EXAMINING THE MULTILEVEL INFLUENCES ON DIABETES AND HYPERTENSION CLINICAL CARE MANAGEMENT AMONG BREAST CANCER PATIENTS

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ABSTRACT OF THE DISSERTATION

Examining the Multilevel Influences on Diabetes and Hypertension Clinical Care Management among Breast Cancer Patients

By MICHELLE DOOSE

Dissertation Directors:

Elisa V. Bandera, MD, PhD and Jennifer Tsui, PhD, MPH

Background: Cancer, type 2 diabetes mellitus, and hypertension are important public health issues for women in the United States given their significant disease burden and impact on mortality. Yet, clinical care management of chronic health conditions before and after a breast cancer diagnosis has not been well evaluated, especially among African American women who disproportionately bear the burden of these chronic illnesses. **Specific Aims:** The specific aims of this dissertation were to evaluate the influence of a breast cancer diagnosis on diabetes and hypertension clinical care management (Chapter 1) and then examine patient (Chapter 1), provider (Chapter 2), and health system (Chapter 3) factors associated with clinical care management and health outcomes after the breast cancer diagnosis. **Methods:** This study included African American women who participated in the Women's Circle of Health Follow-Up Study (WCHFS), an ongoing population-based prospective cohort of breast cancer survivors recruited from ten counties in New Jersey. Women with diabetes and/or hypertension for at least one year prior to the breast

cancer diagnosis (2012-2016) were included in this analytic sample (N=274). The likelihood of receiving all clinical care management measures and achieving all health outcomes after breast cancer diagnosis were compared by patient, provider, and health system factors using binomial regression models. **Results:** The prevalence of diabetes and hypertension diagnosed at least one year prior to the breast cancer diagnosis was 18% and 47%. Less than half (41%) of the participants had all key clinical care management measures met and only 15% reached all key health outcomes after breast cancer diagnosis. Patients who did not have optimal management *before* diagnosis were 29% less likely to have optimal management *after* breast cancer diagnosis (aRR: 0.71; 95% CI: 0.53, 0.95). Participants with shared care (i.e., cancer specialist, primary care provider, and/or medical specialist involved in patient care) were five times more likely to have all clinical care measures met compared with participants who only saw cancer specialists (aRR: 5.07; 95% CI: 1.47, 17.51). Patient and provider factors were not associated with optimal health outcomes. Participants who did not receive both primary care and cancer care within the same health system were 27% less likely to have all clinical care measures met compared with those participants who sought care at the same health system (aRR: 0.73; 95% CI: 0.56, 0.97). Accreditation of cancer program was not associated with having all clinical care measures met (aRR: 0.92; 95% CI: 0.59, 1.45). **Conclusion:** Findings from these studies can be used to identify gaps in care delivery, improve chronic disease management guidelines for breast cancer patients with comorbidities, and address health equity for African American women with

multimorbidities. Future work is needed from a multilevel perspective – health policy, health system, organizational/practice settings, providers/medical teams, and patient level factors – to improve the delivery of care and ultimately impact health outcomes.

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Chapter 2

INTRODUCTION

Cancer, type 2 diabetes mellitus (referred to as diabetes), and hypertension are important public health issues for women in the United States given their significant disease burden and impact on mortality.[1,2] Breast cancer is the most common cancer diagnosis and the second leading cause of cancer death for women.[3] The prevalence of having a chronic condition (i.e., comorbidity) at cancer diagnosis is approximately 32% for the general breast cancer population.[4-6] Two of the most common comorbidities that affect this population are diabetes (affecting 16–20% of women with cancer) and hypertension (32%).[7-10]

Women with a co-occurring health condition at breast cancer diagnosis are more likely to be African American and to be diagnosed with advanced stage breast cancer.[9,11-15] This may be due to the fact that the prevalence of diabetes and hypertension in the U.S. population is higher among African American women (13% and 40%, respectively) compared with non-Hispanic White (NHW) women (7% and 26%, respectively).[16,17] Comprehensive disease management can lead to better health outcomes.[18,19] However, African American women have historically received less clinical care management and treatment for chronic illnesses.[20-22] Consequentially, African American women with comorbidities have higher mortality rates for all-causes including for breast cancer.[8,23-26] The most recent data from the Centers for Disease Control and Prevention (2017) show that compared with White women, African American women were 2.25 times more likely to die from diabetes (age adjusted death rate was 32.9 per 100,000

for African American women and 14.6 per 100,000 for NHW women), 2.03 times more likely to die from cardiovascular disease (age adjusted death rate was 37.8 per 100,000 for African American women and 18.6 per 100,000 for NHW women), and 1.41 times more likely to die from breast cancer (age adjusted death rate was 28.5 per 100,000 for African American women and 20.3 per 100,000 for NHW women).[27,28]

Having a comorbidity may account for half of the Black-White breast cancer survival disparity.[8] Specifically, Braithwaite et al. found that hypertension may account for a third of the racial disparity in survival rates.[8] Women diagnosed with early stage breast cancer are also more likely to die from other health causes, such as cardiovascular disease, than the breast cancer itself.[5,29-31] Therefore, it is imperative that disease management continue to be delivered throughout the patient's breast cancer treatment in order to prevent disease-specific mortality and to reduce disparities in breast cancer mortality.

The context of where and who delivers care also matters. It is important to recognize the multilevel systems that influence clinical care management either directly or indirectly. For example, breast cancer patients who had their primary care physician involved during cancer care experienced lower all-cause mortality and cancer-specific mortality.[32] Another study found that hospital factors (i.e., hospital patient volume, hospital racial mix) explained 26% of the excess overall mortality experienced by African American women with breast cancer compared with NHW women.[33]

Therefore, we used the Taplin's Quality of Cancer Care Model, Anderson's Behavioral Model of Health Services Utilization, and the Donabedian Quality-of-Care Model as a conceptual framework to guide this dissertation research (Appendix I).[34-37] From a health system perspective, organizational structures, delivery system design, clinical information systems (i.e., interoperable electronic medical records), and accreditations can influence the way care is delivered. From a provider/medical team perspective, co-managing both cancer and chronic health conditions require a coordinated care team (including oncologist, primary care physician, medical specialists, social workers, navigators, etc.), communication and coordination of care, and sharing of medical records. Lastly, from a patient's perspective, education, income, insurance status, and disease severity can affect the delivery and receipt of clinical care in the context of a breast cancer diagnosis. However, missing from the literature is a broader picture of how comorbidities are being managed for African American women with breast cancer, who share a disproportionate burden of diabetes and hypertension morbidity and mortality.[27]

By understanding the multilevel influences on diabetes and hypertension clinical care management during breast cancer care, targeted multilevel interventions in cancer care delivery can be developed and implemented. Improving care coordination across multiple cancer and non-cancer care settings is timely and necessary for the growing number of cancer patients with complex health and social needs. Cancer care and comorbid care will only become more complex and costly with the advent of precision medicine. The moral imperative

remains to eliminate racial disparities in health care that drive lower-quality care in order that African American women may achieve their best health during and after breast cancer.

REFERENCES

1. Centers for Disease Control and Prevention. Leading Causes of Death by Race/Ethnicity, All Females-United States, 2015. 2015; https://www.cdc.gov/women/lcod/2015/race-ethnicity/index.htm.
2. DeSantis CE, Miller KD, Goding Sauer A, Jemal A, Siegel RL. Cancer Statistics for African Americans, 2019. *CA Cancer J Clin.* 2019.
3. American Cancer Society. *Breast Cancer Facts & Figures 2017-2018.* Atlanta, GA: American Cancer Society;2017.
4. Snyder CF, Frick KD, Herbert RJ, et al. Comorbid Condition Care Quality in Cancer Survivors: Role of Primary Care and Specialty Providers and Care Coordination. *J Cancer Surviv.* 2015; 9(4): 641-9.
5. Edwards BK, Noone A-M, Mariotto AB, et al. Annual Report to the Nation on the Status of Cancer, 1975-2010, Featuring Prevalence of Comorbidity and Impact on Survival among Persons with Lung, Colorectal, Breast or Prostate Cancer. *Cancer.* 2014; 120(9): 1290-314.
6. Yabroff KR, Dowling E, Rodriguez J, et al. The Medical Expenditure Panel Survey (Meps) Experiences with Cancer Survivorship Supplement. *J Cancer Surviv.* 2012; 6(4): 407-19.
7. Srokowski TP, Fang S, Hortobagyi GN, Giordano SH. Impact of Diabetes Mellitus on Complications and Outcomes of Adjuvant Chemotherapy in Older Patients with Breast Cancer. *J Clin Oncol.* 2009; 27(13): 2170-6.
8. Tammemagi C, Nerenz D, Neslund-Dudas C, Feldkamp C, Nathanson D. Comorbidity and Survival Disparities among Black and White Patients with Breast Cancer. *JAMA.* 2005; 294(14): 1765-72.
9. Lipscombe LL, Fischer HD, Austin PC, et al. The Association between Diabetes and Breast Cancer Stage at Diagnosis: A Population-Based Study. *Breast Cancer Res Treat.* 2015; 150(3): 613-20.
10. Wolf I, Sadetzki S, Catane R, Karasik A, Kaufman B. Diabetes Mellitus and Breast Cancer. *Lancet Oncol.* 2005; 6(2): 103-11.
11. Deckelbaum RJ, Williams CL. Childhood Obesity: The Health Issue. *Obes Res.* 2001; 9 Suppl 4: 239s-43s.
12. Spanakis EK, Golden SH. Race/Ethnic Difference in Diabetes and Diabetic Complications. *Current diabetes reports.* 2013; 13(6): 10.1007/s11892-013-0421-9.
13. Boyle P, Boniol M, Koechlin A, et al. Diabetes and Breast Cancer Risk: A Meta-Analysis. *Br J Cancer.* 2012; 107(9): 1608-17.
14. Han H, Guo W, Shi W, et al. Hypertension and Breast Cancer Risk: A Systematic Review and Meta-Analysis. *Scientific Reports.* 2017; 7: 44877.
15. Stark Casagrande S, Cowie CC. Health Insurance Coverage among People with and without Diabetes in the U.S. Adult Population. *Diabetes Care.* 2012; 35(11): 2243-9.
16. Centers for Disease Control and Prevention. *National Diabetes Statistics Report, 2017: Estimates of Diabetes and Its Burden in the United States.* Atlanta, GA: U.S. Department of Health and Human Services;2017

17. Fryar C, Ostchega Y, Hales C, Zhang G, Kruszon-Moran D. *Hypertension Prevalence and Control among Adults: United States, 2015–2016.* National Center for Health Statistics Centers for Disease Control and Prevention;2017.
18. Wagner EH. Chronic Disease Management: What Will It Take to Improve Care for Chronic Illness? *Eff Clin Pract.* 1998; 1(1): 2-4.
19. Reddy SS. Health Outcomes in Type 2 Diabetes. *Int J Clin Pract Suppl.* 2000; (113): 46-53.
20. Belgrave FZ, Abrams JA. Reducing Disparities and Achieving Equity in African American Women's Health. *Am Psychol.* 2016; 71(8): 723-33.
21. Institute of Medicine Committee on Understanding and Eliminating Racial and Ethnic Disparities in Health Care. *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care.* Washington, DC: National Academies Press; 2003.
22. Chou AF, Brown AF, Jensen RE, Shih S, Pawlson G, Scholle SH. Gender and Racial Disparities in the Management of Diabetes Mellitus among Medicare Patients. *Womens Health Issues.* 2007; 17(3): 150-61.
23. Charlot M, Castro-Webb N, Bethea TN, et al. Diabetes and Breast Cancer Mortality in Black Women. *Cancer Causes Control.* 2017; 28(1): 61-7.
24. Peairs KS, Barone BB, Snyder CF, et al. Diabetes Mellitus and Breast Cancer Outcomes: A Systematic Review and Meta-Analysis. *J Clin Oncol.* 2011; 29(1): 40-6.
25. Gold HT, Makarem N, Nicholson JM, Parekh N. Treatment and Outcomes in Diabetic Breast Cancer Patients. *Breast Cancer Res Treat.* 2014; 143(3): 551-70.
26. Luo J, Virnig B, Hendryx M, et al. Diabetes, Diabetes Treatment and Breast Cancer Prognosis. *Breast Cancer Res Treat.* 2014; 148(1): 153-62.
27. Centers for Disease Control and Prevention. Cdc Wide-Ranging Online Data for Epidemiologic Research (Cdc Wonder). 2018; https://wonder.cdc.gov/. Accessed March 14, 2019.
28. American Cancer Society. *Cancer Facts & Figures for African Americans 2019-2021.* Atlanta, GA: American Cancer Society;2019.
29. Riihimäki M, Thomsen H, Brandt A, Sundquist J, Hemminki K. Death Causes in Breast Cancer Patients. *Ann Oncol.* 2012; 23(3): 604-10.
30. Chapman JA, Meng D, Shepherd L, et al. Competing Causes of Death from a Randomized Trial of Extended Adjuvant Endocrine Therapy for Breast Cancer. *J Natl Cancer Inst.* 2008; 100(4): 252-60.
31. Park NJ, Chang Y, Bender C, et al. Cardiovascular Disease and Mortality after Breast Cancer in Postmenopausal Women: Results from the Women's Health Initiative. *PLoS One.* 2017; 12(9): e0184174.
32. Roetzheim RG, Ferrante JM, Lee JH, et al. Influence of Primary Care on Breast Cancer Outcomes among Medicare Beneficiaries. *Ann Fam Med.* 2012; 10(5): 401-11.
33. Breslin TM, Morris AM, Gu N, et al. Hospital Factors and Racial Disparities in Mortality after Surgery for Breast and Colon Cancer. *J Clin Oncol.* 2009; 27(24): 3945-50.

34. Andersen RM. Revisiting the Behavioral Model and Access to Medical Care: Does It Matter? *J Health Soc Behav.* 1995; 36(1): 1-10.
35. Taplin SH, Anhang Price R, Edwards HM, et al. Introduction: Understanding and Influencing Multilevel Factors across the Cancer Care Continuum. *J Natl Cancer Inst Monogr.* 2012; 2012(44): 2-10.
36. Zapka JG, Taplin SH, Solberg LI, Manos MM. A Framework for Improving the Quality of Cancer Care. *Cancer Epidemiol Biomarkers Prev.* 2003; 12(1): 4.
37. Donabedian A. Evaluating the Quality of Medical Care. *Milbank Mem Fund Q.* 1966; 44(3): Suppl:166-206.

EXAMINING DIABETES AND HYPERTENSION CLINICAL CARE MANAGEMENT AMONG AFRICAN AMERICAN BREAST CANCER PATIENTS

By

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ABSTRACT OF CHAPTER 1 OF 3

Examining Diabetes and Hypertension Clinical Care Management among African American Breast Cancer Patients

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Background: Diabetes and hypertension are two of the most common comorbidities that affect the breast cancer population. Yet, clinical care management of chronic health conditions before and during cancer treatment has not been well evaluated. **Objective:** The aims of this study was to 1) evaluate the influence of a breast cancer diagnosis on diabetes and hypertension clinical care management, and 2) examine patient factors associated with clinical care management and health outcomes after the breast cancer diagnosis. **Methods:** African American women were enrolled in the Women's Circle of Health Follow-Up Study, a population-based prospective cohort of breast cancer survivors recruited from ten counties in New Jersey. Women with diabetes and/or hypertension for at least one year prior to breast cancer diagnosis were included in this analytic sample (N=274). Clinical care management measures and health outcomes were reported before and after breast cancer diagnosis and were compared using McNemar's tests. The likelihood of receiving all clinical care management measures, and the likelihood of achieving all health outcomes, after

a breast cancer diagnosis were compared by patient factors using binomial regression models. **Results:** Less than half (41%) of this population reached all key clinical care management indicators after breast cancer diagnosis: for patients with diabetes, an HbA1c test was ordered for 83% of the population, an LDL-cholesterol test was ordered for 78%, and medical attention for nephropathy was ordered for 71%; and for patients with hypertension, a lipid screen was ordered for 50% of the population, and a prescription for hypertension medication was given for 52%. Only 15% of the total population reached all key health outcomes after diagnosis: for patients with diabetes, 46% achieved an optimal HbA1c level (< 8%), 37% achieved an optimal LDL-cholesterol level (<100 mg/dL), and 60% achieved an optimal blood pressure level (< 140/90 mmHg); and for patients with hypertension, 20% achieved an optimal LDL-cholesterol level (<100 mg/dL), and 73% achieved an optimal blood pressure level (< 140/90 mmHg). Patients who did not have optimal management *before* diagnosis were 29% less likely to have care measures met *after* breast cancer diagnosis (RR: 0.71; 95% CI: 0.53, 0.95). We found that patient-level factors were not associated with health outcomes. **Conclusions:** Diabetes and hypertension unequally burden African American breast cancer patients. Gaps in care delivery were observed and illustrate the need for improved disease management for breast cancer patients with comorbidities.

EXAMINING DIABETES AND HYPERTENSION CLINICAL CARE MANAGEMENT AMONG AFRICAN AMERICAN BREAST CANCER PATIENTS

INTRODUCTION

Disruption of usual diabetes and hypertension clinical care management at breast cancer diagnosis has been speculated, but not well evaluated. Comprehensive disease management can lead to better health outcomes and lower health care utilization and cost.[1,2] Only one study conducted among Medicare breast and colorectal cancer patients with diabetes found that diabetes clinical care management worsened after the cancer diagnosis.[3] Research is sparse in chronic disease management of co-occurring health conditions (i.e., comorbidities) during breast cancer. Such research is needed to address the complex health needs of the growing population of breast cancer patients with chronic diseases who are more likely to die from their chronic disease than breast cancer itself.[4] This is particularly important for African American women who historically receive less clinical care and treatment for chronic diseases and disproportionally share the burden of comorbidities, including diabetes, hypertension, and breast cancer.[5-9]

Diabetes and Breast Cancer

Diabetes is the seventh leading cause of death for U.S. women and the fourth leading cause of death for African American women.[10] The prevalence of diabetes in the general U.S. population is higher among African American

women (13%) compared with their non-Hispanic White (NHW) counterparts (7%).[11] Likewise, African Americans are also more likely to experience diabetes-related complications (e.g., lower-extremity amputations, end stage renal disease, hospitalizations) and experience risk factors for diabetes (e.g., obesity, less physical activity).[12,13] Compared to NHW and privately insured diabetic patients, both African Americans and Medicaid enrollees are also less likely to report having received diabetes-related care.[14,15]

Having diabetes at breast cancer diagnosis increases the risk for infection, hospitalization, poor physical function, and mortality.[16-19] Although there are no specific guidelines for the management of diabetes during breast cancer, there are well-established, evidence-based clinical guidelines for the management of diabetes for the general non-cancer population. Recommendations include: glycated hemoglobin (HbA1c) test every 6-months and annual low-density lipoprotein-cholesterol (LDL-C) test, dilated retinal exam, sensory foot exam, and medical attention for nephropathy (microalbuminuria test, documentation of treatment for nephropathy, or patient receiving angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) therapy).[20,21] Adherence to guideline-recommended diabetes clinical care management is associated with improved patient outcomes and preventable complications (i.e., retinopathy, cardiovascular disease, microvascular events, mortality).[22] However, African Americans are less likely to have access to diabetes-related preventive screenings (i.e., retinal exam and foot exam).[13]

Keating et al. evaluated the quality of diabetes care and clinical outcomes among cancer survivors who were diagnosed with diabetes after cancer,

compared with non-cancer patients with diabetes.[23] They found that 66% of cancer survivors received HbA1c testing and 73% reached optimal HbA1c control, which were statistically better than non-cancer controls. The non-cancer controls had 64% HbA1c testing and 71% HbA1c control. LDL-C testing (84%), retinal examination (67%), and blood pressure control (31%) did not differ by cancer status. Bayliss et al. found that HbA1c levels did not change over time among diabetic patients who later developed cancer.[24] Yao et al. found that diabetes care measures of the rates of HbA1c testing, LDL-C testing, and retinal exams decreased during cancer treatment (58%, 70%, 56%) compared to the one-year period prior to diagnosis (73%, 80%, and 58%) among Medicare breast or colorectal cancer (CRC) patients.[3] Among CRC patients within a single Veteran's Administration hospital system, diabetes care measures and outcomes were high and did not differ before and after the cancer diagnosis.[25] However, none of these studies focused on African American women.

Hypertension and Breast Cancer

Cardiovascular disease (CVD) is the leading cause of death for women in the United States (followed by cancer), with hypertension being the most common risk factor for CVD.[10] Control of blood pressure and LDL-C can decrease the risk of CVD morbidity and mortality.[26] The prevalence of hypertension is higher in African American women (40%) compared with White women (26%).[27] The incidence of and death from CVD is higher for older breast cancer survivors than is recurrence and mortality from breast cancer.[28] Unfortunately, having hypertension at breast cancer diagnosis increases the risk

for cardiac events and related deaths; this is due to treatment toxicities associated with chemotherapy, radiation, and monoclonal therapy.[28,29] Compared with NHW women, African American women at all ages are more likely to die from breast cancer and CVD.[28] Hypertension and hyperlipidemia, which are more prevalent among African Americans, are known risk factors for anthracycline cardiotoxicity.[30-32] Unfortunately, there remains a paucity of research and clinical guidelines that recommend optimal surveillance of CVD and cardiotoxicity from breast cancer treatment.[32] To prevent CVD and to treat hypertension, as well as to maintain an optimal LDL-C level, the gold standard remains pharmacological intervention.[33,34]

Adherence to guideline-recommended hypertension medication is associated with improved health outcomes, preventable hospitalizations, and lower overall medical cost.[35-38] Several studies have evaluated hypertension medication adherence among breast cancer patients in the Medicare population, at a single integrated health system, and with employee-based insurance.[3,25,39-41] Non-adherence to hypertension medications ranged from 17% to 37% and declined by 26% post-cancer diagnosis among patients with private insurance. Significant predictors of non-adherence to hypertension medications were found to be older age and having multiple chronic health conditions.[41]

There are no specific guidelines for the management of hypertension during breast cancer; however, there are clinical guidelines for the management of hypertension for the general population.[33,42] Laboratory measurements, which are only required at the time of a new diagnosis of hypertension, are: fasting blood glucose, complete blood count and lipid panel, serum creatinine with

estimated glomerular filtration rate, serum sodium, potassium, and calcium, thyroid-stimulating hormone urinalysis, and electrocardiogram.[43] However, the U.S. Preventive Services Task Force (USPSTF) and the Canadian Cardiovascular Society recommend as part of a cardiovascular risk assessment: blood glucose screening in adults aged 40–70 years and lipid disorder screening in adults older than 20.[44-46] Clinical guidelines identify the optimal LDL-C level as 100 mg/dL, especially for women at higher CVD risk, but the optimal interval of testing remains uncertain.[47,48] Urine microalbumin has been shown to be a predictor of renal and CVD risk.[49]

In order to address the critical gaps in the literature, we used the Women's Circle of Health Follow-Up Study (WCHFS), a prospective, ongoing population-based cohort of African American women diagnosed with breast cancer, to:

1) Evaluate the influence of a breast cancer diagnosis on diabetes and hypertension clinical care management, and
2) Examine patient-level factors (e.g., age, socioeconomic status, cancer stage, chronic disease severity) associated with clinical care management and health outcomes.

