Effectiveness of Interventions for Breast Cancer Screening in African American Women: A Meta-Analysis

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Objective. The purpose of this study was to report the results of a meta-analysis conducted on the effects of clinical trials in breast cancer screening for African American women between 1997 and 2017.

Data Sources. Articles published in English and in the United States, between January 1997 and March 2017, were eligible for inclusion if they (1) conducted psychosocial, behavioral, or educational interventions designed to increase screening mammography rates in predominantly African American women of all ages; (2) utilized a randomized, controlled trial (RCT) design; and (3) reported quantitative screening rates following the intervention.

Study Design. Randomized clinical trials on breast cancer screening in African American women, published between January 1997 and March 2017, were selected from database searches.

Data Collection Methods. Data collected included effect size of screening versus comparison interventions, intervention characteristics, and a number of study characteristics to explore potential moderators. Search results yielded 327 articles, of which 14 met inclusion criteria and were included in analyses.

Principal Findings. Findings indicated that screening interventions for African American women were significantly more likely to result in mammography than control (OR = 1.56 [95 percent CI = 1.27–1.93], $p < .0001$). Although no patient or study characteristics significantly moderated screening efficacy, the most effective interventions were those specifically tailored to meet the perceived risk of African American women.

Conclusions. Screening interventions are at least minimally effective for promoting mammography among African American women, but research in this area is limited to a small number of studies. More research is needed to enhance the efficacy of existing interventions and reduce the high morbidity and mortality rate of this underserved population.

Key Words. Health disparities, breast cancer, screening, African Americans, women, meta-analysis

Mortality rates for all major causes of death are higher for African Americans than for whites. African Americans have the highest mortality rate of any racial and ethnic group for all cancers, and this contributes, in part, to a lower life expectancy for both men and women. In 2008, African American women were 10 percent less likely to have been diagnosed with breast cancer, but almost 40 percent more likely to die from breast cancer, as compared to non-Hispanic white women (HHS, 2014). In 2000, the National Institutes of Health presented the draft of a strategic research plan to reduce and ultimately eliminate health disparities (U.S. Department of Health and Human Services [HHS], 2000). Despite the remarkable improvements in the overall health of our citizenry, during the previous decades, disparities in the burden of illness and death experienced by African Americans and other ethnic and racial minority groups have continued to grow (Copeland 2005). The focus of the 5-year NIH plan, fiscal years 2002–2006, included specific areas of research, research infrastructure, and public information and community outreach. At that time, African Americans had both the highest death rate and overall incidence of cancer than any other racial or ethnic group. The federal initiatives to address health disparities focused on the following areas: infant mortality; cancer screening and management; cardiovascular disease; diabetes; HIV Infection/AIDS; and immunization (HHS, 2000).

Cancer is one of the nation's biggest medical challenges. Breast cancer is a leading cause of death among women and the second leading cause of death in African American women (Ashing-Giwa et al. 2004, West et al. 2004; Champion et al. 2006; Sadler et al. 2011; ACA, 2013a,b). A cancer diagnosis can feel like a death sentence to many when the news is initially received. The fear and anxiety about mortality can be paralyzing.

Breast cancer deaths rates declined for African American women after 1992 because of improvements in early detection and treatment. However, compared to white women, the decline was slower (ACS 2013a,b) or remained stable (West et al. 2004). Researchers attribute the difference in decline to the growing racial and ethnic disparities in women's health care; the lower rates of screening among African American women, who may seek health care later in

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the progression of the disease (West et al. 2004); and different segments of the population have not equally benefitted from the gains made in cancer prevention and control efforts (Jibaja-Weiss et al. 2003). During 2000–2009, African American women had lower incidence of breast cancer, but higher death rates from breast cancer. While the breast cancer death rate has continued its decline, for women who are poor, the decline has been much slower.

Despite these advances in breast cancer detection and treatment, death rates for all cancers combined continue to be higher for African Americans (ACS 2013a,b). “African Americans have a higher death rate from breast, lung, and colorectal cancer than any other racial or ethnic group” (Kaiser Family Foundation 2007, p. 11). In addition to the higher proportion of cancer deaths for African Americans, their life expectancy is lower than for white men and women, 69.8 versus 75.7 years and 76.5 versus 80.8 years, respectively.

