8-2016

Geographical Location and Stage of Breast Cancer Diagnosis: A Systematic Review of the Literature

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Citation Information

Williams, Faustine; James, Aimee S.; and Jeanetta, Stephen. 2016. Geographical Location and Stage of Breast Cancer Diagnosis: A Systematic Review of the Literature. *Journal of Health Care for the Poor and Underserved*. Vol.27(3). 1357-1383. https://doi.org/10.1353/hpu.2016.0102 ISSN: 1548-6869

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Comments
Errata of article published in *Journal of Health Care for the Poor and Undeserved*, 28(1), February 2017: https://muse.jhu.edu/article/648782

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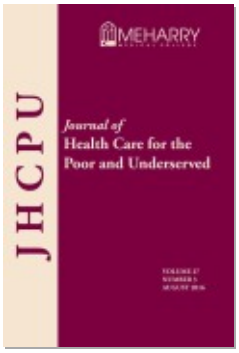

Journal of Health Care for the Poor and Underserved, Volume 27, Number 3, August 2016, pp. 1357-1383 (Article)

Published by Johns Hopkins University Press
DOI: *https://doi.org/10.1353/hpu.2016.0102*

Geographical Location and Stage of Breast Cancer Diagnosis: A Systematic Review of the Literature

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Abstract: **Objective**: To examine systematically the literature on the effect of geographical location variation on breast cancer stage at diagnosis, race/ethnicity, and socioeconomic status. **Methods**. Eight electronic databases were searched using combination of key words. Of the 312 articles retrieved from the search, 36 studies from 12 countries were considered eligible for inclusion. **Results**. This review identified 17 (47%) of 36 studies in which breast cancer patients residing in geographically remote/rural areas had more late-stage diagnosis than urban women. Ten (28%) studies reported higher proportions of women diagnosed with breast cancer resided in urban than rural counties. Nine (25%) studies reported no statistically significant association between place of residence and stage at diagnosis for breast cancer patients residing in rural and urban areas. **Conclusions**. Cancer patients residing in rural and disadvantaged areas were more likely to be diagnosed with distant breast metastasis. Efforts to reduce these inequalities and subsequent mortality are needed.

Key words: Breast neoplasm, staging at diagnosis, rural-urban, rural population, urban population, place of residence.

Except for skin cancer, breast cancer is the most frequent malignancy among women in the United States, affecting women across all racial and ethnic groups. In 2015 it was projected that 231,840 new cases of invasive breast cancer were expected to occur among women in the United States (U.S.), and about 2,350 new cases were expected in men. In addition to invasive breast cancer, 60,290 new cases of in situ breast cancer were expected to occur among women in 2015.[1,2]

Studies have indicated that disparities in access to primary care, especially access to screening services such as mammogram and Papanicolaou smear, exist throughout the United States primarily due to uneven distribution of health facilities.[3,4] Disparities in the prevention and early detection of cancer lead to disparities in cancer outcomes and

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survival. Much of the disparity in mortality can be attributed to the stage of diagnosis at the time of cancer detection. Research shows that certain groups of people, namely those who are poor, less educated, uninsured, and/or immigrants, are more likely to be diagnosed at a later stage of disease, more likely to receive substandard care, and are more likely to die from cancer.[5] Nationally, 61% of White women but only 51% of Black women were diagnosed with breast cancer at the local stage.[6] The five-year survival rate for White women diagnosed with breast cancer between 2002 and 2008 was 90% while the survival rate for Black women was just 78%.[6]

Other studies on cancer survival from cancer in various countries have noted that geographical location is strongly associated with survival and that could also reflect stage at diagnosis and the kind of treatment patients are likely to receive.[7–13] In contrast, some studies have reported that no significant difference exists between breast cancer stage at diagnosis and place of residence or travel time/distance travel to the nearest mammography facility.[14–22] The aim of this review was to examine systematically the literature on the effect of geographical location variation on breast cancer stage at diagnosis, race/ethnicity, and socioeconomic status rather than rural-urban differences in mammography use or risk factors for breast cancer development.

Methods

In the process of identifying studies, searches were conducted in the following bibliographic databases: Academic Search Complete (1984–2013), CINAHL (1982–2013), Compendex and GEOBASE (1969–2013), Medline (1966–2013), PubMed (1951–2013), EMBASE (1947–2013), Cochrane (1993–2013) and Scopus (1960–2013) using key words and phrases. The key words and phrases: *breast neoplasm* or *cancer*, *staging at diagnosis*, *rural-urban*, *rural* po*pulation*, *urban* po*pulation*, or p*lace of residence*. Additionally, we systematically searched the references sections of all articles retrieved to identify additional citation. There was no limitation of publication date in the search; however, the earliest eligible article was published in 1992. Inclusion criteria were studies comparing the differences in breast cancer stage at diagnosis and geographical place of residence, and were published in English. Based on the inclusion criteria, studies that focus solely on access to health care services, influence of socioeconomic status and race on stage at diagnosis, and geographic differences in treatment and/or survival of breast cancer were excluded.

Results

Based on the selection criteria established, 36 out of 312 studies from 12 countries remained eligible.[11,14–49] Figure 1 shows the summary of criteria used for inclusion of eligible studies in this review. Of the eligible papers selected, 23 were from the United States, two each from Australia and New Zealand, and one each from Canada, Denmark, Egypt, Estonia, Italy, Poland, South Africa, Switzerland, and the United Kingdom. Tables 1 and 2 list studies included in this review. Table 1 identifies the type of cancer registry database used and findings, whereas Table 2 focuses on the primary factors addressed and the major conclusions reached by the authors. For the purpose

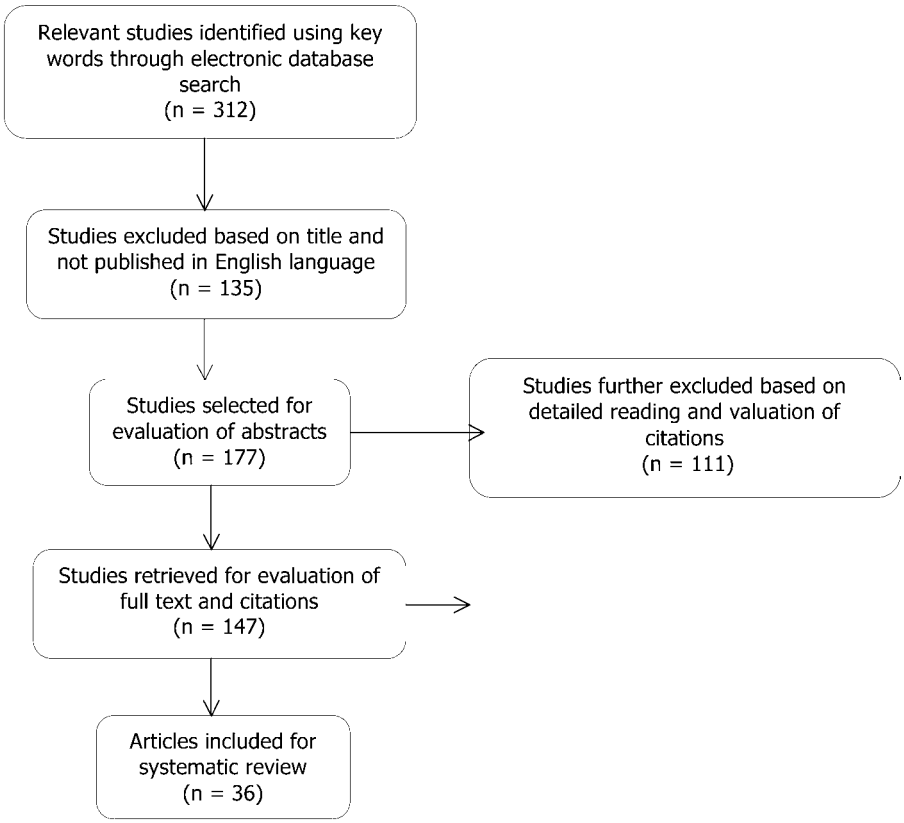

Figure 1. Flow diagram for literature search results and application of eligibility criteria.

of this review, we began analysis by summarizing all of the findings in each study. Second, common themes that emerged in these findings were identified, and finally, the review was structured according to three major general themes. These include: (1) variation by geographic location; (2) variation by race/ethnicity; and (3) variation by socioeconomic status.

