Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

Qual Life Res. Author manuscript; available in PMC 2018 July 01.

Published in final edited form as:

Qual Life Res. 2017 July ; 26(7): 1733–1743. doi:10.1007/s11136-017-1533-5.

Examining Health-Related Quality of Life Patterns in Women with Breast Cancer

Laura C. Pinheiro, MPH,
Department of Health Policy and Management, University of North Carolina at Chapel Hill

Xianming Tan, PhD,
Department of Biostatistics, Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill

Andrew F. Olshan, PhD,
Department of Epidemiology, Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill

Stephanie B. Wheeler, PhD,
Department of Health Policy and Management, Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill

Katherine E. Reeder-Hayes, MD, MBA,
University of North Carolina Breast Cancer, Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill

Cleo A. Samuel, PhD, and
Department of Health Policy and Management, Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill

Bryce B. Reeve, PhD
Department of Health Policy and Management, Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill

Abstract

Purpose—We aimed to identify subgroups of women with breast cancer who experience different health-related quality of life (HRQOL) patterns during active treatment and survivorship and determine characteristics associated with subgroup membership.

Methods—We used data from the third phase of the population-based Carolina Breast Cancer Study and included 2,142 women diagnosed with breast cancer from 2008–2013. HRQOL was measured, on average, 5- and 25-months post-diagnosis. Latent profile analysis was used to

Compliance with Ethical Standards:

Conflict of Interest: Authors Dr. Samuel and Dr. Wheeler have received a research grant from Pfizer for another unrelated study. All other authors (Ms. Pinheiro, Dr. Reeder-Hayes, Dr. Olshan and Dr. Reeve) declare that they have no conflicts of interest to disclose. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent from study subjects was not needed as the University of North Carolina at Chapel Hill IRB granted this research exemption from review.
This article does not contain any studies with animals performed by any of the authors.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

identify HRQOL latent profiles (LPs) at each time point. Latent transition analysis was used to determine probabilities of women transitioning profiles from 5- to 25-months. Multinomial logit models estimated adjusted odds ratios (aORs) and 95% confidence intervals for associations between patient characteristics and LP membership at each time point.

Results—We identified four HRQOL LPs at 5- and 25-months. LP1 had the poorest HRQOL and LP4 the best. Membership in the poorest profile at 5-months was associated with younger age aOR 0.95; 0.93–0.96, White race aOR 1.48; 1.25–1.65, being unmarried aOR 1.50; 1.28–1.65, and having public aOR 3.09; 1.96–4.83 or no insurance aOR 6.51; 2.12–20.10. At 25-months, Black race aOR 1.75; 1.18–1.82 was associated with poorest profile membership. Black race and smoking were predictors of deteriorating to a worse profile from 5- to 25- months.

Conclusions—Our results suggest patient-level characteristics including age at diagnosis and race may identify women at risk for experiencing poor HRQOL patterns. If women are identified and offered targeted HRQOL support, we may see improvements in long-term HRQOL and better breast cancer outcomes.

Introduction

Health-related quality of life (HRQOL) is a multidimensional concept representing an individual's perception of well-being, including spiritual, functional, physical, emotional, and social well-being [1,2]. Women with breast cancer (BC) in the United States experience HRQOL decrements following diagnosis, during active treatment, and through BC survivorship [3–5]. HRQOL concerns include fear of BC recurrence or death, lymphedema, fatigue, early menopause, and difficulty returning to work [1,3,6,7]. Poorly managed HRQOL is associated with increased mortality risk [8]. Incorporating HRQOL assessments into cancer care management may help ensure more patient-centered care and improve BC outcomes [9].

HRQOL is often presented as a single global score, which limits understanding of nuances in HRQOL and the utility of such scores as screening tools for poor health outcomes. For example, a woman may experience optimal physical well-being throughout BC treatment, but suffer significant decrements in psychosocial well-being. Thus, by focusing only on a single, overall score; a clinician may inadvertently overlook decrements in their patients' HRQOL [5].

Although many studies continue to use global indicators of HRQOL, domain-specific measures are also often used to represent the multidimensional nature of HRQOL. However, traditional methods to analyzing differences or changes in domain-specific HRQOL, which compare means and standard deviations, are criticized for not representing heterogeneity in HRQOL experiences [10]. Examining mean differences in HRQOL scores alone may lead us to erroneous conclusions regarding outliers or subgroups [10]. That is, small differences or patterns may be masked and subgroups of women who experience improvements or decrements may be missed [10]. While mean differences in HRQOL scores reflect group-level HRQOL effects of diagnosis or treatment, these overall scores may conceal subgroups of patients experiencing unusually large decrements in a particular domain, or decrements

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

across multiple domains. Such patients may benefit from more targeted HRQOL intervention.

Cluster analysis has been used to identify subgroups of patients at increased risk of poor health outcomes with the expectation of tailoring treatment choices to patient-specific needs [11–15]. Previous studies found that meaningful subgroups of cancer patients could be identified and clinical interventions may have seen better outcomes if an individual's HRQOL had been considered in care decisions [11,13]. For example, women who were identified to be in emotionally unhealthy clusters could have been supported with psychotherapy sessions following diagnosis to ameliorate the emotional impacts of BC and to help them cope with diagnosis and treatment [11,13,16]. However, the work that has focused on identifying clusters of women with BC using HRQOL measures has been somewhat limited. Several studies combined multiple cancer types, many were conducted abroad, most were cross sectional, and all had sample sizes of fewer than 500 women [17–21]. Using a large, population-based study of over 2,000 women with BC offers an opportunity to expand upon previous HRQOL cluster analysis work and draw conclusions more generalizable to women with BC in the U.S.

The objectives of this study were to 1) employ latent profile analysis (LPA) to identify subgroups of women with BC who experienced different HRQOL patterns at 5- and 25-months after diagnosis, 2) determine patient-level characteristics associated with membership in the HRQOL subgroups, 3) assess the probability of transitioning from one subgroup to another between the two distinct phases of the BC care continuum, and, finally, 4) identify patient-level characteristics associated with transitioning from one LP to another LP between 5- and 25-months. To our knowledge, no studies have used LPA and LTA in a large, population-based BC cohort in the U.S. to examine HRQOL pattern. The clinical meaningfulness of HRQOL subgroups will help inform and may improve targeted HRQOL management for women with BC in the U.S.