We hypothesized that clinical care management of diabetes and hypertension will be lower for the one year *after* breast cancer diagnosis compared with the one year *before* the breast cancer diagnosis given the competing care demands of the breast cancer diagnosis.

MATERIALS AND METHODS

Data Source and Study Population

The WCHFS is an "ongoing longitudinal study of lifestyle, obesity, obesity-related comorbidities, and breast cancer outcomes among African American breast cancer survivors."[50] Participants include African American women in ten New Jersey counties newly diagnosed with non-invasive ductal carcinoma in situ (DCIS) or with invasive breast cancer. The study population for this analysis included women who consented after February 2014 to have their medical records requested from medical providers participating in comorbid care. Previously only medical records were requested from medical providers participating in breast cancer care. This study is ongoing and therefore our study population (N=563) only includes participants whose medical records were abstracted for breast cancer information through July 2018.

We restricted our study sample for analysis to breast cancer participants who had a clinical diagnosis of diabetes or hypertension at least 12 months prior to breast cancer diagnosis. A patient was considered to be diagnosed with diabetes when their medical records in the 12 months prior to diagnosis included physician documentation showing type 2 diabetes mellitus. Diabetes is diagnosed when an HbA1c test result of ≥ 6.5% occurs on two separate tests.[51] A patient was considered to be diagnosed with hypertension when their medical records included physician documentation showing hypertension in the 12 months prior to diagnosis. Hypertension is diagnosed when the systolic pressure is above 140 mmHg prior to 2017, or above 130 mmHg starting in 2017, or when the diastolic pressure is above 90 mmHg on two or more separate readings.[42]

Inclusion criteria in this analytical sample was: having primary, histologically confirmed DCIS or invasive breast cancer; having physician documentation of diabetes and/or hypertension for at least one year prior to the breast cancer diagnosis; and being 20–75 years old at breast cancer diagnosis. Exclusion criteria was: having Stage IV breast cancer, having a diabetes or hypertension diagnosis at or after breast cancer diagnosis; having died within one year of breast cancer diagnosis; or provider refused to send medical records.

Procedures

The study procedures have been described in detail elsewhere.[50,52-57] In brief, eligible participants were first identified through the New Jersey State Cancer Registry (NJSCR) using rapid case ascertainment methodology (i.e., cases identified via pathology report within two months of cancer diagnosis).[58] Then the NJSCR contacted eligible patients and obtained verbal consent from the patient to be contacted by the WCHFS research staff at the Rutgers Cancer Institute of New Jersey. Approximately 9 months after diagnosis, a face-to-face home interview (or at a mutually agreed upon location) is conducted with each participant by a highly trained WCHFS research team member to obtain written informed consent from those who agreed to participate in the study, including medical and pharmacy records releases. During the interview, trained staff administered questionnaires to obtain information about participant's personal history (e.g., education, annual household income, marital status) and medical history (e.g., age at diabetes/hypertension diagnosis, insulin use, smoking status) as well as collected biospecimens and anthropometric measurements via a

standardized protocol including height, weight, waist and hip circumferences, body composition (lean and fat mas), and blood pressure measurements.[59]

Consenting participants provided contact information for all providers who were involved in their breast cancer care and comorbid care one-year prior to their breast cancer diagnosis through the day they consented for medical release (i.e., 9–12 months following the diagnosis of breast cancer). Then the Medical Records Team at Rutgers School of Public Health requested medical records from surgical, medical, and radiation oncologists; primary care physicians (i.e., internal medicine, family medicine); medical specialists (i.e., endocrinologist, cardiologist, nephrologist, podiatrist, ophthalmologist, optometrist); and hospitals where surgeries and any treatments were performed. Specifically, requests were made on initial diagnostic information (breast surgery and biopsy reports), operating notes, pathology reports, and discharge summaries from hospitalization either for surgery or chemotherapy. Requests were also made for medical records for non-cancer related care.

Trained abstractors abstracted breast cancer information using a standard abstraction form for information on sociodemographic, medical history, diagnostic work up, breast cancer treatment as well as comorbidity types, severity, and date of onset. For example, for patients with diabetes, we specifically looked for the presence of eye, foot, heart, and kidney disease. For patients with hypertension, we looked for the presence of CVD, including congestive heart failure, myocardial infarction, angina, stroke, and coronary artery disease. For this analysis, two abstractors collected additional information related to clinical care management and health outcomes related to diabetes and hypertension. Data at

the visit level were abstracted, including: date of visit or test order, name of physician who ordered the test, facility name and location, type of test ordered, and result of test ordered. This study was approved by the Institutional Review Boards of all participating institutions and written informed consent was obtained from all study participants.

Outcome Measures

Diabetes Clinical Care Management Measures and Health Outcomes

The six diabetes clinical care management measures selected for this study are:

1) HbA1c testing,[60-64]
2) LDL-C testing,[60,62]
3) eye exam – retinal or dilated eye exam by an optometrist or ophthalmologist,[61,62,64]
4) foot exam – visual inspection, sensory exam with monofilament and pulse exam,[62,65]
5) medical attention for nephropathy – microalbuminuria test (i.e., urinary test for albumin), documentation of treatment for nephropathy (i.e., referral to nephrologist), or participant receiving angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) therapy,[60-62,66] and
6) prescription for hypertension medication – prescription for thiazide-type diuretic, calcium channel blocker (CCB), ACE inhibitor, or ARB.[33,42]

Prescription for hypertension medication only pertains to participants with both diabetes and hypertension. We chose not to create a separate category for participants with diabetes-only since there were only eight participants; therefore,

their data are included in the category “Participants with diabetes and hypertension.” Medical records were reviewed and abstracted for documentation of a medical provider ordering a test for HbA1c, LDL-C, eye, foot, or microalbuminuria and the results of such a test; referring patient to an optometrist or ophthalmologist for eye exam, to a podiatrist for foot exam, or to a nephrologist for treatment of kidney disease; and ordering or refilling an order for hypertension medication (see Appendix II).

All available health outcomes for HbA1c and LDL-C measures were averaged per participant for each measurement time period before and after breast cancer diagnosis. Blood pressure was collected at one time before diagnosis (i.e., last blood pressure measurement available in the medical record before primary surgery) and one time after diagnosis (i.e., average blood pressure readings at home interview conducted 9–12 months post breast cancer diagnosis). These measures are from well-established quality indicators of clinical care management from the Diabetes Quality Improvement Project (DQIP),[67] Health Plan Employer Data and Information Set (HEDIS) Comprehensive Diabetes Care,[61] American Diabetes Association,[68] National Committee for Quality Assurance,[69,70] Centers for Medicare and Medicaid Services (CMS) Accountable Care Organization diabetes measures,[71] and previous studies such as the Translating Research into Action for Diabetes (TRIAD) Study.[72]

Hypertension Clinical Care Management Measures and Health Outcomes

The four hypertension clinical care management measures selected for this study are:

1) lipid screening – high-density lipoprotein cholesterol (HDL-C), LDL-C, total cholesterol, and triglycerides,[45,46]
2) glucose screening – glucose or HbA1c test[44]
3) nephropathy screening – microalbuminuria test or referral to nephrologist[49]
4) prescription for hypertension medication – prescription for thiazide-type diuretic, CCB, ACE inhibitors, or ARB.[33,42]

Medical records were reviewed and abstracted for documentation of a physician ordering a lipid panel or a test for glucose, HbA1c, or microalbuminuria and the results of such panel or test; referring to nephrologist for treatment of kidney disease; and ordering or refilling an order for hypertension medication. All available LDL-C results were averaged per participant for each time period. Blood pressure and glucose results were collected at one time before diagnosis and one time after diagnosis.

These hypertension measures are based on the Seventh and Eighth Joint National Committee (JNC 7 and JNC 8), USPSTF, Canadian Cardiovascular Society, 2017 American Heart Association (AHA)/ American College of Cardiology (ACC) guidelines for the management of high blood pressure in adults, and HEDIS measure for controlling high blood pressure.[33,34,42,46,61,73] The USPSTF and Canadian Cardiovascular Society recommend blood glucose screening in adults aged 40–70 years and lipid disorder screening in adults older than 20 as part of cardiovascular risk assessment.[44-46] Screening for

microalbuminuria should be considered for hypertension patients, given that it is correlated with kidney function and cardiovascular outcomes.[49] JNC 8 and AHA/ACC recommend the initiation of pharmacologic treatment for African Americans, including patients with diabetes, to receive thiazide-type diuretic or calcium channel blocker.[33,74]

First, we examined item-by-item each of these diabetes and hypertension clinical care measures and health outcomes. Each clinical care management measure was considered met if there was at least one physician's order within the measurement period. Health outcomes were considered optimal when HbA1c < 8%, LDL-C < 100mg/dL, albumin-to-creatinine ratio (ACR) or microalbumin (MA) was normal (i.e., < 30), eye or foot exam was normal, and blood pressure level < 140/90 mmHg. Health outcome was considered not optimal when the test result was abnormal, a test was not ordered, or a test was ordered by the physician but was not done by the patient.

A binary composite measure was constructed using the "All-or-None" approach. For participants with diabetes, HbA1c testing, LDL-C testing, and medical attention for nephropathy were included in the "All-or-None" clinical care measure, and the HbA1c, LDL-C, and ACR or MA results were included for the "All-or-None" health outcome measure. For participants with hypertension only (and not diabetes), lipid screening and prescription for hypertension medication were included in the "All-or-None" clinical care measure, and the results of the LDL-C test and blood pressure were included for the "All-or-None" health outcome measure. If the patient was ordered all measures, then she was considered having met all clinical care measures. If the patient was not ordered

all measures, then she was considered not having met all clinical care measures. If all health outcomes were all optimal, then the patient was considered achieving all health outcomes. If the patient did not have all health outcomes as optimal, then she was not considered to have achieve all health outcomes.

Main Predictors

Time Periods

The clinical care management measures were compared at two time periods: the one-year period prior to the date of breast cancer diagnosis (i.e., date of biopsy), and the one-year period following the date of breast cancer diagnosis. The one-year measurement period has been used for several studies.[3,25] Many quality indicators use a one-year time period for which all processes of care measures should be delivered; however, finding an appropriate time to delineate one-year intervals is difficult. The breast cancer diagnosis allows us to apply the “episode of care” approach, where the person’s diabetes or hypertension care can be practically divided into two distinct time intervals.[75]

Patient-level factors

We abstracted patient-level factors, including sociodemographics, tumor characteristics, and clinical comorbidity characteristics from medical records and home interviews. We abstracted from medical records: health insurance status at breast cancer diagnosis, cancer stage, diabetes and hypertension disease

severity, and types of health conditions at or before breast cancer diagnosis. Mutually exclusive categories for disease severity for diabetes included:

- Category I: No complications
- Category II: Eye or foot disease, but no heart or kidney disease
- Category III: Diabetic heart or kidney disease
- Category IV: Diabetic heart and kidney disease

Categories for disease severity for hypertension included:

- Category I: No complications; without congestive heart failure (CHF) and diastolic blood pressure (DBP) < 100 mmHg or systolic blood pressure (SBP) < 160 mmHg
- Category II: Without CHF and DBP ≥ 100 mmHg or SBP ≥ 160 mmHg
- Category III: CHF and DBP ≥ 100 mmHg or SBP ≥ 160 mmHg

Then we created a variable for overall disease severity from diabetes and/or hypertension that dichotomized the highest severity as organ damage or no organ damage.

We obtained the following from home interviews: marital status, annual income, education, health insurance one year prior to breast cancer diagnosis, duration of diabetes and hypertension, insulin use, smoking status, and body mass index. If type of health insurance at diagnosis was not noted in medical records, then we used the health insurance status one year prior to breast cancer diagnosis from the home interview (i.e., assuming insurance status did not change over time). Primary health insurance was defined by the following four categories:

- Medicaid only or Medicaid in combination with Medicare
- Medicare only
- Private insurance only or coverage by the Veteran's Health Administration only, or in combination with Medicare
- No insurance, charity care, or unknown insurance type.

We used the Taplin's Quality of Cancer Care Model, Anderson's Behavioral Model of Health Services Utilization, and the Donabedian Quality-of-Care Model as a conceptual framework to inform the analytic framework (Appendix I).[76-79] For example, disease severity is a known confounder for disease management.[80] Type of insurance and having a usual source of medical care (e.g., care management before diagnosis) are predisposing and enabling factors for disease management. We explored these variables and accounted for them in the analyses. All missing data were coded as unknown.

Statistical Analysis

We generated summary statistics (means and standard deviations for continuous data, and counts and proportions for categorical data) to describe patient-level characteristics of the total population and characteristics by comorbid condition. Clinical care management measures and health outcomes were reported by time period. We used McNemar's tests for matched pairs to determine if clinical care management and health outcomes measures for each participant differed by time periods. We compared the likelihood of receiving all clinical care management measures and the likelihood of achieving all health

outcomes after a breast cancer diagnosis for the total population by patient-level factors using multivariable binomial regressions. When the binomial regressions fail to converge, modified Poisson regression was used to approximate the binomial regression.[81] We also conducted a sensitivity analysis to examine if medical records not available for at least 6 months before and after breast cancer diagnosis changed our study findings. We report relative risks (RR) along with 95% confidence intervals (CIs). Associations with p-values less than 0.05 were considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

This study used data from the first 563 women enrolled in the WCHFS, of which 274 women were eligible for inclusion in the analysis. Among this cohort of African American women diagnosed with breast cancer between 2012 and 2016, 18% had diabetes and 47% had hypertension at least one year prior to their breast cancer diagnosis. Table 1.1 displays selected sociodemographics, tumor characteristics, and comorbidity characteristics of the total study population and of sub-populations by comorbid condition (participants with both diabetes and hypertension and participants with hypertension only). The majority (92%) of the participants with diabetes also had hypertension except for eight participants. The first section of the table shows sociodemographics; a few items to note from the final column are: the mean age at breast cancer diagnosis for the total study population was 58 years; two-thirds of all participants were not married (i.e., single, divorced, widow); and half had private health insurance before and after

diagnosis. The second and third sections of Table 1.1 show tumor characteristics and comorbidity characteristics; a few items to note in the final column are: 10% of all participants were diagnosed with Stage III breast cancer, and the majority of all participants (94%) were classified as overweight or obese. Among the participants with diabetes, the mean duration of having diabetes was 11 years and having hypertension was 16 years; a third were insulin-dependent; and most (69%) had no complications from their diabetes. Among the participants with hypertension only, the mean duration of having hypertension was 13 years, and 87% did not have any complications from their hypertension.

Table 1.2a shows measures of diabetes clinical care management for the one year prior to and the one year following breast cancer diagnosis. Overall, for all measures, care management did not statistically differ by time period. The majority of participants had an HbA1c test ordered before and after breast cancer diagnosis (80% vs. 83%), had an LDL-C test ordered before and after (81% vs. 78%), and had medical attention for nephropathy (69% vs. 71%); however, the proportion of participants receiving an eye exam before and after cancer diagnosis (35% vs. 31%) and a foot exam before and after cancer diagnosis (23% vs. 30%) was poor. Most participants had at least one HbA1c test (69%) and at least one LDL-C test (63%) ordered in both time periods (data not shown). There was an 8% increase in foot exams after the breast cancer diagnosis, yet most (62%) of the foot exams were ordered for the same participants in both time periods (data not shown). Many of the participants received medical attention for nephropathy in both time periods, with almost half having a urine test for albumin ordered (47%) and being prescribed ACE/ARB medications (45%) (data not

shown). Among diabetic participants with hypertension (excluding the 8 participants with diabetes only), half were prescribed at least one prescription for hypertension medications during each time period (see last row in Table 1.2a).

Table 1.2b shows measures of hypertension clinical care management for the one year before and the one year following breast cancer diagnosis. Lipid screening decreased following breast cancer diagnosis (65% vs. 50%), while screening for blood glucose increased (73% vs. 91%). However, 79% had a lipid screening ordered at least once in either time period (data not shown). There was no change by time period in nephropathy screening (12% vs. 11%) and prescribed hypertension medications (44% vs. 52%).

Table 1.3a shows that optimal health outcomes for all diabetes measures did not differ in the year before and the year after breast cancer diagnosis. Optimal HbA1c levels (< 8%) were found for less than half of participants before and after diagnosis (49% vs. 46%), with similar mean HbA1c levels for each time period (7.7% vs. 7.5%). Only a third of participants had optimal LDL-C less than 100 mg/dL at each time period (34% vs. 37%). For eye exams, 16 of the 24 participants who received an eye exam in one of the time periods, but not both, all had normal exams (data not shown). For foot exams, the same 11 participants received a foot exam before and after their breast cancer diagnosis; 9 of these 11 had normal results and 2 were abnormal (data not shown). Optimal blood pressure levels less than 140/90 mmHg was achieved for 57% of the population before breast cancer diagnosis and for 60% after diagnosis.

Table 1.3b shows that, for participants with only hypertension, optimal health outcomes did statistically differ by time period for normal blood glucose

and blood pressure control. More than 80% of participants had a normal blood glucose level after breast cancer diagnosis, compared to 64% before diagnosis (p=0.001); an increase of 16%. More than 72% of participants had a normal blood pressure (<140/90 mmHg) after diagnosis, compared to 58% before diagnosis (p=0.004); an increase of 14%. Less than 5% of participants had a normal albumin level in any time period, and those who received an albumin test only received it once (either before or after diagnosis). Only 20% of participants had optimal LDL-C less than 100 mg/dL at each time period with the mean LDL-C at 117mg/dL before diagnosis and 109 mg/dL after diagnosis.

Table 1.4 shows the proportion of measures met and the “All-or-None” measures met for clinical care management and for health outcomes; most results did not differ by time period. For the entire study sample, the average proportion of clinical care measures met was 50% before and 52% after the breast cancer diagnosis. For the “All-or-None” clinical care measures met, 44% of participants had all measures met before diagnosis and 41% of participants had all measures met after diagnosis. The average proportion of health outcome measures met was 34% before and 39% after the breast cancer diagnosis (this is significantly different). For the “All-or-None” health outcome measures met, 13% of participants had all measures met before diagnosis and 15% of participants had all measures met after diagnosis.

Table 1.5 shows patient-level factors associated with diabetes and hypertension clinical care management after breast cancer diagnosis. The multivariable analysis found that comorbidity type, disease severity, and optimal management *before* diagnosis were associated with clinical care management

being met *after* diagnosis, adjusting for age, health insurance status at diagnosis, and cancer stage. Participants with diabetes and hypertension were twice as likely to have all care measures met compared with participants with hypertension only (adjusted RR: 2.00; 95% CI: 1.48, 2.69). Participants with organ damage related to their diabetes or hypertension were 45% less likely to have all care measures met compared with participants with no organ damage (adjusted RR: 0.55; 95% CI: 0.34, 0.89). Participants who did not have optimal management before diagnosis were 29% less like to have care measures met after breast cancer diagnosis (adjusted RR: 0.71; 95% CI: 0.53, 0.95). Table 1.6 shows patient-level factors associated with diabetes and hypertension health outcomes after breast cancer diagnosis. Multivariable analyses found no patient-level factors associated with health outcomes.

The sensitivity analysis showed that our results did not change when we excluded ten participants (4 with diabetes and 6 with hypertension only) whose medical records were not available for at least 6 months before and 6 months after breast cancer diagnosis.

DISCUSSION

This population-based cohort study of African American breast cancer survivors recruited from the NJSCR is among the first to examine clinical comorbid care management and health outcomes before and after breast cancer diagnosis. Among the 563 women in this cohort, 18% had diabetes and 47% had hypertension at least one year prior to their breast cancer diagnosis. We found that most diabetic breast cancer patients are receiving HbA1c tests (83%), lipid

screenings (78%), and medical attention for nephropathy (71%) after diagnosis, while only half of hypertensive breast cancer patients received a lipid screening. We observed disparate care management in eye exams, foot exams, and hypertension medications. Overall, only 41% of this population reached *all* key clinical care management indicators, and only 15% reached *all* key health outcomes after breast cancer diagnosis.

Diabetes Clinical Care Management and Health Outcomes

Our findings were consistent with other studies that have examined diabetes clinical care before and after cancer. Rate of HbA1c test ordering after breast cancer diagnosis was 83% in our study, which is on par or better than the results of other studies: 58% among Medicare patients with breast cancer or CRC, 84% among CRC patients in a single health system, and 66% among cancer survivors in a single health system.[3,23,25] In our study, rate of LDL-C test ordering after breast cancer diagnosis was 78% for patients with diabetes, which is similar to other findings: 70% of Medicare breast cancer or CRC patients with diabetes, 84% of CRC diabetic patients in a single health system, and 84% of cancer survivors in a single health system.[3,23,25] Eye exam orders or referrals to an ophthalmologist/ optometrist was low in our study (31%) compared with other studies, which ranged from 56% of Medicare breast cancer or CRC patients with diabetes to 84% among CRC patients with diabetes.[3,25] Bulger et al. found that 65% of African Americans with diabetes had a foot exam and 70% had an eye exam, while we found much lower proportions.[82]

We should also note that we did not find a decrease in diabetes management after breast cancer diagnosis, which is in contrast to one previous study using Medicare claims data linked with a central cancer registry in the Appalachia region.[3] Our study population is different to Yao et al. study among breast and CRC patients (AJCC stages I-IV) enrolled in Medicare, over the age of 65, and predominately NHW. This difference in diabetes management may be due to gender differences in that women with breast cancer may be more engaged in their care compared with men or severity of cancer stage or diabetes, which was not robustly accounted for in their analysis. Additionally, differential access to care by geographic area and health care environments may account for this difference (i.e., rural versus urban) in that rural areas have fewer oncologists, treatment facilities, and increased travel burden for patients to access care.[83,84] Cancer care in this rural region may have superseded the comorbid care, which may not be the case for urban areas such as New Jersey.

