

Effect of Uncertainty on Adherence and Quality of Life in Breast Cancer Survivors: A Systematic Review

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Abstract--- *Quality of life takes precedence in the terminal stages of disease, such as breast cancer survivor, when a cure is considered impossible and all alternative methods to prevent disease progression have been exhausted. Given the distress associated with a cancer diagnosis, the treatments and their side effects, as well as the uncertainty of outcomes, it has been suggested that psychosocial factors ought to be considered as an important aspect of breast cancer treatment. The purpose of this research was to assess the effect of uncertainty on adherence and quality of life in breast cancer survivors. A systematic review of the literature concerning uncertainty, adherence and quality of life for patients with breast cancer was conducted by searching PubMed (including Medline), Web of Science, CINAHL Plus, Embase, Breast Cancer Research, The Cochrane Library and Google Scholar Database for articles featuring the terms “uncertainty”, “adherence”, “quality of life”, “cancer” and “breast cancer”. Eligible studies were those whose title or abstract specifically indicated the inclusion of breast cancer patients. There were no restrictions regarding participants’ age, number of participants, or disease stage and the studies were analyzed using prisma. The results of the studies confirmed that the effects of uncertainty were significant, alluding to the possibility to enhance adherence and quality of life in breast cancer survivors. Distress from prognostic uncertainty are associated with adherence and quality of life in breast cancer patients. The findings of this review encourage efforts to further research to enhance quality of care and better quality of life in breast cancer survivors.*

Keywords--- *Uncertainty; Adherence; Quality of life; Breast Cancer Survivor*

I. INTRODUCTION

Breast cancer is the most frequent cancer among women, impacting millions of women each year, and also causes the greatest number of cancer-related deaths among women. In 2018, it is estimated that 627,000 women died from breast cancer – that is approximately 15% of all cancer deaths among women (World Health Organization, 2018). Breast cancer has become the leading malignancy in developed countries worldwide [1]. In China, 169 000 women are diagnosed with breast cancer every year, and about 45 000 die of breast cancer [2]. In Indonesia, breast cancer is the number 1 type of cancer and increasingly 17% each year. In East Jawa Indonesia, breast cancer was reported in 2018 in over 5000 patients. Studies have indicated that the diagnosis and treatment of breast cancer provokes a series of negative emotional changes [3], such as considerable stress, anxiety, fear, and depression [4].

Breast cancer and another chronic illnesses generate psychological challenges that, traditionally, have been treated through problem-focused strategies [5], [6], [7]. Many interventions have been developed to help women to cope with both the physical and psychological negative effects of the diagnosis and the treatment [8], [9]. ¹On the other hand, there is

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evidence that extremely significant events, such as cancer, can impact on people's self-concept, their relationships, and their values, which can mean a reorganization of life's priorities as the person attempts to achieve a better and healthier life [10], [11], [7].

Cancer survivors, unlike the healthy population, are under psychosocial threats from diagnosis, treatment, and living with late effects induced by cancer therapies.[12] Cancer's treatment takes times and several procedures and self-care are crucial for managing chronic disease, and patients' own efforts are particularly important [13]. Because of the demands of continuous self-care, patients with chronic diseases often experience repetitive psychological stress, social intimidation, and reduced self-esteem, in addition to an exacerbation of physical symptoms, meaning they can be vulnerable to maladaptation and depression [14].

Many women report dealing with extensive long-standing ailments such as lymphedema and fatigue, as well as a fear of illness recurrence [15], [16]. However, women post-treatment also reported finding benefit and meaning from their cancer occurrence [17]. These orthogonal outcomes may be related to the uncertainty an individual is able to tolerate [5]. Given the distress associated with a cancer diagnosis, the treatments and their side effects, as well as the uncertainty of outcomes, it has been suggested that psychosocial factors ought to be considered as an important aspect of breast cancer treatment [18], [19], [20], [21], [22], [23], [6].

