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Associations of social networks with cancer mortality: A meta-analysis

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Abstract

This meta-analysis integrates results of 87 studies on the associations of perceived social support, network size, and marital status with cancer survival. In controlled studies, having high levels of perceived social support, larger social network, and being married were associated with decreases in relative risk for mortality of 25%, 20%, and 12%, respectively. Moderator analyses revealed that never married patients had higher mortality rates than widowed and divorced/separated patients. Associations of social network with mortality were stronger in younger patients, and associations of marital status with mortality were stronger in studies with shorter time intervals, and in early-stage cancer. Relationships varied by cancer site, with stronger associations of social support observed in studies of patients with leukemia and lymphomas and stronger associations of network size observed in studies of breast cancer. Further randomized intervention studies are needed to test causal hypotheses about the role of social support and social network for cancer mortality.

Keywords

Cancer; Social support; Social network; Marital status; Survival length; Meta-analysis

1. Introduction

Profound scientific and public interest exists in whether social factors and psychosocial interventions could change the course of cancer. To provide a broader perspective on the treatment literature [1], it is crucial to examine some of its many assumptions, one of which is the subject of this meta-analysis: there is a relationship between social network and mortality of cancer patients in naturalistic (non-intervention) contexts. If such a relationship exists, then carefully targeted social interventions could be recommended for promoting cancer survival. Specifically, one would expect that patients with lower levels of social integration at baseline are most likely to gain from these interventions. However, if no such relationship exists, social interventions should focus on promoting psychological adaptation as such an effect is likely to be found [2].

Despite well-documented associations between the presence of supportive, nurturing relationships and an array of health outcomes including mortality in community samples [3–

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5], it is unclear whether mortality in cancer patients is associated with indicators of social network such as marital status, network size, and perceived social support. No consensus has been reached largely because the results of the individual studies have been inconsistent and the topic has not yet been subject to quantitative meta-analysis. A qualitative review concluded that seven studies revealed a positive association of social involvement and/or social support with the longevity of cancer patients, but another eight did not [6]. These authors emphasized the need for a quantitative meta-analysis that integrates the available literature and identifies variables that may affect the size of the observed relationship, including subgroups defined demographically or with respect to disease characteristics that may appear to derive special benefit from social network. The demonstration of such an association would lend some credibility to the idea that interventions designed to enhance social support may affect longevity.

The present meta-analysis had two goals: (1) to analyze whether three indicators of social network are associated with cancer mortality: perceived social support, network size, and marital status; (2) to test whether the size of the observed relationships is moderated by sociodemographic variables, disease characteristics, such as cancer stage, and important study parameters such as length of study interval and statistical control for confounding variables.

2. Social support, social network, and marital status as predictors of cancer mortality

Eight non-mutually exclusive explanations have been suggested for the apparent connection between indicators of social network and mortality in cancer patients. The first six explanations are substantive, and suggest that social network affect cancer mortality either directly or indirectly via an as yet unidentified mechanism. The other two explanations invoke statistical confounding.

Substantive explanations

First, the effects of social network may be *biologically mediated*, particularly through neuroendocrine or neuroimmune pathways. For example, social support may limit or mitigate the effects of stress-related endocrine changes possibly associated with tumor proliferation [7]. In fact, Levy et al. [8] found higher natural killer cell activity in breast cancer patients with high-quality emotional support, and Turner-Cobb et al. [9] found an association between higher levels of social support and lower cortisol levels in metastatic breast cancer patients. Second, social network may affect *health behavior*, either specific with regard to cancer or in general. For example, as members of the social network may prompt at-risk individuals to seek health care, married patients and those with a larger network may be diagnosed earlier and thus have a better prognosis. Although some studies found the expected effect of marital status on the delay of seeking treatment (e.g., [10,11]), other studies did not (e.g., [12]). Similarly, Mor et al. [13] found no significant effect of social support on treatment delay, indicating that the average effects may be small and difficult to detect. Beyond treatment-seeking, other health behaviors may also be relevant. Members of the social network may encourage cancer patients to maintain a more healthful diet, abstain from health-damaging behaviors such as cigarette smoking or excessive alcohol consumption, engage in regularly physical activity, and diligently attend all scheduled follow-up visits with oncologists and primary care providers. Of course, some if not all of these health behaviors (e.g., cigarette smoking, alcohol consumption) may also affect psychological and physiological function. Third, after being diagnosed with cancer, patients with better social networks may have greater or more reliable *access to the health care system* and assistance with navigating its complexities. Consequently, these patients may

also be able to maintain higher levels of treatment compliance. Specifically, patients with higher levels of instrumental support may be more likely to receive assistance in getting to medical appointments or to the pharmacy. They may also be more likely to receive reminders to take medications and assistance with nutrition and mobility which might protect against disability and contribute to improved survival [14,15]. Fourth, patients with better social networks may be more likely to receive vigorous, aggressive, *active cancer treatment*. There are three reasons for this: (a) Network members may provide vital information about best practices in cancer treatment, as well as information about providers and care-delivery systems (hospitals, cancer centers). This information is relevant for treatment choice. Members of the social network may steer cancer patients toward relatively more effective treatments, providers, or settings. Alternatively, the patients themselves, on account of their own enhanced health literacy by virtue of having access to more information channels, may make more effective treatment decisions. (b) Network members may enhance the motivation for seeking effective treatment, for example mediated through a stronger will to live because patients experience their life as more fulfilling or feel needed by network members. In fact, it has been observed that patients with more social support are more willing to agree to chemotherapy [16], and that married patients are more likely to receive chemotherapy than unmarried patients [17], although not all available studies found such relationships [18]. (c) As married individuals have, on average, higher incomes [19], they may have better access to cost-intensive treatments. Fifth, associations of social network with cancer survival may be *psychologically mediated.* For example, low levels of social support may be related to depression [20] which may influence cancer mortality [6]. Sixth, higher levels of mortality in nonmarried patients may be a *response to loss* through death or divorce or an effect of the loss of other important sources of social support rather than an effect specific to cancer [21]. The effect of social losses may be, again, mediated through physiological, psychological, or health behavior channels, such as impaired mental health, compromised immune function, or deteriorating health habits. To the extent that the effects of social network on longevity can be explained by the mechanisms listed here, then statistical control for these putative mediators (e.g., alcohol consumption, depression) would be expected to diminish the effect size.