It is important to note that our study (using medical records) found that 30% of participants with diabetes had a foot exam ordered and 31% had an eye exam ordered, which were considerably lower than patient-reported foot exams (61%) and eye exams (58%) among the general New Jersey population with diabetes.[85] We found that less than half of the participants with diabetes were ordered albumin testing and less than half received a prescription for ACE/ARB medication. In comparison, 59% of cancer survivors with diabetes had albumin testing and 76% received ACE/ARB medications;[23] and 74% of African Americans with diabetes (but not cancer) had albumin testing and 80% received ACE/ARB medications.[82] Given the increased medical interaction due to the

breast cancer diagnosis, there seems to be missed opportunities for comprehensive diabetes care for African American breast cancer survivors, specifically, eye and foot exams, albumin testing, and ACE/ARB medication.

Diabetes health outcomes in our study were similar to other studies among African Americans, but were worse compared to other racial/ethnic populations. Optimal HbA1c < 8% was 73% for non-cancer diabetic patients and 71% for patients with diabetes and cancer in a single health system, which is much higher than the 46% of women in our study.[23] Our finding that only 37% of breast cancer patients with diabetes had an LDL-C level < 100 mg/dL was similar to two other studies. Keating et al. found that 42% of diabetic cancer survivors and 41% of non-cancer diabetics had optimal LDL-C. Bulger et al. found that 39% of diabetic African Africans had optimal LDL-C.[23,82] Future interventions are needed to promote glycemic control, which is associated with better breast cancer prognosis.[86,87]

Hypertension Clinical Care Management and Health Outcomes

Hypertension clinical care management among breast cancer patients has been less studied in the literature. We found that lipid screening decreased in the year after breast cancer diagnosis, while blood glucose screening increased. The increase in blood glucose screening is not surprising, as glucose screening is part of the comprehensive metabolic panel usually done as part of cancer care. We also observed that nephropathy screening was not part of the usual care for patients with hypertension, although it can be used as a marker for CVD and renal disease. Given that these women were at increased risk for CVD, and may

be at additional increased risk for CVD due to breast cancer treatment, this study highlights the need for clinical guidelines for optimal lipid management and cardiac surveillance in breast cancer patients.[88]

The hypertension health outcomes were similar to other studies among African American women. We observed that 20% of our population had optimal LDL-C < 100 mg/dL with a mean LDL-C of 109 mg/dL after breast cancer diagnosis. This LDL-C level was similar to the levels found in two studies among African American women with breast cancer (119 mg/dL and 110mg/dL) and was lower than the levels found among African American women without breast cancer (135 mg/dL and 114mg/dL).[89,90] The proportion of our cohort with optimal blood pressure (< 140/90 mmHg) did improve from 58% before breast cancer diagnosis to 72% after, which is higher than the national average among African American women (49%).[27] This difference may be due to the "white coat" effect in that the blood pressure after diagnosis was taken by WCHFS research staff in the participant's home, whereas the blood pressure prior to diagnosis was taken by medical staff in a clinical setting.[91]

Although there is no agreed upon method for using and reporting composite measures, they have been used to evaluate diabetes processes of care since 2002. Our "All-or-None" composite measures consisted of well-established measures that are of clinical significance. There are clear advantages over using the "All-or-None" approach, which looks at the entire sequence of care and not solely the parts, thereby encouraging a system-of-care perspective.[92-94] When we examined patient-level factors associated with all clinical care measures being met, patients who received optimal clinical care

before diagnosis were also likely to receive optimal clinical care after diagnosis. Calip et al. found that nonadherence to comorbid medications was associated with less primary care visits, which also supports the importance for interacting with medical providers.[40] Contrary to other studies, we did not find socioeconomic (e.g., income, education, health insurance) disparities in clinical care.[95] Our null findings may be due to the homogeneity of our population being all African American women recruited from only ten counties in New Jersey. As a result, we may have lacked variation and sufficient sample size to detect a difference. However, our findings suggest that there is a need to look beyond the individual and examine the context in which care is provided (i.e., medical team, health care system), which may have direct and indirect effects on clinical care management.[77,96]

Strengths and Limitations

Our study had many strengths, including being a population-based, prospective cohort study that utilized robust data abstracted from medical records as well as from patient interviews. Medical records were abstracted for all medical providers involved in the time period of observation (12 months pre and 12 months post diagnosis). Clinical care measures were considered met if a provider *ordered* or *referred* a patient; this data is more robust than administrative claims data, which can only ascertain if care was *received* by the patient.

We recognize the potential for selection, information, and confounding biases that could have decreased the internal validity of our study and distorted

our results. First, there could have been participation bias. Women with greater disease severity of diabetes or hypertension or those with less engagement with medical care may have been less likely to participate in the study. Therefore, our results may be overestimated.

Secondly, there could be information bias on how the outcome measures were ascertained. There could be bias if a participant forgot or chose to not disclose all providers seen during the home interview, then we could not request nor abstract those medical records, which could underestimate our findings. Also, medical records were abstracted in a standardized method, but providers' document medical visits differently, which may have misclassified outcomes. However, we chose measures for the "All-or-None" composite measure based on longstanding, nationally recognized quality indicators used by employee-based health insurance companies and Medicare and Medicaid programs for reimbursement and to monitor the quality of patient care and outcomes. Additionally, only one blood pressure measurement per time period was used, which may not be a true representation of the participant's overall blood pressure. Due to the limitation of manually abstracting all blood pressure and glucose measurements from medical records, we chose to use only one test result for each of these; likewise, national quality studies use the last measurement in a given year. We recognize the limitations with using the "All-or-None" approach, but we think it is important to look at the entire process of care.

Lastly, we recognize limitations in how confounders were measured and then accounted for in the analyses. Known confounders were chosen from the conceptual framework, including age, socioeconomic status, health insurance,

usual source of medical care, and disease severity. However, there could be other unknown confounders that drive clinical care management (e.g., patient preferences, patient activation, medical mistrust/ implicit bias, distance travel, co-pays) that were not accounted for in this analysis. Finally, our target population is to African American breast cancer patients with diabetes and hypertension in New Jersey. Therefore, our findings may not be generalizable to other populations of breast cancer patients who have differential access to medical care.

In conclusion, we found in our study that key clinical care management measures for diabetes and hypertension as well as related health outcomes among African American breast cancer patients were poor overall. We also found that these outcomes were not associated with age, socioeconomic status, or cancer severity. The prevalence of hypertension and diabetes, related complications, risk factors, and mortality can be attributed to social and environmental factors (e.g., less access to healthy foods, less-walkable communities, and discrimination) that unequally burden African Americans and individuals of lower socioeconomic status.[13,14] Research needs to go beyond the individual patient and address systems of care and the agencies and policies that lead to inferior quality of care and differential access.[5,97-99] Multilevel interventions that recognize and address systematic discrimination (i.e., differential access to care, disparate quality of care, and medical mistrust[5]) are needed to achieve health equity for African American breast cancer survivors.

REFERENCES

1. Wagner EH. Chronic Disease Management: What Will It Take to Improve Care for Chronic Illness? *Eff Clin Pract.* 1998; 1(1): 2-4.
2. Reddy SS. Health Outcomes in Type 2 Diabetes. *Int J Clin Pract Suppl.* 2000; (113): 46-53.
3. Yao N, Camacho FT, Chukmaitov AS, Fleming ST, Anderson RT. Diabetes Management before and after Cancer Diagnosis: Missed Opportunity. *Ann Transl Med.* 2015; 3(5): 72.
4. Weaver SJ, Jacobsen PB. Cancer Care Coordination: Opportunities for Healthcare Delivery Research. *Transl Behav Med.* 2018; 8(3): 503-8.
5. Belgrave FZ, Abrams JA. Reducing Disparities and Achieving Equity in African American Women's Health. *Am Psychol.* 2016; 71(8): 723-33.
6. Institute of Medicine Committee on Understanding and Eliminating Racial and Ethnic Disparities in Health Care. *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care.* Washington, DC: National Academies Press; 2003.
7. Chou AF, Brown AF, Jensen RE, Shih S, Pawlson G, Scholle SH. Gender and Racial Disparities in the Management of Diabetes Mellitus among Medicare Patients. *Womens Health Issues.* 2007; 17(3): 150-61.
8. Centers for Disease Control and Prevention. Cdc Wide-Ranging Online Data for Epidemiologic Research (Cdc Wonder). 2018; https://wonder.cdc.gov/. Accessed March 14, 2019.
9. American Cancer Society. *Cancer Facts & Figures for African Americans 2019-2021.* Atlanta, GA: American Cancer Society;2019.
10. Centers for Disease Control and Prevention. Leading Causes of Death by Race/Ethnicity, All Females-United States, 2015. 2015; https://www.cdc.gov/women/lcod/2015/race-ethnicity/index.htm.
11. Centers for Disease Control and Prevention. *National Diabetes Statistics Report, 2017: Estimates of Diabetes and Its Burden in the United States.* Atlanta, GA: U.S. Department of Health and Human Services;2017
12. U.S. Office of Health and Human Services, Office of Minority Health. Diabetes and African Americans. 2016; https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=4&lvlid=18. Accessed May 7, 2018.
13. Spanakis EK, Golden SH. Race/Ethnic Difference in Diabetes and Diabetic Complications. *Current diabetes reports.* 2013; 13(6): 10.1007/s11892-013-0421-9.
14. Heisler M, Smith DM, Hayward RA, Krein SL, Kerr EA. Racial Disparities in Diabetes Care Processes, Outcomes, and Treatment Intensity. *Med Care.* 2003; 41(11): 1221-32.
15. Hu R, Shi L, Rane S, Zhu J, Chen C-C. Insurance, Racial/Ethnic, Ses-Related Disparities in Quality of Care among Us Adults with Diabetes. *J Immigr Minor Health.* 2014; 16(4): 565-75.
16. Pettit S, Cresta E, Winkley K, Purssell E, Armes J. Glycaemic Control in People with Type 2 Diabetes Mellitus During and after Cancer Treatment:

A Systematic Review and Meta-Analysis. *PLoS One.* 2017; 12(5): e0176941.
17. Srokowski TP, Fang S, Hortobagyi GN, Giordano SH. Impact of Diabetes Mellitus on Complications and Outcomes of Adjuvant Chemotherapy in Older Patients with Breast Cancer. *J Clin Oncol.* 2009; 27(13): 2170-6.
18. Barone BB, Yeh H, Snyder CF, et al. Long-Term All-Cause Mortality in Cancer Patients with Preexisting Diabetes Mellitus: A Systematic Review and Meta-Analysis. *JAMA.* 2008; 300(23): 2754-64.
19. Hershey DS, Given B, Given C, Von Eye A, You M. Diabetes and Cancer: Impact on Health-Related Quality of Life. *Oncol Nurs Forum.* 2012; 39(5): 449-57.
20. 6. Glycemic Targets: Standards of Medical Care in Diabetes-2018. *Diabetes Care.* 2018; 41(Suppl 1): S55-s64.
21. 10. Microvascular Complications and Foot Care: Standards of Medical Care in Diabetes-2018. *Diabetes Care.* 2018; 41(Suppl 1): S105-s18.
22. Oh S-W, Lee HJ, Chin HJ, Hwang J-I. Adherence to Clinical Practice Guidelines and Outcomes in Diabetic Patients. *Int J Qual Health Care.* 2011; 23(4): 413-9.
23. Keating NL, Zaslavsky AM, Herrinton LJ, Selby JV, Wolf RE, Ayanian JZ. Quality of Diabetes Care among Cancer Survivors with Diabetes. *Med Care.* 2007; 45(9): 869-75.
24. Bayliss EA, Blatchford PJ, Newcomer SR, Steiner JF, Fairclough DL. The Effect of Incident Cancer, Depression and Pulmonary Disease Exacerbations on Type 2 Diabetes Control. *J Gen Intern Med.* 2011; 26(6): 575-81.
25. Chiao EY, Nambi PV, Naik AD. The Impact of Diabetes Process and Outcome Quality Measures on Overall Survival in Patients with Co-Morbid Colorectal Cancer. *J Cancer Surviv.* 2010; 4(4): 381-7.
26. Baigent C, Blackwell L, Emberson J, et al. Efficacy and Safety of More Intensive Lowering of Ldl Cholesterol: A Meta-Analysis of Data from 170,000 Participants in 26 Randomised Trials. *Lancet.* 2010; 376(9753): 1670-81.
27. Fryar C, Ostchega Y, Hales C, Zhang G, Kruszon-Moran D. *Hypertension Prevalence and Control among Adults: United States, 2015–2016.* National Center for Health Statistics Centers for Disease Control and Prevention;2017.
28. Mehta LS, Watson KE, Barac A, et al. Cardiovascular Disease and Breast Cancer: Where These Entities Intersect: A Scientific Statement from the American Heart Association. *Circulation.* 2018.
29. Chapman JA, Meng D, Shepherd L, et al. Competing Causes of Death from a Randomized Trial of Extended Adjuvant Endocrine Therapy for Breast Cancer. *J Natl Cancer Inst.* 2008; 100(4): 252-60.
30. Von Hoff DD, Layard MW, Basa P, et al. Risk Factors for Doxorubicin-Induced Congestive Heart Failure. *Ann Intern Med.* 1979; 91(5): 710-7.
31. Swain SM, Whaley FS, Ewer MS. Congestive Heart Failure in Patients Treated with Doxorubicin: A Retrospective Analysis of Three Trials. *Cancer.* 2003; 97(11): 2869-79.

32. Bird BRJH, Swain SM. Cardiac Toxicity in Breast Cancer Survivors: Review of Potential Cardiac Problems. *Clinical Cancer Research.* 2008; 14(1): 14.
33. James PA, Oparil S, Carter BL, et al. 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report from the Panel Members Appointed to the Eighth Joint National Committee. *JAMA.* 2014; 311(5): 507-20.
34. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 Acc/Aha Guideline on the Primary Prevention of Cardiovascular Disease. *Circulation.* 2019: Cir0000000000000678.
35. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of Medication Adherence on Hospitalization Risk and Healthcare Cost. *Med Care.* 2005; 43(6): 521-30.
36. Corrao G, Parodi A, Nicotra F, et al. Better Compliance to Antihypertensive Medications Reduces Cardiovascular Risk. *J Hypertens.* 2011; 29(3): 610-8.
37. Dragomir A, Cote R, Roy L, et al. Impact of Adherence to Antihypertensive Agents on Clinical Outcomes and Hospitalization Costs. *Med Care.* 2010; 48(5): 418-25.
38. Grassi G, Seravalle G, Mancia G. Cardiovascular Consequences of Poor Compliance to Antihypertensive Therapy. *Blood Press.* 2011; 20(4): 196-203.
39. Santorelli ML, Steinberg MB, Hirshfield KM, et al. Effects of Breast Cancer on Chronic Disease Medication Adherence among Older Women. *Pharmacoepidemiol Drug Saf.* 2016; 25(8): 898-907.
40. Calip GS, Elmore JG, Boudreau DM. Characteristics Associated with Nonadherence to Medications for Hypertension, Diabetes, and Dyslipidemia among Breast Cancer Survivors. *Breast Cancer Res Treat.* 2017; 161(1): 161-72.
41. Yang J, Neugut AI, Wright JD, Accordino M, Hershman DL. Nonadherence to Oral Medications for Chronic Conditions in Breast Cancer Survivors. *J Oncol Pract.* 2016; 12(8): e800-9.
42. U.S. Department of Health and Human Services, National Institute of Health, National Heart Lung and Blood Institute. *The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.* Bethesda, MD: National Heart, Lung , and Blood Institute;2004.
43. Whelton PK, Carey RM, Aronow WS, et al. 2017 Acc/Aha/Aapa/Abc/Acpm/Ags/Apha/Ash/Aspc/Nma/Pcna Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. *A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines.* 2017.
44. U.S. Preventive Services Task Force. Abnormal Blood Glucose and Type 2 Diabetes Mellitus: Screening. 2005; https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/screening-for-abnormal-blood-glucose-and-type-2-diabetes.

45. U.S. Preventive Services Task Force. Archived: Lipid Disorders in Adults (Cholesterol, Dyslipidemia): Screening. 2008; https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/lipid-disorders-in-adults-cholesterol-dyslipidemia-screening.
46. Anderson TJ, Gregoire J, Hegele RA, et al. 2012 Update of the Canadian Cardiovascular Society Guidelines for the Diagnosis and Treatment of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult. *Can J Cardiol.* 2013; 29(2): 151-67.
47. Lipsy RJ. Introduction. *J Manag Care Pharm.* 2003; 9(1 Supp A): 2-5.
48. Grundy Scott M, Stone Neil J, Bailey Alison L, et al. 2018 Aha/Acc/Aacvpr/Aapa/Abc/Acpm/Ada/Ags/Apha/Aspc/Nla/Pcna Guideline on the Management of Blood Cholesterol. *Circulation.* 0(0).
49. Basi S, Fesler P, Mimran A, Lewis JB. Microalbuminuria in Type 2 Diabetes and Hypertension: A Marker, Treatment Target, or Innocent Bystander? *Diabetes Care.* 2008; 31 Suppl 2: S194-201.
50. Qin B, Llanos AAM, Lin Y, et al. Validity of Self-Reported Weight, Height, and Body Mass Index among African American Breast Cancer Survivors. *Journal of Cancer Survivorship.* 2018; 12(4): 460-8.
51. Mayo Clinic. Diabetes Diagnosis. https://www.mayoclinic.org/diseases-conditions/diabetes/diagnosis-treatment/drc-20371451. Accessed May 7, 2018.
52. Ambrosone CB, Ciupak GL, Bandera EV, et al. Conducting Molecular Epidemiological Research in the Age of Hipaa: A Multi-Institutional Case-Control Study of Breast Cancer in African-American and European-American Women. *J Oncol.* 2009; 2009: 871250.
53. Bandera EV, Chandran U, Zirpoli G, et al. Body Size in Early Life and Breast Cancer Risk in African American and European American Women. *Cancer Causes Control.* 2013; 24(12): 2231-43.
54. Ambrosone CB, Zirpoli GR, Bovbjerg DH, et al. Associations between Estrogen Receptor-Negative Breast Cancer and Timing of Reproductive Events Differ between African American and European American Women. *Cancer Epidemiol Biomarkers Prev.* 2014; 23(6): 1115-20.
55. Llanos AA, Chandwani S, Bandera EV, et al. Associations between Sociodemographic and Clinicopathological Factors and Breast Cancer Subtypes in a Population-Based Study. *Cancer Causes Control.* 2015; 26(12): 1737-50.
56. Llanos AAM, Rabkin A, Bandera EV, et al. Hair Product Use and Breast Cancer Risk among African American and White Women. *Carcinogenesis.* 2017; 38(9): 883-92.
57. George P, Chandwani S, Gabel M, et al. Diagnosis and Surgical Delays in African American and White Women with Early-Stage Breast Cancer. *J Womens Health (Larchmt).* 2015; 24(3): 209-17.
58. Rutgers Cancer Insitute of New Jersey. Epidemiology Services - Services. 2018; http://www.cinj.org/research/epidemiology-services-services. Accessed March 13, 2019.
59. Bandera EV, Chandran U, Zirpoli G, et al. Body Fatness and Breast Cancer Risk in Women of African Ancestry. *BMC cancer.* 2013; 13: 475-.

60. American Diabetes Association. Strategies for Improving Care. *Diabetes Care.* 2016; 39(Supplement 1): S6.
61. National Committee for Quality Assurance. Hedis 2018. 2018; http://www.ncqa.org/Portals/0/HEDISQM/HEDIS2018/HEDIS 2018 Measures.pdf?ver=2017-06-28-134644-370. Accessed May 19, 2018.
62. Mangione CM, Gerzoff RB, Williamson DF, et al. The Association between Quality of Care and the Intensity of Diabetes Disease Management Programs. *Ann Intern Med.* 2006; 145(2): 107-16.
63. Centers for Medicare & Medicaid Services. 2018 Core Set of Adult Health Care Quality Measures for Medicaid (Adult Core Set). 2018; https://www.medicaid.gov/medicaid/quality-of-care/downloads/performance-measurement/2018-adult-core-set.pdf. Accessed May 22, 2018.
64. Centers for Medicare & Medicaid Services. *Medicare Shared Savings Program, Accountable Care Organization (Aco) 2018 Quality Measures Narrative Specifications Document* 2018.
65. National Quality Forum. Diabetes: Foot Exam. 2018; http://www.qualityforum.org/QPS/MeasureDetails.aspx?standardID=1224&print=0&entityTypeID=1. Accessed March 13. 2019.
66. National Quality Forum. Comprehensive Diabetes Care: Medical Attention for Nephropathy. 2018; http://www.qualityforum.org/QPS/MeasureDetails.aspx?standardID=1226&print=0&entityTypeID=1. Accessed March 13. 2019.
67. Fleming BB, Greenfield S, Engelgau MM, Pogach LM, Clauser SB, Parrott MA. The Diabetes Quality Improvement Project. *Moving science into health policy to gain an edge on the diabetes epidemic.* 2001; 24(10): 1815-20.
68. Health Systems, Patients Factors, and Quality of Care for Diabetes. *Diabetes Care.* 2010; 33(4): 940.
69. National Committee for Quality Assurance. Diabetes Recognition Program. 2018; http://www.ncqa.org/programs/recognition/clinicians/diabetes-recognition-program-drp. Accessed March 08, 2018.
70. National Committee for Quality Assurance. Disease Management Performance Measures. 2018; http://www.ncqa.org/programs/accreditation/disease-management-dm/dm-performance-measures. Accessed March 9, 2018.
71. Centers for Medicare and Medicaid Services. Core Measures: Aco and Pcmh/ Primary Care Measures. 2017; https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/QualityMeasures/Downloads/ACO-and-PCMH-Primary-Care-Measures.pdf.
72. Saaddine JB, Cadwell B, Gregg EW, et al. Improvements in Diabetes Processes of Care and Intermediate Outcomes: United States, 1988–2002. *Ann Med.* 2006; 144(7): 465-74.

