The Impact of Marital Status on Stage at Diagnosis and Survival of Female Patients with Breast and Gynecologic Cancers: A Meta-Analysis

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Abstract

Background: The aim of this meta-analysis is to evaluate the effect of marital status on the stage at diagnosis and survival of female patients with breast and gynecologic cancers.

Methods: A systematic literature search was conducted on electronic databases (PubMed, Cochrane and EMBASE) till March 31, 2020. Publications investigating the association of marital status with stage at diagnosis and/or cancer-specific mortality (CSM) and/or overall survival (OS) in female patients with breast or gynecologic cancers were retrieved. After studies were selected according to inclusion criteria, data extraction, quality assessment and data analysis were performed.

Results: 55 articles were eligible for inclusion, consisting of 1195773 female cancer patients with breast, vulvar, cervical, endometrial and ovarian cancers. Unmarried female cancer patients had higher odds of being diagnosed at later stage [odds ratio (OR) = 1.28, 95% confidence interval (CI): 1.22-1.36)] and worse survival outcomes in CSM [hazard ratio (HR) = 1.22, 95% CI: 1.16-1.28] and OS (HR = 1.20, 95% CI: 1.14-1.25). This estimate did not vary by level of social support, number of adjustment factors, or between America and Europe.

Conclusions: Being married is associated with timely diagnosis and favorable prognosis in most women's cancers. Unmarried female cancer patients have a higher risk of late-stage diagnosis and worse survival outcomes than the married. Greater concern shall be demonstrated towards unmarried female cancer patients. Furthermore, the impact of lacking economic and emotional support on survival outcomes in unmarried female cancer patients deserves particular attention.

Background

According to World Health Organization, cancer is the second leading cause of death worldwide [1]. As reported by GLOBOCAN estimates of cancer incidence and mortality in 2018, for women worldwide, breast cancer was the most common cancer (about 2.1 million cases) and the leading cause of cancer deaths (626,679 deaths). For gynecologic cancers, the most common incident cancers were cervical cancer (569,847 cases), uterine cancer (382,069 cases), and ovarian cancer (295,414 cases). The leading causes of gynecologic cancer deaths were cervical, ovarian, and uterine cancer, with estimated 311365, 184799 and 89,929 deaths in 2018, respectively [2].

In recent years, many studies [3–5] have been carried out to investigate the factors related to stage at diagnosis and survival in female cancer patients. They identified age, race, stage, grade, socioeconomic status, living areas and surgical treatment were factors influencing breast cancer survival and recurrence. Some socio-demographic factors are reported to have predictive role in survival of patients with women's cancers, such as marital status. As reported by Wang et al [6], for patients with ovarian cancer, unmarried ones had an increased risk of mortality [hazard ratio (HR) = 1.11 for single, HR = 1.21 for divorced, HR = 1.12 for widowed] than the married. However, Thomas et al [7] reported reversed results, suggesting that being unmarried at the time of diagnosis is associated with better survival of breast cancer.

Evidence to clarify the role of marital status in predicting survival of patients with women's cancers is still lacking. In this study, we carried out a meta-analysis to evaluate the impact of marital status on stage at diagnosis and cancer survival among women with breast and gynecologic cancers. Furthermore, we determined the direction and extent of the effect of marital status in each individual cancer type, comparing each unmarried status (single, divorced and widowed) with the married.

Methods

Search strategy

We conducted the systematic literature search of PubMed, Cochrane and EMBASE databases, from inception to March 31, 2020. The searches were limited to English-language articles. The search strategy, in PubMed database for example, was ((marital status) OR (marriage) OR (married)) AND ((breast) OR (vulvar) OR (vaginal) OR (cervical) OR (endometrial) OR (uterine) OR (fallopian tube) OR (ovarian) OR (gynecologic)) AND ((cancer) OR (carcinoma) OR (malignancy) OR (tumor) OR (tumor) OR (sarcoma)).

Study inclusion criteria

Studies eligible for inclusion met the following criteria:

1) Patients were women with breast or gynecologic cancers (vulvar cancer, vaginal cancer, cervical cancer, endometrial cancer, fallopian tube cancer and ovarian cancer).

2) Studies provided information of patients' marital status, which was divided into married or unmarried (including single, divorced/separated and widowed patients).

3) Studies assessed at least one of the three cancer-related outcomes: stage of cancer at diagnosis, cancer-specific mortality (CSM) and overall survival (OS).

4) Studies contained quantitative data regarding the association of marital status with cancer-related outcomes and adjusted for factors that are known to be associated with outcomes in the statistical analysis.

5) Articles were published in English.

6) When patient populations were included in at least one study, we only collected the dataset once, according to the priority order: accessibility of data, larger sample size and more recent publications.

Data extraction

All data were extracted independently by two reviewers using a standardized collection form, with disagreements discussed until resolved by consensus between authors.

For each included study, we entered descriptive information including the year of publication, title, authors' names, cancer site and the length of follow-up (years). To place all the included studies on a

common scale in our analysis, marital status at the time of diagnosis was categorized into two major groups: married and unmarried (including single, divorced and widowed). Never married individuals were treated as “single” for all comparisons, while “separated” was treated as “divorced”.

Data for statistical analysis were also collected, including sample size, HR estimates, odds ratio (OR) (in terms of relative risk, RR), relative 95% confidence intervals (CIs), statistical adjustments and the impact factors for which the data was adjusted.

Cancer stage at diagnosis was classified as early and late stage as indicated in the articles, with “localized”/“local” tumor intended as “early” stage and “delayed”/“advanced”/“metastatic” tumor treated as “late” stage. If not indicated in the included articles, American Joint Committee on Cancer (AJCC) stages I and II of breast cancer were defined as early stage of the disease [8, 9].

