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## A conceptual model of social networks and mechanisms of cancer mortality, and potential strategies to improve survival

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#### Abstract

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© Society of Behavioral Medicine 2018. All rights reserved. For permissions, please e-mail: journals. permissions@oup.com. Women with larger personal social networks have better breast cancer survival and a lower risk of mortality. However, little work has examined the mechanisms through which social networks influence breast cancer outcomes and cancer outcomes more generally, potentially limiting the development of feasible, clinically effective interventions. In fact, much of the emphasis in cancer research regarding the influence of social relationships on cancer outcomes has focused on the benefits of the provision of social support to patients, especially through peer support groups, and only more recently through patient navigation. Though critically important, there are other ways through which social relationships might influence outcomes, around which interventions might be developed. In addition to social support, these include social resources, social norms, social contagion, social roles, and social burdens and obligations. This narrative review addresses how social networks may influence cancer outcomes and discusses potential strategies for improving outcomes given these relationships. The paper (a) describes background and limitations of previous research, (b) outlines terms and provides a conceptual model that describes interrelationships between social networks and relevant variables and their hypothesized influence on cancer outcomes, (c) clarifies social and psychosocial mechanisms through which social networks affect downstream factors, (d) describes downstream behavioral, treatment, and physiological factors through which these subsequently influence recurrence and mortality, and (e) describes needed research and potential opportunities to enhance translation. Though most literature in this area pertains to breast cancer, this review has substantial relevance for cancer outcomes generally. Further clarification and research regarding potential mechanisms are needed to translate epidemiological findings on social networks into clinical and community strategies to improve cancer outcomes.

#### Keywords

Social networks, Social support, Cancer outcomes, Conceptual model

#### INTRODUCTION

Women with larger personal social networks, defined as the web of social relationships that surround an individual [1], have often been shown to have better breast cancer survival [2–6] and larger social networks have been associated with lower mortality generally [7]. However, exceedingly little work has examined the mechanisms through which social networks influence breast cancer outcomes and cancer outcomes more generally, inhibiting the development of feasible, clinically effective interventions [8–12].

#### Implications

**Practice:** Peer support groups, patient navigation, and acute and social services have been predominant strategies to augment support in cancer patients though other potential strategies could include caregiver training in late-stage patients, family and community social network interventions, patient communication and relationship skill interventions, and online support resources.

**Policy:** While it is important to augment social support to cancer patients, policymakers should also consider the many resources social networks bring that transcend social support; such resources may provide clues regarding the types of strategies that could be leveraged to improve cancer survival.

**Research:** This paper provides a conceptual model describing mechanisms through which social networks influence cancer outcomes though further clarification and research will be needed to translate epidemiological findings into clinical and community strategies to improve outcomes.

This narrative review addresses how social networks may influence cancer outcomes and discusses potential strategies for improving outcomes given these relationships. Though the review references breast cancer extensively given that the bulk of the literature in this area focuses on this cancer, the model has considerable relevance for cancer outcomes generally.

It is divided into five parts. The first section describes background and limitations of previous research. The second section begins with a conceptual model that describes interrelationships between social networks and relevant variables and their hypothesized influence on cancer outcomes. In that section, I define relevant terms and describe advances afforded by the model. In the third section, I clarify social and psychosocial mechanisms through which social networks affect downstream factors. In the fourth section, I describe downstream behavioral, treatment, and physiological factors through which social relationships influence recurrence and mortality. The fifth section describes needed research and potential points of leverage, that is, opportunities and strategies, limitations of those, and alternative potential strategies.

#### BACKGROUND AND LIMITATIONS OF PREVIOUS RESEARCH

Substantial interest in the area of social support and cancer survival emerged with a paper published by Spiegel et al. [13] in which the authors reported that a peer emotional social support intervention, designed to improve quality of life (QoL) in metastatic breast cancer patients, was related to two-fold higher survival compared with the controls (36.6 vs. 18.9 months). This was an incidental finding; the study was not powered to examine survival, and only 11 participants remained in the control group by study end. Goodwin et al. [9] attempted to replicate this intervention. They powered the study to examine survival, and Spiegel was a consultant involved in developing the intervention. However, in 2001, in the New England Journal of Medicine, Goodwin et al. reported no effect of the social support intervention on survival. Spiegel et al. [8] also reported no benefit of another, more recent peer support intervention on survival though results suggested a possible benefit in the small subset of triple-negative metastatic breast cancer patients.

Social support interventions have focused primarily on providing informational and emotional support [4, 14], and these have been conducted in women with metastatic breast cancer. Though peer support interventions are generally, though not always [11, 12], related to improvements in QoL, most trials have failed to show improvements in survival [8–10]. A meta-analysis of previous trials further corroborates the lack of significant survival benefit [15].

Clinical trials are generally considered the gold standard in research, superior to results obtained from observational studies. However, there are well-known limitations of clinical trials, which could negate the influence of an intervention even when there is a true causal effect. An intervention may be of insufficient duration, or support from strangers could be less efficacious than support from people already known. The study population may be inappropriate. Most previous trials have been in metastatic patients in whom it may be difficult to extend life though opportunities might exist in evaluating the benefit of emotional support in earlier stage patients. There are several types of support including emotional, tangible/instrumental, appraisal, and informational support, positive interaction, and affection [1, 16], and potentially others including spiritual support. Types of support relevant to survival may include any or all of these; emotional support itself may be insufficient to affect survival. Moreover, there is a multiplicity of social and psychosocial mechanisms through which social networks may influence or be leveraged to improve survival. As a result, implications regarding the influence of social support on breast cancer survival based on previous trials are unclear.

