

Review

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Outcomes and quality of life following breast cancer treatment in older women: When, why, how much, and what do women want?

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Abstract

Background: There are few comprehensive reviews of breast cancer outcomes in older women. We synthesize data to describe key findings and gaps in knowledge about the outcomes of breast cancer in this population.

Methods: We reviewed research published between 1995 and June 2003 on breast cancer quality of life and outcomes among women aged 65 and older treated for breast cancer. Outcomes included communication, satisfaction, and multiple quality of life domains.

Results: Few randomized trials or cohort studies that measured quality of life after treatment focused exclusively on older women. Studies from older women generally noted that, with the exception of axillary dissection, type of surgical treatment generally had no effect on long-term outcomes. In contrast, the processes of care, such as choosing therapy, good patient-physician communication, receiving treatment concordant with preferences about body image, and low perceptions of bias, were associated with better quality of life and satisfaction.

Conclusions: With the exception of axillary dissection, the processes of care, and not the therapy itself, seem to be the most important determinants of long-term quality of life in older women.

Introduction

Breast cancer is an important disease and one where health care services have the potential to improve the quality and quantity of life. Breast cancer is also largely a disease of old age [1,2]. By the year 2030, one in five women in the United States will be 65 years of age or older (hereinafter referred to as "older") [3]. This demographic imperative, coupled with the dramatic increases in rates of breast cancer with advancing age, is expected to translate into a large absolute increase in the number of older women treated for and surviving breast cancer [4]. These older breast cancer survivors are likely to be a phys-

iologically, socially, and racially heterogeneous group with varying numbers of comorbid conditions and varying outcomes following treatment for their disease [4,5].

Older women diagnosed with breast cancer today have many different treatment options from which to choose. While most women will choose treatments that maximize survival, information about quality of life can be an important component in decision-making in several clinical situations. For instance, if a woman is considering two treatments with equivalent survival, such as mastectomy and breast conservation, then quality of life outcomes

may be important considerations in her treatment decision-making. Likewise, in clinical trials of equivalent approaches, quality of life may be the identifying factor in determining the most "effective" treatment. Quality of life may also be important to women, providers, and researchers comparing the overall benefits of very toxic, but very effective regimens with those of less toxic approaches that yield somewhat lower survival. The balance of effectiveness, harms, and quality of life is especially important for older women, since treatment decisions must also factor in interactions of comorbid conditions and treatment.

Unfortunately, until recently, older women were not included in sizable numbers in breast cancer research. In addition, the inclusion of quality of outcomes into clinical and observation trials is also a fairly recent trend [6]. Thus, there is only limited information available on quality of life outcomes after different treatment regimens among diverse older populations. In this paper we review what is known about quality of life outcomes in older women with breast cancer. We highlight findings across multiple domains, discuss special considerations in measuring outcomes in this age group, and make some recommendations for future research. This review is intended to serve as a focal point for discussion and extension of existing efforts to improve the quality of breast cancer care for the growing older population.

Methods

For the purposes of this review, quality of life outcomes associated with breast cancer care are defined as the net effects of the health care structure and process on the health and well-being of women diagnosed with this disease [7]. As such, quality of life is a multidimensional construct encompassing clinical, financial, functional, and psychosocial domains affected by treatment and its interactions with baseline comorbidity and circumstances (Figure 1) [6–9]. We use the term quality of life to be synonymous with the expression 'health-related quality of life' [10].

To identify relevant articles for this review, we conducted a search of published literature indexed on MedLine, CancerLit, CINAHL, and PsychInfo between 1995 and June 2003. We chose 1995 as the earliest year for review to ensure that results would be consistent with current standards of care. To capture literature encompassing a broad set of domains that might be affected by breast cancer or its treatments, we included the following terms in our searches: "breast neoplasms" and "aged" or "elderly" with "quality of life," "pain," "fatigue," "mental health," "adjustment," "body image," "satisfaction," "sexuality," "social support," "function," "communication," "cognition," or "economics." We also examined the bibliogra-