Quality assessment

The quality assessment of included studies was performed independently by two reviewers. All disagreements were resolved by consensus through detailed discussion among authors. The Newcastle-Ottawa Quality Assessment Scale (http://www.ohri.ca/home.asp) was recommended as a quality assessment tool for evaluating the quality of cohort and case-control studies, including 9 items from 3 domains. To assess the methodological quality of included cross-sectional studies, we used an adapted form of the NOS [10, 11].

Statistical analysis

This meta-analysis examined the impact of marital status (married or unmarried) on stage of cancer at diagnosis, CSM and OS, in female patients with breast and gynecologic cancers.

Subgroup analyses were carried out with three aims. Firstly, the association between marital status and clinical outcomes was assessed in subgroups with each cancer type. Secondly, we evaluated the specific contribution of each unmarried status, by comparing cancer-related outcomes of single vs. married, divorced vs. married, and widowed vs. married. Thirdly, the potential impact of sample provenance and level of social support between marital status and clinical outcomes was examined by subgroup analysis, as well as the influence of numbers of adjustment factors in statistical models.

Data from studies were pooled by the generic inverse variance method. Estimates of relative risk (HR and OR) were assessed, with corresponding point estimates and 95% CIs. Statistical heterogeneity among studies was assessed using Chi-square test and I^2 statistic. The random effect model was used if the heterogeneity was significant ($P \leq 0.1$, $I^2 \geq 50\%$). Otherwise, the fixed effect model should be adopted [12]. If results from multiple models were reported in one study, we extracted the results from the model adjusting for more factors. Funnel plots were constructed to visually assess the potential publication bias [13].

Results

Characteristics of included studies

Using the search strategy described above, we identified 3283 articles in PubMed, 71 in Cochrane Library and 2409 in EMBASE. According to the inclusion and exclusion criteria, a total of 55 eligible studies were included in this meta-analysis. The flow diagram of literature search and selection is shown in Fig. 1. Characteristics of included studies are summarized in Table 1. Quality assessment for each included study is shown in Table S1.

Table 1
Brief description of the studies included in the meta-analysis

Study included	N	Cancer type	Marital status	Follow-up (years)	Outcome
Neale et al., 1986 [41]	1261	breast cancer	widowed VS married	10	CSM
	1261	breast cancer	widowed VS married	--	Stage
Timm, 1973 [42]	74	ovarian cancer	single VS married	5	OS
			divorced VS married		
LeMarchand et al., 1984 [43]	2290	breast cancer	single VS married	5	OS
Palmer et al., 1982 [44]	688	breast cancer	single VS married	5	OS
			widowed VS married		
Neale, 1994 [45]	10464	breast cancer	single VS married	10	CSM
			divorced VS married		
			widowed VS married		
Kvikstad et al., 1994 [46]	4025	breast cancer	divorced VS married	--	Stage
			widowed VS married		
Kvikstad and Vatten, 1996 [47]	3831	breast cancer	unmarried VS married	25	CSM
	1618	cervical cancer			
	1120	ovarian cancer			
	501	endometrial cancer			
Gajalakshmi et al., 1997 [48]	1325	breast cancer	single VS married	5	OS

Study included	N	Cancer type	Marital status	Follow-up (years)	Outcome
			widowed VS married		
Meng et al., 1997 [49]	3344	breast cancer	single VS married	5	CSM
			divorced VS married		
			widowed VS married		
Wojcik et al., 1998 [50]	5939	breast cancer	single VS married	13.3	OS
			divorced VS married		
			widowed VS married		
Ferrante et al., 2000 [51]	852	cervical cancer	married VS unmarried	--	Stage
Studzijnski and Zajewski, 2003 [52]	121	endometrial cancer	single VS married	5	CSM
			widowed VS married		
Yeole et al., 2004 [53]	2476	breast cancer	single VS married	5	CSM
			widowed VS married		
Taplin et al., 2004 [54]	2534	breast cancer	single VS married	--	Stage
			divorced VS married		
Vinh-Hung et al., 2007 [55]	27999	cervical cancer	married VS unmarried	10	CSM
Kaku et al., 2008 [56]	337	cervical cancer	single VS married	--	Stage
			divorced VS married		
Ali et al., 2008 [31]	496	breast cancer	single VS married	--	Stage

Study included	N	Cancer type	Marital status	Follow-up (years)	Outcome
			divorced VS married		
Berz et al., 2009 [57]	109848	breast cancer	married VS unmarried	5	CSM
Adams et al., 2009 [58]	1749	cervical cancer	single VS married	10	CSM
			divorced VS married		
Celaya et al., 2010 [59]	5833	breast cancer	unmarried VS married	--	Stage
Chang and Kuo, 2010 [60]	1134	breast cancer	unmarried VS married	12.5	CSM
Mahdi et al., 2013 [61]	41858	ovarian cancer	unmarried VS married	--	Stage
Ibrahim et al., 2011 [62]	197	cervical cancer	unmarried VS married	--	Stage
Kroenke et al., 2012 [63]	4530	breast cancer	unmarried VS married	6.8	CSM
			unmarried VS married	6.8	OS
Li et al., 2012 [64]	4321	cervical cancer	unmarried VS married	no	CSM
Lan et al., 2013 [65]	948	breast cancer	unmarried VS married	5	CSM
Rauh-Hain et al., 2013a [66]	5474	vulvar cancer	unmarried VS married	5	CSM
			unmarried VS married		OS
Rauh-Hain et al., 2013b [67]	21960	cervical cancer	unmarried VS married	5	CSM
Rauh-Hain et al., 2013c [68]	14289	ovarian cancer	unmarried VS married	5	CSM
Bhuyan et al., 2014 [69]	4739	breast cancer	unmarried VS married	5	CSM
Mohaghegh et al., 2014 [70]	318	breast cancer	single VS married	--	Stage