73. Siu AL. Screening for High Blood Pressure in Adults: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med.* 2015; 163(10): 778-86.
74. Cifu AS, Davis AM. Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. *JAMA.* 2017; 318(21): 2132-4.
75. O'Connor PJ. *Towards a Comprehensive Diabetes Quality Measure Set: New Measurement Opportunities and Methodological Challenges.* National Quality Forum;2008.
76. Andersen RM. Revisiting the Behavioral Model and Access to Medical Care: Does It Matter? *J Health Soc Behav.* 1995; 36(1): 1-10.
77. Taplin SH, Anhang Price R, Edwards HM, et al. Introduction: Understanding and Influencing Multilevel Factors across the Cancer Care Continuum. *J Natl Cancer Inst Monogr.* 2012; 2012(44): 2-10.
78. Zapka JG, Taplin SH, Solberg LI, Manos MM. A Framework for Improving the Quality of Cancer Care. *Cancer Epidemiol Biomarkers Prev.* 2003; 12(1): 4.
79. Donabedian A. Evaluating the Quality of Medical Care. *Milbank Mem Fund Q.* 1966; 44(3): Suppl:166-206.
80. Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for Enhancing Medication Adherence. *Cochrane Database Syst Rev.* 2008; (2).
81. Zou G. A Modified Poisson Regression Approach to Prospective Studies with Binary Data. *Am J Epidemiol.* 2004; 159(7): 702-6.
82. Bulger JB, Shubrook JH, Snow R. Racial Disparities in African Americans with Diabetes: Process and Outcome Mismatch. *Am J Manag Care.* 2012; 18(8): 407-13.
83. Charlton M, Schlichting J, Chioreso C, Ward M, Vikas P. Challenges of Rural Cancer Care in the United States. *Oncology (Williston Park).* 2015; 29(9): 633-40.
84. American Society of Clinical Oncology. Key Trends in Tracking Supply of and Demand for Oncologists. 2015; https://www.asco.org/sites/new-www.asco.org/files/content-files/research-and-progress/documents/2015-cancer-care-in-america-report.pdf. Accessed June 28, 2018.
85. Centers for Disease Control and Prevention. *Diabetes Report Card 2017.* Atlanta, GA: Centers for Disease Control and Prevention, US Dept of Health and Human Services;2018.
86. Erickson K, Patterson RE, Flatt SW, et al. Clinically Defined Type 2 Diabetes Mellitus and Prognosis in Early-Stage Breast Cancer. *J Clin Oncol.* 2010; 29(1): 54-60.
87. Chang Y-L, Sheu WH-H, Lin S-Y, Liou W-S. Good Glycaemic Control Is Associated with a Better Prognosis in Breast Cancer Patients with Type 2 Diabetes Mellitus. *Clin Exp Med.* 2018; 18(3): 383-90.
88. Carver JR, Shapiro CL, Ng A, et al. American Society of Clinical Oncology Clinical Evidence Review on the Ongoing Care of Adult Cancer Survivors: Cardiac and Pulmonary Late Effects. *J Clin Oncol.* 2007; 25(25): 3991-4008.

89. Llanos AA, Makambi KH, Tucker CA, Wallington SF, Shields PG, Adams-Campbell LL. Cholesterol, Lipoproteins, and Breast Cancer Risk in African American Women. *Ethn Dis.* 2012; 22(3): 281-7.
90. Griffith KA, Chung SY, Zhu S, Ryan AS. Insulin Resistance and Inflammation in Black Women with and without Breast Cancer: Cause for Concern. *Ethn Dis.* 2016; 26(4): 513-20.
91. Tanner RM, Shimbo D, Seals SR, et al. White-Coat Effect among Older Adults: Data from the Jackson Heart Study. *J Clin Hypertens (Greenwich).* 2016; 18(2): 139-45.
92. Curnow R, Knight T, Harris R, Linscott K. Advancing Care with Ncqa's Diabetes Recognition Program. Paper presented at: NCQA's Diabetes Recognition Program (DRP) Summit: Leaders Advancing Quality of Care for Patients with Diabetes2012.
93. Kelley E. All or None Measurement: Why We Know So Little About the Comprehensiveness of Care. *Int J Qual Health Care.* 2006; 19(1): 1-3.
94. Nolan T, Berwick DM. All-or-None Measurement Raises the Bar on Performance. *JAMA.* 2006; 295(10): 1168-70.
95. Gaskin DJ, Thorpe RJ, Jr., McGinty EE, et al. Disparities in Diabetes: The Nexus of Race, Poverty, and Place. *Am J Public Health.* 2014; 104(11): 2147-55.
96. Sampson UK, Kaplan RM, Cooper RS, et al. Reducing Health Inequities in the United States: Recommendations from the Nhlbi's Health Inequities Think Tank Meeting. *J Am Coll Cardiol.* 2016; 68(5): 517-24.
97. Daly B, Olopade OI. A Perfect Storm: How Tumor Biology, Genomics, and Health Care Delivery Patterns Collide to Create a Racial Survival Disparity in Breast Cancer and Proposed Interventions for Change. *CA Cancer J Clin.* 2015; 65(3): 221-38.
98. Gravlee CC. How Race Becomes Biology: Embodiment of Social Inequality. *Am J Phys Anthropol.* 2009; 139(1): 47-57.
99. Wheeler SB, Reeder-Hayes KE, Carey LA. Disparities in Breast Cancer Treatment and Outcomes: Biological, Social, and Health System Determinants and Opportunities for Research. *Oncologist.* 2013; 18(9): 986-93.

TABLES

Table 1.1. Characteristics of study participants (N=274)

	Participants with diabetes & hypertension[1]		Participants with hypertension only		Total participants	
	n=102		n=172		n=274	
Patient Characteristics	n	%	n	%	n	%
Sociodemographics						
Mean ± SD age at diagnosis, years	61 ± 8		57 ± 9		58 ± 9	
<55	24	23.53	72	41.86	96	35.04
55-64	36	35.29	58	33.72	94	34.31
65-75	42	41.18	42	24.42	84	30.66
Marital status						
Married	34	33	63	36.63	97	35
Not Married	68	67	109	63.37	177	65
Education						
≤ High school	44	43.14	69	40.12	113	41.24
> High school	58	56.86	103	59.88	161	58.76
Annual household income						
Less than $35,000	54	52.94	68	39.53	122	44.53
$35,000-$69,999	21	20.59	44	25.58	65	23.72
$70,000 or more	19	18.63	54	31.40	73	26.64
Unknown	8	7.84	6	3.49	14	5.11
Health insurance one year prior to breast cancer diagnosis						
Medicaid	15	14.71	15	8.72	30	10.95
Medicare	29	28.43	39	22.67	68	24.82
Private	43	42.16	93	54.07	136	49.64
None/charity/unknown	15	14.71	25	14.53	40	14.60
Health insurance at breast cancer diagnosis						
Medicaid	23	22.55	25	14.53	48	17.52
Medicare	39	38.24	38	22.09	77	28.10
Private	38	37.25	97	56.40	135	49.27
None/charity/unknown	2	1.96	12	6.98	14	5.11
Tumor Characteristic						
AJCC stage						
0 (DCIS)	27	26.47	41	23.84	68	24.82
I	34	33.33	53	30.81	87	31.75
II	32	31.37	60	34.88	92	33.58
III	9	8.82	18	10.47	27	9.85

Patient Characteristics	Participants with diabetes & hypertension[1] n=102 n	%	Participants with hypertension only n=172 n	%	Total participants n=274 n	%
Clinical Comorbidity Characteristics						
Mean ± SD duration of diabetes, years	11 ± 9		-	-	11 ± 9	
Insulin-dependent						
Yes	30	29.41	-	-	30	10.95
No	72	70.59	-	-	72	26.28
Not applicable	-	-	-	-	172	62.77
Diabetes disease severity						
Category I (No complications)	70	68.63	-	-	70	25.55
Category II (Eye or foot disease, but no heart or kidney disease)	8	7.84	-	-	8	2.92
Category III (Diabetic heart or kidney disease)	19	18.63	-	-	19	6.93
Category IV (Diabetic heart and kidney disease)	5	4.90	-	-	5	1.82
Not applicable	-	-	-	-	172	62.77
Mean ± SD hypertension duration, years	16 ± 13		13 ± 12		14 ± 12	
Hypertension disease severity						
Category I (No complications)	82	80.39	157	91.28	239	87.23
Category II (Without CHF and DBP ≥ 100 or SBP ≥ 160 mmHg)	8	7.84	13	7.56	21	7.66
Category III (CHF and DBP ≥ 100 or SBP ≥ 160 mmHg)	4	3.92	2	1.16	6	2.19
Not applicable	8	7.84	-	-	8	2.92
Smoking status						
Never	55	53.92	87	50.58	142	51.82
Former	32	31.37	53	30.81	85	31.02
Current	15	14.71	32	18.60	47	17.15
Count of comorbidities[2]						
1	4	3.92	96	55.81	100	36.50
2	40	39.22	51	29.65	91	33.21
≥3	58	56.86	25	14.53	82	29.93
Type of health conditions						
Hypertension	94	92.16	172	100.00	266	97.08
Diabetes	102	100.00	0	0.00	102	37.23
Chronic kidney disease	6	5.88	6	3.49	12	4.38
Cardiovascular disease[3]	22	21.57	9	5.23	31	11.31
Hyperlipidemia	42	41.18	34	19.77	76	27.74
High cholesterol	15	14.71	17	9.88	32	11.68

Patient Characteristics	Participants with diabetes & hypertension[1] n=102		Participants with hypertension only n=172		Total participants n=274	
	n	%	n	%	n	%
Body mass index (kg/m^2) (mean ± SD)	34 ± 7		33 ± 7		33 ± 7	
Normal (24.9 and less)	3	2.94	13	7.56	16	5.84
Overweight (25.0-29.9)	29	28.43	55	31.98	84	30.66
Obese Class I (30.0-34.9)	28	27.45	49	28.49	77	28.10
Obese Class II (35.0-40.0)	23	22.55	30	17.44	53	19.34
Obese Class III (40.0+)	19	18.63	25	14.53	45	16.42

Abbreviations: SD, standard deviation; AJCC, American Joint Committee on Cancer; CHF, congestive heart failure; SBP, systolic blood pressure; DBP, diastolic blood pressure

[1] Patients with diabetes-only (without hypertension) (n=8) were included.

[2] Count of comorbidities present at or before breast cancer diagnosis excludes breast cancer but includes diabetes and hypertension, as well as: HIV/AIDS, arthritis, asthma, congestive heart failure, chronic liver disease, ascites, hepatic encephalopathy, myocardial infarction, angina, premature ventricular contractions, chronic renal disease, other cancer, osteoporosis, and COPD.

[3] Cardiovascular disease includes congestive heart failure, myocardial infarction, angina, stroke, and coronary artery disease.

Table 1.2a. Diabetes clinical care management among breast cancer patients in the year before and after breast cancer diagnosis (N=102)

	Before Breast Cancer Diagnosis		After Breast Cancer Diagnosis		
	n	%	n	%	P-value[1]
Measures of diabetes care					
Hemoglobin A1c tests	82	80.39	85	83.33	0.564
LDL-cholesterol screening	83	81.37	80	78.43	0.736
Eye exam	36	35.29	32	31.37	0.505
Foot exam	23	22.55	31	30.39	0.103
Medical attention for nephropathy	70	68.63	72	70.59	0.752
Prescribed hypertension medications[2,3]	54	57.45	52	55.32	0.715

[1] P-value from McNemar's tests comparing clinical care management measures met before and after diagnosis.

[2] Hypertension medications include thiazide-type diuretic, calcium channel blocker, angiotensin-converting enzyme inhibitor, and angiotensin receptor blocker.

[3] Patients with diabetes-only (without hypertension) (n=8) are not eligible for this measure.

Table 1.2b. Hypertension clinical care management among breast cancer patients in the year before and after breast cancer diagnosis (N=172)

	Before Breast Cancer Diagnosis		After Breast Cancer Diagnosis		
	n	%	n	%	P-value[1]
Measures of hypertension care					
Lipid screening	111	64.53	86	50.00	**0.004**
Screening for abnormal blood glucose	125	72.67	156	90.70	**<0.001**
Nephropathy screening	20	11.63	18	10.47	0.655
Prescribed hypertension medications[2]	76	44.19	89	51.74	0.085

[1] P-value from McNemar's tests comparing clinical care management measures met before and after diagnosis.
[2] Hypertension medications include thiazide-type diuretic calcium channel blocker, angiotensin-converting enzyme inhibitor, and angiotensin receptor blocker.

Table 1.3a. Optimal health outcomes among breast cancer patients with diabetes in the year before and the year after breast cancer diagnosis (N=102)

	Before Breast Cancer Diagnosis			After Breast Cancer Diagnosis			
	n	%	Mean Value ± SD[1]	n	%	Mean Value ± SD[1]	P-value[2]
Optimal Health Outcomes							
Hemoglobin A1c < 8.0%	50	49.02	7.71 ± 1.93	47	46.08	7.48 ± 1.57	0.590
LDL-cholesterol < 100 mg/dL	35	34.31	103.63 ± 28.89	38	37.25	99.28± 31.02	0.590
Normal eye exam	14	13.73	-	10	9.80	-	0.455
Normal foot exam	9	8.82	-	9	8.82	-	1.000
Normal albumin (ACR < 30)	20	19.61	-	27	26.47	-	0.178
Blood pressure control < 140/90 mmHg	58	56.86	-	61	59.80	-	0.647
Systolic blood pressure			135.43 ± 16.68			132.34 ± 22.74	
Diastolic blood pressure			78.16 ± 11.16			77.36 ± 12.84	

Abbreviations: SD, standard deviation; LDL, low-density lipoproteins; ACR, albumin-to-creatinine ratio.
[1] Mean and standard deviation from results of test performed.
[2] P-value from McNemar's test comparing optimal test results before and after breast cancer diagnosis. If no test was ordered, then health outcome was considered not optimal.

Table 1.3b. Optimal health outcomes among breast cancer patients with hypertension in the year before and the year after breast cancer diagnosis (N=172)

	Before Breast Cancer Diagnosis			After Breast Cancer Diagnosis			
	n	%	Mean Value ± SD[1]	n	%	Mean Value ± SD[1]	P-value[2]
Optimal Health Outcomes							
LDL-cholesterol < 100 mg/dL	35	20.35	117.05 ± 34.91	34	19.77	109.12 ± 38.24	0.876
Normal blood glucose level	110	63.95	-	137	79.65	-	**0.001**
Hemoglobin A1c < 8.0%	51	29.65	6.08 ± 0.77	48	27.91	6.28 ± 1.21	
Blood glucose level < 120 mg/dL	101	58.72	98.26 ± 25.88	126	73.26	104.47 ± 23.51	
Normal albumin (ACR < 30)	8	4.65	-	7	4.07	-	1.000
Blood pressure control < 140/90 mmHg	99	57.56	-	123	71.51	-	**0.004**
Systolic blood pressure			136.05 ± 16.19			129.15 ± 16.93	
Diastolic blood pressure			80.50 ± 9.45			79.63 ± 11.98	

Abbreviations: SD, standard deviation; LDL, low-density lipoproteins; ACR, albumin-to-creatinine ratio.
[1] Mean and standard deviation from results of test performed.
[2] P-value from McNemar's test comparing optimal test results before and after breast cancer diagnosis. If no test was ordered, this considered not optimal.

Table 1.4. Diabetes and hypertension clinical care management among breast cancer patients in the year before and the year after breast cancer diagnosis (N=274)

	Before Breast Cancer Diagnosis			After Breast Cancer Diagnosis			
	n	%	Mean ± SD	n	%	Mean ± SD	P-value[1]
Clinical Care Management Measures							
Proportion met	-	-	50.49% ± 28.63%	-	-	52.31% ± 25.17%	0.369
All-or-None met[2]	121	44.16	-	112	40.88	-	0.380
Health Outcomes							
Proportion met	-	-	34.31% ± 22.26%	-	-	39.14% ± 20.89%	**0.002**
All-or-None met[3]	36	13.14	-	41	14.96	-	0.515

[1] P-value from paired t-test for continuous variables and McNemar's test for categorical variables.

[2] All-or-none refers to whether provider ordered for patients with diabetes A1c test, LDL test, and medical attention for nephropathy and for patients with hypertension-only provider ordered lipid panel and prescribed hypertension medication at least once. All-or-none variable is dichotomized as all measures met or not all measures met.

[3] All-or-none refers to whether HbA1c, LDL-C, and microalbuminuria test results were optimal for patients with diabetes, and LDL test result and blood pressure measurement were optimal for patients with hypertension-only.

Table 1.5. Patient-level factors associated with diabetes and hypertension clinical care management after breast cancer diagnosis (N=274)

	All Clinical Care Measures Met[1]					
	n= 112		Unadjusted		Adjusted	
	n	%	RR	95% CI	RR	95% CI
Age at diagnosis, years						
65-75	40	35.71	1.00	Ref.	1.00	Ref.
55-64	42	37.50	0.94	(0.68, 1.29)	1.00	(0.73, 1.38)
<55	30	26.79	**0.66**	**(0.45, 0.95)**	0.74	(0.50, 1.09)
Health insurance at diagnosis						
Private	49	43.75	1.00	Ref.	1.00	Ref.
Medicaid	22	19.64	1.26	(0.86, 1.85)	1.12	(0.79, 1.57)
Medicare	37	33.04	1.32	(0.96, 1.83)	1.06	(0.75, 1.49)
None/charity/unknown	4	3.57	0.79	(0.33, 1.86)	0.88	(0.37, 2.12)
AJCC stage						
0 (DCIS)	29	25.89	1.00	Ref.	1.00	Ref.
I	33	29.46	0.89	(0.61, 1.31)	0.94	(0.65, 1.35)
II-III	50	44.64	0.99	(0.70, 1.39)	1.05	(0.75, 1.46)
Comorbidity type						
Hypertension=only	51	45.54	1.00	Ref.	1.00	Ref.
Diabetes and hypertension[2]	61	54.46	**2.02**	**(1.52, 2.67)**	**2.00**	**(1.48, 2.69)**
Hypertension/diabetes disease severity[3]						
No organ damage	99	88.39	1.00	Ref.	1.00	Ref.
Organ damage	13	11.61	0.93	(0.59, 1.46)	**0.55**	**(0.34, 0.89)**
Optimal management before diagnosis						
Yes	64	57.14	1.00	Ref.	1.00	Ref.
No	48	42.86	**0.59**	**(0.44, 0.79)**	**0.71**	**(0.53, 0.95)**

[1] "All Clinical Care Measures Met" refers to whether provider ordered for patients with diabetes all of the following: HbA1c test, LDL test, and medical attention for nephropathy; and whether, for patients with hypertension-only, provider ordered an LDL test and prescribed hypertension medication at least once. This variable is dichotomized as: all measures met or not all measures met.
[2] Patients with diabetes-only (without hypertension) (n=8) were included.
[3] Disease severity from diabetes or hypertension; or if patient has both, then highest severity used.

Table 1.6. Patient-level factors associated with diabetes and hypertension health outcomes after breast cancer diagnosis (N=274)

	All Health Outcomes Measures Met[1]					
	n= 41		Unadjusted		Adjusted	
	n	%	RR	95% CI	RR	95% CI
Age at diagnosis, years						
65-75	14	34.15	1.00	Ref.	1.00	Ref.
55-64	14	34.15	0.96	(0.48, 1.93)	0.77	(0.38, 1.55)
<55	13	31.71	0.94	(0.47, 1.89)	0.78	(0.38, 1.60)
Health insurance at diagnosis						
Private	22	53.66	1.00	Ref.	1.00	Ref.
Medicaid	8	19.51	1.02	(0.49, 2.14)	0.89	(0.42, 1.90)
Medicare	8	19.51	0.64	(0.30, 1.36)	0.49	(0.23, 1.05)
None/charity/ unknown	3	7.32	1.31	(0.45, 3.85)	1.52	(0.52, 4.48)
AJCC stage						
0 (DCIS)	10	24.39	1.00	Ref.	1.00	Ref.
I	16	39.02	1.25	(0.61, 2.58)	1.18	(0.56, 2.48)
II-III	15	36.59	0.86	(0.41, 1.80)	0.82	(0.39, 1.69)
Comorbidity type						
Hypertension-only	23	56.10	1.00	Ref.		Ref.
Diabetes and hypertension[2]	18	43.90	1.32	(0.75, 2.32)	1.04	(0.53, 2.05)
Hypertension/diabetes disease severity[3]						
No organ damage	34	82.93	1.00	Ref.	1.00	Ref.
Organ damage	7	17.07	1.45	(0.70, 3.02)	1.58	(0.70, 3.59)
Optimal management after diagnosis						
Yes	22	53.66	1.00	Ref.	1.00	Ref.
No	19	46.34	0.60	(0.34, 1.05)	0.56	(0.31, 1.03)

[1] "All Health Outcomes Measures Met" refers to whether HbA1c, LDL-C, and microalbuminuria test results were optimal for patients with diabetes; and whether or not LDL test result and blood pressure measurement were optimal for patients with hypertension-only. This variable is dichotomized as: all health outcomes measures met or not all measures met.

[2] Patients with diabetes-only (without hypertension) (n=8) were included.
[3] Disease severity from diabetes or hypertension; or if patient has both, then highest severity used.