phies of retrieved articles for additional relevant citations. For citations of articles published prior to 1995, we only included sentinel articles pertinent to older women. We confined our review to original reports of randomized trials and cohort studies to examine data by age group and domain of quality of life. We excluded methodological articles, reviews, case series, and case reports, and non-English language articles. Articles were reviewed for inclusion of older women and data were abstracted on post-treatment quality of life or other outcomes for this age group. It should be noted that most observational studies to date have only examined short-term side effects and symptoms of treatment and future research is need on long-term side effects of treatments in older breast cancer survivors. We confine citations of data to results that were statistically significant, highlighting findings that are controlled for key confounding variables, such as baseline functioning [11]. We present a qualitative summary of these results. We did not attempt to conduct a meta-analysis of results since each study was conducted using varying time horizons, used different measurement tools and definitions of quality of life domains, included heterogeneous populations with a variety of tumor stages, and was conducted in different countries and cultural perspectives.

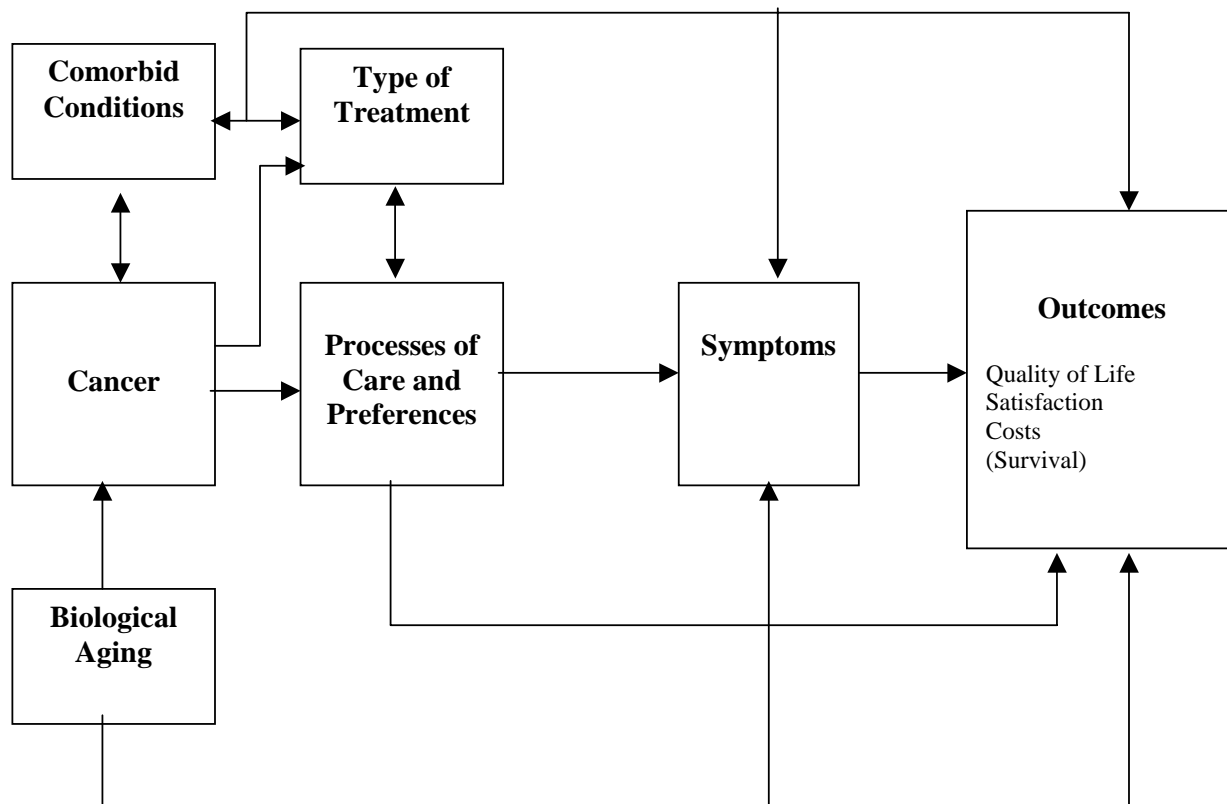
Results

Overall, few randomized trials or cohort studies measured quality of life after treatment and focused exclusively on older women [12–14]. With rare exceptions, [15–17] studies involving breast cancer outcomes were conducted in non-minority populations.

