Title: The effect of mode of detection of breast cancer on stress and distress

Short title: Mode of detection of breast cancer

[1, 2]Andrea Gibbons, [2]AnnMarie Groarke, [2]Ruth Curtis, [2]Jenny Groarke.

[1]Health Psychology Research Unit, Royal Holloway, University of London

[2]School of Psychology, National University of Ireland, Galway, Ireland.

Address for correspondence:

Dr. Andrea Gibbons

Health Psychology Research Unit,

Royal Holloway, University of London,

Egham,

Surrey, TW20 0EX

Email: andrea.gibbons@royalholloway.ac.uk

Tel: +44 (0)1784 276521

Fax: +44 (0)1784 414657

Abstract

Objective: The number of women with screen-detected breast cancer is increasing, but it is not clear if these women experience the same levels of distress as women with symptomatic breast cancer. The current study compared stress and distress in women with screen-detected or symptomatic breast cancer at diagnosis and 12 months post-diagnosis.

Methods: Ninety-two women with screen-detected breast cancer and 129 women with symptomatic breast cancer completed measures of perceived stress, anxiety, and depression at diagnosis and 12 months post-diagnosis. Women also completed a measure of cancer-related stress 12 months post-diagnosis.

Results: Both groups reported similar levels of perceived stress, anxiety, and depression at diagnosis. A third of women in both groups reported clinical levels of anxiety at diagnosis, which decreased over time. There were no differences in depression. Analyses revealed that at 12 months post-diagnosis, the symptomatic group reported a significant reduction in anxiety but the screen-detected group reported a non-significant trend for a reduction over time. The screen-detected group reported significantly higher cancer-related stress at 12 months than the symptomatic group.

Conclusions: Screen-detected women report similar distress at diagnosis, but may be more at risk for greater distress requiring further psychological support one year after diagnosis. Future interventions which focus on preparation for screening may help to reduce ongoing levels of anxiety and cancer-related stress for this group.

Background

Breast cancer is the most common form of cancer in women, with over 1.38 million women diagnosed worldwide in 2008, accounting for 23% of all new cancer cases [1]. Due to the availability of national screening programmes more women are being diagnosed, and mortality from the disease has reduced [2-3]. Despite these benefits, research has also focused on the costs of possible screening outcomes, for example the impact of over-diagnosis and false positive results [4]. Women may be diagnosed with non-invasive cancer such as ductal carcinoma in situ (DCIS), which is unlikely to be detected outside of screening. As screening is directed at the apparently healthy public [5] an unexpected diagnosis of breast cancer may have different psychological consequences to women presenting with symptomatic disease.

Distress is a common response to a diagnosis of breast cancer, with a significant minority of women reporting clinical levels of anxiety and depression [6-8]. Research on distress focuses almost exclusively on women who have symptomatic disease but it has been reported that women with screen-detected disease also experience significant anxiety and high levels of shock [5, 9-10]. Only one study to date has compared the distress trajectories of women with screen-detected DCIS or invasive breast cancer and found no differences over nine months, but the sample was small (9 vs 33) [11]. Two earlier comparison studies had focused on psychiatric morbidity only. Burgess and colleagues [12] conducted psychiatric interviews in 52 screen-detected women and 80 symptomatic women at 5 and 18 months post-diagnosis. Haddad, Maguire and Jones [13] interviewed 82 screen-detected women with 213 symptomatic women at 2 and 14 months post-diagnosis. Neither study showed differences in the likelihood of a psychiatric episode between the two groups. There is, therefore, a dearth of research examining the impact of mode of detection on levels of general distress in women with breast cancer.

Diagnosis of breast cancer has also been associated with high levels of perceived stress [14]. Perceived stress predicts poor adjustment in breast cancer patients [15]. No studies to date have compared stress appraisal in screen-detected and symptomatic women. This may be of particular relevance since it is known that exposure to an unpredictable and unexpected stressor (e.g. a diagnosis of breast cancer through screening), can have a deleterious psychological and physiological effect [16-17]. To advance existing literature, the present study is the first to assess the level of stress and distress reported by a broad breast

cancer sample presenting with screen-detected breast cancer or symptomatic disease at diagnosis and 12 months follow-up.

Methods

Participants and procedure

The study protocol was approved by the University Hospital Ethics Committee, and the Research Ethics Committee of the National University of Ireland, Galway before data collection commenced. Inclusion criteria were women with a diagnosis of non-metastatic breast cancer awaiting surgery who were referred from their general practitioner based on the presentation of symptoms, or were diagnosed via the national screening programme, BreastCheck. To avoid any confounding of distress from previous experience, women with a previous diagnosis of cancer were excluded. Women with a diagnosis of intellectual disability, or lack of English literacy skills, which would preclude women from being able to complete the questionnaires, were also excluded. Women older than 75 years and who had medical conditions that precluded receiving treatment for breast cancer were also excluded.