EXAMINING MEDICAL PROVIDERS' INVOLVEMENT IN CHRONIC DISEASE MANAGEMENT DURING BREAST CANCER CARE

By

MICHELLE DOOSE

Chapter 2 of 3 of dissertation entitled

EXAMINING THE MULTILEVEL INFLUENCES ON DIABETES AND HYPERTENSION CLINICAL CARE MANAGEMENT AMONG BREAST CANCER PATIENTS

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Written under the direction of

Elisa V. Bandera, MD, PhD and Jennifer Tsui, PhD, MPH

ABSTRACT OF CHAPTER 2 OF 3

Examining Medical Providers' Involvement in Chronic Disease Management during Breast Cancer Care

By MICHELLE DOOSE

Dissertation Directors:

Elisa V. Bandera, MD, PhD and Jennifer Tsui, PhD, MPH

Background: Co-managing both breast cancer and other chronic illnesses requires a coordinated team of medical providers. Shared care between cancer specialists, primary care providers, and comorbidity specialists may lead to improved quality of care and health outcomes. **Objective:** To examine the relationship between shared care on diabetes and hypertension clinical care management and health outcomes after the breast cancer diagnosis. **Methods:** We used a prospective cohort of African American breast cancer survivors diagnosed between 2012 and 2016 to examine clinical care management of diabetes and hypertension at the provider level (N=274). Clinical care management measures were reported by type of provider who ordered the test or made the referral. The median day from breast cancer diagnosis to provider visit and to the order of test/referral were reported. The likelihood of receiving all clinical care management measures and achieving all health outcomes after a breast cancer diagnosis were compared by type of physician team (shared care

or not) using binomial regression models. **Results:** 90% of participants received shared care during breast cancer care. Participants with shared care were five times more likely to have all clinical care measures met compared with participants who did not have shared care (that is, they only saw cancer specialists; aRR: 5.07; 95% CI: 1.47, 17.51). Type of physician team was not associated with having met all health outcomes (aRR: 4.32; 95% CI: 0.57, 32.66). **Conclusions:** Our findings suggest that shared care may be associated with high-quality care for diabetes and hypertension during breast cancer care.

EXAMINING MEDICAL PROVIDERS' INVOLVEMENT IN CHRONIC DISEASE MANAGEMENT DURING BREAST CANCER CARE

INTRODUCTION

In 2019, an estimated 268,600 women will be diagnosed with breast cancer, of which 50% will have a co-occurring health condition at diagnosis.[1] Having a chronic condition can limit breast cancer treatment options and breast cancer treatment can exacerbate current chronic illnesses.[2-4] Co-managing both breast cancer and comorbidities requires a comprehensive, coordinated team of medical providers, with the patient at the center of treatment decisions. Given that patients often have a longer relationship with their primary care provider than with their new cancer specialist,[5,6] primary care providers may play an important role for managing comorbidities during breast cancer treatment.

Traditionally, the role of primary care providers includes the prevention, detection, and survivorship phases of the cancer care continuum, with little acknowledgement of their roles during cancer treatment.[7,8] A survey among primary care physicians and oncologists found that over two-thirds of primary care physicians report actively assisting patients in determining their initial cancer treatment, and almost a third of oncologists report actively managing their patients' comorbidities.[9] Another survey within five hospitals found that 88% of primary care providers report being involved during the cancer diagnosis, and 44% report being involved during active treatment.[10] A recent study evaluating

primary care physicians' involvement during cancer care demonstrated that Medicare breast cancer patients who reported greater primary care interaction had lower all-cause mortality and cancer-specific mortality.[11] Qualitative studies have shown that primary care providers are willing to be involved in cancer care.[12-14] Yet, there exists the belief that once the primary care provider refers the patient to the oncologist, the oncologist will assume all non-cancer care and the cancer diagnosis will supersede all other health problems; this belief is referred to in the literature as "cancer exceptionalism."[14,15]

Overall, there remains limited understanding of medical providers' involvement in chronic disease management during breast cancer treatment and whether a team of medical providers is associated with better clinical care and health outcomes. This team of medical providers providing shared care, also known as team-based or collaborative care, may include cancer specialists (e.g., medical, surgical, and/or radiation oncologists), primary care providers (e.g., internal medicine, family medicine), and other medical specialists (e.g., endocrinologists, cardiologists, nephrologists) jointly participating in the patient's care.[16-18] Since the 1980s, research examined shared care of diabetes between primary care physicians and hospital specialists.[19] These studies, including randomized controlled trials (RCTs), demonstrated that shared care improved care coordination and patient outcomes (e.g., morbidity, mortality).[19-24]

Limited studies of team-based care across the cancer care continuum demonstrated improved symptom management, treatment initiation, and adherence, yet none of these studies were conducted among breast cancer

patients during active treatment.[21,25,26] Most of the literature on the shared care model focus on the survivorship phase of care. For example, Zhao et al. systematic review of the effectiveness of shared care defined shared care as a "formal interaction between primary care and secondary care." The multisite RCT entitled "Shared care of Colorectal cancer survivors" defined the shared care intervention group as receiving alternating visits between cancer specialists and primary care physicians.[27] Another study considered shared care when the cancer patient was referred to the palliative care team.[26] Two studies have found that 30–50% of breast cancer patients reported shared care during breast cancer care.[28,29] African American breast cancer patients and patients with comorbidities were more likely to report primary care involvement in breast cancer care compared with White women and patients with no comorbidities.[28] Insurance type at treatment was also found to be associated with shared care.[29]

Given the lack of empirical studies on medical providers' involvement in chronic disease management during breast cancer care, we sought to examine whether shared care was associated with diabetes and hypertension clinical care management and health outcomes after the breast cancer diagnosis. We hypothesized that participants who only see a cancer specialist after breast cancer diagnosis will be less likely to 1) receive diabetes and hypertension clinical care management in the 12 months post-diagnosis, and 2) have optimal diabetes and hypertension health outcomes in the 12 months post-diagnosis, compared with participants who have shared care (i.e., care provided by cancer

specialist, primary care provider, and/or a medical specialist), after controlling for patient-level factors.

MATERIALS AND METHODS

Data Source and Study Population

The Women's Circle of Health Follow-Up Study (WCHFS) is an ongoing, prospective study among African American women diagnosed with breast cancer in ten counties in New Jersey. The study population includes women who consented after February 2014 to have their medical records requested from medical providers participating in comorbid care. Previously only medical records were requested from medical providers participating in breast cancer care. Our study population (N=563) only includes participants whose medical records were abstracted for breast cancer information through July 2018. These women were diagnosed with breast cancer between 2012 and 2016.

We restricted our study sample for this analysis to breast cancer participants who had a clinical diagnosis of diabetes or hypertension at least 12 months prior to breast cancer diagnosis. For a participant to be eligible, her medical records had to include a physician documentation of diabetes or hypertension for at least one year prior to the date of breast cancer diagnosis. Inclusion criteria: primary, histologically confirmed non-invasive ductal carcinoma in situ (DCIS) or invasive breast cancer; being 20–75 years old; being able to understand and read English; and providers sent all medical records. Exclusion criteria: Stage IV breast cancer, diabetes or hypertension diagnosed at or after

breast cancer diagnosis; death within one year of breast cancer diagnosis; or provider refused to send medical records.

Procedures

The study procedures have been described in detail in chapter 1. In brief, participants were first identified through the New Jersey State Cancer Registry (NJSCR) using rapid case ascertainment methodology. WCHFS research staff consented participants and obtained medical records releases at an in-person home interview approximately 9-12 months following the breast cancer diagnosis. Data were collected from the home interviews and abstracted from medical records. For this analysis, two abstractors collected additional information related to clinical care management and health outcomes related to diabetes and hypertension. Data at the visit level was abstracted, including: date of visit or test order, name of physician who ordered the test, facility name and location, type of test ordered, and result of test ordered. This study was approved by the Institutional Review Boards at the Rutgers Cancer Institute of New Jersey and Roswell Park Cancer Institute. Written informed consent was obtained from all study participants.

Measures

Outcome Measures – Clinical Care Management and Health Outcomes

Medical records were reviewed and data was abstracted at the visit level, including: date of testing, physician who ordered the test / made a referral /

prescribed medication, facility name and location, type of test / referral / prescription, and result of test ordered. Type of test / referral / prescription included glycated hemoglobin (HbA1c) test, low-density lipoprotein-cholesterol (LDL-C) screening, microalbuminuria testing, referral to nephrologist for treatment of kidney disease, and order for hypertension medication. All available health outcomes for HbA1c and LDL-C measures were averaged per participant from one year after the date of diagnosis. Blood pressure was collected at one time after diagnosis. This is the average blood pressure reading collected by study staff at home interview 9-12 months post diagnosis.

From the data abstracted, binary composite measures were constructed using the “All-or-None” approach. For participants with diabetes, measurements included in the “All-or-None” clinical care measure were HbA1c testing, LDL-C testing, and medical attention for nephropathy; measurements included in the “All-or-None” health outcomes measure were the results of these tests (i.e., HbA1c, LDL-C, and microalbuminuria). For participants with hypertension only, measurements included in the “All-or-None” clinical care measure were lipid screening and prescription for hypertension medication; measurements included in the “All-or-None” health outcomes measure were the results of the LDL-C test and the blood pressure reading. If the patient was *ordered* all measures, then she was considered as having met all clinical care measures. If the patient was not ordered all measures, then she was considered as not having met all measures. The median number of days, including interquartile range (IQR), from diagnosis (i.e., date of biopsy) to first test ordered or first referral made were

examined, along with the type of medical provider who provided the first clinical care management following breast cancer diagnosis.

Main Predictor – Type of Physician Team

Types of physician seen included cancer specialist (e.g., medical oncologist, radiation oncologist, and breast surgeon), primary care physician (e.g., internal medicine, family medicine), and medical specialists related to diabetes or hypertension (e.g., endocrinologist, cardiologist, and nephrologist). In this study, if a participant had a visit with any cancer specialist, primary care provider, or medical specialists, then that provider was considered involved in care regardless of the type of tests ordered or referrals made, including none. We then dichotomized the types of physician into two categories: 1) shared care, where the participant received care from both a cancer specialist and a primary care physician and/or a medical specialist within the 12 months following a breast cancer diagnosis; and 2) not shared care, where the participant received care from only a cancer specialist.

Covariates

Covariates were selected from the conceptual framework derived from the Taplin's Quality of Cancer Care Model, Andersen's Behavioral Model of Health Services Utilization, and Donabedian's Quality-of-Care Model (Appendix I). Patient-level factors were abstracted from medical records, including age at diagnosis, health insurance at diagnosis, American Joint Committee on Cancer

(AJCC) cancer stage from pathology reports, and all comorbidities diagnosed before and after breast cancer diagnosis (type, severity, and year of onset). From the home interviews, participants reported their education level, health insurance status one year prior to diagnosis, annual household income, and all comorbidities (type and date of diagnosis). Health insurance was defined by the following four categories: private insurance only, or coverage by the Veteran's Health Administration only, or in combination with Medicare; Medicaid only or Medicaid in combination with Medicare; Medicare only; and no insurance, charity care, or unknown insurance type. We also accounted for the management of diabetes and/or hypertension before diagnosis (i.e., all clinical care management measures met or not). All missing data were coded as unknown.

Statistical Analysis

Descriptive statistics were generated for provider characteristics of the total population and by comorbid condition. Clinical care management measures were reported by type of provider who ordered the test or made the referral. Given the skewedness of the data, we calculated the median number of days, with IQR, from diagnosis to provider visit, and the median number of days from diagnosis to test order/referral/prescription. The likelihood for the total population of receiving all clinical care management measures and achieving all health outcomes after a breast cancer diagnosis were compared by type of physician team (shared care versus cancer specialist only) using binomial regression models. When the binomial regression fails to converge, the modified Poisson

regression was used to approximate the binomial regression.[30] Relative risks (RR) and 95% confidence intervals (CIs) were reported. P-values less than 0.05 were considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

A total of 274 breast cancer participants with diabetes and/or hypertension were included in the final analytic cohort, of which 90% received shared care in the year following their breast cancer diagnosis: 62% saw a cancer specialist and a primary care provider; 24% saw a cancer specialist, a primary care provider, and a medical specialist; and 4% saw a cancer specialist and a medical specialist. Shared care was statistically associated with meeting all clinical care management measures for diabetes and hypertension, but *not* for achieving all diabetes-related and hypertension-related health outcome measures.

Most (83%) participants saw a primary care provider at least once in the 12 months before diagnosis, and 86% saw their primary care provider at least once in the 12 months after diagnosis (Table 2.1). However, 7% had no primary care visit before or after diagnosis (data not shown). In the year after their breast cancer diagnosis, 12% had at least one primary care visit, 15% had two visits, and 59% had three or more visits (data not shown). There was no difference in the number of participants who had a visit to a primary care provider before or after cancer diagnosis (p=0.19). Likewise, there was no statistical difference in the number of participants who had a visit with a medical specialist before or

after diagnosis (p=0.09). A quarter (24%) had visits to two or more medical providers related to their diabetes or hypertension care one year prior to their breast cancer diagnosis. After diagnosis, 24% saw five or more medical providers; all participants saw a surgeon; 94% saw an oncologist; and 77% saw a radiation oncologist.

We also explored time to medical visits with providers and clinical care measures along with identifying the first provider who ordered tests, referrals, or prescriptions. The median number of days to first primary care visit after breast cancer diagnosis was 42 (IQR: 17-94); to first cardiology visit was 63 days (IQR: 28-166); and to first nephrology visit was 163 days (IQR: 70-210) excluding those without any medical visit (Figure 2.1). For participants with diabetes, the median number of days from diagnosis to first endocrinology visit was 58 days (IQR: 38-111). The median number of days to clinical care are detailed in Table 2.2. Of the participants with diabetes, 83% had an HbA1c ordered by a medical provider of which half had it ordered by the 89th day (IQR: 39-151) after the breast cancer diagnosis. For lipid screening, 78% of the participants with diabetes had the test ordered of which half had it ordered by the 99th day (IQR: 44-170), and 50% of the participants with hypertension only had it ordered of which half had the test ordered by the 135th day (IQR: 50-230) after the breast cancer diagnosis. Most (55-88%) clinical care measures were ordered by a primary care provider (Figure 2.2). Cancer specialists were mostly involved in ordering the first prescription for angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker

(ARB) medications (11%) and LDL-C screening (8%) for participants with diabetes.

Tables 2.3 and 2.4 show the association between shared care and clinical care management and health outcomes after breast cancer diagnosis adjusting for patient-level factors. In the adjusted regression model, participants with shared care were five times more likely to have all clinical care measures met compared with participants who only saw cancer specialists (RR: 5.07; 95% CI: 1.47, 17.51). Type of physician team was not associated with achieving all health outcomes (RR: 4.32; 95% CI: 0.57, 32.66) as well as other patient-level factors adjusted for in the model.

DISCUSSION

Ninety percent of participants had shared care during breast cancer care, which was associated with an increased likelihood of having met all clinical care measures for diabetes and hypertension. The proportion of participants with shared care was significantly higher (90%) in our study population compared with two previous studies among general breast cancer patients and breast and colorectal cancer patients with comorbidities (66% and 62%, respectively).[28,29] The difference may be due to the fact that these two studies used patient-reported data with different demographic populations. In this population of African American women with breast cancer, we did not find that “cancer exceptionalism” existed in that most participants were engaged with their primary care provider following breast cancer diagnosis, and their cancer specialists did not assume all

diabetes- and hypertension-related care. This is the first study to our knowledge to examine the relationship between medical providers' involvement in chronic disease management among minority breast cancer patients. This is important given that the Black-White breast cancer survival disparity may be due in large part to the higher prevalence of comorbidities and disparate access to care and treatment experienced by African American women.[31,32]

We found that a higher proportion of participants had a primary care visit both before and after the breast cancer diagnosis. Primary care providers are also managing most of the clinical care for diabetes and hypertension for the 12 month post-diagnosis. Given the growing demand for diabetes care and the shortage of endocrinologists, 90% of patients with diabetes in the general population are managed by a primary care physician than an endocrinologist.[33,34] Participants in our study were also engaged with primary care early on (within 3 months) after the cancer diagnosis; including chronic disease management. Half of the participants with diabetes had their HbA1c testing and lipid screening ordered within 3 months of diagnosis.

It was surprising that there was no statically significant increase in participants seeing a medical specialist related to their diabetes or hypertension in the year following the breast cancer diagnosis. This null finding may be due to length of observation in that the one-year period is focused on cancer treatment and not the post-treatment, survivorship phase. For participants with diabetes, only 22% had a visit with an endocrinologist and 25% with a cardiologist, and for participants with hypertension only, 16% had a visit with a cardiologist after

breast cancer diagnosis. Retrospective studies of chart reviews found that diabetes care at an endocrinology clinic was superior at delivering quality diabetes care than at primary care clinics.[35,36] Also, a referral to a cardiologist to assess and monitor the risk for cardiotoxicity may have been warranted for this patient population. In fact, the 2019 American College of Cardiology/ American Heart Association Task Force guidelines for the prevention of cardiovascular disease (CVD) explicitly state that "a team-based care approach is recommended for the control of risk factors associated with atherosclerotic cardiovascular disease.[37]" The women in this study are already at increased risk for CVD given their comorbidities and the prevalent risk factors such as obesity and older age. In addition, breast cancer treatment, including radiation, anthracycline, and other chemotherapy agents (e.g., trastuzumab), may place these women at additional risk for CVD.[38] Although the area of cardio-oncology is growing, evidence-based guidelines are missing and should include risk-stratified guidelines to screen and monitor women for cardiotoxicity during treatment and into survivorship.[39]

Strengths and Limitations

The strength of this study is that it is a large cohort of African American breast cancer survivors covering many providers. We also used abstracted medical records instead of relying solely on patient-reported data. However, there are several limitations that should be noted. The small sample size and lack of variation in types of physician team limits the study's power. Also, we only

included care for diabetes and hypertension; other comorbidities and visits with those providers (e.g., pulmonologist) were not examined. We did not examine how shared care impacted cancer care delivery concurrently. Also, we only examined care through the first year following the breast cancer diagnosis and acknowledge that patients may be more engaged with medical specialist in the survivorship phase of care.

Additionally, there is no agreed upon defined of shared care. We considered shared care when the patient had at least one visit with a primary care provider or medical specialist regardless of the medical visit's purpose. One visit may not be indicative of the provider participating in the patient's care compared with multiple visits. Studies are needed to validate the construct of shared care. Providers may be working independently or as a team interdependent on each other to achieve specific patient's care goals and outcomes.[40] Also, we did not examine the underlying care coordination mechanisms that led to improved comorbid clinical care, which warrants further exploration to determine: if providers communicated with one another; if providers explicitly defined each other's roles during treatment; if interoperable medical records facilitated communication, or if shared care was driven by the patient.

In conclusion, most participants in our study are engaged with shared care, and comorbid care by primary care providers continues even after the breast cancer diagnosis. There may be missed opportunities for the delivery of high-quality comorbid care and cancer care when patients are not engaged with

primary care and with medical specialists. These findings are important in that shared care may promote optimal clinical care management for diabetes and hypertension. However, we did not examine if there was a formal delineation of providers' roles or duplication of services. Future research is needed to explore the processes of shared care to determine whether medical providers are performing clinical care independently or via interdependency and teamwork in which providers are communicating to mutually achieve goals and outcomes.[40,41]

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2019. *CA Cancer J Clin* 2019; 69(1): 7-34.
2. Sarfati D, Koczwara B, Jackson C. The Impact of Comorbidity on Cancer and Its Treatment. *CA Cancer J Clin* 2016; 66(4): 337-50.
3. Abdel-Rahman O, Xu Y, Kong S, et al. Impact of Baseline Cardiovascular Comorbidity on Outcomes in Women with Breast Cancer: A Real-World, Population-Based Study. *Clin Breast Cancer.* 2018.
4. Unger JM, Hershman DL, Fleury ME, Vaidya R. Association of Patient Comorbid Conditions with Cancer Clinical Trial Participation. *JAMA Oncol.* 2019.
5. Balogh EP, Ganz PA, Murphy SB, Nass SJ, Ferrell BR, Stovall E. Patient-Centered Cancer Treatment Planning: Improving the Quality of Oncology Care. Summary of an Institute of Medicine Workshop. *The Oncologist.* 2011; 16(12): 1800-5.
6. Del Giudice ME, Grunfeld E, Harvey BJ, Piliotis E, Verma S. Primary Care Physicians' Views of Routine Follow-up Care of Cancer Survivors. *J Clin Oncol.* 2009; 27(20): 3338-45.
7. Nekhlyudov L, O'Malley D M, Hudson SV. Integrating Primary Care Providers in the Care of Cancer Survivors: Gaps in Evidence and Future Opportunities. *Lancet Oncol.* 2017; 18(1): e30-e8.
8. Hudson SV. Continuous Primary Care Is Central to Comprehensive Cancer Care: Are We Ready to Meet Growing Needs? *J Am Board Fam Med.* 2013; 26(6): 623-5.
9. Klabunde CN, Ambs A, Keating NL, et al. The Role of Primary Care Physicians in Cancer Care. *J Gen Intern Med.* 2009; 24(9): 1029-36.
10. Aubin M, Vézina L, Verreault R, et al. Patient, Primary Care Physician and Specialist Expectations of Primary Care Physician Involvement in Cancer Care. *J Gen Intern Med.* 2012; 27(1): 8-15.
11. Roetzheim RG, Ferrante JM, Lee JH, et al. Influence of Primary Care on Breast Cancer Outcomes among Medicare Beneficiaries. *Ann Fam Med.* 2012; 10(5): 401-11.
12. Dossett LA, Hudson JN, Morris AM, et al. The Primary Care Provider (Pcp)-Cancer Specialist Relationship: A Systematic Review and Mixed-Methods Meta-Synthesis. *CA Cancer J Clin.* 2017; 67(2): 156-69.
13. Shen MJ, Binz-Scharf M, D'Agostino T, et al. A Mixed-Methods Examination of Communication between Oncologists and Primary Care Providers among Primary Care Physicians in Underserved Communities. *Cancer.* 2015; 121(6): 908-15.
14. Rubinstein EB, Miller WL, Hudson SV, et al. Cancer Survivorship Care in Advanced Primary Care Practices: A Qualitative Study of Challenges and Opportunities. *JAMA Intern Med.* 2017; 177(12): 1726-32.
15. Weiner J. Precision Medicine Meets Cancer Exceptionalism. 2017; https://ldi.upenn.edu/healthpolicysense/precision-medicine-meets-cancer-exceptionalism. Accessed December 26, 2017.