Processes of Care and Satisfaction

Satisfaction with breast cancer treatment is primarily a function of the process of care, and not the actual treatment received. A summary of these processes of care issues is found in Table 1. As one example, women who felt their surgeons initiated a conversation about treatment concerns reported higher satisfaction six months post-treatment than women who felt their surgeons communicated less, controlling for treatment and other factors [18]. Of note, surgeons who received additional training in surgical oncology have been noted by their older patients to bring up a discussion about patient concerns 60% more often (95% CI 1.02–2.56) than surgeons without specialty training [18].

Older patients may prefer and rely on physician-initiated quality of life discussions [19] and may prefer that their physicians provide information in person as opposed to written materials [20]. Higher levels of communication, both physician and patient-initiated, also affect women's perceptions of having a choice of treatment. For instance, in one study, older women who reported that their physicians asked them caring questions, asked about their con-



Adapted (in part) from Buchner and Wagner, 1992[98] and Mandelblatt, Bierman, et al. 1999[5]

Figure 1
Conceptual Model of Quality of Life in Older Breast Cancer Patients

Table 1: Key issues in processes of care in older breast cancer patients

Issue	Comment
Communication	<ul style="list-style-type: none"> • Physician-initiated communication and shared-decision making related to increased satisfaction • Increased communication related to increased perception of choice
Perceptions of ageism	<ul style="list-style-type: none"> • Higher levels of perceived ageism related to decreased satisfaction with care • Higher levels of perceived ageism related to higher levels of self-reported pain
Setting of care	<ul style="list-style-type: none"> • In-patient rehabilitation or case management may improve outcomes in women with multiple comorbidities
Social support	<ul style="list-style-type: none"> • Inadequate social support associated with less satisfaction with care
Preferences for treatment	<ul style="list-style-type: none"> • Concordance between preference for appearance and type of surgical treatment related to better mental health

cerns, or who discussed a number of options were more than twice as likely to report that they felt they were given a choice of treatment, controlling for other factors [18].

Interestingly, there appears to be a positive health benefit to having had a choice per se. In one cohort, by six months after surgery, women who reported having had a choice of therapy also reported higher adjusted global

health on a linear rating scale than women who felt they had no choice (78.7 vs. 75.3 on a zero to 100 scale, $p = .03$) [21]. Women reporting a choice also felt more satisfied with their treatments than women who reported having no choice, considering other factors. Other investigators have also noted that women who share in the decision-making process are more likely to report being satisfied, have better post-treatment adjustment to cancer, than women who feel that they did not participate [9,22–25]. Of note, in one longitudinal cohort, older women who received treatment that was consistent with their preferences around body image reported better mental health at follow-up than those who received surgery that was inconsistent with their preferences (e.g., receiving mastectomy without reconstruction despite a concern about maintaining body image) [26]. Interventions to facilitate decision-making that is consistent with preferences, such as CD-ROM programs, appear to have the potential to improve satisfaction with treatment decisions and with interactions with health care providers, as well as increase overall self-reported health and physical functioning [27].

Other features of women's interactions with the medical care system appear to be significant predictors of satisfaction, including perceptions of ageism ($p = .01$) and racism ($p = .03$) [16]. For example, women who perceive high levels of ageism have reported less general satisfaction with their breast cancer care than women who felt there was less ageism in their interactions in the health care system.

The setting of care may also influence outcomes. For instance, for older women with multiple comorbid illnesses (>3), in-patient rehabilitation has been noted to improve multiple domains of quality of life, and many of these effects appeared to be maintained after discharge [28]. Similarly, intensive nurse case management programs have been found to improve mood and reduce feelings of uncertainty [29].

Experiences outside of the health care system, such as having less social support, have also been associated with being less satisfied with one's breast cancer care [13]. In addition, Silliman and colleagues found that older women with inadequate social support had poor psychosocial outcomes after breast cancer treatment [30].

Preferences for Treatment

In the studies conducted to date, older patients are able to state their preferences, and generally want to be fully informed about their treatment options [31–34]. Preferences are important considerations in treatment choices [35]. For example, in two studies, older breast cancer patients were willing to select a risky treatment option (chemotherapy with major toxicity) for a small increase in

life expectancy (e.g., 6 months) [31,36]. In another study, 80% of older women indicated that chemotherapy would be worthwhile if they could live an additional two years,[37] but others have found that women in this age group would accept aggressive chemotherapy for as little as a 1% increase in survival [38,39]. Overall, these results suggest that older women are willing to trade-off short-term physical well-being, such as occurs with chemotherapy, for increased survival.