Variation by geography or location. Geographic barriers are important for breast cancer patients, especially those who live in rural areas. Over the past decades, numerous studies have confirmed that patients residing in rural and medically underserved areas are more likely to have unstaged tumors and advanced stage breast cancer diagnosis than their urban counterparts.[11,23–38] However, we found inconsistency in the definition of *rural* and/or *urban*. For example, all 23 studies[11,16–21,23,25,26,29–32,34,35,38–40,43–46,49] from the U.S. used different definitions and measurements for rural and urban. Six studies[11,17,18,21,39,40] used the rural urban commuting area (RUCA) codes measurement and definition. The RUCA codes classify all census tracts in the U.S. using measures of population density, urbanization, and daily commuting.[50] The rural urban continuum or Beale code system was used in four studies.[20,23,43,46] Other definitions such as the urban influence code, U.S. Census Bureau rural urban classification, population density, state-specific minor division, ZIP code and census tract, and federally designated medically underserved

Table 1.

DATABASE STUDIES, SAMPLE CHARACTERISTICS, COUNTRY AND PRIMARY FINDING

Author	Database/Source	Sample Population and Data Year	Size *(N)*	Country	Rural-Urban Definition	Primary Finding
Amey et al. 1997 (23)	Florida Cancer Data System and Area Resource File	All women residing in the state of Florida between 1981 and 1989 who were diagnosed with breast cancer	79,946	U.S.A.	Rural Urban Continuum Code (RUCC) classification—Metropolitan and Non-metropolitan counties	Rural black women are diagnosed with breast cancer much later than black urban women or whites of either residence.
Armstrong & Borman 1996 (14)	National Cancer Registry	Persons diagnosed as having cancer of the breast through the National Cancer Registry between 1978 and 1992	20,090	New Zealand	Based on Regional Health Authority regions. Rural centers as population ranging from 10,000 to 30,000 and urban areas as with population greater than 30,000	Study but no significant difference between stage at diagnosis and rural-urban place of residence.
Baade et al. 2011 (24)	Queensland Cancer Registry	Women aged 30–79 years diagnosed as having breast cancer between 1997 and 2006	18,658	Australia	Accessibility/Remoteness index of Australia classification into five areas based on distance to the closet service center (Major City, Inner Regional, Outer Regional, Remote and Very Remote areas)	The rates of advanced breast cancer were significantly higher for women residing in Outer Regional areas (OR 1.13, 95% CI = 1.02, 1.24) and those who lived in the most disadvantaged areas (OR 1.16, 95% CI = 1.02, 1.32).
Barry & Breen 2005 (25)	Surveillance, Epidemiology, and End Results (SEER)	Cancer data from 1989 to 1990	12,395	U.S.A.	Federally designated medically underserved area developed by Health Resources and Services Administration	Residence in an underclass neighborhood or an extremely poor neighborhood also contributes to a late stage diagnosis.
Bennett et al. 2007 (15)	New Zealand Cancer Registry	Women diagnosed with breast cancer between January 1998 and 31 December 2002	11,340	New Zealand	Statistics New Zealand Classification, based on population size. Urban areas: (i) Main urban areas ≥30,000 population, (ii) Secondary urban areas (10–29,999 population, and (iii) Minor urban areas 1000–9999 population. Rural areas <1000 population	Urban/rural residence, however classified, did not have any significant effect on the odds of late stage at diagnosis for women diagnosed with breast cancer in New Zealand. Also no trend to increasing odds with increasing rurality or distance.

(*Continued on p. 1361*)

Table 1. (*continued*)

Author	Database/Source	Sample Population and Data Year	Size (*N*)	Country	Rural-Urban Definition	Primary Finding
Blair et al. 2006 (16)	The California Cancer Registry	Patients with breast, melanoma, and colon cancer from 1988 to 2003	59,615 (breast cancer)	U.S.A.	California Rural Health Commission definition. Rural counties represent a population density of 250 people/less per square mile and no incorporated communities of more than 50,000 people	There was no difference in percentage of patients presenting with early summary stage disease between rural and urban dwellers. For example, in 2003, 70% of urban patients presented with early stage disease and 69% of urban patients were diagnosed with early summary stage breast cancer.
Celaya et al. 2010 (17)	New Hampshire State Cancer Registry	Female residents of New Hampshire diagnosed with breast cancer between January 1, 1998 and December 31, 2004	5,966	U.S.A.	Rural Urban Commuting Area (RUCA) classification scheme. Grouping: urban, large rural, and small rural	No significant association between rural residence and stage of diagnosis was found.
Cho et al. 2011 (26)	Illinois State Cancer Registry in conjunction 1990 and 2000 Census tract	Women diagnosed with breast cancer in Cook County between 1994 and 2003	42,714	U.S.A.	United States (U.S.) Census tract	Residing in poor concentrated immigration neighborhoods was associated with being diagnosed with late breast cancer.
Cuthbertson et al. 2009 (27)	Trent Cancer Registry	Women diagnosed with invasive breast cancer from 1998 to 2006	31,551	U.K.	Primary Care Trust boundaries derived from postcode	Women resident in nine Trent primary care trusts (PCTs) have significant higher risk diagnosis with late stage breast cancer than those resident in Nottingham City PCT.
Dalton et al. 2006 (28)	Danish Breast Cancer Cooperative	Women with a primary invasive breast cancer diagnosed between 1983 and 1999	28,765	Denmark	Degree of urbanicity: capital areas, suburbs, provincial cities and rural areas	There was an urban-rural gradient, with higher risk among rural women (OR 1.10; 95 % CI = 1.02, 1.18) and lower risk among women in the capital suburbs (OR, 0.85; 95% CI = 0.78, 0.93) and capital area (OR, 0.93; 95% CI = 0.84, 1.02).

