestimated the associations of interest. Finally, EOD can only be considered as a proxy measure of timing of diagnosis, and factors associated with EOD cannot be assumed to be causing a delay in diagnosis.

In conclusion, in people who develop cancer, we investigated previously recorded depressive and anxiety symptoms as risk factors for beyond-local EOD at diagnosis. In analyses adjusted for age alone, depressive symptoms were associated with higher likelihood of beyond-local EOD and anxiety symptoms with a lower likelihood of this outcome. These parallel associations of depressive and anxiety symptoms with cancer mortality previously reported in the same cohort (i.e. higher risk associated with depressive symptoms, lower risk with anxiety symptoms).[4] However, importantly, neither association with EOD was statistically significant in fully adjusted models. For anxiety, this might be explained by inclusion of health and lifestyle factors, such as smoking, as covariates so that better health, and therefore possibly increased help-seeking, might have accounted for the protective association. For depression, coefficients remained relatively unaltered and close to statistical significance in most models, so an independent association might have been observed in a larger sample. Considering implications, at the very least the findings suggest that associations with mental health conditions are potentially complex; in this instance, suggesting that two very closely related syndromes (depression and anxiety) may have opposing influences on help-seeking behaviour and/or other factors determining cancer detection. Similar models of investigation could be informative with respect to other disorders, such as cardiovascular disease, whose prognosis is also known to be associated with mental health status and whose presentation and subsequent management have important implications on outcome. Physical health complaints, perhaps particularly in depression, risk being overlooked and attributed to the mental disorder, so there are important potential implications for primary and secondary care vigilance. The potential influence of mental disorder symptoms on how important somatic disorders present to healthcare (and/or are detected and diagnosed) clearly needs to be borne in mind when considering ways in which well-recognised health inequalities in people with mental disorders are to be addressed.

Robert Stewart, Researcher, Institute of Psychiatry, Psychology and Neuroscience, King's College London; and The National Institute for Health Research (NIHR), South London and Maudsley NHS Foundation Trust, UK; **Sophie Dorothea Fosså**, Researcher, Department of Oncology and University of Oslo, Institute of Clinical Medicine, Oslo University Hospital, Norway; **Matthew Hotopf**, Researcher, Institute of Psychiatry, Psychology and Neuroscience, King's College London; and South London and Maudsley NHS Foundation Trust, UK; **Arnstein Mykletun**, Researcher, Division of Mental Health, Norwegian Institute of Public Health; Department of Community Medicine, University of Tromsø; Center for Work and Mental Health, Nordland Hospital Trust; and Centre for Research and Education in Forensic Psychiatry and Psychology, Haukeland University Hospital, Norway

Correspondence: Arnstein Mykletun, Haukeland University Hospital, Sandviken Hospital, Sandviksleitet 1, 5036 Bergen, Norway. Email: arnstein.mykletun@helse-bergen.no

First received 21 Feb 2019, accepted 13 Aug 2019

Funding

No specific funding was obtained for this analysis and there was no study sponsor. R.S. and M.H. are part-funded by the National Institute for Health Research Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. R.S. has received research support in the past from Janssen, GSK, Roche and Takeda. A.M. received funding from Research Council of Norway at the time of the study and later.

References

1 Prince M, Patel V, Saxena S, Maj M, Maselko J, Phillips MR, et al. Global Mental Health 1: no health without mental health. *Lancet* 2007; **370**: 859–77.

2 Heila H, Haukka J, Suvisaari J, Lonnqvist J. Mortality among patients with schizophrenia and reduced hospital care. *Psychol Med* 2005; **35**: 725–32.

3 Osby U, Brandt L, Correia N, Ekbom A, Sparen P. Excess mortality in bipolar and unipolar disorder in Sweden. *Arch Gen Psychiatry* 2001; **58**: 844–50.

4 Mykletun A, Bjerkeset O, Dewey M, Prince M, Overland S, Stewart R. Anxiety, depression and cause-specific mortality. The HUNT study. *Psychosom Med* 2007; **69**: 323–31.