Physical Function and Pain

While many have hypothesized that breast conservation will result in better post-treatment functioning than mastectomy, in reviewing the literature we found that adjusted physical function scores were not significantly different by treatment group, [12] but rather, largely related to women's general pre-morbid level of illness [16,17,40–43].

The physical function outcome of treatment relates to use of axillary node dissection [44]. In one series, the cumulative risk of having arm problems two years post-treatment were three times higher (95% CI 1.94–4.67) among women who underwent axillary surgery compared to women without axillary surgery, controlling for covariates. Arm problems after axillary dissection were reported by up to 60% of women and had a consistent negative impact on long-term functional abilities [16]. Of note, one study reported that the effects of having axillary dissection and arthritis were multiplicative two years post-surgery (Figure 2) [45]. The expected benefit of having fewer concerns about recurrence after axillary dissection has not been demonstrated [16]. Using a decision analytic approach, Parmigiani and colleagues also noted that axillary dissection had an overall negative impact on the quality-adjusted survival of 60-year-old women [46]. Other researchers have noted that long-term decrements in physical function can affect activities of daily living that are critical to an older woman's ability to live independently [42,43]. Thus, in a Medicare population, the risks of axillary surgery may outweigh any benefits in guiding adjuvant therapy or of more detailed knowledge of prognosis [47–56]. Sentinel node biopsy has been shown to have lower morbidity than axillary dissection, [57] and may be particularly useful in older patients, especially those with arthritis or other pre-existing mobility limitations [58]. Final conclusions about the value of axillary dissection will rest on the accuracy of sentinel biopsy and women's preferences.

Radiation has not been found to increase pain or affect quality of life (measured on the EORTC breast module) in older women participating in clinical trials [14]. For older women undergoing chemotherapy, quality-adjusted benefits are similar to those seen in younger women when