By contrast, observational data strongly suggest a potential role of naturally occurring social relationships on breast cancer-specific survival [4, 17]. In 2,835 postmenopausal breast cancer survivors in the Nurses' Health Study (NHS), Kroenke et al., found that socially isolated women, that is, women with small networks, assessed prior to diagnosis were twice as likely to die of breast cancer than were socially integrated women [4]. In a more recent study, in 9,267 women from the After Breast Cancer Pooling Project (ABCPP), socially isolated women with small networks had higher risks of recurrence (HR = 1.43, 95% CI: 1.15-1.77), breast cancer-specific mortality (HR = 1.64, 95% CI: 1.33-2.03), and total mortality (HR = 1.69, 95% CI: 1.43-1.99), compared with socially integrated women [17]. A recent meta-analysis corroborates these findings [18].

Observational studies have substantial limitations, most notably that those with more salutary social networks generally also have other characteristics or behaviors that are related to survival. Women with larger networks tend to have greater physical activity and a lower prevalence of smoking, obesity, and alcohol overconsumption [19]. However, in analyses of social network size and breast cancer survival, adjustment for lifestyle factors has not explained and in fact has only slightly attenuated associations [4, 17]. It is possible that there are confounding factors, for example, personality factors such as extraversion and conscientiousness, which could influence a person's social networks and their health behaviors. However, previous research shows modest or weak relationships between personality and health behaviors [20-22] and no association between personality factors and breast cancer outcomes [23, 24]. Indeed, the magnitude of the association between social networks and breast cancer survival has been larger than associations of either lifestyle factors or personality factors and breast cancer survival. Some scientists might disregard observational findings given findings from trials. But, given the multiplicity of different types of social support as well as other mechanisms through which social relationships may influence breast cancer survival, disparate findings should instead signal the need for additional research to develop and evaluate other strategies. To date, few other types of social interventions have been conducted. Current efforts are underway to evaluate the influence of support provided, for example, by peer navigators, individuals who have previously undergone diagnosis and treatment of breast cancer, on QoL [25] in cancer patients and on timeliness of cancer care [26, 27]. Considerable recent research has evaluated the TBM

Table 1   Social network terms	
Social network terms	Definition
General terms	
Social networks	The web of social relationships that surround an individual
Social ties	Members of a social network
Sociocentric social networks	A social network comprised of a web of social ties in which the complete set of ties in a group is known
Egocentric social networks	A personal network approach that studies ties from the reference point of the pa- tient. A social network is comprised of a web of ties (egos and alters) with the patient (ego) at the center of the network.
Ego	The central person in an egocentric social network
Alters	Members within a social network
Structural social support	Often measured in terms of social ties and is conceptualized as the social support that derives from the social network
Strong ties	Close friends and family
Weak ties	Acquaintances or ties to acquaintances
Structural dimensions of social networks	
Strength of ties	Represents the strength of relationships and is a function of the amount of time a person has known an alter and the closeness/intensity of the relationship
Diversity	Represents the number of different types of ties in a person's network.
Multiplexity	Refers to overlap in relationships
Density	The extent to which the ties are directly connected to, that is, know and associate with, one another
Network	Refers to the ties that connect a specific set of alters
Degree	Quantifies the connections an individual has in a network; akin to social network size
Psychosocial mechanisms of social networks	
Social support (or functional social support)	The perception and reality of the exchange of assistance through social relationships
Social strain	The negative aspects of social relationships that result from stressful relationships or the burdens that arise from social obligations
Social regulations	Restrictions designed to discourage harmful behavior or encourage socially desir- able behavior
Social norms	Rules of behavior considered acceptable in a group or society
Social contagion	The spread of ideas, attitudes, moods, or behaviors in a group
Social roles	The roles an individual fills (e.g., parent, employee, volunteer, spouse)

influence of patient navigation. However, further observational studies are needed to inform possible intervention strategies. The development of a conceptual model may help to inform these strategies.

## TERMS, CONCEPTUAL MODEL, AND THE IMPORTANCE OF SOCIAL NETWORK MEASURES

#### Defining and distinguishing terms

Social network terms described in this paper are found in Table 1. Previous studies have often equated social terms including social networks, social ties, social function, social well-being, and social support. Though these may be correlated, they are not synonymous. Other terms including social regulation, social norms, and social contagion, have not been explored in the context of cancer survivorship research.