Methods

Data

We used data from the third phase of the Carolina Breast Cancer Study (CBCS-III). Through rapid case ascertainment, CBCS-III enrolled 2,998 women diagnosed with incident, invasive, pathologically confirmed BC between 2008 and 2013 across 44 counties in North Carolina [22,23]. By oversampling young and Black women, the population-based CBCS-III cohort is 50% Black and 50% under the age of 50. CBCS-III intended to be representative of women across the state and, therefore, enrolled those in rural and urban regions, women with private, public or no insurance, and of varying income levels [22]. Demographics, lifestyle factors, and HRQOL data were first collected in-person by nurses within 9-months of BC diagnosis and at a median of 5.2 months post-diagnosis (range 1.8–8.9 months) [22,24]. At the initial interview, participants consented for researchers to abstract their medical records [22–24]. Women also completed a follow-up survey, which included additional HRQOL questionnaires at a median of 25 months post-diagnosis (range 20–36 months), which is referred to as the "25-month survey". Medical record abstraction data included comorbidities and BC treatments. Pathology report data provided information

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

regarding tumor stage and grade. This study was approved by the Institutional Review Board at the University of North Carolina at Chapel Hill.

Participants

We limited our sample to women who completed both 5-and 25-month surveys (82% of total women enrolled). Additional exclusions included: women identifying as Hispanic or "other race" due to their small representation (3%), distant stage BC (3%), women who completed their initial survey more than 9 months after diagnosis (7%), and those who completed their follow-up survey more than 36 months after diagnosis (<1%). Therefore, 2,142 Non-Hispanic Black and White women with Stage I-III BC were included in this study.

HRQOL Measures

The Functional Assessment of Cancer Therapy for Breast Cancer (FACT-B) and Functional Assessment of Chronic Illness Therapy for Spiritual Well-Being (FACIT-SP) were used to measure HRQOL at both 5- and 25-months. The FACT-B is a BC-specific instrument with domains for: physical, social, emotional, and function well-being, and BC-specific concerns [25]. The FACT-B has been psychometrically validated and shown to be sensitive to changes over time in women with BC [26]. The FACIT-SP is a validated chronic disease instrument commonly used to measured spiritual well-being [26–28]. FACT-B and FACIT-SP domains are treated as continuous measures with higher scores indicating better HRQOL [26,28,29]. Minimally important differences (MID) or smallest differences in HRQOL that are considered meaningful to the patient or provider are 2–4 points per HRQOL domain [30].

Independent Variables

Primary predictors of HRQOL subgroup membership at 5- and 25-months reflect self-reported individual characteristics captured on the 5-month survey, including age at diagnosis, race, marital status, education, and insurance status.

Covariates

Self-reported smoking status, medical-record confirmed comorbid conditions (e.g., diabetes, chronic obstructive pulmonary disease, obesity, hypertension, heart disease), tumor stage and grade, surgery type, and receipt of radiation, chemotherapy, and Herceptin were included in analyses [31].

Statistical Analysis

Analyses were performed in R (Version 3.2.3) and SAS 9.3 with two-sided statistical tests and significance level of 5%.

LPA Models

Using the six continuous FACT-B and FACIT-SP domains, we used the "mclust" model-based clustering package in R to implement a more generalized version of latent profile analysis (LPA) to identify clusters of women who experienced distinct HRQOL patterns [32]. Probabilistic clusters of women were grouped together as HRQOL latent profiles (LP) at 5 and 25-months post-diagnosis, separately [33–36]. To perform the LPA, we assumed

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

homogeneity within and across LPs and LP separation (i.e., item-response probabilities allow for clear differentiation between LPs) [35–37]. However, we did not assume local independence, which enabled us to use a more general version of LPA [38,39]. A combination of underlying theory, interpretability of findings, and model fit indices guided model selection and, thus, the ideal number of LPs at each time point [35]. We used the Bayesian Information Criteria (BIC) to compare fits of models with different covariance structures and number of LPs and selected the model with the lowest BIC value [35,36]. We then calculated prevalence rates or the proportion of women with BC expected in each LP at 5- and 25-months [35,40]. We also determined mean FACT-B and FACIT-SP scores in each LP and compared scores across LPs and to U.S. norm scores (considering both MIDs and statistical significance).

Predicting LP Membership

We employed a one-step approach, which simultaneously estimates a LP model and a multinomial logit structural model to determine if patient-level characteristics were significantly associated with LP membership [41,42]. The highest HRQOL LP served as the reference category. In this approach, we adjusted for smoking status, comorbid conditions, treatment, and tumor characteristics, which could influence HRQOL at a single time point and HRQOL changes over time [31,43]. Variables presented in Table 1 were potential covariates for adjusted models. Before selecting which variables to include in the models, we conducted univariable analyses to determine covariates that were significantly associated with LP membership. We used a significance level of 0.05 to select relevant covariates to include in multivariable analyses.

Analysis of Transition

To assess transition probabilities and to determine patient-level characteristics associated with transitioning, we estimated four separate multinomial logit models (MLMs) (one for each 5-month profile) to predict LP transitions from 5- to 25-months, adjusting for covariates presented in Table 1 [33,40,44]. Given the 16 possible transitions, we adjusted for multiple comparisons using Bonferroni. In these models, 25-month HRQOL LPs (four categories) were used as the outcomes. The highest HRQOL LP at 25-months was the reference category in all MLMs. We also used MLM to examine patient-level predictors of improving to a better LP and deteriorating to a worse LP from 5- to 25-months.