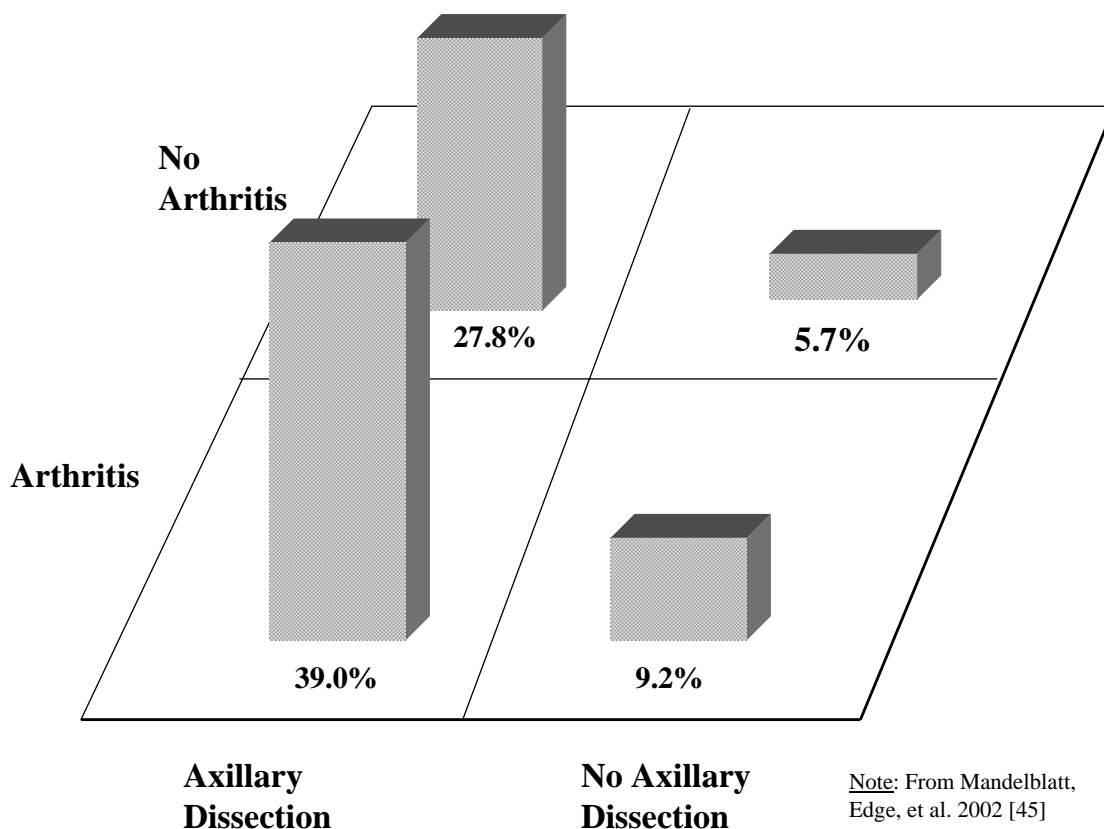


Figure 2
Percent of older women reporting arm problems after axillary dissection: Relationship to presence of arthritis.

considering women with estrogen receptor negative tumors. For older women with estrogen positive disease, quality adjusted survival is significantly improved with chemotherapy, albeit at a somewhat lower level than seen in younger women [59].

The process of care also seems to affect physical outcomes. For instance, Mandelblatt and colleagues found that older women who perceived high levels of ageism (vs. lower levels) in the health care system or felt that they had no choice of treatment (vs. having a choice) reported significantly more bodily pain [13].

Symptoms

Symptoms, such as hot flashes on tamoxifen treatment, have been noted to decrease general quality of life in older women, either directly, or through associated disturbed sleep and fatigue [60]. Fatigue from treatment, especially

in association with pain or other symptoms, can increase anxiety and depression [61]. In a cross-sectional study of 841 older patients, pain, fatigue, and insomnia were significantly related to losses in physical functioning, even after controlling for cancer treatment and comorbid conditions [62]. In a one-year follow-up of the same cohort, chemotherapy was related to reports of fatigue in the short-term, but not at one-year post-treatment [63]. A recent randomized controlled trial of exercise training[64] suggests that overall quality of life, as measured by the FACT-B scale, increases significantly in the postmenopausal breast cancer survivors who exercise regularly. Reductions in fatigue and improvements in mood were also reported, indicating that further testing of exercise interventions in older breast cancer survivors is warranted.

Mental Health and Overall Impact

The processes of care, including feeling like one had a choice of treatment also are important predictors of health outcomes. For example, in one cohort of older women, choice was independently associated with reports of better mental health [13]. Recently, Keating and colleagues extended these results and demonstrated that the concordance between desired and actual decision-making was actually more important than the actual process itself [65].

Receipt of chemotherapy (yes vs. no) has not been related to any long-term mental health outcomes except for having a perception that breast cancer had a greater impact on one's life, even after considering stage and other factors [13]. One aspect of this negative impact has been distress about weight gain associated with chemotherapy [66].

Interestingly, better educated women report that breast cancer has a greater impact on their lives than their less well educated counterparts, but the oldest women (75+ years) rate breast cancer as having less of an impact on their lives than younger women (67 to 74 years) [13]. The experience of having breast cancer has also been noted to have positive effects on women's lives, [67] and feeling a sense of purpose in life has been found to have a greater impact on quality of life than breast cancer itself [67].

Interestingly, older women are less likely to use mental health (or alternative medicine) services than younger patients [68]. However, participation in mental health support, such as performing expressive journaling has been found to improve short-term (i.e., 3 months) mental health outcomes and vitality and to decrease the number of medical appointments for cancer-related symptoms [69].

Cognition

Patients with breast cancer frequently complain of problems with their memory and concentration. Such reports are known colloquially as "chemobrain" or "chemofog" <http://www.pinkribbon.com/chemobr.htm>. Empirical evidence is accumulating that cognitive problems are associated with use of surgery and chemotherapy (e.g., Ahles et al, 2002) [70]. For example, Cimprich [71] examined attention and reported decrements in attention-related tasks in older, but not in younger breast cancer patients. Tamoxifen has also been found to negatively affect cognition [72] in a sample of women aged 57-75.

As cognitive problems interact with fatigue, pain, depression, and sleep quality in their impact on functioning, interventions to improve cognition (and/or reduce these other symptoms) could lead to improvements in other domains. Cognitive behavior therapy has been found to

be effective in improving sleep, cognition, and quality of life in younger groups [73] and such interventions could be expanded to include older women. Examination of long-term cognitive effects of adjuvant treatment using validated neuropsychological batteries and evaluation of fatigue prior to and after surgery and adjuvant therapy is warranted. Improving cognition may also have long-term effects on survival, since impaired cognitive status has been associated with poorer survival, controlling for age, stage, and treatment [41].