Social networks are defined as the web of social relationships that surround an individual [1]. A social network is comprised of a web of social ties (egos and alters). Social networks and social ties are structural factors, that is, economic, social, policy, organizational or other aspects of the environment that serve as barriers to or facilitators of behaviors and other predictors of risk, and have been called structural social supports. Social support, the perception and reality of the exchange of assistance through social relationships, is also called functional social support. Thus, the individuals make up the structure and the assistance provided the function. However, the term "structural social support" is problematic; while social relationships can and do provide social support, this terminology disregards the negative aspects of social relationships, that is, social strain, as a result of stressful relationships or the burdens that arise from the obligations of social relationships. The quality of social relationships is affected by both support and strain, and the influence of both positive and negative relationship factors on health should be considered in studies of cancer patients. Social well-being and social function, also sometimes used interchangeably with social support, do not describe the support provided in relationships but rather refer to OoL outcomes-feelings of satisfaction with social relationships or the ability to maintain social obligations. Social regulations are restrictions designed to

discourage harmful behavior or encourage socially desirable behavior. Social norms are the rules of behavior considered acceptable in a group or society, and social contagion is the spread of ideas, attitudes, moods, or behaviors in a group. Social roles refer to the roles an individual fills (e.g., parent, employee, volunteer, spouse). In most cancer research, investigators explore the influence of strong ties, that is, close friends and family, on outcomes. However, weak ties or ties to acquaintances [28] could also have an important role in cancer outcomes.

#### Conceptual model

The conceptual model presented below (Fig. 1) was informed in part by an influential model of social networks and health developed by Berkman and Glass [1]. However, the model presented here focuses specifically on cancer outcomes and is informed by major current topics in the cancer literature. While the broad social context is highly relevant, this model eliminates explicit reference to embeddedness within social-structural conditions, to focus attention on social networks and because social network characteristics reflect that embeddedness. Moreover, by necessity, studies of cancer survivorship focus on individual cancer patients and survivors. While the measures of interest are not limited to the individual level, the model centers around the individual. The model also emphasizes the need for direct measures of social networks and their structural characteristics. Clarification is provided in Fig. 1 regarding interrelationships between these variables as well as how social relationships influence cancer outcomes.

In this conceptual model, social networks influence cancer outcomes through several social and psychosocial pathways including social support, social regulation/norms, social roles, social burdens, and institutional social resources. Through these pathways, social networks influence downstream factors including treatment and lifestyle factors as well as psychophysiologic pathways, which in turn influence recurrence, cancer mortality, and mortality from other causes. These relationships are further modified by social contextual factors and factors related to disease severity. Understanding how social networks influence cancer treatment and the ability to identify patients at risk are critical to being able to devise effective social strategies.

#### Advances afforded by this conceptual model

Useful conceptual models are sufficiently broad to stimulate thinking and apply to a variety of situations but also point to the need to consider ideas that might be overlooked. This model motivates consideration of the following: (a) the structural, not just the individual, effects of social networks on cancer outcomes, (b) the context in which social networks exert their influence leading to potentially positive and negative effects, and (c) psychosocial mechanisms other than social support through which social networks exert influences. It also points to the need to consider behavioral and biological mechanisms and the need to consider associations in different cancers.

## Need to examine structural, not just individual, effects of social networks

In cancer research to date, approaches to examining the influence of social networks have employed individual-level data including epidemiologic social network indexes including information on numbers of (close) friends and relatives, religious and

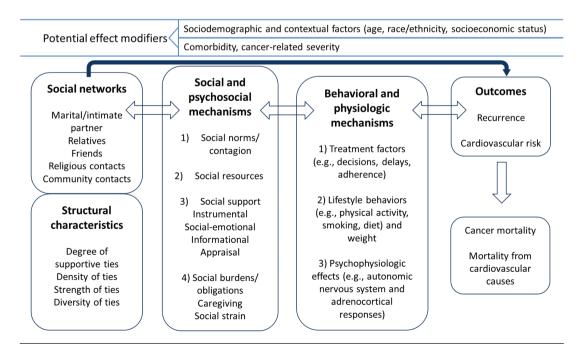


Fig 1 | Social networks and mechanisms through which social relationships influence cancer survival

community participation, marital status and work status, and measures of social support. These have provided useful information, and the approach is appropriate given the types of data that typically exist in cohort studies (a limited set of social ties) or cancer registries (usually marital status only). However, the social environment is not optimally characterized only by measures of individual social ties.

The influence of social networks on health outcomes is also a function of *characteristics or the structure* of the network and of actors' positions in the network. In sociocentric social networks, the complete set of ties in a group is known (e.g., friendship ties in a school classroom). When resources constrain the ability to evaluate the universe of ties or when it is more advantageous to understand the ties of a specific individual, researchers can collect data on egocentric social networks. In this personal network approach [29], the egocentric approach studies ties from the reference point of the patient.

In current work, colleagues and I are beginning to explore potential insights that may be developed from egocentric social network methods. In egocentric data, social networks are naturally occurring groups within which members ("alters") may influence each other's behaviors. A "network" formally refers to the ties that connect a specific set of alters [30, 31]. Social network analysis is an effort to describe the social environment by quantifying social relationships among this group of alters [32]. Using social network data collection and analysis, several new dimensions can be characterized and analyzed; these enable examination of the influence of social networks beyond size and individual ties.