Results

Unadjusted

5-month LPs—We identified four HRQOL LPs at 5-months (Figure 1). The profiles were generally well-ordered with mean overall FACT-B scores of: 84.6, 102.8, 120.1, and 132.5, respectively. LP1 had the poorest HRQOL scores across all domains (up to one standard deviation below U.S. norms) and is considered the “poorest HRQOL profile.” LP4 had the highest HRQOL scores across domains (one standard deviation above U.S norms) and is considered the “highest HRQOL profile.” The second poorest HRQOL LP (LP2) had physical and functional well-being scores below U.S. norms, but not as low as LP1 (Figure 1). Differences between the two poorest HRQOL profiles exceeded MID thresholds of 2-

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

points for every domain except physical well-being. As such, we refer to LP2 as the “poor physical HRQOL, but well-supported mental well-being profile.” LP3 had physical and functional well-being scores above U.S norms, but below LP4. Mean differences between LP 3 and 4 were above MID thresholds for social, functional, and spiritual well-being and BC-specific concerns. LP3 had mean BC-specific concerns scores 4-points higher than LP2 and 7-points higher than LP1, which both well exceed the MID threshold. Therefore, we consider LP 3 the “second highest HRQOL profile”. Patient prevalence rates at 5-months for LPs 1–4 are as follows: 32%, 29% 28% and 11%, respectively. Over 60% of women with BC were in the two poorest HRQOL LPs during active treatment.

25-month LPs—We also identified four HRQOL profiles at 25-months (Figure 2). Similar to 5-month LPs, the profiles were well ordered with mean overall FACT-B scores of: 86.1, 99.6, 108.6, and 122.3, respectively. As at 5-months, the poorest HRQOL LP was LP1 and the highest HRQOL LP was LP4. Scores across all domains were low for the poorest HRQOL profile, but especially in physical and functional domains, which are more than one standard deviation below U.S. norm scores. Women in the poor physical HRQOL, but better mental well-being profile (LP2) at 5- months reported mean physical and spiritual well-being scores higher than the second highest HRQOL profile at 25-months, but lower functional, social and emotional well-being and BC-specific concerns (Figure 2). At 25-months, the poor physical HRQOL profile also had scores in social and emotional HRQOL were below U.S. norms. The second highest HRQOL profile scores were generally high across all domains, but lower than scores in the highest HRQOL profile. The proportion of patients within each profile at 25-months for LPs 1–4 are as follows: 26%, 12%, 37% and 25%, respectively. More than 60% of the women with BC were in the highest HRQOL LPs at 25-months post-diagnosis.

5- to 25-month Transitions—Overall, mean HRQOL scores in the poorest HRQOL profile were lower at 25-months than at 5-months, but scores at 25-months were higher than 5-months in the best HRQOL profile. Compared to mean scores at 5-months, scores at 25-months in LP2 were higher for physical and functional well-being, lower for social, emotional and spiritual domains, and remained the same for BC-specific concerns. Mean scores at 5- and 25-months for the second highest HRQOL profile were generally the same. There were 951 (44%) women who improved to a better HRQOL profile from 5- to 25-months, 864 (40%) who remained in the same profile over time, and 327 (15%) who deteriorated to a worse profile. Among women in the poorest HRQOL profile at 5-months, 52% remained in the poorest HRQOL profile at 25-months, and 48% transitioned to a higher HRQOL profile at 25-months (Table 2). Of the women in the poor physical HRQOL, but better mental well-being profile at 5-months, 11% remained in that profile, 22% declined to the poorest HRQOL profile and 67% transitioned to a higher HRQOL profile at 25-months. We observed the largest change in mean domain-specific scores from 5- to 25-months in the poor physical HRQOL, but better mental well-being profile. Among women in the second highest profile at 5-months, 18% declined in HRQOL to one of the two poorest HRQOL profiles, and 35% improved to the highest HRQOL profile at 25-months. Finally, among those in the highest HRQOL at 5-months most remained in the highest HRQOL profile

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

(65%), 24% declined to LP3, and 11% to one of the two poorest HRQOL profiles at 25-months.

Adjusted

Relevant covariates for adjusted models, which met the 0.05 threshold included: race, age at diagnosis, smoking status, marital status, education, insurance status, diabetes, COPD, heart disease, hypertension, obesity, surgery, chemotherapy, Herceptin, and stage of disease (Table 1).

5-month LPs—Compared to the highest HRQOL LP, White race, younger age at diagnosis, being unmarried, having public or no insurance (versus private), prevalence of COPD, and receiving chemotherapy were significantly associated with membership in the poorest HRQOL LP (Table 3). Compared to the highest HRQOL profile, membership in the poor physical, but good mental well-being profile was significantly associated with younger age, COPD, obesity and receipt of chemotherapy. Membership in the second highest profile was significantly associated with White race, higher level of education, COPD, and not receiving chemotherapy compared to membership in the highest profile.

25-month LPs—Compared to the highest HRQOL profile, membership in the poorest HRQOL profile at 25-months was significantly associated with Black race, being a current or former smoker, COPD, heart disease, obesity, receiving chemotherapy and having more advanced stage BC (Table 4). Membership in the poor physical, but good mental well-being profile was significantly associated with younger age, smoking, being unmarried, COPD, heart disease, obesity, chemotherapy, Stage 2 or 3 BC, and having public or no insurance (compared to membership in the highest HRQOL profile). Finally, relative to the highest HRQOL profile, membership in the second highest profile was significantly associated with White race, younger age at diagnosis, higher education and prevalence of COPD.

Transitions—Prior to adjusting for multiple comparisons, there were no patient-level characteristics significantly associated with transitioning from a particular HRQOL profile to another profile from 5- to 25-months. Compared to women who improve from one HRQOL LP to a better LP or remain in the same LP, Black race aOR1.32, 95% CI 1.02–1.72 and being a current smoker aOR 1.54, 95% CI 1.13–2.12 were significant predictors of HRQOL LP deterioration from 5-to 25-months. Compared to women who improve to a better HRQOL, the only predictor of remaining in the same HRQOL over time was having public (versus private) or no insurance aOR 1.52, 95% CI 1.18–1.96 and aOR 2.10, 95% CI 1.34–3.29, respectively.