(*Continued on p. 1362*)

Table 1. (*continued*)

Author	Database/Source	Sample Population and Data Year	Size (*N*)	Country	Rural-Urban Definition	Primary Finding
Dey et al. 2010 (42)	Gharbiah population-based cancer Registry	Women diagnosed with primary breast cancer with known estrogen receptor positive (ER+) or progesterone receptors(PR) status for a period of 6 years (2001–2006)	3,673	Egypt	Central Agency for Public Mobilization and Statistics coding of urban and rural areas. Urban areas consisted of capital cities, and rural consisted of villages surrounding the capital cities	Urban ER+ incidence rate (per 100,000 women) was 2–4 times (IRR = 3.36, 95% CI = 4.84, 2.34) higher than rural incidence rate. ER-incidence rate was 2–3 times (IRR = 1.86, 95% CI = 2.38, 1.45) higher in urban areas than in rural areas.
Elliott et al. 2004 (29)	Lake Superior Rural Cancer Care Project	All eligible cancer cases diagnosed between 1993 and 1997	831	U.S.A.	U.S. Census Bureau rural and urban classification	Urban patients were more likely to be diagnosed at earlier stage than rural.
Ess et al. 2010 (30)	Seven Swiss Population based Cancer Registries	Women diagnosed with invasive breast cancer between January 1, 2003 and December 31, 2005	4,820	Switzerland	Regions - undefined	Considerable differences in the detection and management of breast cancer across all the seven regions with regards to urbanity and affluence.
Friedell et al. 2003 (43)	Kentucky Cancer Registry	Incidence and mortality of breast cancer among women for the period 1995–2000	18,205	U.S.A.	Beale code/Rural Urban Continuum Code counties classification	Using Beale code 0–3 for "urban" and 4–9 for rural, incidence rates for early stage cases are slightly higher in the urban areas. Incidence rates for late stage cases are slightly higher for urban compared to rural areas over the reporting period.
Gregorio et al. 2002 (44)	Connecticut Tumor Registry	Women diagnosed with breast cancer between 1991 to 1995	10,601 invasive and 1,814 *in situ breast cancers*	U.S.A.	Connecticut census block groups	The most probable location of low incidence was rural northeastern Connecticut where risk of disease, relative to elsewhere around the state, was 0.70 (p=.0001); the most probable place of elevated incidence was north central Connecticut where a relative risk of 1.34 (p=.002) was observed. Incidence of *in situ disease was estimated to be significantly high for north central Connecticut (RR = 1.84; p=.0001).*

(*Continued on p. 1363*)

Table 1. (*continued*)

Author	Database/Source	Sample Population and Data Year	Size (*N*)	Country	Rural-Urban Definition	Primary Finding
Hall et al. 2005 (45)	North Carolina Central Cancer Registry	Women with a first case of invasive or in situ breast cancer diagnosed between January 1995 and December 1999	27,989	U.S.A.	Urban Influence Code: (i) Metropolitan, (ii) Non-Metropolitan – adjacent to a metropolitan area, (iii) Non-Metropolitan – non-adjacent to metropolitan area	For white women, incidence rate ratios (IRRs) comparing the most urban with the most rural counties were 1.60 for in situ and 1.18 for invasive cancer. For non-white women, IRRs were 1.27 and 0.99, respectively.
Hausauer et al. 2009 (46)	North American Association of Central Cancer Registries resource	Invasive and in situ breast cancer incidence data for the years 1997 to 2004	475,523 invasive and 111,885 in situ	U.S.A.	2003 U.S. Department of Agriculture nine-point rural/urban codification scheme, which distinguishes counties by population size, degree of urbanization, and adjacency to a metropolitan area	Overall patterns of invasive breast cancer were comparable among women living in both urban and suburban counties but differed for women in rural counties.
Henry et al. 2011 (18)	10 state-wide population based cancer registries (Arkansas, California, Idaho, Iowa, Kentucky, North Carolina, New Hampshire, New York, New Jersey, and Oregon	Women aged 40 years and older, diagnosed between January 1, 2004 and December 31, 2006,	161,619	U.S.A.	Rural Urban Commuting Area codes based on U.S. Census Bureau urbanized area and work commuting patterns. Urban (central places >50,000 population), small town (central places of 10,000–49,000 population), and small rural town (<10,000 population)	Proportion of late stage was nearly identical among women living in small rural towns (31%) compared to women living in urban areas (30%). Rural/urban residence type was not a significant predictor of breast cancer stage at diagnosis.
Higginbotham et al. 2001 (31)	Mississippi State Department of Health Central Cancer Registry	All patients who were diagnosed and/or treated for cancer in 1996	9,685	U.S.A.	U.S. Census Bureau rural urban classification	There was a significant difference between rural and urban residents for stage of disease at initial diagnosis. Secondly, the proportion of tumors unstaged at diagnosis is greater for rural compared to urban residents.
Hoffman et al. 2000 (47)	South African Cancer Registry	Women under the age of 50 diagnosed with breast cancer	485	South Africa	Undefined	The odds of being diagnosed with localized stage breast cancer was more than twice for women in urban areas.

(*Continued on p. 1364*)

Table 1. (*continued*)

Author	Database/Source	Sample Population and Data Year	Size (*N*)	Country	Rural-Urban Definition	Primary Finding
Howe et al. 1992 (32)	Illinois State Cancer Registry	All female breast cancer cases diagnosed in 1986–87	781	U.S.A.	1990 U.S. Census population counts. Rural – population density of <100 persons/square mile and urban 210 persons/square mile	Compared with urban cases, rural cases diagnosed in rural hospitals were less likely to have a staged tumors and more likely to have node dissections.
Huang et al. 2009 (19)	Kentucky Cancer Registry	Female diagnosed with breast cancer between 1999 and 2003	12,322	U.S.A.	Residence in urban/rural counties was categorized as metropolitan or nonmetropolitan	There was no significant association between rural/urban residence and poverty at Census tract level.
Innos et al. 2011 (33)	Estonia Cancer Registry	Female breast cancer cases reported in 1995–2006	6,936	Estonia	County and region - undefined	Significant differences in the number of patients diagnosed with late stage cancer across regions of residence (Tallinn, Tartu, Ida-Viru County).
Klein et al. 2011 (20)	Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute	Male patients diagnosed with breast cancer from 1988 to 2006	4,222	U.S.A.	Rural Urban Continuum Code – Metropolitan and Nonmetropolitan counties	A significant difference was not found between region and stage at diagnosis, indicating that the stage at diagnosis was not associated with the region. A significant difference was not found between region and tumor size at diagnosis, indicating that the tumor grade size at diagnosis was also not associated with the region.
Krzyzak et al. 2010 (48)	Voivodship Cancer Registry	Women diagnosed with breast cancer during 2001–2002	696	Poland	National Official Register of Territorial Division of the Country – urban and rural	The proportion of localized stage was 35.5% in urban and 29.5% in rural women. Even more than half of the women were diagnosed in regional stage at disease in both urban and rural areas (52.4% *vs* 52.0%).
Liff et al. 1991 (34)	Georgia Center for Cancer Statistics	All incident cancers among residents of metropolitan Atlanta and ten neighboring rural counties between 1978 and 1985.	35,6 10	U.S.A.	Rural urban - undefined	Residents of the rural area were twice as likely to have unstaged cancers 18.3%) as were urban residents (9.6%]. Among patients with known stage at diagnosis, rural patients tended to have more advanced disease than urban patients. The relative excess of nonlocalized malignancies in rural Georgia was 21% for whites and 37% for blacks.

