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Prevalence and risk factors for cancer-related fatigue in women with malignant gynecological tumors: a meta-analysis and systematic review

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Abstract

Background Cancer-related fatigue (CRF) is one of the most prevalent symptoms, but its prevalence and associated risk factors remain inconsistent across studies.

Objective To identify the prevalence and risk factors for CRF in women with malignant gynecological tumors.

Methods A comprehensive search of databases, including Web of Science, Cochrane Library, PubMed, Embase, CNKI, VIP, Wan Fang, and CBM, was conducted for relevant studies published from the inception of the database until September 7, 2023. Two reviewers used EndnoteX9 software to independently review, extract data, cross-check, and use the Newcastle-Ottawa quality assessment scale and the Agency for Healthcare Research and Quality tool for risk of bias assessment to evaluate bias risk. Stata 17.0 software was used to perform a traditional meta-analysis.

Results The meta-analysis included 33 studies, of which 29 reported the prevalence of CRF. The combined prevalence of CRF was 89% (95% confidence interval *[CI]*: 80–95%), and the combined prevalence of chronic CRF was 25% (95%*CI*: 22–28%). The combined prevalence of CRF in patients with ovarian cancer, cervical cancer, endometrial, and gynecological malignancies (including but not limited to cervical, ovarian, vaginal and other mixed types of gynecological cancers) was 77%, 94%, 90%, and 93%, respectively. The variability in CRF measurement is due to the different scales used across studies. Its prevalence varies by country, and developing countries, especially China, have a high prevalence of CRF. The following risk factors were associated with CRF: age (odds ratio *[OR]* = 1.43, 95%*CI* = 1.12–1.83), psychological factors (*OR* = 1.40, 95%*CI* = 1.14–1.72), disease stage (*OR* = 1.65, 95%*CI* 1.14–2.40), and social support (*OR* = 0.77, 95%*CI* 0.67–0.87).

Conclusion The prevalence of CRF is significant in women with gynecological cancers, especially in developing countries. Age, psychological factors, and disease stage are risk factors for CRF, while social support serves as a

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protective factor. Healthcare professionals can obtain a clearer picture of CRF in women with gynecological malignant tumors and identify risk factors to support subsequent interventions in these patients.

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Keywords Gynecological malignant tumors, Cancer-related fatigue, Prevalence, Risk factors, Meta-analysis, Systematic review

Introduction

Malignant gynecological tumors, including cervical, endometrial, and ovarian cancers, pose significant threats to women's health. According to the data released by the International Agency for Research on Cancer in 2020, approximately 1.33 million new cases of gynecological malignancies are diagnosed globally each year, accounting for 14.4% of all female cancers[1]. Additionally, around 0.54 million women die from these cancers each year, representing 12.4% of female cancer deaths[1]. Recently, platinum-based chemotherapy has made significant advancements in treating these malignancies and has become the third most important method after surgical treatment and radiotherapy. However, chemotherapy also leads to side effects such as nausea, vomiting, and bone marrow toxicity, of which cancer-related fatigue is one of the most common symptoms[2]. Treatment of malignant gynecological tumors often leads to cancer-related fatigue (CRF)[2, 3].

According to the National Comprehensive Cancer Network (NCCN), CRF is defined as a distressing and persistent in the subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activities that interfere with usual functioning[4, 5]. Approximately 25–99% of patients with gynecological malignant tumors are plagued by CRF. Severe CRF can lead to treatment interruptions, significantly impacting social functioning, self-management, and quality of life[6]. CRF has a devastating effect on patients with malignant gynecological tumors. In addition, gynecological cancer patients experience CRF that is a persistent and dynamic challenge. In terms of duration, its impact on patients is more severe than other symptoms, such as pain and psychological depression[7]. Poort et al. has identified six distinct patterns of fatigue in ovarian and endometrial cancer patients, including sustained high, sustained low, and fluctuating levels of fatigue[8]. Zheng et al. found that patients with gynecological cancers experience varying degrees of fatigue both before and after chemotherapy, with the fatigue progressively worsening throughout the treatment process, and potentially lasting for several years[9, 10].

The prevalence of CRF in patients with malignant gynecological tumors remains inconsistent across studies. For example, Sekse et al.[11] identified the prevalence of symptoms among 120 patients treated for various types of gynecological cancers, with a prevalence of 53%. Obama et al.[12] found that the prevalence of CRF in cervical cancer and endometrial cancer survivors was 34%. This variation may be partially attributed to differences in cancer type and stage, as well as the use of different assessment scales and treatment regimens[5]. Moreover, although several reviews have examined the prevalence and risk factors for CRF in cancer patients, these studies may not be directly applicable to gynecological cancer patients due to the unique characteristics of the type of cancer[13, 14, 15]. Patients with gynecological malignant tumors may experience greater mental stress and more severe fatigue than those with other malignant tumors, warranting increased attention[16]. Investigating risk factors for CRF is essential to identify patients at risk of experiencing more fatigue during cancer treatment. Therefore, it is necessary to systematically review the risk factors for CRF in patients with malignant gynecological tumors in an evidence-based manner. The variation in prevalence discussed above also indicates that it is necessary to perform a meta-analysis of the prevalence in these articles.

The primary objectives of this meta-analysis were to (1) determine the summary level of the CRF prevalence in gynecological malignancies, (2) explore the risk factors of CRF in gynecological malignant tumors, and (3) provide an evidence-based basis for formulating scientific, effective, and reasonable nursing intervention measures to help alleviate patients' fatigue.

Materials and methods

This systematic review was conducted according to the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) guidelines. The protocol was successfully registered in PROSPERO (no. CRD42023489433).