Study included	N	Cancer type	Marital status	Follow-up (years)	Outcome
Lowery et al., 2015 [71]	42678	endometrial cancer	unmarried VS married	20.8	CSM
			single VS married		
			divorced VS married		
			widowed VS married		
	47420	endometrial cancer	married VS widowed	--	Stage
Saghari et al., 2015 [72]	13624	cervical cancer	single VS married	--	Stage
			divorced VS married		
Jatoi et al., 2016 [73]	325	breast cancer	unmarried VS married	2	OS
Cheng et al., 2015 [74]	52	breast cancer	unmarried VS married	--	Stage
Parikh et al., 2015 [75]	756	breast cancer	unmarried VS married	--	OS
Leung et al., 2016 [76]	195	breast cancer	unmarried VS married	--	Stage
Mwaka et al., 2016 [77]	144	cervical cancer	divorced VS married	--	Stage
			widowed VS married		
El Ibrahimi and Pinheiro, 2017 [36]	30235	cervical cancer	unmarried VS married	10.9	OS
			single VS married		
			divorced VS married		
			widowed VS married		
	30235	cervical cancer	single VS married	--	Stage

Study included	N	Cancer type	Marital status	Follow-up (years)	Outcome
			divorced VS married		
			widowed VS married		
Binder et al., 2016 [78]	2062	endometrial cancer	single VS married	15	OS
			divorced VS married		
			widowed VS married		
Eskander et al., 2016 [79]	3307	breast cancer	unmarried VS married	5	OS
Hinyard et al., 2017 [80]	77381	breast cancer	unmarried VS married	5	OS
Hsu et al., 2017 [81]	52048	breast cancer	unmarried VS married	5	CSM
			unmarried VS married	--	Stage
Martinez et al., 2017 [82]	139542	breast cancer	single VS married	10	CSM
			widowed VS married		
	139542	breast cancer	single VS married	--	Stage
			widowed VS married		
Mahdi et al., 2017 [83]	6373	endometrial cancer	unmarried VS married	25	OS
Dianatinasab et al., 2018 [9]	497	breast cancer	unmarried VS married	--	Stage
Wang et al., 2017 [6]	10905	ovarian cancer	single VS married	5	OS
			divorced VS married		
			widowed VS married		

Study included	N	Cancer type	Marital status	Follow-up (years)	Outcome
Sathwara et al., 2017 [84]	1210	breast cancer	single VS married	--	Stage
			divorced VS married		
Renna Junior and Silva, 2018a [85]	87783	breast cancer	single VS married	--	Stage
			divorced VS married		
			widowed VS married		
Parise and Caggiano, 2018 [86]	12773	breast cancer	single VS married	13.3	CSM
			divorced VS married		
			widowed VS married		
	22782	breast cancer	single VS married	--	Stage
			divorced VS married		
			widowed VS married		
Gauri et al., 2018 [87]	18279	cervical cancer	single VS married	--	Stage
			divorced VS married		
Renna Junior and Silva, 2018b [88]	40554	cervical cancer	single VS married	--	Stage
			divorced VS married		
			widowed VS married		
Wu et al., 2018 [21]	4001	vulvar cancer	single VS married	--	Stage
			divorced VS married		

Study included	N	Cancer type	Marital status	Follow-up (years)	Outcome
			widowed VS married		
Dunyo et al., 2018 [89]	142	cervical cancer	unmarried VS married	--	Stage
dos-Santos-Silva et al., 2019 [90]	121174	breast cancer	unmarried VS married	--	Stage

Main meta-analysis: unmarried versus married

Overall, results of the 27 studies focusing on the effect of marriage on stage at diagnosis showed that, unmarried female cancer patients had a significant higher risk of presenting at late stage of cancer than the married (OR = 1.28, 95% CI: 1.22–1.36, $P < 0.0001$) (Fig. 2).

21 studies focused on the association of marital status with CSM (Fig. 3). The pooled HR of CSM for unmarried versus married female cancer patients was 1.22 (95% CI: 1.16–1.28), indicating that marriage is a significant protective factor against mortality ($P < 0.0001$).

Figure 4 displays the overall HR for OS in married and unmarried female cancer patients, by pooling data of 15 included studies. Results showed that unmarried female cancer patients had significantly worse OS compared with married ones, with a pooled HR of 1.20 (95% CI: 1.14–1.25, $P < 0.0001$).

Subgroup analyses

Table 2 shows the association of marital status with late stage at diagnosis, by cancer type. For breast cancer, vulvar cancer, cervical cancer and endometrial cancer, after pooling studies that met the inclusion criteria (n = 15, 1, 9 and 1, respectively), compared to married female patients, the pooled OR of unmarried ones to be diagnosed at late stage was 1.25 (95% CI: 1.17–1.33), 1.14 (95% CI: 1.01–1.28), 1.36 (95% CI: 1.31–1.41) and 1.50 (95% CI: 1.42–1.58), respectively. Nevertheless, based on the only 1 study included in the subgroup analysis for ovarian cancer, being unmarried is a protective factor against late stage at diagnosis (OR = 0.85, 95% CI: 0.82–0.89).

