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THE PSYCHOLOGICAL IMPACTS OF FALSE POSITIVE OVARIAN CANCER
SCREENING: ASSESSMENT VIA MIXED AND TRAJECTORY MODELING

DISSERTATION

A dissertation submitted in partial fulfillment of the requirements for the degree of
Doctor of Philosophy in the College of Public Health at the University of Kentucky

By Amanda Thaxton Wiggins

Lexington, Kentucky

Director: Dr. Wayne Sanderson, Professor of Epidemiology

Lexington, Kentucky

2013

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ABSTRACT OF DISSERTATION

THE PSYCHOLOGICAL IMPACTS OF FALSE POSITIVE OVARIAN CANCER SCREENING: ASSESSMENT VIA MIXED AND TRAJECTORY MODELING

Ovarian cancer (OC) is the fifth most common cancer among women and has the highest mortality of any cancer of the female reproductive system. The majority (61%) of OC cases are diagnosed at a distant stage. Because diagnoses occur most commonly at a late-stage and prognosis for advanced disease is poor, research focusing on the development of effective OC screening methods to facilitate early detection in high-risk, asymptomatic women is fundamental in reducing OC-specific mortality. Presently, there is no screening modality proven efficacious in reducing OC-mortality. However, transvaginal ultrasonography (TVS) has shown value in early detection of OC.

TVS presents with the possibility of false positive results which occur when a woman receives an abnormal TVS screening test result that is deemed benign following repeat testing (about 7% of the time). The purpose of this dissertation was to evaluate the impact of false positive TVS screening test results on a variety of psychological and behavioral outcomes using mixed and trajectory statistical modeling. The three specific aims of this dissertation were to 1) compare psychological and behavioral outcomes between women receiving normal and false positive results, 2) identify characteristics of women receiving false positive results associated with increased OC-specific distress and 3) characterize distress trajectories following receipt of false positive results.

Analyses included a subset of women participating in an experimental study conducted through the University of Kentucky Ovarian Cancer Screening Program. 750 women completed longitudinal assessments: 375 false positive and 375 normal results. Mixed and group-based trajectory modeling were used to evaluate the specific aims.

Results suggest women receiving false positive TVS result experience increased OC-specific distress compared to women receiving normal results. Among those

receiving false positives, less education, no history of an abnormal screening test result, less optimism and more social constraint were associated with increased OC-specific distress. Family history was associated with increased distress among women with monitoring informational coping styles. Three distinct trajectories characterize the trajectory of distress over a four-month study period. Although decreasing over time, a notable proportion of women experience sustained high levels of OC-specific distress.

KEYWORDS: false positive, ovarian cancer screening, cancer-specific distress, mixed modeling, group-based trajectory modeling

Amanda Wiggins
Student's Signature

November 22, 2013
Date

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This dissertation is dedicated to my husband, Craig. Thank you for your continued support and encouragement throughout my academic career.

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1 Introduction

Ovarian cancer (OC) is the fifth most common cancer among women and has the highest mortality of any cancer of the female reproductive system [1]. In the United States, the age-adjusted incidence rate for OC from 2005-2009 was 12.7 per 100,000 women, while the age-adjusted mortality rate was 8.2 per 100,000 women [2]. In 2012, it is estimated that 22,280 incident cases will be diagnosed in the US, accounting for nearly 3% of all cancers among women. An estimated 15,500 deaths from OC are expected to be reported in 2012 in the United States alone. OC represents the fourth leading cause of death for women aged 40-59, and the 5th leading cause of death for women aged 60-79 [3]. From 2005-2009, the median age at diagnosis for OC was 63 years of age, with the highest percentage of diagnoses occurring in women between 55 and 64 years of age (23%).

The stage at OC diagnoses distribution is disproportionately late-stage with 15% of cases diagnosed in localized, 16% in regional and 61% distant [3]. When diagnosed at a localized stage, 5-year relative survival is very high (92%), with rates dropping considerably for diagnoses in regional and distant stages (72% and 27%, respectively) [4]. Because diagnoses occur most commonly at a late stage, and prognosis for advanced disease is poor, research focusing on the development of effective ovarian cancer screening methods to facilitate early detection in high-risk, asymptomatic women is fundamental to decreasing mortality from ovarian cancer.

Presently, there is no screening modality proven effective to reduce OC-specific mortality. Methods have been proposed for early detection consisting of any combination of pelvic examination, transvaginal ultrasound (TVS) and blood tests for cancer antigen

125 (CA125). Currently, only four screening trials have been conducted to test the efficacy of different screening methods, two of which have been completed with the other two ongoing. In these trials, combinations of screening modalities (pelvic examination, CA125 testing and TVS) were considered [5]. As of now, only results from the Prostate, Lung, Colorectal and Ovary (PLCO) trial have been reported and showed equivalent rates of OC-specific mortality among women receiving screening and those in the usual care group [6]. In the other three trials, presentation of results is pending. While the efficacy of these methods in reducing OC-specific mortality has not been proven in prospective, randomized trials, CA125 assay and TVS have been tested alone and in combination, and have shown value in early detection of OC [7-9]. Further, investigators have found TVS to be significantly more accurate in defining the dimensions of the ovaries compared to clinical pelvic examination alone [10].

Although early detection through OC screening is critical to improving prognosis of OC, it does not come without limitations. Similar to other cancer screening modalities, OC screening modalities, such as TVS, present with the possibility of false positive test results. Research has shown receipt of a false positive screening test result in any cancer screening setting to be associated with affective, cognitive and behavioral outcomes [11, 12].

False positive screening test results occur when patients receive an abnormal test result, which after repeat screening or further follow-up procedures, confirms no disease exists. Researchers have found that false positive mammograms were associated with significantly more symptoms of distress, anxiety and worry about future screening and breast cancer, illness and death [13]. Additionally, false positive results were associated

with generally more breast cancer-specific thoughts such as greater distress, anxiety, worry, and more perceived risk of receiving positive results for breast cancer in the future [13]. From the University of Kentucky OC screening program, Andrykowski et al. found that after receipt of a false positive TVS screening test, women reported elevated OC-specific stress, but distress returned near baseline levels at four month follow-up [11]. Investigators found receipt of an abnormal, yet ultimately benign TVS test to be associated with responses to cancer-specific distress rather than generic measures of distress, and suggested using cancer-specific distress measures in future studies.

Recent studies suggest the trajectory of response to an abnormal cancer screening test result is associated with how an individual processes information after the occurrence of health-threatening events. In order to better characterize the impact of an abnormal TVS screening test result, it is important to identify factors that moderate the impact. Two conceptual frameworks are used to help understand the trajectory of response to abnormal cancer screening results: Monitoring Process (MP) model and the Cognitive-Social Health Information Processing (C-SHIP) model [14, 15]. The MP model suggests that individuals differ in coping styles for dealing with health-threatening events. The theory characterizes individuals' informational coping styles as monitoring (attending to) or blunting (avoiding). Termed “monitors”, these individuals seek health-related information while “blunters” tend to minimize or avoid health-relevant information. Consistent with the MP model, Wardle et al. found that monitors experienced greater distress after receipt of an abnormal TVS result [16].

C-SHIP model theory follows from the MP model but additionally suggests that dispositional or situational characteristics can modify monitors' tendency to amplify

threat. Consistent with the C-SHIP model, Andrykowski et al. found that the combination of a monitoring informational coping style with low optimism was associated with elevated OC-specific stress after receipt of an abnormal TVS screening result, whereas high dispositional optimism combined with a monitoring style restrained the response [11, 17]. Further, the MP and C-SHIP models predict that family history of OC is associated with an increased risk for an adverse response due to an increased perception of cancer risk posed by a false positive TVS result. Through specific aims (2) and (3) of this dissertation, we will evaluate the association between potential predictors suggested by these models and the magnitude and trajectory of OC-specific distress.

The purpose of this dissertation is to investigate affective, cognitive and behavioral responses of women after receipt of an abnormal, yet ultimately benign, TVS screening test result for OC. The specific aims of this study are:

1. Compare affective, cognitive and behavioral outcomes between women receiving false positive TVS screening test results and women receiving routine, normal screening test results.
2. Identify a comprehensive set of demographic, clinical, dispositional and social environmental characteristics that moderate the magnitude of OC-specific distress after receipt of a false positive TVS screening test result for OC.
3. Use group-based trajectory modeling to characterize trajectories of response to a false positive cancer screening test result for OC, and identify characteristics associated with likelihood of group membership.

We hypothesize that an abnormal, yet ultimately benign, TVS test result will be associated with increased OC-specific distress, increased perceptions of personal OC risk, reduced perceptions about the efficacy of TVS screening for OC and curability of OC and reduced intentions to participate in future TVS screening for OC. For positive affective outcomes, we predict that an abnormal TVS result will result in less reassurance and well-being but greater “benefit-finding”. Further, we hypothesize that a monitoring informational coping style combined with low dispositional optimism or a family history of OC will be associated with greater immediate OC-specific distress, and more sustained OC-specific stress over the study period.

While previous research has addressed some of these research questions, this study allows for the largest, most comprehensive study of response to a false positive cancer screening test result in the OC setting. Because of the large numbers of women receiving abnormal results, we have sufficient power to detect more subtle and complex interaction effects to test the associations proposed by the MP and C-SHIP models. Although OC cancer screening is not currently recommended by any professional organization, the availability of study subjects through the University of Kentucky OC screening program provides a “natural laboratory” for examining affective, cognitive and behavioral responses to a potentially health-threatening event. Of most importance, study findings have implications translatable to understanding clinical management of response to false positive screening test results for other types of cancers.

2 Consequences of False Positive Cancer Screening Test Results for Ovarian Cancer: A Literature Review

Among cancers of the female reproductive system, the disease etiology of OC is least well understood. As the fourth or fifth leading cause of cancer death among women in the United States, OC causes upwards of 140,000 deaths among women worldwide [18]. While the etiology is well established among other cancers of the female reproductive system (cervical, endometrial), little is known about causes of this highly fatal disease.

Descriptive epidemiology of ovarian cancer

The highest age-adjusted rates of OC are present in developed parts of the world such as North America, Northern Europe and Western Europe [19]. The disease occurs more commonly among Whites (14.3 per 100,000), with slightly lower rates among African-Americans (10.1 per 100,000). Over time, incidence rates of OC in North America and Europe have remained fairly constant with a slight decline since the 1990s. A slight decline in OC-related mortality for all races combined has been seen in the United States over time, likely due to advances in treatment methods. Geographical and racial variation in OC incidence is likely due to differences in oral contraceptive use and pregnancy, as these factors are associated with decreased risk for developing OC.

OC is typically viewed as an asymptomatic disease as symptoms associated with OC have low specificity and low positive predictive value. Common symptoms include persistent bloating, abdominal pain, feeling full quickly or frequent or urgent urination patterns [2]. The most common symptom is abdominal enlargement, caused by the

accumulation of fluid. Although these symptoms are common among women without OC, it is recommended to seek medical attention if persistent symptoms occur.

The cause of OC is not known. The risk for developing ovarian cancer has been associated with factors relating to family history, hormones, menstrual history, pregnancy, oral contraceptive use and lifestyle factors [19]. Factors associated with reduced OC risk are pregnancy, lactation and long-term oral contraceptive use. While parity is associated with a decreased OC risk in the general population, a study by Vachon et al. found family history of OC in first degree relatives (FDR) to have a mediating effect on OC risk [20]. Among women with history of OC in FDR, nulliparous women were at significantly higher risk [RR=2.7; 95% CI= (1.1-6.6)] for OC compared to parous women, while among women without family history of OC in FDR, the effect of parity was marginal. Further, results from a population-based study suggested having ever breastfed was associated with a 22% reduction in OC risk among parous women [21]. Oral contraceptive use is one the most significant protective risk factors for OC, with estimated protection ranging from 30-40% for ever oral contraceptive users, and almost a 50% risk reduction in women using oral contraceptives for at least ten years [22]. The most well-established risk factor for OC is family history, with a threefold to sevenfold increased risk among women with history of disease in FDR [19]. Women who take estrogen replacements for 5 years or more are at increased risk for developing OC [23]. Inherited germline mutations in BRAC1 or BRAC2 are associated with increased lifetime risk of OC. With the lifetime risk of OC for the general population in the United States being 1.2%, the estimated lifetime risk of OC significantly raises for women with the BRAC1 and BRAC2 mutations (39%-60% and 12%-20%, respectively) [24].

Analogous to many other cancer types, the risk of OC increases with increased age [1]. Because no definitive symptoms are present with OC, it is estimated that for only 15% of patients is the disease confined to the ovary [25].

Surgery is the primary treatment for OC. Surgery may involve anything from a total hysterectomy, bilateral salpingo-oophorectomy, partial or complete removal of the omentum or biopsy of the lymph nodes and other tissues in the pelvis and abdomen [1]. Chemotherapy is typically used after surgery to treat remaining disease. Over time 5-year relative survival rates after an OC diagnoses have increased significantly, likely due to improvements in treatment methods. More specifically, survival rates have climbed from 36% in 1975-1977 to 44% in 2001-2007 for all stages at diagnoses [3].

Overview of cancer screening

Early detection is a fundamental process in the cancer control continuum. For all types of cancer, early detection of disease is associated with improved prognosis. The primary purpose of cancer screening is to detect cancer before symptoms present, because by the time symptoms occur it is likely that the disease may have grown or spread, making it harder to treat. For localized cancer, treatment is more effective and sometimes cancer is curable. Cancer screening modalities may include physical exams, laboratory tests, imaging procedures or genetic testing for genetic predispositions to specific cancers. According to the National Cancer Institute, in any cancer screening program there are many factors that must be considered when evaluating its necessity [26]. One, the disease should be a serious health problem, with the disease having high incidence rates and posing substantial threats on morbidity and mortality. Two, the target population to be

screened should be clearly defined, with sufficient disease prevalence to justify screening costs. Three, the level of expected participation should be sufficient enough to produce results that can be meaningfully analyzed. And most importantly, the screening test must have acceptable performance characteristics such as sensitivity and specificity.

Performance characteristics in cancer screening

Performance characteristics pertain to the diagnostic accuracy of the testing procedure. Test performance is often summarized using three quantitative measures: sensitivity, specificity and predictive value. Sensitivity is a measure representing the accuracy of a testing procedure to adequately identify the presence of disease, while specificity refers to the precision of a test to correctly identify non-diseased individuals. These measures are a function of possible outcomes of screening: true positives, true negatives, false positives and false negatives. The true positive rate is also called sensitivity, and one minus the true negative rate is termed specificity. A graphical representation of these rates is called a receiver operating curve (ROC), and is frequently presented. It is ideal for a cancer screening diagnostic test to have a very low false-positive rate, minimizing the number of individuals required to return for further diagnostic or surgical follow-up. Figure 2.1 is an example of a hypothetical ROC curve adapted illustrated by Baker, with sensitivity along the y-axis and 1-specificity along the x-axis [27]. True positives defined as individuals who have the disease of interest and are identified positive by the screening test, are the only people who can benefit from screening. Positive predictive value is the proportion of individuals with positive screening tests who actually have the disease, and is a function of sensitivity, specificity and disease prevalence. In any cancer screening modality, high measures of test performance are desired, but the possibility of diagnostic

errors (false negative, false positives) always exists. In addition to diagnostic errors, cancer screening programs also present with concerns about costs and potential risks of harm.

Ovarian cancer screening trials

Because no distinct symptoms are present with OC, the overwhelming majority of OC cases are diagnosed at a distant stage when prognosis is poor. Therefore, recent studies have focused on the development of OC screening methods to aid in early detection of the disease. As of today, four prospective trials have been conducted to test the efficacy of screening modalities in reducing OC-related mortality. Of the four trials, two have been completed and two are ongoing and study locations vary geographically: two have been conducted in the United States, one in Japan and one in the United Kingdom.

The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial was a large, multicenter, randomized controlled trial conducted in the United States aimed to evaluate the efficacy of transvaginal ultrasound and serum cancer antigen 125 (CA125) as screening tools to reduce OC-specific mortality [6]. The trial was conducted from 1993-2001 with follow-up for 13 years from randomization. Women were randomized to either the intervention group or usual care group, with the intervention consisting of annual TVS and serum CA125 levels measured through blood testing. Eligible participants were women who were 55-74 years of age who: had no previous diagnosis of lung, colorectal or ovarian cancer, had not previously undergone oophorectomy surgery and were not currently using tamoxifen. Women in the intervention group were offered TVS and CA125 blood testing at baseline, with an annual TVS for an additional three years and an

annual CA125 for an additional five years. The primary outcome of interest in this study was mortality from OC, with secondary outcomes of interest including OC incidence and complications associated with screening and diagnostic procedures. Results from this trial did not show that combination screening reduced OC-related mortality. Almost 10% of women in the intervention group experienced a false positive screening test result, and 15% of them experienced at least one serious complication after surgical follow-up. The primary conclusions from this study were that simultaneous TVS and CA125 screening compared with usual care does not reduce OC mortality, and follow-up procedures after receipt of a false positive screening test results were associated with complications.

The only other OC screening trial in the United States is being conducted at the University of Kentucky [28]. This population-controlled (one-arm) trial began in 1986 and offers annual TVS screening to asymptomatic, postmenopausal women aged 50 years or older as well as premenopausal women 25 years of age or older with a documented family history of OC in at least one FDR. This trial has up to 27 years of follow-up and remains ongoing. Preliminary results suggest TVS is useful in detecting early stage OC (70.2% stage I and II, compared with 27% in general population comparison group). Because OC is a very rare disease, an enormous amount of women must be screened to detect a small number of cases. According to 2013 trial results, 47 true positives have been detected out of over 200,000 women screened. Data from this trial indicate almost 7% of women with abnormal TVS results present with no evidence of OC after surgical follow-up (false positives) [28].

Hirosaki University Ovarian Cancer Screening Program offers annual TVS screening for asymptomatic women [7]. The randomized, controlled trial offered TVS screening along

with CA125 testing to women at least 30 years of age who presented for cervical cytologic screening. Preliminary results from this trial indicate early detection of OC (stage I and II) in 82% of women with the disease. Over 40,000 women were screened for this trial and 27 true positive OC cases were detected.

The final OC screening trial is the United Kingdom Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) [29]. This randomized, controlled trial accrued participants from 2001-2005 and included post-menopausal women aged 50-74. The intervention arms received annual TVS screening alone or annual TVS screening combined with CA125 testing. Results from the trial indicated 50% stage I and II OC cases, with high rates of sensitivity and specificity in both multimodal and TVS alone intervention groups. Evidence offered promising characteristics of the proposed screening modalities and results are pending for additional follow-up to evaluate the efficacy of screening in reducing OC-specific mortality.

Although results from these trials indicate that OC screening modalities have the ability to detect early stage disease, annual screening for OC is not recommended by any professional society. Although TVS and CA125 prove effective in the early detection of OC with high sensitivity, false positive test results occur and can cause adverse psychological and behavioral outcomes as well as complications resulting from invasive follow-up and diagnostic procedures. Of interest in this dissertation are the affective, cognitive and behavioral outcomes associated with receipt of an abnormal, yet ultimately benign, OC screening test result.

Outcomes associated with receipt of a false positive cancer screening test

Abundant literature exists that demonstrates the impact of an abnormal, yet ultimately benign, cancer screening test result, with the overwhelming majority focusing on breast and cervical cancer screening. Current research suggests that receipt of a false positive cancer screening test during annual, routine screening has a significant impact on psychological and behavioral outcomes.

Affective outcomes

Extensive research focusing on affective endpoints such as general anxiety, depression and overall well-being suggests that receipt of an abnormal screening test result is associated with increased adverse outcomes within this domain. Researchers have found that women receiving false positive cancer screening test results experience significantly more distress [30-33], report lower quality of life [34] and suffer from higher levels of anxiety [30].