5 Chan CMH, Ahmad WAW, Yusof MMD, Ho GF, Krupat E. Effects of depression and anxiety on mortality in a mixed cancer group: a longitudinal approach using standardised diagnostic interviews. *Psychooncology* 2015; **24**: 718–25.

6 Cuijpers P, Vogelzangs N, Twisk J, Kleiboer A, Li J, Penninx BW. Comprehensive meta-analysis of excess mortality in depression in the general community versus patients with specific illnesses. *Am J Psychiat* 2014; **171**: 453–62.

7 Ristvedt SL, Trinkaus KM. Psychological factors related to delay in consultation for cancer symptoms. *Psychooncology* 2005; **14**: 339–50.

8 Ristvedt SL, Trinkaus KM. Sex differences in responding to rectal cancer symptoms. *Psychol Health* 2008; **23**: 935–44.

9 Burgess CC, Ramirez AJ, Smith P, Richards MA. Do adverse life events and mood disorders influence delayed presentation of breast cancer? *J Psychosomatic Res* 2000; **48**: 171–5.

10 Nosarti C, Crayford T, Roberts JV, Elias E, McKenzie K, David AS. Delay in presentation of symptomatic referrals to a breast clinic: patient and system factors. *Br J Cancer* 2000; **82**: 742–8.

11 Burgess CC, Potts HWW, Hamed H, Bish AM, Hunter MS, Richards MA, et al. Why do older women delay presentation with breast cancer symptoms? *Psychooncology* 2006; **15**: 962–8.

12 Robertson R, Campbell NC, Smith S, Donnan PT, Sullivan F, Duffy R, et al. Factors influencing time from presentation to treatment of colorectal and breast cancer in urban and rural areas. *Br J Cancer* 2004; **90**: 1479–85.

13 Desai MM, Bruce ML, Kasl SV. The effects of major depression and phobia on stage at diagnosis of breast cancer. *Int J Psychiatry Med* 1999; **29**: 29–45.

14 Larsen IK, Småstuen M, Johannesen TB, Langmark F, Parkin DM, Bray F, et al. Data quality at the Cancer Registry of Norway: an overview of comparability, completeness, validity and timeliness. *Eur J Cancer* 2009; **45**: 1218–31.

15 World Health Organization. *Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death: Seventh Revision*. WHO, 1957.

16 Holmen J, Midthjell K, Krüger O, Langhammer A, Holmen TL, Bratberg GH, et al. The Nord-Trøndelag Health Study 1995–97 (HUNT 2): objectives, contents, methods and participation. *Norsk Epidemiologi* 2003; **13**: 19–32.

17 Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983; **67**: 361–70.

18 Bjelland I, Dahl AA, Haug TT. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosomatic Res* 2002; **52**: 69–77.

19 Roness A, Mykletun A, Dahl AA. Help-seeking behaviour in patients with anxiety disorder and depression. *Acta Psych Scand* 2005; **111**: 51–8.

https://doi.org/10.1192/bjp.2019.211 Published online by Cambridge University Press

20 Fernando MS, Ince PG. MRC Cognitive Function and Ageing Neuropathology Study Group. Vascular pathologies and cognition in a population-based cohort of elderly people. *J Neurol Sci* 2004; **226**: 13–7.

21 Oerlemans ME, van den Akker M, Schuurman AG, Kellen E, Buntinx F. A meta-analysis on depression and subsequent cancer risk. *Clin Pract Epidemiol Ment Health* 2007; **3**: 29.

22 Prasad SM, Eggener SE, Lipsitz SR, Irwin MR, Ganz PA, Hu JC. Effect of depression on diagnosis, treatment and mortality of men with clinically localized prostate cancer. *J Clin Oncol* 2014; **32**: 2471–8.