Among these, *degree* quantifies the connections an individual has, akin to social network size. Because of the potentially substantial burden on study participants, researchers using egocentric social network data collection generally limit the number of alters. In this case, the degree or number of supportive ties, or alternatively, the degree of strained ties, may be useful measures of the quality of the network. The strength of a patient's ties represents the strength of relationships and is a function of the amount of time a person has known an alter in combination with the closeness and intensity of the relationship. Diversity of ties represents the number of different types of ties in a person's network. If a patient has a large network that consists primarily of family members, the influences on health may differ from those who have a greater number of different types of ties including people they know through work, volunteering, community participation, and religious participation. Multiplexity refers to overlap in relationships and it may be more or less advantageous to have persons in one's network assuming multiple roles. Density is the extent to which the ties are directly connected to, that is, know and associate with, one another. Greater network density, occurring when the ties mentioned by the patient also know each other well, could help with the coordination of patient care in seriously ill patients. Alternatively, a denser network may limit the influx of new information influencing decisions about or persistence with treatment. Given that caregiving is predominantly provided by women, a higher proportion of female network members could potentially translate to better health outcomes. Higher bridging potential of a participant in a network may afford greater access to resources to otherwise disconnected networks, but it can also reflect greater burden on an actor as that person navigates, connects, and meets the needs of actors from separate networks, with possible positive or negative effects on a patient. Social networks can also include weak ties, that is, acquaintances, that connect patients with opportunities, experts, and information. To our knowledge, no research has examined sociocentric social networks and cancer outcomes though work in egocentric social network data collection may provide new insights about the nature of the impact of social networks on cancer survivorship.

#### Researchers should consider the context of social relationships

Effects may differ by sociodemographic factors. It is important to consider that while social network measures measure an individual's immediate social environment, they also capture information about the macro-level social environment. Thus, it is also important to consider the social context of people's relationships. Most studies of social networks and health outcomes report findings from predominantly white populations [7]. However, in recent work in the ABCPP, the largest observational study of social networks and breast cancer mortality to date, Kroenke and colleagues found that associations with mortality outcomes depended considerably on sociodemographic factors [33]. Specifically, associations between social ties and breast cancer mortality differed by race, age, and country of origin. Family and friendship ties were critical predictors of the outcome in the subgroup of African-American, Asian, and Hispanic women. A partner or spouse was predictive in older white women. Community ties predicted lower breast cancer mortality in older white women and in Asian women. There were no ties that predicted outcomes in younger white women. The social networks of different race/ethnic groups may differ substantially due to cultural factors and socioeconomic structures since education, income, and race determine access to healthful networks. Moreover, the ability to leverage assistance in relationships from naturally occurring networks may be strongly shaped by sociodemographic characteristics. Most cancer cohorts have extensive cancer data but limited social data. Because of this, a common approach to examining the social environment has been to look at effects of social networks in page 633 of 642

conjunction with or stratified by sociodemographic factors. To capture the influence of social networks on health, collecting information about context (e.g., egos' and alters' race/ethnicity, socioeconomic status, supportiveness, strain, health beliefs) is important. Fortunately, collection and analyses of these data are facilitated by processes in egocentric social network data collection.

*Effects may differ by treatment severity.* Cancer stage may also modify effects of social relationships on outcomes. In the ABCPP, higher breast cancer-specific and overall mortality were apparent in socially isolated women with stage I and II, but not in those with stage III and IV, breast cancer. In the Pathways study, affection predicted better QoL in early-stage breast cancer patients but worse QoL in late-stage patients [34]. In contrast, tangible support was related to better QoL in late, but not early stage, patients. This may be related to the differing needs of cancer patients by stage as well as the abilities within naturally occurring social networks to meet those needs.

## Researchers should consider psychosocial mechanisms beyond social support

Many investigators have collected information on socially supportive relationships to attempt to understand the influence of social relationships on health outcomes. This is an important start. However, the exploration of the influence of social relationships on cancer outcomes should not be limited to the study of supportive relationships and should include examination of other psychosocial mechanisms such as social norms, social resources, social roles, and social burdens. In fact, previous research in cancer almost uniformly presumes benefits in social support and social relationships, though this idea has never been explicitly stated. This means that research should reflect the potential negative aspects of social relationship on outcomes. A Women's Health Initiative study showed among those with caregiving obligations or highly strained relationships that a larger network of relatives was related to poorer survival after a diagnosis of breast cancer [35]. In addition, a study in the Life After Cancer Epidemiology (LACE) cohort showed that women with small but supportive relationships had no higher mortality than women with large networks though women with small, unsupportive networks did have higher mortality [36].

This approach may help address criticisms regarding replication of findings and ensuring scientific rigor, particularly in regard to social relationships and their complex influence on health. It may also help to devise approaches to translate findings to cancer care. In the cancer literature, associations between social relationships and cancer outcomes have been somewhat mixed, even within studies such as the recent study in the ABCPP [33]. Understanding the context of relationships, including their positive and negative aspects, may help to explain these "mixed" findings, which may simply reflect the complexity of social relationships. They may also facilitate a clear-eyed view of what is feasible and necessary given the context of people's relationships. For example, a patient with few supportive social ties might benefit from peer emotional support groups. However, a patient with supportive relationships who provides caregiving to others might better be helped through provision of services to dependents. At a minimum, it is important to collect information on the quality of relationships. However, the collection of data on context also extends to understanding the sociocultural and socioeconomic contexts of patients' social networks.

#### Researchers should consider associations in varied cancers

The literature on social networks and cancer has focused largely on breast cancer but work is needed to evaluate relationships with other types of cancer.

#### PSYCHOSOCIAL MECHANISMS THROUGH WHICH SOCIAL NETWORKS OPERATE

Little is known about how social networks influence cancer prognosis, and as indicated, the primary focus in cancer research has been on evaluating the influence of social support, critically important but insufficient to describe the influence of social relationships on cancer outcomes. Other relevant social and psychosocial mechanisms include access to social structures and resources, social roles, social regulation and relatedly social norms and social "contagion," social strain, and social/caregiving roles.