Statistical explanations

There are two types of statistical confounding. First, associations of marital status and network size with cancer mortality may, in part, reflect *health-driven social selection*. Healthy individuals probably have a higher chance of getting married and remarrying after the loss of the partner [22,23]. Similarly, they may be more likely to build and maintain a larger social network. If network size or marital status were mainly proxies for health or vitality, then associations between network variables and mortality should no longer be significant after statistically controlling for indicators of physical health such as the presence or severity of medical comorbidity. Second, associations of social support, network size and marital status may be based on *demographic confounding variables*, such as age, gender, or socioeconomic status (SES) rather than on causal effects of support and network variables. For example, mortality rates in general and cancer-related mortality rates increase with age (e.g., [24]), and older individuals have smaller networks (e.g., [25]) and may have lower levels of social support, in part because they are more likely to have been widowed [26] and to have survived the deaths of numerous relatives and friends. Similarly, there are well-documented socioeconomic gradients in morbidity and mortality [27]. If indicators of social network were mainly proxies for age or SES, then bivariate associations of perceived social support, network size, and being married with cancer mortality may, at least in part, be based on the higher mortality of older patients or socioeconomically disadvantaged patients [28]. Thus, associations of perceived social support, network size, and marital status with

mortality might be reduced or even become nonsignificant after statistical controlling for sociodemographic and other confounders.

Although at least six substantive and two statistical reasons for an association of social support, social network, and marital status with cancer survival have been suggested, the available studies on these associations have been inconclusive. A qualitative review found positive associations of indicators of social involvement and perceived social support with length of survival of cancer patients in about half of the studies reviewed [6]. With regard to differences in mortality between married and unmarried (never married, divorced/separated, widowed) respondents, a recent meta-analysis not specific to cancer found higher mortality in widowed older adults (risk ratio (RR): 1.11, 95% confidence interval (CI): 1.08–1.14), divorced/separated (RR = 1.16, CI: 1.09–1.23), and never married (RR = 1.11, CI: 1.07–1.15) older adults than in married seniors [29]. However, the size of the association may differ for cancer patients, where other variables, beyond baseline health and bereavement, may be important. A narrative literature review found no evidence for an influence of marital status on prognosis of cancer [19]. Nonetheless, some recent large-scale studies found longer survival of married than of unmarried cancer patients [30,31] but a few studies found shorter survival in married than in unmarried patients [15,32,34 in breast cancer patients only].

The apparently null findings of some studies may simply reflect a small as opposed to nil association because effects are more difficult to detect in smaller samples. In addition, part of the heterogeneity of the results may be based on differences in study characteristics, such as the proportion of subjects with advanced cancer or significant functional impairments. For example, the level of receipt of emotional and instrumental support may, in part, reflect the level of support needs (e.g., of being emotionally distressed, and of having impaired functional status, respectively) which could even be associated with lower length of survival (e.g., [30,34]). Similarly, being married may indicate availability of high levels of emotional support and having a high will to live, but might, in the cases of terminal illness, also lead to feelings of guilt and burdensomeness [35]. Thus, there may be overall small protective effects of social support, network size, and being married on cancer survival, but these effects may be detected only when accounting for instrumental or emotional needs.

In sum, we expected that perceived social support, network size, and being married would be associated with lower cancer mortality when the effects are pooled across available studies. Most explanations for an association between social network and cancer mortality suggest that the effect of the network and of marital status on survival is mediated through aspects of social support (e.g., providing relevant information, help with getting optimal therapy, promotion of mental health [14,17]). Thus, there may be stronger associations of social support with survival than of network size and marital status with survival because social support is more proximal. From the perspective of translational research this would be especially interesting, given that perceived support is perhaps more modifiable than network size and definitely more so than marital status. Nonetheless, Cohen [36] suggested that associations between social network variables and survival may be attributable to both health-promoting mechanisms associated with social integration and support and to disease-promoting mechanisms that operate among the most isolated. In this case, associations of network size with cancer survival may even be stronger than associations between support and survival. Nonetheless, differences in the size of the association of marital status, social network, and perceived social support with cancer survival may be smaller than expected because available studies rarely focus on those aspects that may have the strongest effect on survival (e.g., serious social isolation, receiving good medical advice, etc.).

3. Moderating effects of demographics, disease parameters, and study characteristics

Several demographic, disease, and study characteristics may moderate the size of the association between perceived social support, network size, and marital status with cancer mortality.

3.1. Demographic characteristics

3.1.1. Age—As the average size of social network declines with age (e.g., [25]), and support needs increase due to growing numbers of chronic diseases and physical impairments (e.g., [26]), older cancer patients may be at greater risk for having insufficient network members as sources of support. Thus, we expected that associations with cancer mortality of social network indicators to increase with age. In fact, Funch and Marshall [37] found a stronger association of social involvement in the 5-year period before diagnosis with length of survival among older patients. Similarly, Vogt et al. [38] found that larger network scope predicted longer cancer survival in individuals 75+ years but not in younger persons. However, associations of two other network measures with length of survival in that study did not vary by age.

3.1.2. Gender—It has been suggested that marriage might have a stronger effect on men's health than women's in part because wives are more likely to promote healthy habits in husbands than vice versa [39]. In fact, Lai et al. [40] found that marital status explained up to 19% of the mortality difference in men with late-stage cancer, as compared to 9% among women with this disease. However, a meta-analysis that did not focus specifically on cancer but instead examined survival among older adults in general did not reveal gender differences [29]. Therefore, we do not offer a directional hypothesis about gender differences in the associations of survival with indicators of social network.

3.1.3. Subgroups of nonmarried patients—On the one hand, divorced and widowed patients may have larger social networks than never married patients (e.g., due to a higher probability of having children [41]) and may, therefore be more likely to activate social support after facing a severe illness. Thus, never married patients could be expected to show elevated mortality rates compared to divorced/separated and widowed patients. On the other hand, associations of marital status with mortality may be based on the effect of the loss of the spouse, thus suggesting elevated mortality of divorced and widowed compared to never married patients [21]. However, this would no longer be relevant with increasing duration of being divorced or widowed and should therefore not outweigh the effects of singlehood on mortality.