23 Boyd CA, Benarroch-Gampel J, Sheffield KM, Han YM, Kuo YF, Riall TS. The effect of depression on stage at diagnosis, treatment, and survival in pancreatic adenocarcinoma. *Surgery* 2012; **152**: 403–13.

24 Andersen BL, Cacioppo JT, Roberts DC. Delay in seeking a cancer diagnosis: delay stages and psychophysiological comparison processes. *Br J Soc Psychol* 1995; **34**: 33–52.

25 Ramirez AJ, Westcombe AM, Burgess CC, Sutton S, Littlejohns P, Richards MA. Factors predicting delayed presentation of symptomatic breast cancer: a systematic review. *Lancet* 1999; **353**: 1127–31.

26 Chang C-K, Hayes RD, Broadbent MTM, Hotopf M, Davies E, Møller H, et al. A cohort study on mental disorders, stage of cancer at diagnosis and subsequent survival. *BMJ Open* 2014; **4**: e004295.

27 Mykletun A, Bjerkeset O, Overland S, Prince M, Dewey M, Stewart R. Levels of anxiety and depression as predictors of mortality: the HUNT study. *Br J Psychiatry* 2009; **195**: 118–25.

psychiatry in literature

Language and style for psychiatrists: honing our words on Flann O'Brien's grindstone

Alistair Stewart

Psychiatrists, and not only those in training, often communicate about their patients' mental worlds and struggles in a way which suggests that they have abandoned the resources of everyday language without gaining anything useful in return. This is probably due in part to laziness, in part to the strange vocabulary which grows out of the soil of psychology and in part to absorption of bureaucratic jargon.

I find that a useful antidote to all this is regular immersion in the writings of Flann O'Brien, otherwise known as Brian O'Nolan, or Brian Ó Nualláin or Myles na cGopaleen. As Flann, he is known for a number of mind-bending novels, in particular *The Third Policeman*. As Myles, for over 20 years from the 1940s he wrote The Cruiskeen Lawn, a regular column in *The Irish Times*, addressing many different subjects in a range of voices and styles. In these pieces, now collected in various volumes, he lampooned without mercy: blaggers, conmen and hypocrites of all ranks and stations. Since we are all capable of a bit of blagging, we can find ourselves there too. In the Catechism of Cliché, which Myles often rehearsed, he laid bare the ridiculous quality of the stock phrases we use so readily:

> 'Is treatment, particularly bad treatment, ever given to a person?
> No. It is always meted out.
> Is anything else ever meted out?
> No. The only thing that is ever meted out is treatment.
> And what does the meting out of treatment evoke?
> The strongest protest against the treatment meted out'

(the Catechism was contemporaneous with George Orwell's observations on the dangerous effects of cliché in political language).

Myles also introduced a cast of characters who remain familiar today. A certain class of civil servant, for example:

> 'In his view, there is pressure of work. The work is, however, under consideration. Certain separate matters are under review, others are under active consideration. A decision will be taken only on consideration of the facts in all their aspects. The facts will in the meantime be under continuous and active review and a decision will be announced at an early date.'

And not forgetting the intellectuals:

> 'Suppose I write a symphony. No, that is a crude way of putting it. Suppose that contained in my cranium is a work of dimension so vast, of nature so autonomous, supreme, trisgemistous in its modes that it cannot be noted down on paper. Suffice it that it… explores, discovers, dismantles, inaugurates… stuns!'

Writers of Irish heritage have enriched the English language to a quite disproportionate degree. Myles na cGopaleen offered the following explanation for this:

> 'It is worth remembering that if Irish were to die completely, the standard of English here, both in the spoken and written word, would sink to a level probably as low as that obtaining in England, and it would stop there only because it could go no lower.'

Those of us in England, if not elsewhere, should do our best to prove him wrong, at least on this point.

The British Journal of Psychiatry (2020) 217, 433. doi: 10.1192/bjp.2020.66

https://doi.org/10.1192/bjp.2019.211 Published online by Cambridge University Press