Discussion

The objective of this study was to employ a novel, patient-centered approach to characterizing HRQOL patterns in women from a large population-based BC cohort and to determine patient-level characteristics associated with patterns. We identified four distinct HRQOL LPs at 5- and 25-months. Membership in poorer HRQOL LPs at 5-months was significantly associated with younger age, White race, lack of social support, public insurance or being uninsured, comorbid conditions (e.g., obesity, COPD), being a smoker,

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

and more intensive BC treatment. At 25-months, membership in poorer HRQOL LPs was associated with modifiable patient-level factors such as smoking and obesity, as well as non-modifiable factors such as younger age, Black race, and prevalence of comorbid conditions. More advanced stage of BC and receipt of chemotherapy was also associated with poorer HRQOL LPs at 25-months. To our knowledge, no previous study has used LPA and LTA methods in a BC cohort to describe and characterize HRQOL patterns [40].

Traditional LPA and LTA are considered more patient-centered approaches to identifying women susceptible to poor HRQOL [35,40]. LPA is appealing for identifying patterns within large, heterogeneous groups of individuals because it takes individual HRQOL patterns into account rather than aggregating scores across individuals [35,36,40]. This is a probabilistic model-based approach, which groups patients together based on probabilities rather than grouping symptoms or HRQOL scores together based on pre-determined distances [16].

Identifying subgroups of women with BC can offer clinically meaningful guidance on distinct HRQOL patterns experienced by this population [20]. For example, a previous study in pediatric oncology suggested that LPA could be used to develop prediction models that preemptively identify individuals who might be vulnerable to membership in poor HRQOL LPs so action can be taken early on in their care trajectories [16]. Furthermore, LTA might be able to help predict patients who are likely to transition to poorer HRQOL LPs as they move through the cancer continuum. This type of prediction tool could be especially relevant for women with BC who are in the BC care continuum for several years and could benefit from targeted HRQOL management.

We also identified patient-level characteristics associated with membership in the 5- and 25-month LPs, which offers insights for interventions wishing to target specific groups of patients who are risk for poor HRQOL. As these are non-modifiable characteristics routinely collected in clinic, these factors could be used to easily identify women who are most susceptible to membership in a poor HRQOL LP. Characteristics associated with lower HRQOL LP membership were generally similar at 5- and 25-months including younger age at diagnosis, race, comorbid conditions, and receipt of chemotherapy. However, some distinct differences that may help inform better HRQOL support exist. For example, membership in the poorest HRQOL LP at 5-months was associated with White race as well as socioeconomic factors such as lack of partner support, and insurance coverage and type. At 25-months, Black race was actually associated with membership in the poorest HRQOL profile, but no other socioeconomic factors were associated with poorest HRQOL profile membership. Understanding which patient-level characteristics might be most associated with poor HRQOL LP membership at different phases of the BC care continuum helps inform HRQOL management strategies, which can vary over time [31]. For example, if clinicians are aware that particular characteristics are associated with worse HRQOL patterns at specific BC continuum phases, they might be better equipped to provide the necessary support for patients. Conversely, if supportive resources such as counseling or nursing support are limited, they could be targeted to the patients most in need. Furthermore, some modifiable patient factors such as obesity and smoking status were also strongly associated with membership in poorer HRQOL profiles as well as deteriorating to a worse

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

HRQOL profile over time, and could potentially be intervened upon in order to help support HRQOL management in women with BC.

Limitations

Our study was limited to Non-Hispanic White and Black women with Stage 1–3 disease residing in North Carolina from 2008–2013. As such, results may not be generalizable to women of other races/ethnicities, those with advanced stage BC, and women in other states. Furthermore, given that there are not software packages developed to perform a traditional, one-step LTA, we performed an ad hoc version of this approach, limiting the generalizability of our findings. Performing separate MLMs at each time point could have yielded a different number of profiles, which could have complicated interpretation of our findings. As these methods continue to develop and evolve, it would be of interest to replicate these analyses. Finally, although we had a large sample size, when we estimated individual MLMs for each 5-month HRQOL LP in order to predict transitions, our sample sizes for each model became small, which may partially explain why we did not find statistically significant predictors of LP transitions. Future studies with larger samples of women with BC should further explore predictors of LP transitions.

Conclusions

LPA is a probabilistic model-based approach used to identify subgroups of individuals who share similar characteristics that might be associated with their HRQOL patterns [16]. By identifying women with BC who are likely to belong to poor HRQOL LPs, this approach offers a unique opportunity for women with BC to be offered targeted HRQOL support early in the BC care continuum [16]. This could potentially lead to downstream effects such as improved long-term HRQOL, greater adjuvant treatment adherence, and ultimately, better BC outcomes (i.e., BC recurrence and survival) [21,45,46]. Results from this work suggest that we can potentially use routinely collected patient characteristics to help identify women at increased risk for experiencing poor HRQOL during active treatment and survivorship phases of their BC care. These findings are clinically relevant, as there is a national emphasis on patient-centered care that encourages clinicians to routinely collect and monitor HRQOL through electronic health records [47–52]. Furthermore, patient-level characteristics such as age at diagnosis and race are regularly collected in clinic and could easily be used to identify women at risk for poor HRQOL. If these women were identified following BC diagnosis, they could be connected to mental health specialists, support groups from the onset of active treatment, nutritionists to control weight gain or loss, and physical therapists to help manage physical and functional well-being ailments following treatments. Leveraging LP membership to preemptively anticipate HRQOL needs of women with BC is in line with providing cancer care that reflects patient needs, preferences, and values.