Search strategy

Two reviewers (Zhao and Zhan) independently and systematically searched Web of Science, Cochrane Library, PubMed, Embase, CNKI, VIP, Wan Fang, and CBM from the inception of the database until September 07, 2023. The literature search time is from September 07 to November 05, 2023. Search strategies were performed using a combination of the subject terms and free-text terms. We manually retrieved references from

relevant papers to ensure a comprehensive search. The search terms including 'genital neoplasms, female,' 'fallopian tube neoplasms,' 'ovarian neoplasms,' 'uterine neoplasms,' 'endometrial neoplasms,' 'uterine cervical neoplasms,' 'vaginal neoplasms,' 'vulvar neoplasms,' 'Fatigue,' 'cancer-related fatigue,' 'CRF,' 'lassitude,' 'tiredness,' 'tried,' 'exhaust,' 'Risk factors,' 'epidemiology,' 'incidence,' 'prevalence,' etc. This systematic review did not require approval from an ethics committee because it was based on previously published studies. The detailed search strategy is available in Supplementary Material 2.

Inclusion and exclusion criteria

The inclusion criteria were: (1) Patients with gynecological malignancies were included in the study, including fallopian tube neoplasms, ovarian neoplasms, uterine neoplasms, endometrial neoplasms, uterine cervical neoplasms, vaginal neoplasms, vulvar neoplasms; (2) CRF being assessed using a scale; (3) Prevalence and risk factors of cancer-related fatigue have been reported; (4) Study types including case-control studies, cohort, and cross-sectional studies. The exclusion criteria were: (1) incomplete research data or only abstracts, (2) publications not in English or Chinese, and (3) low-quality evaluation results.

Study selection and data extraction

After removing duplicate studies, two reviewers (Zhao and Zhan) independently evaluated the studies by screening the titles and abstracts. When at least one researcher determined that an abstract met the inclusion criteria, the full text was retrieved and evaluated according to the inclusion and exclusion criteria by reading the abstract and the full text. Disagreements were resolved by a third reviewer (Shen). The extracted contents included the first author, year of publication, country of study, type of study, sample size, diagnostic criteria, prevalence of cancer-related fatigue, reported odds ratio of risk factors, and its 95% confidence interval (95% *CI*).

Quality assessment

The quality of the included studies was independently evaluated by two evaluators (Zhao and Zhan). The quality of the case-control and cohort studies was assessed using the Newcastle-Ottawa Scale (NOS), a validated 9-item measurement tool17. The evaluation mainly focuses on selection, comparability, and results. The total score ranged from 0 to 9 points. The higher the score, the lower the risk of bias, and 0–3 was classified as low quality, 4–6 as medium quality, and 7–9 as high quality. The risk of bias in cross-sectional studies was assessed using 11 measurement tools recommended by the Institute for Health Research and Quality (AHRQ)18. The total score ranged from 0 to 11 points: 0–3 points for low quality, 4–7 points for medium quality, and 8–11 points for high quality. Disagreements were resolved by a third researcher (Shen).

Data analysis

Meta-analysis was performed using Stata 17.0 (Stata Corp, College Station, TX) software. Statistical heterogeneity was expressed as I^2 and p-value. When $p \geq 0.1$ and $I^2 < 50\%$, the study was considered to be homogeneous, and the fixed effect model (FEM) was used to combine the effect size. Otherwise, a random-effects model (REM) was used. To explore the potential source of high heterogeneity, subgroup analyses were conducted by following variables: country, type of cancer, and level of national development. Sensitivity analysis was performed by excluding individual studies and observing the difference between the combined effect size of the remaining studies and the total effect size of all the studies. $p < 0.05$. significant.

Results

Search results

Overall, 2081 articles were retrieved during the initial search, of which 876 were duplicates. The remaining 1205 studies were screened using EndNote X9. According to the inclusion and exclusion criteria, 1144 studies were excluded after reading their titles and abstracts. After reading the full texts for rescreening, 28 studies were excluded. The reasons for exclusion are shown in the flowchart. Finally, 33 articles were included, 15 in English and 18 in Chinese. A flowchart of the literature screening process is shown in Fig. 1.

Characteristics of included studies

A total of 33 studies were included in the meta-analysis, including 7 case-control studies, 20 cross-sectional studies, and 6 cohort studies, with a total of 5949 participants. All studies were published between 2003 and 2023. These 33 studies included both developed and developing countries, of which 18 were from developing countries and 15 were from developed countries. These studies came from four continents and ten countries, including 22 studies from Asia, seven from Europe, three from North America, and only one from Oceania.

The quality evaluation results were as follows: 10 articles were 'high quality,' 23 articles were 'medium quality,' and one article of 'low quality' was deleted. The characteristics of the 33 studies are summarized in Table 1.

*Prevalence of chronic fatigue. Among the types of studies, one represented a case-control study, two represented a cross-sectional study, and three represented a cohort study. Among the different types of cancer, a represents cervical cancer, b, ovarian cancer, c, endometrial cancer, d, choriocarcinoma, and e, vaginal