Cancer-specific psychological morbidities have also been studied, and results suggested that women receiving false positive cancer screening results suffered from greater cancer-specific anxiety, distress and worry [12, 35, 36]. More specifically, a study by Anderson et al. found that women with abnormal test results were more than twice as likely to report increased levels of cancer worry over a two year screening interval compared to women receiving all normal breast cancer screening results [37]. In a meta-analysis of the effect of false positive mammograms on psychosocial outcomes, results suggested that effects were associated with cancer-specific indices rather than general affective indices of psychological morbidities (i.e. distress, anxiety, worry) [38].

Although considerable literature demonstrates the association between an abnormal cancer screening test result and adverse affective outcomes, little research has been devoted to positive affective outcomes associated with participating in cancer screening programs. There is growing literature that investigates the positive ways in which individuals' lives change as a result of a traumatic event, and it has been suggested that types of "post-traumatic growth" and benefit-finding are related to improved physical and psychological outcomes [39, 40]. A 2006 review of literature examining positive consequences after a traumatic life event found for health-threatening stressors, benefit-finding was associated with decreased depression, global distress and subjective physical health, and increased positive well-being. Results from this study indicated that time since trauma (both health-threatening and personal traumas) was the most significant moderator in the effect sizes for depression, anxiety, positive well-being and global distress. Although researchers have examined benefit-finding after the occurrence of various stressors (i.e. diagnoses of primary cancers, chronic diseases) [41, 42], little work has been done in the context of cancer screening.

In a study of psychological outcomes of familial ovarian cancer screening, Brain et al. found no long term differences in reassurance between women who received a normal result and women receiving false positive test results [43]. However, Gaugler et al. found that receipt of a normal OC screening test result was associated with positive affective outcomes over a four month study period [44]. With conflicting study results, the impact of cancer screening test results on positive affective outcomes is not yet well characterized.

Cognitive outcomes

Few studies have been conducted that focus on the impact of an abnormal, yet ultimately benign, cancer screening result on cognitive outcomes such as personal and comparative perceptions of cancer risk and attitudes and beliefs about the efficacy of cancer screening. A study by Lipkus et al. found that receipt of a false positive mammogram was associated with increased perceptions of lifetime personal breast cancer risk [45]. In a more recent study, researchers at the University of Kentucky examined the effect of a false positive screening result for OC on perceived personal OC risk as well as comparative risk, defined as a woman's lifetime perceived risk for OC compared to a typical woman's risk for OC [46]. Results from this study suggested that women in the false positive group reported greater perceived personal risk for OC than women in the regular screened group. While women in both groups reported their perceived OC risk to be less than a typical woman's OC risk, the magnitude of comparative risk was significantly smaller in the false positive screening group. In a meta-analysis investigating perceived breast cancer risk and the relation between perceived risk and breast cancer screening, researchers found that women who were asked about their perceived lifetime breast cancer risk by way of a numerical question tended to overestimate their risk, while those asked in a verbal question tended to present their risk more optimistically [47]. Further, the investigators suggested that women held an optimistic bias in the verbal scale but significantly overestimated their risk in the numerical scale, suggesting that the two measures should be combined to represent a composite measure of risk perception.

Results pertaining to general attitudes and beliefs about cancer screening programs in various cancer settings have been reported. In a population-based study of United States

residents, researchers found that most adults (87%) believe routine cancer screening is “almost always a good idea”, and the majority believe that early detection saves lives “most” or “all of the time” [48]. Specific to OC screening, baseline analysis from the UKCTOCS showed that almost all women (99%) believed committed participation in OC screening would reduce mortality and 96% of participants believed that cancers detected early would have improved prognosis [49]. Although the general population seems to agree that early detection through cancer screening is useful in detecting early cancer and subsequently improving survival, little is known about how these beliefs are affected by a false positive cancer screening test result.

Schwartz et al. examined women’s attitudes about false-positive mammograms, and results indicated that a majority of women (62%) did not take the possibility of false-positive screening results into account when deciding about screening. While perceptions of personal and comparative lifetime cancer risk and worry about cancer after an abnormal cancer screening test result have been reported, very limited research has been done to examine how attitudes and beliefs about cancer screening are affected after receipt of a false positive test result. Lipkus et al. conducted a study to assess attitudes towards mammography screening in women who had history of an abnormal mammogram and those who did not [45]. Investigators hypothesized that women with an abnormal mammogram within the past 2 years would have more positive attitudes towards mammography screening than women who had regular mammograms. Results from this study suggested a marginally significant trend ($p=0.09$) that women who had a recent abnormal mammogram reported more positive attitudes towards mammograms than women who had not had an abnormal result. However, no such differences were

found when comparing women with abnormal mammograms more than two years ago to those with normal results. In the breast cancer screening literature, it has been suggested that women are aware of the possibility of false-positive screening results, but the possibility does not affect their attitudes and beliefs about the efficacy of mammography testing. Rather, receipt of a false-positive screening test may heighten their beliefs in the efficacy of the screening modality in early detection. While studies have suggested such cognitive effects of an abnormal cancer screening test, further research is needed to better characterize the impact, especially in the OC screening context.

Behavioral outcomes

Although literature exists examining the association between receipt of an abnormal cancer screening test result and future participation in cancer screening programs, most studies focus on the cervical and breast cancer screening setting. Lipkus et al. conducted a cross-sectional study to investigate whether previous history of an abnormal mammogram affected screening outcomes [45]. Results from this study indicated that women with previous history of abnormal mammograms (within the past 2 years) were more likely to have had a clinical breast examination over the past two years, and more likely to adhere to mammography screening recommendations, compared to women who had never had an abnormal test result. Similarly, in a study of adherence to mammography screening, Burman et al. found that women who received a false-positive mammography were 20% more likely to return to their next recommended mammography screening, compared to women with true-negative index screening test results [50]. A meta-analysis of studies conducted in the United States found conflicting results that women who received false positive results during routine breast cancer

screening were slightly more likely to return to routine screening than women who received normal results [RR=1.07; 95% CI=(1.02-1.12)], although no statistically significant differences were found among studies of European women [13]. However, for the meta-analysis including two studies of Canadian women, receipt of a false-positive mammography was associated with a decrease in the likelihood of returning to routine screening [RR=0.63; 95% CI=(0.50-0.80)]. With conflicting results, further research examining the impact of a false positive screening test result is necessary to better distinguish the impact on return for screening.

Differing theories have been proposed to explain women's participation in future cancer screening programs after receipt of a false positive screening test. In the context of breast cancer screening, one may suggest that receiving an abnormal, yet ultimately benign, mammogram may discourage women from participating in routine screening, due to testing errors weakening women's beliefs in the efficacy of mammography in early detection [51]. Another theory suggests that false-positive cancer screening results may not have an effect on return for routine screening. In a study aimed to determine the public's enthusiasm for cancer screening, 98% of subjects were glad they had participated in the initial cancer screening even though 29% of individuals characterized the experience of receiving false positive results as "very scary"[48]. In this same study, among women who have had a false positive mammography test result, 73% reported that they are still having mammography tests the same as before. A third, less commonly argued theory is that false positive may be associated with increased participation in future screening, due to increases in anxiety, worry and/or perceived risk experienced after the event [52]. Whatever the reason may be, understanding behavioral outcomes

following false positive cancer screening results is fundamental in understanding the impact of a significant health-threatening event.

Per the theory of planned behavior, it is reasonable to assume that stated intentions are positively correlated with behaviors, and stated intentions to participate is useful as a surrogate in investigating the effect of an abnormal cancer screening test result on return for routine, recommended cancer screening [53]. To our knowledge, no previous study has been conducted to examine this relationship in the context of OC screening.

Throughout the literature it has been well established that abnormal cancer screening tests are associated with adverse affective outcomes. While general distress and cancer-specific distress have been addressed, cognitive outcomes such as attitudes and beliefs about cancer screening, or behavioral outcomes pertaining to intentions to participate in future cancer screening programs have not yet been explored in the OC screening context. Although researchers have examined general (and cancer-specific) indices of affective outcomes, the impact of an abnormal cancer screening test result on positive affective outcomes, such as benefit-finding and reassurance, is not yet well characterized. Further, factors associated with the trajectory of psychological response over time remain unknown.

Factors associated with the magnitude and trajectory of psychological response over time

It is reasonable to assume the magnitude and trajectory of psychological response to a health-threatening event is determined in part by an individual's situational factors and dispositional characteristics. The monitoring process (MP) model was developed to

analyze how informational styles relate to coping when dealing with potentially life-threatening events. Termed “high monitors”, these individuals scan for information pertaining to the event, and tend to translate neutral or ambiguous information as threatening, leading to exaggerated perceptions of personal risk [54]. While low monitors, or “blunters”, tend to avoid threat-relevant information. In a study by Wardle et al., researchers found evidence supporting the MP model that women with an information-seeking coping style (i.e. monitors) were more adversely affected by abnormal screening results for OC than women with blunting coping styles (i.e. blunters) [16]. In a study of women participating in an annual TVS screening program for OC, results supported the impact of informational coping style on OC-specific distress after an abnormal screening test result [17]. Findings suggested that a combination of a monitoring coping style and low optimism was associated with elevated OC-specific distress after an abnormal TVS screening result. The authors proposed that the impact of a monitoring coping style was restrained when high optimism was also present in the context of an abnormal screening test result as a health-threatening event. Because informational coping styles have been shown to be associated with psychological responses to health-threatening events, identification and treatment of individuals at high-risk, who are more likely to experience distress, may lead to improved quality of life and may help promote early detection of cancer [54].

More recently, Andrykowski et al. conducted a study to test the Cognitive-Social Health Information Processing (C-SHIP) model [14] theory that proposes dispositional or situational characteristics combined with coping style may moderate the trajectory of OC-specific distress triggered by an abnormal TVS screening test result [17]. In this

study, researchers found a high monitoring coping style combined with family history of OC was associated with increased OC-specific distress after a false positive screen. Consistent with findings from a previous study of cancer-specific distress after breast biopsy, family history of disease seemed to induce additional distress already experienced among monitoring women [12]. It has been well established that receiving false positive cancer screening test results is associated with increased, short-term cancer-specific distress [13, 55]. Although, little research has examined factors associated with the magnitude and trajectory of cancer-specific distress over time.

Steffens et al. conducted a study to determine the demographic and clinical factors associated with the magnitude of distress during the benign breast biopsy (BBB) experience after abnormal mammography results [56]. In this study, researchers found lower age, less education and no family history of breast cancer to be significantly associated with greater distress. Contradicting these results, a study on the impact of BBB found number of first degree relatives with breast cancer to be significantly associated with greater avoidance scores (as a measure of OC-specific distress) [12]. Further, this study evaluated dispositional factors associated with magnitude of distress. Results showed that among women in the BBB group, a monitoring informational coping style was most strongly associated with distress when optimism was low, supporting theories proposed by the MP model.

Through specific aims (2) and (3) of this dissertation, we examine the features – out of a comprehensive set of demographic, clinical, dispositional and situational factors – that are associated with high-risk profiles for OC-specific distress. As these demographic, clinical and situational factors are easily identifiable, they provide a simple, cost-effective

means of stratifying risk for distress in the OC screening setting. Further, categorization of dispositional characteristics allows identification of women who are more likely to suffer from increased distress. It is clinically relevant to identify these factors to provide interventional programs to moderate OC-specific distress after the occurrence of a potentially health-threatening event.

Several studies have demonstrated that a high monitoring information coping style is associated with not only elevated levels of distress, but more persistent distress in response to threatening events [16, 57, 58]. In a study by Andrykowski et al. examining the psychological impact of benign breast biopsy, researchers found a decrease in breast cancer-specific distress over time, with significant differences between baseline and 4-month follow-up assessments [12]. Although previous studies have identified decreases in adverse psychological responses over time in women participating in cancer screening trials, to our knowledge, no study has examined factors associated with the trajectory of cancer-specific distress within the false positive group alone. By modeling intraindividual OC-specific distress trajectories, we will be able to identify factors associated with changes over time. Further, we will be able to identify which women are at high risk for experiencing long-term adverse psychological distress to better characterize which individuals need treatment to moderate their response to a potentially health-threatening event.

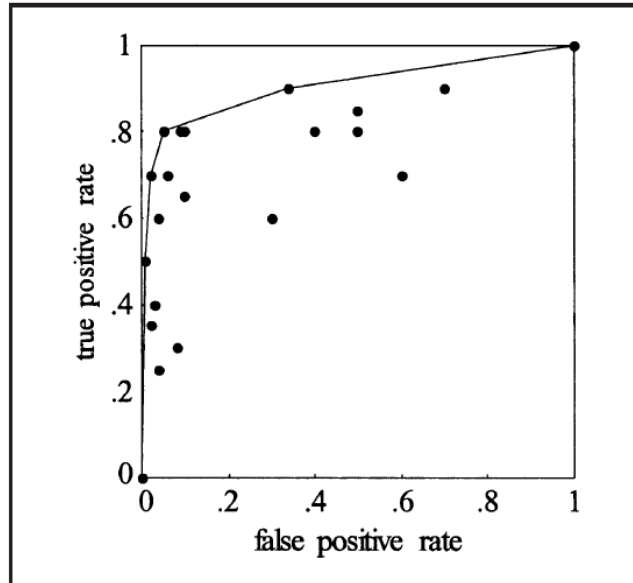


Figure 2.1 Example receiver operator curve

3 Affective, Cognitive and Behavioral Outcomes Associated with a False Positive Screening Test Result for Ovarian Cancer

Introduction

Ovarian cancer (OC) is the fifth most common cancer among women and has the highest mortality of any cancer of the female reproductive system [1]. In 2012, an estimated 22,280 incident cases were, accounting for nearly 3% of all cancers among women and approximately 15,500 deaths were reported in the United States. OC represents the fourth leading cause of death for women aged 40-59, and the fifth leading cause of death for women aged 60-79 [3].

The distribution of stage at OC diagnosis is disproportionately late-stage with 15% of cases diagnosed with localized disease, 16% with regional and 61% with distant disease [3]. When diagnosed at a localized stage, 5-year relative survival is very high (92%), with rates dropping considerably for diagnoses in regional and distant stages (72% and 27%, respectively) [4]. Because diagnoses occur most commonly at a late stage, and prognosis for advanced disease is poor, research focusing on the development of effective OC screening methods to facilitate early detection in high-risk, asymptomatic women is fundamental to decreasing mortality from ovarian cancer. Presently, there is no screening method proven effective in reducing OC-specific mortality. Methods have been proposed for early detection of OC including pelvic examination, transvaginal ultrasonography (TVS) and blood tests for cancer antigen 125 (CA125), alone or in combination. While the efficacy of these methods in reducing OC-specific mortality has not been proven in

prospective, randomized trials, the CA125 assay and TVS have been tested alone and in combination, and have shown value in early detection of OC [7-9].

Although early detection through OC screening is critical to improving prognosis of OC, it does not come without limitations. Similar to other cancer screening modalities, TVS screening for OC presents with the possibility of false positive screening test results.

False positive screening test results occur when patients receive an abnormal screening test result, after which repeat screening or further follow-up procedures confirms no disease exists. Research has shown receipt of a false positive screening test result in any cancer screening setting can impact a variety of affective, cognitive and behavioral outcomes [11, 12].

Affective outcomes

Extensive research focusing on affective endpoints such as general anxiety, depression and overall well-being suggests a false positive screening test result is associated with increased adverse outcomes. Researchers have found that women receiving false positive cancer screening test results experience significantly more distress [30-33], report lower quality of life [34] and suffer from higher levels of anxiety [30]. Cancer-specific psychological morbidities have also been studied, suggesting that women receiving false positive cancer screening results report greater cancer-specific anxiety, distress and worry [12, 35, 36]. In the OC screening setting, researchers found women receiving false positive TVS screening test results for OC reported elevated short-term OC-specific stress. Distress declined over time, but remained elevated at four month follow-up [11]. Additionally, investigators found that receipt of an abnormal, yet ultimately benign, TVS

test result was associated with increased cancer-specific distress rather than generic measures of distress, and suggested using cancer-specific distress measures in future studies [13].

Although considerable literature demonstrates the association between a false positive screening test result and adverse affective outcomes, little research has been devoted to examining potential positive affective outcomes associated with participating in cancer screening programs or false positive screening test results. There is a growing literature that investigates the positive ways in which individuals' lives change as a result of a traumatic event, and it has been suggested that benefit-finding is related to improved physical and psychological outcomes [39, 40]. A 2006 review of literature examining positive consequences after a traumatic life event found for health-threatening stressors, benefit-finding was associated with decreased depression, global distress and subjective physical health, and increased positive well-being[39]. Although researchers have examined benefit finding after the occurrence of various stressors (i.e. diagnoses of primary cancers, chronic diseases, etc. [41, 42]), little work has been done in the context of cancer screening. In a study of psychological outcomes of familial ovarian cancer screening, Brain et al. found no long term differences in perceived positive consequences of cancer screening between women receiving normal results and women receiving false positive test results [43]. However, a study by Gaugler et al. found receipt of a normal OC screening test result to be associated with positive affect over a four month study period [44]. These studies focused on different target populations, with conflicting study results; the impact of cancer screening test results on positive affective outcomes remains unclear.

Cognitive outcomes

Few studies have been conducted on the impact of a false positive screening test result on cognitive outcomes such as perceptions of lifetime cancer risk and attitudes and beliefs about the efficacy of cancer screening. A study by Lipkus et al. found that receipt of a false positive mammogram was associated with increased perceptions of lifetime personal breast cancer risk [45]. In a more recent study, researchers at the University of Kentucky examined the effect of a false positive screening test result for OC on perceived personal OC risk as well as comparative OC risk, defined as perceived personal lifetime risk for OC compared to perceptions of a typical woman's risk for OC [46]. Results suggested women receiving false positive results report greater perceived personal risk for OC than women receiving normal screening test results. While women in both groups reported their perceived OC risk to be less than what they perceived to be a typical woman's OC risk, the magnitude of comparative risk was significantly smaller in the false positive screening group.

Results pertaining to general attitudes and beliefs about cancer screening procedures in various cancer settings have been reported. In a population-based study of U.S. residents, researchers found most adults (87%) believe routine cancer screening is "almost always a good idea", and the majority of adults believe early detection saves lives "most" or "all of the time" [48]. Specific to OC screening, baseline analysis from the University of Kentucky Ovarian Cancer Screening Program showed almost all women (99%) believed committed participation in OC screening would reduce mortality and 96% of participants believed cancers detected early would have improved prognosis [49]. Although the general population seems to agree early detection through cancer screening is useful in

detecting early cancer and subsequently improving survival, little is known about how these beliefs are affected by a false positive cancer screening test result.

Behavioral outcomes

Literature examining the association between receipt of a false positive screening test result and future participation in cancer screening programs has focused on cervical and breast cancer screening. Lipkus et al. conducted a cross-sectional study to investigate whether a previous history of a false positive mammogram affected subsequent screening behavior [45]. Results indicated women with a previous history of abnormal, yet ultimately benign, mammograms (within the past 2 years) were more likely to have had a clinical breast examination over the past two years, and more likely to adhere to mammography screening recommendations, compared to women who had never had an abnormal mammogram result. Similarly, in a study of adherence to mammography screening, Burman et al. found women who received a false positive mammogram were 20% more likely to return to their next recommended mammography screening, compared to women with normal mammogram results [50]. A meta-analysis of studies conducted in the United States concluded women who received false positive results during routine breast cancer screening were slightly more likely to return for routine screening than women who received normal results. In contrast, no statistically significant differences were found among studies of European women [13]. However, for the meta-analysis including two studies of Canadian women, receipt of a false positive mammogram was associated with a decrease in the likelihood of returning for routine screening. With conflicting results, further research examining the impact of a false

positive screening test result is necessary to determine the impact of a false positive test on return for screening.