A lot of evidence supported that the uncertainty model has been employed to maintain the mental health of vulnerable populations experiencing stressful events [3], [24],[25], [26], [27]. It means that this model is a defense mechanism to deal with cancer diagnosis and treatment-related difficulties. Research has shown that uncertainty is associated with negative mood, concurrent and elevated level of symptoms of fatigue, sleep disturbance [28] and poorer quality of life [3], [11], [29]. Furthermore, to identify the features of such studies and related variables, a comprehensive review of uncertainty studies should precede the development of positive acceptance in breast cancer survivors [30], [31], [26]. Thus, this study aims to contribute the effect of uncertainty to enhance quality of life for patients with breast cancer by performing a systematic review of the literature concerning the adherence or uncertainty model designed for breast cancer patients.

II. METHODS

- Strategy for searching studies in the literature search

Studies published in English were searched for on PubMed (including Medline), Science Direct, Web of Science, CINAHL Plus, Embase, Breast Cancer Research, Cochrane Library and Google Scholar from 2 January to 11 January 2020. We included all relevant literature published prior to 11 January 2020.

Search Terms

The search terms used were "uncertainty", "adherence", "quality of life", "cancer," "breast cancer" and "nursing".

- Study selection - type of study

Published primary studies were eligible for inclusion and reviews, editorials, and letters, and case reports were excluded. No limitations regarding study design or outcome measures were used. All studies found relating to quality of life in patients with breast cancer were included. Eligible studies were those whose title or abstract specifically indicated the inclusion of breast cancer patients. The studies were included even if the sample was not exclusively composed of breast cancer patients. There were no restrictions regarding participants' age, number of participants, or disease stage.

The exclusion criteria were the following: studies that were published more than once, not intervention studies, and studies that mentioned uncertainty in the text, but excluded or did not measure uncertainty in their actual investigation.

Nursing intervention

Eligible articles were empirical studies applying at least one of the following nursing interventions to enhance coping and decrease the uncertainty for breast cancer patients: positive psychotherapy, hope therapy, well-being therapy, QoL therapy, mindfulness, PTG therapies, self-management therapy, family or community therapy and strength-centered therapies.

In addition, interventions focused on developing personal strengths, meaning-making, enhancing positive emotions, engagement, positive relationships, accomplishment, life satisfaction, and personal growth and others to increase and better quality of life were also included.

- Review methods

A list of relevant descriptors was used to obtain the articles. The abstracts of the identified publications were screened for relevance to the selection criteria. An article was rejected if it was determined from the abstract that the study failed to meet these criteria. When an abstract could not be rejected with certainty, the full article was appraised. A review template was developed specifying key information about each study.

- Assessment of study quality

The quality of included studies was assessed using the Downs and Black Checklist, a quality index with high internal consistency, high retest reliability, and good interrater reliability [32] (Downs & Black, 1998). This checklist consists of 27 items that are distributed over the five subscales of reporting, external validity, internal validity: bias, internal validity: confounding, and power. The Downs and Black checklist may be used to assess the methodological quality of both randomized controlled trials (RCTs) and nonrandomized studies, with scores greater than or equal to 20 considered good, between 15 and 19 considered fair, and 14 or below considered poor. Two investigators selected original studies on the basis of the inclusion criteria and reviewed the quality of each. Any disagreement between the two investigators regarding the extracted data was resolved through discussion. As study quality was the issue of concern, the score for each of the included studies should exceed 14.