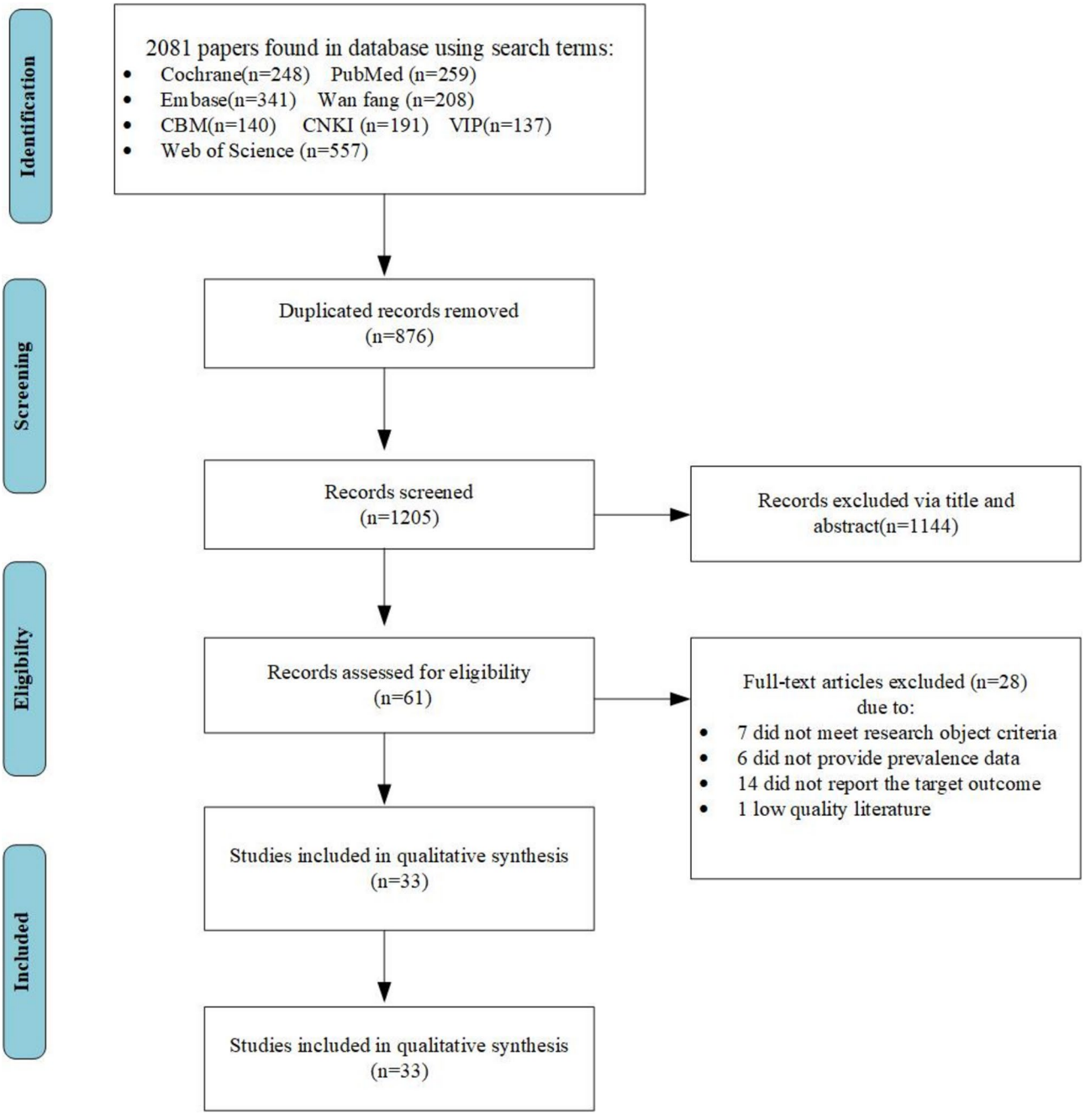

Fig. 1 Meta-analysis literature screening flow chart

cancer. MFI-20 = the Multidimensional Fatigue Inventory-20; EORTC QLQ-C30 = the European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire C30; FQ = the Fatigue Questionnaire; BFI: The Brief Fatigue Inventory; PFS-R = The Revised Piper Fatigue Scale; PFS = The Piper Fatigue Scale; MSAS = Memorial Symptom Assessment Scale; CFS = Cancer Fatigue Score; POMS-SF = the Profile of Mood States-Short Form; FACIT-F = the Functional Assessment of Chronic Illness Therapy-Fatigue; FAS: Fatigue Assessment Scale.

Prevalence of CRF in patients with gynecological malignant tumors

The prevalence of CRF in patients with gynecologically malignant tumors is between 36.7% and 100%, while the incidence of chronic CRF ranges from 22 to 32.7%. In the study, 28 articles reported on the CRF, with a heterogeneity analysis (I^2=98.73%, p = 0.000), followed by a

Table 1 Characteristics of included studies

Authors	Publication Years	Country	Time	Type of study	Age	Sample size	CRF	CRF Prevalence	Diagnostic criteria	Severity of CRF	Type of cancer	Recurrent of cancer	Treatment	Risk factors assessed	NOS/AHRQ
Bernhard Holzner [19]	2003	Austria	2000.2–2000.10	1	57.4 ± 12.5	98	32	32.7%*	MFI-20	—	b	Both	End	—	8
I Vistad [20]	2007	Norway	2005.1	2	59.1 ± 11.4	79	24	30.4%*	FQ	—	a	—	End	depression	4
Liavaag, A. H. [21]	2007	Norway	1977–2003	1	50.6 ± 9.7 53.3 ± 7.8	189	42	22%*	FQ	—	b	Both	End	pain body image scale score	7
Yaping Ye [22]	2009	China	2006.10–2008.3	2	48.01 ± 10.16	96	89	92.71%	BFI	low 23 moderate 49 high 17	a, b, c, d, e	—	Undergoing	treatment, depression, sleep disturbance, anemia, lower white blood cell count	4
Fangfang Xiong [23]	2013	China	2010.8–2010.11	2	47.32 ± 9.99	106	99	93.40%	PFS-R	—	a, b, c,	No	Undergoing	—	8
Sekse [11]	2014	Norway	2009–2012	2	56 ± 13	118	63	53.40%	FQ	—	a, b, e	—	End	age, anxiety, depression	5
Teng [24]	2014	Canada	2012.1–2012.5	2	58	102	72	71.00%	EORTC QLQ-C30	—	b	Both	Undergoing/End	disease stage	7
Xiaobin Zheng [25]	2014	China	2011.7–2012.11	3	47.83 ± 13.12	82	78	95.12%	PFS	low 20 moderate 49 high 9	a, b, c	No	Undergoing	—	7
Hwang [26]	2015	Korea	2012.5–2013.6	2	49.3	192	182	94.80%	Self-designed according to MSAS	—	b	Both	Undergoing	—	8
Kyoko Obama [12]	2015	Japan	2013.5–2013.8	2	44.9 ± 5.5	64	64	100.00%	BFI	low 42 moderate to high 22	a, c	—	End	—	9
Jianfen Tan [27]	2016	China	2013.11–2014.6	2	≥ 18	110	109	99.09%	CFS	—	a, b, c, d, e	—	Undergoing	—	4
Cun [28]	2017	United States	2013	3	63.2	30	9	30%*	POMS-SF	—	b	Both	End	cortisol levels	7
Nho [29]	2017	Korea	2014.7–2015.5	2	54.67 ± 9.16	210	77	36.70%	FACIT-F	—	b	Both	Undergoing	—	6