The present study characterizes the impact of a false positive screening test result during routine participation in a TVS screening program for OC. More specifically, we examined differences in affective, cognitive and behavioral outcomes in women receiving false positive screening test results and those receiving normal results during routine screening. We hypothesized that an abnormal, yet ultimately benign, TVS test result would be associated with increased OC-specific distress, less positive consequences of screening but greater benefit-finding, increased perceptions of personal OC risk, reduced perceptions about the efficacy of cancer screening and reduced intentions to participate in future cancer screening programs in general.

Methods

Sample

Participants represent a subset of individuals participating in a broader, quasi-experimental study evaluating affective, cognitive and behavioral outcomes associated with receipt of an abnormal, yet ultimately benign, TVS screening test result identified during routine screening through the University of Kentucky Ovarian Cancer Screening Program (UKOCSP). Ethical approval for this study was obtained from the University of Kentucky Institutional Review Board.

The UKOCSP offers free, annual screening to asymptomatic women at least 50 years of age and asymptomatic women 25-50 years of age with at least one first degree relative

with OC. Women receiving an abnormal TVS screening test result during the course of routine, annual screening are asked to return within 2-12 weeks for a repeat TVS test. Eligibility for participation in this study of psychosocial and behavioral response to TVS screening was dependent upon study group definition. Eligible women were identified from UKOCSP records. Women who received an abnormal TVS screening test result within the past 12 weeks, and were scheduled to return for additional follow-up were identified. Upon arrival at the clinic at the time of their scheduled follow-up appointment, these women met with research staff and consented to participate in the study. These women comprised the abnormal screening (AS) group. To be included in the routine screening (RS) study group, a woman must have matched with a woman already enrolled in the AS study group based on the following criteria: 1) age (+/- 5 years), 2) number of prior routine screening tests received on the program (+/- 1 test), and 3) history of prior abnormal TVS test result (yes vs. no). Women in the RS study group were identified through clinic records and were enrolled at the clinic prior to receipt of their annual, routine TVS screening test. All participants were enrolled in the study from 2004 to 2009.

Procedure

A baseline interview was completed following study enrollment immediately prior to the participant's scheduled repeat or routine TVS screening test. Women in the RS study group received a normal TVS screening test result and completed two follow-up telephone interviews, one month and four months following their baseline interview. Women in the AS study group completed their baseline assessment prior to their scheduled repeat TVS screening test. Women in the AS study group also completed two follow-up telephone interviews, one month and four months after their baseline

assessment. All women in the AS study group were notified prior to the one month follow-up interview that results of their repeat TVS screening test were benign. Less than 5% of eligible women invited to participate declined participation. Figure 3.1 provides a graphical depiction of participant flow and longitudinal administration of assessments.

Measures

All participants completed questionnaires assessing demographic and clinical information, dispositional information, mental and physical functioning, distress, benefit-finding, positive consequences of screening, perceived OC risk, beliefs about cancer screening, and intentions to participate in future cancer screening programs.

Demographic, clinical and dispositional information were assessed only at baseline, whereas all other measures were completed at all baseline and follow-up assessments by both study groups. Only the AS group was assessed for benefit-finding and positive consequences of screening at the baseline assessment.

Demographic and clinical information

Demographic information assessed by self-report included age, race/ethnicity, partner status, education, income and clinical information relevant to OC risk including personal history of breast cancer and family history of OC. Family history of OC (yes vs. no) was determined based on whether or not the woman had a first-degree relative (FDR) with OC (mother, sister or daughter). Clinical information collected from clinic records included number of previous TVS screening tests and prior lifetime history of abnormal TVS screening test result (yes versus no).

Dispositional characteristics

Dispositional optimism was assessed using the Life Orientation Test-Revised (LOT-R) [59]. The LOT-R is a standardized, commonly used 10-item measure of dispositional optimism and yields a total optimism score. Informational coping style was measured using the Miller Behavioral Styles Scale-Short Form (MBSS-SF) [60]. The MBSS-SF consists of 2 stressor scenarios followed by 8 statements representing different coping strategies for that stressor. Separate Monitoring and Blunting scores were computed, only the Monitoring score was used in subsequent analyses.

Mental and Physical Functioning

Mental and physical functioning were assessed using the Medical Outcomes Study 12-Item Short Form Health Survey (SF-12) [61]. The SF-12 is a standardized, commonly used measure of physical and mental health status in both medical and healthy examples. Only the physical and mental health subscale scores were used in subsequent analyses.

Outcome measures

Distress

General distress was assessed by the Centers for Epidemiologic Studies Depression Scale (CESD) [62]. The CESD is a 20-item measure of current depressive symptoms and yields a total depression symptom score. As such, it is a measure of general distress.

OC-specific distress was assessed by the Impact of Events Scale (IES) [63]. The IES is a standardized, commonly used 15-item measure of current distress associated with a specific stressor. Women completed the IES with regard to "the possibility that you will develop ovarian cancer in your lifetime." The IES yields subscale scores for Intrusion and

Avoidance. The Intrusion subscale consists of 7 items which measure intrusive symptoms (intrusive thoughts, nightmares, unpleasant feelings and imagery). The Avoidance subscale consists of 8 items which measure avoidance symptoms (numbing of responsiveness, avoidance of feelings, situations and ideas). Respondents are asked to rate the frequency of each item occurring within the past 7 days according to the scale: (0) not at all, (1) rarely, (3) sometimes and (5) often. Responses are summed over each subscale, with the following possible range of responses: Intrusion (0-35) and Avoidance (0-40). A copy of the IES instrument is available in the Appendix.

Positive consequences of screening

Benefits were assessed using the Benefit-Finding Questionnaire (BFQ) [64]. The BFQ is a 17-item instrument assessing benefits derived following a specific event, in this case – “my most recent experience with the University of Kentucky Ovarian Cancer Screen Program.” The BFQ yields a total benefit-finding score.

Positive consequences of cancer screening were assessed using the Psychological Consequences Questionnaire (PCQ) [65]. The PCQ is a standardized 22-item measure of positive (i.e. reassurance) and negative consequences of breast cancer screening. While developed for use in the breast cancer screening setting, the authors indicate the PCQ can be modified for use in other screening settings. Only the 10-item positive consequences subscale was used and the PCQ was modified by changing references from "breast cancer" and "breast cancer screening" to "ovarian cancer" and "ovarian cancer screening".

Perceived OC-risk

Two estimates of lifetime OC risk were obtained: personal and comparative. Personal lifetime risk for OC was assessed based on responses from two questions. First, women estimated personal lifetime risk for OC by providing a percentage between 0 and 100 in response to the question "What do you think are the chances that you will develop ovarian cancer during your lifetime?" [12] Second, women were asked "How likely do you think you are to develop ovarian cancer at some point during your life?" with ordinal response options ranging from (1) "no chance" to (6) "certain to happen". Responses from these two questions were standardized with respect to baseline mean and standard deviation and summed to create a composite measure of personal lifetime OC risk.

Typical lifetime risk for OC was formed using women's personal and typical lifetime perceived OC risk estimates. Typical lifetime risk for OC was assessed based on responses from two questions. First, women estimated typical lifetime OC risk by providing a percentage between 0 and 100 in response to the question "What do you think the chances are that the typical woman your age will develop ovarian cancer during her lifetime?" [12, 66]. Second, women were asked "Compared to other women your age, do you think your chances of getting ovarian cancer during your lifetime are: (1) higher than other women my age, (2) about the same as other women my age or (3) lower than other women my age?". Responses from these two questions were standardized (to baseline mean and standard deviation) and summed to create a composite measure of typical lifetime OC risk.

Finally, a comparative measure of OC risk was calculated by subtracting the typical risk measure from the personal risk measure. Thus, a positive comparative OC risk value indicated a perception that personal risk of OC was greater than a typical woman's OC

risk. The personal and comparative OC risk measurements were used in subsequent analyses.

Cancer screening beliefs

Participants indicated their extent of agreement with two statements: “A Transvaginal Sonography screening test can find ovarian cancer early” and “Ovarian cancer can be cured if found early” [66]. Responses were recorded on identical 4-point Likert scales ranging from strongly disagree to strongly agree. Responses were summed to create a single index of OC screening effectiveness with higher scores reflecting stronger beliefs in the effectiveness of OC screening. Similar questions were asked regarding mammography for breast cancer and sigmoidoscopy for colorectal cancer, and screening effectiveness scores for each were calculated in the same manner.

Cancer screening intentions

Intentions for participation in future OC screening were assessed with the following question: “How likely is it that you will return for another TVS screening test for ovarian cancer by ___?” Here, research staff filled in the blank with the appropriate date for next recommended screening (i.e. one year from last screening date), with ordinal response options ranging from (1) “I definitely will” to (5) “I definitely will not”. The same questions were asked regarding intentions to participate in mammography screening.

Statistical analyses

Data were summarized descriptively, including means and standard deviations for continuous variables and frequency distributions for categorical variables. Bivariate

analyses to evaluate the unadjusted associations between demographic/clinical characteristics and study group were performed using linear mixed models (LMM) and generalized linear mixed models (GLMM) to account for potential correlations between individual matches. Multivariate associations for normally distributed outcomes of interest were conducted using a two-group (AS versus RS) LMM repeated measures analysis [67]. Two-group (AS versus RS) GLMM repeated measures analysis was used for non-normally distributed outcomes. Because a considerable proportion of respondents exhibited none of the responses (i.e. a zero response) measured by the CESD or the Intrusion and Avoidance subscales of the IES, the Zero-Inflated Poisson (ZIP) distribution was the assumed underlying probability distributions for these three models. Results of adjusted (G)LMM analyses were reported as estimates of mean differences or mean ratios, as appropriate, with accompanying 95% confidence intervals. Multivariate models were adjusted for education, mental and physical functioning (SF-12), MBSS-SF Monitoring and LOT-R Optimism scores. The effect size calculated was Cohen's *d*. All analyses for this paper were generated using SAS software, Version 9.3 of the SAS System for Windows.

Results

The study sample consisted of 750 women: 375 in the AS group and 375 in the RS group. The demographic and clinical characteristics by study group are shown in Table 3.1. Women in AS and RS study groups were very similar with respect to demographic characteristics, with the only exception being years of education. Women in the AS group were significantly more educated than women in the RS group (Mean (SD)_{AS}=14.0 (2.8) versus Mean (SD)_{RS}=13.6 (2.9); $p=0.03$). Study group participants were similar on the

majority of clinical characteristics pertaining to OC, but a significantly higher proportion of women in the AS study group reported ever being diagnosed with breast cancer (12.5% in AS versus 5.9% in RS; $p=0.002$).

Results of the adjusted GLMM and LMM analyses are reported in Table 3.2. Table values include estimates of mean ratios (AS vs. RS) or mean differences (AS-RS), confidence intervals, appropriate p -values for tests of differences at each time point and effect sizes. Mean ratios greater than 1 suggest increased distress responses in the AS group compared to the RS group.

Distress

There was no significant Group*Time interaction effect for CESD depression scores ($p=0.57$). Women in the AS group expressed somewhat lower depression scores but no significant difference was observed between AS and RS women over the four month interval post-screening.

According to the first IES ZIP model there was a significant Group*Time interaction effect for IES-Avoidance scores. This interaction, shown in Figure 3.2, suggests women in the AS group exhibited higher IES-Avoidance measures at each time point relative to the RS group, with observed differences decreasing over time. For baseline and one-month assessments AS women reported over three times as many estimated mean avoidant thoughts as RS women, and still almost two times as many at the four-month follow-up. Small to medium effect sizes were observed, ranging from 0.19-0.54 deviations. A trend toward significance ($p=0.06$) was observed in the Group*Time interaction effect in IES-Intrusion scores. This interaction, shown in Figure 3, resembles

the changes in group differences over time in IES-Intrusion scores. Although the overall Group*Time interaction effect was not significant at the 0.05 level, AS women reported significantly higher mean intrusive thoughts compared to women in the RS group at each time point. Again, small to medium effect sizes were observed ranging from 0.22-0.44 deviations.

Positive Consequences

No significant Group*Time interaction effect was observed in benefit-finding. No significant differences were observed at either assessment between AS and RS women (see Table 2).

Although there was no significant Group*Time interaction effect for positive consequences of screening ($p=0.16$), AS women reported significantly lower mean positive consequences of screening at each time point compared to RS women (one-month: $MD_{AS-RS} = -1.42, p=0.03$; four-month: $MD_{AS-RS} = -2.27, p=0.002$). Effect sizes were in the small to medium range.

Perceived OC-risk

Although no significant Group*Time interaction effect was observed for personal or comparative lifetime perceived OC-risk, AS women reported significantly higher perceived personal and comparative risk at almost every assessment (see Table 2 and Figure 4). For personal OC-risk, AS women reported significantly higher perceived lifetime OC risk at baseline and one-month assessments with small to moderate effect sizes ranging from 0.22-0.23.

Lifetime perceived comparative OC-risk differed significantly between groups at each time point, with AS women perceiving the magnitude of their comparative (personal-typical) OC-risk greater than RS women at all assessments with small to moderate effect sizes ranging from 0.23-0.31. Unadjusted mean comparative OC-risk estimates by groups over time are displayed in Figure 3.5.

Cancer Screening Beliefs

For ovarian cancer, breast cancer and colorectal cancer screening effectiveness, no differences in the beliefs of AS and RS women were observed at any time point, nor were any significant Group*Time interaction effects observed.

Cancer Screening Intentions

As shown in Table 2, there was no significant Group*Time interaction effect observed in intentions to participate in future TVS screening for OC. However, women in the AS group reported significantly elevated intentions at the one-month assessment ($MD_{AS-RS} = 0.09, p=0.01$). Analyses limited to women at least 50 years of age ($N=590$) indicated no significant Group*Time interaction effect, nor significant group differences at any time point, in intentions to participate in future mammography screening for breast cancer.

Discussion

In general, the study results support the hypotheses that receipt of a false positive TVS test result during routine OC screening impacted a variety of affective, cognitive and behavioral outcomes.

With respect to affective outcomes, receipt of a false positive TVS result had little impact on a generic measure of distress (CESD) but had significant impact upon a more cancer-specific measure of distress (IES). This is consistent with other studies which suggest false positive cancer screening test results are associated with increased cancer-specific distress [12, 35, 36]. Consistent with findings from Andrykowski et al., our results indicate a short-term effect on OC-specific distress that dissipates over time [11], but still remains significantly elevated at 4-months relative to the RS group. As suggested by previous researchers [11, 38], results from the current study indicate event-specific measures of distress to be more appropriate in measuring the impact of a health-threatening event than generic distress measures.

The heightened distress after receipt of a false positive TVS result may warrant the development and testing of interventions to minimize distress. Cancer-specific distress not only decreases overall well-being and quality-of-life, but may also adversely impact future cancer-related preventive behavior, such as participation in screening. Future research should identify variables associated with greater distress in response to false positive TVS test results so that interventions might be appropriately targeted to the most vulnerable, at risk women.

This study also examined the impact of a false positive TVS result on positive affective outcomes, including measures of benefit-finding and perceived positive consequences of screening. Contrary to our hypothesis, results showed no effect of screening test results on benefit-finding. In contrast, as hypothesized, receipt of a normal TVS screening test result was associated with reports of increased positive consequences of screening such as reassurance and feelings of well-being. This is consistent with findings from previous

research suggesting women with normal OC screening test results reported higher positive consequences of screening [44].

Study findings supported our hypotheses related to the impact of false positive TVS results on cognitive outcomes. Consistent with findings in the breast cancer screening setting [45], our results indicate an increased perception of lifetime OC risk following a false positive screening test result, with this effect observed in both measures of personal and comparative OC risk. Similar to findings from a previous smaller study [46], we observed an increased perception of lifetime OC risk in AS women at each assessment, with the largest effects observed in the short-term. Women in the AS study group reported significantly higher perceptions of comparative OC risk at all assessments. Again, the most significant impact of receipt of a false positive TVS result on comparative OC risk was observed in the short-term. Heightened risk perceptions may negatively impact quality of life or motivate avoidant behavior that could result in a reduced likelihood of participation in future cancer screening [68, 69]. Conversely, increased risk perception may have a positive impact if it motivates participation in risk-reducing behavior, such as participation in cancer screening programs [47, 70].

The effect of false positive screening test results on cognitive outcomes – including beliefs about screening efficacy for OC, breast and colorectal cancer have not previously been examined in the literature. While we did not observe any impact of a false positive result on screening efficacy beliefs for ovarian, breast or colorectal cancer screening, lack of significant findings may have been due to the insensitivity of the measurement used. Specifically, we observed a "ceiling effect", as the overwhelming majority of women agreed, or strongly agreed, the selected screening methods are effective and the selected

cancers can be cured if detected early. This finding indicates that within our study population, the belief that cancer screening is highly effective is so well in-grained that a false positive screening test result had little effect on women's beliefs. It would be interesting to see if this result is observed in other populations.

With respect to behavioral outcomes, at best, our results indicate a small, temporary increase in intention to participate in future TVS screening in the AS group. Again, lack of significant findings may be due to the insensitivity of the one-item measurement used. In fact, at least 90% of women reported they "definitely will" return in one year for TVS screening when asked at each assessment. While intentions are known to be an important precursor to actual behavior [53], further research is needed to identify the impact of false positive screening test results on actual OC screening participation.

Strengths and limitations

The present study is the largest, most comprehensive study to date focusing on the impact of a false positive cancer screening test result on psychosocial and behavioral outcomes. While previous research has examined the impact of false positive OC screening test results on a variety of outcomes, samples sizes were limited with only 33 women included in the AS group [11]. In the present study, relatively large sample sizes in both groups permitted the inclusion of potential confounding factors while also examining the role of time in the association between receipt of a false positive screening test result and outcomes of interest. Further, the use of advanced statistical techniques allowed for the appropriate specification of the underlying probability distribution of the distress outcome measures (CESD, IES-Intrusion and IES-Avoidance). Additionally, this study

evaluated the association between false positive screening test results and positive outcomes (i.e. benefit-finding and positive consequences of screening), which have received only limited attention in the cancer screening setting.

Several limitations to our study should be noted. First, because TVS screening for OC is not presently recommended for mass screening of asymptomatic women, it is unknown whether our results can be generalized to other cancer screening tests that are broadly recommended (i.e. mammography). However, it should be noted that while TVS screening for OC is not endorsed for the general population, the women in this study generally endorsed very strong beliefs in the value of TVS screening. Second, as noted in other publications from studies conducted through the UKOCSP, our sample consisted of predominantly Caucasian women. Thus, our findings may not be generalizable to racial/ethnic minority women. Although this study's large sample size allowed for the examination of complex associations of interest, results with respect to cancer screening beliefs and intentions to participate in future screening are likely limited due to the relative insensitivity of the measurements used. Therefore, a more thorough examination of the impact of false positive cancer screening test results is warranted within these domains.

Conclusions

Results from this study suggest receipt of a false positive TVS screening test result is associated with increased OC-specific distress, less perceived positive consequences of screening and increased perceptions of lifetime OC risk. The impact upon future screening behavior not yet well-characterized for OC. This study indicates that women's

beliefs in the effectiveness and intentions to participate in future ovarian, breast and colorectal cancer screenings were not affected by false positive OC screening test results. However, it is unknown whether women's actual behavior in participating in future screening was affected. If women who received a false positive TVS test result were found to reduce their participation effective cancer screening such as for breast, colorectal or cervical cancer, this would support the argument for not recommending OC screening test with low specificity and positive predictive values.