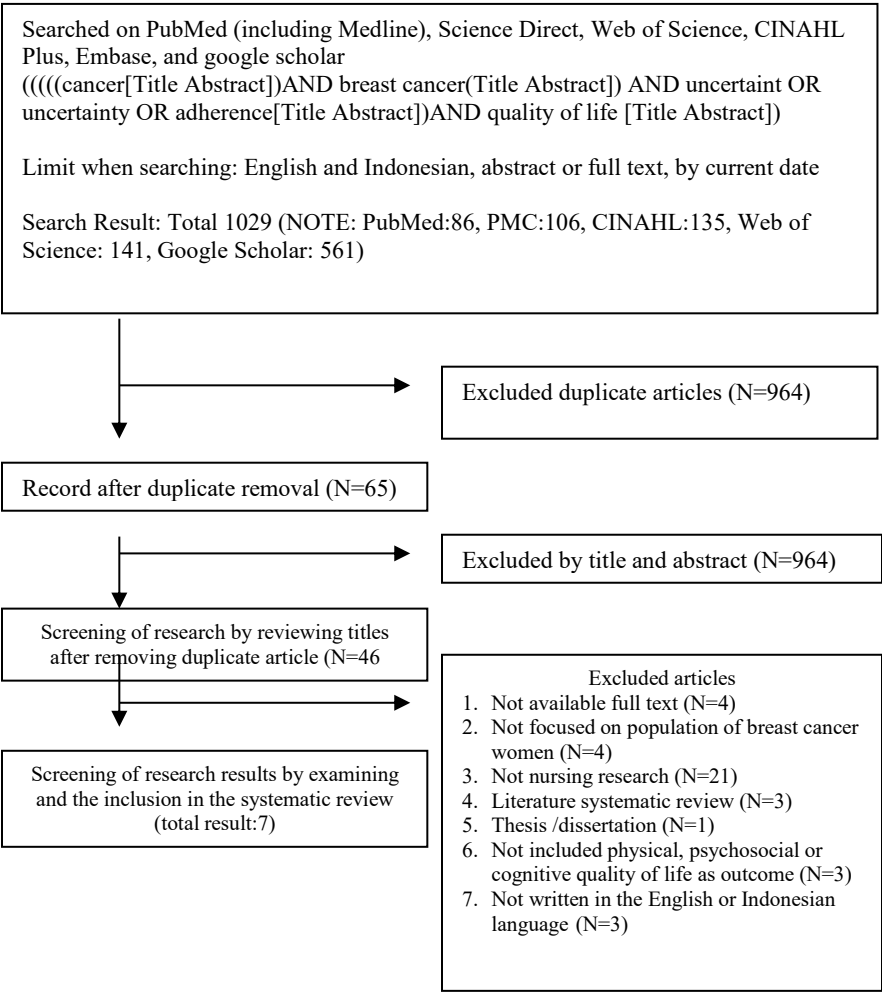


Figure 1 Inclusion stages of studies, adapted from the diagram prism (2009)

III. RESULTS

The electronic database searches yielded 65 bibliographic records (after removing duplicates). After applying the aforementioned filter, 7 studies met the inclusion criteria and were included in the review.

- Study Characteristics

Seven studies with similar designs were included. The years of publishing the articles were 2010 to 2019. Sample size varied from 44 to 313. In relation to demographic characteristics, all studies reported the mean age of patients. Participants were mainly married or partnered. Four studies reported family support and economic income. In total, 4 different instruments were used.

An analysis of research design found that six of the studies used an RCT design and one used Quasi experimental using posttest only with a control group. An analysis of research settings revealed that the intervention periods were 1-24 weeks, with the intervention period for study varying. Moreover, differences were observed in terms of the numbers of sessions.

- Study Quality

Six studies reported the participants' drop-out rates. One study reported that 13 participants dropped out of the follow-up research for several reasons. And there was one study that reported no participant drop out. The attrition rate in these studies ranged from 0% to 19.4%, and scores on the quality index checklist ranged between 16 and 25 (Table 1).

- Study Content

Two studies were based on mindfulness theory and using mindfulness intervention. Two studies were based on uncertainty management interventions, and three studies were based on communication, counseling, stress management and adherence theory.

All study meaning to enhance certainty and reduce fear was used both in the intervention programs and focused on strengthening mindfulness and managing uncertainty. All of the study design was a controlled pre and posttest design.