In 2007, approximately 39 million African Americans lived in the United States, representing 13 percent of the total population (ACS 2007). Approximately one-third of all African Americans are poor. As a social determinant of health, poverty is consistently correlated with poor health outcomes (Jaynes and Williams 1989; Jibaja-Weiss et al. 2003; Copeland and Butler 2007). The rate of poverty and lack of and/or limited access to a usual source of health care leave many African Americans at risk for several chronic health conditions, including cancer. African Americans are less likely to have private or employment-based health insurance coverage, relative to whites; are more likely to be covered by Medicaid or other publicly funded insurance; and are twice as likely to be uninsured (Copeland 2005).

In the study of health disparities, regarding breast cancer screening, the prevention of excessive deaths through increased screening with African American women is the end point. The prevention of excess deaths, among African American women, can occur with increased and early breast cancer screening. While health disparities are prevention-focused, breast cancer screening is the end point. For patient-centered outcomes, mortality is the end point. Although screening rates are not a traditional patient-centered outcome, screening was the focus of this research because of the large body of evidence indicating that screening is strongly related to patient-centered outcomes of mortality and morbidity (Phillips, Cohen, and Tarzian 2001; Davis, Emerson, and Husaini 2005; Newman, 2005) and that African American women utilize screening interventions less than other racial and ethnic groups (Davis et al. 2005; Newman 2005). It is well documented that African American women have higher mortality from breast cancer due to lack of

screening (Davis et al. 2005; Marshall et al. 2015), but little information is known on the efficacy of interventions designed to promote screening among this population. As such, we believe understanding the efficacy of such interventions on screening participation in African American women is a meaningful and important outcome for patients and the field.

The purpose of this study was to report the results of a meta-analysis conducted on the effects of clinical trials in breast cancer screening for African American women between 1997 and 2017. To what extent have health services researchers been successful in developing culturally appropriate primary interventions to decrease the overall incidence of and death rate from breast cancer for this group of women? Given the influx of research funding, to decrease racial and ethnic disparities in health status, we sought to investigate if we have succeeded in closing the gap by developing effective interventions to promote breast cancer screening among this population.

METHODS

This study was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) that evaluate health care interventions (Moher et al. 2009).

Search Strategy and Selection of Studies

An extensive literature search was performed to locate articles published between January 1997 and March 2017. Studies published in English and conducted in the United States were eligible for inclusion if they (1) conducted psychosocial, behavioral, or educational interventions designed to increase screening mammography rates in predominantly African American women of all ages; (2) utilized a randomized, controlled trial (RCT) design; and (3) reported quantitative screening rates following the intervention. Current intervention designs to promote mammography screening among ethnically minority women broadly fall into three major categories: psychosocial, behavioral, and educational interventions. These intervention approaches are frequently guided by several theoretical perspectives, such as health belief model, transtheoretical model, and social learning (social cognitive) theory, and they highlight psychosocial, behavioral, and educational constructs. A great deal of evidence indicates significant positive correlations between these intervention approaches and breast cancer screening behavior (e.g., Janz,

Champion, and Strecher 2002; Wood et al. 2002; Russell, Champion, and Skinner 2006). Therefore, defining intervention as psychosocial, behavioral, and educational interventions in this study provided a comprehensive assessment of the current evidence base, and no intervention studies using RCT among African American women were excluded through the application of our search criteria. We used the following databases to complete our search: Medline, PsycINFO, ProQuest Psychology Journals, PsycARTICLES, Pubmed, Social Work Abstracts, SocINDEX, The Cumulative Index to Nursing, and Allied Health Literature. This was accomplished by conducting keyword searches using the search strings “breast cancer screening” or “mammography” combined with “randomized” and “African American women.” The search through Medline and PsycINFO databases yielded 31 and 20 articles, respectively, and 110 articles were identified using Pubmed. The combined search through ProQuest Psychology Journals and PsycARTICLES yielded 140 articles. Another combined search generated 23 articles using the following databases: Social Work Abstracts, SocINDEX, The Cumulative Index to Nursing, and Allied Health Literature. Additionally, references of relevant studies were examined to identify additional studies, and one article was identified. From these abstract searches conducted between January 1997 and May 2014, 12 studies met the inclusion criteria and were reviewed (Figure 1). An additional search was conducted during March 2017 to identify newly published studies between 2014 and 2017, and two articles met the inclusion criteria. In total, 14 studies were reviewed for this meta-analysis, including articles published between January 1997 and March 2017 (Figure 1).