(*Continued on p. 1365*)

Table 1. (*continued*)

Author	Database/Source	Sample Population and Data Year	Size (*N*)	Country	Rural-Urban Definition	Primary Finding
Markossian & Hines 2012 (21)	The Atlanta and Rural Georgia Cancer Registries	All incident breast tumors diagnosed for non-Hispanic white and non-Hispanic African American women for the years 1992–2007	23,500	U.S.A.	Rural Urban Comminuting Area Codes. Urban counties have codes ≤3, and rural counties have codes ≥6	Rural residents were less likely to be diagnosed with in situ tumors (14.6% versus 18.0%) and stage I tumors (32.7% *vs* 34.9%), and more likely to be unstaged (7.0% *vs* 5.5%) (p<.0001). Urban and rural residents did not differ significantly regarding tumor grade. Urban residents were more likely to have estrogen receptor positive tumors (49.9% *vs 43.1%, p<.0001) and progesterone receptor positive tumors (44.0% vs 37.7%, p<.0001).*
McLafferty et al. 2011 (40)	Illinois State Cancer Registry	Breast cancer cases among Illinois residents in two time periods, 1988–92 and 1998–2002. Cases among Illinois residents that were diagnosed in neighboring states such as Missouri and Wisconsin are included	37,392 (1988–92) 15,454 (1998–2002)	U.S.A.	Rural Urban Commuting Areas classification scheme. Urban regions: (i) Chicago city, (ii) Chicago suburbs, (iii) Other metropolitan areas. Rural areas: (i) Large towns, towns with population sizes from 10,000–50,000, (ii) Small towns with population sizes 10,000	In both time periods, the risk of late-stage diagnosis is highest among patients living in the most urbanized areas, an indication of urban disadvantage. Thus, late-stage diagnosis decreases with increasing rurality, with a slight upturn in the most rural settings. However, For black breast cancer patients, the rural-urban gradient is reversed, with higher risks among patients living outside the city of Chicago.
McLafferty & Wang 2009 (39)	Illinois State Cancer Registry	Cancer cases from 1998 to 2002	44,070	U.S.A.	Rural Urban Commuting Areas classification. (i) Urban core areas, (ii) Suburban areas, (iii) Large town areas (urbanized population 10,000–49,999) and (iv) Small town and isolated rural areas	The risk of late-stage diagnosis is less for those living in other metropolitan and large town settings.
Menck et al. 2001 (35)	California Cancer Registry	Breast cancer cases diagnosed between 1994 and 1997	54,541	U.S.A.	County/county groups: (i) Nonurban (counties that include at least 10,000 acres and a population density <30 inhabitants/acre), (ii) Urban	Lower percentages of early diagnosis breast carcinomas were reported for the nonurban county/county groups.
Mitchell et al. 2006 (22)	Western Australia Cancer Registry	Women diagnosed with invasive breast cancer in 1999 in Western Australia	1,025	Australia	Urban and rural - undefined	No significant differences in stage at diagnosis between urban and rural women with breast cancer.

(*Continued on p. 1366*)

Table 1. (*continued*)

Author	Database/Source	Sample Population and Data Year	Size (*N*)	Country	Rural-Urban Definition	Primary Finding
Montella et al. 2006 (36)	Campania Institute Hospital Tumor Registry	Women diagnosed with breast cancer between January 1991 and December 1993	976	Italy	Italian Central Institute of Statistics classification into urban (including semi-urban) and rural (including semi-rural	Rural municipal women are at greater risk to have a delayed breast cancer diagnosis.
Olson et al. 2012 (37)	British Columbia Cancer Agency Cancer Registry	All patients diagnosed with breast cancer during 2002	2,869	Canada	Ministry of Health administrative local authorities. Large/urban if at least 95% of its residents lived in a community >100,000. Rural greater than 50% of its population resided in communities of <10,000	Patients from rural communities presented with more advanced disease (p=.01).
Sariego 2009 (38)	The American College of Surgeons National Cancer Data Base	American College of Surgeons National Cancer Data Base	811,652	U.S.A.	U.S. Census Bureau regions: Northeast, Midwest, South, and West	A statistically significant relationship (p<.001) identified between stage of breast cancer at the time of presentation and region of the country. The greatest percentage of early-stage disease (stage I) was recorded in the Northeast region (61%), whereas the lowest percentage was recorded in the South (57%). Conversely, as expected, a higher percentage of patients presented with advanced disease (stages III and IV) in the South when compared with the rest of the country (11.2% *vs* 10.3%).
Sheehan et al. 2005 (49)	Massachusetts Cancer Registry	Female invasive breast cancer diagnosed between 1988 and 1997	46,666	U.S.A.	Minor civil division (town code), ZIP Code, and census tract	Results showed that incidence is related to urban/rural status with urban tracts having an incidence rate on average 2.7% higher than rural tract.
Wang et al. 2008 (11)	Illinois State Cancer Registry	Late stage cancer incidence in Illinois from 1998 to 2000	9,077	U.S.A.	Rural Urban Commuting Areas classification. (i) Chicago city, (ii) Other urban, (iii) Suburban, (iv) Large town, (v) Small town and isolated rural	Poor geographical access to primary health care significantly increases the risk of late diagnosis for persons living outside the city of Chicago.

Table 2.

STUDIES, MAJOR FOCUS OF PAPER, AND CONCLUSION

Author	Primary Issue(s) Addressed in Terms of Stage at Diagnosis	Conclusion
Amey et al. 1997 (23)	Variation by Geography/Location	Rural residents are more likely to be diagnosed for breast cancer later in the disease progression than their urban counterparts. The most disadvantaged are the most geographically remote, suggesting that proximity to services plays some role in determining the stage at diagnosis.
	Variation by Race/Ethnicity	The disadvantage of residence applies only to black women. Even the most rural white women suffer no significant disadvantage from residence.
Armstrong & Borman 1996 (14)	Geography/Location	There are small differences between rates of breast cancer in rural and urban residences in New Zealand, as compared to other countries.
Baade et al. 2011 (22)	Geography/Location	A woman's risk of being diagnosed as having advanced breast cancer depends on where she lives, separate from the individual characteristics of the woman herself.
	Variation by Socioeconomic status (SES)	Both the rurality and socio-economic characteristics of the geographical area in which women lived were important. The socio-economic factors contributing to advanced breast cancer, existing in both urban and rural environments.
Barry & Breen 2005 (25)	Geography/Location	Overall, health care markets in the United States have performed imperfectly in serving poor, less educated, and uninsured women.
Bennett et al. 2007 (15)	Geography/Location	The study did not show an urban/rural disparity in stage at diagnosis or survival for women with breast cancer in New Zealand.
Blair et al. 2006 (16)	Geography/Location	People in rural and urban areas have their cancers diagnosed at comparable stages.
Celaya et al. 2010 (17)	Geography/Location	Most women living in New Hampshire have good geographical access to mammography, and no indication was found that travel time or travel distance to mammography significantly affected stage at breast cancer diagnosis. Health insurance, age and marital status were the major factors associated with later stage breast cancer.
Cho et al. 2011 (26)	Geography/Location	Neighborhood disadvantage is strongly associated with late stage diagnosis of breast cancer. Specifically, breast cancer patients residing in neighborhoods that became relatively more disadvantaged over the 1990–2000 decade experienced an additional risk of late stage diagnosis.
	Variation by Race/Ethnicity	Increasing concentration of immigrant populations within neighborhoods over the course of that decade additionally contributed to the risk of late stage diagnosis of breast cancer among women in those communities.