Consecutive women with symptomatic breast cancer presenting at the Breast Symptomatic Unit, or women with a confirmed diagnosis of screen-detected breast cancer at BreastCheck Services were invited to participate in research which examined aspects of the psychological impact of cancer. Both services are located in the same university-affiliated hospital. Patients in each group were accrued from April 2010 to September 2011.

For both groups, informed written consent was obtained after diagnosis in the assessment results clinics. Within two weeks of diagnosis, and before surgery, principal researchers administered the questionnaires within a semi-structured interview assessing anxiety, depression, and perceived stress. These interviews were conducted in clinics women were attending prior to surgery. Twelve months later, women in both groups were contacted via post, and asked to complete the same measures along with a measure of cancer-related stress.

One hundred and twenty nine women diagnosed in the symptomatic breast clinic (57% of eligible patients) and 92 women with screen-detected breast disease (44% of eligible patients) took part in the study at diagnosis. Although reasons for non-participation were not recorded, some women reported being too stressed or ill to participate. At follow-up (12 months post-diagnosis), 111 of the 129 women (86%) diagnosed in symptomatic breast

clinics, and 51 of the 92 women (55%) with screen-detected breast disease, returned the questionnaires, giving an overall response rate of 73%.

Measures

Age, type of surgery, stage of disease, and the type of treatment received (radiotherapy, chemotherapy), were obtained from medical records of participants.

The Perceived Stress Scale (PSS) [18] is a 14-item scale designed to measure subjective appraisals of events over the past month. Items ask how often participants have felt or thought in a certain way in the past month. Items are rated from 0 (*never*) to 4 (*very often*). Items are reverse-scored and summed. Higher scores indicate higher levels of general perceived stress. In previous studies internal consistency ranged from .75 to .84 [15, 18]. Reliabilities in the current study were .80 at diagnosis and .77 at 12 months post-diagnosis.

The Hospital Anxiety and Depression Scale [HADS; 19] was used to measure general anxiety and depression levels. The HADS is a 14-item scale (7 items for anxiety, 7 for depression) that asks individuals to indicate their level of agreement with statements on a four point scale from 0 (*e.g. most of the time*) to 3 (*e.g. not at all*). Higher scores indicate greater levels of anxiety or depression. A score of 11 is considered the cut-off for detecting mood disorders, and displays a sensitivity score of 70% and a specificity score of 88% when compared to clinical interviews and other psychological measures [20]. Internal consistency has been reported to be .93 for anxiety and .90 for depression [21]. Reliabilities in the current study for anxiety were .90 at diagnosis and .85 at 12 months, and .85 at diagnosis and .86 at 12 months for depression.

The Impact of Events Scale (IES) [22] was used to measure cancer-related stress at 12 months. The measure consists of 15 statements that ask individuals to rate their agreement on a four point Likert scale that is scored as 0 (*not at all*), 1 (*rarely*), 3 (*sometimes*), or 5 (*often*). Seven items relate to intrusion, and 8 items measure avoidance. Participants were asked to answer items based on their response to diagnosis and treatment. Items are summed to give a total cancer-related stress (impact) score. Higher scores indicate higher levels of cancer-related stress. Reported internal consistencies of the measure ranged from .87 to .90 [15, 23]. In the current study internal consistency was .90. The IES was not used at diagnosis, as its impact may have been difficult to express immediately following diagnosis.

Statistical Analysis

Chi-Squared analyses were conducted to examine differences in responders and non-responders on medical variables, and to assess differences in medical variables in women with screen-detected or symptomatic disease. An independent samples *t* tests was conducted to examine the difference in cancer-related stress at 12 months across the two groups. A series of two-way mixed ANOVAs were conducted to examine the differences between those with symptomatic or screen-detected disease on measures of general perceived stress, anxiety, and depression from diagnosis to 12 months post-diagnosis.

Results

Sample characteristics

The screen-detected group were older (M = 56.57, SD = 4.32, range = 50-65) than the symptomatic group *(*M = 53.75, SD = 10.91, range = 32-78; $t_{(173.45)} = 2.62$, $p = .009$). All women in the screen-detected group had breast conserving surgery, whilst 47 (36.40%) of the symptomatic group required a mastectomy (see Table 1). Nine women in the screen-detected group (9.80%) had non-invasive cancer (DCIS), whilst all women with symptomatic disease had invasive cancer. Chi-Squared analyses revealed that the symptomatic group were more likely to have a higher stage of disease ($\chi^2 = 57.82$, $df = 4$, $p < .001$).