16. Sada Y, Street RL, Singh H, Shada R, Naik AD. Primary Care and Communication in Shared Cancer Care: A Qualitative Study. *Am J Manag Care.* 2011; 17(4): 259-65.
17. O'Toole E, Step MM, Engelhardt K, Lewis S, Rose JH. The Role of Primary Care Physicians in Advanced Cancer Care: Perspectives of Older Patients and Their Oncologists. *J Am Geriatr Soc.* 2009; 57 Suppl 2: S265-8.
18. Oeffinger KC, McCabe MS. Models for Delivering Survivorship Care. *J Clin Oncol.* 2006; 24(32): 5117-24.
19. Greenhalgh PM. Shared Care for Diabetes. A Systematic Review. *Occas Pap R Coll Gen Pract.* 1994; (67): i-viii, 1-35.
20. Hickman M, Drummond N, Grimshaw J. A Taxonomy of Shared Care for Chronic Disease. *J Public Health Med.* 1994; 16(4): 447-54.
21. Bosch M, Faber MJ, Cruijsberg J, et al. Review Article: Effectiveness of Patient Care Teams and the Role of Clinical Expertise and Coordination: A Literature Review. *Med Care Res Rev.* 2009; 66(6 Suppl): 5s-35s.
22. Griffin S. Diabetes Care in General Practice: Meta-Analysis of Randomised Control Trials. *BMJ.* 1998; 317(7155): 390-6.
23. Shojania KG, Ranji SR, McDonald KM, et al. Effects of Quality Improvement Strategies for Type 2 Diabetes on Glycemic Control: A Meta-Regression Analysis. *JAMA.* 2006; 296(4): 427-40.
24. Walsh JME, McDonald KM, Shojania KG, et al. Quality Improvement Strategies for Hypertension Management: A Systematic Review. *Medical Care.* 2006; 44(7): 646-57.
25. Taplin SH, Weaver S, Salas E, et al. Reviewing Cancer Care Team Effectiveness. *J Oncol Pract.* 2015; 11(3): 239-46.
26. Jack B, Hillier V, Williams A, Oldham J. Hospital Based Palliative Care Teams Improve the Symptoms of Cancer Patients. *Palliat Med.* 2003; 17(6): 498-502.
27. Jefford M, Emery J, Grunfeld E, et al. Score: Shared Care of Colorectal Cancer Survivors: Protocol for a Randomised Controlled Trial. *Trials.* 2017; 18(1): 506-.
28. Wallner LP, Abrahamse P, Uppal JK, et al. Involvement of Primary Care Physicians in the Decision Making and Care of Patients with Breast Cancer. *J Clin Oncol.* 2016; 34(33): 3969-75.
29. Doose M, McGee-Avila J, Stroup AM, et al. Shared Care During Breast and Colorectal Cancer Treatment: Is It Associated with Patient-Reported Care Quality? *J Healthc Qual.* 2019.
30. Zou G. A Modified Poisson Regression Approach to Prospective Studies with Binary Data. *Am J Epidemiol.* 2004; 159(7): 702-6.
31. Tammemagi C, Nerenz D, Neslund-Dudas C, Feldkamp C, Nathanson D. Comorbidity and Survival Disparities among Black and White Patients with Breast Cancer. *JAMA.* 2005; 294(14): 1765-72.
32. Institute of Medicine Committee on U, Eliminating R, Ethnic Disparities in Health C. In: Smedley BD, Stith AY, Nelson AR, eds. *Unequal Treatment:*

Confronting Racial and Ethnic Disparities in Health Care. Washington (DC): National Academies Press; 2003.

33. Shrivastav M, Gibson W, Shrivastav R, et al. Type 2 Diabetes Management in Primary Care: The Role of Retrospective, Professional Continuous Glucose Monitoring. *Diabetes Spectrum.* 2018; 31(3): 279.
34. Davidson JA. The Increasing Role of Primary Care Physicians in Caring for Patients with Type 2 Diabetes Mellitus. *Mayo Clinic proceedings.* 2010; 85(12 Suppl): S3-S4.
35. Leinung MC, Gianoukakis AG, Lee DW, Jeronis SL, Desemone J. Comparison of Diabetes Care Provided by an Endocrinology Clinic and a Primary-Care Clinic. *Endocr Pract.* 2000; 6(5): 361-6.
36. Ho M, Marger M, Beart J, Yip I, Shekelle P. Is the Quality of Diabetes Care Better in a Diabetes Clinic or in a General Medicine Clinic? *Diabetes Care.* 1997; 20(4): 472-5.
37. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 Acc/Aha Guideline on the Primary Prevention of Cardiovascular Disease. *Circulation.* 2019: Cir0000000000000678.
38. Mehta LS, Watson KE, Barac A, et al. Cardiovascular Disease and Breast Cancer: Where These Entities Intersect: A Scientific Statement from the American Heart Association. *Circulation.* 2018; 137(8): e30-e66.
39. Xie Y, Collins WJ, Audeh MW, et al. Breast Cancer Survivorship and Cardiovascular Disease: Emerging Approaches in Cardio-Oncology. *Curr Treat Options Cardiovasc Med.* 2015; 17(12): 60-.
40. Taplin SH, Weaver S, Chollette V, et al. Teams and Teamwork During a Cancer Diagnosis: Interdependency within and between Teams. *J Oncol Pract.* 2015; 11(3): 231-8.
41. Kosty MP, Bruinooge SS, Cox JV. Intentional Approach to Team-Based Oncology Care: Evidence-Based Teamwork to Improve Collaboration and Patient Engagement. *J Oncol Pract.* 2015; 11(3): 247-8.

TABLES AND FIGURES

Table 2.1. Provider characteristics among study participants (N=274)

	Participants with diabetes and hypertension[1]		Participants with hypertension only		Total participants	
	n=102		n=172		N=274	
	n	%	n	%	n	%
Before breast cancer diagnosis						
Medical provider seen[2]						
PCP	87	85.29	140	81.40	227	82.85
Endocrinologist	16	15.69	-	-	-	-
Cardiologist	23	22.55	22	12.79	45	16.42
Nephrologist	3	2.94	6	3.49	9	3.28
Podiatrist	6	5.88	-	-	-	-
Eye doctor	12	11.76	-	-	-	-
Number of providers seen[3]						
0	6	5.88	27	15.70	33	12.04
1	53	51.96	123	71.51	176	64.23
2 or more	43	42.16	22	12.79	64	23.72
Type of physician team[4]						
None	8	7.84	27	15.70	35	12.77
PCP only	57	55.88	118	68.60	175	63.87
Medical specialist only	7	6.86	5	2.91	12	4.38
PCP and medical specialist	30	29.41	22	12.79	52	18.98
After breast cancer diagnosis						
Medical provider seen[2]						
Surgeon	102	100.00	172	100.00	274	100.00
Oncologist	95	93.14	163	94.77	258	94.16
Radiation oncologist	75	73.53	135	78.49	210	76.64
PCP	88	86.27	148	86.05	236	86.13
Endocrinologist	22	21.57	-	-	-	-
Cardiologist	26	25.49	27	15.70	53	19.34
Nephrologist	9	8.82	5	2.91	14	5.11
Podiatrist	8	7.84	-	-	-	-
Eye doctor	10	9.80	-	-	-	-
Number of providers seen[3]						
1	0	0.00	0	0.00	0	0.00
2	4	3.92	12	6.98	16	5.84
3	16	15.69	40	23.26	56	20.44
4	42	41.18	96	55.81	138	50.36
5 or more	40	39.22	24	13.95	64	23.36
Type of physician team[4]						

Cancer specialist only[5]	5	4.90	22	12.79	27	9.85
PCP and cancer specialist	51	50.00	120	69.77	171	62.41
Medical specialist and cancer specialist	9	8.82	2	1.16	11	4.01
PCP, medical specialist, and cancer specialist	37	36.27	28	16.28	65	23.72

Abbreviation: PCP, Primary care provider

[1] Most diabetic patients (92%) also have hypertension.

[2] At least one visit with provider between date of diagnosis and one year from date of diagnosis.

[3] Number of providers includes endocrinologist, cardiologist, and nephrologist before cancer diagnosis and includes medical oncologist, radiation oncologist, and breast surgeon after the cancer diagnosis.

[4] Medical specialist includes endocrinologist, cardiologist, and nephrologist only.

[5] Cancer specialist includes medical oncologist, radiation oncologist, and breast surgeon only.

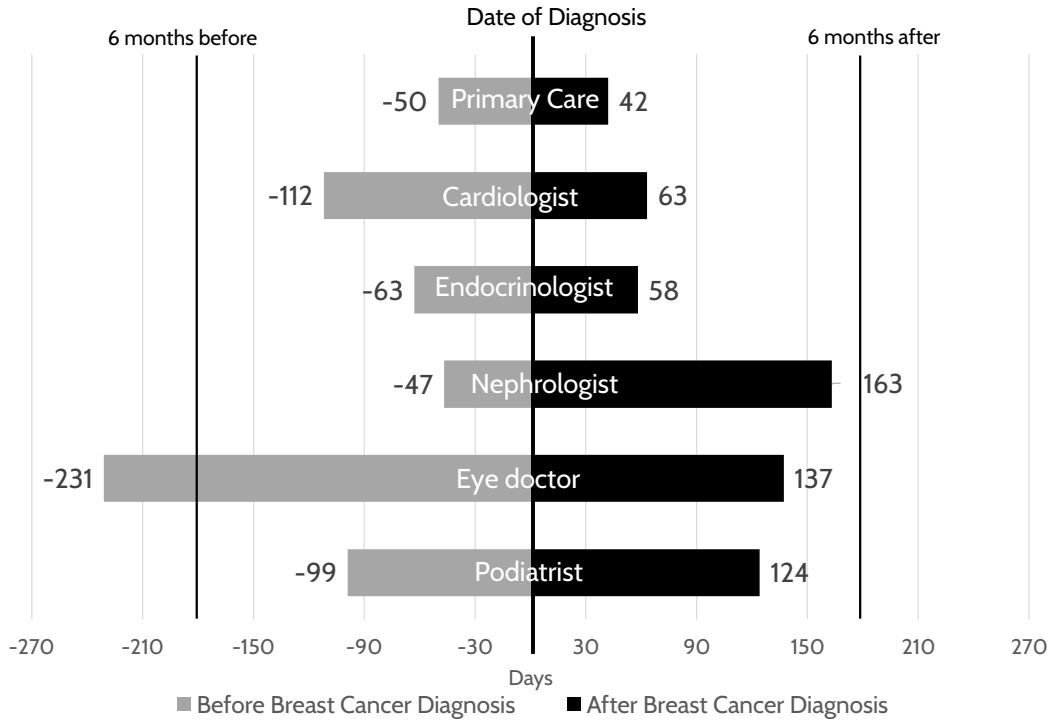


Figure 2.1. Median Number of Days between Last Provider Visit and Breast Cancer Diagnosis, and between Breast Cancer Diagnosis and First Provider Visit

Table 2.2. Number of days between clinical care for diabetes and hypertension and breast cancer diagnosis (N=274)

	Before Breast Cancer Diagnosis					After Breast Cancer Diagnosis				
	n	%	Q1 Days	Median days	Q3 Days	n	%	Q1 Days	Median days	Q3 Days
Measures of diabetes care (N=102)										
HbA1c test	82	80.39	25	70	117	85	83.33	39	89	151
LDL-cholesterol screening	83	81.37	33	75	165	80	78.43	44	99	170
Eye exam	36	35.29	38	77	170	32	31.37	108	145	193
Foot exam	23	22.55	41	106	168	31	30.39	66	138	224
Urine test for albumin	48	47.06	42	95	233	48	47.06	92	157	246
Prescribed ACE or ARB meds	46	45.10	34	76	141	46	45.10	43	111	167
Measures of hypertension care (n=174)										
Lipid screening	111	64.53	34	64	136	86	50.00	50	135	230
Prescribed hypertension meds	76	44.19	34	74	231	89	51.74	50	125	197
Urine test for albumin	16	9.30	85	127	171	16	9.30	85	127	171

Abbreviations: ACE, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; Q1, first quartile where 25% of the measures lie below and 75% lie above this day; Q3, third quartile where 75% of the measures lies below and 25% lie above this day.

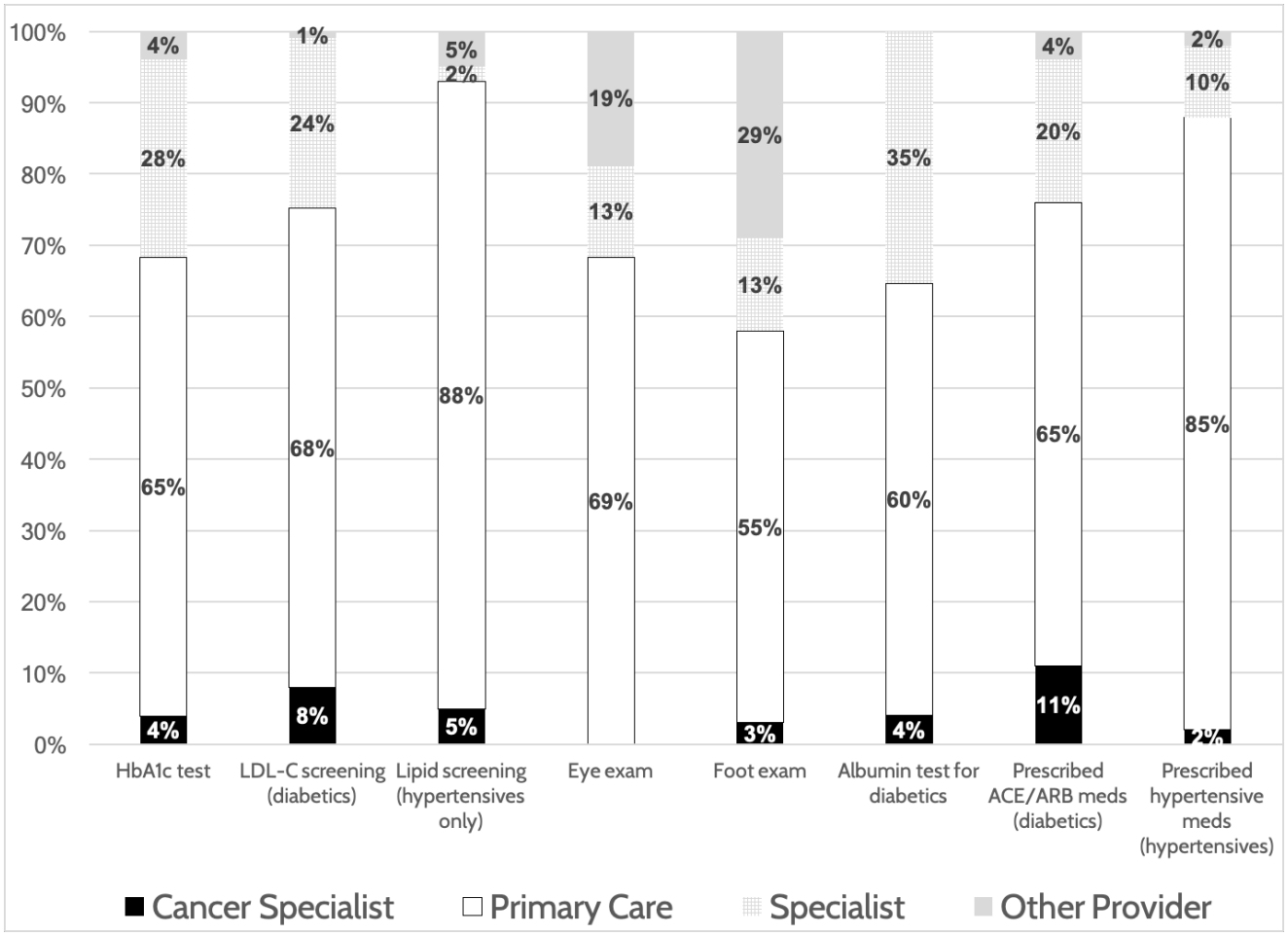


Figure 2.2. Provider Who Managed Diabetes and Hypertension Clinical Care After Breast Cancer Diagnosis[1]
[1]Other providers for eye exam includes ophthalmologists and optometrists and for foot exam include podiatrists.

Table 2.3. Shared care associated with diabetes and hypertension clinical care management (N=274; 112 participants met all clinical care measures)

	All Clinical Care Measures Met[1]					
	n=112		Unadjusted		Adjusted	
	n	%	RR	95% CI	RR	95% CI
Physician involvement						
Cancer specialist only	2	1.79	1.00	Ref.	1.00	Ref.
Shared care[2]	110	98.21	**6.01**	**(1.57, 22.98)**	**5.07**	**(1.47, 17.51)**
Age at diagnosis, years						
65-75	29	25.89	1.00	Ref.	1.00	Ref.
55-64	33	29.46	0.94	(0.68, 1.29)	1.06	(0.78, 1.43)
<55	50	44.64	**0.66**	**(0.45, 0.95)**	0.70	(0.54, 1.15)
Health insurance at diagnosis						
Private	49	43.75	1.00	Ref.	1.00	Ref.
Medicaid	22	19.64	1.26	(0.86, 1.85)	1.12	(0.79, 1.58)
Medicare	37	33.04	1.32	(0.96, 1.83)	1.07	(0.77, 1.49)
None/charity/unknown	4	3.57	0.79	(0.33, 1.86)	0.88	(0.39, 2.01)
AJCC stage						
0 (DCIS)	29	25.89	1.00	Ref.	1.00	Ref.
I	33	29.46	0.89	(0.61, 1.31)	0.94	(0.65, 1.36)
II-III	50	44.64	0.99	(0.70, 1.39)	1.08	(0.78, 1.49)
Comorbidity type						
Hypertension-only	51	45.54	1.00	Ref.		Ref.
Diabetes and hypertension[3]	61	54.46	**2.02**	**(1.52, 2.67)**	**2.08**	**(1.56, 2.76)**
Hypertension/diabetes disease severity[4]						
No organ damage	99	88.39	1.00	Ref.	1.00	Ref.
Organ damage	13	11.61	0.93	(0.59, 1.46)	**0.55**	**(0.35, 0.88)**

[1] "All Clinical Care Measures Met" refers to whether provider ordered for patients with diabetes all of the following: HbA1c test, LDL test, and medical attention for nephropathy, and whether provider ordered for patients with hypertension only an LDL test and prescribed hypertension medication at least once. This variable is dichotomized as: all measures met or not all measures met.
[2] Shared care defined as medical visits with cancer specialist and at least one visit with primary care and/or medical specialist (i.e., cardiologist, endocrinologist, nephrologist) within the year after the breast cancer diagnosis.
[3] Patients with diabetes-only (without hypertension) (n=8) were included.
[4] Disease severity from diabetes or hypertension; or if patient has both, then highest severity used.

Table 2.4. Shared care associated with diabetes and hypertension health outcomes (N=274; 41 participants met all health outcomes)

	All Health Outcomes Measures Met[1]					
	n=41		Unadjusted		Adjusted	
	n	%	RR	95% CI	RR	95% CI
Physician involvement						
Cancer specialist only	1	2.44	1.00	Ref.	1.00	Ref.
Shared care[1]	40	97.56	4.37	(0.63, 30.55)	4.32	(0.57, 32.66)
Age at diagnosis, years						
65-75	14	34.15	1.00	Ref.	1.00	Ref.
55-64	14	34.15	0.96	(0.48, 1.93)	0.80	(0.40, 1.93)
<55	13	31.71	0.94	(0.47, 1.89)	0.78	(0.38, 1.59)
Health insurance at diagnosis						
Private	22	53.66	1.00	Ref.	1.00	Ref.
Medicaid	8	19.51	1.02	(0.49, 2.14)	0.92	(0.44, 1.93)
Medicare	8	19.51	0.64	(0.30, 1.36)	0.50	(0.23, 1.08)
None/charity/ Unknown	3	7.32	1.31	(0.45, 3.85)	1.48	(0.49, 4.44)
AJCC stage						
0 (DCIS)	10	24.39	1.00	Ref.	1.00	Ref.
I	16	39.02	1.25	(0.61, 2.58)	1.18	(0.57, 2.46)
II-III	15	36.59	0.86	(0.41, 1.80)	0.86	(0.42, 1.77)
Comorbidity type						
Hypertension-only	23	56.10	1.00	Ref.	1.00	Ref.
Diabetes and hypertension[3]	18	43.90	1.32	(0.75, 2.32)	1.20	(0.62, 2.34)
Hypertension/diabetes disease severity[4]						
No organ damage	34	82.93	1.00	Ref.		Ref.
Organ damage	7	17.07	1.45	(0.70, 3.02)	1.37	(0.60, 3.12)

[1] All-or-none refers to whether A1c and LDL test results and medical attention for nephropathy were optimal for diabetics and whether LDL test result and blood pressure were optimal for hypertensives. All-or-none variable is dichotomized as all health outcomes measures met or all not met.

[2] Shared care defined as medical visits with cancer specialist and at least one visit with primary care and/or medical specialist (i.e., cardiologist, endocrinologist, nephrologist) within the one year period after the breast cancer diagnosis.
[3] Patients with diabetes-only (without hypertension) (n=8) were included.
[4] Disease severity from diabetes or hypertension; or if patient has both, then highest severity used.