Acknowledgments

Jessica Tse, and Mary Beth Bell

Funding: This study was supported by the University Cancer Research Fund of North Carolina, the National Cancer Institute Specialized Program of Research Excellence in Breast Cancer at UNC (NIH/NCI P50-CA58223), the Susan G. Komen for the Cure Foundation, and 3 R01 CA150980 05S1.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

References

1. Lopez-Class M, Gomez-Duarte J, Graves K, Ashing-Giwa K. A contextual approach to understanding breast cancer survivorship among Latinas. Psycho-oncology. 2012; 21(2):115–124. DOI: 10.1002/pon.1998 [PubMed: 21674680]
2. Hennessy CH, Moriarty DG, Zack MM, Scherr PA, Brackbill R. Measuring health-related quality of life for public health surveillance. Public health reports (Washington, DC : 1974). 1994; 109(5): 665–672.
3. Cho J, Jung SY, Lee JE, Shim EJ, Kim NH, Kim Z, Sohn G, Youn HJ, Kim KS, Kim H, Lee JW, Lee MH. A review of breast cancer survivorship issues from survivors' perspectives. Journal of breast cancer. 2014; 17(3):189–199. DOI: 10.4048/jbc.2014.17.3.189 [PubMed: 25320616]
4. Kappel ML. It's not the model that matters--still lost in transition. Journal of oncology practice / American Society of Clinical Oncology. 2013; 9(3):128–129. DOI: 10.1200/jop.2013.001016
5. Smith AW, Alfano CM, Reeve BB, Irwin ML, Bernstein L, Baumgartner K, Bowen D, McTiernan A, Ballard-Barbash R. Race/ethnicity, physical activity, and quality of life in breast cancer survivors. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. 2009; 18(2):656–663. DOI: 10.1158/1055-9965.epi-08-0352
6. Bloom JR, Petersen DM, Kang SH. Multi-dimensional quality of life among long-term (5+ years) adult cancer survivors. Psycho-oncology. 2007; 16(8):691–706. DOI: 10.1002/pon.1208 [PubMed: 17628036]
7. Tomich PL, Helgeson VS. Five years later: a cross-sectional comparison of breast cancer survivors with healthy women. Psycho-oncology. 2002; 11(2):154–169. [PubMed: 11921331]
8. Ganz PA, Lee JJ, Siau J. Quality of life assessment. An independent prognostic variable for survival in lung cancer. Cancer. 1991; 67(12):3131–3135. [PubMed: 1710541]
9. Basch E, Deal AM, Kris MG, Scher HI, Hudis CA, Sabbatini P, Rogak L, Bennett AV, Dueck AC, Atkinson TM, Chou JF, Dulko D, Sit L, Barz A, Novotny P, Fruscione M, Sloan JA, Schrag D. Symptom Monitoring With Patient-Reported Outcomes During Routine Cancer Treatment: A Randomized Controlled Trial. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2016; 34(6):557–565. DOI: 10.1200/jco.2015.63.0830 [PubMed: 26644527]
10. Buijs C, de Vries EG, Mourits MJ, Willemse PH. The influence of endocrine treatments for breast cancer on health-related quality of life. Cancer treatment reviews. 2008; 34(7):640–655. DOI: 10.1016/j.ctrv.2008.04.001 [PubMed: 18514425]
11. Trask PC, Griffith KA. The identification of empirically derived cancer patient subgroups using psychosocial variables. Journal of psychosomatic research. 2004; 57(3):287–295. DOI: 10.1016/j.jpsychores.2004.01.005 [PubMed: 15507256]
12. Hack TF, Degner LF. Coping with breast cancer: a cluster analytic approach. Breast cancer research and treatment. 1999; 54(3):185–194. [PubMed: 10445417]
13. Nagel GC, Schmidt S, Strauss BM, Katenkamp D. Quality of life in breast cancer patients: a cluster analytic approach. Empirically derived subgroups of the EORTC-QLQ BR 23--a clinically oriented assessment. Breast cancer research and treatment. 2001; 68(1):75–87. [PubMed: 11678311]
14. Shapiro DE, Boggs SR, Rodrigue JR, Urry HL, Algina JJ, Hellman R, Ewen F. Stage II breast cancer: differences between four coping patterns in side effects during adjuvant chemotherapy. Journal of psychosomatic research. 1997; 43(2):143–157. [PubMed: 9278904]
15. Shapiro DE, Rodrigue JR, Boggs SR, Robinson ME. Cluster analysis of the medical coping modes questionnaire: evidence for coping with cancer styles? Journal of psychosomatic research. 1994; 38(2):151–159.
16. Buckner TW, Wang J, DeWalt DA, Jacobs S, Reeve BB, Hinds PS. Patterns of symptoms and functional impairments in children with cancer. Pediatric blood & cancer. 2014; 61(7):1282–1288. DOI: 10.1002/pbc.25029 [PubMed: 24634396]
17. Kenne Sarenmalm E, Browall M, Gaston-Johansson F. Symptom burden clusters: a challenge for targeted symptom management. A longitudinal study examining symptom burden clusters in

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

breast cancer. Journal of pain and symptom management. 2014; 47(4):731–741. DOI: 10.1016/j.jpainsymman.2013.05.012 [PubMed: 23916827]