3.2. Disease characteristics

3.2.1. Stage—In advanced stages of cancer, biological functions may become increasingly important in regard to patient mortality while psychosocial factors may play a larger role in the outcomes of less progressed cancer [42]. In fact, Ell et al. [33] observed that perceived adequacy of social support was associated with better survival in patients with localized cancer but not in those with advanced cancer. However, Reynolds et al. [43] observed that associations of emotional support and breast cancer survival were even stronger in women with later stage of the disease. No such differential effects were found in that study for marital status, instrumental support, and network size. Due to the heterogeneity of available results, no directional hypothesis was offered.

3.2.2. Cancer site—Similarly, it is unclear whether the size of associations of social network with cancer mortality would vary by cancer site. Some of the biological mediators may vary by cancer site. For example, as social factors affect hormone production [7] such an effect on survival would be relevant mainly for hormone dependent tumors [44]. Lai et al. [40] analyzed associations between marital status and survival in patients with different cancer sites. Whether married patients lived significantly longer than unmarried patients seemed to depend more on the sample size of the subgroups than on cancer site.

3.3. Study design and methods

3.3.1. Time of assessment of the independent variables—It has been observed that being diagnosed with cancer can be associated with change in social contact with family members and in available social support [45]. Similarly, employed cancer patients may not be able to maintain social contact with their co-workers during their sick leave or because of having to quit the job. Thus, the network size and perceived social support assessed prior to or concurrent with the diagnosis of cancer may be weaker predictors of cancer mortality than assessments made after being diagnosed. This question has not yet been systematically tested.

3.3.2. Length of study interval—On the one hand, the perceived availability of social support, network size, and marital status may change over time, so that scores at the first time of data collection lose predictive power with increasing time interval. For example in the first one to 6 years after being diagnosed with cancer, Villingshøj et al. [45] found a change in partner status in about 7.5% of the cancer patients assessed, and change in frequency of contact with their children in about 15%. On the other hand, effects of social variables may be more difficult to detect in the first few months after being diagnosed because of the strong cancer- and treatment-related biological processes during that time. According to this view, associations between social network and cancer mortality may become stronger over time. In fact, some studies found that the effects of social support [32] and marital status [22] on cancer survival accumulated over time. No directional hypothesis is offered.

3.3.3. Control for other variables—Associations of perceived social support, network size, and martial status with mortality may be stronger in uncontrolled studies than in studies that controlled for medical or sociodemographic characteristics that may, in part, explain or mediate the effects on survival of social network. In fact, DeGraef et al. [46] observed that marital status and social activity were univariate predictors of survival but were no longer significant in multivariate analysis that controlled for confounding variables. Nonetheless, as very few of the putative mediators of the association between social network and survival are controlled for in multivariate analyses, we expected that statistical control for confounding variables would reduce but not eliminate the effects on survival of social network.

In sum, with respect to moderators, we compared the effects on mortality of perceived social support, network size and marital status as a function of age, gender, cancer stage, cancer site, time of assessment of independent variables, length of study interval, and statistical control for confounders. Evaluating the quality of individual studies is controversial [47]. In the present meta-analysis, we focused on an important indicator of study quality, namely whether the studies controlled for confounding variables.

4. Methods

4.1. Identification of studies

We identified a comprehensive sample of studies searching electronic data bases (MEDLINE, Cochrane Data Base, Psyclit, PSYN-DEX); search terms: [(malignant or cancer or carcinoma) and (social support or network or frequency of contact, or marital status or married or widowed or divorced or separated) and (survival or mortality or death or Kaplan–Maier or Cox)] and cross-referencing. Criteria for inclusion in the meta-analysis were:

1. The participants were cancer patients or were enrolled in a prospective community-based sample for which cancer mortality is reported.
2. Information about the level of perceived social support, network characteristics, and/or marital status is provided.
3. Information on general or cancer-specific mortality is provided.
4. Statistics about associations between perceived social support, network size, and/or marital status with mortality could be computed or estimated (e.g., based on risk ratios and their confidence intervals, survival curves, *p*-values of Cox regression or Kaplan–Maier analysis).

We did not include the effects of “supportive interventions” or “psychosocial interventions” or “psychotherapy” in our meta-analysis as these interventions often include other components in the addition to the provision of social support, such as cognitive restructuring, and go beyond the provision of emotional and instrumental support [48]. Moreover, the literature on this topic has recently been reviewed [1]. Recognizing that supportive interventions involve more than merely providing support, this review is conceptualized in part as an examination of one of the premises underlying the presumed health consequences of such interventions.

Of the 94 empirical papers initially identified, 87 met all inclusion criteria with a total *N* of 10,795,137 [10,11,14,15,17,22,30–34,37,38,40,43–45,49–118]. The remainder were excluded because they provided insufficient information about effect sizes (five studies), duplicated published results (one study) or did not distinguish between individuals married at the time of first assessment and previously married persons (one study). Eleven of the remaining 87 studies reported results for multiple samples (e.g., for men and women or for different cancer sites), yielding a total of 104 samples.

4.2. Coding of variables

We entered the year of publication, the numbers of participants, age, gender, method to assess perceived social support and assessing network size, sample composition (1 = cancer patients only, 0 = community sample), cancer site (1 = breast, 2 = leukemia/lymphoma, 3 = lung, 4 = other sites, 5 = mixed sites), cancer stage (1 = early [I, II], 2 = mixed/not reported, 3 = late [III, IV]), timing of assessment of support, network size and/or marital status (1 = prior to cancer diagnosis, 2 = after diagnosis), and study interval (years). With regard to control for other variables, we created six dummy variables (1 = yes, 0 = no) indicating whether the study controlled for cancer site, health status (stage, functional status, medical comorbidities), age, gender, SES (educational attainment and/or income) and alcohol/tobacco use. Associations of perceived social support, network size, and marital status with mortality were coded as risk ratios. The risk ratio is a summary of the difference between two Kaplan–Meier curves or Cox regression curves and represents the overall increase in the risk of death over the period of follow-up. It has been especially useful for comparing two survival curves because it allows for censoring.

For studies reporting data for more than one follow-up, we included the results of all follow-ups but adjusted their weight so that the sum of the subresults' weight would be equal to the weight when only including one result [119].

4.3. Statistical integration of research findings

Calculations for the meta-analysis were performed using random-effects models and the noniterative method of moments [120] given the expected variability in effect sizes between studies beyond subject-level sampling error. Calculations were conducted as follows.