(*Continued on p. 1368*)

Table 2. (*continued*)

Author	Primary Issue(s) Addressed in Terms of Stage at Diagnosis	Conclusion
Cuthbertson et al. 2009 (27)	Geography/Location	Despite uniform breast cancer care programmes within regions and within countries, geographical differences in breast cancer survival and stage at diagnosis persist.
	Race/ Ethnicity	The risk of diagnosis with late-stage breast cancer is greater for those women from ethnic minority groups than for White British women. In particular, the Black/Black British and Chinese/Other ethnic groups had a greater than 25% increased risk of diagnosis with late-stage breast cancer.
	SES and Stage at Diagnosis	Women in the three most deprived quintile groups all have a significantly increased risk of diagnosis with the most advanced stage of breast cancer (Stage IV), compared with the least deprived women, which suggests that deprived women are less likely to participate in the screening programme and that they are more likely to ignore symptoms for longer. Consequently, the delay in diagnosis and treatment affords the most deprived women the poorest prognosis.
Dalton et al. 2006 (28)	Geography/Location and SES	Result shows an increased risk for being diagnosed with a high-risk breast cancer with shorter education, with lower disposable income, with a residence in rural areas, and with having no access to organized mammography screening.
Dey et al. 2010 (42)	Geography/Location	Urban women have a higher incidence ER+ incidence than rural women and xenoestrogen might be a significant cause of this in developed countries and urban areas of developing countries.
Elliott et al. 2004 (29)	Geography/Location	Rural patients as compared with their urban counterparts were disadvantaged in proportion staged, stage at diagnosis, initial management procedures, post-treatment surveillance testing and participation in cancer clinical trials.
Ess et al. 2010 (30)	Geography/Location	Important regional variations in the whole chain of care for breast cancer patients (early diagnosis, malignancy confirmation, therapeutic approach and therapies) were found across regions in Switzerland.
Friedell et al. 2003 (43)	Geography/Location	Efforts to improve screening rates should be increased in all parts of Kentucky, but most needed improvement will have to be in rural and particularly Appalachian areas.
Gregorio et al. 2002 (44)	Geography/Location	Geographic differences of invasive and in situ breast cancer incidence were observed.
Hall et al. 2005 (45)	Geography/Location	Excess incidence in urban counties, but appeared to be explained through the urban preponderance of registry hospitals.
Hausauer et al. 2009 (46)	Geography/Location and SES	Higher proportions of women diagnosed with breast cancer resided in urban than rural and low or middle- than high-poverty counties, irrespective of invasive status.

(*Continued on p. 1369*)

Table 2. (*continued*)

Author	Primary Issue(s) Addressed in Terms of Stage at Diagnosis	Conclusion
Henry et al. 2011 (18)	Geography/Location	Travel time to diagnosing facility or nearest mammography facility was not a determinant of late stage of breast cancer at diagnosis, and better geographic proximity did not assure more favorable stage distributions.
	Race/Ethnicity and SES	Non-geographic factors such as poverty, race/ethnicity, and health insurance independently present more substantial risks for a late-stage diagnosis of breast cancer.
Higginbotham et al. 2001 (31)	Geography/Location and Race	Findings suggest that rural residents in Mississippi and rural African American women in particular, have less access to, or utilization of, early cancer detection programs and/or quality medical care.
Hoffman et al. 2000 (47)	Geography/Location	Area of residence was among the strongest determinants of the stage at diagnosis, and the odds of having localized rather than advanced breast cancer was more than twofold among women resident in urban areas.
	Race/Ethnicity	Incidence rates of breast cancer in coloured and urban women were higher than in black and rural women.
	SES and Family History	Early stage at diagnosis was associated with a higher educational level, being resident in an urban area, being on medical aid and having a family history of breast cancer.
Howe et al. 1992 (32)	Geography/Location	This study demonstrates urban-rural differences in tumor staging. The proportion of unstaged breast cancer in our rural population was much higher (31%) compared with White rural women in Georgia (7.1%). Unstaged cases also made up a larger proportion of our urban cases (five percent) compared with the urban White cases in Georgia (2.5%).
Huang et al. 2009 (19)	Geography/Location	Although socioeconomic status, race, and age may help explain advanced diagnoses, longer travel distance also adversely affects early detection for rural populations.
Innos et al. 2010 (33)	Geography/Location	Place of residence appeared to be the strongest predictor of advanced stage diagnosis in all age groups. Younger and elderly women, those living in remote areas and of lower socio-economic status should be addressed with specific measures to promote earlier detection of breast cancer, particularly in view of current economic difficulties and a sharply rising unemployment rate.
Klein et al. 2011 (20)	Geography/Location	Result showed that metropolitan/nonmetropolitan differences in tumor grade size and cancer stage at diagnosis were not statistically significant.
Krzyzak et al. 2010 (48)	Geography/Location	The proportion of early breast cancer in Podlaskie Voivodship is low, and also related to place of residence, adversely to the rural population. Also, the urban-rural differentiation in breast cancer incidence and stage distribution should be considered as the appearances of health inequalities in the Polish population

(*Continued on p. 1370*)

Table 2. (*continued*)

Author	Primary Issue(s) Addressed in Terms of Stage at Diagnosis	Conclusion
Liff et al. 1991 (34)	Geography/Location	Differences in access to or utilization of early detection methods may contribute to the rural-urban differential in the extent of disease at diagnosis.
	Race/Ethnicity	Black Georgia rural residents were more likely to have nonlocalized malignancies than whites.
Markossian & Hines 2012 (21)	Geography/Location	No significant association between geographic residency status and late stage breast cancer diagnosis.
McLafferty et al. 2011 (40)	Geography/Location	No evidence of rural disadvantage in either time period. In fact the percentage of breast cancer cases diagnosed late is higher in the highly urbanized city of Chicago than it is in other regions of the state-an indication of urban disadvantage.
	Race/Ethnicity	For the black population, rural-urban disparities were markedly different: there is clear evidence of rural disadvantage as opposed to the urban disadvantage observed for the population as a whole.
McLafferty & Wang 2009 (39)	Geography/Location	In the most rural areas, the lower rates of late-stage diagnosis primarily reflect the greater presence of elderly patients who have a lower risk of late-stage diagnosis
Meck et al. 2001 (35)	Geography/Location	Lower percentages of early diagnosis breast carcinomas were reported for the nonurban county/county groups. Elderly women, Hispanic and black women, and women who reside in nonurban areas should be targeted as high priority subpopulations for mammographic screening.
	Race/Ethnicity	Non-Hispanic white women were diagnosed with 14.4% in situ breast carcinoma and 51.4% localized breast carcinoma with small tumor size. Hispanic women were diagnosed with lower levels of in situ breast carcinoma: 12.0%. Hispanic and black women were diagnosed with less localized breast carcinoma with small tumor size: 41.4% and 39.1%, respectively. Asian/Pacific Islander women were diagnosed with 16.6% in situ breast carcinoma, and 45.1% localized breast carcinoma with small tumor size. These findings were statistically significant (*P*, 0.0001).
	SES	Breast carcinoma was diagnosed at an early stage most frequently in women of younger age, in non-Hispanic white women or women of Asian and Pacific Island ancestry, in women who lived in urban counties characterized by higher household incomes, and in women who were diagnosed in more recent years.

(*Continued on p. 1371*)

Table 2. (*continued*)

Author	Primary Issue(s) Addressed in Terms of Stage at Diagnosis	Conclusion
Mitchell et al. 2006 (22)	Geography/Location	Despite similarities in mode of presentation and tumor characteristics, women with breast cancer from rural Western Australia experience a poorer survival outcome than their urban counterparts.
Montella et al. 2006 (36)	Geography/Location	Residents of rural municipalities, as well as poorly educated subjects, are more likely than their respective counterparts to have a delayed diagnosis of breast cancer.
Olson et al. 2012 (37)	Geography/Location	The study identified disparities in use of breast cancer screening, stage distribution and breast-conserving therapy by the population size of the patients' local health authority at the time of diagnosis.
Sariego 2009 (38)	Geography/Location/Race/Ethnicity	A relationship exists between the pattern of breast cancer presentation and geographical location within the United States. The Northeast-with the highest percentage of urban areas and white population-reported the highest percentage of early-stage breast cancer at presentation. Conversely, the South-with more rural and nonwhite population-had the highest percentage of later-{\h}stage disease.
Sheehan et al. 2005 (49)	Geography/Location	Only one area of excess late stage breast cancer diagnoses was identified in the space-time analyses for the first three years of the study and remained statistically significant after covariate adjustment.
Wang et al. 2008 (11)	Geography/Location	Living in areas with poor geographical access to primary care physicians increases the likelihood of late diagnosis for breast cancer.
	SES/Access	Sociocultural barriers and spatial access to primary care (access) have statistically significant associations with late breast cancer diagnosis. As expected, socioeconomic disadvantage and sociocultural barriers have positive relationships, indicating that persons living in areas where income and education levels are low and linguistic and sociocultural barriers are high have a greater risk of late-stage disease. Spatial access to primary care physicians is inversely related to late-stage risk.

area (among others) were used in 12 studies[16,19,25,26,29,31,32,35,38,44,45,49] while one study[34] did not provide information on the measurement type used.