Body Image and Sexuality

In the multi-center EORTC trial of mastectomy versus breast conservation (plus tamoxifen) there was a trend towards better body image one year after treatment among women 70 years and older [12]. In other studies, older women undergoing breast conservation have reported better body image (and mental health) two-years post-treatment compared to the women who had undergone mastectomy, [26,74] although results have been inconsistent [75,76]. National estimates of breast reconstruction rates following mastectomy demonstrate lower use among older women, with only 1.3% to 4.1% of women over age 70 having reconstruction compared to 17.9% of younger women [77,78].

There is a paucity of data on sexual feelings and outcomes in older women with breast cancer. In our own research, we observed that 15.1% of women had been sexually active prior to breast cancer diagnosis and that many women reported that breast cancer had either a "very negative" or "somewhat negative" impact on their sexual feelings and interest (Mandelblatt, unpublished data, 2003).

Social and Role Function

Social and role functions are inextricably linked to social support and integration prior to breast cancer diagnosis. Breast cancer survivors who are more socially integrated before their breast cancers report better post-treatment role function and vitality than less socially integrated women [79]. In fact, Michael and colleagues report that social integration accounts for greater variance in quality of life than treatment itself [79]. As a result, others have developed social support interventions targeted to breast cancer survivors with poor support systems. In a recent randomized, prospective trial, the quality of life of older women improved when communicating with a community-based nurse case manager who provided help with managing comorbid conditions, assistance with activities of daily living (ADLs), and help navigating the health care system [80]. Similarly, Silliman and colleagues [30] found that older women relied heavily on their physicians for support and they suggest enhanced physician-patient communication may improve emotional health outcomes in these women. With intense support, women

generally report better well-being and lower distress, [81] although some studies have not been able to demonstrate this effect [82].

Economic Outcomes

Breast cancer accounted for between one-fifth and one-quarter of the \$157 billion dollars in cancer costs in the United States in 2001 [83]. Lower costs per woman have been reported for older women compared to costs for younger women [84] and is probably partly explained by less aggressive treatment offered to older women [35]. Interestingly, economic market forces affect costs and patterns of care in older women. For example, Hadley and colleagues examined Medicare claims and demonstrated that women living in areas with the highest ratio of mastectomy fees relative to breast conservation fees were significantly more likely to have mastectomy, while women in areas where there was less of a fee differential between the two procedures were most likely to get breast conservation [85].

In one economic analysis spanning a five year horizon after breast cancer treatment, Polsky and colleagues found that the initial costs of six weeks of radiation makes breast conservation more expensive than mastectomy, with no significant differences in quality-adjusted survival. Summing costs and outcomes over five years post-treatment, breast conservation and radiation cost more than \$200,000 per quality adjusted life year saved (QALY) compared to mastectomy. In an alternative formulation, where breast conservation and radiation are compared to open choice, and choice is assumed to have a utility in and of itself (as noted above), the cost-effectiveness ratio for breast conservation drops to as low as approximately \$50,000 to \$75,000 per QALY, well within the threshold for current medical expenditures [86].

Caregiver Burden

There is a paucity of data about the impact of breast cancer in older women on their family members and caregivers. Female gender, older age, and past grief experiences have been associated with increased distress and grief in spousal caregivers of cancer patients [87]. In one study, daughters and sisters of women with breast cancer perceived that their information and support needs were not well met [88]. In another report, Northouse and colleagues found that family members of patients with recurrent disease experienced decrements in emotional well being, and that negative impact was mediated by family hardness and social support [89]. Among caregivers of a small sample of cancer patients sleep problems predicted 63.6% of the variance in caregiver depression [90]. Since older women are likely to be primary caregivers for their spouses or grandchildren, when they are undergoing breast cancer treatment or terminally ill, caregiver burden

is compounded by loss of this key family resource. Overall, more research is needed to assess caregiver needs and develop appropriate interventions geared to older patients and their families.