Table 1 (continued)

Authors	Publication Years	Country	Time	Type of study	Age	Sample size	CRF	CRF Prevalence	Diagnostic criteria	Severity of CRF	Type of cancer	Recurrent of cancer	Treatment	Risk factors assessed	NOS/AHRQ
Rita Steen [30]	2017	Norway	2012.12.31	3	32–75	382	88	23.04%*	FQ	—	a	No	End	depression, quality of lives	5
Cheong [31]	2018	Korea	2016.6–2016.8	1	54.26 ± 10.54	168	106	63.10%	——	—	b	Both	Undergoing	number of chemotherapy cycles	6
Huiling Huang [32]	2018	China	2016.12–2017.8	2	45.24 ± 10.05	143	119	83.22%	BFI	low 63 moderate 38 high 18	a	—	Undergoing	marriage state, treatment	5
Jianjian Wei [33]	2018	China	2016.5–2017.5	2	18–60	300	292	97.30%	PFS-R	—	a, b, c, d, e	—	Undergoing	—	7
Jinlian Ma [34]	2018	China	2016.7–2017.6	2	55.12 ± 3.37	200	187	93.50%	PFS	low 62 moderate 93 high 32	a, b, c	—	Undergoing	—	7
Juan Ji [35]	2019	China	2016.1–2016.9	2	52.81 ± 11.02	321	200	62.31%	PFS	low 44 moderate 100 high 56	a	—	Undergoing	—	6
Salome Adam [36]	2019	Netherlands	2008.1–2012.12	3	63.7 ± 8.9	600	252	42.00%	FAS	—	c	No	——	—	5
Beesley [37]	2020	Australia	2012.1–2015.5	3	60 ± 10.4	527	300	57.00%	FACIT-F	—	b	No	Undergoing	—	6
Dongfang Han [38]	2020	China	2019.3–2019.7	2	47.36 ± 7.29	228	228	100.00%	BFI	low 118 moderate 102 high 8	a	No	Undergoing	age, disease stage, treatment	7
François Gernier [39]	2020	French	2007	1	58.1	45	45	100.00%	MFI-20	low 23 moderate 16 high 6	a	No	End	—	7
Qian Wei [40]	2020	China	2019.7–2020.1	2	49.6 ± 3.2	90	66	73.33%	CFS	—	b	No	Undergoing	disease course, payment methods, degree of disease awareness, social support, adjuvant chemotherapy	5

Table 1 (continued)

Authors	Publication Years	Country	Time	Type of study	Age	Sample size	CRF	CRF Prevalence	Diagnostic criteria	Severity of CRF	Type of cancer	Recurrent of cancer	Treatment	Risk factors assessed	NOS/AHRQ
Tingting Zhang [41]	2020	China	2019.2–2019.11	2	49.61 ± 7.98	115	113	98.26%	CFS	—	a	—	Undergoing	—	4
Xuesong Sun [42]	2020	China	2018.1–2018.12	2	56.4 ± 9.7	131	131	100.00%	CFS	—	c	No	Undergoing	—	7
Jing Wang [43]	2021	China	2020.1–2020.6	2	49.36 ± 7.38	210	210	100.00%	BFI	low 108 moderate to high 102	a	—	Undergoing	age, disease stage, disease course	7
Yingying Li [44]	2021	China	2020.3–2020.11	2	49.86 ± 12.97	283	283	100.00%	PFS-R	low 69 moderate 196 high 18	b	—	Undergoing	age, income, sleep disturbance, disease stage, disease course	7
Crystal J. Hare [45]	2022	Canada	2014.9–2016.8	3	58 ± 11.2	202	109	54.00%	FACIT-F	—	b	Both	Undergoing/End	—	4
Ling Huang [46]	2022	China	2019.1–2021.9	1	≥ 18	219	143	65.30%	BFI	—	a	—	Undergoing	age, education, adjuvant chemotherapy, hypoproteinemia, depression	9
Na Huang [47]	2022	China	2017.3–2019.6	2	56.41 ± 2.87	122	122	100.00%	PFS	low 18 moderate 72 high 32	c	No	Undergoing	anxiety, depression, social support, sleep disturbance	6
Yuling Pan [48]	2022	China	2020.5–2021.5	1	61.56 ± 11.27 54.47 ± 9.87	116	116	100.00%	PFS-R	low 67 moderate to high 49	b	—	Undergoing	age, disease stage, disease course, tumor metastasis	7
Xiuping Xiao [49]	2023	China	2020.7–2022.4	1	52.65 ± 5.83	71	71	100.00%	PFS-R	low 37 moderate to high 34	a	No	Undergoing	family function, marriage state, social support, multiple chronic diseases	8

meta-analysis using a random effects model. The combined prevalence of CRF in patients with gynecological malignant tumors was 89% (95%*CI*: 80–95%). The results are depicted in Fig. 2. Five studies reported on chronic CRF, with a heterogeneity analysis (I^2=29.7%, p = 0.223), and a fixed effect model was used in the meta-analysis. The results showed that the pooled prevalence of chronic CRF was 25% (95%*CI*: 22–28%). The results are shown in Fig. 3.