Data Extraction

Data extraction was undertaken by the second author and checked by the first and third authors. Disagreements were resolved by discussion between the two review (the first and third) authors. After assembling the studies to be included in this research, the information needed for this meta-analysis was collected from each study (Table 1). The study authors were contacted to obtain the information if it could not be extracted from the articles. The following data were extracted from each article: mean sample age, sample size, study duration, and description of interventions. In addition, the number of participants and breast cancer screening rates postintervention for both intervention and control groups were extracted from each article. Further, interventions were categorized by consensus as being high (e.g., tailored in-person

Figure 1: Flow Diagram for the Inclusion and Exclusion of Studies

counseling) or low (e.g., reminder letters) in participant contact, and information was recorded on whether the intervention was culturally tailored for African American women. As studies varied considerably in the type of control intervention used, which may affect differential efficacy of the experimental interventions, the type of control was coded as either an active or usual care control for the purposes of moderator analysis.

Risk of Bias Assessment

Risk of bias was assessed by the second author and independently checked by the third author. In the case of discrepancies, consensus was reached through discussion. To ascertain the validity of eligible randomized trials, each study was assessed for the following components based on the Cochrane risk of bias tools and the PRISMA guidelines (Liberati et al. 2009; Higgins, Altman, and Sterne 2011): (1) random sequence generation; (2) allocation concealment; (3) blinding of outcome assessment; (4) incomplete outcome data; (5) selective

Table 1: Randomized, Controlled Trials of Breast Cancer Screening Interventions for African American Women

Study	N_i	N_e	Mean Age	Months Follow-up		Screened _i %	Screened _e %	Absolute Difference %	Intervention Description	Cultural Components	Intervention Fidelity	Intervention Frequency	Active Comparison
Sung et al. (1997)	71	54	39.50	6	50.40	39.40	11.81		Lay health advisor intervention	Yes	Unclear	4 ×/11 months	Yes
Champion et al. (2000)	139	139	55.00	12	75.54	71.22	4.32		Tailored counseling intervention	Yes	High	3 ×/year	No
Young, Waller, and Smitherman (2002)	43	38	52.00	3	66.00	38.00	28.28		On-site screening intervention	Yes	High	1 hour total	No
Zhu et al. (2002)	162	162	76.00	12	55.00	53.00	1.85		Lay health advisor intervention	Yes	High	3 ×/year	No
Zhu et al. (2002)	162	162	76.00	24	66.00	68.00	−1.85		Lay health advisor intervention	Yes	High	3 ×/year	No
Jibaja-Weiss et al. (2003) – Tailored Letter	106	105	46.75	12	12.26	20.00	−7.74		Personalized tailored letters	Yes	High	1 × total	No
Jibaja-Weiss et al. (2003) – Form Letter	83	105	47.50	12	26.51	20.00	6.51		Personalized formletters	Yes	High	1 × total	No

Continued

Table 1. *Continued*

<i>Study</i>	<i>N_i</i>	<i>N_c</i>	<i>Mean Age</i>	<i>Months Follow-up</i>	<i>Screened_i</i> %	<i>Screened_c</i> %	<i>Absolute Difference</i> %	<i>Intervention Description</i>	<i>Cultural Components</i>	<i>Intervention Fidelity</i>	<i>Intervention Frequency</i>	<i>Active Comparison</i>
West et al. (2004)	140	141	65.00	6	15.71	15.60	0.11	Stage 1: Reminder letter Stage 2: Tailored call	Yes	High	1 ×/6 months	No
West et al. (2004)	113	113	65.00	6	15.93	13.00	2.66		Yes	High	1 ×/6 months	Yes
Kreuter et al. (2005) – Behavioral Tailoring	48	55	48.67	18	64.60	54.50	10.03	Received behaviorally tailored magazines	No	High	6 ×/18 months	No
Kreuter et al. (2005) – Cultural Tailoring	44	55	48.69	18	63.60	54.50	9.09	Received culturally tailored magazines	Yes	High	6 ×/18 months	No
Kreuter et al. (2005) – Both	45	55	49.00	18	75.60	54.50	21.01	Received both magazines	Yes	High	6 ×/18 months	No
Champion et al. (2006) – Computer vs. Pamphlet	125	56	50.51	6	40.00	32.14	7.86	Interactive computer-assisted instruction program	Yes	High	3 ×/6 months	Yes
Champion et al. (2006) – Video vs. Pamphlet	56	118	50.51	6	32.14	24.58	6.78	Culturally appropriate video	Yes	High	3 ×/6 months	Yes