Using a population-based cancer registry data from Georgia, Liff et al.[34] [N = 35,610] (rural, urban, not defined) revealed rural patients were twice as likely to have unstaged cancer (18.3%) as urban residents (9.6%). Among patients with known stages, rural residents tended to have more advanced stage of the disease. Similarly in a Danish study, Dalton et al.[28] [N = 28,765] found that women living in rural areas of Denmark had a 10% higher odds (OR) of high-risk breast cancer than their urban counterparts (95% CI: 1.02, 1.18), while those living in the capital suburban areas had a 15% lower OR (95% CI: 078, 0.93) than those living in provincial cities.

Long distance travel time to health care services has been shown to influence both access and utilization.[11,39,40] There is also an assumption that the greater the distance to travel, the higher the incidence of psychological morbidity and the poorer the compliance with treatment.[11,41] A study by Wang and colleagues[11] [N = 9,077] on late-stage breast cancer diagnosis and health care access in Illinois, argued that spatial access to primary care doctors and time travel is critically important in achieving high rates of early breast cancer detection in Illinois and surrounding states. Consequently, living in areas with poor geographical access to primary care physicians increases the likelihood of late diagnosis for breast cancer.[11]

On the other hand, other studies have reported that rural disadvantage does not contribute to distant metastasis breast cancer diagnosis.[39,40,42–49] Gregorio et al.[44] [N = 12,415] examined geographical differences in breast cancer according to precise geographic coordinates in Connecticut, 1991–1995. Results showed that breast cancer rates were lower than expected for the rural, outermost counties of northeast (risk of disease among residents relative to elsewhere in the state [RR] was .67; p=.001) and northwest (RR = .88; p = .03) Connecticut. However, a higher incidence rate was found for a predominantly suburban/urban county of southwest Connecticut (RR = 1.06; p=.004).

Additionally Hall et al.[45] [N = 27,989] used the Urban Influence Code (UIC) measurement to analyze urbanization and breast cancer incidence in North Carolina, 1995–1999. The authors found that, *in situ* breast cancer incidence rates were highest in the most urbanized counties among Whites (incidence rate ratio (IRR = 1.60) comparing most urban with most rural) and among non-Whites (IRR = 1.27 for the same comparison). Invasive breast cancer rates were also shown to be higher in the most urban counties for Whites (IRR = 1.18 comparing most urban with most rural) but not non-Whites (IRR = .99 for the same comparison). In another study, using the Gharbiah population-based cancer registry to determine urban-rural differences in breast cancer incidence in Egypt, Dey et al.[42] [N = 3,673] suggest that compared with rural incidences, urban incidences showed that for all hormone receptor status (HRS) was higher in urban areas than rural areas for all age-groups with the urban incidence of estrogen receptor positive (ER+) cancer being the highest in all age-groups.

In contrast to these findings Amey et al.,[23] Armstrong and Borman,[14] Bennett et al.,[15] Blair et al.,[16] Celaya et al.,[17] Henry et al.,[18] Huang et al.,[19] Klein et al.,[20] Markossian and Hines,[21] and Mitchell et al.[22] found no statistically significant difference in stage of breast cancer and rural-urban geographic location and distance travel to mammography screening facility. Markossian and Hines's.[21] [N = 23,500] analysis of Atlanta and

Rural Georgia Cancer Registry to assess disparities in late stage diagnosis and rural residence found that rural-urban designation was not significantly associated with late stage breast cancer diagnosis, and late stage did not vary significantly across counties (p=1.0). Additionally, while rural patients had over 22% increased odds of unknown tumor type compared with urban patients, the association was not statistically significant.

Using the rural urban continuum code (RUCC) classification system definition and Florida cancer data system and area resource file, Amey et al.[23] [N = 79,946] analyzed the role of race and residence on stage at breast cancer diagnosis. Results indicated that residents of rural counties that are adjacent to a metropolitan county have the highest percentage (64.5%) of women whose breast cancer was detected at an early stage compared with their urban counterparts. This stood in contrast to the findings of Farley and Flannery[51] who reported that adequately served rural counties were better off than their urban counterparts. The authors also reported that even nonadjacent rural counties had a slightly higher percentage of women diagnosed early (63.1%) than did urban counties (62.9%). However, the last difference was not statistically significant, suggesting proximity to services seems not to inhibit the residents of these most rural counties from receiving a timely diagnosis. Celaya et al.[17] [N = 5,966] used the Rural Urban Commuting Area codes to classify the rural-urban areas in New Hampshire, and found no significant association between rural residence and stage of breast cancer diagnosis. Similarly, Klein et al.[20] [N = 4,222] analyzed differences in male breast cancer stage, tumor size, and stage at diagnosis using metropolitan and non-metropolitan classification and found no statistical differences in proportions of stage or tumor size at diagnosis.

Variation by race or ethnicity. Large disparities in cancer burden and health outcomes exist between Whites and ethnic/racial minorities. For many decades, African American women experienced a lower incidence rates of breast cancer, but a higher mortality rates than White women.[1,2,6] Nonetheless, recent new evidence concerning disparities in breast cancer has demonstrated that the incidence rates of breast cancer in African American women have increased slightly (by 0.4% per year) while the rates in White women have remained stable.[1,2] Rural populations are generally disadvantaged in terms of access to medical care services.[23,35,38,40,47] Particularly for Black and Hispanic White women, living in rurally remote areas is likely to affect their cancer health prognosis and survival.[4,27] Amey et al.[23] [N = 79,946] revealed that place of residence had a differential impact on stage at diagnosis across racial groups. While the odds of receiving a late diagnosis for Black women in nonadjacent rural counties are approximately 46% higher than for Black urban residents, it is inconsequential for White women. The study further reported that even low-risk Black women in remote rural counties have approximately a 17% chance of receiving a late diagnosis, and the 12% probability for the most disadvantaged Whites is equivalent to the probability of the most advantaged Black group.