#### Social support

One of the primary ways social networks are hypothesized to influence cancer outcomes is through provision of social support. In addition to tangible, emotional, informational, and appraisal support [1], Sherbourne and Stewart identified affectionate support and "positive social interaction" in patients with chronic illness [16]. Tangible support includes rides to the hospital, trips to the pharmacy, or provision of healthy meals [37, 38]. Network members may provide informational support through referrals to physicians and clinics, alternative types of treatment, or may buffer stress [39] through provision of emotional support, "positive interaction," or other types of support. Affection includes hugs and other signs of tenderness, warmth, and caring. Positive interaction is defined as the availability of someone with whom to have fun and get one's mind off things for a while and was the most predictive type of support in a Pathways study of social support and QoL [34]. In addition to emotional and

social dimensions of QoL, higher "positive interaction" predicted better physical QoL; it was related to significantly lower levels of pain, less need for bed rest, and higher levels of energy [34]. Among patients who require caregiving, their caregivers' social networks may also exert indirect effects on patient outcomes through levels of caregivers' perceived social support [40].

## Social resources (social capital, social structures, resources)

Though social structures provide the context in which social networks operate, being a part of a social network can afford opportunities to connect to resources available within (the structure of) a network. This overlaps with the concepts of social support and social capital [41], the latter leading to benefits to an individual even without individual connection to actors within a network (e.g. social capital and the trust within a community it affords making the community a safer place to live). However, it is distinguished from these concepts to the degree that the resources derive from connections to others based on position within a specific network. A person from one's social network may facilitate referrals and connections to highly experienced oncologists or doctors in larger clinics or comprehensive cancer centers, those who can help navigate issues with health insurance, referrals to scientists and groups conducting clinical trials, those who have experienced cancer, others with financial resources to help, or other people in the network with access to institutions that can increase access to resources, information, or opportunities to bring about change (e.g., increasing political will to fund cancer research grants, develop philanthropic organizations, build educational organizations, or organize fund-raising walks and other activities). Thus, depending on network structure [28], cancer patients may have different levels of access to resources, referrals, advice, opportunities to participate in clinical trials, and knowledge about the side effects and outcomes of treatment. These then lead to differences in decisions about treatment, influencing prognosis. Thus, beyond direct provision of resources, the network brings with it access to other people and to the social institutions, power, and resources that go along with knowing and being able to access others in the network.

#### Social regulation, social norms, and "contagion"

Social relationships and interactions influence behaviors and health outcomes by "contagion" [42, 43] through norms [1, 43], peer modeling [44], and social regulation. Identification with social network members may increase the likelihood of adopting behaviors [45, 46] through influences on shared behaviors and norms. One's health-related behaviors including smoking, diet, alcohol intake, and obesity status may influence the behaviors of others in a network. It is unknown whether attitudes around adjuvant endocrine therapy (AET) could influence others' decisions to start or persist with AET, though it is an intriguing question given low levels of adherence currently reported in breast cancer patients [47-52].

#### Social and caregiving roles

Social networks may also bring costs or burdens that can adversely influence health [35]. Larger social networks may increase caregiving obligations since women comprise 75% of informal caregivers [53, 54]. While potentially rewarding, caregiving can be physically and emotionally demanding, leading to poorer self-care and worse health outcomes [55–60]. However, the "mission" African-American women reported in caring for others in one study promoted continuation with treatment [61].

#### Social strain and stress

Though social isolation is considered to be stressful, and that is the major underlying hypothesis of most research on social isolation and physiological factors, social relationships can also be stressful. Family communication issues can also lead to higher levels of stress. Social relationships can be burdensome, strained, or even abusive. Though being married has often been associated with better health and lower mortality, marital quality may modify the influence on health, especially in women.

## DOWNSTREAM BEHAVIORAL AND PHYSIOLOGICAL MECHANISMS

Social networks influence cancer outcomes through several downstream factors including behavioral, treatment, and physiologic factors.

#### Behavioral

Social network members may influence lifestyle through different types of social support [16]. Social norms and identification with social network members increase the likelihood of adopting lifestyle behaviors similar to those members [45, 46]. Low social network diversity, defined as the variety of social ties (connections) or roles, has been related to alcohol dependency, smoking, low levels of physical activity [62, 63], and poorer health generally [64]. Norms have been shown to influence screening [65]. Social relationships may also adversely affect health-related outcomes through relationship obligations or social strain, and related to this, higher levels of psychological distress and reduced motivation for self-care. Lifestyle risk factors, including poor diet quality [66], physical inactivity [67], smoking [68], and related to these, obesity [69] have each been associated with poorer cancer-specific and overall survival and may be mechanisms through which social relationships influence cancer outcomes.