Table 3.1 Unadjusted associations among demographic and clinical characteristics and study group

	AS group N ^a =375 N (%)	RS group N ^a =375 N (%)	<i>P</i>
Demographic characteristics			
Mean age at study entry (SD)	56.8 (11.7)	58.0 (10.6)	.13
Race			.49
White	364 (97.1)	367 (97.9)	
Non-white	11 (2.9)	8 (2.1)	
Ethnicity			.21
Hispanic	4 (1.1)	1 (0.3)	
Non-Hispanic	371 (98.9)	374 (99.7)	
Partnered status			.23
Partnered	292 (77.9)	278 (74.1)	
Non-partnered	83 (22.1)	97 (25.9)	
Mean number years of education completed (SD)	14.0 (2.8)	13.6 (2.9)	.03
Household income (\$)			.10
≤ 20,000	52 (14.1)	63 (17.3)	
20,001 - 40,000	97 (26.2)	108 (29.7)	
40,001 - 80,000	131 (35.4)	113 (31.0)	
> 80,000	90 (24.3)	80 (22.0)	
Clinical characteristics			
Mean number of previous TVS tests (SD)	4.2 (4.98)	4.0 (4.53)	.70
History of abnormal TVS test result			--
Yes	78 (20.8)	78 (20.8)	
No	297 (79.2)	297 (79.2)	
Family History of OC in FDR			.11
No	211 (64.3)	225 (70.1)	
Yes	117 (35.7)	96 (29.9)	
Ever had BC			.002
Yes	47 (12.5)	22 (5.9)	
No	328 (87.5)	353 (94.1)	

Abbreviations: SD, standard deviation, TVS, transvaginal ultrasonography FDR, first-degree relative, OC, ovarian cancer, BC, breast cancer

^a Numbers vary due to sporadically missing data

Table 3.2 Multivariate associations among study group and outcome measures

	Baseline	1-month	4-month	Group*Time effect
	Estimated MR _{AS vs. RS} (95% CI) <i>ES^b</i>	Estimated MR _{AS vs. RS} (95% CI) <i>ES^b</i>	Estimated MR _{AS vs. RS} (95% CI) <i>ES^b</i>	<i>p^a</i>
Distress				
<u>CESD^c</u>	0.88 (0.76, 1.02) <i>0.13</i>	0.92 (0.79, 1.08) <i>0.06</i>	0.86 (0.74, 0.99) [*] <i>0.15</i>	.57
<u>IES</u>				
Avoidance	3.67 (2.72, 4.95) ^{***} <i>0.54</i>	3.70 (2.62, 5.23) ^{***} <i>0.39</i>	1.91 (1.35, 5.23) ^{**} <i>0.19</i>	.01
Intrusion	3.08 (2.31, 4.12) ^{***} <i>0.44</i>	3.42 (2.49, 4.79) ^{***} <i>0.36</i>	2.29 (1.66, 3.17) ^{***} <i>0.22</i>	.06
	Estimated MD _{AS-RS} (95% CI) <i>ES^b</i>	Estimated MD _{AS-RS} (95% CI) <i>ES^b</i>	Estimated MD _{AS-RS} (95% CI) <i>ES^b</i>	<i>p^a</i>
Positive outcomes				
Benefit-finding^d	--	1.67 (-1.52, 4.86) <i>.08</i>	-0.29 (-3.17, 2.85) <i>-.01</i>	.13
Positive Consequences of screening^d	--	-1.42 (-2.64, -0.20) [*] <i>.19</i>	-2.27 (-3.46, -1.08) ^{**} <i>.31</i>	.16
Lifetime perceived OC risk				
Personal	0.23 (0.09, 0.37) ^{**} <i>.23</i>	0.17 (0.03, 0.31) [*] <i>.22</i>	0.12 (-0.04, 0.26) <i>.13</i>	.13

Table 3.2 cont.

Comparative	0.37 (0.19, 0.55) ^{***} .31	0.31 (0.13, 0.49) ^{**} .23	0.24 (0.06, 0.42) ^{**} .24	.14
Cancer screening beliefs				
OC screening effectiveness	-0.02 (-0.16, 0.13) .02	-0.01 (-0.16, 0.13) .01	-0.02 (-0.16, 0.12) .03	.99
BC screening effectiveness	-0.08 (-0.23, 0.07) .09	-0.01 (-0.17, 0.14) .03	-0.02 (-0.17, 0.12) .03	.66
CRC screening effectiveness	-0.12 (-0.27, 0.02) .13	0.08 (-0.03, 0.20) .11	-0.10 (-0.25, 0.04) .12	.37
Intentions to participate in future screening				
TVS	0.05 (-0.01, 0.12) .12	0.09 (0.02, 0.16) [*] .20	0.001 (-0.07, 0.07) .002	.15
MAM^e	0.02 (-0.12, 0.16) .02	-0.08 (-0.22, 0.06) .09	0.05 (-0.09, 0.19) .04	.27

Abbreviations: CI, confidence interval, ES, effect size, OC, ovarian cancer, TVS, transvaginal ultrasonography,

MAM, mammography, BC, breast cancer, SIG, sigmoidoscopy, CRC, colorectal cancer

Models adjusted for education, mental and physical functioning, MBSS-SF-Monitoring score and LOT-R optimism **p*<.05, ***p*<.01, ****p*<.001

^a *p*-value from overall group*time interaction fixed effect F test

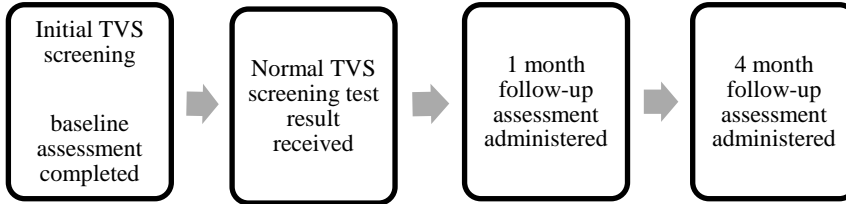
^b Effect size is Cohen's *d*

^c Model adjusted for education, physical functioning, MBSS-SF-Monitoring score and LOT-R optimism

^d Evaluated at 1-month and 4-month assessments only

^e Analysis limited to women at least 50 years of age (*n*=590)

Routine screening (RS) group



Abnormal screening (AS) group

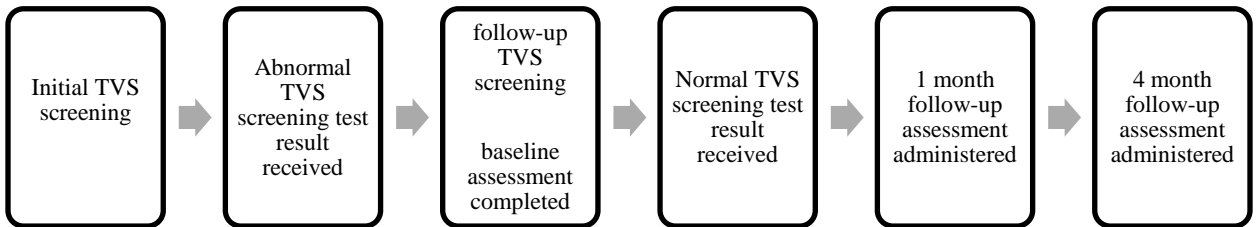


Figure 3.1 Participant flow and longitudinal assessment administration

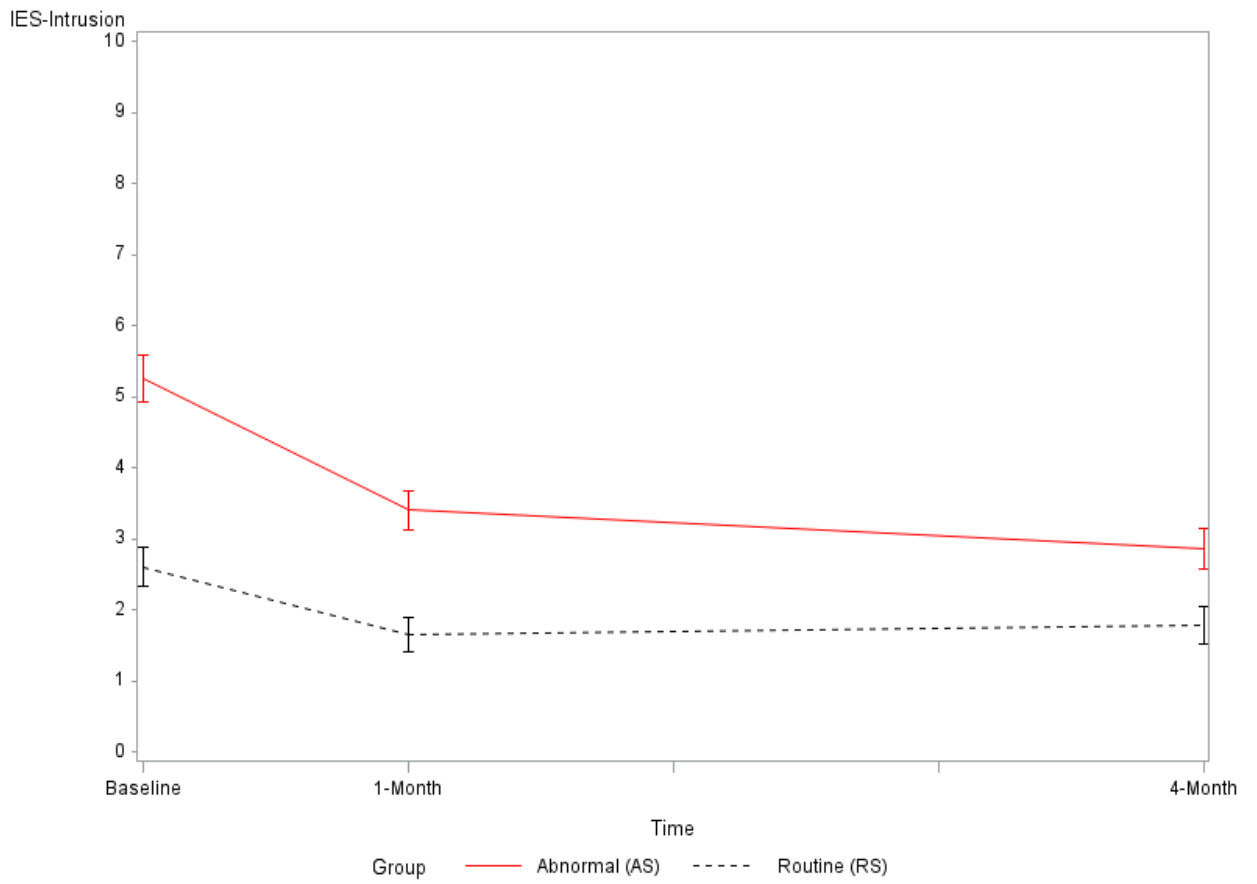


Figure 3.2 Estimated average IES-Intrusion score +/- 1 SE

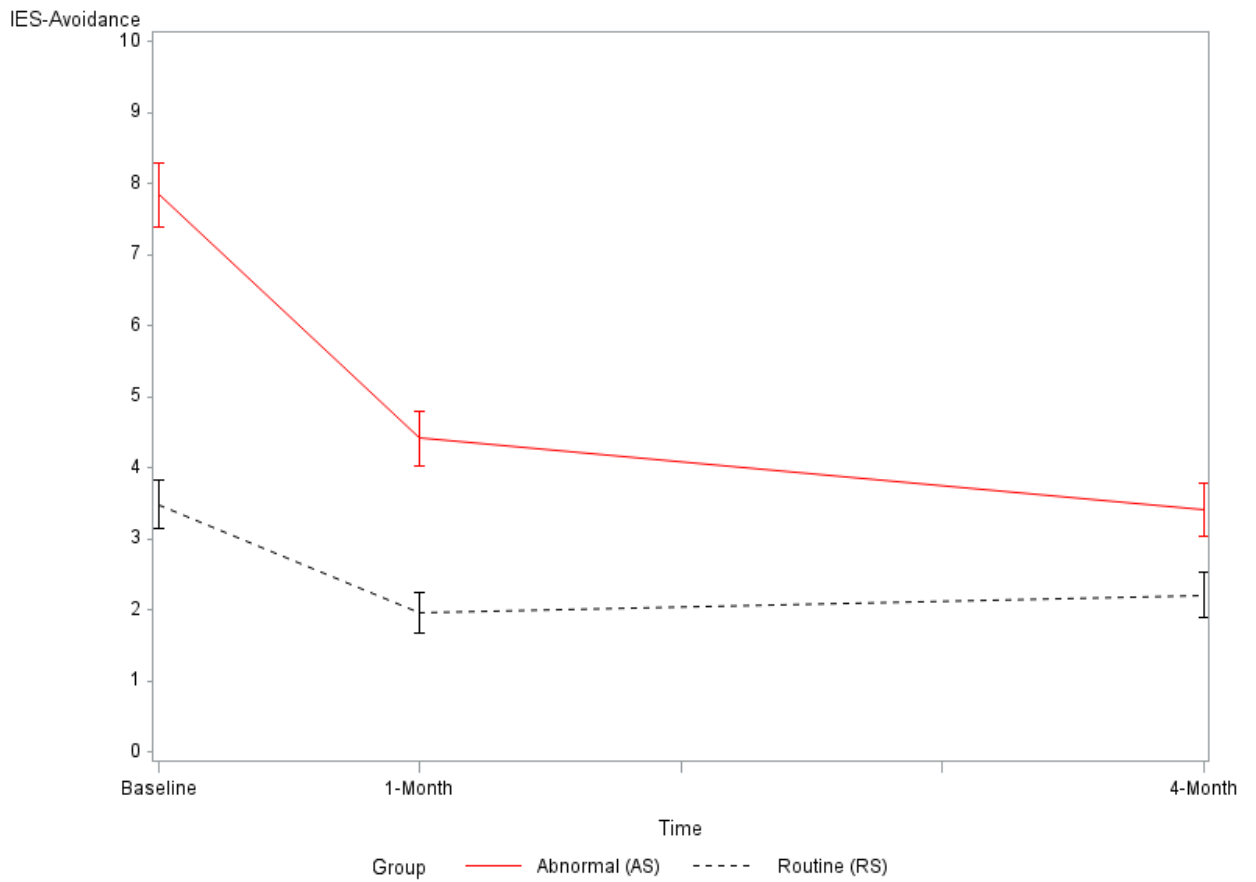


Figure 3.3 Estimated average IES-Avoidance score +/- 1 SE

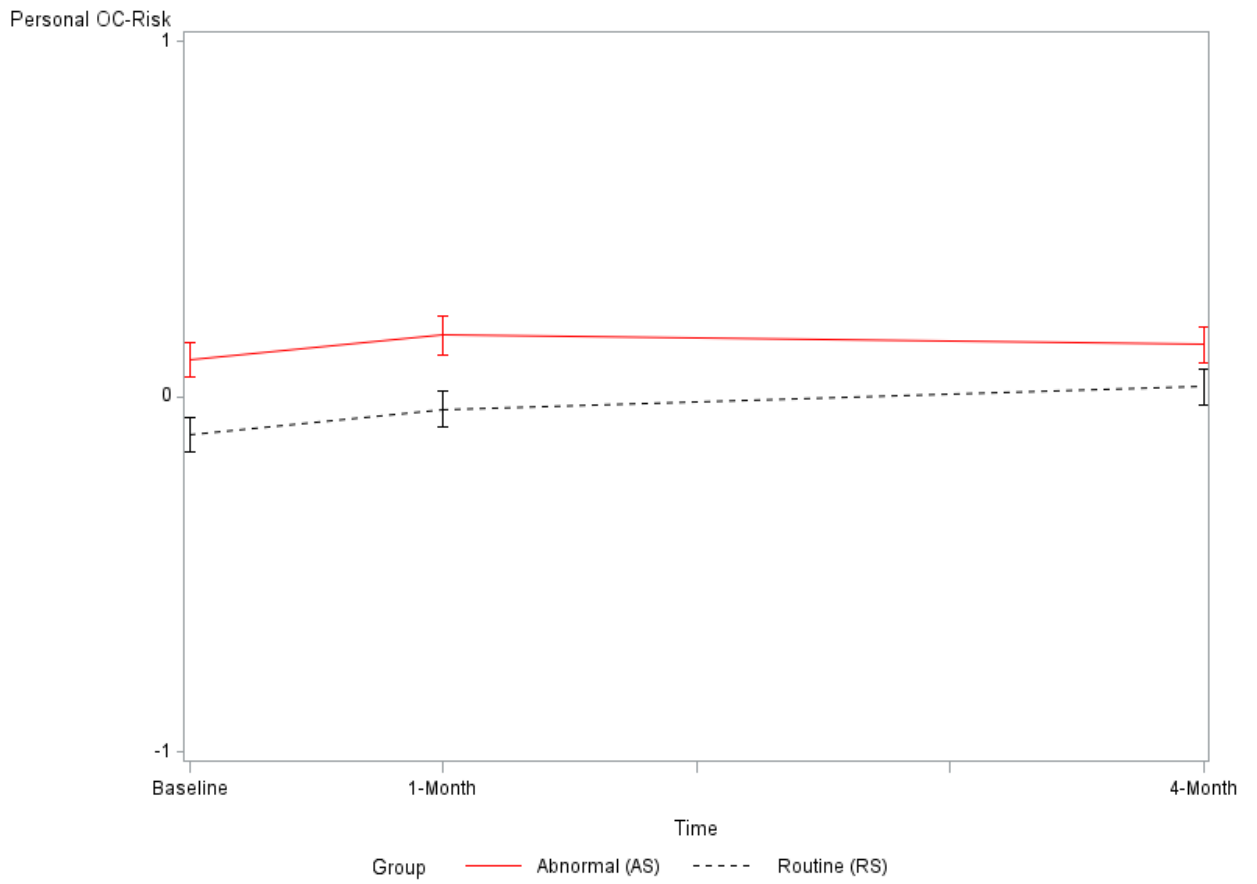


Figure 3.4 Estimated average standardized personal OC risk +/- 1 SE

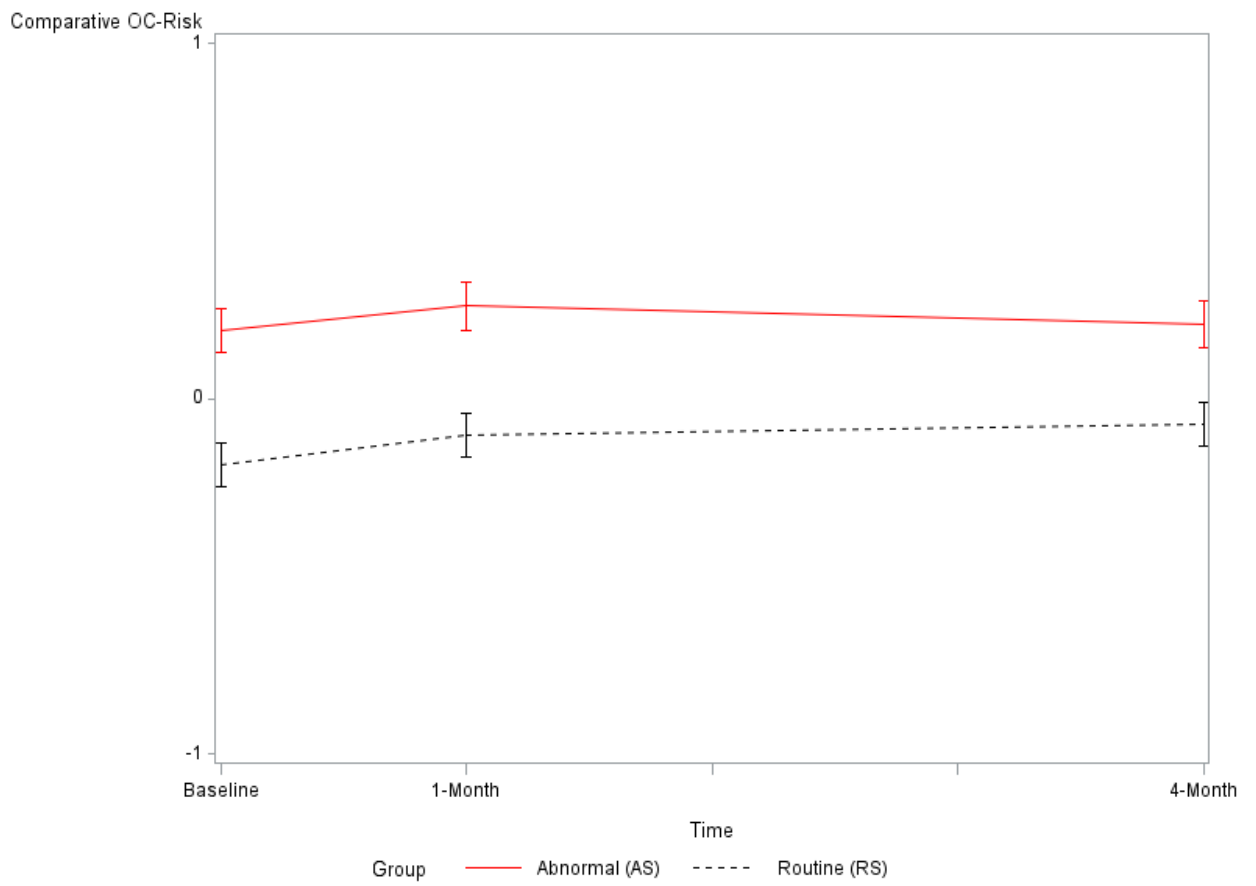


Figure 3.5 Estimate average standardized comparative OC risk +/- 1 SE

4 Demographic, Clinical, Dispositional and Social Environmental Characteristics Associated with Cancer-Specific Distress and Perceived Risk Following a False Positive Screening Test Results for Ovarian Cancer: A Longitudinal Study