Continued

Table 1. Continued

Study	N_i	N_e	Mean Age	Months Follow-up		Screened _i %	Screened _e %	Absolute Difference %	Intervention Description	Cultural Components	Intervention Fidelity	Intervention Frequency	Active Comparison
Goel, George, and Burack (2008)	450	487	52.40	6	29.78	23.00	32.78		Telephone call reminder	No	High	1 × total	Yes
Russell et al. (2010)	89	90	51.25	6	50.60	1780	16.43		Combined interactive computer program and lay health advisor intervention	Yes	High	6 ×/6 months	Yes
Sadler et al. (2011)	112	120	40.66	6	46.00	30.00	17.07		Lay health advisor intervention	Yes	Low	2 ×/6 months	Yes
Hendren et al. (2014)	41	41	51.55	12	26.83	9.76	5.76		Multimodal intervention	No	High	10 ×/52 weeks	No
Marshall et al. (2015)	638	720	–	24	93.26	87.50	7.56		Printed educational materials and patient navigation services	No	Unclear	8 ×/2 years	Yes

Continued

Table 1. *Continued*

<i>Study</i>	N_i	N_c	<i>Mean Age</i>	<i>Months Follow-up</i>	<i>Screened_i</i> %	<i>Screened_c</i> %	<i>Absolute Difference</i> %	<i>Intervention Description</i>	<i>Cultural Components</i>	<i>Intervention Fidelity</i>	<i>Intervention Frequency</i>	<i>Active Comparison</i>
Gathirua-Mwang et al. (2016)—DVD	83	71	51.30	6	40.96	35.21	5.75	Mailed interactive DVD	Yes	High	3×/6 months	No
Gathirua-Mwang et al. (2016)—Telephone	83	71	51.70	6	42.17	35.21	6.96	Computer-tailored telephone counseling	No	High	3×/6 months	No

outcome reporting, and (6) other source of bias. The assessment of the risk of bias was summarized in Table 2.

Data Analysis

A series of random-effects multivariate meta-analytic models were constructed to examine the pooled efficacy of proscreening interventions on mammography screening in African American women using metafor in R 3.0.2 (Viechtbauer 2010; R Development Core Team 2013). Odds ratios were computed based on sample size and screening rates and weighted based on their variance estimates. As a single study could contribute multiple effect sizes, random-effects models were used with study as a nesting factor to account for dependency among effect sizes coming from a single study. Heterogeneity in effect sizes was assessed using the *Q* statistic, which follows a chi-squared distribution with $k - 1$ degrees of freedom; significant results from the *Q* statistic suggest significant heterogeneity in study effect sizes (Hedges and Olkin 1985). In the presence of significant heterogeneity between

Table 2: Risk of Bias Assessment of Included Studies

<i>Study</i>	<i>Random Sequence Generation</i>	<i>Allocation Concealment</i>	<i>Blinding of Outcome Assessment</i>	<i>Incomplete Outcome Data</i>	<i>Selective Outcome Reporting</i>	<i>Other Source of Bias</i>
Sung et al. (1997)	L	U	U	H	L	L
Champion et al. (2000)	L	U	U	L	L	L
Young, Waller, and Smitherman (2002)	L	U	U	L	L	L
Zhu et al. (2002)	L	U	U	L	L	L
Jibaja-Weiss et al. (2003)	L	U	L	L	L	L
West et al. (2004)	L	U	U	L	L	L
Kreuter et al. (2005)	L	U	U	H	L	L
Champion et al. (2006)	L	U	U	L	L	L
Goel, George, and Burack (2008)	L	U	U	L	L	L
Russell et al. (2010)	L	H	U	L	L	L
Sadler et al. (2011)	L	L	L	L	L	L
Hendren et al. (2014)	L	L	L	L	L	L
Marshall et al. (2015)	L	U	U	H	L	L
Gathirua-Mwang et al. (2016)	L	L	U	L	L	L

H, high risk of bias; L, low risk of bias; U, unclear risk of bias.

studies, moderators were examined using mixed-effects moderator models based on a priori defined study characteristics. Finally, to assess the degree to which publication bias might affect meta-analytic results, fail-safe n was calculated based on Rosenthal's (1979) approach to examine the number of unpublished null finding studies needed to eliminate any significant positive benefits observed from proscreening interventions.