#### Treatment

Social relationships may influence delays in diagnosis and treatment and affect treatment decisions. Greater social integration has been related to a higher likelihood of mammography [70], though not in all studies [71]. Perceptions that screening is normative, encouragement by family/friends, and religious support are associated with screening adherence [65, 72-74]. Women's social relationships (e.g., spouse, family, friends) influence choice of mastectomy or lumpectomy [75], whether to pursue chemotherapy [76], and other treatment decisions [76]. Supportive relationships have been related to higher treatment adherence in people with coronary heart disease, hypertension, emerging diabetes [77-82], and other conditions [83]. As previously indicated, the "mission" women feel in caring for others may promote continuation with treatment [61]. However, strained family relationships may lower treatment adherence, mediated by risky health behaviors [84] or reduced self-management of disease [85]. Caregiving burdens may reduce adherence [86]. A lack of support or social resources may lead to treatment delays which are associated with poorer cancer outcomes [87]; delays as short as 3-6 months from diagnosis to the start of treatment decreased 5-year breast cancer survival rates by 12% [87]. These may also alter treatment decisions (e.g., radiotherapy [88, 89], chemotherapy [90]), which may influence survival. A substantial literature shows that suboptimal treatment jeopardizes breast cancer survival.

#### Physiological

Recent reviews by Hinzey et al. [91] and Lutgendorf and Andersen [92] have described possible biological mechanisms by which social relationships might have direct effects on cancer survival. In the context of the "hallmarks of cancer" [93, 94], those are described by the effects of social relationships on physiologic changes that underlie and determine cancer progression.

In particular, social isolation, considered a chronic psychological stressor, is well known to activate the hypothalamic-pituitary axis resulting in the secretion of catecholamines (stress hormones), which have downstream effects on tumorigenic markers through adrenergic pathways. Biomarkers involved in cancer progression include interleukins (IL), vascular endothelial growth factor (VEGF), matrix metalloproteinases (MMPs), prolactin, and tumor necrosis factor (TNF)-a. Stress hormones such as norepinephrine have been shown to cause upregulation of cytokines such as IL-6 and IL-8, which are proangiogenic and support tumor progression by regulating hallmarks of cancer [93, 94]. IL-6 also protects cancer cells from therapy-induced DNA damage, oxidative stress, and apoptosis. Hypothalamic-pituitary-adrenal-axis activation has also been related to higher VEGF expression; overexpression of VEGF enables a tumor to develop the vascular architecture needed to grow and metastasize. VEGF is higher in cancer patients [95]; numerous studies show decreased overall and disease-free survival in tumors overexpressing VEGF, and elevated VEGF-A has been related to poor breast [96, 97] and colorectal [98] cancer prognosis. Psychological stress has also been related to elevated MMPs, which are enzymes that degrade the extracellular matrix and promote carcinogenesis through tissue remodeling, cell proliferation, apoptosis, angiogenesis, and metastasis. Prior research has also found caregiving stress to be related to elevated levels of IL-6[99] and to prolactin [100], important in cancer progression by inhibiting apoptosis, increasing cell proliferation, and enhancing cell migration in certain cancer cell lines, as well as inducing malignant transformation in human immortalized normal epithelial cells. TNF- $\alpha$  is a cell signaling protein (cytokine) involved in systemic inflammation and is also strongly implicated in cancer prognosis [101]. Measures of psychological stress have been related to higher levels of TNF- $\alpha$ , IL-6, VEGF, and prolactin in healthy populations and in breast and ovarian cancer patients [92].

In cancer patients, social isolation has also been related to higher levels of VEGF, IL-6, and TNF- $\alpha$ , factors that support angiogenesis and further growth of a tumor [101, 102]. Normally, there is inhibition of unchecked cell growth. However, social isolation is related to inactivation of tumor suppressor genes. A lack of social support has also been related to elevated levels of MMPs, enzymes which stimulate invasion into the cell matrix leading to metastasis of the tumor. Social support has been linked to greater natural killer cell activity in ovarian cancer patients [103]. Each of these biological markers has been related to cancer survival.

#### NEEDED RESEARCH AND OPPORTUNITIES FOR TRANSLATION TO CLINICAL CARE

Relatively few strategies to leverage social relationships to improve cancer survival have been developed or tested. A possible presumption to date is that social networks are clinically irrelevant because changes in the social environment may require nonclinical strategies. And yet, advances could be made at individual, clinical, and community levels. To date, in the clinical setting, strategies have focused on providing social support through peer groups or through peer navigators or by meeting acute needs that might otherwise usually be provided by personal supports (e.g., rides to the doctor). This next section details strategies for augmenting support to patients focusing on potential clinical strategies including caregiver training, patient (peer or nurse) navigation, provision of acute (social) services, social support in early-stage patients, resources available in religious and community groups, online resources, relationship skills improvement, family interventions to improve medication adherence, and other social resources and opportunities including social network behavioral interventions [104, 105]. It will be important to

evaluate these strategies in continued research; their benefits cannot be presumed. Effective clinical strategies will capitalize on information about the specific types of resources afforded by social networks within specific populations of cancer patients.

#### Patient navigation: Nurse navigator and peer navigators

An important direction in research over the past several years has been the area of patient navigation. Patient navigation programs were initially developed to assist breast cancer patients, particularly minority and low income women, with navigating the complex network of cancer diagnosis and treatment services with the goal of reducing barriers to earlier diagnosis and treatment. Some address QoL and psychosocial outcomes [106]. Patient navigators were originally envisioned as members of the community they were serving, that is, cancer patients or peer navigators. However, navigators include cancer survivors, nurses, social workers, other health professionals, or lay/community health workers [107]. The role of the navigator varies between programs but usually involves coordination of care and encouraging patients to pursue continued care, if needed [106]. Navigators may also provide health education about breast cancer and its treatment, emotional support, informational support, assessment of barriers, and assistance with and resources related to financial and health insurance issues, transportation services, child care, and translation.