There were no differences in age between those women who did and did not participate at diagnosis ($t_{(366)} = -0.72$, $p = .474$). Non-responders at diagnosis were more likely to have received a mastectomy ($\chi^2 = 32.96$, $df = 4$, $p < .001$). At diagnosis, responders in the screen-detected group were more likely to have invasive cancer ($\chi2 = 14.49$, $df = 4$, $p = .006$). There were no differences in stage of disease at diagnosis or at 12 months, but the symptomatic group were more likely to have a higher stage of disease compared with the screen-detected group ($\chi2 = 57.82$, $df = 4$, $p < .001$).

There were no differences in anxiety, depression, perceived stress, or age at diagnosis between women who did not respond and those who participated at 12 months. For the symptomatic group, non-responders at 12 months were more likely to have received a mastectomy ($\chi^2 = 6.86$, $df = 2$, $p = .032$). No other differences were found.

Prevalence of anxiety, depression, and cancer-related stress

Cut-off scores for the HADS were assessed. As can be seen in Table 2, 28 women (30.40%) with screen-detected disease and 46 women (35.60%) with symptomatic disease reported probable levels of anxiety at diagnosis, which fell to 8 (8.70%) and 10 women

(7.80%) respectively at 12 months post-diagnosis. Chi-Squared tests indicated that there were no differences in the frequency of women reporting mild, moderate, or probable levels of anxiety (χ^2 = 2.33, *df* = 2, *p* = .313) or depression (χ^2 =3.35, *df* = 2, *p* = .187) between screen-detected or symptomatic groups at diagnosis or at 12 months (anxiety: χ^2 = 1.56, *df* = 2, *p* = .458; depression: χ^2 = 1.69, *df* = 2, *p* = .430).

Cancer-related stress was measured at 12 months post-diagnosis using the IES. A cut-off score of 33 has been suggested as a way to measure a high impact of cancer stress [24]. Of those women who took part at 12 months post-diagnosis, 17 women (33.30 %) in the screen-detected group and 15 women (13.50%) in the symptomatic group reported scores of 33 or more. An independent samples *t* test was conducted to examine differences in cancer-related stress across the groups at 12 months post-diagnosis. Findings showed that the screen-detected group was significantly more stressed by their cancer at 12 months (*M* = 25.06, *SD* = 16.91) than the symptomatic group (*M* = 16.57, *SD* = 15.56; $t_{(159)}$ = 3.12, *p* = .002).

Differences between groups one year post-diagnosis

A series of 2 (time) x 2 (group) mixed ANOVAs were conducted to examine the differences between those with symptomatic or screen-detected disease on measures of perceived stress, anxiety, and depression from diagnosis to 12 months post-diagnosis.

ANOVA analyses for perceived stress indicated that there was a main effect for time ($F_{(1, 156)}$ = 7.60, *p* = .007). Irrespective of mode of detection, general perceived stress decreased from diagnosis (*M* = 23.46, *SD* = 7.80), to 12 months post-diagnosis (*M* = 21.20, *SD* = 8.61). There was no main effect for group ($F_{(1, 156)}$ = 1.75, *p* = .187), and no interaction effect ($F_{(1, 156)}$ = 1.76, *p* = .187). For depression, there were no main effects for time ($F_{(1, 157)}$ = 1.33, *p* = .251) or group ($F_{(1, 157)}$ = 1.39, *p* = .240), and no interaction effect ($F_{(1, 157)}$ = 1.20, *p* = .275).

There was a main effect for time on anxiety ($F_{(1, 156)}$ = 32.51, *p* < .0001). Irrespective of group, women reported greater anxiety at diagnosis (*M* = 8.34, *SE* = 0.41) than at 12 months post-diagnosis (*M* = 6.08, *SE* = 0.33). There was no main effect for group ($F_{(1, 156)}$ = 0.25, *p* = .617). Irrespective of time, the screen-detected group (*M* = 7.05 *SE* = 0.52) reported similar levels of anxiety to the symptomatic group (*M* = 7.37, *SE* = 0.35). There was; however, a significant interaction effect ($F_{(1, 156)}$ = 5.84, *p* = .017). Post-hoc comparisons revealed that the screen-detected group reported similar levels of anxiety at diagnosis (*M* = 7.70, *SE* = 0.68) to the symptomatic group (*M* = 8.97, *SE* = 0.46; *p* = .355). The symptomatic

group reported a significant reduction in anxiety over time (M = 5.76, SE = 0.37; $p < .001$). In contrast, the screen-detected group showed a trend for a reduction in anxiety levels, but this was not statistically significant (M = 6.40, SE = 0.55; p = .077; Figure 1).