1. If the risk ratio was not reported, it was computed from logrank statistics, survival curves, or from information about the numbers of deceased and living patients with low versus high levels of perceived social support, high versus low network size, and married versus unmarried respondents [121]. Then, log risk ratios were computed because they are approximately normally distributed and allow for combining results across studies.
2. Weighted mean effect sizes were computed [119]. The homogeneity of effect sizes was tested by use of the homogeneity statistic *Q*. The significance of the mean was tested by dividing the weighted mean effect size by the estimated standard error of the mean. Then confidence intervals (CI) that include 95% of the effects were computed for each effect size. Differences between two conditions were interpreted as significant when the 95% CIs did not overlap.
3. Summary statistics of the effect size and the 95% CI were converted back to risk ratios by taking the antilogarithms.
4. Weighted ordinary least squares regression analysis [122] was used to conduct multivariate analyses of the influence of moderator variables.
5. Funnel plots were used as an indicator for publication bias [119].

5. Results

Of the 104 samples, 27 included patients with mixed cancer sites, 24 focused on breast cancer, 10 on leukemia and lymphomas, 9 on lung cancer, and 34 samples on other cancer sites (e.g., colon, pancreas). The majority combined patients with early and late stages of the disease ($N = 93$); three focused on patients with early-stage cancer (I/II) and eight on late-stage disease (III/IV). Most ($N = 85$) assessed support, network size and/or marital status after cancer diagnosis; 19 examined the influence of these variables prior to cancer diagnosis. The latter were community-based cohort studies that assessed risk for different sources of mortality. For the present analyses, only data on cancer mortality were used. Forty studies reported only bivariate associations between social network and survival, 27 only multivariate associations that controlled for some confounders, and 19 bivariate as well as multivariate associations. Studies with multivariate analyses controlled for (some) confounding variables, such as age ($k = 35$ studies), cancer site ($k = 35$), gender ($k = 34$), stage ($k = 31$), SES ($k = 11$), medical comorbidities ($k = 8$), functional status ($k = 7$), and alcohol/tobacco use ($k = 7$). Thus, the controlled studies varied regarding which confounding variables were controlled. The included studies are identified in the Reference section.

A large number of different measures ($N = 22$) were used for assessing perceived social support, such as the MOS Social Support Survey ([123]; $k = 2$). Social network indicators were assessed with single-item indicators (e.g., contact frequency, number of confidants; $k = 9$) and multi-item scales ($k = 6$), such as the Social Network Inventory [124]). The marital status of the respondents was assessed with single-item indicators ($k = 66$).

The participants had a mean age of 65.9 years (SD = 6.2), 57% were women, and 14.3% were members of ethnic minorities. About 86% of the respondents were married. The average study interval between assessment of social network and of survival was 7.1 years (SD = 5.2). Intervals were longer in community-based studies (M = 12.2 years, SD = 5.5) than in clinical studies with cancer samples (M = 5.9 years, SD = 4.3; $t(103) = 5.71$, $p < .001$). During this interval, about 40.2% of the participants were deceased.

We used funnel plots to check for publication bias. With regard to associations of network size with mortality, we found that studies with below-average risk ratios were more likely to have sample sizes of 2000–4000 whereas those with above-average risk ratio were more likely to have sample sizes of 5000–6000 patients. In studies on the association of marital status with mortality, we found more studies with below-average risk ratio with 5000–7000 patients and more studies with above-average risk ratio with ≥10,000 patients. As there was no evidence for publication bias (i.e., large and significant effect sizes were not overrepresented among studies with small sample sizes), it is unlikely that small studies with nonsignificant results would be less likely to be published.

Because community-based studies on mortality usually start with people having no life-threatening disease, initially measured network variables may affect disease onset and disease whereas studies with cancer patients analyze effects of network variables on disease progression. Thus, we first checked whether the association of network variables with mortality differed between these groups of studies. Because no differences were found for social support (RR = .86, CI: .63–1.17 versus RR = .79, CI: .71–.89), network size (RR = .81, CI: .68–.95 versus RR = .78, CI: .68–.90), and marital status (RR = .87, CI: .84–.89 versus RR = .87, CI: .82–.91), both groups of studies were collapsed for the following analyses.

With regard to the first research question, we analyzed whether perceived social support, network size and marital status would be associated with cancer mortality. Separate effect sizes were computed for uncontrolled studies and for studies that controlled for one or more confounding variables (age, gender, SES, health status/cancer stage, alcohol/tobacco use). In line with our expectations, both groups of studies showed lower mortality in individuals with higher levels of perceived social support, larger social networks, and in married as compared to nonmarried respondents (Table 1). For example, the controlled risk ratio of .75 of the association between perceived social support and survival indicates that the relative risk of mortality was reduced by 25% when the level of perceived support increases by one standard deviation unit. Similarly, the relative risk for mortality was reduced in controlled studies by 20% when the size of the network increases by a standard deviation. In controlled studies, the relative risk for mortality of married respondents was 12% lower than the relative risk for mortality in unmarried persons. As indicated by overlap of the 95% confidence intervals, the effect sizes of the association of perceived social support, network size, and marital status with mortality did not differ significantly.

As shown by the overlap of the 95% CI, effect sizes of uncontrolled studies and controlled studies did also not differ significantly (Table 1). Thus, we computed average effect sizes across controlled and uncontrolled studies that replicated the results of the analysis of uncontrolled and controlled effects.

We next checked whether associations of marital status with mortality would differ between never married, divorced/separated, and widowed individuals. Risk rations were computed that compare the relative risk for mortality in these groups against the relative risk in married individuals. As shown in Table 2, never married, divorced/separated, and widowed individuals had higher mortality rates than married individuals. As indicated by the non-

overlap of the CI, the survival disadvantage of never married persons in controlled studies was significantly larger than the survival disadvantage of divorced/separated and widowed individuals. Similarly, when combining controlled and uncontrolled studies, never married respondents had a larger survival disadvantage than divorced/separated and widowed individuals.

As shown by the *Q*-statistics, the size of the associations of perceived social support, network size, and marital status with mortality varied between studies, underscoring the need to identify moderators (study characteristics that moderate the size of the observed association of network variables with mortality). Thus, weighted multiple linear regression analyses were computed for analyzing the effects of moderating variables.