Despite the rapid proliferation of patient navigation programs for patients with cancer, particularly for breast cancer, research on the efficacy of these programs has been limited. A recent systematic review found that while patient navigation programs improved surveillance and mammography rates, there are few high quality studies of the effect on treatment outcomes [108]. Of seven studies that looked at timeliness of treatment initiation, all found that women who received navigation initiated treatment earlier, but only two demonstrated statistically significant differences [108]. One study found that that receiving patient navigation was associated with higher rates of receiving AET among women with hormone receptor-positive breast cancer though assistance from a navigator was not associated with rates of chemotherapy or radiation therapy [109]. Two studies found improvements in psychosocial measures after receiving navigation. However, neither included a control group [110, 111]. A third study found that women with suspicious mammogram results randomized to patient navigation had lower mean anxiety scores and higher satisfaction with care compared with usual care controls one month after final resolution of mammogram results [112]. No studies have examined associations with survival; such research is greatly needed.

#### Peer social support interventions in early-stage patients

Given that patient needs differ by stage, needs for and the influence of social support may also differ by stage. Though peer support group interventions have been associated with modest psychosocial benefits [9, 113, 114], as indicated, there is little evidence that peer social support interventions improve cancer survival in metastatic patients even when conducted by well-trained experts. Corroborating this was the aforementioned finding from the ABCPP in which associations showing potentially salutary effects of larger social networks on breast cancer mortality were apparent only in early-, not late, stage patients. To influence survival, social interventions might target patients with earlier stage cancer, a strategy which has not been tested in research. Another potential opportunity, investigators might consider the possible merits of augmenting types of social support other than emotional support to influence patient outcomes.

#### Acute services and social services

Given barriers to and a lack of supportive care, social workers may be called on to communicate with patients about social resources to meet acute needs during treatment. Delays in treatment may be related to the inability to get a ride to the hospital in a timely manner, or opting against treatment may be related to the anticipated difficulties in meeting one's own needs or in coping with the combined demands of treatment and work and caregiving responsibilities. A person's ability to complete treatment with chemotherapy, for example, could be influenced by a lack of help in managing day-to-day responsibilities, which may lead to the desire to end treatment early; acute services could promote treatment completion. Kaiser Permanente, for example, is piloting strategies to provide low-cost meals during acute illness, and social workers are connecting patients with financial need to resources to help pay for care. The Road to Recovery program, offered by the American Cancer Society, provides rides to cancer patients to treatment appointments. There are also numerous educational and emotional support online resources. Among these and partnering with the American Cancer Society, "I Can Cope" is an online cancer education and support program for people facing cancer and the caregivers supporting them. Each of these support resources merits evaluation.

#### Caregiver training in late-stage patients

Nonsignificant associations in late-stage cancer patients in the ABCPP also suggested that resources provided within naturally occurring networks may not be well matched to the needs of those with latestage cancer [115]. Managing relationships with family and friends providing caregiving may be difficult when both patients and caregivers are coping with feelings of high distress [116] and expectations regarding needs differ [117]. As mentioned, in the Pathways Study, tangible support was important to QoL but only in women with late, not early, stage breast cancer [36]. Specific training may be needed to help assist late-stage cancer patients to improve QoL. Deserving mention are the frequent economic sacrifices made by caregivers to provide support and care; consideration should be given to providing resources or paid support for otherwise unpaid, "informal" caregivers and evaluating the effects on those receiving caregiving.

## Interventions involving naturally occurring social network members

There has been limited exploration of the ways through which naturally occurring networks affect cancer survival and thus no exploration of ways to clinically address the needs met by patients' personal social networks. Relatedly, there has been no research to evaluate or test how network characteristics might be influenced to alter survival.

#### Family interventions

However, opportunities potentially exist to involve family members in interventions with cancer survivors. Relevant here, family interventions have been used to improve lifestyle factors in persons with other medical conditions. The British Family Heart Study [118] showed that counseling about diet and exercise delivered to both marital partners reduced the number of cardiovascular risk factors for both partners over time compared with a protocol that only addressed the patient. Also, a major study of a family intervention for patients with hypertension demonstrated that a single home visit to develop a customized plan for families to assist with medication and lifestyle change resulted in reduced blood pressure and patient mortality and increased cost savings, relative to control families [119, 120]. Though unknown, it is possible that such strategies could be applied to populations of cancer survivors with similar issues with medication adherence and lifestyle. In addition, in non-cancer populations, social network behavioral interventions are being used to reduce risky behaviors or to prompt solicitation of support [104, 105]. The translation to cancer populations is yet unclear though insights about cancer patients' social networks may help patients to request the assistance they need and set boundaries for relationships that might compromise their care or well-being.

#### Religious and community groups

Churches are settings that have been used to promote screening [121–123] particularly in African-Americans. Also in the community setting, peer network strategies are being tested [124–126] to improve support in African-American breast cancer patients. In the future, the development of community cancer volunteer networks could also more widely help provide critical support to survivors with limited social networks. Considerably more work in this area is warranted.