Discussion

A third of women with screen-detected or symptomatic disease reported clinical levels of anxiety at diagnosis, which fell to less than 10% twelve months later. This is in line with previous research that has shown that although women may respond initially to their diagnosis with shock and anxiety, these levels decrease over time [6, 11, 15]. The number of women reporting probable cases of anxiety was the same in both groups. The level of depression was low overall in both groups and showed no change over time. Previous research has also found that anxiety but not depression, is more likely to be associated with a breast cancer diagnosis [25].

At diagnosis, there were no differences in anxiety or depression in screen-detected and symptomatic women. There was, however, an interaction effect for anxiety over time. Women with screen-detected cancer showed a trend towards anxiety reduction, whilst women with symptomatic breast cancer experienced a significant reduction in anxiety. This contrasts with research on screening which reports that long-term adverse effects of screening are comparatively rare [5], and that women with screen-detected cancer have a similar risk of developing psychiatric morbidity as women with symptomatic disease [13]. However, Keyzer-Dekker and colleagues [26] found that women with benign breast disease who were recalled after an abnormal mammogram reported greater anxiety twelve months later compared with women who presented with a palpable lump. Perhaps differences in coping explain these results. Coping styles can impact levels of anxiety in women with breast cancer [8, 15, 27], so it may be that strategies employed by screen-detected women are less adaptive over time. Women with self-detected cancer may have increased knowledge of the disease, perhaps having had more time to inform and prepare themselves prior to seeking medical attention. This may equip these women with greater opportunities for adaptive coping during treatment and recovery. Future research examining the impact of coping on anxiety in these two groups over time would be useful.

While no group differences emerged in general stress, anxiety, or depression at follow-up, the screen-detected group reported significantly greater cancer-related stress. Many women are nearing the end of treatment and awaiting their first surveillance

mammogram, so this may lead to greater anxiety and stress. The heightened level of cancer-related stress and more limited reduction in anxiety in women with screen-detected disease is of concern, so psychological interventions should note that these women may require prolonged or differing levels of support. Stress management programmes have been useful in improving health outcomes in patients awaiting test results for HIV status [28], and have reduced cancer-specific stress, depression, and anxiety in women with breast cancer [29-31]. Offering these programmes to women undergoing screening or after diagnosis may help to reduce subsequent stress and anxiety. Little research to date has examined cancer-related stress, so future research could usefully examine the trajectory of cancer-related stress over time, as well as its potential interaction with distress.

Women diagnosed through screening may require more preparation for what a diagnosis may mean. Farmer [32] asserts that the diagnosis of non-invasive breast cancers such as DCIS via screening is communicated in a much more positive and reassuring way. Women are often told that the disease is not as serious as other breast cancers, but receive the same treatments as women with invasive disease [25, 33-34]. Anxiety levels may be greater in women who are given a diagnosis and prognosis that are seemingly contradictory. Communicating the diagnosis and treatment options in a more comprehensive manner may reduce confusion and so alleviate levels of anxiety in both groups.

It is important to note that at 12 months most women have completed their treatment, but are likely to be waiting or undergoing their first mammogram post-treatment. Women may find it difficult to cope when treatment is completed [35]. Making the transition from patient to survivor may be more difficult for screen-detected women, as they may be more anxious about their ability to detect any future recurrence. Jones et al [36] found that lower levels of self-efficacy predicted greater distress in women with breast cancer post-treatment, so it may be that screen-detected women have lower self-efficacy in relation to detecting future disease, which increases their levels of anxiety and cancer-related stress once treatment is complete. It has been shown previously that women with asymptomatic gynaecological disease may be more anxious and have a greater fear of recurrence [37]. Likewise Clements et al. [38] interviewed 12 women after treatment for screen-detected breast cancer and found that although women were reassured that they would be treated successfully, they reported considerable anxiety regarding future mammography screening and what it may find. Psychological services and interventions based on such factors as perceived risk, self-efficacy, and adaptive coping strategies can help to communicate the possibility of a cancer

diagnosis in a way that does not lead to heightened anxiety for prospective screen-detected cancer patients [10]. Research has suggested that risk-stratified screening should be offered to women in the United Kingdom [39]. Such screening would avoid unnecessary testing in women at low risk of developing breast cancer, whilst increasing testing in women at greater risk. Although the number of women awaiting their first mammogram post-treatment was not recorded, the current study suggests that women who are screened in such services and considered high-risk should receive support and preparation such as stress management to improve their adjustment to a possible diagnosis.