Introduction

Although the benefits of early detection and diagnosis are well recognized in a variety of cancer settings, it is less well recognized that participation in cancer screening programs can have a negative psychological impact, even when a malignancy is not found [12, 13, 17, 55]. Because the cancer screening setting has the potential for false positive test results, it provides a “natural laboratory” for examining psychological response to a potentially health threatening event – here, receipt of an abnormal, yet ultimately benign, transvaginal sonography (TVS) screening test result for ovarian cancer (OC). This setting provides an opportunity to examine theories or models of coping and adaptation of psychological responses to stressful or threatening events. It is also of interest to examine the demographic and clinical characteristics that moderate the psychological response following receipt of a false positive TVS screening test result for OC. Determining the factors associated with adverse psychological reactions following false positive test results would enable professionals to recognize women who may need additional psychological support as they progress through the follow-up procedures after receiving a false positive screening test result.

A model relevant to understanding individual differences in psychological response to an abnormal cancer screening test result is the Cognitive Social Health Information Processing (C-SHIP) model [15]. The C-SHIP model is a broad conceptual framework

for understanding response to potentially health-threatening events. The C-SHIP model is an expansion of the Monitoring Process model (MP) [14]. The MP model suggests individuals differ in regard to their informational coping style, the extent to which they seek health-relevant information, and the manner in which they respond to health-threatening events. Termed “monitors”, these individuals scan for information pertaining to the event, and tend to translate neutral or ambiguous information as threatening, leading to exaggerated perceptions of personal risk [54]. In contrast, low monitors, or “blunters”, tend to avoid threat-relevant information. The C-SHIP model extends the MP model by suggesting the tendency of monitors to amplify threat can be modified by dispositional and situational characteristics.

Wardle et al. found evidence supporting the MP model, suggesting monitors were more adversely affected by abnormal screening test results for OC than blunters [16].

Consistent with the C-SHIP model, a monitoring informational coping style was most strongly associated with distress when optimism was low following a benign breast biopsy [12]. Following receipt of a false positive screening test for OC, distress was highest in monitors with low dispositional optimism and a family history of OC [11]. Similarly, a 2011 study found monitoring to be associated with increased OC-specific distress when family history of OC in a first-degree relative (FDR) was present [17].

Although both the MP and C-SHIP models have been examined in the OC setting, results of these cross-sectional studies are based on small samples of women receiving false positive test results. The present study involves a larger sample (n=375) of women receiving false positive OC screening test results, and investigates factors associated with distress and risk perception through longitudinal follow-up.

Social environmental characteristics (social support and constraint) have also been suggested to impact adaptation to stressful events across a variety of health and medical settings (i.e. cancer survivorship, cardiovascular disease, chronic disease diagnosis, [71, 72]). Social support may serve as a buffer in the mental adaptation process after stressful life events. Social constraint refers to the direct or indirect efforts of the social environment (i.e. family and friends) to limit or punish an individual's attempts to discuss thoughts or feelings referring to their trauma-related experience [73]. Social constraint has been associated with less desirable psychological outcomes (i.e. greater distress) following medically health-threatening events [17, 74]. According to the Social Cognitive Process (SCP) model [75], successful adaptation is achieved through adequate cognitive and emotional processing of a stressful event, which can be fostered by a social environment which is high in social support and low in social constraint. Results from the most recent study conducted in the OC screening setting found higher social constraint levels were associated with increased OC-specific distress following a false positive TVS screening test result [17]. In contrast, results from this study did not indicate a significant association between social support and OC-specific distress.

Demographic and clinical factors may also moderate psychological response following receipt of a false positive OC screening test result. The majority of research has been conducted within the breast cancer screening setting and includes both women receiving false positive mammography results as well as normal (no malignancy suspected) results. Steffens et al. conducted a study examining the impact of the benign breast biopsy (BBB) experience and found lower age, less education and no family history of breast cancer to be significantly associated with greater distress [56]. Conversely, another study of the

BBB experience found the number of first-degree relatives (FDR) with breast cancer to be significantly associated with greater baseline breast cancer-specific distress [12].

In 2008, Brain et al. examined predictors of breast cancer-related distress following mammography screening among younger women with a family history of breast cancer [76]. Results from this study suggested higher baseline perceived breast cancer risk, higher baseline distress, having previously undergone breast cancer screening, having been recalled for further tests, and low levels of optimism to be associated with higher cancer worry at one-month follow-up. At six months follow-up, baseline worry, higher perceived risk, death of a relative from breast cancer within the past year and having previously been part of the screening program were significantly associated with breast cancer worry.

The purpose of the present study is to identify factors – out of a comprehensive set of demographic, clinical, dispositional and social environmental characteristics – associated with increased OC-specific distress and perceptions of OC risk over the four month study period. This study is the largest, most comprehensive study of response following a false positive screening test result in the OC setting, employing a longitudinal design and examination of affective and cognitive responses. Though no previous studies have examined perceptions of lifetime cancer risk in this context, it has been reported that women receiving false positive TVS screening test results have increased perceptions of personal OC risk [46, 77].

We hypothesize that lower age, less education, no prior history of abnormal screening test results, lower optimism, greater social constraint and a monitoring informational

coping style combined with family history of OC in a FDR will be associated with OC-specific distress.

Methods

Sample

Participants represent a subset of individuals participating in a broader, quasi-experimental study evaluating affective, cognitive and behavioral outcomes associated with receipt of an abnormal, yet ultimately benign, TVS screening test result identified during routine screening through the University of Kentucky Ovarian Cancer Screening Program (UKOCSP). Ethical approval for this study was obtained from the University of Kentucky Institutional Review Board.

The UKOCSP offers free, annual screening to asymptomatic women at least 50 years of age and asymptomatic women 25-50 years of age with at least one first degree relative with OC. Women receiving an abnormal TVS screening test result during the course of routine, annual screening are typically asked to return within 2-12 weeks for a repeat TVS test. Women who received an abnormal TVS screening test result within the past 12 weeks, and scheduled to return for additional follow-up were identified from clinic records. Upon arrival at the clinic at the time of their scheduled follow-up appointment, these women met with research staff and consented to participate in the study. All participants were enrolled in the study from 2004-2009.

Procedure

Figure 1 displays a graphical representation of longitudinal assessment administration. A baseline interview was conducted by project research staff and was completed following study enrollment immediately prior to the participant's scheduled repeat TVS screening test. Women completed their baseline assessment prior to their scheduled repeat TVS screening test. Following, women also completed two follow-up telephone interviews, one month and four months after their baseline assessment. All women were notified prior to the one month follow-up interview that results of their repeat TVS screening test were benign. Less than 5% of eligible women who were invited to participate declined participation.

Measures

All participants completed questionnaires assessing demographic and clinical information, dispositional characteristics, social environmental characteristics, mental and physical functioning, risk perception, and distress. Demographic, clinical, dispositional and physical functioning information was assessed only at baseline, whereas risk perception, social environmental and distress information was captured at baseline and both follow-up assessments. Only baseline measures of social environmental variables were used in subsequent analyses.

Demographic and clinical information

Demographic information assessed by self-report included age, race/ethnicity, partner status, education, income and clinical information relevant to OC risk including personal

history of breast cancer and family history of OC. Family history of OC (yes vs. no) was determined based on whether or not the woman had a FDR (mother, sister or daughter) with OC. Clinical information collected from clinic records included number of previous TVS screening tests and history of abnormal TVS screening test result prior to their most recent abnormal screening test result (yes versus no).

Dispositional characteristics

Dispositional optimism was assessed using the Life Orientation Test-Revised (LOT-R) [59]. The LOT-R is a standardized, commonly used 10-item measure of dispositional optimism and yields a total optimism score. Informational coping style was measured using the Miller Behavioral Style Scale-Short Form (MBSS-SF) [60]. The MBSS-SF consists of 2 stressor scenarios followed by 8 statements representing different coping strategies for that stressor. Separate Monitoring and Blunting scores were computed; only the Monitoring score was used in subsequent analyses.

Social environmental characteristics

Social support was assessed using the Duke-UNC Functional Social Support Questionnaire (Duke-SSQ) [78]. The Duke-SSQ is a standardized, commonly used, 8-item measure of functional social support yielding a total functional (i.e. affective) social support score. Social constraint was assessed using the 15-item "Friends and Family" version of Social Constraint Scale (SCS) [73]. The SCS is a commonly used measure of the extent an individual's social environment inhibits expression of thoughts and feelings about a stressful event – in this case, "your experience with ovarian cancer screening". A total social constraint score is calculated.

Physical Functioning

Physical functioning was assessed using the Medical Outcomes Study 12-Item Short Form Health Survey (SF-12) [61]. The SF-12 is a standardized, commonly used measure of physical and mental health status in both medical and healthy examples. The physical functioning subscale score was used in subsequent analyses.

OC risk perception

Perceptions of absolute lifetime risk for OC were assessed based on responses from two questions. First, women estimated personal lifetime risk for OC by providing a numerical response (0-100) to the question “What do you think are the chances that you will develop ovarian cancer during your lifetime?” [12] Second, women were asked to provide a verbal response to the question "How likely do you think you are to develop ovarian cancer at some point during your life?" with ordinal response options ranging from (1) "no chance" to (6) "certain to happen". Because researchers have suggested women tend to overestimate their risk in the numerical scale and underestimate their risk in the verbal scale [47], a composite measure of risk was created. Responses from these two questions were standardized (with respect to baseline mean and standard deviations) and summed to create a composite measure of personal lifetime perceived OC risk.

OC-Specific distress

OC-specific distress was assessed by the Impact of Events Scale (IES) [63]. The IES is a standardized, commonly used 15-item measure of current distress associated with a specific stressor. Women completed the IES with regard to “the possibility that you will

develop ovarian cancer in your lifetime." The IES yields subscale scores for Intrusion and Avoidance. The Intrusion subscale consists of 7 items which measure intrusive symptoms (intrusive thoughts, nightmares, unpleasant feelings and imagery). The Avoidance subscale consists of 8 items which measure avoidance symptoms (numbing of responsiveness, avoidance of feelings, situations and ideas). Respondents are asked to rate the frequency of each item occurring within the past 7 days according to the scale: (0) not at all, (1) rarely, (3) sometimes and (5) often. Responses are summed over each subscale, with the following possible range of responses: Intrusion (0-35) and Avoidance (0-40). A copy of the IES instrument is available in the Appendix.

Statistical Analyses

Study sample characteristics were presented descriptively, including frequencies or means and standard deviations, as appropriate. Summary statistics of longitudinal outcome measures were presented as means and standard deviations for normally distributed outcomes, or medians and interquartile ranges for non-normally distributed outcomes. A shared random effects generalized linear mixed model was used to identify factors associated with the magnitude of OC-specific distress over time. As the two subscales scores of the IES were highly correlated, a shared random effect (intercept per subject) was assumed to account for the correlation among observations per individual. Thus, the intercept was allowed to vary by individual but shared over each outcome. Because a notable proportion of participants exhibited none of the items measured by the subscales of the IES (i.e. a zero response), the Zero-Inflated Poisson (ZIP) distribution was the assumed underlying probability distribution in the GLMM.

A linear mixed model was used to identify factors associated with the magnitude of OC risk perception at each time point. A random intercept was used to account for correlations among observations per individual.

Both initial models included age, education, family history of OC in a FDR, history of an abnormal TVS screening test result, number of prior routine TVS screens, physical functioning, monitoring informational coping style, dispositional optimism, social support, social constraint and the interaction between monitoring coping style and family history of OC in a FDR. However, because the interaction was not significant in the personal OC risk model, it was removed for final analyses. For the OC-specific distress models, the effect of family history was estimated at different levels (low, medium and high) of monitoring informational coping style to better explain the interaction. These levels were determined based on the first (25%), second (50%) and third (75%) quartiles of the distribution of monitoring. All analyses were conducted using SAS Software, Version 9.3 for Windows, with an alpha level of 0.05 throughout (Cary, NC).

Results

Analysis included 375 women who received false positive TVS screening test results during routine screening through the UKOCSP. The mean age was 56.7 years (SD=11.7) and the mean years of education completed was 14.0 years (SD=2.8). The majority of women were married or partnered (78%), White (97%), had no history of an abnormal TVS screen for OC (79%) and had no history of OC in a FDR (69%) (Table 4.1).

Longitudinal descriptive statistics for IES subscale scores and OC risk perception indices are displayed in Table 4.2. Participant retention was very good throughout the study, with

92% and 88% of women responding at the one- and four-month assessments, respectively. General longitudinal patterns were similar between IES subscale scores, with ranges narrowing over time. Regardless of IES subscale, the majority of OC-specific distress scores decreased over time, as expected. A slight increase in OC risk perception was observed at one-month, with a decline at the four-month assessment.

Tables 4.3 and 4.4 display results from the multivariate models examining factors associated with OC-specific distress and OC risk perception, respectively. Cell values in Table 4.3 represent estimated mean ratios and can be interpreted as the mean change in response corresponding to a one unit-increase for a continuous covariate, adjusting for all other factors in the model. For categorical covariates, the estimated mean ratios correspond to the estimated mean change in response associated with one level of the covariate compared to the other level (i.e. yes versus no). Estimated mean ratios greater than 1 indicate an increase in distress associated with an increase in the factor.

In general, controlling for all other covariates in the model, less education, a greater number of previous routine TVS screens, no history of an abnormal screening test result, less optimism and more social constraint were associated with greater OC-specific distress (Table 4.3). Factors associated with greater perceptions of personal OC risk included: lower age, less education, less optimism and more social constraint, adjusting for all other factors in the model (Table 4.4).

During the period of uncertainty (from the abnormal TVS test result to the time of the baseline assessment) experiencing an abnormal TVS result for the first time, increased social constraint and low optimism were associated with increased OC-specific distress.

However, once the results of the abnormal TVS test were resolved and concluded to be benign, having been through the abnormal result experience no longer affected distress. While lower optimism was associated with an increased distress in women even after the results of the test were resolved (at one-month), optimism was not associated with distress at the four-month assessment. While the previous characteristics were associated with a short-term response, lower education and being newer to the UKOCSP appeared to have a more intermediate response. Lower education was associated with increased distress at both the one- and four-month assessments as measured by both subscales of the IES. Fewer previous routine TVS screens was associated with increased distress at the four-month assessment (estimated $MR_{int}=0.94$, 95% CI=(0.89, 0.98); Table 4.3.).

The effect of monitoring on OC-specific distress was dependent on family history of OC in a FDR. When monitoring was low, family history of OC in a FDR did not have much of an effect, but when medium to high monitoring was present, family history was associated with an increase in both intrusive and avoidant thoughts. The highest effect was observed at the four-month follow-up assessment, as women with history of OC in a FDR reported over three times the OC-specific distress among high monitors, compared to those with no family history of OC in a FDR (estimated $MR_{avd}=3.17$, 95% CI=(1.92, 5.21); Table 4.3) . The effect of monitoring was associated with slightly increased distress at baseline when family history of OC in a FDR was absent. However, this effect was only observed at the baseline assessment.

While characteristics were associated with affective responses at some time points and not others, this was not observed for the cognitive outcome. For perceptions of absolute lifetime OC risk, younger age, less education, lower optimism and higher social

constraint were associated with an increased risk perception at all three points of assessment. Moreover, the effect of family history of OC in a FDR on perceptions of OC risk was not dependent on level of monitoring. Regardless of the level of monitoring, family history of OC in a FDR was associated with increased perceptions of OC risk at all assessments. Monitoring coping style had no effect on OC risk perception, regardless of family history status.

Discussion

Results supported the majority of our hypotheses regarding OC-specific distress. Based on the C-SHIP model, we hypothesized a monitoring informational coping style combined with family history of OC in a FDR would be associated with increased OC-specific distress. As measured by both subscales of the IES, women characterized by family history of OC in a FDR and medium or high informational coping styles experienced greater OC-specific distress at all assessments. This replicates prior research conducted in the breast cancer [12] and OC settings [17] and demonstrates the C-SHIP model's theory of the presence of dispositional characteristics with situational factors – in this case, family history of OC in a FDR, to amplify threat associated with potentially health-threatening events.

Also consistent with our hypotheses, increased OC-specific distress was associated with lower dispositional optimism and higher social constraint. Our findings replicate results reported from a recent, cross-sectional study examining factors associated with OC-specific distress following false positive TVS screening test results [17]. This study found higher social constraint and lower optimism to be associated with increased OC-specific

distress at baseline. Not only does our study replicate findings, but results extend to one- and four-month participant follow-up. At the one-month assessment, when results of repeat TVS screening are known to be benign, lower optimism remained significantly associated with increased distress and by the four-month follow-up, optimism was no longer associated with distress. For social constraint, our results replicate baseline findings suggested by Andrykowski et al. [17], and further show increased social constraint to be significantly associated with increased OC-specific distress through to the four-month follow-up.

Overall, we conclude no prior history of an abnormal TVS screening test result to be the most significant demographic or clinical predictor of OC-specific distress immediately following receipt of an abnormal result. However, once the test result is known to be benign, this association disappears and lower education has the most significant intermediate effect on distress, with this effect remaining at the four-month follow-up. Months after the results of the abnormal test are known to be false positives, less experience with the screening program (fewer previous routine TVS screening tests) is associated with increased OC-specific distress. Based on our findings, we can conclude that lower education, less experience with the screening program, a social environment characterized by high social constraint and family history among high monitors are associated with increased OC-specific distress several months after the false positive screening test result experience.