Subgroup analysis

The combined prevalence of CRF in patients with ovarian cancer, cervical cancer, endometrial, and gynecological malignancies (including but not limited to cervical, ovarian, vaginal and other mixed types of gynecological cancers) was 77%, 94%, 90%, and 93%, respectively. The incidence of CRF varied significantly depending on the assessment scale used. Among the scales used over 2 times, the highest incidence of CRF measured by the Revised Piper Fatigue Scale (PFS-R) was 99%, and the lowest incidence of CRF measured by Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) was 49.0%. Furthermore, the estimated incidences of CRF vary across countries. The incidence of CRF in patients with gynecological malignancies in developing countries (95%) is much higher than that in developed countries (71%). Among the countries that have published more than two articles, China had the highest reported

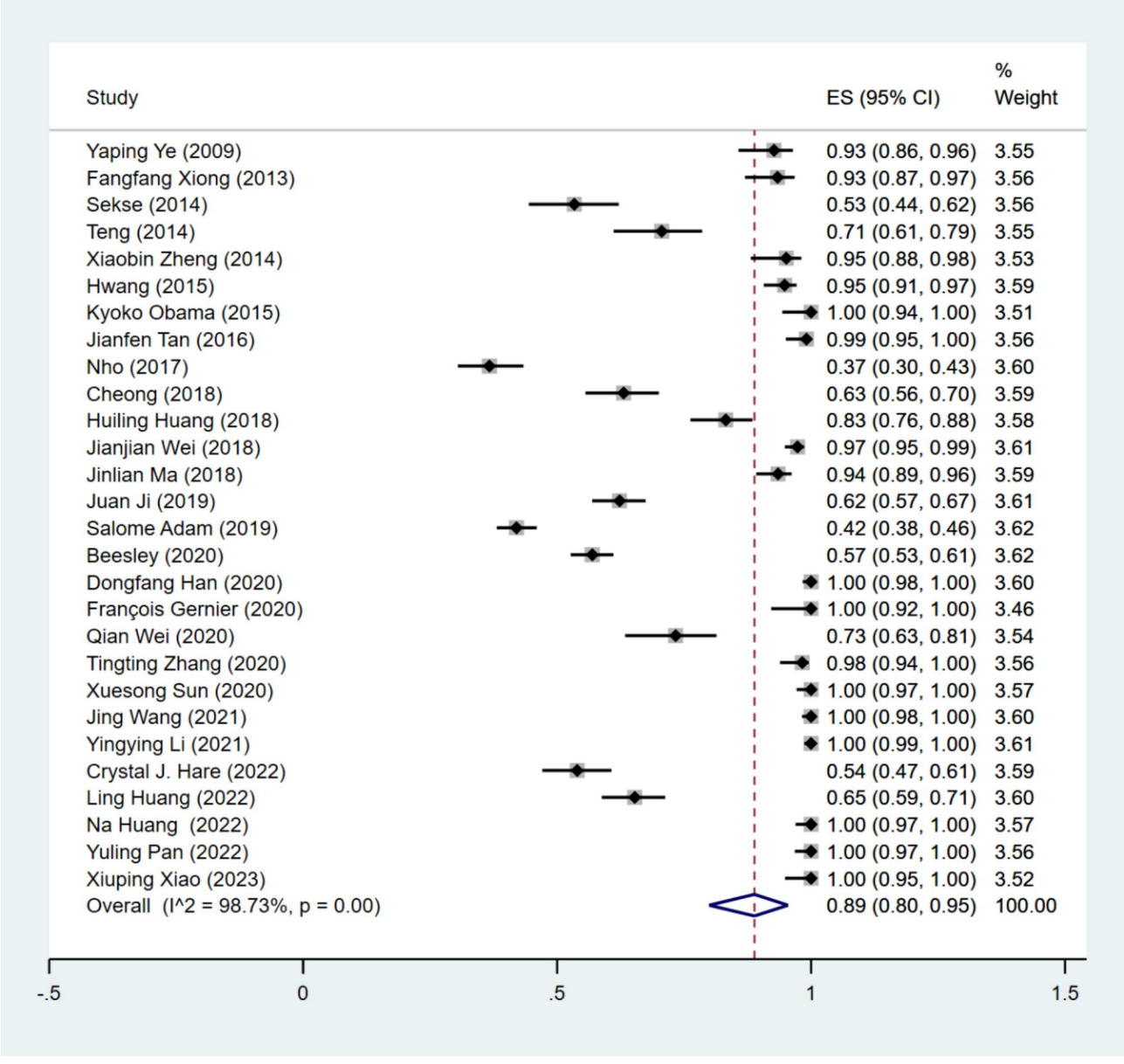

Fig. 2 Prevalence of cancer-related fatigue in patients with gynecological malignant tumors