As cancer mortality varies by age, gender, SES, health status/cancer stage, and alcohol/tobacco use [34,47,49,85,87,94], we checked whether studies controlled for all of these variables. Unfortunately, only one of the studies did. Because we could not compare high-quality studies that controlled for all relevant variables with other studies, we built a count variable that sums up the number of controlled variables. With weighted multiple regression analysis we tested whether the association of the network variables with mortality varied by the number of control variables. Interestingly, the association of network with mortality did not vary by the number of controlled variables (social support: $B = .08$, $\beta = .23$, $Z = 1.11$; network size: $B = -.00$, $\beta = -.01$, $Z = -.04$; marital status: $B = -.02$, $\beta = -.11$, $Z = -.60$).

In the next step, we tested whether the association between social network and cancer survival observed in multivariate analyses would vary by the inclusion of individual control variables. As shown in Table 3, the association of social support with cancer mortality was weaker in studies that controlled for gender and SES. In addition, the association of social network with cancer mortality became stronger in studies that controlled for alcohol/tobacco use and weaker in studies that controlled for gender, functional status, and comorbidities (potential confounders). Finally, the strength of the association of martial status and mortality became stronger in studies that controlled for gender, cancer site, and comorbidity.

In the second set of regression analyses, we tested whether the association of social network with mortality would vary by other study characteristics, such as age, gender, cancer site, and stage. Because eight studies were available on late stage of cancer, as compared to three studies on early stage, we included a dummy variable that compares studies with late-stage cancer to other studies (mixed stage, early stage). In addition, a sufficient number of studies for inclusion in the meta-analysis were available for breast cancer and leukaemia/lymphoma but not for other sites. Due to the large number of methods used for the assessment of perceived social support and network size, we could not include individual measures as predictor variables.

As shown in Table 4, we found a stronger association of perceived support and survival in studies on patients with leukaemia and lymphomas than in studies with other cancer sites. In addition, associations of network size and cancer mortality were stronger in studies with older patients and in studies with breast cancer patients. Finally, weaker associations of being married with mortality were observed in studies with late-stage cancer patients as compared to studies on early and mixed stages, and in studies with longer intervals between baseline and follow-up.

6. Discussion

The present meta-analysis showed that the longevity of cancer patients is related to their perceptions of social support, the size of their social networks, and their marital status. We found no evidence for stronger associations of social support with mortality than of network

size and marital status with cancer mortality. In addition, the observed effects varied by study characteristics.

Whereas a previous narrative review on this topic yielded inconsistent results [6], the present meta-analysis provides clear and unequivocal evidence for the association of social network with longevity in cancer patients. Reductions of relative risk for mortality by 12–25% in patients with high levels of perceived social support, large social networks and in married patients (controlled studies) show that the effects are clearly clinically meaningful, even though they may be too small to detect in studies that are not sufficiently powered.

We did not find significantly stronger associations of social support with mortality than of marital status with survival. Although some available explanations for effects of social network on survival suggest stronger effects of social support than of network size (for example because closely knit networks may be more supportive than large numbers of acquaintances [125]), some relevant aspects of reported social support provision that may promote survival were rarely measured. This would include getting help with accessing the best available treatment, which would be considered instrumental support. Thus, effects of perceived support on cancer mortality may have been underestimated in the present studies.

As bivariate associations of perceived social support, network size, and marital status with cancer mortality may, in part, be based on the effects of statistical confounding variables (e.g., demographics), we were interested in whether uncontrolled studies would yield higher effect sizes than controlled studies. We found some empirical evidence for the assumption that the association between social network and cancer mortality may, at least in part, be based on confounding effects of SES as the association of perceived social support with mortality became weaker in studies that controlled for SES. However, no evidence was found for the suggestion that the association of network variables with mortality could be explained by the fact that low support or lack of social ties may lead to higher levels of smoking and alcohol use. The association of social network size with mortality became even stronger in studies that controlled for smoking and alcohol use. Larger networks might confer both health-damaging effects (through more opportunities for drinking and smoking) and health-promoting effects. By accounting for smoking and alcohol, we were able to detect the salutary effects of social networks more readily.

Studies that controlled for gender differences in mortality found weaker associations of social support with survival but stronger associations of marital status with survival. Associations of marital status with mortality are underestimated in studies that did not control for gender because women are more likely to be widowed *and* to live longer than men. However, because women receive, on average, more emotional support than men [126], associations of perceived support with cancer mortality are, in part, confounded with gender differences in life expectancy.

Associations of network size and marital status with cancer mortality varied between studies that controlled and those that did not control for comorbidity. Weaker associations of network size with mortality in controlled studies may indicate that comorbidities impair the pursuit of many social contacts and decrease length of survival. In this regard, the comorbidity variable behaved like a confounder. However, controlling for comorbidities strengthened the association between marital status and length of survival. Thus, lower cancer mortality of married patients could not be explained by their better general physical health.

We had expected that associations of perceived support, network size, and marital status with cancer mortality would be stronger in older patients. This assumption was empirically supported for network size, but not for marital status and perceived support. The benefits of

expanded social networks accrue early in expansion, with the most benefits occurring for some members versus very few members of the social network [127]. Because older adults invest more energy in maintaining close and supportive social ties than in maintaining large social networks [25] they may be at higher risk for not having a sufficient number of social ties than for lacking emotional support.

We had explored whether the association of social network with mortality may vary by cancer sites. Unfortunately, only a very limited number of cancer sites could be compared. Perceived social support showed a stronger association with reduced mortality in leukeamia and lymphoma patients than in other patients; network size showed a stronger association with reduced mortality in breast cancer patients than in other patients. As lymphoma and leukaemia patients receive highly aggressive therapy with strong side effects they may profit more from available social support. Given the fact that breast cancer is the most frequent cancer site in women and that social recommendations promote breast cancer screening practices and early detection of breast cancer [128], women with larger networks may be more likely to receive and use these recommendations, and may therefore survive longer. Alternatively, the stronger association of network size with mortality in breast cancer patients may indicate that network size affects hormonal changes and has, therefore, stronger effects on mortality in hormone dependent tumors.

Given the fact that the level of perceived social support, the network size and marital status may change over time, we had expected that the associations with cancer mortality would decline with increasing study intervals. This hypothesis was supported for marital status but not for the other independent variables. As more studies and larger sample sizes were available for the former analysis, the small effect of the length of the study interval was probably only detected in the analysis with the largest data base. However, associations of network variables with mortality did not vary between prospective community-based studies of initially healthy adults and clinical studies with cancer patients. This result indicates that social network variables may have similar effects on cancer progression and on cancer onset.