#### Communication and relationship skill interventions

Little considered, interventions to improve relationship skills (e.g., social sensitivity, communication) within existing relationships could also have beneficial influences on cancer health outcomes. Research has demonstrated the difficulties to families when a member is diagnosed with cancer, particularly in those families with communication problems prior to diagnosis [127–130]. Considerable emphasis in the literature has also focused on patient-physician communication and most particularly physician communication skills [131–137]. Emphasis might also be devoted to empowering patients through improvements in patient communication skills to facilitate interactions with the many clinicians with whom they interface.

#### Online resources

The proliferation of disease-specific online support groups, both self-directed and professionally led, has resulted in additional resources for cancer patients. The literature on online peer social support is, however, nascent and the effects of online peer support networks on cancer outcomes are unknown. There is also no published research regarding the influence of online networks on cancer treatment. a major predictor of survival. Initial research has focused on general reasons for use and level of engagement [138-141]. Breast cancer patients seek online peers for information (91.3%) and symptom management (69.6%) and less so for emotional support (47.8%) [142]. In an online network of prostate cancer patients, patients also asked for treatment recommendations (66%) [143]. In another online network forum, among breast cancer patients taking aromatase inhibitors (AIs), 12.8% mentioned discontinuing AIs, and another 28.1% mentioned switching AIs [138]. Online participation could have ramifications for treatment decision-making and survival since patients use the Internet to help make decisions about type of surgery [144], and social norms influence cancer patients' decisions about chemotherapy [145], but this is untested in research.

Online groups may also be useful for those who are unable to access in-person groups, for example, those who live in rural areas, have mobility limitations, or have rare cancers or subtypes. To date, limited evidence exists regarding the use and efficacy of online support groups, and results regarding their influence on QoL, the major focus of research conducted to date, are mixed [146–151]. The Comprehensive Health Enhancement Support System (CHESS) and related trials, for example, may help to address questions regarding the impact of online resources on cancer outcomes in the future [152–154].

Crowdfunding sites are also intriguing in their potential to assist patients and families after a cancer diagnosis though this may ultimately reach only a select set of patients. Regardless, considerable work will be needed to be able to characterize the influence of online support on survival.

#### Implications for future research

The conceptual model outlined here may motivate research examining structural aspects of social networks, as well as multiple and potentially competing psychosocial and downstream mechanisms of cancer outcomes. This model also has considerable relevance for health disparities in cancer outcomes. More research must be done to understand the influence of social networks on cancer outcomes. Though ongoing research is being undertaken to improve outcomes in cancer patients, other clinically relevant hypotheses are suggested by this model, which may also point to new areas of research.

Hypothesis (Hyp) 1. Patients with large, diverse social networks may have better cancer outcomes generally.

As mentioned, most prior work has been in breast cancer patients though these relationships should be examined in other cancers as well. And as indicated, work will be needed to understand the structural aspects including the positive and negative aspects of social networks on cancer outcomes.

Hyp 2. Certain cancer patients may have healthier behaviors if they have smaller, less diverse social networks, leading to better cancer survival.

This model has substantial relevance for work in health disparities. In the general research literature, larger, more diverse social networks are related to lower mortality and healthier behaviors. However, these may not always lead to better outcomes such as when social networks lead to unhealthy behaviors. For example, immigrants from countries with healthier lifestyle patterns who live in higher co-ethnic neighborhoods and have social networks with higher proportions of recent immigrants, may have healthier behaviors, leading to better cancer outcomes. Understanding these relationships may help clarify social factors that may enhance or impede individual-level clinical interventions and recommendations.

Hyp 3. Social networks may not lead to better cancer outcomes in late-stage patients due to a mismatch between caregiver knowledge and resources and patient needs.

Many people depend on close friends and relatives to provide care in the case of cancer, but many of these people do not have the training or resources to take on this care, particularly for patients with late-stage cancer. This has broader clinical and policy implications both with regard to concerns about medical care being handed off to non-clinicians without training as well as the ethics of unpaid caregiving in the USA in which substantial resources go to unproven medical interventions, but few resources are provided to caregivers. Research is needed to understand the implications of this on cancer outcomes. Hyp 4. The structural characteristics of social networks may influence treatment management.

Network density may have a role in the optimization of treatment if it enables better coordination of care. Alternatively, highly dense networks may limit influx of relevant information. Research is needed to explore the influence of structural characteristics on cancer and outcomes.

Hyp 5. Social norms matter in decision-making about cancer treatment where treatment options are not clear cut.

In settings where norms may influence behaviors as is possible in an unmoderated online network, the attitudes and beliefs of certain participants may influence the attitudes and beliefs of others. Research is needed to explore social norms as a conduit to decision-making about treatment particularly when treatment options are not predetermined.

These are a few examples of hypotheses that derive from the conceptual model. Thus, this model provides the basis for these and other questions about social networks that are relevant to cancer patients and survivors.

#### CONCLUSION

Ultimately, it is important to consider both macroand micro-level processes of how social networks influence outcomes. There is a variety of potential interventions, with direct influences on social relationships or indirect influences on the resources they provide, some strategies which are currently in use and some the effects of which are unknown, that may serve to improve cancer outcomes. The relevance and potential of each of these types of strategies will be informed by knowledge of mechanisms. The size and quality of one's social networks are also influenced by the broader social environment as well as individual-level factors such as quality of relationships. The context in which patient social networks operate also influence the resources accessible to patients. Considerable work has been done in the area of patient navigation. Other social strategies have received much less attention. Further work will be needed to identify and test new strategies to leverage social relationships to improve cancer survival.

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