Special Considerations in Quality of Life Measurement

To date, quality of life assessments in older women have employed a wide variety of methods and tools to assess outcome. Some limitations of prior evaluations include use of a limited number of domains, lack of standard agreement on the appropriate comparison groups (e.g., other cancer patients, women without cancer) or failure to compare results to any control group, and inclusion of narrow segments of the breast cancer population (e.g., only well-educated, non-minority women). Furthermore, few prior studies were designed to specifically evaluate outcomes for older women, particularly to assess the interactions of decrements in function or well being associated with treatment with comorbid conditions. For example, mild treatment related peripheral neuropathy might significantly impair ambulation in an older diabetic woman with pre-existing neuropathic changes. Visual problems associated with tamoxifen could be especially detrimental to older women with underlying visual impairment. Lack of control for baseline function may also over-estimate the magnitude of treatment-related decrements in quality of life.

Certain domains of quality of life may be more salient to older women than other groups of breast cancer patients. For instance, for older women, ambulation and mobility impairments may make the difference between independent living and assisted living [43,91]. Likewise, mild fatigue may have a multiplicative effect in impairing activities of daily living in a frail older woman, while only being bothersome to a younger woman. Presence of comorbid conditions may also limit discussion of treatment options [92] or complicate delivery of treatment such as chemotherapy [40,93,94]. Conversely, it is important to recognize heterogeneity in elderly women such that special subsets will have few chronic diseases and greater functional status; such patients will be able to tolerate more intensive therapy (i.e. "fit elderly") [95].

Administration of quality of life evaluations for older patients may also be difficult and can compromise the quality of data obtained. For instance, visual or hearing problems may lead to miscomprehension of survey items, and memory impairments may lead to obtaining inaccurate data, especially about more distal events. Older women also may telescope time and discount the importance of health events that are in the future versus those in the present.

Table 2: Recommendations for Future Research with Older Breast Cancer Patients

Area of research	Recommendations
Methodological issues	<ul style="list-style-type: none"> • Long-term follow-up needed • Increase sample sizes
Body image and sexuality	<ul style="list-style-type: none"> • Integrate quality of outcomes into clinical and observation trials • Include reliable and valid measures of body image and sexuality concerns • Discuss preferences
Effects of comorbid conditions	<ul style="list-style-type: none"> • Design studies to specifically evaluate interactions of decrements in function or well being associated with treatment of comorbid conditions. • Use of multiple informants approach with cognitively impaired women [96] • Use of Comprehensive Prognostic Index [97]
Cognitive effects of treatments and evaluation of fatigue	<ul style="list-style-type: none"> • Examine long-term cognitive effects of adjuvant treatment using validated neuropsychological batteries
Interventions to improve quality of life	<ul style="list-style-type: none"> • Evaluate fatigue prior to and after surgery, and adjuvant therapy • Educate medical staff on older women's unique concerns and needs • Develop interventions to improve patient-physician communication • Use decision aides to elicit preferences and enhance shared decision making • Tailor interventions to account for cultural factors
Caregiver burden	<ul style="list-style-type: none"> • Examine caregiver sleep problems and their role in depression • Increase social support • Assess quality of the dying experience for patient and caregiver • Test models to relieve caregiver burden

Thus, as indicated by the pathways depicted in Figure 1, consideration of comorbidity data is essential for future outcomes research among older women. Exclusion of older women with multiple comorbidities from clinical trials may result in less representative samples of breast cancer patients and interfere with improving understanding of the impact that such conditions have on quality of life. Specialized tools and methodologies may need to be developed and applied to research with older female populations to fully capture non-cancer influences on outcomes. Examples could include the multiple informants approach when working with cognitively impaired women [96] or the Comprehensive Prognostic Index [97] which is created by combining indices of comorbidities that impact breast cancer survival with age and cancer stage.

Thus, there are many methodological challenges inherent in working with older populations. Researchers interested in studying older women's quality of life will need to be cognizant of these special issues to ensure high quality results. Further research is necessary to ensure that we are using the proper approaches to obtain valid information and to improve the quality of care for older women.

Future Directions

This review is intended to highlight key outcomes among older women surviving breast cancer. Our results can be used to inform clinical decision-making and design interventions to improve quality of care and optimize func-

tioning in this growing population (Table 2). Additional research is needed to understand dynamic interactions between cancer survivorship, comorbidities, aging per se, poverty, ethnicity, and the processes of interaction with the medical care system in producing the observed outcomes of care.

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