In the United Kingdom (U.K.) Cuthbertson et al.[27] [N = 31,551] examined racial inequalities in breast cancer diagnosis between ethnic minorities and British White women in the Trent region. Results showed that ethnic minority groups have a significantly increased risk of diagnosis with late stage breast cancer relative to the White British group. For the Black/Black British and Chinese/Other ethnic groups, risk

of diagnosis with late stage breast cancer is more than 25% higher [RR = 1.28 (95% CI: 1.11, 1.49) and RR = 1.26 (95% CI: 1.04, 1.53)]. Analysis further revealed women residing in nine primary care trusts (PCT) have a significant risk of being diagnosed at late stage, compared with women residing in the Nottingham City PCT. The differences in risk range from an increase of 22% in Doncaster [RR = 1.22 (95% CI: 1:00, 1.48)] to 42% for women in Bassetlaw [RR = 1.42 (95% CI: 1.15, 1.77)] and Leicester City [RR = 1.41 (95% CI: 1.18, 1.17)] PCTs. Liff et al.[34] [N = 35,610] also reported that the relative excess of non-localized malignancies in rural Georgia was almost twice for Blacks (37%) as for Whites (21%). This finding suggests that for Black and other minority populations, the rural-urban disparities are markedly different.[40]

Consistent with these variations by stage at diagnosis and race, Menck and Mills[35] [N = 54,541], descriptive analysis of the California Cancer Registry (1994–1997) showed that non-Hispanic White women were diagnosed with 14.4% in situ breast carcinoma and 51.4% localized breast carcinoma with small tumor size. Hispanic women were diagnosed with lower levels of in situ breast carcinoma (12.0%). Hispanic and Black women were diagnosed with less localized breast carcinoma with small tumor size: 41.4% and 39.1%, respectively. Asian/Pacific Islander women were diagnosed with 16.6% in situ breast carcinoma, and 45.1% localized breast carcinoma with small tumor size. These differences were statistically significant (p=.0001).

Geographic location variability in rural vs. urban and White vs. Black populations differs within the U.S. The Northeast regions are considered urban and have the largest proportion of Whites. On the other, the Southeast is predominantly rural has the largest number of African Americans.[38,52] To assess whether geography matters, Sariego[38] [N = 811,652] used the American College of Surgeons' national cancer database to examine the distribution patterns of breast cancer patterns in the U.S. His findings indicated that a large geographic variation exists in proportion of patients diagnosed in stage with regard to race. Results indicated a statistically significant dependent relationship between race and region with regard to breast cancer tumor size (p<.001). Results indicated a statistically significant dependent relationship between race and region with regard to breast cancer tumor size (p<.001). There were more White women in all four regions of the U.S. than Black women. However, when stage at diagnosis was compared across the U.S. as a whole, a higher percentage of the White women (90.1%) were diagnosed with early stage breast cancer (stages I and II) than of the Black women (85.3%). These differences were statistically significant (p<.001). Similarly, in terms of rural or non-urban population distribution, more women lived in the Midwest (23.6%) than in the South (20.4%). Even though the Midwest has a larger number of women residing in rural areas than the South, more late stage breast cancer was reported among women in the South than among women in the Midwest. This association was also statistically significant (p<.002). Finally, in terms of urbanicity, the Northeast has a larger proportion of urban areas as well as White population than the South. Nonetheless, an inverse relationship exists between early stage at diagnosis and the proportion of rural population.[38] Thus, women residing in rural areas (South and West) experienced more late stage breast cancer diagnosis than those in urban areas.

Variation by socioeconomic status. There is a strong relationship between low socioeconomic status and an increased risk of being on the losing end of health dispari-

ties.[53] A study by Adler and Newman[53] on socioeconomic disparities in health reported that whether assessed by income, level of education, or occupation, socioeconomic status clearly predicts the health status of an individual. These three measurements of socioeconomic status influence minority populations only indirectly, but it remains important to consider these three main SES determinants of health.

In Australia, Baade et al.[24] [N = 18,658] analyzed Queensland Cancer Registry data to investigate links between geographic remoteness, area disadvantage, individual-level factors and advanced breast cancer. Results showed that women who lived in the most socioeconomically disadvantaged regions were significantly more likely (OR 1.21, 95% CI 1.07, 1.37) than residents of the most economically advantaged areas to be diagnosed with more advanced breast cancer. Further, when place of residence and socioeconomic status were adjusted, the effect of geographic region/resident and area advantage were statistically significant, and the rates of late detection remained significantly higher for women in the most geographically remote and disadvantaged areas compared with women who lived in the cities. Celaya et al.[17] [N = 5,966] and Henry et al.[18] [N = 161,619], however, found no association between rural and urban residence and stage at diagnosis. Ceyala et al.[17] for instance noted that New Hampshire women were more likely to be diagnosed with breast cancer at later stages if they lacked private health insurance (p=<.001), were not married (p=<.001) and were older (p=<.001). There was also a borderline association with diagnosis during non-winter and winter months (p=.074). Barry and Breen[25] [N = 12,395] revealed that late diagnosis was prevalent in socially distressed and medically underserved areas.

Henry et al.[18] [N = 161,619] analyzed 10 population-based state cancer registries and suggested that for women living in census tracts with poverty rates greater than 20%, the odds of late stage breast cancer were 1.34 times (95% CI = 1.29, 1.39) greater than the odds for women living in census tracts with poverty rates less than 5%. Other studies have suggested socioeconomic status and residing in urban areas provide an advantage for early diagnosis.[28,35,47] Dalton et al.[28] [N = 28,765] results showed that the risk for late diagnosis decreased with increasing education, income, and urbanicity in women diagnosed with breast cancer in Denmark. Similarly, Cho et al.[26] [N = 42,714], Hoffman et al.[47] [N = 485] and Wang et al.[11] [N = 9,077] also reported an association between socioeconomic status and late stage breast cancer diagnosis. In a study of the association between changes in immigrant population and the likelihood of distant metastasis stage at diagnosis of breast cancer in Cook County Illinois, Cho et al.[26] [N = 42,714] discovered that neighborhood disadvantage is strongly associated with late stage diagnosis of breast cancer. Specifically, breast cancer patients residing in neighborhoods that became relatively more disadvantaged over the 1990-2000 decade experienced an additional risk of late stage diagnosis.[26] Hoffman and colleagues[47] also [N = 485] suggested that early stage at diagnosis was associated with a higher educational level, being resident in an urban area, on medical aid and having a family history of breast cancer. Similarly, Wang et al.[11] [N = 9,077] revealed that socioeconomic disadvantage and sociocultural barriers have positive relationships indicating that people living in areas where income and education levels are low and linguistic and sociocultural barriers are high have a greater risk of late stage disease compared with those in high socioeconomic neighborhoods.

Discussion

Disparities in breast cancer between White and Black have been well documented over the years. Causes of these disparities have been linked to social, behavioral, and economic factors such as persistent inequalities in access to care, unhealthy environments, and racial discrimination.[11,41,54–57] Our systematic review identified 17 (47%) of 36 studies in which breast cancer patients residing in geographically remote/rural areas had a distant metastasis than urban women. Ten (28%) studies reported higher proportions of women diagnosed with breast cancer resided in urban than rural counties. Nine (25%) studies on the other hand, reported no statistically significant effect association between place of residence and stage at diagnosis for women residing in rural and urban areas.

It is clear from the review that, compared with urban residents, rural residents with breast cancer faced unique experiences and challenges with regard to diagnosis. For example, the studies that reported a significant difference in the distant metastasis of the disease between urban and rural patients indicated uniformly that rural breast cancer patients were less likely to be diagnosed with early stage breast cancer due to difficulty accessing cancer screening services in rural areas.[11,23–38] Additionally, rural patients are more likely to travel greater distances for screening mammography to receive primary breast cancer treatment, and to stay away from home during this treatment, which may factor into why women in rural areas were more likely to be detected with late stage breast cancer in these studies.[11,33,4142,55]

Our review of the studies further demonstrated the ever-increasing racial disparities in breast cancer stage at diagnosis between African American and White women. This literature review suggests that—irrespective of place of residence—African American women were more likely to be diagnosed with later stage breast cancer compared with White women. All 10[39,40,42–49] studies that reported the risk for late stage diagnosis was highest among patients living in urban and metropolitan areas suggest that for Black breast cancer patients the rural-urban difference was reversed. Additionally, when analysis was examined within urban areas among Black women and White women, differences still remained statistically significant in terms of place and socioeconomic status. Similar findings were reported in nine[14–22] studies that showed no significant difference between stage at diagnosis and rural-urban place of residence.