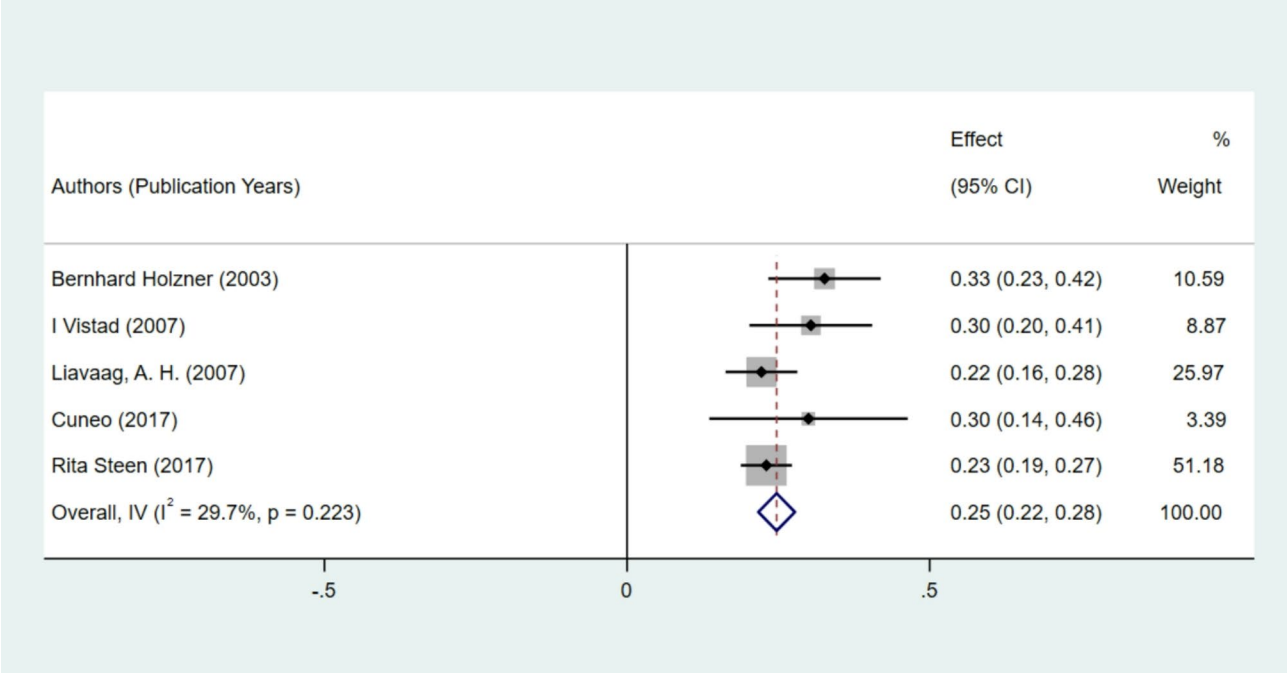

Fig. 3 Prevalence of cancer-related chronic fatigue in patients with gynecological malignant tumors

incidence (95%), followed by Korea (68%) and Canada (60%). The results of this study are presented in Table 2.

Risk factors of CRF in patients with gynecological malignant tumors

This meta-analysis examines five potential risk factors: age, psychological factors, disease stage, social support, and disease course. Of these, age, psychological factors, and disease stage were identified as risk factors for CRF, while social support was identified as a protective factor. The disease course was not statistically significant. The results are shown in Table 3.

Publication bias

The Galbraith plot demonstrated that all studies fell within the 95% confidence interval, indicating the absence of publication bias. Egger's test ($P = 0.972$) confirmed the absence of publication bias. The results are shown in Fig. 4.

Discussion

Assessing the prevalence of fatigue in cancer patients is essential to understand the impact of the symptom and to determine the most effective management strategies. To our knowledge, this study is the first to estimate the overall prevalence and identify the risk factors of CRF in patients with gynecological cancer.

Prevalence of cancer-related fatigue

In the meta-analysis, 33 studies included 5949 patients with gynecological malignancies. The combined prevalences of CRF and chronic CRF were 89% and 25%, respectively.

The results of the types of cancer subgroup showed that except for the gynecological malignant tumor group, the incidence of CRF in patients with cervical cancer was the highest (94.0%), followed by endometrial cancer (90.0%), and ovarian cancer was the lowest (77.0%). This may be related to the main treatment methods used for these three types of malignant tumors. Radiotherapy can directly damage cells, and chemotherapy can cause blood toxicity and gastrointestinal reactions in patients due to cytotoxicity50. Treatment for cervical cancer typically involves a combination of modalities such as surgery, radiotherapy, and chemotherapy. These treatments often lead to side effects, including bone marrow suppression, gastrointestinal disturbances, and immunosuppression, all of which contribute to the worsening of fatigue. Relevant studies38, 51 have shown that patients receiving both radiotherapy and chemotherapy experience the highest degree of CRF, followed by those receiving chemotherapy alone, with patients only receiving radiotherapy showing the lowest degree of CRF. Endometrial cancer, an estrogen-dependent tumor, is primarily diagnosed in postmenopausal women52. During treatment, patients often experience poor tolerability and slow postoperative recovery, which are key factors in the onset of fatigue. Additionally, fluctuations in hormone levels not

Table 2 Subgroup analysis results table

Subgroups		Number of studies	CRF Prevalence	95%CI	I^2	*P*
Types of cancer	Ovarian Cancer	9	77%	57–93%	98.87%	0.000
	Cervical Cancer	8	94%	80–100%	98.37%	0.000
	Endometrial Cancer	3	90%	34–100%	-	-
	Gynecological Cancer	8	93%	85–99%	95.15%	0.000
Scales for CRF	BFI	6	94%	80–100%	97.88%	0.000
	PFS-R	5	99%	96–100%	83.81%	0.000
	PFS	4	91%	69–100%	98.27%	0.000
	CFS	4	96%	84–100%	95.03%	0.000
	FACIT-F	3	49%	37–61%	-	-
	FQ	1	53%	44–62%	-	-
	EORTC QLQ-C30	1	71%	61–79%	-	-
	MSAS	1	95%	91–97%	-	-
	FAS	1	42%	38–46%	-	-
	MFI-20	1	100%	92–100%	-	-
Developed Degree	Developed Country	10	71%	57–84%	98. 04%	0.000
	Developing Country	18	95%	90–99%	97.83%	0.000
Countries	China	18	95%	90–99%	97.28%	0.000
	Korea	3	68%	29–96%	-	-
	Canada	2	60%	54–65%	-	-
	Norway	1	53%	44–62%	-	-
	Japan	1	100%	94–100%	-	-
	Netherlands	1	42%	38–46%	-	-
	Australia	1	57%	53–61%	-	-
	French	1	100%	92–100%		

Table 3 Cancer-related fatigue risk factors

Risk factor	Number of included studies	I^2	OR	95%CI		*p*
Age	5	91.80%	1.43	1.12	1.83	0.005
Psychological Factor	5	93.70%	1.40	1.14	1.72	0.001
Disease Stage	3	50.70%	1.65	1.14	2.40	0.008
Social Support	2	42.20%	0.77	0.67	0.87	0.000
Disease Course	2	81.70%	2.09	0.91	4.80	0.083

only contribute directly to fatigue, but also induce symptoms such as hot flushes and insomnia, further exacerbating feelings of exhaustion. By the time ovarian cancer is diagnosed, many cases are already at an advanced stage, and the standard treatment typically includes oophorectomy before chemotherapy[53]. Following oophorectomy, patients experience dramatic hormonal changes that trigger a range of menopausal symptoms, including hot flushes, mood swings, sleep disturbances, and sexual dysfunction[54, 55]. These symptoms further contribute to fatigue. The incidence of CRF is significant in women with gynecological cancers. It is a major cause of debilitation and reduced quality of life[19]. CRF has long-term negative effects on physical health, psychological well-being, and social functioning[56]. It can also lead to a loss of confidence and hope, significantly reducing quality of life and potentially affecting survival outcomes.