IV. DISCUSSION

In previous research, uncertainty has been studied from multiple perspectives. Mindfulness is an intervention that should be considered by advanced practice RNs as well as oncology nurses. Results from Crane-Okada et al. and Schell et al. suggest that mindfulness, when performed by the patient after professional instruction, results in a decrease in FCR. Incorporating and encouraging purposeful and mindful movement has the potential to improve quality of life and, in turn, decrease fear and uncertainty [33], [34].

When considering implementing any change in clinical practice, the limitations of these research findings must be examined. Both studies demonstrated that mindfulness interventions that significantly managed fear and uncertainty had small sample sizes and there was no ethnically diverse. Measuring the effectiveness and success of an interventions would be enhanced with longer periods of follow up as well as larger and more diverse samples.

The uncertainty in illness, especially for cancer survivors and particularly for young breast cancer survivors, can be difficult for the patients. Germino et al. and Ha et al. used an intervention to address uncertainty, but unlike the two mindfulness studies examined previously, Germino et al. and Ha et al. were successful in recruiting a large sample size of women to examine. However, the attention control condition for Germino et al. made drawing meaningful conclusions difficult. After all, the intervention group did express decreased fear and, as a result of decreased uncertainty, increased knowledge about long-term side effect of treatment, and increased awareness of the cancer and adherence of their treatment that could provide a basis for additional research in cancer survivorship [35], [36].

Communication is a critical point of care and can develop an environment of mutual trust and understanding. Communication was effective to empower patients to express their concerns to their physician and it was significantly correlated to decreased anxiety [37]. These studies showed that the patients who felt more empowered became more self-effective and might clearly discuss their worries, therefore reducing their anxiety and increasing adherence to their treatment.

[38], [37].

In other words, increasing communications was less related to overcoming a chronic disease, but largely concerned with helping patients to discuss their physical and social situations and comply with therapeutic care, which could ultimately lead to a healthier life.

However, it was difficult to conclude that nursing intervention programs for chronic patients such as breast cancer are effective for reducing depression, anxiety, and stress [39]. Thus, follow-up studies should adopt multiple approaches to pinpoint program components that directly contribute to enhancing quality of life and other significant dependent variables. This review illustrates the need to decrease uncertainty in patients with chronic disease for a better quality of life [8].

This review also found that uncertainty-improving interventions for patients with breast cancer survivors should be designed with adequate session time and program length to foster temporary behavior changes as well as changes in one's internal belief system and values.

V. CONCLUSION

This systematic review aimed to identify nursing interventions to increase coping and reduce uncertainty for patients who were breast cancer survivors by systematically reviewing the literature on nursing programs. A total of 1 029 studies were found, of which 7 satisfied the study selection criteria. All of the study designs had a controlled pre and posttest design. The result of all the studies confirmed that the effects of nursing intervention programs were significant, alluding to the possibility of developing a more positive psychological intervention and self-management program to enhance coping and reduce fear and anxiety among breast cancer survivors.

Each study reported that such intervention programs were effective for improving positive coping and reducing uncertainty around illness. Various nursing intervention studies have been conducted with chronic patients such as those with breast cancer, which served as stepping stones to develop adherence for therapy or treatment enhancement program for the quality of life of breast cancer survivors. Nevertheless, this study only included randomized control trials and did not include qualitative analyses such as a concept analysis or interviews about uncertainty. Therefore, future studies should employ more integrative methods to elucidate the concept of uncertainty. Consequently, the findings of this review encourage efforts for further research on developing coping, mindfulness and better quality of life among breast cancer survivors.

CONFLICT OF INTEREST

All authors declare that there is no potential conflict of interest regarding the research, authorship, or publication of this article.