Table 2
Results of subgroup analyses

Variables	Late Stage at Diagnosis			CSM			OS		
	NO.	OR (95% CI)	I^2 (%)	NO.	HR (95% CI)	I^2 (%)	NO.	HR (95% CI)	I^2 (%)
Cancer Type (unmarried VS. married)									
Breast Cancer	15	1.25(1.17–1.33)	89	12	1.19(1.14–1.25)	75	9	1.19(1.08–1.30)	65
Vulvar Cancer	1	1.14(1.01–1.28)	24	1	1.01(0.90–1.14)	NA	1	1.22(1.13–1.31)	NA
Cervical Cancer	9	1.36(1.31–1.41)	26	6	1.36(1.10–1.68)	95	1	1.32(1.27–1.38)	NA
Endometrial Cancer	1	1.50(1.42–1.58)	NA	4	1.85(1.11–3.10)	76	2	1.26(1.09–1.45)	54
Ovarian Caner	1	0.85(0.82–0.89)	NA	3	1.16(1.01–1.34)	16	2	1.15(1.05–1.27)	66
Marital Status (VS. married)									
Single	13	1.38(1.32–1.44)	57	13	1.17(1.09–1.26)	53	10	1.28(1.13–1.46)	80
Divorced	8	1.28(1.18–1.39)	72	5	1.32(1.09–1.60)	89	8	1.18(1.08–1.29)	41
Widowed	8	1.27(1.16–1.39)	85	5	1.31(1.18–1.45)	80	6	1.17(1.00-1.37)	90

In the subgroup analysis evaluating the impact of cancer type on the association between marital status and CSM (Table 2), data of included studies were pooled for each cancer type (n = 12 for breast cancer, n = 1 for vulvar cancer, n = 6 for cervical cancer, n = 4 for endometrial cancer, n = 3 for ovarian cancer). The overall HR for unmarried versus married cancer patients was 1.19 (95% CI: 1.14–1.25), 1.01 (95% CI: 0.90–1.14), 1.36 (95% CI: 1.10–1.68), 1.85 (95% CI: 1.11–3.10) and 1.16 (95% CI: 1.01–1.34), respectively.

The subgroup analysis assessing the impact of cancer type on the association of marital status with OS is shown in Table 2. For breast cancer, pooled data of 9 studies showed an overall HR of 1.19 (95% CI: 1.08–1.30) for unmarried versus married individuals. For vulvar and cervical cancer, only one study was available. The HR was 1.22 (95% CI: 1.13–1.31) for vulvar cancer and 1.32 (95% CI: 1.27–1.38) for

cervical cancer. For endometrial and ovarian cancer, 2 studies were included for each of them. The pooled HR for unmarried versus married patients was 1.26 (95% CI: 1.09–1.45) and 1.15 (95% CI: 1.05–1.27), respectively.

In the subgroup analyses for each marital status (Table 2), studies reporting data on cancer stage at diagnosis (n = 13), CSM (n = 8) and OS (n = 8) of single versus married female cancer patients were included in this subgroup analysis. The pooled OR of late stage at diagnosis for single versus married female cancer patients was 1.38 (95% CI: 1.32–1.44). The pooled HR of CSM and OS was 1.17 (95% CI: 1.09–1.26) and 1.28 (95% CI: 1.13–1.46), respectively. *P* values were < 0.0001 for all 3 comparisons.

Data of studies comparing clinical outcomes of divorced versus married individuals (n = 13 for cancer stage at diagnosis, n = 5 for CSM, n = 5 for OS) were pooled in this subgroup analysis. Divorced subjects were significantly more likely to be diagnosed at late stage (pooled OR = 1.28, 95% CI: 1.18–1.39), having increased risk of CSM (pooled HR = 1.32, 95% CI: 1.09–1.60) and worse OS (pooled HR = 1.18, 95% CI: 1.08–1.29) than the married. *P* values were < 0.0001 for all 3 comparisons. (Table 2)

10 studies comparing the stage at diagnosis of widowed versus married patients were available. Compared with the married, the widowed were more likely to be diagnosis at late stage of cancer (pooled OR = 1.27, 95% CI: 1.16–1.39). 8 studies focusing on the CSM and 6 studies focusing on the OS of widowed versus married persons, with pooled HR = 1.31 (95% CI: 1.18–1.45) and 1.17 (95% CI: 1.00-1.37), respectively. *P* values were < 0.0001 for all 3 comparisons. (Table 2)

All the included studies reported patients' provenances. In America, unmarried female cancer patients had a higher risk of late-stage diagnosis and worse prognosis than the married (17 studies for cancer stage at diagnosis, 15 for CSM and 12 for OS). The pooled effects of late stage at diagnosis, CSM and OS were 1.13 (95% CI: 1.05–1.22), 1.15 (95% CI: 1.09–1.22) and 1.18 (95% CI: 1.12–1.26), respectively. In European female cancer patients, the unmarried had worse CSM (3 studies included), with pooled HR = 1.74 (95% CI: 1.01–3.02) (Table 3).

Table 3
The influence of certain factors on outcomes comparing unmarried versus married female cancer patients.

Variables	Stage			CSM			OS		
	NO.	OR (95% CI)	I^2 (%)	NO.	HR (95% CI)	I^2 (%)	NO.	HR (95% CI)	I^2 (%)
Patient's provenance									
America	17	1.13 (1.05–1.22)	99	15	1.15 (1.09–1.22)	93	12	1.18 (1.12–1.26)	91
Europe	1	0.87 (0.63–1.22)	NA	3	1.74 (1.01–3.02)	97	2	3.41 (0.16-71.0)	79
Asia	6	1.35 (0.13–1.63)	71	3	0.86 (0.57–1.29)	70	1	1.13 (0.84–1.53)	NA
Africa	3	1.05 (0.90–1.24)	42						
Level of social support									
High				2	1.13 (1.10–1.16)	0	1	1.49 (1.03–2.13)	NA
Low				2	0.93 (0.66–1.30)	91	1	0.76 (0.55–1.05)	NA
NO. of adjustment factors									
≤ 5	20	1.10 (1.02–1.19)	98	10	1.15 (1.06–1.25)	88	10	1.22 (1.13–1.31)	74
> 5	7	1.29 (1.17–1.42)	94	11	1.19 (1.10–1.29)	94	5	1.13 (1.06–1.21)	82

Subgroup analyses were conducted to examine the relationship between marital status and survival outcomes of female cancer patients with different levels of social support. Results showed that among patients with high level of social support, the unmarried had worse survival outcomes than the married,

with pooled HR of CSM = 1.13 (95% CI: 1.10–1.16) and pooled HR of OS = 1.49 (95% CI: 1.03–2.13) (Table 3).