Our findings further suggest that geographical differences exist not only between rural and urban areas, but also within urban areas in terms of socioeconomic status and stage at breast cancer diagnosis. Generally, socioeconomically disadvantaged populations may experience reduced access to medical care. In addition, lack of health insurance, limited access to care, and lower rates of cancer screening among residents of rural and more disadvantaged areas may account for their higher rates of late stage cancer diagnoses. In terms of race and minority populations, disparities in neighborhood conditions, lower education level, and income may reflect inequities in health care access, cancer screening, and treatment.

Overall, this review suggests that remote rural breast cancer patients are diagnosed at a more advanced stage of the disease than their urban counterparts. At the same time,

our literature review also pointed to the continuing debate regarding the difficulty in defining and measuring rurality in America. According to Berk et al.[58] almost one fifth of the U.S. population lives in a rural area, but defining what constitutes rural or urban America is complex. As noted by Brown and Schafft[59] the word rural is ambiguous: there is no consensus among researchers and policymakers about how to define it or how to classify localities. Over two dozen definitions that are currently in use by various agencies. The use of various definitions reflects the multidimensionality of these concepts—the defining criteria can be population size, population density, administrative boundaries, proximity to urban settings, and economic activities. In addition, researchers and policy makers face several challenges when defining or classifying rural and urban, such as defining thresholds and building blocks (geographic unit), and data availability.[60–62] This issue became evident in the two Georgia studies that used the same database but came to different conclusion on their findings. For instance, an earlier study by Liff et al.[34] showed that the risk for advanced stage diagnosis for rural women were more than twice when compared with urban women. On the other hand, a recent follow up study by Markossian and Hines[21] did not find a significant association between geographic location and late stage breast cancer diagnosis.

This evidence-based review of the literature on geographical location variation on breast cancer stage at diagnosis, race/ethnicity, and socioeconomic status has some limitations. The first relates to differences in definition and measurement for rural and urban in each study. While we believe the variability in measurement might not have affected the results greatly, using a standardized definition across board would have eliminated any confusion. Secondly, the review was limited only to studies that were published in English. This means potential publications meeting the established inclusion, but in other languages were excluded from the review.

Conclusions and future directions. Our study investigated rural-urban differences in the breast cancer stage at diagnosis over the years. Thirty six (36) studies from 12 countries around the world were identified and we provided a comprehensive summary on variations in diagnosis and stage between rural and urban populations. This review suggests that there are inequalities associated with geographical place, race/ethnicity, and stage at diagnosis of breast cancer all over the world. Overall, breast cancer patients residing in rural, remote, and socioeconomically disadvantaged neighborhoods were more likely to be diagnosed with distant breast metastasis. At the same time, a large geographic variations exists in the proportions of sub-populations—such as African American, Hispanic and White women—living in rural areas. Minority women were more likely to be diagnosed at advanced stage compared with their White counterparts irrespective of geographical place of residence.

Given that geographic access is an essential determining factor of a patient's treatment-seeking behavior, it is important to study and develop measures of spatial availability and accessibility of health care facilities for rural areas (and to define the terms rural and urban carefully and consistently). We suggest future studies on breast cancer stage at diagnosis and geographic place of residency address these issues as a way to understand more fully the difference in stage at diagnosis between rural remote (nonmetropolitan) and urban metropolitan areas.

Acknowledgments

The study is supported by the Transdisciplinary Research on Energetics and Cancer (TREC) Center at Washington University in St. Louis. The TREC Center is funded by the National Cancer Institute at National Institutes of Health (U54 CA155496).

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Errata: Williams F, Jeanetta S, James AS. Geographical Location and Stage of Breast Cancer Diagnosis: A Systematic Review of the Literature. Journal of Health Care for the Poor and Underserved 27 (2016): 1357–1383.

Page 1359: Correct display of diagram is shown here:

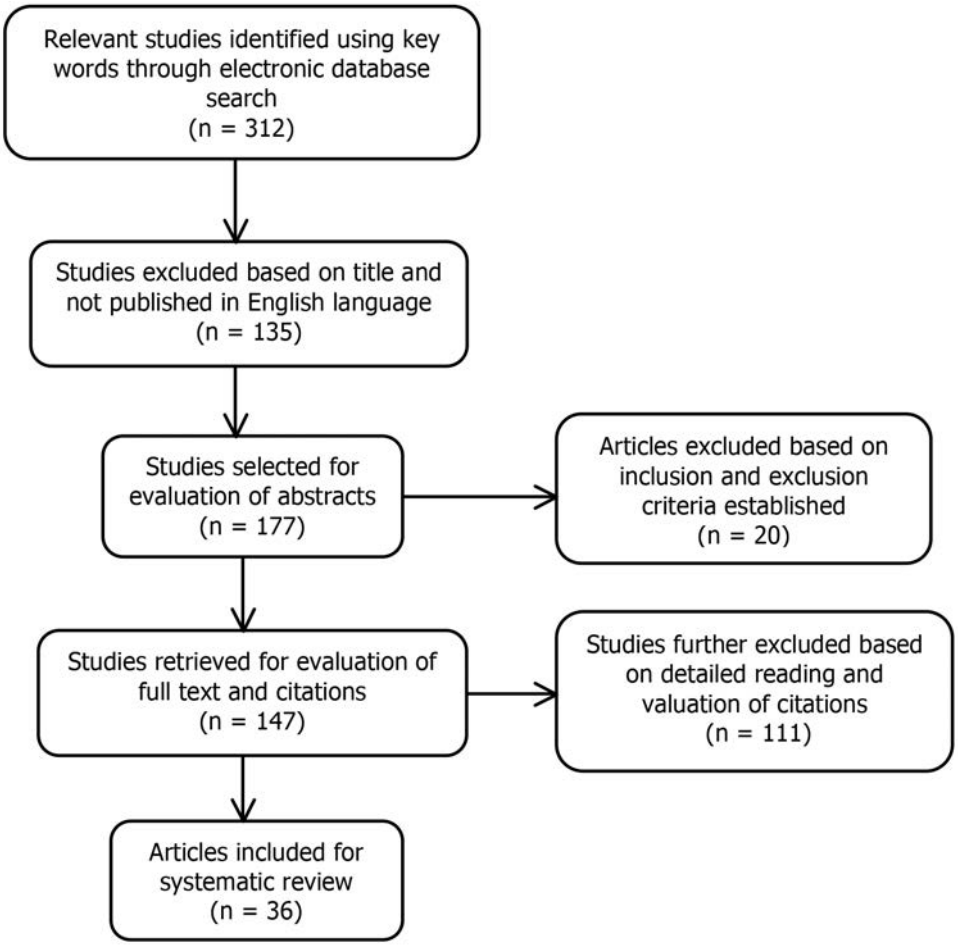

Figure 1. Flow diagram for literature search results and application of eligibility criteria

Page 1377: Table 1: (continued) Elliott et al. 2004 (29). Rural patients as compared with their urban counterparts were disadvantaged in proportion staged, stage at diagnosis, initial management procedures, post-treatment surveillance testing and participation in cancer clinical trials. [Correction: Rural patients compared with their urban counterparts were disadvantaged in proportion of stage at diagnosis, initial management procedures, post-treatment surveillance testing, and participation in cancer clinical trials.]