In line with the suggestion that associations of psychosocial variables with cancer mortality would be more difficult to detect in patients with late stages of cancer than in earlier stages [42], we found that the negative association of marital status with mortality was weaker in late-stage cancer than in early and mixed stages. A univariate analysis even shows that being married is associated with *elevated* mortality risk in the six studies with late-stage cancer (RR = 1.11, CI: 1.02–1.21, $Z = 2.46$, $p < .05$), whereas the reverse is true in other samples (RR = .85, CI: .83–.88, $Z = -9.97$, $p < .001$). This surprising result may indicate that late-stage cancer patients psychologically suffer from burdening their spouse as a caregiver, which again reduces their will to live [129]. Feeling demoralized, spouses of late-stage patients may begin the grieving process, with implications for the emotional environment in the family and for patient survival.

Although it has been suggested that men may profit more from being socially integrated than women [39,40], associations of perceived social support, network size and marital status with mortality did not vary by gender. The assumption about gender differences was based on men's larger needs for social control over their health behavior. However, in the case of cancer, health behavior is to a large extent controlled by the medical staff (e.g., during stays in hospital), so that unmarried patients may experience sufficient social control over their health behaviors irrespectively of their gender. Alternatively, as Manzoli et al. [29] did not find gender differences in the association between marital and mortality of older adults in general, health behaviors may be less relevant as a mediator of the association between marital status and mortality.

7. Limitations and conclusions

Some limitations of the present study have to be mentioned: First, although our meta-analysis included 87 studies and a total of more than one million participants, sub-analyses could only be computed for two cancer sites. Second, some potential moderators of the size of the association of perceived social support, network size and marital status with cancer mortality could not be tested due to the lack of sufficient data (e.g., ethnicity, level of psychological distress, religious involvement). Third, available multivariate studies controlled only for a very limited number of confounders. For example, they usually did not control for psychological health and personality variables. Thus, studies are needed that control for a larger range of potential confounders. In addition, randomized intervention would help excluding the possibility that the observed effects could be based on unmeasured confounding variables. Such interventions in natural social networks may be targeted at building stronger (more supportive) ties to existing network members, creating close ties with members of the community, and reducing negative interactions [36].

Fourth, because most available studies did not differ between cancer-related mortality and other causes of mortality in cancer patients, we were not able to test for effects of specific causes of death. Fifth, we did not have sufficient data for testing the effects of different subaspects of social network and support, such as contact with friends versus family members, and instrumental versus emotional support. Sixth, insufficient data were available for the analysis of simultaneous effects of perceived social support, network size, and marital status on mortality in cancer patients. Finally, we were not able to meta-analyze mediators of the relationship of support, network size, and marital status with mortality.

Despite these limitations, we conclude that cancer patients with lower levels of perceived support, smaller network size, and unmarried patients are at a higher risk for mortality and that this effect cannot be explained by sociodemographic confounders. Second, we conclude that some of the explanations for the association between social network and mortality are not supported by the present meta-analysis: The observed association with network size and marital status could not be explained by an effect of SES because statistical control for SES did not change the size of the association of these variables with mortality. Similarly, the association of social network with cancer survival could not be explained by effects of the loss of the spouse due to divorce or widowhood because controlled studies found even stronger effects of marital status for never married than for divorced and widowed patients. In addition, statistical control for health-related variables had no consistent effect on the association between social network and mortality, thus ruling out the possibility that the effect of social network is a proxy for the effect of good health or vitality. Our results rule out the possibility that the association of social network with cancer mortality is based on these confounders, although we could not test for other confounding variables, such as psychological health. With regard to future research needs, strict control for confounding variables would be recommended in order to increase the quality of the studies. Third, more studies on associations of perceived social support, network size, and marital status with mortality are welcomed for those cancer sites that could not be included in the analysis of site-specific associations. This would enlarge our knowledge about whether effects of social network are site specific or global. Fourth, more efforts are needed for analyzing whether perceived social support, network size, and marital status would have independent effects on mortality by simultaneously including the three predictors and also including psychosocial confounders or mediators, such as depressive symptoms. Fifth, studies are needed that assess mediators of the association of perceived social support, network size, and marital status with cancer survival. As several mediators have been suggested [16,130,7], studies with large sample sizes would be needed for identifying these mediators. Finally, prospective longitudinal studies cannot test causal hypotheses because the observed effects of social

support, network size and marital status might also be explained by unmeasured third variables. For testing causal effects of network variables and perceived social support on mortality, randomized intervention studies are welcomed that increase availability of social support or the level of social contact in patients with low levels of available support and small social networks. If present, effects of supportive interventions designed to enhance perceived support would most likely be found in patients reporting lower levels of support in their daily lives. Similarly, effects of activation and network-building interventions would most likely be found in those with smaller networks.

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Biography

Martin Pinquart, Ph.D. studied psychology at Friedrich Schiller University of Jena and Humboldt University at Berlin. He is currently full professor at the Department of Psychology at Philipps University of Marburg. He has worked on a large interdisciplinary research project on the older cancer patient. His special interests lie in the role of critical life events and stressors on human life.

Table 1

Association of perceived social support, network size, and being married with cancer survival.

Study characteristic	*k*	*N*	RR	95% Confidence interval		*Z*	*p*	*Q*	*p*
Association of social support with mortality in cancer patients									
Uncontrolled effect sizes	18	2,867	.92	.84	.99	−2.03	.0427	42.94	.0005
Controlled effect sizes	21	17,481	.75	.65	.87	−3.79	.0002	80.52	.0001
Averaged effect size	31	18,828	.82	.75	.89	−4.56	.0001	109.77	.0001
Associations of social network with mortality of cancer patients									
Uncontrolled effect sizes	6	94,794	.73	.60	.88	−3.30	.001	6.27	.2810
Controlled effect sizes	23	3,997	.80	.72	.89	−4.30	.0001	48.95	.0008
Averaged effect size	23	97,088	.80	.72	.88	−4.33	.0001	45.95	.0030
Associations of being married with mortality in cancer patients									
Uncontrolled effect sizes	64	11607,245	.84	.81	.86	−12.52	.0001	372.36	.0001
Controlled effect sizes	40	610,837	.88	.82	.94	−3.74	.0002	474.97	.0001
Averaged effect size	88	12159,656	.87	.84	.90	−7.92	.0001	543.35	.0001

Note. k: number of samples, *N*: number of participants, RR: risk ratio. Values >1 indicate that the risk for cancer mortality is increased in subjects with higher levels of social support, larger networks, and in married respondents, respectively. *Z*: test for the significance of the mean effect size. *Q*: test for heterogeneity of effect sizes.