The included studies used 10 different scales, which varied in sensitivity and specificity, potentially leading to discrepancies in the reported incidence of CRF. In the meta-analysis, a subgroup analysis revealed significant differences in the incidence of CRF when measured by different scales. The highest incidence was reported using the PFS-R scale (99.0%), followed by the CFS, Brief Fatigue Inventory (BFI), and PFS. The incidence of CRF in gynecological malignant tumors measured using the above four scales was more than 90%. In contrast, the incidence of CRF measured by the FACIT-F scale was the lowest (49.0%). As seen in Table 1, nine articles reported a 100% incidence of CRF in gynecological malignancies patients. Among them, five researchers, Dongfang Han (BFI), Kyoko Obama (BFI), François Gernier (Multidimensional Fatigue Inventory-20, MFI-20), Yuling Pan (PFS-R), and Xiuping Xiao (PFS-R) recorded different scales ≤ 3 as low fatigue, while the original scale was 0 as no fatigue, and 1–3 as low fatigue. In this case, the CRF measured using each scale was higher than the actual level. To address these discrepancies, future research

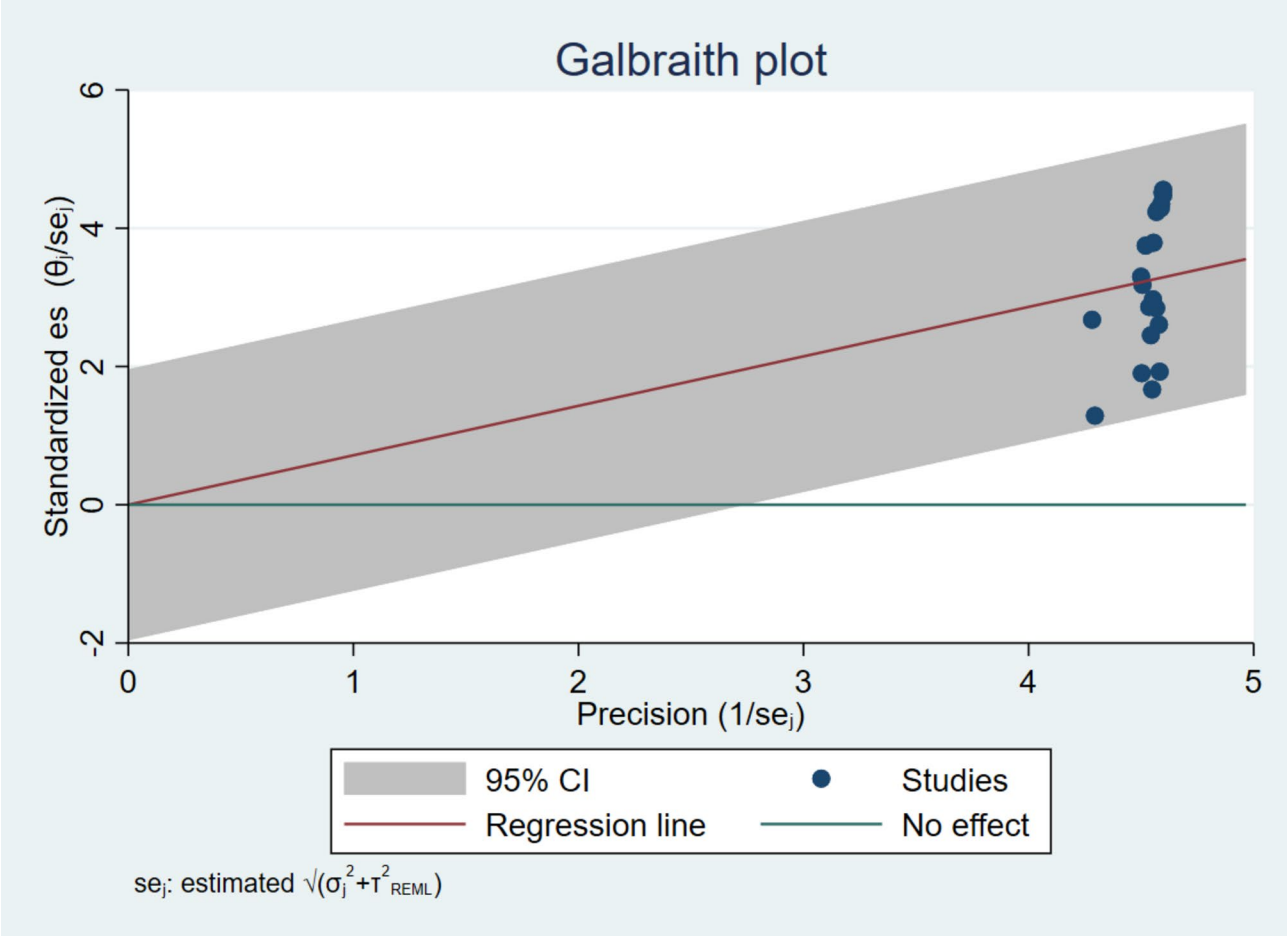

Fig. 4 Galbraith plot for assessing publication biases

should consider developing a standardized scale to measure CRF in patients with gynecological malignancies, reducing the variability caused by different scales and facilitating more accurate clinical assessments.