When analyzing the impact of marital status on timely diagnosis and survival outcomes, most studies adjusted for influencing factors. These studies were split into two groups depending on whether the numbers of adjustment factors were ≤ 5 or > 5. The results of the subgroup analyses showed that in both groups, unmarried female cancer patients had a higher risk of late-stage diagnosis and worse survival outcomes than the married (OR > 1 and HR > 1, $P < 0.05$) (Table 3).

Publication bias

In funnel plots (Figure S1) for studies evaluating the association of marital status with late stage at diagnosis, CSM and OS, each circle represents one study. The vertical line represents the pooled effect estimate. Most points are distributed in the top of the funnel plots, indicating that included studies are with large sample size and high precision and there is no evidence for publication bias.

Discussion

The correlation between marital status and health has been demonstrated [14]. Manzoli et al. examined the association of marital status and survival in old cancer patients [15]. Huynh-Le et al. evaluated the impact of marital status on receipt of brachytherapy and survival outcomes in cancer patients diagnosed at late stage [16]. Siddiqui et al. investigated the relationship between marital status and clinical outcomes in patients with lung cancer [17]. According to these studies, being married or having good relationship with partners is associated with early diagnosis of cancer, and can act as a protective factor for cancer survival [18]. In the present study, we conducted a meta-analysis to examine the impact of marital status on stage of diagnosis and cancer survival in female patients with breast and gynecologic cancers. Our meta-analysis of 107 datasets from 55 studies, including 1195773 female cancer patients, confirms that unmarried women are more likely to be diagnosed at late stage and have poorer survival rates than the married. Pooled OR and HR showed that, compared to the married, unmarried female cancer patients had a 28% increased risk to be diagnosed at late stage and a 20% higher risk of death.

Marriage offers protective benefits on the diagnosis and prognosis of female patients with women's cancer in several ways. The first is the effect on behavior. Living with a spouse or a partner has a positive effect on lifestyle and health behaviors in women. One explanation is that sexually active women present early symptoms for some cancers, such as cervical cancer [19], since postcoital bleeding is a typical symptom. Moreover, close partners may notice early symptoms [20] and encourage their wives to seek medical care instantly once symptoms develop. Another possible explanation is that spouses may promote timely health screenings [21]. Studies have shown that married women are more likely to receive surveillance mammography [22, 23] and participant in cervical cancer screening [24–26]. In addition, marriage may reduce risk-taking behavior and exert social control on behavior, such as diet and exercise [27, 28].

Secondly, economic and social support may lead to timely diagnosis and favorable prognosis [29, 30]. Compared with the unmarried, married women may receive financial assistance from spouses and other family members, therefore having an increased opportunity to seek and receive effective medical treatments [31]. Moreover, marriage may offer a protective benefit through family assistance and care, as well as larger social support networks [32]. Consequently, marriage is positively associated with physical and mental health. In addition, married cancer patients perceive more social support through extended family network and enjoy overall better health. Furthermore, family members can share the emotional burden; therefore, patients display less depression, fatigue and anxiety [33]. In contrast, unmarried women lack social and economic support, thus suffer from psychological distress and physical symptoms.

Since breast cancer is the most frequent cancer and the second leading cause of cancer death in women, breast cancer-related studies accounted for the largest number of studies included in the subgroup analysis. Compared to married women with breast cancer, the unmarried had a 25% higher risk to be diagnosed at late stage and a 19% increased risk of death. Studies suggest that married women have a higher rate of breast cancer screening than the unmarried [34], and the married breast cancer survivors are more optimistic than the unmarried, especially within 5 years since diagnosis [35]. In cervical cancer patients, marriage is positively associated with early diagnosis and better survival. This can be explained by better health behaviors, more comprehensive health insurance coverage and greater socio-economic support in married women with cervical cancer [36]. However, it should be noticed that, from the only one eligible study, the married ovarian cancer patients have a higher risk of being diagnosed at late stage than the unmarried, although the evidence level of this conclusion was not improved.

Results of the subgroup analysis showed that single, divorced and widowed female cancer patients are associated with late stage at diagnosis and worse prognosis. Unmarried female cancer patients (especially the single individuals) showed a distinct tendency to receive no surgery compared with those of married status, partly resulting in their survival disadvantages [37]. Potential explanations could be that, divorce or death of a spouse can cause not only severe disruption of the patient's social support network, but also great emotional stress such as anxiety and depression [38, 21]. Moreover, women of divorced and widowed status have lost the spousal effect which may promote cancer screening and the seeking of medical attention and treatment. In addition, they are less likely to receive surgical treatments and chemotherapy.

Marriage and marital status are closely related to cultural background and social status. Therefore, we conducted subgroup analyses for provenances: patients from America, Europe, Asia and Africa. Marriage showed a protective effect in patients from America and Europe, whereas its influence was not significant in patients from Asia and Africa. In addition, marriage plays a significant protective role in women with high social support, whereas its influence was not statistically significant under low social support. However, due to the limited number of studies, any conclusions regarding the potential impact of cultural background and social status shall be avoided until further evidence is available.

The present meta-analysis study has some limitations that should be addressed. The first methodological limitation of this meta-analysis is the quality of included studies. All the included studies were observational studies (cross-sectional studies and cohort studies). 80% of the studies had a sample size of over 500 patients. To assess the methodological quality of included studies, two authors independently evaluated each study using an adapted form of the NOS scale, with consensus reached following discussion of any differences. Nevertheless, data of some studies could not be further extracted, resulting in relatively few eligible studies included in the subgroup analysis for some clinical outcomes. For example, when evaluating the impact of marital status on the CSM of women with vulvar cancer and on the survival of women with high social support, only 1 or 2 studies were included, which was unable to improve the evidence level. The second methodological limitation is heterogeneity. Like most meta-analyses, among the included studies in our analysis, there was a high heterogeneity in study design, sample size, characteristic of patients, etc. This heterogeneity persisted even in subgroup analyses conducted for cancer type, unmarried status, social characteristic of patients, and number of adjustment factors. Nonetheless, the investigation of heterogeneity could be essential for identifying high-risk individuals.