While a few studies have examined perceptions of lifetime personal OC-risk following a false positive TVS screening test results [77], no previous research has identified

demographic, clinical, dispositional or social environmental characteristics associated with changes in OC risk perception. Following a false positive TVS screening test result, we found younger age, less education, lower optimism, higher social constraint and family history of OC in a FDR to be associated with increased perceptions of lifetime OC-risk. Because perceptions of risk are elements of contemporary models evaluating health behavior, including cancer screening behavior [79], it is critical to identify what characteristics are associated with women who experience increased perceptions of cancer risk, as increased risk may motivate or hinder participation in cancer screening programs which are recommended for mass screening.

Strengths and limitations

This study extends earlier research on response to false positive TVS screening test results for OC during participation in a routine screening program by including a larger number of women with false positive results and including longitudinal assessment of distress and risk perception outcomes. Because OC screening is not currently recommended for asymptomatic women and a greater proportion of the women who chose to participate in the screening were White, married or partnered and more educated than the general population, our sample does not represent the general population who would participate in a generally recommended cancer screening program.

Conclusions

Results from this study replicate findings from a smaller, similar study conducted in similar setting [17] as well as provide additional information regarding characteristics of women associated with likelihood of experiencing adverse psychological response over

time. Based on findings from this study, women with no history of an abnormal screen, low dispositional optimism and a social environment characterized by high social constraint are at high risk for experiencing increased *immediate* OC-specific distress following receipt of a false positive TVS screening test result for OC. Further, women who are newer to the screening program, have lower dispositional optimism or constraining social environments experience increased distress at four-month follow-up.

Additionally, results indicate younger age, less education, lower dispositional optimism, a social environment characterized by high social constraint and family history of OC are associated with increased OC risk perception at all assessments. Because we can easily identify characteristics of individuals associated with adverse psychological and cognitive responses following this potentially health-threatening event, interventional programs can be targeted to moderate these effects among high risk women.

Table 4.1 Characteristics of the study sample

	Frequency or Mean (SD)
Demographic	
Age	56.7 (11.7)
Marital status	
Married or partnered	292
Single or non-partnered	83
Years of education completed	14.0 (2.8)
Race	
White, Non-hispanic	364
Other	11
Clinical	
History of abnormal OC screening test	
Yes	78
No	297
History of OC in FDR	
Yes	117
No	258
Number of previous OC screening tests	4.2 (5.0)
Number of days between abnormal OC screening test and baseline assessment	53.4 (27.5)

Abbreviations: SD, standard deviation, OC, ovarian cancer, FDR, first-degree relative.

Table 4.2 Longitudinal descriptive statistics for IES subscale scores and OC risk perception

	Baseline (N=374)	1-month (N=347)	4-month (N=331)
IES-Avoidance			
Median (IQR)	5 (0-13)	0 (0-5)	0 (0-3)
Mean (SD)	7.85 (8.70)	4.41 (7.03)	3.40 (6.75)
Range	0-38	0-36	0-34
IES-Intrusion			
Median (IQR)	3 (0-9)	0 (0-5)	0 (0-4)
Mean (SD)	5.26 (6.39)	3.40 (5.23)	2.86 (5.10)
Range	0-30	0-27	0-24
OC Risk Perception			
Mean (SD)	0.00 (0.92)	0.17 (1.01)	0.15 (0.94)

Abbreviation: IQR, interquartile range

Table 4.3 Results from multivariate analysis examining factors associated with OC-specific distress

Coefficient	OC-Specific Distress			
	Estimated Mean Ratio (95% CI)			P ^a
	Baseline	1-Month	4-Month	
Age^b				
Avoidance	0.972 (0.834, 1.134)	1.046 (0.878, 1.246)	1.159 (0.951, 1.412)	.239
Intrusion	1.000 (0.851, 1.175)	1.023 (0.857, 1.220)	1.165 (0.958, 1.418)	.632
Education				
Avoidance	0.948 (0.895, 1.004)	0.905 (0.849, 0.964) [†]	0.882 (0.817, 0.951) [†]	.003
Intrusion	0.931 (0.877, 0.987) [*]	0.921 (0.864, 0.982) [*]	0.909 (0.846, 0.978) [*]	.026
Physical Functioning				
Avoidance	1.005 (0.999, 1.011)	1.006 (0.999, 1.013)	1.001 (0.994, 1.009)	.150
Intrusion	1.005 (0.999, 1.010)	1.006 (0.999, 1.013)	0.998 (0.991, 1.006)	.070
Previous # routine TVS screens				
Avoidance	1.001 (0.964, 1.039)	0.991 (0.951, 1.034)	0.930 (0.882, 0.980) [†]	.022
Intrusion	1.003 (0.966, 1.042)	0.973 (0.933, 1.015)	0.936 (0.890, 0.983) [†]	.015
History of abnormal TVS screen				
Avoidance	0.573 (0.340, 0.965) [*]	0.634 (0.376, 1.067)	0.983 (0.544, 1.777)	.050
Intrusion	0.534 (0.332, 0.858) [†]	0.843 (0.507, 1.403)	1.043 (0.588, 1.849)	.024
Optimism				
Avoidance	0.935 (0.895, 0.976) [†]	0.915 (0.871, 0.961) [‡]	0.983 (0.929, 1.040)	<.001
Intrusion	0.917 (0.876, 0.960) [‡]	0.934 (0.889, 0.982) [†]	0.952 (0.902, 1.006)	.003
Social Support				
Avoidance	0.999 (0.972, 1.030)	0.981 (0.951, 1.012)	0.989 (0.954, 1.024)	.486
Intrusion	1.009 (0.979, 1.039)	0.990 (0.959, 1.022)	1.001 (0.966, 1.040)	.615
Social Constraint				
Avoidance	1.067 (1.045, 1.089) [‡]	1.091 (1.067, 1.116) [‡]	1.134 (1.106, 1.163) [‡]	<.001
Intrusion	1.062 (1.040, 1.085) [‡]	1.088 (1.063, 1.113) [‡]	1.107 (1.080, 1.135) [‡]	<.001
Family history of OC in a FDR^c				
Avoidance	2.348 (1.093, 5.043) [*]	1.278 (0.539, 3.026)	0.746 (0.274, 2.032)	.026
Intrusion	1.498 (0.676, 3.323)	1.137 (0.479, 2.696)	0.668 (0.244, 1.829)	.356
Monitoring^c				
Avoidance	1.161 (1.041, 1.295) [†]	1.021 (0.890, 1.151)	1.021 (0.890, 1.171)	.010
Intrusion	1.136 (1.016, 1.271)	1.024 (0.905, 1.159)	1.056 (0.923, 1.209)	.103

Table 4.3 cont.				
Monitoring* family history of OC in a FDR				
Avoidance				<.001
Intrusion				.026
Effect of family history when monitoring is:				
Low				
Avoidance	1.922 (1.197, 3.087) †	1.516 (0.888, 2.588)	1.330 (0.713, 2.483)	
Intrusion	1.622 (0.990, 2.655)	1.492 (0.871, 2.554)	1.243 (0.661, 2.336)	
Medium				
Avoidance	1.573 (1.107, 2.236) *	1.799 (1.218, 2.657) †	2.371 (1.529, 3.674) ‡	
Intrusion	1.755 (1.220, 2.523) †	1.957 (1.322, 2.896) ‡	2.312 (1.497, 3.571) ‡	
High				
Avoidance	1.423 (0.940, 2.154)	1.960 (1.243, 3.088) †	3.165 (1.921, 5.213) ‡	
Intrusion	1.825 (1.193, 2.794) †	2.241 (1.423, 3.529) ‡	3.153 (1.938, 5.128) ‡	

^a *P* value from overall *F*-test of fixed effect with 3 degrees of freedom

^b Corresponds to a 10 unit increase in age

^c Cell values cannot be directly interpreted as estimated mean ratios, as coefficients are involved in interaction term

* *P* < .05

† *P* < .01

‡ *P* < .001

Table 4.4 Results from multivariate analysis examining factors associated with OC personal risk

Coefficient	OC Risk Perception			<i>P</i> ^a
	Estimated Mean Response (95% CI)			
	Baseline	1-Month	4-Month	
Age^b	-0.172 (-0.260, -0.034) [‡]	-0.160 (-0.258, -0.074) [‡]	-0.166 (-0.258, -0.074) [‡]	<.001
Education	-0.054 (-0.086, -0.022) [‡]	-0.059 (-0.090, -0.027) [‡]	-0.052 (-0.085, -0.019) [†]	.002
Physical Functioning	-0.003 (-0.006, 0.001)	-0.002 (-0.005, 0.002)	-0.003 (-0.006, 0.005)	.327
Previous # routine TVS screens	0.009 (-0.012, 0.030)	0.007 (-0.014, 0.028)	0.010 (-0.011, 0.032)	.804
History of abnormal TVS screen	0.104 (-0.144, 0.353)	0.153 (-0.097, 0.404)	0.086 (-0.171, 0.343)	.691
Optimism	-0.054 (-0.080, -0.028) [‡]	-0.044 (-0.070, -0.018) [‡]	-0.052 (-0.078, -0.026) [‡]	<.001
Social Support	0.008 (-0.007, 0.024)	-0.001 (-0.018, 0.016)	-0.004 (-0.021, 0.013)	.371
Social Constraint	0.016 (0.004, 0.028) [*]	0.019 (0.007, 0.031) [†]	0.018 (0.005, 0.031) [†]	.020
Family history of OC in a FDR	0.577 (0.373, 0.780) [‡]	0.507 (0.302, 0.713) [‡]	0.387 (0.179, 0.594) [‡]	<.001
Monitoring	0.033 (-0.019, 0.086)	0.049 (-0.004, 0.102)	0.042 (-0.012, 0.095)	.319

^a *P* value from overall F-test of fixed effect with 3 degrees of freedom

^b Corresponds to a 10 unit increase in age

^{*} *P* < .05

[†] *P* < .01

[‡] *P* < .001

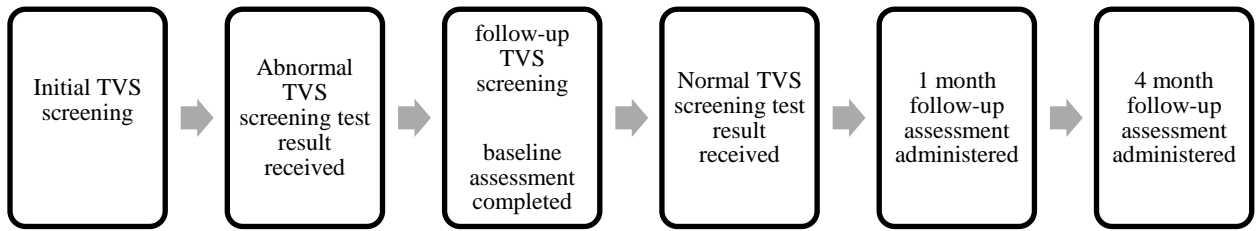


Figure 4.1 Graphical representation of participant flow and longitudinal assessment

5 Characteristics Associated with the Trajectory of Cancer-Specific Distress Following a False Positive Screening Test Result for Ovarian Cancer

Introduction

Previous studies have examined the association between receipt of a false positive TVS screening test result for OC and OC-specific distress [17]. Additionally, studies have identified characteristics – out of a comprehensive set of demographic, clinical, dispositional and social environmental characteristics – are associated with increased distress over time. However, little is known about the trajectory of OC-specific distress experienced by these women when followed over time or what factors influence trajectories of distress.

Characterizing the distinct trajectories of OC-specific distress following receipt of a false positive TVS screening test result for OC increases our understanding of responses to a potentially health-threatening event and identifies the types of women most likely to experience detrimental effects of screening. Because increased levels of cancer-specific distress are associated with decreased quality of life, it is important to focus interventions following this experience on moderating the negative effects.

Results from longitudinal studies examining the changes in breast cancer-specific distress over time among women experiencing false positive mammography or benign breast biopsies indicate that distress declines over time [12, 55]. Similarly in the OC screening setting, investigators observed OC-specific distress among women receiving false positive TVS screening test results to be elevated in the short term but decline over time, although remaining elevated at four months [11].

No previous studies have modeled trajectories of OC-specific distress following receipt of an abnormal, yet ultimately benign, TVS screening test result for OC; we expect the estimated trajectories to identify women experiencing high, medium and low distress levels gradually decreasing over time. Further, based on our previous research, we hypothesize lower education, fewer previous routine OC screening tests on the program, family history of OC in a FDR, lower dispositional optimism and higher social constraint to be associated with an increased likelihood in membership in the highest distress trajectory.

Methods

Sample

Participants represent a subset of individuals participating in a broader, quasi-experimental study evaluating affective, cognitive and behavioral outcomes associated with receipt of an abnormal, yet ultimately benign, TVS screening test result identified during routine screening through the University of Kentucky Ovarian Cancer Screening Program (UKOCSP). Ethical approval for this study was obtained from the University of Kentucky Institutional Review Board.

The UKOCSP offers free, annual screening to asymptomatic women at least 50 years of age and asymptomatic women 25-50 years of age with at least one first degree relative with OC. Women receiving an abnormal TVS screening test result during the course of routine, annual screening are typically asked to return within 2-12 weeks for a repeat TVS test. Women who received an abnormal TVS screening test result within the past 12 weeks, and scheduled to return for additional follow-up were identified from clinic

records. Upon arrival at the clinic at the time of their scheduled follow-up appointment, these women met with research staff and consented to participate in the study. All participants were enrolled in the study from 2004-2009.

Procedure

A baseline interview was conducted by project research staff and was completed following study enrollment immediately prior to the participant's scheduled repeat TVS screening test. Women completed their baseline assessment prior to their scheduled repeat TVS screening test. Following, women also completed two follow-up telephone interviews, one month and four months after their baseline assessment. All women were notified prior to the one month follow-up interview that results of their repeat TVS screening test were benign. Less than 5% of eligible women who were invited to participate declined participation.

Measures

All participants completed questionnaires assessing demographic and clinical information, dispositional characteristics, social environmental characteristics, mental and physical functioning, risk perception, and distress. Demographic, clinical, dispositional and physical functioning information was assessed only at baseline, whereas risk perception, social environmental and distress information was captured at baseline and both follow-up assessments. Only baseline measures of social environmental variables were used in subsequent analyses.

Demographic and clinical information

Demographic information assessed by self-report included age, race/ethnicity, partner status, education, income and clinical information relevant to OC risk including personal history of breast and colorectal cancer and family history of OC. Family history of OC (yes vs. no) was determined based on whether or not the woman had a FDR with OC (mother, sister or daughter). Clinical information collected from clinic records included number of previous TVS screening tests and history of abnormal TVS screening test result (yes versus no).

Dispositional characteristics

Dispositional optimism was assessed using the Life Orientation Test-Revised (LOT-R) [59]. The LOT-R is a standardized, commonly used 10-item measure of dispositional optimism and yields a total optimism score. Informational coping style was measured using the Miller Behavioral Styles Scale-Short Form (MBSS-SF) [60]. The MBSS-SF consists of 2 stressor scenarios followed by 8 statements representing different coping strategies for that stressor. Separate Monitoring and Blunting scores were computed. Only the Monitoring score was used in subsequent analyses.

Social environmental characteristics

Social support was assessed using the Duke-UNC Functional Social Support Questionnaire (Duke-SSQ) [78]. The Duke-SSQ is a standardized, commonly used, 8-item measure of functional social support yielding a total functional (i.e. affective) social support score. Social constraint was assessed using the 15-item "Friends and Family" version of Social Constraint Scale (SCS) [73]. The SCS is a commonly used measure of the extent an individual's social environment inhibits expression of thoughts and feelings

about a stressful event – in this case, "your experience with ovarian cancer screening". A total social constraint score is calculated.

Physical Functioning

Physical functioning was assessed using the Medical Outcomes Study 12-Item Short Form Health Survey (SF-12) [61]. The SF-12 is a standardized, commonly used 12-item measure of physical and mental health status in both medical and healthy examples. The physical functioning subscale score was used in subsequent analyses.

OC-Specific distress

OC-specific distress was assessed by the Impact of Events Scale (IES) [63]. The IES is a standardized, commonly used 15-item measure of current distress associated with a specific stressor. Women completed the IES with regard to "the possibility that you will develop ovarian cancer in your lifetime." The IES yields subscale scores for Intrusion and Avoidance. The Intrusion subscale consists of 7 items which measure intrusive symptoms (intrusive thoughts, nightmares, unpleasant feelings and imagery). The Avoidance subscale consists of 8 items which measure avoidance symptoms (numbing of responsiveness, avoidance of feelings, situations and ideas). Respondents are asked to rate the frequency of each item occurring within the past 7 days according to the scale: (0) not at all, (1) rarely, (3) sometimes and (5) often. Responses are summed over each subscale, with the following possible range of responses: Intrusion (0-35) and Avoidance (0-40). A copy of the IES instrument is available in the Appendix.

Statistical Analyses

Two group-based trajectory models [80, 81] were fit to identify the trajectories of psychological response - one for each subscale of the IES instrument. Each group-based trajectory model assumes that there exist two or more groups having modest within-group variation but notable between-group variation. A latent categorical variable - here, referred to as *class* - is introduced to define group membership. At each level of class, a typical trajectory is estimated. The estimated relative probability of membership in a group is then expressed in terms of the independent variables.

The underlying distribution is assumed to follow a Zero-Inflated Poisson distribution to account for the excess presence of zeros in the response data. The number of groups and shape of each trajectory were chosen in such a way to simultaneously optimize the Bayesian Information Criterion (BIC) and restriction that an estimated 20% of the population be represented in each trajectory. BIC is a commonly used statistic to compare goodness of fit between models. BIC is comprised of measures of how well the model fits the sample and model complexity. BIC favors more parsimonious models. The final model was chosen such that the trajectories were distinct and interpretable.

After the specification of the appropriate number of groups and trajectory shapes, time-invariant covariates were added to the model to examine the association of demographic, clinical, dispositional and social environmental characteristics on group membership. Mean and standard deviations, medians and interquartile ranges, or frequencies of covariates across estimated trajectories were reported for both outcomes, as appropriate. Estimated ratios of probabilities of group membership from the multivariate model were

presented as estimated odds-like ratios (OLR), with accompanying 95% confidence intervals (CI) and p values. All analyses were performed using SAS Version 9.3 (Cary, NC) for Windows, with an alpha level of 0.05 throughout.

Results

The group-based trajectory analysis included 373 women receiving false positive TVS screening test results during routine screening through the UKOCSP. Figures 5.1 and 5.2 represent the estimated trajectories for Avoidance and Intrusion subscale scores respectively, as measured by the IES. Three distinct trajectories of similar shape were identified: class 1- no distress, class 2-medium decreasing and class 3- high decreasing for both the IES-Avoidance and IES-Intrusion subscales. For the Avoidance model the class proportions were 30.0%, 48.2% and 21.8%, respectively (Figure 5.1). For the Intrusion model the class proportions were 34.4%, 36.7% and 28.9%, respectively (Figure 5.2).

To identify predictors associated with the probabilities of group membership in various trajectories both models were re-estimated with the inclusion of time-invariant covariates. Descriptive statistics of covariates by class membership are displayed in Table 5.1. It is important to note this table does not take into account uncertainty regarding group membership, but mean posterior probabilities of group membership, given covariates were very high. For the Avoidance models, estimated probabilities over subjects were 94%, 96% and 95% for class 1, class 2 and class 3, respectively. For the Intrusion model, mean probabilities were 94%, 93% and 94% for class 1, class 2 and class 3, respectively.