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APPENDIX

Table 1 Literature Matrix

Author, Year, Country	Participant	Study Design	Delivery Personnel/ Setting	Intervention Duration/Frequency/Complexity
Mindfulness Intervention				
Crane Okada et al., California USA	1. N = 49 (48 completed the study, 1 DO) 2. Age 50-90 avg 3. 69% are single/widow/divorce 4. 62% are retired/not working	Randomized, controlled pilot feasibility study	Mindful movement program	Completed a dance and movement program for 12 weeks.
Schell, Monsef, Wöckel, & Skoetz, 2019, Germany	1. N = 42 (control group) 2. N = 40 (intervention)	Randomized clinical trial	Mindfulness training	Two-hour mindfulness training session from psychologist.
Uncertainty Management Interventions				
Ha, Thanasilp, & Thato, 2019, Vietnam	1. N = 57 (intervention group) 2. N = 58 (control groups) 3. Age 40-60 years avg 4. 71% are married 5. 71% are homemakers or farmers	Quasi experimental using post test only with control group	Uncertainty management program (UMP)	First section: 3 days before mastectomy Second section: 3 days post mastectomy Third section: 7 days post mastectomy Following 2 weeks at home: received 2 phone calls.
Germino et al., 2013, USA	1. N = 313 (196 Caucasian) 2. 117 African American)	Randomized Clinical Trial	Uncertainty Management Intervention (UMI)	Participants received a CD with cognitive and behavioral strategies. Data were collected at the time of a stress event (follow up appointment with oncologist).
Communication, Counseling, Handling Stress and Adherence Interventions				
Shields et al., 2010, USA	1. N = 22 (intervention) 2. N = 22 (control group)	Randomized Clinical Trial	Coaching telephone call	Participants received coaching telephone call from an oncology nurse

				practitioner to help with worries and concerns. Data (survey of symptoms) were collected at four different points.
Lai et al., 2019	1. N = 63 (control) 2. N = 63 (intervention)	Randomized Clinical Trial	Nurse-led care program	The intervention arm received nurse-led care plus routine hospital care.
Krikorian et al., 2019, USA	1. 181 female patients receiving an adjuvant AI treatment randomly assigned to one of three groups. 2. The first group received reminder letters and information booklets. 3. The second group was reminded and informed through telephone calls. 4. The control group received neither.	Randomized Clinical Trial single center, three-armed, randomized and partially blinded parallel group study	Education adherent to oral antineoplastic medication	The primary analysis at 12 and a secondary analysis planned for 24 months. The primary endpoint was the rate at which patients were classified as adhering to treatment after twelve months.

Table 1 Literature Matrix, Continued

Outcome Measure and Follow up Frequency	Result	Quality assessment Score	Reason for drop out	Drop-out Rate
1. Three 12-week series of MMP sessions were held with 3 groups of EG participants 2. Instrument QoL and Mindful Attention Awareness Scale (MAAS)	Fear of recurrence was reduced in the EG ($P = .02$), who also improved in mindfulness attitude ($P = .026$), whereas the CG reported improvement in upper body symptoms ($P = .04$) at 12 weeks.	21	1 participant drop out at first week; 6 participants in experimental group dropped out at second week because of work conflict, illness, car trouble and family need.	14.5 % (7/48)
1. Two-hour mindfulness training session from psychologist 2. Participants received a training manual and four audio tapes for practice 3. Instrument MAAS	In the intervention group, statistically significant changes were seen from baseline to the six-week data point. Improvements were seen in FCR concerns ($p=0.007$), FCR problems ($p=0.02$), emotional and informational support ($p=0.09$), depression ($p=0.04$), physical functioning ($p=0.01$) and energy ($p=0.07$). Outcomes included decreased FCR and anxiety.	21	4 participants in control group dropped out because of their health status.	4.8 % (4/82)
1. Post test only with control group 2. Participant were assessed 2 times 3. Instrument QoLI	QoL intervention group was higher than control group $t=6.45$.	25	2 participants in control group dropped out because of their health status, 1 subject for experimental group left the program because unstable vital signs, dizziness and low blood pressure.	2.6 % (3/115)
1. Intervention received a CD with cognitive and behavioral strategies to control uncertainty. 2. Also received a guide with resources and telephone calls from a nurse. 3. Control: attention control with telephone calls from a psychology graduate	The YS UMI group had decreased uncertainty ($p=0.01$) and increased knowledge about long term side effects of treatment ($p=0.02$), and were able to report more sources of information ($p<0.001$) and helpfulness of resources received ($p<0.001$). The intervention group had increased self efficacy ($p=0.003$). African American women in the intervention group were	22	No one dropped out.	0 %