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Table 2

Cancer mortality in never-married, divorced/separated, and widowed persons.

Study characteristic	*k*	*N*	RR	95% Confidence interval		*Z*	*p*	*Q*	*p*
Comparison of cancer survival in never married versus married persons									
Uncontrolled effect sizes	39	276,063	1.17	1.09	1.25	4.51	.0001	398.50	.0001
Controlled effect sizes	52	458,121	1.23	1.19	1.28	10.65	.0001	295.92	.0001
Averaged effect size	77	567,622	1.19	1.18	1.20	11.48	.0001	430.84	.0001
Comparison of cancer survival of divorced/separated versus married persons									
Uncontrolled effect sizes	31	355,627	1.14	1.05	1.24	3.07	.0021	274.31	.0001
Controlled effect sizes	68	731,652	1.16	1.13	1.19	10.37	.0001	188.74	.0001
Averaged effect size	93	838,694	1.14	1.11	1.17	10.55	.0001	242.47	.0001
Comparison of cancer survival of widowed versus married persons									
Uncontrolled effect sizes	31	281,170	1.13	1.01	1.26	2.07	.0385	396.03	.0001
Controlled effect sizes	45	445,334	1.14	1.10	1.17	8.40	.0001	133.50	.0001
Averaged effect size	69	565,699	1.10	1.07	1.13	6.94	.0001	303.50	.0001

Note. k: number of samples, *N*: number of participants, RR: risk ratio. Risk ratios >1 indicate higher mortality in unmarried than in married individuals. *Z*: test for the significance of the mean effect size. *Q*: test for heterogeneity of effect sizes.

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Table 3

Moderating effects of control for confounding variables on the multivariate association of social network with cancer mortality.

Control variables	Association of perceived social support with cancer mortality		Association of network size with cancer mortality		Association of being married with cancer mortality	
	B	***β***	***B***	***β***	***B***	***β***
Age	.01	.02	.18	.26	.17	.29
Gender	.88*	.59	1.22**	1.78	−.18**	−.46
Socioeconomic status	1.92*	.47	_a		−.03	−.07
Cancer site	.09	.06	−.02	−.03	−.27*	−.45
Cancer stage	.53	.37	_a		−.03	−.07
Functional status	.32	.26	1.10*	1.30	.17	.24
Comorbidity	−.03	−.03	1.63**	3.07	−.17*	−.35
Smoking/alcohol use	.45	.36	−1.54**	−2.84	.00	.016
(Constant)	−1.72*		1.58		−.07	
k	21		23		37	
R^2	.51		.56		.39	

Dummy variables were coded as follows: Control for confounder = 1, no control = 0. *β* (*B*) unstandardized (standardized) regression coefficient, *k*: number of samples, R^2: variance explained by the predictor variables.

[a] Variable had to be excluded from the analysis due to the lack of variance.

* $p < .05$.

** $p < .01$.

Table 4

Analysis for moderating effects on the association of perceived social support, network size, and being married with cancer mortality.

Variable	Association of social support with cancer mortality		Association of network size with cancer mortality		Association of being married with cancer mortality	
	B	**β**	***B***	**β**	***B***	**β**
Age	.00	.01	−.03*	−.56	.00	.07
%Women	−.00	−.28	.00	.33	−.00	−.07
Time of assessment (1 = prior to being diagnosed, 2 = after being diagnosed)	−.12	−.11	.15	.23	.03	.07
Stage (1 = late (III/IV, 0 = others))	−.08	−.05	−.08	−.08	.20**	.30
Breast cancer (1 = yes, 0 = no)	.22	.30	−.74***	−.77	−.01	−.03
Leukaemia/lymphoma (1 = yes, 0 = no)	−.53*	−.47	_[a]		.01	.01
Length of study interval (in years)	−.00	−.04	.01	.08	.01*	.25
Control for confounders (1 = yes, 0 = no)	−.31	−.41	.30	.19	−.03	−.07
(Constant)	.36		.80		−.35	
R^2	.27		.45		.17	
k	32		24		86	

β(*B*) unstandardized (standardized) regression coefficient, *k*: number of samples, R^2: variance explained by the predictor variables.

[a] No studies on leukaemia/lymphomas were available for that analysis. A negative regression coefficient indicates that the size of the risk ratio is reduced (the protective effect of social support, network size or being married gets stronger) in studies with large values of the independent variable.

* $p < .05$.

** $p < .01$.

*** $p < .001$.

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Appendix A

Studies included in the present meta-analysis.

Author	Country	*N*	Length of study interval (years)	Cancer sites	Design	Target variables
Akechi et al. [49]	Japan	122	2	Lung	uc	n
Allison et al. [50]	Canada	96	1	Head/neck	uc, c	n
Ben-Schlomo et al. [51]	U.K.	18,403	18	Mixed	uc	m
Broers et al. [52]	Netherlands	123	7.2	Mixed	uc	m
Burns et al. [53]	Australia	163	3	Mixed	c	m, n
Butow et al. [54]	Australia	125	2	Melanoma	uc	m, s
Butow et al. [55]	Australia	99	5.5	Breast	c	s
Cassileth et al. [32]	U.S.	204	8	Mixed	uc, c	m, n
Chang and Barker [56]	U.S.	10,987	n.r.	Glioblastoma	c	m
Chung et al. [57]	Taiwan	57	2	Mixed	uc	m, s
Colón et al. [58]	U.S.	100	2	Leukemia	uc	s
Cousson-Gélie et al. [59]	France	75	10	Breast	uc, c	m, s
Cronin-Fenton et al. [17]	Ireland	1,257	n.r.	Non-Hodgkin's lymphoma	c	m
DeGraef et al. [46]	Netherlands	208	3.75	Head, neck	uc	m
Ehlers [60]	U.S.	130	2.67	Head, neck	uc	m
Ell et al. [33]	U.S.	410	6.9	Breast, colorectal, lung	uc, c	m, s
Forsén [61]	Finland	87	8	Breast	c	m
Foster et al. [62]	U.S.	131	n.r.	Leukemia	uc	m, s
Frick et al. [63]	Germany	99	2.4	Myelom, lymphoma	uc, c	m, s
Funch and Marshall [37]	U.S.	208	20	Breast	c	n
Gajalakshmi et al. [64]	India	1,325	n.r.	Breast	uc	m
Ganz et al. [65]	U.S.	40	1.5	Lung	uc	m
Ghori et al. [66]	U.S.	292	10	Thyroid	uc	m
Gilliland et al. [67]	U.S.	15,698	10	Thyroid	uc	m
Giraldi et al. [68]	Italy	96	6	Breast	uc	s
Goodwin et al. [69]	U.S.	646	10	Mixed	c	s
Goodwin et al. [30]	U.S.	24,696	n.r.	Breast	c	m
Gore et al. [70]	U.S.	5,854	3.3	Bladder	uc, c	m
Grulke et al. [71]	Germany	72	9	Leukemia	uc	s