Results of the covariate-adjusted models are displayed in Table 5.2. Cell values contain estimated odds-like ratios and accompanying 95% confidence intervals and p values. For continuous covariates, the class 2 versus class 1 OLR represents the factor by which the estimated relative probability of group membership in class 2 versus class 1 is multiplied for every unit increase in the covariate, controlling for all other factors. For categorical covariates, the class 2 versus class 1 OLR represents the ratio of the estimated probability of group membership in class 2 to class 1 at the first level of the covariate versus the second level of the covariate, controlling for all other factors.

From Table 5.2 we can see family history of OC in a FDR, no history of an abnormal TVS test result and greater social constraint are associated with an increased likelihood of membership in class 2 versus class 1 for Avoidance and Intrusion. In other words, women with family history of OC in a FDR are more likely to belong to the medium decreasing distress trajectory than the no distress trajectory. Similar results are apparent for women with no previous history of an abnormal TVS screening test result versus women who have gone through the experience of an abnormal test result in the past (estimated $OLR_{avd} = 2.27$, 95% CI= (1.01, 5.00); estimated $OLR_{int} = 2.44$, 95% CI= (1.04, 5.88); Table 5.2).

Covariates associated with an increased likelihood of membership in the high decreasing trajectory versus the no distress trajectory were family history of OC in a FDR, lower optimism and increased social constraint, controlling for all other factors. Similar results were observed for family history of OC in a FDR as seen in comparing probability of class 2 membership to class 1 membership. For both subscale scores of the IES, an

increase in dispositional optimism was associated with an increased likelihood of membership in the highest decreasing trajectory versus the no distress trajectory.

Finally, results suggest higher social constraint to be significantly associated with increased likelihood of probability in the high decreasing trajectory versus the medium decreasing trajectory for both outcomes. For the intrusive model, lower dispositional optimism was associated with an increased likelihood of membership in class 3 versus class 2 (estimated $OLR_{int} = 0.85$, 95% CI= (0.77, 0.94); Table 5.2).

Discussion

In general, results supported our hypotheses regarding the distinct number of groups and trajectory shapes. Estimated trajectories were similar for both models and consistent with our expectations. According to results of the group-based trajectory modeling, three trajectories adequately characterized women's responses to false positive TVS screening test results. Of clinical importance however, is the identification of women likely belonging to the high decreasing trajectory. These women, representing over 20% of the sample of women in the study, suffer from the most adverse psychological effects of the false positive experience. Among this group, distress decreases from baseline to one-month, the period when results are confirmed to be benign, but remains elevated even at the four-month assessment when compared to women in the other trajectories.

Although no previous studies have conducted similar trajectory analyses, results from the adjusted models are consistent with previous literature evaluating factors associated with increased distress in the false positive cancer screening setting. In the present study, lower dispositional optimism, family history of OC in a FDR and high social constraint

were associated with a higher likelihood of membership in the high decreasing trajectory versus the no distress trajectory for both models, which is consistent with our hypotheses. Results from our previous studies suggest lower dispositional optimism, family history of OC in a FDR and higher social constraint to be associated with increased OC-specific distress. This finding is also consistent with previous research in the breast and ovarian cancer setting [17, 55].

Of most interest are the characteristics distinguishing membership probabilities in class 3 versus class 2: the high decreasing trajectory versus the medium decreasing trajectory. Even after the results of the abnormal test are known to be benign (one-month), distress remains elevated at the four-month assessment. For both measures of OC-specific distress, high social constraint was consistently associated with an increased likelihood of group membership in class 3 versus class 2. This finding may be due to the likely membership of women with the highest levels of social constraint in the high decreasing (class 3) trajectory, as shown in Figure 5.3. For the Intrusion model, lower dispositional optimism was also associated with an increased likelihood in membership in class 3 versus class 2.

One may have suspected monitoring informational coping style to be associated with an increased likelihood of membership in one of the elevated distress trajectories versus the no distress trajectory, as suggested by the Monitoring Process (MP) model[82]. This result may be due to the lack of inclusion of the combination of monitoring coping style and family history of OC in a FDR in the adjusted models, as suggested by the Cognitive Social Health Information Processing (C-SHIP) model [15], as this interaction has been

identified with increased OC-specific distress, measured by both subscales of the IES, at baseline, one- and four-month assessments [17].

Contrary to previously conducted studies finding lower education to be associated with increased OC-specific distress, we did not observe education to be significantly associated with group membership in class 2 or 3 versus class 1, which is likely due to the apparent balanced educational level between trajectory members. In Table 5.2, without considering the uncertainty associated with group membership, we can see the mean number of years of education completed is similar among members of all trajectories.

Strengths and Limitations

To our knowledge, the present study is the first to use group-based trajectory modeling in the context of response to an abnormal, yet ultimately benign, cancer screening test result – for any cancer screening test, not just TVS for OC. Also, this study is the largest study of response to false positive TVS screening test results over time for OC to date.

Several limitations to the present study should be noted. OC screening is not currently recommended for mass screening of asymptomatic women, and therefore it is unknown whether our results can be generalized to other cancer screening tests that are broadly recommended (i.e. mammography). Further, our sample was comprised of predominantly Caucasian women and thus our findings may not be generalizable to racial/ethnic minority women.

Conclusions

Results from this study suggest distinct, interpretable trajectories of OC-specific distress not only exist, but follow our expectations with regard to their characterization. Based on findings from previous studies and the present study's results, we can infer that a notable proportion of women experiencing false positive screening test results suffer high levels of OC-specific distress that only slightly dissipates over a four month period. Further research should determine whether results can be extrapolated to other cancer screening settings, i.e. mammography, where there exists a higher likelihood of false positive results and mass screening of asymptomatic women is recommended. If we can identify women at highest risk for suboptimal responses, we can focus interventions to aid in the moderation of OC-specific distress following this event. For the OC screening setting, this would include women with low dispositional optimism and a social environment characterized by high constraint.

Table 5.1 Distribution of demographic, clinical, dispositional and social environmental characteristics by estimated trajectory

Avoidance			
Covariates	Class 1 No distress N=118	Class 2 Medium decreasing N=181	Class 3 High decreasing N=74
	Mean (SD), median (IQR) or %	Mean (SD), median (IQR) or %	Mean (SD), median (IQR) or %
Age	58.3 (11.7)	56.1 (12.2)	55.7 (10.3)
Years of education	14.2 (2.9)	14.0 (2.7)	13.8 (2.9)
Number of previous routine TVS tests	2.5 (1.0-8.0)	2.0 (1.0-8.0)	1.5 (0.0-5.0)
No history of abnormal TVS test result	72.9	82.3	82.4
Family history of OC in a FDR	22.0	36.5	32.4
Physical functioning	79.0 (28.0)	78.7 (29.5)	77.0 (27.7)
Optimism	17.6 (3.4)	16.3 (3.7)	15.1 (3.7)
Monitoring	3.3 (1.6)	4.0 (1.7)	3.9 (1.8)
Social support	38.0 (34.0-40.0)	36.0 (31.0-39.0)	33.0 (28.5-37.0)
Social constraint	16.0 (15.0-18.0)	19.0 (15.5-25.0)	27.0 (20.5, 34.5)
Intrusion			
Covariates	Class 1 No distress N=143	Class 2 Medium decreasing N=140	Class 3 High decreasing N=90
	Mean (SD), median (IQR) or %	Mean (SD), median (IQR) or %	Mean (SD), median (IQR) or %
Age	57.7 (11.6)	57.9 (10.8)	53.3 (12.6)
Years of education	14.5 (2.9)	13.9 (2.7)	13.6 (2.8)
Number of previous routine TVS tests	2.0 (1.0-8.0)	2.0 (0.0-7.5)	1.0 (0.0-4.0)
No history of abnormal TVS test result	72.0	83.6	84.4
Family history of OC in a FDR	22.4	32.9	42.2
Physical functioning	78.0 (29.4)	80.9 (26.9)	75.6 (30.2)
Optimism	17.7 (3.3)	16.6 (3.3)	14.3 (4.0)
Monitoring	3.3 (4.2)	3.7 (1.7)	4.3 (1.9)
Social support	38.0 (33.0-40.0)	36.0 (30.0-39.0)	36.0 (31.0-39.0)
Social constraint	16.0 (15.0-19.0)	20.0 (15.0-26.0)	25.5 (19.0-32.0)

Table 5.2 Multivariate associations between demographic, clinical, dispositional and social environmental characteristics and estimated OC-specific distress trajectories

	Medium decreasing versus no distress (Class 2 versus Class 1)	High decreasing versus no distress (Class 3 versus Class 1)	High decreasing versus medium decreasing (Class 3 versus Class 2)
	Estimated OLR (95% CI)	Estimated OLR (95% CI)	Estimated OLR (95% CI)
Age^a			
Avoidance	1.02 (0.75, 1.37)	1.07 (0.72, 1.59)	1.05 (0.75, 1.47)
Intrusion	1.28 (0.94, 1.76)	1.05 (0.70, 1.56)	0.82 (0.56, 1.19)
Years of education			
Avoidance	0.96 (0.86, 1.06)	0.94 (0.8, 1.09)	0.98 (0.87, 1.11)
Intrusion	0.91 (0.81, 1.02)	0.86 (0.74, 0.99)	0.94 (0.83, 1.07)
Number of previous routine TVS tests			
Avoidance	1.01 (0.93, 1.07)	0.97 (0.89, 1.07)	0.97 (0.90, 1.05)
Intrusion	0.99 (0.92, 1.07)	0.92 (0.83, 1.01)	0.93 (0.85, 1.02)
No history of abnormal TVS test result			
Avoidance	2.27 (1.01, 5.00)*	2.27 (0.76, 6.67)	1.02 (0.39, 2.63)
Intrusion	2.44 (1.04, 5.88)*	2.08 (0.68, 1.46)	0.86 (0.30, 2.47)
Family history of OC in a FDR			
Avoidance	2.59 (1.27, 5.25)**	2.86 (1.13, 7.20)*	1.10 (0.51, 2.36)
Intrusion	3.00 (1.42, 6.33)**	5.01 (2.07, 12.14)*	1.66 (0.78, 3.53)
Physical functioning			
Avoidance	1.01 (0.99, 1.02)	1.01 (0.99, 1.03)	1.01 (0.99, 1.02)
Intrusion	1.01 (1.01, 1.03)*	1.01 (0.99, 1.02)	0.99 (0.98, 1.02)
Optimism			
Avoidance	0.95 (0.97, 1.04)	0.88 (0.78, 0.99)*	0.93 (0.84, 1.02)
Intrusion	0.92 (0.83, 1.02)	0.78 (0.70, 0.88)*	0.85 (0.77, 0.94)**
Monitoring			
Avoidance	1.20 (1.01, 1.44)*	1.19 (0.94, 1.50)	0.99 (0.82, 1.20)
Intrusion	1.17 (0.98, 1.40)	1.36 (1.09, 1.70)	1.17 (0.96, 1.42)

Table 5.2 cont.			
Social support			
Avoidance	0.89 (0.93, 1.04)	1.01 (0.93, 1.08)	1.02 (0.96, 1.09)
Intrusion	1.02 (0.96, 1.08)	1.39 (1.03, 1.21)	1.09 (1.02, 1.17) [*]
Social constraint			
Avoidance	1.17 (1.08, 1.26) ^{***}	1.29 (1.19, 1.41) ^{***}	1.11 (1.06, 1.16) ^{***}
Intrusion	1.15 (1.08, 1.23) ^{***}	1.26 (1.17, 1.36) ^{***}	1.10 (1.04, 1.15) ^{***}

^{*} $p < .05$, ^{**} $p < .01$, ^{***} $p < .001$

^a Corresponds to a 10-unit increase in age

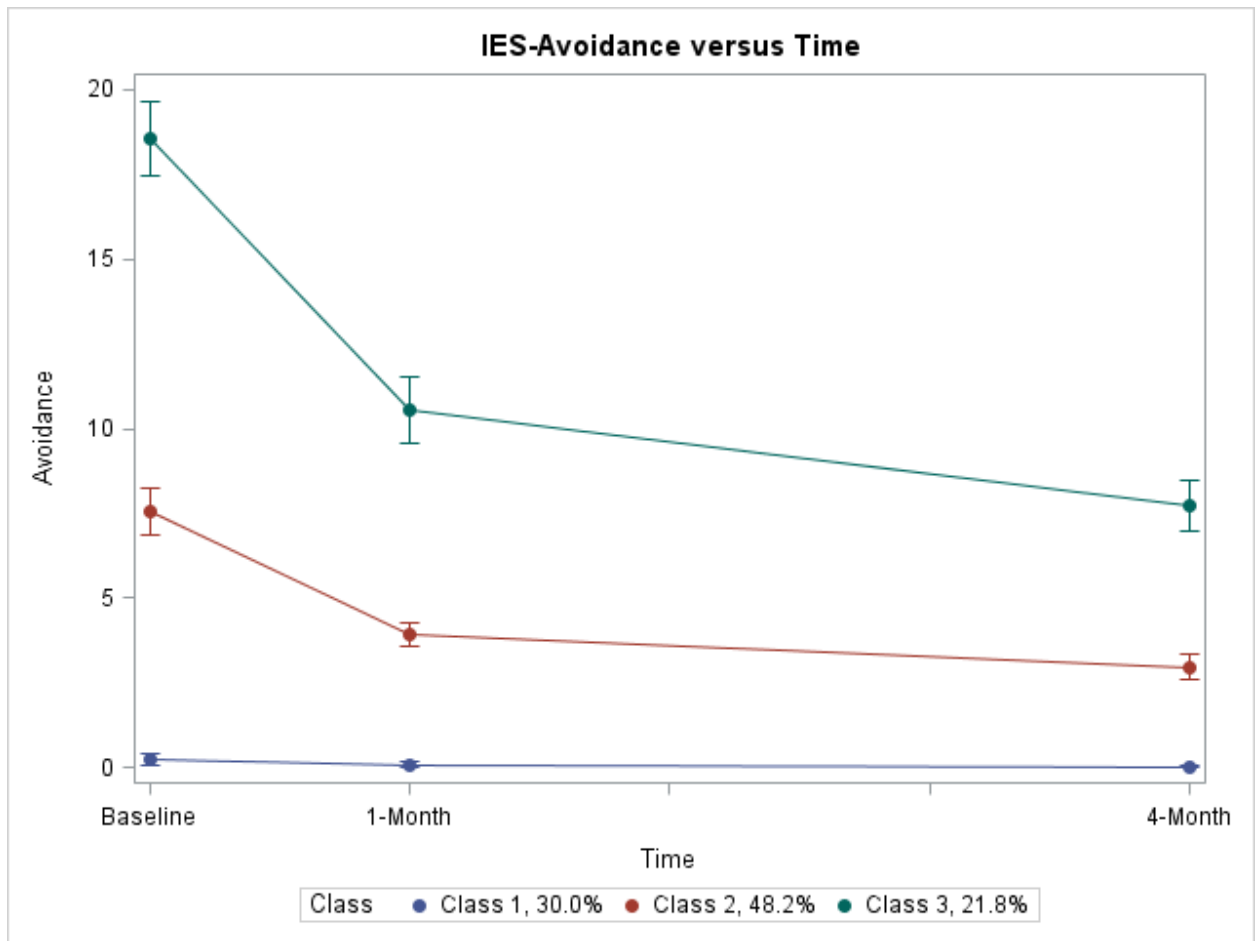


Figure 5.1 Estimated trajectories: IES-Avoidance

Figure 5.1 Estimated trajectories of OC-specific distress as measured by the IES Avoidance subscale in group-based trajectory modeling (N=373). Class membership based on posterior probabilities from unconditional model. The lines represent the fitted means and 95% confidence intervals.

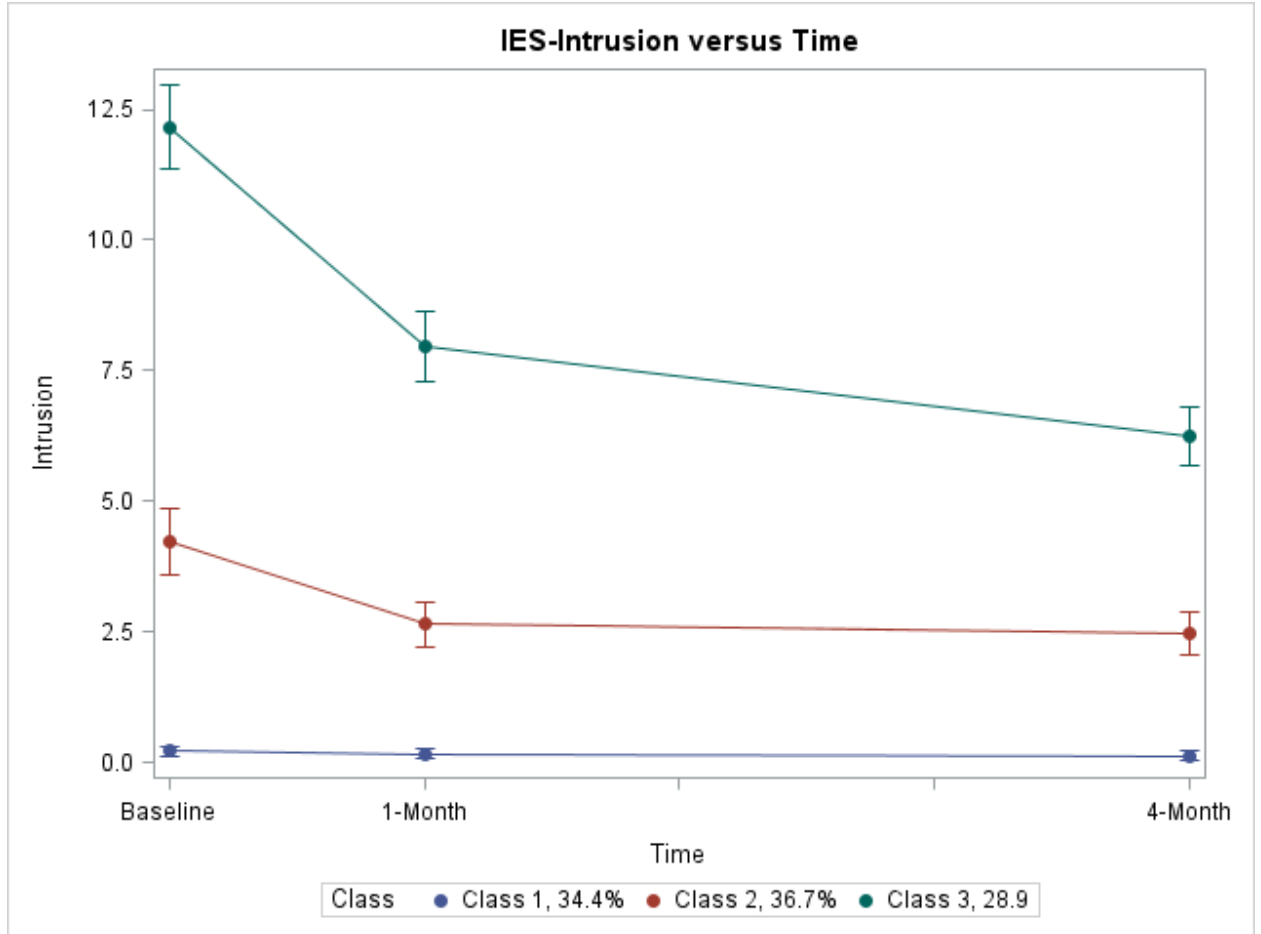


Figure 5.2 Estimated trajectories: IES-Intrusion

Figure 5.2. Estimated trajectories of OC-specific distress as measured by the IES Intrusion subscale in group-based trajectory modeling (N=373). Class membership based on posterior probabilities from unconditional model. The lines represent the fitted means and 95% confidence intervals.