Additionally, several limitations to this study must be considered in interpreting the results. First, diverse cultural backgrounds may lead to different concepts and institutions of marriage, as well as difference in the age at first marriage, the age at first birth, breastfeeding, etc. Therefore, we carried out subgroup analyses stratified by different provenances of female cancer patients. Second, marriage is a double-edged sword for health. Studies [39, 40] have shown that high marital quality is associated with better physical and mental health, while low marital quality may increase the risk of stress, depression and worse health outcomes.

In this study, we focused on the relationship between marital status (being married or unmarried) and the clinical outcomes of female cancer patients. However, the potential effect of marital quality is difficult to delineate. Finally, although some factors are known to affect the survival of cancer patients (e.g. genetics, treatments, medical resource utilization, etc.), this is not against our investigation into the impact of marriage on cancer survival. From the perspective of public health and population health intervention, this topic is of utmost importance to pay specific attention to high-risk populations and develop screening strategies. Furthermore, most of the included studies in this meta-analysis had adjusted for known factors when constructing the influencing factor analysis models.

Conclusions

Breast and gynecologic cancers are significant global public health problems threatening women’s health and causing great psychological burden to women. Therefore, it is necessary to specifically promote cancer screening, provide psychosocial support and personalized treatment to female cancer patients with different marital status. The results of our meta-analysis suggest that being married is associated with timely diagnosis and favorable prognosis in most women’s cancers. This conclusion emphasizes the development of specific interventions for unmarried population to achieve early diagnosis and improved

survival. Additionally, particular attention should be paid to the impact of lacking economic and emotional support on survival outcomes in unmarried female cancer patients.

List Of Abbreviations

CSM: cancer-specific mortality

OS: overall survival

OR: odds ratio

CI: confidence interval

HR: hazard ratio

RR: relative risk

AJCC: American Joint Committee on Cancer

Declarations

Ethical approval

The present study was approved by the Ethics Committee of the First Affiliated of Zhengzhou University and the Ethical Approval Number was 2020-KY-167.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors contributed to the study conception and design. Literature search and data collection were performed by QL and NH. RY and MJ re-checked data. Statistical analysis was performed by CZ. The first draft of the manuscript was written by RY, MJ and NH. All authors read and approved the final manuscript.