RESULTS

A total of 14 randomized, controlled trials of breast cancer screening interventions in African American women met inclusion criteria for this meta-analysis, and their characteristics are described in Table 1. Included studies provided 21 effect size estimates across 5,791 participants. Study sample size ranged from 81 to 1,358 individuals, with an average participant age of 55.44 (SD = 9.82) years and a mean study duration of 10.71 (SD = 6.33) months. Approximately 62 percent of studies used high-contact interventions that provided significant in-person or tailored contact with participants to encourage screening. Most (76 percent) studies made use of interventions that provided specific cultural tailoring of educational and intervention components for African American women.

Characteristics of the intervention and comparison groups of the included studies are presented in Supplemental Table 1. Regarding the types of interventions, six studies used complex interventions, including letter, pamphlet, prompts, DVD, video, phone calls, interactive computer, and lay health advisors. Three studies were identified as lay health advisor interventions. One study employed a tailored counseling intervention, and another study examined an on-site screening intervention. Three studies solely used letters, magazines, or telephone reminders, respectively. Eleven studies included cultural component relevant to African American women. In terms of the fidelity of the planned interventions, 11 studies had high fidelity, one study had low fidelity, and two studies were deemed unclear. Frequency and duration of interventions varied, ranging from once to ten times and from 1 hour to 52 weeks, respectively. The comparison groups received no intervention or various interventions, including educational materials, postcard reminder, tailored letter, pamphlet, video, interactive computer, and diabetes education program.

Figure 2 presents the results of a random-effects meta-analysis across all 14 randomized trials of breast cancer screening interventions for African American women. Overall, results indicated that women who were

randomized to experimental screening interventions were significantly more likely to obtain a mammogram at post-treatment follow-up compared to those receiving usual care or a comparator control intervention, $OR = 1.56$, $p < .0001$. Average effect size was modest in magnitude and indicated that African American women were approximately 1.5 times more likely to receive a mammogram when they were randomized to proscreening interventions. Analysis of number needed to treat to achieve an effective of screening indicated that screening interventions needed intervene with 11 African American women in order for one to obtain screening. Study effect sizes ranged from $OR = 0.56$, indicating a detrimental effect of screening interventions, to $OR = 4.73$, with significant between-study variability in effects, $Q(20) = 35.66$, $p = .017$. There were no significant differences in effect size of screening interventions for those studies that used active versus to usual care comparison groups, $Q_m(1) = 2.94$, $p = .086$.

Investigation of systematic moderators of proscreening intervention efficacy indicated that neither study sample size nor duration was associated with variability in the effect of screening interventions on receiving a mammography, all $p > .50$. Studies of high versus low contact outreach interventions were also similarly effective, $Q_m(1) = 0.49$, $p = .489$. Given that the majority of studies used cultural tailoring to personalize interventions to the African

Figure 2: Meta-Analytic Results of the Efficacy of Breast Cancer Screening Interventions in African American Women

American female population, examination of the moderating impact of such tailoring was not feasible. A nonsignificant trend did suggest that proscreening intervention efficacy decreased with mean participant age, $Q_m(1) = 3.02$, $p = .082$, which reduced the heterogeneity of study effect sizes to a nonsignificant level, $Q_e(18) = 25.90$, $p = .102$. No other moderators were assessed that significantly accounted for variability in effect sizes. File-drawer analysis indicated that 255 unpublished null studies of proscreening interventions would need to exist to reduce the effect size of proscreening interventions observed in this meta-analysis to nonsignificant levels.

DISCUSSION

Given the correlation between breast cancer screening and mortality, increasing mammography rates are both primary and secondary intervention strategies to decrease cancer death rates in African American women. In our analysis of clinical trials, for breast cancer screening with African American women, some interventions found to be effective were specifically tailored to meet the perceived risk of African American women. However, the circumstances under which the interventions were effective were unique. The intervention approaches assessed, as effective, were based on social cognition models for health education and health promotion. These strategies varied and included educational awareness; constructs from both the health beliefs and stages of change model were utilized. The interventions took place in various community locations and the home of participants.