EXPLORING THE HEALTH SYSTEM INFLUENCES ON CHRONIC DISEASE MANAGEMENT DURING BREAST CANCER CARE

By

MICHELLE DOOSE

Chapter 3 of 3 of dissertation entitled

EXAMINING THE MULTILEVEL INFLUENCES ON DIABETES AND HYPERTENSION CLINICAL CARE MANAGEMENT AMONG BREAST CANCER PATIENTS

A dissertation submitted to the

School of Graduate Studies

Rutgers, The State University of New Jersey

In partial fulfillment of the requirements

For the degree of

Doctor of Philosophy

Graduate Program in Public Health

Written under the direction of

Elisa V. Bandera, MD, PhD and Jennifer Tsui, PhD, MPH

ABSTRACT OF CHAPTER 3 OF 3

Exploring the Health System Influences on Chronic Disease Management During Breast Cancer Care

By MICHELLE DOOSE

Dissertation Directors:

Elisa V. Bandera, MD, PhD and Jennifer Tsui, PhD, MPH

Background: Research is lacking on the impact of the health care setting (i.e., delivery systems and accreditation) on quality of care for breast cancer patients with comorbidities especially for racial/ethnic minorities who disproportionally bear the burden of multimorbidities. **Objective:** To explore health system factors associated with diabetes and hypertension clinical care management after breast cancer diagnosis. **Methods:** We used a prospective cohort of African American breast cancer survivors diagnosed between 2012 and 2016 to examine clinical care management of diabetes and hypertension at the health system level (N=274). Clinical care management measures were explored by type of primary care practice (solo practice, part of a health system, etc.) and type of cancer program (part of a teaching hospital, accredited or not, etc.). Using multivariable binomial regressions, the likelihoods of receiving all clinical care management measures for comorbid conditions (diabetes and hypertension) after a breast cancer diagnosis were compared by 1) whether or not the participants used the

same health system for both cancer care and comorbid care, and 2) whether or not the cancer program was accredited by the American College of Surgeons' Commission on Cancer (CoC). **Results:** 18% of participants received both primary care and cancer care within the same health system, and 87% received cancer care at a CoC-accredited cancer program. Participants who did not receive both primary care and cancer care within the same health system were 27% less likely to have all clinical care measures for their comorbid conditions met compared with those participants who received both primary care and cancer care at the same health system (adjusted RR: 0.73; 95% CI: 0.56, 0.97). CoC accreditation of cancer program was not associated with having met all clinical care measures for diabetes and hypertension (adjusted RR: 0.92; 95% CI: 0.59, 1.45). **Conclusions:** Health system was found to be associated with quality comorbid care following the cancer diagnosis while CoC accreditation was not associated. It is important and timely to understand the health system factors that drive quality in patient's care given recent and ongoing reforms of the U.S. health care system.

EXPLORING THE HEALTH SYSTEM INFLUENCES ON CHRONIC DISEASE MANAGEMENT DURING BREAST CANCER CARE

INTRODUCTION

A diagnosis of cancer for patients with chronic illnesses represents a time for care coordination and greater interactions between physicians and health systems. This is especially salient for African American women diagnosed with breast cancer, who are more likely to present with a chronic illness (i.e., hypertension, diabetes) at diagnosis and to die from breast cancer or a comorbidity compared with their White counterparts.[1] Noting that cancer care is not immune to the challenges faced by the fragmented U.S. health care system, the 2013 Institute of Medicine report, *Delivering High-Quality Cancer Care: Charting a New Course for a System in* Crisis, recommends high-quality cancer care that "ensure[s] coordinated and comprehensive patient-centered care," "data collected in cancer research for patients with multiple comorbid conditions," and "reduc[ing] disparities in access to cancer care for underserved populations."[2] It is important to recognize that the health care landscape has been changing and evolving, especially of late with the passing of the Affordable Care Act (ACA) in 2010 and the Medicare Access and CHIP Reauthorization Act of 2015 (MARCA). The direct effects of ACA and MARCA on cancer care delivery includes increased access to care (e.g., health insurance expansion, Medicaid expansion, coverage for pre-existing conditions), new health care

system reform (e.g., Oncology Care Model, Patient-Centered Medical Homes, Accountable Care Organizations, value-based payments), and increased funding for clinical research (e.g., Patient-Centered Outcomes Research Institute).[3,4] Yet, measuring the impact of fragmentation or health system redesign across multiple specialists and non-cancer care settings on the quality of care, health outcomes, costs, and patient experiences are critically missing.[5,6]

A health system factor that may influence the delivery of care is whether or not the cancer specialist and the primary care physician are part of the same health system. The Agency for Healthcare Research and Quality defines a *health system* as "an organization that includes at least one hospital and at least one group of physicians that provides comprehensive care (including primary and specialty care) who are connected with each other and with the hospital through common ownership or joint management."[7] If cancer care and comorbid care are delivered within the same health system, the underlying assumption is that "proximity among providers will improve communication, collaboration, and coordination."[8] Although care within the same health system does not guarantee care coordination, it may increase communication and collaboration between providers who may have an increased opportunity to see each other, and who may see each other's patient notes within the same electronic health record system.

Health systems have been on the rise before the ACA and has accelerated as a result of the ACA.[9,10] Hospital mergers (horizontal consolidation) form health systems as well as when hospitals acquire physician practices (this is

referred to as vertical consolidation).[9] There are over 626 health systems in the U.S. and, among states, New Jersey is in the top quartile with 25 health systems.[11] The percentage of physicians in solo practices has rapidly declined in the past three decades from 41% to 17%.[12] Physicians have also moved from solo or smaller practices into larger medical groups that are independent from hospitals.[13,14] As consolidation continues, oncologists remain in smaller practices, but the number of independent oncology practices has been decreasing.[15] Consolidation provides health systems with negotiation power with insurance companies and provides capital for better care coordination (e.g., interoperable electronic medical records).[10] The downside is that less market competition has resulted in increased health care costs, which are passed on to the patient, and potentially less quality of care.[10,16,17]

Another health system factor that may ensure quality of care between cancer specialists and primary care physicians is the national accreditation of cancer programs. The American College of Surgeons' Commission on Cancer (CoC) is a national standard-setting organization that "recognize[s] cancer care programs for their commitment to providing comprehensive, high-quality, and multidisciplinary patient centered care."[18] At CoC-accredited cancer programs, compliance with National Quality Forum breast cancer care quality measures are high (>90%); however, there remains a paucity of research on the quality of co-managing another chronic disease during cancer care.[19] Breast cancer patients with comorbidities need medical care from primary care and/or medical specialists during breast cancer treatment. Therefore, seeking cancer care at a

CoC-accredited cancer program would, in theory, facilitate care coordination because one of the CoC standards is: “coordination of care among many medical disciplines, including physicians ranging from primary care providers to specialists in all oncology disciplines.[12]” However, the ability of CoC-accredited cancer programs to integrate non-cancer providers (during cancer care) has not be evaluated.

Therefore, to meet this critical gap in the literature, we explored health system factors associated with diabetes and hypertension clinical care management after breast cancer diagnosis. We hypothesized, after controlling for patient-level factors, that:

1) Participants who receive cancer care and comorbid care within the same health system will be more likely to receive diabetes and hypertension clinical care management in the year following the cancer diagnosis compared with participants who receive care at different institutions.
2) Participants who receive cancer care at a CoC-accredited cancer program will be more likely to receive comorbid clinical care management in the year following the cancer diagnosis compared with participants who do not receive care at a CoC-accredited cancer program.

MATERIALS AND METHODS

Data Source and Study Population

The Women’s Circle of Health Follow-Up Study (WCHFS) is an ongoing, prospective study among African American women diagnosed with breast cancer

in ten counties in New Jersey. The study population includes women who consented after February 2014 to have their medical records requested from medical providers participating in comorbid care. Previously only medical records were requested from medical providers participating in breast cancer care. Our study population (N=563) only includes participants whose medical records were abstracted for breast cancer information through July 2018. These women were diagnosed with breast cancer between 2012 and 2016.

We restricted our study sample for analysis to breast cancer participants who had a clinical diagnosis of diabetes or hypertension at least 12 months prior to breast cancer diagnosis. For a participant to be eligible for this analysis, her medical records had to include a physician documentation of diabetes or hypertension for at least one year prior to the date of breast cancer diagnosis. Inclusion criteria: primary, histologically confirmed non-invasive ductal carcinoma in situ (DCIS) or invasive breast cancer; being 20–75 years old; being able to understand and read English; and providers sent all medical records. Exclusion criteria: Stage IV breast cancer, diabetes or hypertension diagnosed at or after breast cancer diagnosis; death within one year of breast cancer diagnosis; or provider refused to send medical records.

Procedures

The study procedures have been described in detail in chapter 1. In brief, participants were first identified through the New Jersey State Cancer Registry (NJSCR) using rapid case ascertainment methodology. WCHFS research staff

consented participants and obtained medical records releases at an in-person home interview approximately 9-12 months following the breast cancer diagnosis. Data were collected from the home interviews and abstracted from medical records. For this analysis, two abstractors collected additional information related to clinical care management and health outcomes related to diabetes and hypertension. Data at the visit level was abstracted, including: date of visit or test order, name of physician who ordered the test, facility name and location (city, state), type of test ordered, and result of test ordered. This study was approved by the Institutional Review Boards at the Rutgers Cancer Institute of New Jersey and Roswell Park Cancer Institute. Written informed consent was obtained from all study participants.

Measures

Outcome Measure – Diabetes and Hypertension Clinical Care Management Measures

We reviewed medical records and abstracted data at the visit level, including: name of physician who ordered the test or made the referral, facility name and location (city, state), test date, type of test ordered, and result of test ordered. We then constructed a binary composite measure for having met all clinical measures (yes/ no), which included:

- For participants with diabetes:
    1. HbA1c testing
    2. LDL-C testing

3. Medical attention for nephropathy, which include microalbuminuria test, referral to nephrologist, and/or participant receiving angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) therapy

- For participants with hypertension only:
  1. Lipid screening
  2. Prescription for hypertension medication, which include prescription for thiazide-type diuretic, calcium channel blocker (CCB), ACE inhibitor, and/or ARB

If the patient was ordered all measures, then she was considered as having met all clinical care measures. A detailed description of measures is in chapter 1.

Main Predictors

We abstracted practice-level information from medical records including name, city, and state of the surgical facility where the first primary breast surgery occurred and name, city, and state of the primary care facility where the patient had her first primary care visit following breast cancer diagnosis.

Same Health System for Both Cancer Care and Comorbid Care

Health systems and affiliated institutions were abstracted from the New Jersey Hospital Association (NJHA) website.[20] We accounted for temporal changes in the health systems (i.e., mergers) using web archives of NJHA (via web.archive.org). If it was unclear whether a facility was part of a health system,

including health systems outside New Jersey, then the facility website and the health system website were reviewed to verify this information. Each surgical facility was coded by the name of its health system or as not part of any health system.

Each primary care facility was then categorized into one of five types of practice:

- Health system – an organization with at least one hospital group and/or one physician group (e.g., Atlantic Health System, The Cooper Health System), including independent hospital organizations (i.e., St. Francis Medical Center, University Hospital)[7,20]
- Medical group – more than one practitioner at one or more practices not affiliated with a hospital health system
- Federally Qualified Health Center (FQHC) – Federally funded community-based health care centers (not a health system for this study)[21,22]
- Solo practice – one provider in a single practice unaffiliated with a health system or organization
- Unknown – not part of a health system; type of practice unknown

Next each primary care facility part of a health system was linked to its respective health system. We created the variable same health system for cancer care and comorbid care when both primary care and surgical facility were part of the same health system. A participant was classified as <u>not</u> receiving care from the same health system if their primary care and their cancer care were

received from different health systems, or if their primary care provider was not part of a health system, or if the facility of either primary care or cancer care was unknown, or if they did not have a primary care visit within one year after their cancer diagnosis.

Commission on Cancer Accreditation

We abstracted CoC accreditation status including type of CoC program from the 2017 American College of Surgeons Commission on Cancer website.[23] CoC accreditation status (yes/no) was assigned to each surgical facility (i.e., hospital) where the primary breast surgery occurred. If the surgical facility name was unknown, then CoC accreditation status was coded as no. Four mutually exclusive accreditation categories, which are assigned by the CoC based on "type of facility, program structure, services provided, and the number of cases accessioned each year,"[18] include:

- National Cancer Institute (NCI)–designated Comprehensive Cancer Center Program: full range of services across the cancer care continuum available onsite
- Academic Comprehensive Cancer Program: participates in postgraduate medical education; 500 newly diagnosed cancer cases each year; full range of services on-site or by referral
- Comprehensive Community Cancer Program: 500 newly diagnosed cancer cases each year; full range of services on-site or by referral

- Community Cancer Program: 100-500 newly diagnosed cancer cases each year; portion of services by referral
- Not a CoC-accredited Cancer Program (including unknowns)

If a surgical facility was part of an NCI-designated or Academic Comprehensive Cancer Program, then it was classified as a “teaching hospital”; all other cancer programs were classified as non-teaching.

Covariates

Covariates were selected from the conceptual framework derived from the Taplin’s Quality of Cancer Care Model, Andersen's Behavioral Model of Health Services Utilization and Donabedian’s Quality-of-Care Model (Appendix I). Patient-level factors were abstracted from medical records, including age at diagnosis, health insurance at diagnosis, American Joint Committee on Cancer (AJCC) cancer stage from pathology reports, and all comorbidities diagnosed before and after breast cancer diagnosis (type, severity, and year of onset). From the home interviews, participants reported their education level, health insurance status one year prior to diagnosis, annual household income, and all comorbidities (type and date of onset). Health insurance was defined by the following four categories: private insurance only, or coverage by the Veteran’s Health Administration only, or in combination with Medicare; Medicaid only or Medicaid in combination with Medicare; Medicare only; and no insurance, charity care, or unknown insurance type. We also accounted for the management of

diabetes and hypertension before diagnosis (i.e., all clinical care management measures met or not). All missing data were coded as unknown.

Statistical Analysis

Statistics were generated to describe health system factors of the total population and by comorbid condition. Clinical care management measures were reported by type of primary care practice and type of cancer program. Using a multivariable binomial regression model, the likelihood of receiving all clinical care management measures after a breast cancer diagnosis were compared by 1) same health system for cancer care and comorbid care, and 2) CoC accreditation of cancer program. Relative risks (RR) were reported along with 95% confidence intervals (CIs). Associations with p-values less than 0.05 were considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

A total of 274 breast cancer participants with diabetes or hypertension were included in the final analytic cohort, of which 18% received both primary care and cancer care within the same health system (Table 3.1). We found that participants who received both primary care and cancer care within the same health system were more likely to have all clinical care measures met compared with those participants who sought care at separate institutions. CoC

accreditation of cancer program was not associated with having all clinical care measures met (Table 3.3).

Participants received primary care at a variety of practice settings: 30% health system, 27% medical group, 7% FQHC, and 20% solo practice (Table 3.1). All participants received their first primary breast surgery at a hospital, either affiliated with a health system (78%), independent hospital (19%), or unknown (3%) (data not shown). The majority (87%) of surgical facilities were CoC-accredited, of which there are 42 CoC accredited cancer programs in New Jersey. In New Jersey, there are 11 Academic Comprehensive Cancer Programs, 20 Comprehensive Community Cancer Programs, 10 Community Cancer Programs, and 1 NCI-designated Comprehensive Cancer Center Program.[18] In our study, 42% of participants received cancer care at an Academic Comprehensive Cancer Program followed by 29% at a Comprehensive Community Cancer Program, 5% at a Community Cancer Program, and 11% at a NCI-designated Comprehensive Cancer Center Program (Table 3.1).

Bivariate associations between type of primary care practice and type of cancer programs were also explored (Table 3.2). Participants whose primary care was at a solo practice were 37% less likely to have all clinical care measures met compared with participants whose primary care was at a practice affiliated with a health system (RR: 0.63; 95% CI: 0.41, 0.97). There were no differences by other primary care practice types or by type of cancer program. In the multivariable model (Table 3.3), participants whose primary care and cancer

care were not part of the same health system were 27% less likely to have all clinical care measures met after adjusting for age, health insurance, education, annual household income, comorbidity type, optimal care management before diagnosis, and CoC accreditation of cancer program (RR: 0.73; 95% CI: 0.56, 0.97). When we re-ran the same model omitting participants without any primary care visits after breast cancer diagnosis (N=236), our results were attenuated (adjusted RR: 0.76; 95% CI: 0.57, 1.01). There was no difference in having all clinical care measures met by CoC accreditation status in the multivariable model (RR: 0.92; 95%: 0.59, 1.45).

DISCUSSION

We observed participants receiving primary care during breast cancer treatment at a variety of practice settings and those who sought primary care at a solo practice were less likely to receive clinical care management of their diabetes and hypertension compared with patients seeking primary care within a health system. Solo practitioners may be overwhelmed with cancer care (i.e., providing medical clearance, participating in treatment decisions, and managing side effects), and they may not have access to electronic medical records to communicate with the cancer center or these practices are not systematically capturing clinical data in medical records. Given our previous finding that cancer specialists are not managing comorbidities, it is not surprising that type of cancer program was not associated with clinical care management of diabetes and hypertension.

As we hypothesized, we found that participants who received both cancer care and primary care within the same health system were more likely to receive clinical care management for their diabetes and hypertension during breast cancer treatment. To date, other studies show mixed findings regarding the relationship between health systems (or integrated delivery systems) and improved quality of care or health outcomes. For cancer care, integrated delivery systems had marginal benefits for prostate cancer treatment and fewer payment differences compared with non-integrated health delivery systems.[24-26] Future studies will need to examine the approaches and characteristics (i.e., processes of care) of health systems that provide high-quality breast cancer care and comorbid care over a fragmented delivery system, especially for racial/ethnic minorities. These characteristics may include level of integrated care (i.e., coordinated, colocated, integrated), electronic medical records, and accreditation (e.g., National Committee for Quality Assurance Diabetes Recognition Program) among others for non-cancer care.[27-30]

We found that CoC accreditation was not associated with clinical care management, which we did not expect to find since accreditation purports to drive quality. Likewise, Yao et al. found that breast and colorectal cancer patients with diabetes treated at CoC-accredited hospitals did not experience improved diabetes care compared with patients treated at non-CoC hospitals.[31] Eighty-seven percent of African American women in our study were more likely to seek care at a CoC-accredited cancer program compared with 64% of breast and colorectal cancer patients in the Yao et al. study who were predominately White,

from the Appalachian region, and covered by Medicare.[31] There is a strong perception among leaders at CoC accredited programs that receiving treatment at a CoC-accredited facility improves a patient's cancer care and outcomes.[19] Yet, cancer is not the only chronic condition affecting patients' lives. Given that non-metastatic breast cancer patients are more likely to die from other chronic illnesses than from cancer and given that cancer treatment itself can exacerbate chronic illnesses or create new health issues (i.e., cardiotoxicity),[32] there may be missed opportunities for cancer programs to integrate primary care, especially for the growing population of cancer patients with comorbidities.

Although there is not much empirical research on the impact of the health system environment on quality of comorbid care during breast cancer, there is a growing body of literature on the geographic/spatial access to breast cancer care. Studies have observed that African American women were less likely to receive care at hospitals with greater volume of breast surgery (an indicator of high quality) and African American women selected their breast surgeon based on a physician's referral while White women selected their surgeon based on reputation.[33,34] Institutional variables (i.e., supply of subspecialty care, wait time to surgery) explained more of the variation between breast conserving surgery and mastectomy than patient-level factors (except for age).[35] Breslin et al. found that hospital factors (i.e., hospital patient volume, hospital racial mix) explained 26% of the excess overall mortality experienced by African American women with breast cancer compared with White women.[36] These studies demonstrate, along

with our study, that variation in quality of care exist by health system factors, which seem to disproportionally affect African American breast cancer patients.

The interpretations of our findings should be in the context of the study's limitations. First, we only looked at whether the patient's *primary care* and their *surgical facility* were part of the same health system. Participants may have received most of their diabetes/hypertension care from an endocrinologist or cardiologist or primary care at various practices, which we did not examine if all practice settings were part of the same health system. In addition, we only explored the surgical facility, which represents one place of care in the cancer care continuum. We also recognize that variation exists between the different types of health systems and within the same health system, which may attenuate our results. Also, CoC accreditation status may have changed from 2013 to 2017, when accreditation status was assigned in this study. The strength of our study is that we used a population-based approach in a large area with variation in practice settings for both comorbid care and cancer care. This enhances the external validity of the study to similar health care markets with large minority populations.

In conclusion, it is important to monitor cancer care quality during this evolving period of health care system reform because payers are shifting to value-based payments where hospitals and providers are being paid based on measures of quality and health outcomes.[37] New yet costly therapeutic drugs on the market will continue to drive up breast cancer care costs (one of the highest cost for cancer care), which were estimated to be $16.5 billion in the U.S. in

2010.[38] At the same time, the diverse cancer patient population is presenting with more complex health and social needs that is burdensome to the health care system.[4,37,39] Key areas of future work includes developing metrics and implementing system level strategies that promote high-quality cancer care and comorbid care concurrently for the breast cancer population with multiple comorbid conditions while reducing disparities in cancer care for racial/ethnic minorities and other underserved populations.

REFERENCES

1. Tammemagi C, Nerenz D, Neslund-Dudas C, Feldkamp C, Nathanson D. Comorbidity and Survival Disparities among Black and White Patients with Breast Cancer. *JAMA.* 2005; 294(14): 1765-72.
2. Institute of Medicine. *Delivering High-Quality Cancer Care: Charting a New Course for a System in Crisis.* Washington, DC: The National Academies Press; 2013.
3. Brooks GA, Hoverman JR, Colla CH. The Affordable Care Act and Cancer Care Delivery. *Cancer J.* 2017; 23(3): 163-7.
4. Findlay S. *Implementing Macra.* Health Affairs Policy Brief;2017.
5. Spinks T, Ganz PA, Sledge GW, Jr., et al. Delivering High-Quality Cancer Care: The Critical Role of Quality Measurement. *Healthcare (Amsterdam, Netherlands).* 2014; 2(1): 53-62.
6. Institute of Medicine Committee on Quality of Health Care in A. *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington (DC): National Academies Press (US); 2001.
7. Agency for Healthcare Research & Quality. Defining Health Systems. 2017; https://www.ahrq.gov/chsp/chsp-reports/resources-for-understanding-health-systems/defining-health-systems.html. Accessed February 23, 2019.
8. Elrashidi MY, Mohammed K, Bora PR, et al. Co-Located Specialty Care within Primary Care Practice Settings: A Systematic Review and Meta-Analysis. *Healthcare.* 2018; 6(1): 52-66.
9. Cuellar AE, Gertler PJ. Trends in Hospital Consolidation: The Formation of Local Systems. *Health Affairs.* 2003; 22(6): 77-87.
10. Gaynor M, Town R. *The Impact of Hospital Consolidation.* Robert Wood Johnson Foundation;2012.
11. Agency for Healthcare Research & Quality. Variation in Health System Characteristics across States, 2016. 2017; https://www.ahrq.gov/sites/default/files/wysiwyg/variation-in-health-system-characteristics-across-states-2016v2.pdf. Accessed February 21, 2019.
12. Squires D, Blumenthal D. Do Small Physician Practices Have a Future? 2016; https://www.commonwealthfund.org/blog/2016/do-small-physician-practices-have-future. Accessed February 21, 2019.
13. Welch WP, Cuellar AE, Stearns SC, Bindman AB. Proportion of Physicians in Large Group Practices Continued to Grow in 2009-11. *Health Aff (Millwood).* 2013; 32(9): 1659-66.
14. Muhlestein DB, Smith NJ. Physician Consolidation: Rapid Movement from Small to Large Group Practices, 2013-15. *Health Aff (Millwood).* 2016; 35(9): 1638-42.
15. Kirkwood MK, Hanley A, Bruinooge SS, et al. The State of Oncology Practice in America, 2018: Results of the Asco Practice Census Survey. *J Oncol Pract.* 2018; 14(7): e412-e20.