There are some limitations to the study. Although we excluded women with a previous diagnosis of cancer, we did not record number of benign breast biopsies experienced. This could have impacted upon on women's responses. Cancer-related stress was only measured at 12 months, so differences over time could not be examined. The response rate was modest, and attrition rates were higher in the screen-detected women at 12 months follow-up. Not all women attended the clinic at 12 months post-diagnosis, so data collection was conducted via post, leading to a lower response rate. No reminders were sent, as to do so may have placed undue pressure on participants. Non-responders were more likely to have had a mastectomy, and no women with screen-detected disease who had a mastectomy participated. The screen-detected group also had on average a less serious stage of disease, and were older, but there were no other differences in clinical factors. Women may also have been distressed awaiting their first surveillance mammogram, potentially impacting the number of screen-detected women participating at 12 months. Despite this, there were no differences in distress at diagnosis in those women who did and did not respond at 12 months. From a medical perspective, it is interesting that although the screen-detected group received less invasive treatment and had less serious disease, they still, despite these advantages, were more vulnerable to heightened anxiety and cancer-related stress post-diagnosis.

Despite the limitations, the study has important implications for understanding adjustment in women with breast cancer. The diagnosis of breast cancer presents many physical and psychological challenges, so examining stress appraisal is an important but often overlooked aspect of adaptation to the disease as perceptions of cancer-related stress are related to impaired quality of life long-term [6, 40]. This is the first study to compare general and cancer-related stress in women with screen-detected or symptomatic breast cancer and is the first study to report differences in anxiety and cancer-related stress based on mode of

detection. The inclusion of both types of stress provides a more comprehensive assessment of how women respond to a cancer diagnosis.

Conclusions

While women with screen-detected and symptomatic disease report similar general stress and anxiety at diagnosis, mode of detection can impact on anxiety reduction and cancer-related stress at 12 months post-diagnosis. Identifying the psychological support required by women undergoing screening, subsequent diagnosis and at future mammogram screening post-diagnosis is important so that adequate care can be provided at this stage of the experience. Specifically, routine psychological assessment may be required in women who are diagnosed through screening programmes to identify those at greater risk of heightened stress and anxiety post-treatment.

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Table 1.

Summary frequencies of medical variables for the symptomatic and screen-detected groups

Variable	Screen-detected		Symptomatic	
	N	%	*N*	%
Surgery				
Lumpectomy	92	100.00	78	60.50
Mastectomy	0	0.00	11	8.50
Mastectomy with reconstruction	0	0.00	36	27.90
Unknown	0	0.00	4	3.10
Stage of Disease				
Stage 0	40	43.50	4	3.10
Stage IA, IB	4	4.30	32	24.80
Stage IIA, IIB	23	25.00	66	51.20
Stage IIIA, IIIB, IIIC, IV	9	9.80	14	10.90
Unknown	16	17.40	13	10.00
Chemotherapy	28	30.40	81	62.80
Radiotherapy	78	84.80	79	61.20

Table 2

Summary of Frequencies for Cut-off Scores for Anxiety and Depression (HADS) at Diagnosis and 12 Months Post-diagnosis

	Screen-detected				Symptomatic			
	Diagnosis		12 months		Diagnosis		12 months	
Distress	*N*	%	*N*	%	*N*	%	*N*	%
Anxiety								
Mild (0-7)	38	41.30	35	38.10	58	45.00	80	62.00
Moderate (8-10)	24	26.10	8	8.70	23	17.80	20	15.50
Probable (>11)	28	30.40	8	8.70	46	35.60	10	7.80
Missing	2	2.20	41	44.50	2	1.60	19	14.70
Total	92	100.00	92	100.00	129	100.00	129	100.00
Mean		7.70		6.40		8.97		5.76
SD		4.08		4.25		5.07		3.68
Depression								
Mild (0-7)	70	76.10	46	50.00	107	82.90	96	74.40
Moderate (8-10)	14	15.20	2	2.20	10	7.80	10	7.80
Probable (>11)	6	6.50	3	3.30	11	8.50	4	3.10
Missing	2	2.20	41	44.50	1	0.80	19	14.70
Total	92	100.00	92	100.00	129	100.00	129	100.00
Mean		3.38		3.36		4.37		3.58
SD		3.19		4.28		3.89		3.19