We found screening interventions which were tailored to connect with women on a socio-cultural, racial, ethnic, and cognitive level were effective, but no systematic moderators supported this finding. Some of the culturally tailored interventions were associated with increased mammography screening rates. Gathirua-Mwang et al. (2016) found the use of a mailed interactive DVD for low-income African American women was five times more effective than usual care for promoting mammography screening at the 6-month follow-up. Marshall et al. (2015) found both patient navigation and printed educational materials increased self-reported mammography utilization.

Tailored messages versus targeted messages appeared to be successful in some situations (Ashing-Giwa 1999; Kreuter et al. 2005). However, Jibaja-Weiss et al. (2003) found personalized tailored letters with more individualized information on cancer risk may decrease the likelihood of follow-up screening and personalized form letters with general information may

increase follow-up screening. It appears the acquired information on individualized risk had a more negative impact on participation screening in their study.

The integration of culture norms with mammography knowledge may enhance the utilization of breast cancer screening services. Kreuter et al. (2005) found women who received behavioral construct tailoring, which included concepts from behavior change theories, and culturally relevant tailoring, which included concepts on religiosity, collectivism, racial pride, and time orientation, were more likely to receive mammograms. When magazines were tailored to increase breast cancer screening, these culturally relevant concepts were integrated with women's health concerns as the major focus. For example, the investigators were deliberate in producing the magazines with beautiful bold colors, knowledge of breast cancer, mammography knowledge, breast cancer treatment knowledge, barriers to mammograms, and stages of readiness, etc. Each magazine was personalized with participant's name, and the artwork of local African American Artists was featured. Text and graphic were developed with participation of staff and volunteers who were African American. The socio-cultural context appears to enhance the effectiveness of tailored message for breast cancer screening for some women, but not all women (Kenny et al. 2004). The systematic attention to integrating culture into interventions enhanced the effectiveness of messages to African American women in the Kreuter et al. (2005) study.

There are limitations to our review. We started out reviewing over 300 date-based breast screening studies. However, when we narrowed our inclusive criteria to randomized clinical trials (RCT), African American women, studies published in English and conducted in the United States, quantitative screening rates post intervention, and conducted psychosocial, behavioral, or education interventions we concluded with 14 studies. Therefore, our findings are limited to the women who were included in the studies we reviewed. Further, few studies examined follow-up beyond 24 months, and thus, the long-term impact of these screening interventions is not clear, which will be an important direction for future research. The studies took place in urban settings. Both age of participants and SES varied across the different projects. Neither findings nor effectiveness of these interventions can be generalized to all African American women. African American women are not a homogeneous group; there are differences within this target population. Interventions must be developed to target the women unique to the research goals. In addition, the knowledge base of African American women varies. With all the attention to cancer risk in the media, some women are unaware of the benefits

of screenings and the availability of affordable mammography screenings, where they exist. For women who may be aware of the benefits of breast cancer screening, information regarding available resources may not be available (Kenny et al. 2004).

We know there are well-documented barriers to health care utilization, like breast cancer screening. This includes low income, lack of access to care such as transportation to a screening center, knowledge of breast cancer risks, recommendation from a provider, cultural differences, and having a usual source of care. This research sheds light on some of the socio-cultural strategies that can be helpful for developing culturally relevant prevention strategies to increase breast cancer screening. One of the sources, which did not meet our inclusive criteria, suggests the importance of connecting on the socio-cultural dimensions, that is, religion, racial pride, the mind, body, and spirit. In our reviews of the literature, religion and racial pride were consistent suggestions among the culturally relevant tailoring strategies for health care utilization. Jibaja-Weiss et al. (2003) findings suggest communications tailored to individual risk based on medical records did on result in more breast cancer screenings for the participants in their study. It appears from the breast cancer screening that interventions targeted at African American women should be more holistic. Screening should be among several strategies for better health outcomes and not just the only focus for health promotion studies.

ACKNOWLEDGMENTS

Joint Acknowledgment/Disclosure Statement: We want to acknowledge the support of the School of Social Work, Center on Race and Social Problems, University of Pittsburgh.

Disclaimer: None.

Disclosures: None.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the supporting information tab for this article:

Appendix SA1: Author Matrix.

Table S1: Characteristics of the Intervention and Comparison Groups of the Included Studies.