The results from the country development level subgroup analysis revealed that the incidence of CRF was significantly lower in developed countries (71.0%) compared to developing countries (95.0%). The national subgroup reported that the high incidence in Japan and France was that the researchers directly identified patients with ≤3 points as low CRF, and there was only one literature. Regardless of the above two countries, among the remaining countries, Chinese patients with gynecologically malignancies had the highest CRF rate of 95%, which was notably higher than that in other countries. China, being the only developing country included in the studies, had a much higher incidence rate than other nations. In developed countries, including South Korea, Canada, Australia, Norway, and the Netherlands, the incidence rates of CRF did not differ significantly. These studies indicate that the incidence of CRF is closely linked to a country's level of development. Developed countries have higher economic and medical levels, more advanced cancer diagnoses and treatments, and more mature coping mechanisms and policies. Moreover, this may be related to the awareness of CRF among healthcare professionals and patients[57]. In developed countries, higher levels of education contribute to increased health awareness, regular physical check-ups and screening for cancer, which enables early diagnosis and treatment, thereby promoting better follow-up care. Developing countries need to enhance medical technologies, introduce corresponding guidelines and policies, and improve public health awareness, and respond better to CRF.

Risk factors for cancer-related fatigue

The review found that disease stage, psychological factors, and age were strongly associated with an increased risk of developing CRF, while social support was identified as a protective factor.

Disease stage

The meta-analysis reported that the disease stage was associated with increased CRF. The effect of disease stage on women receiving chemotherapy for gynecological malignancies is most pronounced in terms of treatment regimens and chemotherapy variations[36]. Patients in advanced stages typically receive more complex chemotherapy regimens with multiple drug combinations, which increases the risk of experiencing chemotherapy-related side effects[58].

Psychological factors

This meta-analysis demonstrates that psychological factors significantly contribute to the increased risk of CRF. The results regarding the elevated incidence of CRF patients with cervical cancer receiving radiation therapy are corroborated by earlier research[20]. Patients may experience physical and psychological discomfort because of the pathological changes caused by malignant gynecological tumors. In addition, fear of cancer, possible hormonal changes, and changes in sexual health following surgery can cause psychological reactions such as anxiety and distress. Prolonged exposure to detrimental psychological elements can also affect neurological, endocrine, and other regulatory systems, leading to weariness and lowered immunity in patients[59].

Age

Age is a risk factor for CRF in patients with gynecological malignancies. Older patients are more likely to experience fatigue symptoms, reduced physical function, and diminished regulatory abilities, as well as lower levels of deliberate physical activity[43, 48]. Furthermore, the integrity of mitochondrial structure and function is essential for energy production, and chemotherapy drugs can reduce physiological energy production in elderly patients. Chemotherapy drugs may disrupt mitochondrial function, interfering with energy metabolism, and increasing the risk of fatigue. Aging can also affect the immune system, resulting in neuroendocrine disorders, which can cause a physiological decline in multiple organ systems. These factors can exacerbate fatigue in elderly patients[60]. To relieve fatigue, healthcare professionals should prioritize the needs of elderly patients and offer individualized comfort care.

Social support

Higher-income individuals often have greater social responsibilities and heavier workloads, which may affect the level of social support they receive. Prolonged chemotherapy-related hospital stays limit patients' daily activities and interfere with their ability to fulfill social obligations, which increases CRF[40].

Disease course

The meta-analysis results did not identify disease course as a significant risk factor for CRF. Wei et al.[40] concluded that as tumors grow and the number of chemotherapy treatments increase, the immune system and cardiopulmonary function of the body deteriorate, making patients more physically exhausted. This finding contrasts with the study's results, possibly due to the limited number of studies included. Further research is needed to clarify this relationship.

Our study has several notable limitations. Firstly, the restriction to literature published in English or Chinese may have introduced publication bias. Secondly, due to insufficient data from the included studies, we could not perform a subgroup analysis of the severity of cancer-related fatigue, so we could not determine the prevalence of different degrees of cancer-related fatigue. In addition, fatigue, a multifaceted construct, was assessed as a generic measure in most studies, limiting our ability to comment on specific dimensions of fatigue. The reliance on patient-reported outcomes may also introduce reporting bias, particularly in studies conducted in specific geographical or cultural contexts.

Conclusions

This study provides insight into the high prevalence of CRF in women with gynecological malignancies, with an overall prevalence of 89%. Age, psychological factors, and disease stage are risk factors for CRF, while social support is a protective factor. Understanding these risk factors provides a sound theoretical framework for nurses and healthcare professionals. CRF screening and management strategies should prioritize addressing these risk factors to facilitate early identification and intervention. However, the variability in CRF measurement methods, due to the use of different assessment tools, limits the ability to compare findings across studies. Future research should focus on developing standardized assessment tools, exploring the long-term trajectory of CRF in this population, and developing appropriate interventions to alleviate CRF symptoms and improve patients' quality of life.

Abbreviations

CRF	Cancer-related fatigue
NOS scale	Newcastle-ottawa quality assessment scale
AHRQ	Agency for healthcare research and quality
CI	Confidence interval
OR	Odds ratio
NCCN	National comprehensive cancer network
MOOSE	Meta-analysis of observational studies in epidemiology
FEM	Fixed effect model
REM	Random-effects model
FACIT-F	Functional assessment of chronic illness therapy-fatigue
FIGO	International federation of gynecology and obstetrics
PFS-R	The revised piper fatigue scale
BFI	Brief fatigue inventory
MFI-20	Multidimensional fatigue inventory-20

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Author contributions
Zhao participated in drafting the manuscript, research conception and design, data analysis and interpretation, literature screening, literature quality assessment. Zhan participated in drafting the manuscript, research conception and design, data analysis and interpretation, literature screening, literature quality assessment. Pang participated in critical revision of the manuscript for important intellectual content. Shujie Shen contributed to the literature quality assessment, literature screening and data extraction. Huang participated in data extraction and interpretation. Zhang participated in data extraction and interpretation. Siqi Wei participated in drafting the article, supervised the design and critically revised the paper. All authors read and approved the final manuscript.

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Data availability
Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate
Due to the publicly available nature of all data used in this study, no ethical approval was required.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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