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Figures

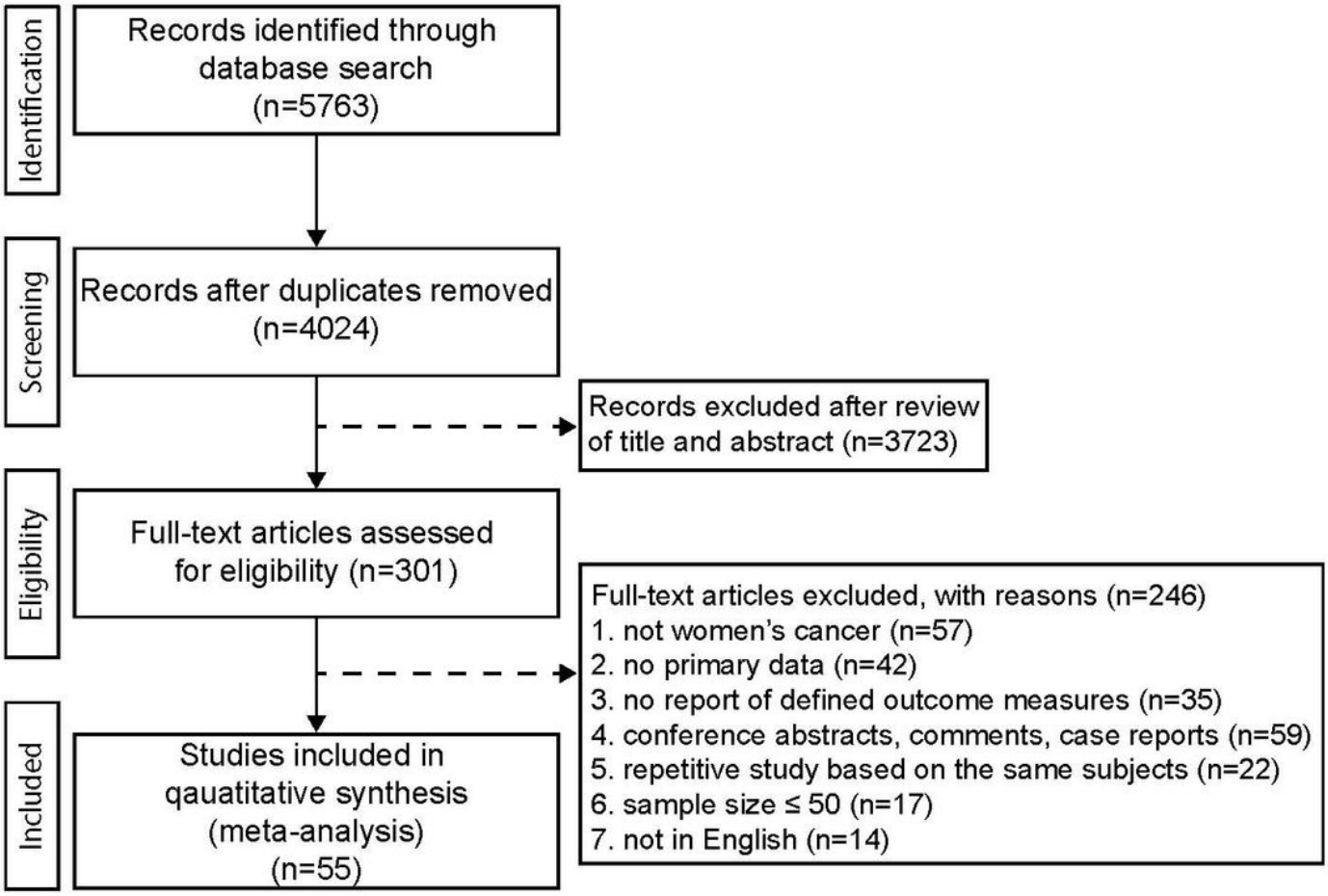

Figure 1

The flow diagram of literature search and selection

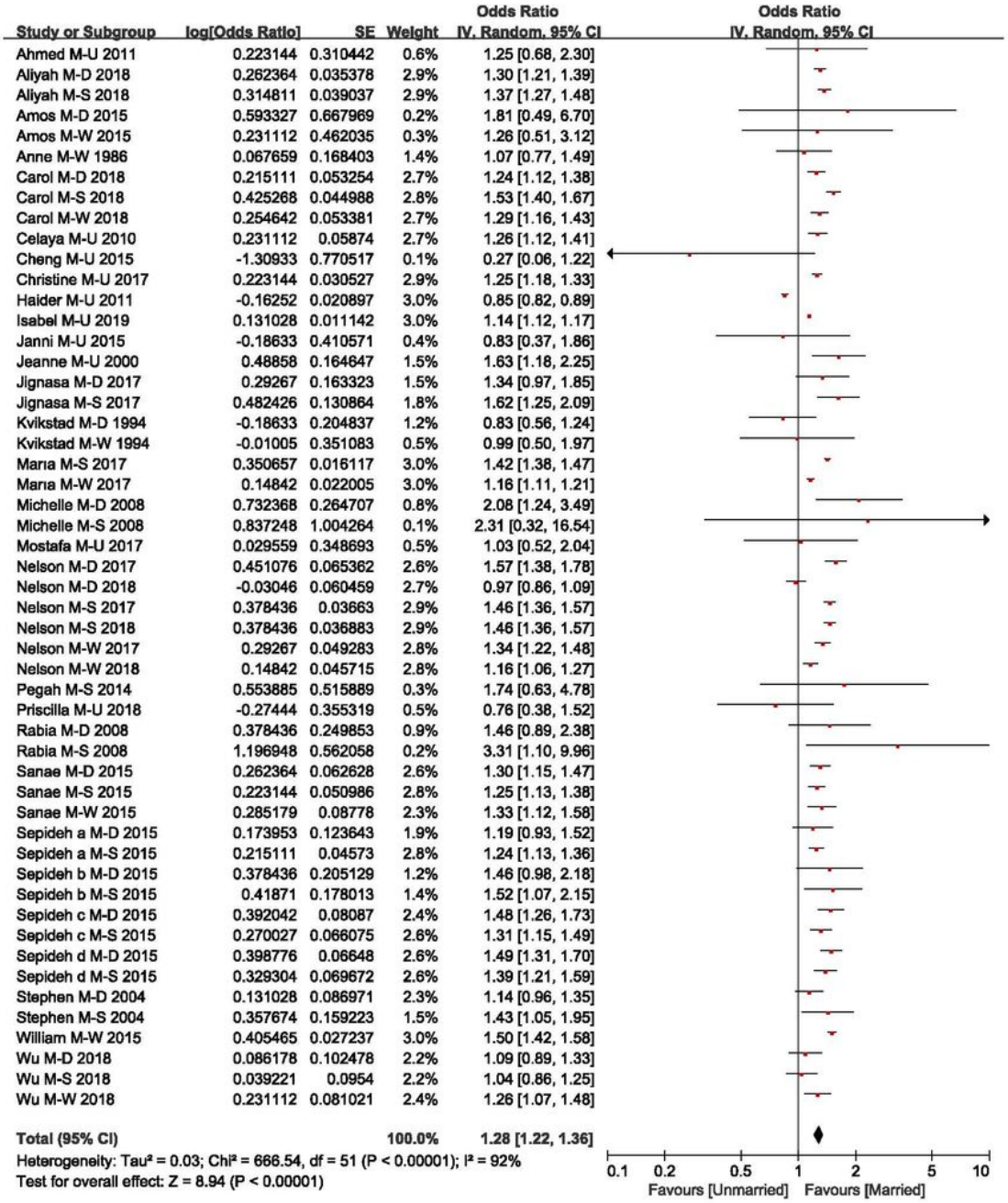

Figure 2

Overall, results of the 27 studies focusing on the effect of marriage on stage at diagnosis showed that, unmarried female cancer patients had a significant higher risk of presenting at late stage of cancer than the married