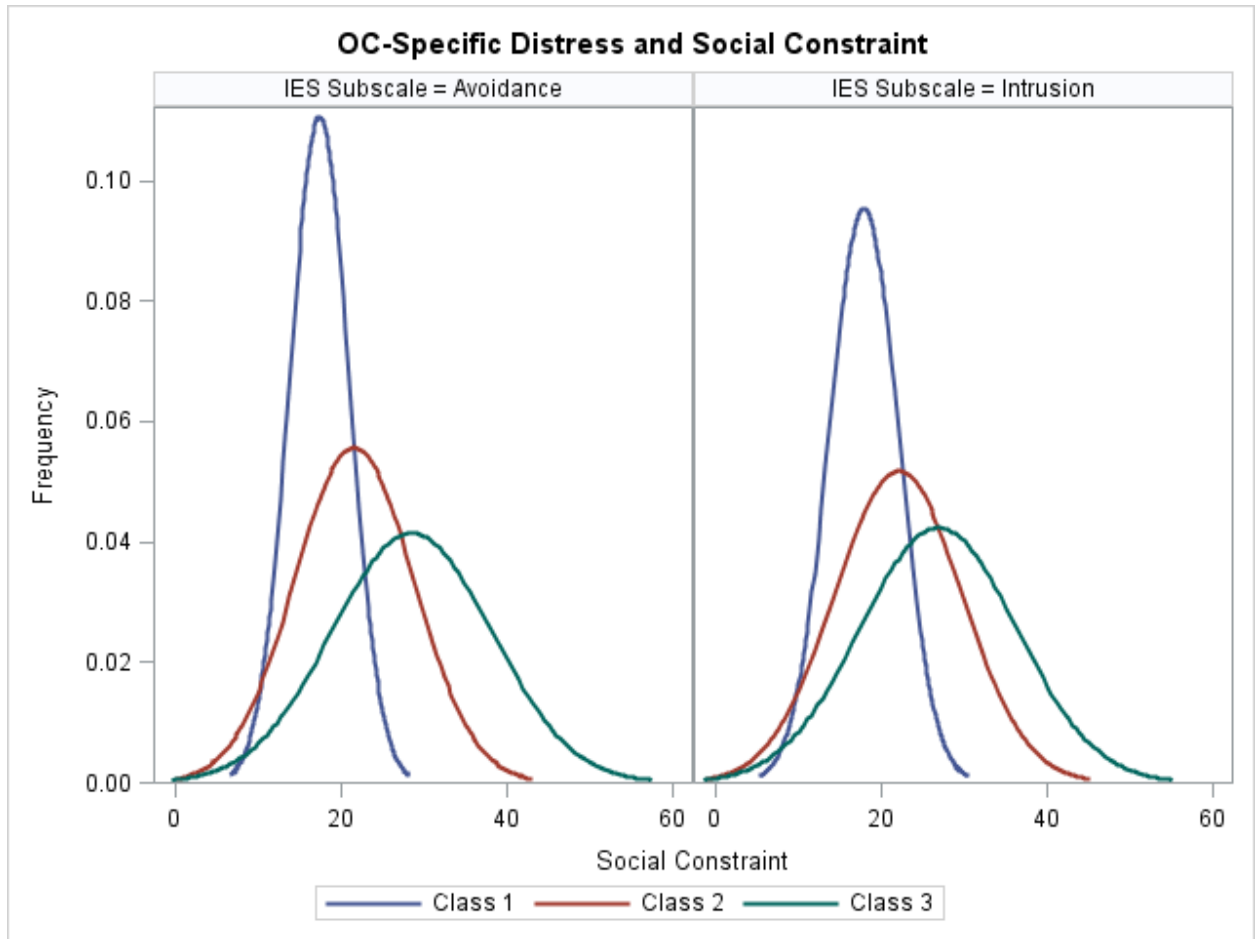


Figure 5.3 Distribution of social constraint by estimated trajectory membership

Figure 5.3. Group membership determined by subject's highest estimated group membership probability from group-based trajectory modeling (N=373).

6 Discussions and Conclusions

Summary

This chapter provides a summary of the previous five chapters as well as discusses the individual and public health implications of our research findings, strengths and limitations of this research and recommendations for future research. Four papers were presented in this dissertation: (1) Consequences of False Positive Cancer Screening Test Results for Ovarian Cancer: A Literature Review; 2) Affective, Cognitive and Behavioral Outcomes Associated with A False Positive Screening Test for Ovarian Cancer; 3) Demographic, Clinical, Dispositional and Social Environmental Characteristics Associated with Cancer-Specific Distress and Perceived Risk Following Receipt of A False Positive Screening Test Result for Ovarian Cancer: A Longitudinal Study; and 4) Characteristics Associated with the Trajectory of Cancer-Specific Distress Following a False Positive Screening Test Result for Ovarian Cancer.

The first paper (Chapter Two) was a comprehensive literature review that focused on responses to false positive cancer screening test results and what factors may moderate the magnitude and trajectory of potential responses. The purpose of this chapter was to evaluate relevant existing literature pertaining to response to a potentially health-threatening event and provide guidance into what factors may explain how one reacts to such an event. The review included studies focused on the breast and ovarian cancer screening settings and examined both negative and positive outcomes experienced following the event.

In general, results from this review suggested that women receiving false positive cancer screening test results experience increased cancer-specific distress which is most apparent immediately following receipt of the test result and dissipates over time but may still remain elevated relative to baseline. Although a multitude of literature evaluates the adverse affective outcomes associated with false positive screening test results, little research has included measures of positive affective outcomes such as benefit-finding and perceived positive psychological consequences of screening. For cognitive outcomes, a few studies have been conducted to evaluate the association between false positive cancer screening test results and perceptions of lifetime personal (absolute) risk and comparative risk. While results suggest perceptions of lifetime risk to be increased among women in the false positive group compared to the routine screening group, sample sizes in each group were fairly small. For general beliefs regarding the efficacy of cancer screening on reducing overall cancer mortality, no studies have directly addressed this question in the context of ovarian cancer screening. From the breast cancer screening literature, results are contradictory. Although literature exists examining the potential behavioral effects of false positive cancer screening test results, most studies focus on the cervical and breast cancer screening setting and results are inconsistent.

Also discussed in the first paper were two theoretical models that provide insight into what factors may moderate women's response to potentially health-threatening events – here, receipt of a false positive TVS screening test result. Throughout Chapter Two, the MP and C-SHIP models showed that a person's informational coping style, situational and dispositional characteristics explain how individuals process and react to threatening information. Additionally, a few studies have examined factors associated with the

magnitude and trajectory of cancer-specific distress over time. However, these studies involved a limited sample of women who have actually received false positive cancer screening test results and the focused on fewer outcomes.

The second paper, Chapter Three, provides the largest, most comprehensive study to date focusing on the impact of false positive cancer screening test results on psychological and behavioral outcomes. The study included 750 women: 375 in the abnormal screening (AS) group and 375 in the routine screening (RS) group. Results from this longitudinal study suggested receipt of a false positive TVS test result impacted a variety of affective, cognitive and behavioral outcomes. Additionally, results suggested women in the AS group experience increased OC-specific distress, less perceived positive consequences of screening and increased perceptions of lifetime OC risk compared to women receiving normal, routine screening results. The majority of our hypotheses were supported and most findings were consistent with the literature. However, this study is the first to examine the effect of a false positive cancer screening test result on positive affective outcomes and beliefs about the efficacy of screening. Although our study lacked significant findings regarding hypotheses in the domains, study results offer guidance to future researchers to better characterize attitudes and beliefs regarding screening efficacy. Further, this study provided the largest evaluation of behavioral outcomes in the false positive cancer screening context. Results indicated women's intentions to participate in future ovarian, breast and colorectal cancer screenings were not affected by a false positive screening test for OC. However, results regarding intention to participate in future screening may have been limited due to lack of variability in the single ordinal measure question which was used in the questionnaire.

Chapter Four included only women in the AS study group, and focused on identifying demographic, clinical, dispositional and social environmental characteristics associated with the magnitude of OC-specific distress over time. Although some studies have addressed factors associated with increased cancer-specific distress in this context, perceptions of personal cancer risk have not formerly been addressed. Additionally, this study evaluated the association between outcomes and a comprehensive set of factors at all assessment points, whereas previous studies have examined outcomes only cross-sectionally. Using a generalized linear shared random-effects mixed model, this study simultaneously addressed both subscales of the IES - Avoidance and Intrusion, while controlling for their assumed correlation. In general, results were consistent with the literature and extended characterization of outcomes to include follow-up assessments. The main findings regarding OC-specific distress suggested less education, more previous routine TVS screens on the program, no history of an abnormal test result, less optimism and more social constraint to be associated with greater OC-specific distress. Additionally, the combination of a monitoring informational coping style with family history of OC in a FDR was association with increased distress at all assessments, as suggested by the C-SHIP model and previous researchers. For perceptions of personal OC risk, lower age, less education, family history of OC, less optimism and increased social constraint were associated with greater perceived risk at all assessments.

The last paper, Chapter Five, modeled trajectories of OC-specific distress response over the four-month study period as well as identified characteristics associated with an increased likelihood of membership in one trajectory versus another. Using group-based trajectory modeling, three distinct classes of trajectories of response were estimated. In

each of the models, the majority of the sample was estimated to belong to the medium decreasing (class 2) group. These women experience immediate increased OC-specific distress when notified their test results are abnormal and require additional follow-up. However, after the results of the additional follow-up TVS test are known to be benign, distress decreases and tends to remain constant up to four-months following. Of most interest in this study, is the identification of characteristics of women more likely to belong to the highest distress estimated trajectory. Although increased social constraint was the only characteristic distinguishing in likelihood of membership in the highest decreasing trajectory and the medium decreasing trajectory (class 3 versus class 2), there were many characteristics associated with increased likelihood of membership in the highest estimated trajectory and lowest (no distress) trajectory. Here, family history of OC in a FDR, lower dispositional optimism and increased social constraint were associated with an increased likelihood of group membership. Although no previous studies have modeled trajectories of response, results were consistent with our expectations based on results from the previously conducted studies in this dissertation.

All studies conducted in this dissertation involve participants from the same study and answer similar questions regarding the psychological and behavioral impact of a false positive TVS screening test result. Together, results provide a comprehensive evaluation of the impact of a false positive screening test result for OC – from evaluating what endpoints are affected to specifically characterizing the types of women most likely to be at high risk for experiencing adverse psychological and cognitive outcomes.

Implications

Results from these studies have implications for women considering participation in cancer screening programs, as well as public health efforts aimed to identify efficacious screening methods to reduce OC mortality and the development of interventional programs to moderate distress following a false positive test result. All previous chapters of this dissertation provide support that women experiencing false positive test results during participation in routine, annual screening programs of asymptomatic individuals are likely to suffer increased cancer-specific distress and perceptions of absolute and comparative cancer risk.

From a public health perspective, it is important to understand whether or not receipt of a false positive cancer screening test result for OC is associated with reduced beliefs about the efficacy of screening or intentions to participate in other screening modalities which are recommended for mass screening, such as mammography by professional organizations. From this dissertation, we can conclude that attitudes and beliefs and the efficacy of OC, breast cancer and colorectal cancer modalities do not appear to be affected by the false positive experience. In fact, results indicated that women in our study believed that cancer screening is highly effective. However, it remains unclear if behavior to participate in these programs is affected.

While our studies identify an increase in negative psychological response, the overall trend seems to dissipate by four-months but remain elevated relative to baseline levels, suggesting the impact is experienced in the immediate and short-term. However, from a public health perspective, it should be noted that over 20% of the women in the abnormal

screening group were estimated to belong to class 3, high decreasing, in the trajectory modeling (Chapter Five). Although distress among these women also decreases over time, it remains elevated even at four-months, compared to the other two trajectories. Because a notable proportion of TVS screening tests are likely to be false positives, these potential effects should be considered to identify women likely to suffer the most adverse responses and intervene to moderate distress levels.

Strengths and Limitations

The compilation of these studies provides the most comprehensive examination of response to a false positive cancer screening test result in the OC setting. Not only in regard to the plethora of outcomes examined, but also the in-depth examination of the false positive study group over time. Our studies include the largest sample sizes, longitudinal assessment of study outcomes and advanced statistical techniques to more appropriately address associations of interest. No previous studies have modeled trajectories of response in the abnormal cancer screening setting. As a whole, this dissertation provides insight into all aspects of response to the abnormal cancer screening experience.

Several limitations to our research should be noted. First, because screening for OC is not recommended by any professional organization, it is unknown whether our results are generalizable to other populations for which mass screening is recommended. Second, the overwhelming majority of women participating in this study were Caucasian and at least high school educated. Additionally, individuals in this study were participants in a free cancer screening program. Therefore, our study may lack external validity, as our

results may not be generalizable to ethnic/minority, less than high school educated women or those willing to participate in a fee-for-service screening program.

Future Research

Findings from this dissertation point to various potential avenues for future research opportunities. Throughout this dissertation we have identified characteristics associated with women at the highest risk for experiencing adverse psychological issues following receipt of an abnormal, but benign, TVS screening test result for OC. The first direction future research should focus on is development of an interventional program designed to moderate adverse effects experienced by these women. The second direction should focus on adequately measuring the impact of false positive screening on actual future participation in cancer screening programs.

Although an extensive review of the literature examining psycho-educational intervention programs for cancer screening is necessary before providing specific recommendations on what kind of program should be developed to moderate responses following abnormal screening test results, we can identify women at highest need for participation in such a program. Findings from this dissertation suggest the intervention be implemented during the 4-8 week period of uncertainty between the initial receipt of an abnormal TVS screening test result and follow-up TVS testing when the highest levels of OC-specific distress are experienced. However, because these women belonging to the high decreasing estimated trajectory (Chapter Five) still have high distress levels at four-months, it would be necessary to evaluate the use of an intervention over the entire

period. The specification of the form of the intervention (clinic-based, telephone-based, etc.) should be determined based on a more extensive literature review.

Because it is unknown whether increased risk perceptions are likely to motivate or hinder participation in risk-reducing behaviors, such as participation in cancer screening programs, future research should be conducted in this context. Further, research is needed to characterize the impact of a false positive cancer screening test result on actual behavior, i.e. returning for recommended screening. Impacts on screening behavior should be evaluated not only for the same screening modality for which the false positive screening test was received, but also cancer screening participation for which an individual is recommended.

Responses to false positive cancer screening test results and their potential harm to individuals should remain a concern for clinicians, public health officials and researchers when considering the potential negative impact of mass screening programs.

Appendix

IMPACT OF EVENT SCALE (IES)

DIRECTIONS: Below is a list of comments made by people after stressful life events. Please check each item, indicating how frequently the comments were true for you DURING THE PAST SEVEN DAYS regarding the possibility of you developing OVARIAN CANCER someday. If they did not occur, please mark the “Not at all” column.

	Not at all	Rarely	Sometimes	Often
1. I thought about it when I didn't mean to.				
2. I avoided letting myself get upset when I thought about it or was reminded of it.				
3. I tried to remove it from memory.				
4. I had trouble falling asleep or staying asleep, because of pictures or thoughts about it that came into my mind.				
5. I had waves of strong feelings about it.				
6. I had dreams about it.				
7. I stayed away from reminders of it.				
8. I felt as if it hadn't happened or it wasn't real.				
9. I tried not to talk about it.				
10. Pictures about it popped into my mind.				
11. Other things kept making me think about it.				
12. I was aware that I still had a lot of feelings about it, but I didn't deal with them.				
13. I tried not to think about it.				

14. Any reminder brought back feelings about it.

15. My feelings about it were kind of numb.

0

1

3

5

Intrusion subset= 1, 4, 5, 6, 10, 11, 14; Avoidance subset= 2, 3, 7, 8, 9, 12, 13, 15.

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Vita

EDUCATION

M.S. in Statistics

2008-2010

University of Kentucky, Lexington, KY

B.S. in Mathematics

2004-2008

University of Kentucky, Lexington, KY

Minor: Statistics

PROFESSIONAL EXPERIENCE

Research Assistant, Biostatistics Shared Resource Facility

August 2010- present

Markey Cancer Center

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Research Assistant

May 2010- August 2011

Kentucky Violent Death Reporting System

University of Kentucky, Lexington, KY

Research Assistant, Statistical Consultant

Summer 2009-Spring 2010

College of Agriculture

University of Kentucky, Lexington, KY

Undergraduate Assistant

Fall 2007

University of Kentucky, Lexington, KY

Ma 109: College Algebra; Dr. Schubert

TEACHING

Part-time Instructor

Summer 2009

University of Kentucky, Lexington, KY

STA 291: Introduction to Statistical Methods 1

Teaching Assistant

Fall 2008, Spring 2009

University of Kentucky, Lexington, KY

STA 580: Biostatistics I; Dr. Charnigo

AWARDS

Certificate of Outstanding Teaching

2009

College of Arts and Sciences, Office of the Dean and Education Policy Committee

R.L Anderson Prize for Best Teaching

2009

University of Kentucky, Department of Statistics

PUBLICATIONS

Vanderpool R, Stradtman L, **Wiggins AT**, New K, VanMeter E, Crosby R. Fatalistic Beliefs and Completion of the Human Papillomavirus (HPV) Vaccine Series Among a Sample of Young Appalachian Kentucky Women, *Cancer Epidemiology, Biomarkers & Prevention*. (submitted)

Christopher KL, **Wiggins AT**, Van Meter EM, Means RT Jr, Roach JP, Hayslip JW. Differences in Vitamin D Nutritional Status between Newly Diagnosed Cancer Patients from Rural or Urban Settings in Kentucky, *Nutrition and Cancer* 2013; 65(5):653-658.

PRESENTATIONS

“An overview of adaptive design clinical trials and FDA recommendations”. Biostatistics Shared Resources Facility journal club presentation. Lexington, KY. May 31, 2012, **Wiggins** presenting.

“Marty Driesler Lung Project: Results of Lung Cancer Screening in Rural Kentucky”. Bensadoun E, Brooks M, Slone S, Baron A, Huang B, Manino D, Hirschowitz E. Weaver A. Khan A. Castle J, Miller J, **Wiggins A**, Arnold S. Markey Cancer Research Day. Lexington, KY. May 16, 2012, Arnold presenting.

“Quantitative evaluation of single-arm versus randomized phase II cancer clinical trials, by Pond and Abbasi”. Biostatistics Shared Resources Facility journal club presentation. Lexington, KY. Fall 2011, **Wiggins** presenting.

POSTERS

Bensadoun E, Brooks M, Slone S, Baron A, Huang B, Manino D, Hirschowitz E, Weaver A, Khan A, Castle J, Miller J, **Wiggins A**, Arnold S. Marty Driesler Lung Project: Results of Lung Cancer Screening in Rural Kentucky. Markey Cancer Research Day. Lexington, KY; May 16, 2012.

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Mills LA, Vanderpool RC, Kilbridge KL, Van Meter E, **Wiggins A**. Assessment of Health Literacy and Colorectal Cancer Knowledge among a Sample of Appalachian Men and Women Participating in a Colorectal Cancer Screening Formative Research Study. Kentucky Conference on Health Communication. Lexington, KY; April 2012.

Christopher K, Van Meter EM, Means RT Jr., Roach J, **Wiggins A**. Vitamin D and Other Nutritional Deficiencies Among in Newly Diagnosed Cancer Patients Living in Kentucky. 2011
American Institute of Cancer Research Annual Research Conference.