18. Dodd MJCMH, Cooper BA, Miaskowski C. The effect of symptom clusters on functional status and quality of life in women with breast cancer. European journal of cancer (Oxford, England : 1990). 2010
19. Ridner SH. Quality of life and a symptom cluster associated with breast cancer treatment-related lymphedema. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer. 2005; 13(11):904–911. DOI: 10.1007/s00520-005-0810-y [PubMed: 15812652]
20. Miaskowski C, Aouizerat BE, Dodd M, Cooper B. Conceptual issues in symptom clusters research and their implications for quality-of-life assessment in patients with cancer. Journal of the National Cancer Institute Monographs. 2007; (37):39–46. DOI: 10.1093/jncimonographs/lgm003 [PubMed: 17951230]
21. Trudel-Fitzgerald C, Savard J, Ivers H. Longitudinal changes in clusters of cancer patients over an 18-month period. Health psychology : official journal of the Division of Health Psychology, American Psychological Association. 2014; 33(9):1012–1022. DOI: 10.1037/a0033497
22. McGee SA, Durham DD, Tse CK, Millikan RC. Determinants of breast cancer treatment delay differ for African American and White women. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. 2013; 22(7):1227–1238. DOI: 10.1158/1055-9965.epi-12-1432
23. Newman B, Moorman PG, Millikan R, Qaqish BF, Geradts J, Aldrich TE, Liu ET. The Carolina Breast Cancer Study: integrating population-based epidemiology and molecular biology. Breast cancer research and treatment. 1995; 35(1):51–60. [PubMed: 7612904]
24. Hair BY, Hayes S, Tse CK, Bell MB, Olshan AF. Racial differences in physical activity among breast cancer survivors: implications for breast cancer care. Cancer. 2014; 120(14):2174–2182. DOI: 10.1002/cncr.28630 [PubMed: 24911404]
25. Garcia SF, Hahn EA. Measure validation is an ongoing process: the Functional Assessment of Cancer Therapy-Breast Symptom Index as a case example. Ann Palliat Med. 2012; 1(3):207–210. DOI: 10.3978/j.issn.2224-5820.2012.10.07 [PubMed: 25841515]
26. Brady MJ, Cella DF, Mo F, Bonomi AE, Tulsky DS, Lloyd SR, Deasy S, Cobleigh M, Shiomoto G. Reliability and validity of the Functional Assessment of Cancer Therapy-Breast quality-of-life instrument. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 1997; 15(3):974–986. [PubMed: 9060536]
27. Bai M, Lazenby M. A systematic review of associations between spiritual well-being and quality of life at the scale and factor levels in studies among patients with cancer. J Palliat Med. 2015; 18(3):286–298. DOI: 10.1089/jpm.2014.0189 [PubMed: 25303461]
28. Peterman AH, Fitchett G, Brady MJ, Hernandez L, Cella D. Measuring spiritual well-being in people with cancer: the functional assessment of chronic illness therapy--Spiritual Well-being Scale (FACIT-Sp). Annals of behavioral medicine : a publication of the Society of Behavioral Medicine. 2002; 24(1):49–58. [PubMed: 12008794]
29. Canada AL, Murphy PE, Fitchett G, Peterman AH, Schover LR. A 3-factor model for the FACIT-Sp. Psycho-oncology. 2008; 17(9):908–916. DOI: 10.1002/pon.1307 [PubMed: 18095260]
30. Cella D, Hahn EA, Dineen K. Meaningful change in cancer-specific quality of life scores: differences between improvement and worsening. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2002; 11(3):207–221.
31. Pinheiro LC, Samuel CA, Reeder-Hayes KE, Wheeler SB, Olshan AF, Reeve BB. Understanding racial differences in health-related quality of life in a population-based cohort of breast cancer survivors. Breast cancer research and treatment. 2016; 159(3):535–543. DOI: 10.1007/s10549-016-3965-y [PubMed: 27585477]
32. Fraley C, Raftery A. Model-based Methods of Classification: Using the mclust Software in Chemometrics. Journal of Statistical Software. 2007; 18(6)
33. Kenzik KM, Martin MY, Fouad MN, Pisu M. Health-related quality of life in lung cancer survivors: Latent class and latent transition analysis. Cancer. 2015; 121(9):1520–1528. DOI: 10.1002/cncr.29232 [PubMed: 25565326]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

34. ALM. Latent Class Analysis. Sage Publications; Beverly Hills, CA: 1987.
35. Collins, LML., ST. Latent Class and Latent Transition Analysis With Applications in the Social, Behavioral and Health Sciences. John Wiley & Sons, Inc; Hoboken, NJ: 2010.
36. Tein JCS, Cham H. Statistical Power to Detect the Correct Number of Classes in Latent Profile Analysis. Structural Equation Modeling: A Multidisciplinary Journal. 2013; 20(4):640–657. [PubMed: 24489457]
37. Gibson W. Three multivariate models: Factor analysis, latent structure analysis, and latent profile analysis. Psychometrika. 1959; 24(3):229–252.
38. Harper D. Local dependence latent structure models. Psychometrika. 1972; (37):53–59.
39. Hagenaars J. Latent structure models with direct effects between indicators—local dependence models. Sociological Methods & Research. 1988; (16):379–405.
40. Lanza ST, Patrick ME, Maggs JL. Latent Transition Analysis: Benefits of a Latent Variable Approach to Modeling Transitions in Substance Use. J Drug Issues. 2010; 40(1):93–120. [PubMed: 20672019]
41. Vermunt J. Latent Class Modeling with Covariates: Two improved three-step approaches. Political Analysis. 2010; (18):450–469.
42. Yamaguchi K. Multinomial logit latent-class regression models: An analysis of the predictors of gender-role attitudes among Japanese women. American Journal of Sociology. 2000; (105):1702–1740.
43. Ferrell BR, Grant M, Funk B, Garcia N, Otis-Green S, Schaffner ML. Quality of life in breast cancer. Cancer Pract. 1996; 4(6):331–340. [PubMed: 9128486]
44. Kim HJ, Abraham I, Malone PS. Analytical methods and issues for symptom cluster research in oncology. Current opinion in supportive and palliative care. 2013; 7(1):45–53. DOI: 10.1097/SPC.0b013e32835bf28b [PubMed: 23196378]
45. Gotay CC, Kawamoto CT, Bottomley A, Efficace F. The prognostic significance of patient-reported outcomes in cancer clinical trials. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2008; 26(8):1355–1363. DOI: 10.1200/jco.2007.13.3439 [PubMed: 18227528]
46. Hershman DL, Kushi LH, Hillyer GC, Coromilas E, Buono D, Lamerato L, Bovbjerg DH, Mandelblatt JS, Tsai WY, Zhong X, Jacobson JS, Wright JD, Neugut AI. Psychosocial factors related to non-persistence with adjuvant endocrine therapy among women with breast cancer: the Breast Cancer Quality of Care Study (BQUAL). Breast cancer research and treatment. 2016; doi: 10.1007/s10549-016-3788-x
47. Higginson IJ, Carr AJ. Measuring quality of life: Using quality of life measures in the clinical setting. BMJ (Clinical research ed). 2001; 322(7297):1297–1300.
48. Velikova G, Booth L, Smith AB, Brown PM, Lynch P, Brown JM, Selby PJ. Measuring quality of life in routine oncology practice improves communication and patient well-being: a randomized controlled trial. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2004; 22(4):714–724. DOI: 10.1200/jco.2004.06.078 [PubMed: 14966096]
49. Hibbard JH, Greene J. What the evidence shows about patient activation: better health outcomes and care experiences; fewer data on costs. Health affairs (Project Hope). 2013; 32(2):207–214. DOI: 10.1377/hlthaff.2012.1061 [PubMed: 23381511]
50. Detmar SB, Muller MJ, Schornagel JH, Wever LD, Aaronson NK. Health-related quality-of-life assessments and patient-physician communication: a randomized controlled trial. JAMA : the journal of the American Medical Association. 2002; 288(23):3027–3034. [PubMed: 12479768]
51. Jensen RE, Snyder CF, Abernethy AP, Basch E, Potosky AL, Roberts AC, Loeffler DR, Reeve BB. Review of Electronic Patient-Reported Outcomes Systems Used in Cancer Clinical Care. Journal of oncology practice /American Society of Clinical Oncology. 2013; doi: 10.1200/jop.2013.001067
52. Glasgow RE, Kaplan RM, Ockene JK, Fisher EB, Emmons KM. Patient-reported measures of psychosocial issues and health behavior should be added to electronic health records. Health affairs (Project Hope). 2012; 31(3):497–504. DOI: 10.1377/hlthaff.2010.1295 [PubMed: 22392660]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