16. Abelson R. When Hospitals Merge to Save Money, Patients Often Pay More. *The New York Times.* November 14, 2018.
17. Capps C, Dranove D. Hospital Consolidation and Negotiated Ppo Prices. *Health Affairs.* 2004; 23(2): 175-81.
18. American College of Surgeons, Commison on Cancer. *Cancer Program Standards: Ensuring Patient-Centered Care.* American College of Surgeons;2016.
19. Knutson AC, McNamara EJ, McKellar DP, Kaufman CS, Winchester DP. The Role of the American College of Surgeons' Cancer Program Accreditation in Influencing Oncologic Outcomes. *J Surg Oncol.* 2014; 110(5): 611-5.
20. New Jersey Hospital Association. Healthcare System. 2018; http://www.njha.com/membership/list-of-nj-providers/healthcare-systems/. Accessed April 30, 2018.
21. State of New Jersey Department of Health. Federally Qualified Health Center (Fqhcs). 2019; https://www.nj.gov/health/fhs/primarycare/fqhc/. Accessed February 21, 2019.
22. Health Resources and Services Administration. Federally Qualified Health Centers. 2018; https://www.hrsa.gov/opa/eligibility-and-registration/health-centers/fqhc/index.html. Accessed March 6, 2019.
23. American College of Surgeons. Searching for Cancer Centers. 2018; https://www.facs.org/search/cancer-programs. Accessed June 4, 2018.
24. Hollenbeck BK, Bierlein MJ, Kaufman SR, et al. Implications of Evolving Delivery System Reforms for Prostate Cancer Care. *Am J Manag Care* 2016; 22(9): 569-75.
25. Kaye DR, Min HS, Norton EC, et al. System-Level Health-Care Integration and the Costs of Cancer Care across the Disease Continuum. *J Oncol Pract.* 2018; 14(3): e149-e57.
26. Herrel LA, Kaufman SR, Yan P, et al. Health Care Integration and Quality among Men with Prostate Cancer. *J Urol.* 2017; 197(1): 55-60.
27. Tsai TC, Jha AK. Hospital Consolidation, Competition, and Quality: Is Bigger Necessarily Better?Hospital Consolidation, Competition, and Qualityviewpoint. *JAMA.* 2014; 312(1): 29-30.
28. Blount A. Integrated Primary Care: Organizing the Evidence. *Families, Systems, & Health.* 2003; 21(2): 121-33.
29. National Institute of Mental Health. Integrated Care 2017; https://www.nimh.nih.gov/health/topics/integrated-care/index.shtml.
30. Taplin SH, Anhang Price R, Edwards HM, et al. Introduction: Understanding and Influencing Multilevel Factors across the Cancer Care Continuum. *J Natl Cancer Inst Monogr.* 2012; 2012(44): 2-10.
31. Yao N, Camacho FT, Chukmaitov AS, Fleming ST, Anderson RT. Diabetes Management before and after Cancer Diagnosis: Missed Opportunity. *Ann Transl Med.* 2015; 3(5): 72.
32. Edwards BK, Noone A-M, Mariotto AB, et al. Annual Report to the Nation on the Status of Cancer, 1975-2010, Featuring Prevalence of Comorbidity

and Impact on Survival among Persons with Lung, Colorectal, Breast or Prostate Cancer. *Cancer.* 2014; 120(9): 1290-314.
33. Keating NL, Kouri E, He Y, Weeks JC, Winer EP. Racial Differences in Definitive Breast Cancer Therapy in Older Women: Are They Explained by the Hospitals Where Patients Undergo Surgery? *Med Care.* 2009; 47(7): 765-73.
34. Freedman RA, Kouri EM, West DW, Keating NL. Racial/Ethnic Differences in Patients' Selection of Surgeons and Hospitals for Breast Cancer Surgery. *JAMA Oncology.* 2015; 1(2): 222-30.
35. Greenberg CC, Lipsitz SR, Hughes ME, et al. Institutional Variation in the Surgical Treatment of Breast Cancer: A Study of the Nccn. *Ann Surg.* 2011; 254(2): 339-45.
36. Breslin TM, Morris AM, Gu N, et al. Hospital Factors and Racial Disparities in Mortality after Surgery for Breast and Colon Cancer. *J Clin Oncol.* 2009; 27(24): 3945-50.
37. Nardi EA, McCanney J, Winckworth-Prejsnar K, et al. Redefining Quality Measurement in Cancer Care. *J Natl Compr Canc Netw.* 2018; 16(5): 473-8.
38. Yabroff KR, Lund J, Kepka D, Mariotto A. Economic Burden of Cancer in the United States: Estimates, Projections, and Future Research. *Cancer Epidemiology Biomarkers & Prevention.* 2011; 20(10): 2006-14.
39. Ganz PA. Improving the Quality and Value of Cancer Care: A Work in Progress—the 2016 Joseph V. Simone Award and Lecture. *J Oncol Pract.* 2016; 12(10): 876-9.

TABLES

Table 3.1. Characteristics of health care settings used by study participants (N=274)

Characteristics of Health Care Settings	Participants with diabetes and hypertension n=102		Participants with hypertension only n=172		Total participants N=274	
	n	%	n	%	n	%
Primary care						
Type of primary care practice[1]						
Health system	37	36.27	46	26.74	83	30.29
Medical group	24	23.53	50	29.07	74	27.01
Federally Qualified Health Center	7	6.86	13	7.56	20	7.30
Solo practice	19	18.63	36	20.93	55	20.07
Unknown	1	0.98	3	1.74	4	1.46
No primary care	14	13.73	24	13.95	38	13.87
Cancer care						
Type of cancer program[2]						
NCI-designated Comprehensive Cancer Program	8	7.84	22	12.79	30	10.95
Academic Comprehensive Cancer Program	47	46.08	69	40.12	116	42.34
Comprehensive Community Cancer Program	27	26.47	52	30.23	79	28.83
Community Cancer Program	7	6.86	7	4.07	14	5.11
Not a CoC-accredited cancer program	13	12.75	22	12.79	35	12.77
Is surgical facility a teaching hospital?[3]						
Yes	55	53.92	91	52.91	146	53.28
No	47	46.08	81	47.09	128	46.72

CoC-accredited cancer program[2]						
Yes	89	87.25	150	87.21	239	87.23
No	13	12.75	22	12.79	35	12.77
Both primary care and cancer care						
Are primary care and cancer care both part of same health system?						
Yes	18	17.65	31	18.02	49	17.88
No	84	82.35	141	81.98	225	82.12

Abbreviations: NCI, National Cancer Institute; CoC, Commission on Cancer

[1] Primary care practice identified from first primary care visit following breast cancer diagnosis.

[2] Cancer program accreditation is designated by the American College of Surgeons for the surgical facility.

[3] Teaching hospital includes NCI-designated Comprehensive Cancer Programs and Academic Comprehensive Cancer Programs.

Table 3.2. Type of primary care practice and type of cancer program associated with diabetes and hypertension clinical care management after breast cancer diagnosis (N=274; 112 participants met all clinical care measures)

	All Clinical Care Measures Met[1]				
	n=112				
	n	%	RR	95% CI	P-value
Type of primary care practice[2]					**0.008**
Health system	43	38.39	1.00	Ref.	
Medical group	34	30.36	0.89	(0.64, 1.22)	
Federally Qualified Health Center	9	8.04	0.87	(0.51, 1.47)	
Solo practice	18	16.07	**0.63**	**(0.41, 0.97)**	
Unknown	1	0.89	0.48	(0.08, 2.67)	
No primary care visit	7	6.25	**0.36**	**(0.18, 0.72)**	
Type of cancer program[3]					0.815
NCI-designated Comprehensive Cancer Program	10	8.93	1.00	Ref.	
Academic Comprehensive Cancer Program	48	42.86	1.24	(0.72, 2.15)	
Comprehensive Community Cancer Program	34	30.36	1.29	(0.73, 2.27)	
Community Cancer Program	7	6.25	1.50	(0.72, 3.11)	
Not a CoC-accredited cancer program	13	11.61	1.11	(0.57, 2.17)	

Abbreviations: NCI, National Cancer Institute; CoC, Commission on Cancer

[1] "All Clinical Care Measures Met" refers to whether provider ordered for patients with diabetes all of the following or not: A1c test, LDL test, and medical attention for nephropathy; and whether or not, for patients with hypertension only, provider ordered an LDL test and prescribed hypertension medication at least once in the year following breast cancer diagnosis.

[2] Primary care practice identified from first primary care visit following breast cancer diagnosis.

[3] Cancer program accreditation is designated by the American College of Surgeons for the surgical facility.

Table 3.3. Health system factors associated with diabetes and hypertension clinical care management after breast cancer diagnosis (N=274; 112 participants met all clinical care measures)

	All Clinical Care Measures Met[1]					
	n=112		Unadjusted		Adjusted	
	n	**%**	RR	95% CI	RR	95% CI
Are primary care and cancer care both part of same health system?						
Yes	27	24.11	1.00	Ref.	1.00	Ref.
No	85	75.89	**0.69**	**(0.51, 0.93)**	**0.73**	**(0.56, 0.97)**
CoC-accredited cancer program[2]						
Yes	99	88.39	1.00	Ref.	1.00	Ref.
No	13	11.61	0.90	(0.57, 1.42)	0.92	(0.59, 1.45)
Age at diagnosis, years						
65-75	29	25.89	1.00	Ref.	1.00	Ref.
55-64	33	29.46	0.94	(0.68, 1.29)	0.99	(0.69, 1.44)
<55	50	44.64	**0.66**	**(0.45, 0.95)**	0.84	(0.55, 1.29)
Health insurance at diagnosis						
Private	49	43.75	1.00	Ref.	1.00	Ref.
Medicaid	22	19.64	1.26	(0.86, 1.85)	1.04	(0.66, 1.63)
Medicare	37	33.04	1.32	(0.96, 1.83)	1.01	(0.66, 1.55)
None/charity/unknown	4	3.57	0.79	(0.33, 1.86)	0.86	(0.36, 2.06)
Education						

> High school	62	55.36	1.00	Ref.	1.00	Ref.
≤ High school	50	44.64	1.15	(0.86, 1.53)	0.99	(0.71, 1.40)
Annual household income						
$70,000 or more	23	20.54	1.00	Ref.	1.00	Ref.
$35,000-$69,999	27	24.11	1.32	(0.85, 2.06)	1.11	(0.72, 1.71)
Less than $35,000	55	49.11	1.43	(0.97, 2.12)	1.04	(0.63, 1.72)
Unknown	7	6.25	1.59	(0.85, 2.96)	1.28	(0.64, 2.57)
Comorbidity type						
Hypertension only	51	45.54	1.00	Ref.	1.00	Ref.
Diabetes	61	54.46	**2.02**	**(1.52, 2.67)**	**1.71**	**(1.23, 2.36)**
Did patient receive optimal management before diagnosis?						
Yes	64	57.14	1.00	Ref.	1.00	Ref.
No	48	42.86	**0.59**	**(0.44, 0.79)**	0.76	(0.56, 1.05)

[1] "All Clinical Care Measures Met" refers to whether provider ordered for patients with diabetes all of the following or not: A1c test, LDL test, and medical attention for nephropathy; and whether or not, for patients with hypertension only, provider ordered an LDL test and prescribed hypertension medication at least once in the year following breast cancer diagnosis.

[2] Cancer program accreditation is designated by the American College of Surgeons for the surgical facility.

CONCLUSION

This dissertation evaluated diabetes and hypertension clinical care management among African American women with breast cancer from a multilevel perspective. The findings from this research can be used to inform multilevel interventions at the levels of patient, provider, and practice/ organization. The first chapter found that the prevalence of diabetes and hypertension, diagnosed at least one year prior to the breast cancer diagnosis, was 18% and 47% respectively, among a cohort of African American women with breast cancer recruited from the population-based New Jersey State Cancer Registry. Overall, key clinical care management measures for diabetes and hypertension and related health outcomes *before* breast cancer diagnosis did not differ *after* breast cancer diagnosis. Common clinical care measures ordered by providers were hemoglobin A1c test, lipid screening, medical attention for nephropathy, and prescription for hypertension medications; however, we found that recommended measures of foot exams and eye exams for diabetic participants were not regularly ordered. Optimal clinical care management before the breast cancer diagnosis was associated with optimal clinical care management after diagnosis. Results from this study can be used to inform clinical practice guidelines and interventions for the management of diabetes and hypertension during breast cancer.

Findings from the second chapter showed that most participants saw multiple providers after their breast cancer diagnosis to manage their diabetes and/or hypertension. Participants who received care from cancer specialists and

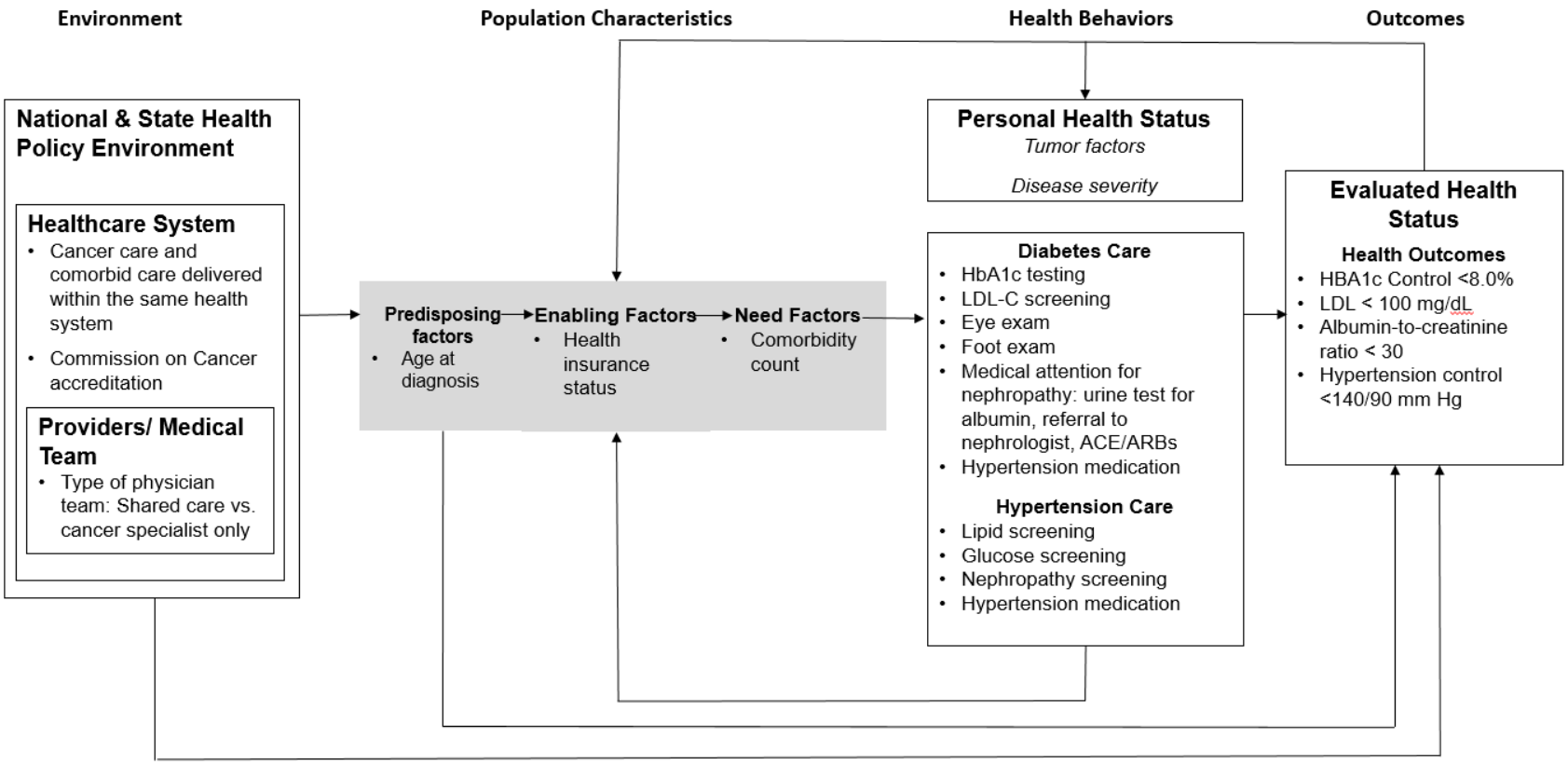
from primary care providers and/or comorbidity specialists were more likely to have all clinical measures met compared with participants who only saw their cancer specialists. “Cancer exceptionalism” is not true for this patient population in that most participants were engaged with primary care and cancer specialists did not assume all non-cancer care. Women in our study are at increased risk for cardiovascular disease from their comorbidities, from prevalent risk factors such as obesity and older age, and now possibly from treatment toxicity from chemotherapy and/or radiation. Therefore, future work is needed to produce evidence-based guidelines to screen for and monitor cardiovascular disease and comorbidities and to implement care coordination approaches including delineating roles of providers involved in shared care during cancer care and into the survivorship phase.

Findings from the third chapter demonstrated that participants who received both cancer care and comorbid care within the same health system were more likely to receive clinical care management for their diabetes and hypertension during breast cancer treatment, while accreditation of the cancer program was not associated with their clinical care management, after adjusting for patient-level factors. The health care landscape is changing and evolving, yet studies remain scarce about the effects of new care delivery models and health system reform on quality of care and health outcomes for the breast cancer population.

In conclusion, we must employ a multilevel perspective to address health equity for African American women with breast cancer and co-occurring diabetes

and hypertension, who disproportionately bear the burden of these diseases. Findings from these studies can be used to identify gaps in care delivery, improve chronic disease management guidelines for breast cancer patients with comorbidities, and inform future research to evaluate health policy, health systems, organizational/practice settings, providers/medical teams, and patient-level factors that influence the delivery of high-quality care and ultimately impact health outcomes.

APPENDIX I. A Conceptual Framework of Patient, Provider, and Health System Level Factors Associated with Diabetes and Hypertension Clinical Care Management among Breast Cancer Patients[1-3]



APPENDIX II. List of Hypertension Medications[4]

Angiotensin converting enzyme (ACE) inhibitors:

- Benazepril (Lotensin)
- Captopril
- Enalapril (Vasotec)
- Fosinopril
- Lisinopril (Prinivil, Zestril)
- Moexipril
- Perindopril (Aceon)
- Quinapril (Accupril)
- Ramipril (Altace)
- Trandolapril (Mavik)

Angiotensin II Receptor Blockers (ARB):

- Azilsartan (Edarbi)
- Candesartan (Atacand)
- Eprosartan
- Irbesartan (Avapro)
- Losartan (Cozaar)
- Olmesartan (Benicar)
- Telmisartan (Micardis)
- Valsartan (Diovan)

Antihypertensive combinations:

- Aliskiren-valsartan
- Amlodipine-benazepril
- Amlodipine-hydrochlorothiazide-valsartan
- Amlodipine-hydrochlorothiazide-olmesartan
- Amlodipine-olmesartan
- Amlodipine-telmisartan
- Amlodipine- perindopril
- Amlodipine-valsartan
- Azilsartan-chlorthalidone
- Benazepril-hydrochlorothiazide
- Candesartan-hydrochlorothiazide
- Captopril-hydrochlorothiazide
- Enalapril-hydrochlorothiazide

- Eprosartan-hydrochlorothiazide
- Fosinopril-hydrochlorothiazide
- Hydrochlorothiazide-irbesartan
- Hydrochlorothiazide-lisinopril
- Hydrochlorothiazide-losartan
- Hydrochlorothiazide-moexipril
- Hydrochlorothiazide-olmesartan
- Hydrochlorothiazide-quinapril
- Hydrochlorothiazide-telmisartan
- Hydrochlorothiazide-valsartan
- Sacubitril-valsartan
- Trandolapril-verapamil

Thiazide-type diuretics:

- Chlorothiazide (Diuril)
- Chlorthalidone
- Hydrochlorothiazide (Microzide)
- Indapamide
- Metolazone
- Bumetanide (Bumex)
- Ethacrynic acid (Edecrin)
- Furosemide (Lasix)
- Torsemide (Demadex)
- Amiloride
- Eplerenone (Inspra)
- Spironolactone (Aldactone)
- Triamterene (Dyrenium)

Calcium channel blockers:

- Amlodipine, Amlodipine Besylate (Norvasc)
- Diltiazem (Cardizem, Tiazac, others)
- Felodipine
- Isradipine
- Nicardipine
- Nifedipine (Adalat CC, Afeditab CR, Procardia)
- Nisoldipine (Sular)
- Verapamil (Calan, Verelan)

REFERENCES

1. Taplin SH, Anhang Price R, Edwards HM, et al. Introduction: Understanding and influencing multilevel factors across the cancer care continuum. *J Natl Cancer Inst Monogr.* 2012;2012(44):2-10.
2. Zapka JG, Taplin SH, Solberg LI, Manos MM. A Framework for Improving the Quality of Cancer Care. *Cancer Epidemiol Biomarkers Prev.* 2003;12(1):4.
3. Andersen RM. Revisiting the behavioral model and access to medical care: does it matter? *J Health Soc Behav.* 1995;36(1):1-10.
4. U.S. Department of Health and Human Services, National Institute of Health, National Heart Lung and Blood Institute. *The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.* Bethesda, MD: National Heart, Lung , and Blood Institute;2004.

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