student.	found to have improved affect at time of stress event ($p=0.001$). the outcome was decreased FCR (as a result of decreased uncertainty).			
1. Intervention: received a coaching telephone call from an oncology nurse practitioner to help with worries and concerns patients wanted to communicate to their oncologist at their next visit, received a typed prompt sheet to use at their doctor's visit.	Most questions (72%) included on the prompt or summary sheet were affect oriented (e.g., worry, anxiety, sadness, anger) change in self efficacy (i.e., improvement) directly predicted concerns at future data points: depression ($p<0.05$) anxiety ($p<0.0001$) womanhood worries ($p<0.05$) and role worries ($p<0.1$) Improved self efficacy was found to lead to decreased anxiety. Decreased anxiety was an outcome; FCR was not directly reported as an outcome but was one of the top three concerns patients expressed desire to talk about with their physicians.	16	Five refused due to a lack of time to participate, four could not be reached by telephone, and two had recently been diagnosed with metastatic breast cancer. Two participants did not complete the final assessment.	19.4 % (13/67)
<p>1. Two types of interventions were delivered in the study (i.e., the routine hospital care and the nurse-led care).</p> <p>2. Participants in the control arm received the routine hospital care, and participants in the intervention arm received both the nurse-led care and the routine hospital care.</p> <p>3. The routine hospital care included a brief education session before chemotherapy, care on the days of drug administration, and access to a patient-initiated hotline service during chemotherapy.</p>	<p>The intervention arm participants reported significantly lower distress levels from oral problems, fatigue, peripheral neuropathy, distressful feelings, and higher satisfaction with care. According to the satisfaction evaluation and the interviews, the participants stated that the service was helpful in providing information and communication opportunities, filling the service gap after drug administration, providing psychological support, relieving discomfort, and building confidence.</p>	21	8 participants in control group dropped out because of their health status.	6.5 % (8/120)
<p>1. Interventions were planned for week 1, 2, 10, 20 and 33 in the first year (after start of therapy) and months 15, 18 and 21 in the second year.</p> <p>2. Group 1 (Control group) – No intervention only standard information provided.</p> <p>3. Group 2 (Letter group) – Patients received a personalized motivational reminder letter, informative content in</p>	<p>Baseline results showed a well-balanced randomization with no significant differences between groups. After 12 months, 48% (CI 35–62) of the control group, 62.7% (CI 49–75) in the telephone group and 64.7% (CI 51–77) in the letter group were adhering to therapy. A post hoc pooled analysis with a one-way hypothesis for both interventions versus control indicated a significant difference between the groups favoring the intervention ($p = 0.039$).</p>	22	10 patients were excluded within four weeks of randomization as they no longer met inclusion criteria (e.g. withdrew consent; 5 without providing a reason, 2 due to other serious disease, 2 due to starting an externally controlled treatment - home care service, 1 restarted menstruation just after randomization and was switched to tamoxifen)	5.5 % (10/181)

combination with a breast
cancer information leaflet
at 1, 2, 10, 20 and 33
weeks and at month 15,
18 and 21.

4. Group 3 (Telephone
group) – Patients were
contacted by a study
nurse at week 1, 2, 10, 20
and 33 and month 15, 18
and 21 via telephone.
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