53. Brucker PS, Yost K, Cashy J, Webster K, Cella D. General population and cancer patient norms for the Functional Assessment of Cancer Therapy-General (FACT-G). Eval Health Prof. 2005; 28(2): 192–211. DOI: 10.1177/0163278705275341 [PubMed: 15851773]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

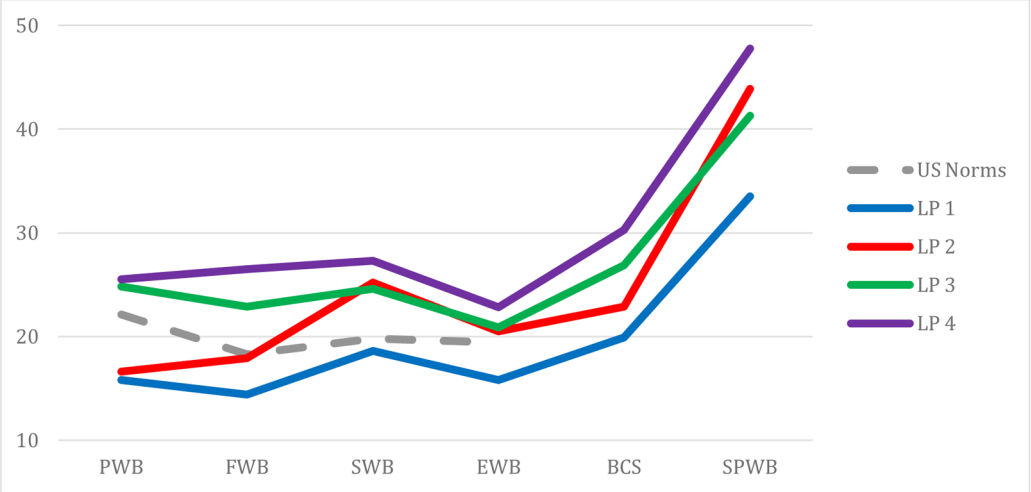

Figure 1.

Mean HRQOL Scores by 5-month Latent Profiles

Note: Mean HRQOL domains by latent profile (LP) are presented above. PWB (Physical Well-Being), SWB (Social Well-Being), EWB (Emotional Well-Being), FWB (Functional Well-Being), BCC (Breast Cancer Specific Concerns), SPWB (Spiritual Well-Being). Normed US scores are only available for Physical, Social, Functional and Emotional FACT-B domains and come from Brucker et al [53].

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

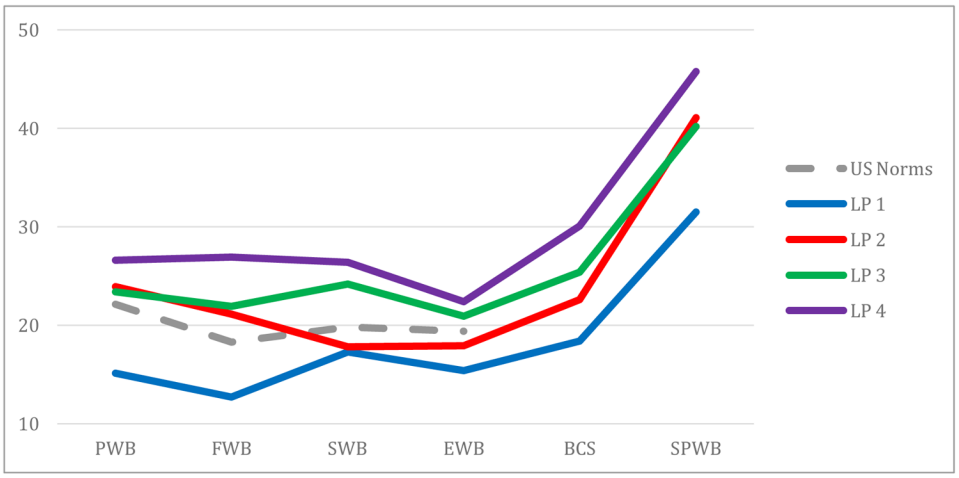

Figure 2.

Mean HRQOL Scores by 25-month Latent Profiles

Note: Mean HRQOL domains by latent profile (LP) are presented above. PWB (Physical Well-Being), SWB (Social Well-Being), EWB (Emotional Well-Being), FWB (Functional Well-Being), BCC (Breast Cancer Specific Concerns), SPWB (Spiritual Well-Being) Normed US scores are only available for Physical, Social, Functional and Emotional FACT-B domains and come from Brucker et al [53].