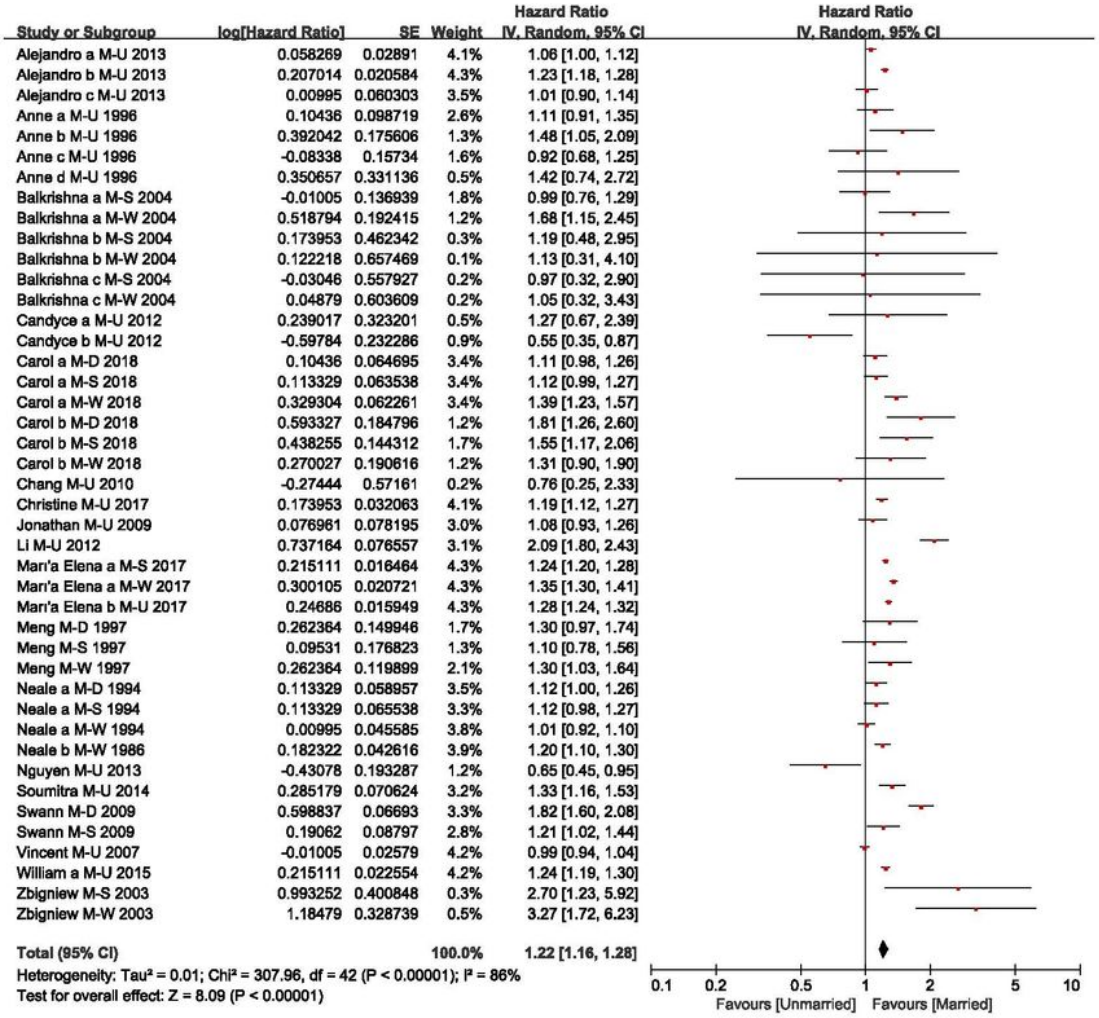

Figure 3

21 studies focused on the association of marital status with CSM

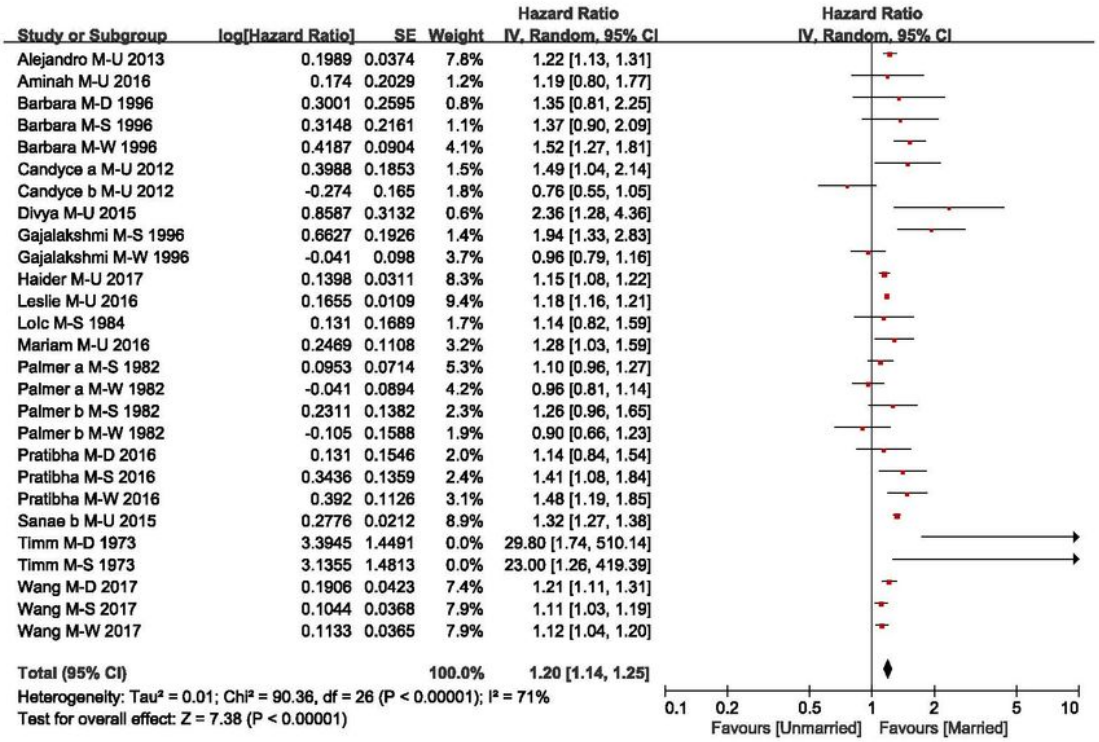

Figure 4

The overall HR for OS in married and unmarried female cancer patients, by pooling data of 15 included studies.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- AdditionalFile1.docx
- AdditionalFile2.docx