Author	Country	*N*	Length of study interval (years)	Cancer sites	Design	Target variables
Hall et al. [72]	Australia	14,587	5	Colorectal	c	m
Harvei and Kravdahl [73]	Norway	30,000	5	Prostate	c	m
Herndon et al. [74]	U.S.	206	4.2	Lung	uc	s
Hill et al. [31]	U.S.	445,423	n.r.	Breast	uc	m
Iwasaki et al. [75]	Japan	11,560	n.r.	Mixed	c	m, n, s
Jaffe et al. [76]	Israel	12,498	10	Mixed	uc	m
Jatoi et al. [77]	U.S.	5,898	6.9	Lung	c	m
Johansen et al. [78]	Denmark	3,896 3,406	24 24	Colon Rectum	uc, c	m
Karvonen-Gutierrez et al. [79]	U.S.	405	n.r.	Head, neck	uc, c	m
Kato et al. [80]	Japan	2,581 4,422	5 5	Colorectal Gastric	uc	m
Konski et al. [81]	U.S.	1,438	2.3	Head, neck	c	m
Kravdal [82]	Norway	>100,000	n.r.	Mixed	uc, c	m
Kravdal [83]	Norway	45,270	10	Mixed	c	m, n
Kroenke et al. [14]	U.S.	2,835	n.r.	Breast	c	m, n
Krongard et al. [84]	U.S.	146,979	12	Prostate	c	m
Krongard et al. [85]	U.S.	1,070 12,636	n.r. n.r.	Bladder Prostate	uc	m
Lai et al. [40]	U.S.	261,070	n.r.	Mixed	c	m
Lehto et al. [86]	Finland	102	n.r.	Breast	c	s
LeMarchand et al. [87]	U.S.	2,956	5	Breast	uc	m
Maunsell et al. [88]	Canada	224	7	Breast	uc, c	s
Murphy et al. [89]	U.K.	1,607	5	Cervix	uc	m
Nakaya et al. [90]	Japan	189	28.5	Mixed	uc	m
Naughton et al. [91]	U.S.	67	1	Lung	c	s
Neale [92]	U.S.	1,261	10	Breast	uc	m
Neale et al. [22]	U.S.	10,778	10	Breast	uc, c	m
Osborne et al. [93]	Australia	61	7	Breast	c	s
Osborne et al. [10]	U.S.	32,268	3	Breast	uc, c	m
Ou et al. [94]	U.S.	4,702	n.r.	Lung	c	m
Phillips et al. [95]	Australia	708	8.2	Breast	uc, c	s
Pinquart et al. [34]	Germany	50	2	Leukemia	uc, c	s

Author	Country	*N*	Length of study interval (years)	Cancer sites	Design	Target variables
Prieto et al. [96]	Spain	1,999	5	Leukemia	uc	m
Reid et al. [97]	U.S.	9,386	n.r.	Neck	uc, c	m
Reyes Ortiz et al. [11]	U.S.	14,180	n.r.	Melanoma	uc	m
Reynolds and Kaplan [98]	U.S.	476	17	Mixed	uc, c	m, n
Reynolds et al. [43]	U.S.	1,011	5	Breast	c	m, s
Reynolds et al. [99]	U.S.	747	8.5	Breast	c	s
Richardson et al. [100]	U.S.	94	5	Hematologic malignancies	uc	m
Ringdal et al. [101]	Norway	231	2	Mixed	uc	m
Ross et al. [102]	Denmark	249	2	Colorectal	c	m
Saito-Nakaya et al. [103]	Japan	238	6.5	Lung	uc, c	s
Saito-Nakaya et al. [104]	Japan	865	2	Lung	uc, c	m
Sakauchi [105]	Japan	6,219	n.r.	Mixed	c	m
Sehlen et al. [106]	Germany	57	7	Brain	uc	m
Soler-Vila et al. [107]	U.S.	322	10	Breast	c	s
Stavratsky et al. [108]	Canada	224	1	Lung	uc	m
Strand et al. [109]	Diverse	10789,239	n.r.	Breast	uc	m
Studzinski and Zajewski [110]	Poland	121	5	Endometrium	uc	m
Tominaga et al. [111]	Japan	398	n.r.	Breast	c	m, n
Tschuschke et al. [112]	Germany	52	5	Leukemia	uc	m
Villingshøj et al. [45]	Denmark	770	4.5	Colorectal	c	m, n
Vogt et al. [38]	U.S.	2,324	15	Mixed	uc	n
Waxler-Morrison et al. [15]	Canada	133	4	Breast	c	m, n, s
Weihs et al. [113]	U.S.	90	8.5	Breast	c	s
Welin et al. [114]	Sweden	989	12	Mixed	uc, c	n
Wojicik et al. [115]	U.S.	6,577	13.33	Breast	uc	m
Wong et al. [116]	Taiwan	1,010	5	Oral	uc, c	m
Wrensch et al. [117]	U.S.	728	n.r.	Brain	uc, c	m
Yeole et al. [118]	India	5,345	5	Head, neck	uc, c	m

n.r.: not reported. c: controlled effect sizes were included in the meta-analysis, uc: uncontrolled effect sizes were included; target variables: m – marital status, n – network size, s – social support.