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 1

Cohort Characteristics collected at 5-months post-diagnosis

	Total Cohort	
	N=2,142	%
Age at diagnosis•		
<35 years	79	4%
35–50 years	922	43%
50–64 years	745	35%
65+ years	396	18%
Race•		
White	1105	52%
Black	1037	48%
Smoking status•		
Never	1200	56%
Former	577	27%
Current	365	17%
Marital status•		
Not married	899	42%
Married	1243	58%
Education level•		
<HS	166	8%
HS & Post HS	1108	52%
College+	868	41%
Insurance status•		
None	108	5%
Private	1535	72%
Public	499	23%
Diabetes•	322	15%
COPD•	53	2%
Heart Disease•	106	5%
Obesity•	1023	48%
Hypertension•	969	45%
Surgery•		
Not specified	17	1%
Lumpectomy	1405	66%
Mastectomy	720	34%
Chemo•	1336	62%
Radiation	1570	73%
Herceptin•	308	14%
Stage•		
I	936	44%
II	837	39%

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

	Total Cohort	
	N=2,142	%
III	256	12%
HR positive	1599	75%
HER 2 positive	336	16%

Note: HS (High School), HR (Hormone receptor), COPD (Chronic Obstructive Pulmonary Disease)

" indicates variables that were include in multivariable models.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 2

Unadjusted Latent Profile Transitions from 5- to 25-months

5-months	25-months			
	LP 1 (N=554)	**LP 2 (252)**	**LP 3 (N=799)**	**LP 4 (N=537)**
LP 1 (N=682)	356 (52%)	114 (17%)	166 (24%)	46 (7%)
LP 2 (N=617)	137 (22%)	65 (11%)	289 (47%)	126 (20%)
LP3 (N=606)	49 (8%)	59 (10%)	288 (47%)	210 (35%)
LP 4 (N=237)	12 (5%)	14 (6%)	56 (24%)	155 (65%)

Note: LP (Latent profiles). The table above displays row percentages. Row 1 shows the number and percent of women who were in LP 1 at 5-months and who remained in LP 1 at 25-months, who transitioned to LP 2, LP 3 and LP 4.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 3

Factors Associated with 5-Month HRQOL Latent Profile Membership

	LP 1		LP 2		LP 3	
	aOR	**95% CI**	**aOR**	**95% CI**	**aOR**	**95% CI**
Race (ref=white)						
Black	0.52	(0.35–0.75)***	1.09	(0.74–1.62)	0.28	(0.18–0.43)***
Age at diagnosis (years)	0.95	(0.93–0.96)***	0.98	(0.96–0.99)*	0.98	(0.96–1.0)
Smoking status (ref=never)						
Former/Current	1.41	(1.10–1.81)**	1.25	(0.97–1.62)	1.09	(0.82–1.45)
Marital status (ref=not married)						
Married	0.50	(0.35–0.72)***	0.71	(0.48–1.03)	1.01	(0.56–1.78)
Education level (ref=<HS)						
>HS, College	0.50	(0.78–1.43)	1.00	(0.73–1.36)	2.15	(1.49–3.09)***
Insurance status (ref=private)						
Public	3.09	(1.96–4.83)***	1.32	(0.81–2.12)	1.35	(0.78–2.34)
Uninsured	6.51	(2.12–20.1)***	2.17	(0.66–7.15)	2.59	(0.64–10.43)
COPD (ref=no)	267.68	(147.61–485.44)***	330.4	(170.71–639.46)	64.91	(23.95–175.91)***
Obesity (ref=no)	1.43	(0.99–2.05)	1.80	(1.24–2.60)***	0.84	(0.56–1.28)
Chemotherapy (ref=no)	1.85	(1.22–2.81)***	4.92	(3.13–7.74)***	0.54	(0.34–0.88)**

Note: Latent Profile (LP) 4 was used as the reference category. Models also included prevalence of diabetes, heart disease, obesity, hypertension, receipt of surgery, radiation, and Herceptin, tumor stage and grade. aOR (adjusted odds ratio), 95% CI (95% confidence interval). Statistical significance is denoted as:

* <0.05,

** <0.01,

*** <0.001

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 4

Factors Associated with 25-Month HRQOL Latent Profile Membership

	LP 1		LP 2		LP 3	
	aOR	**95% CI**	**aOR**	**95% CI**	**aOR**	**95% CI**
Race (ref=white)						
Black	1.75	(1.18–2.60)**	1.03	(0.71–1.47)	0.47	(0.32–0.69)***
Age at diagnosis (years)	0.98	(0.96–1.00)	0.95	(0.93–0.97)***	0.98	(0.96–0.99)*
Smoking status (ref=never)						
Former/Current	1.39	(1.06–1.82)*	1.89	(1.49–2.42)***	1.23	(0.96–1.60)
Marital status (ref=not married)						
Married	1.02	(0.69–1.50)	0.65	(0.46–0.92)*	0.88	(0.61–1.28)
Education level (ref=<HS)						
>HS	1.17	(0.85–1.60)	0.88	(0.65–1.17)	1.78	(1.30–2.44)***
Insurance status (ref=private)						
Public	1.29	(0.80–2.11)	2.79	(1.81–4.33)***	1.06	(0.64–1.78)
Uninsured	3.11	(0.94–10.27)	4.77	(1.53–14.82)**	2.04	(0.55–7.51)
COPD (ref=no)	142.52	(78.84–257.65)***	189.62	(118.23–304.10)***	95.24	(48.62–185.55)***
Heart disease (ref=no)	3.45	(1.24—9.61)*	3.42	(1.27–9.19)*	1.85	(0.59–5.86)
Obesity (ref=no)	2.16	(1.49–3.15)***	1.94	(1.37–2.74)***	0.96	(0.66–1.38)
Chemo (ref=no)	1.92	(1.21–3.05)**	1.76	(1.15–2.69)**	0.93	(0.60–1.45)
Stage 2/3 (ref=Stage 1)	1.45	(1.07–1.97)*	1.34	(1.01–1.78)*	1.12	(0.83–1.53)

Note: Latent Profile (LP) 4 was used as the reference category. Models also included prevalence of diabetes, hypertension, receipt of surgery, radiation and Herceptin, and tumor grade. aOR (adjusted odds ratio), 95% CI (95% confidence interval). Statistical significance is denoted as:

* <0.05,

** <0.01,

*** <0.001