Global and regional geographical prevalence of depression in gastric cancer: a systematic review and meta-analysis

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ABSTRACT

Background Substantial uncertainty exists about the prevalence of depression in patients with gastric cancer. We aimed to summarise the global and regional pooled prevalence of depression among patients with gastric cancer.

Method Up to February 2020, we searched PubMed/MEDLINE, Embase, Scopus, Web of science (ISI) and PsychINFO to identify published studies on the prevalence of depression among patients with gastric cancer. The study selection procedure was in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. We estimated the prevalence of depression in gastric cancer patients using a random-effect pooled estimate analysis approach with subgroup analysis based on WHO regions, and methods of depression measurement.

Results Totally, we retrieved 3781 studies from the previously mentioned databases, of which 18 (12 cross-sectional and 6 cohort studies in design) met the eligibility criteria, which were published from 2001 to 2017 in different regions. The total sample size of the included studied contained 4709 patients with gastric cancer, of which 1885 cases were diagnosed with depression. The pooled prevalence of depression among gastric cancer patients was 37%(95% CI: 26% to 48%). Subgroup analysis showed that the highest prevalence of depression was in Eastern Mediterranean (pooled prevalence=42%; 95% CI: 18% to 65%) followed by the Western Pacific region (pooled prevalence=40%;95% CI: 26% to 54%). The results indicated a significant heterogeneity (I^2=98.8%,P<0.05).

Conclusion Our findings indicated that depression is high among gastric cancer patients. The findings suggest health authorities to provide specially designed social and psychological supportive care services, including screening for depression, among such patients.

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INTRODUCTION

Gastric cancer is a common malignancy worldwide with relatively high case fatality rate, especially among men at older ages.[1] For example, based on a report from GLOBOCAN 2018, gastric cancer is the most frequent malignancy and the third leading cause of cancer-related death with an estimated 783 000 deaths in 2018.[2] As a result, the disease has become an important public health challenge. Recently, for most cancers including gastric cancer, applying multidisciplinary approaches to patients' care is becoming more common. In that regard, the patients are not only provided with diagnosis and treatment services, but also have access to social and psychological supports as an essential part of the patients' care.[3] The increase in the patients' survival is accompanied by a longer exposure to negative psychological pressure on patients and caregivers. When diagnosed with gastric cancer, patients are exposed to many psychological challenges, such as anxiety, depression, pain and fatigue.[3] That is why, focus has turned towards enhancing patients' quality of life (QoL) as they mostly experience psychological problems such as anxiety and depression.[4] It has been suggested that among cancer patients, depression is one of the most important psychological problems, as the condition decreases the patients' QoL and increases healthcare expenditures.[5]

It has been suggested that patients with cancer when comorbid with depression have more suicidal thoughts, anxiety, distress and fatigue.[5] Despite adverse effects of depression on patients' prognosis and QoL, the condition among cancer patients is inadequately monitored.

The few studies on depression among cancer patients have mainly focused on the prevalence and risk factors or management of depression among cancer patients in general with little attention to gastric cancer. As a result, the available evidence provides minimal information on depression among the gastric cancer patients.[6] In addition to poor prognosis and survival when compared with cancers of several other organs, gastrointestinal malignancies, especially gastric cancer, cause disturbing and disabling symptoms such as persistent pain, nausea, vomiting, diarrhoea and malnutrition.[7 8] As a result, patients with gastric cancer are more prone to malnutrition, lower body mass index, less physical activity and social relationship.[9] These mentioned disabling symptoms have negative impacts on patient's QoL and trigger depression.[10] Besides, to achieve curative resection of tumours of the stomach, gastrectomy, a profoundly invasive treatment strategy is considered as the mainstay of treatment choice. The procedure has very deep and detrimental effects on QoL and mental status of the patients.[11] As an unavoidable side effect of the treatment of gastric cancer, total gastrectomy has also detrimental effects on postoperative nutritional status of the patients.[8] Previous studies have found that patients undergoing total gastrectomy will lose 7%–15% of their body weight, usually within the first year of surgery, and will not return to the normal weight.[12]

From clinical and psychological points of view, due to disabling symptoms and the side effects of the invasive treatment of the disease, profound nutritional, social and mental problems in gastric cancer patients are highly common.

Understanding the clinical symptoms of depression and having a precise estimate on the prevalence of the condition among gastric cancer patients in different communities may led to reconsideration of patient's medical and social cares via identifying high-risk populations. It is believed that depression has a negative impact on the prognosis of the disease and poor survival among the patients.[13] The presence of psychological distress is a risk factor for treatment non-compliance and mortality. As a result, providing estimates on depression among gastric cancer patients can help to emphasise the need for screening depression and other mental disorders among gastric cancer patients.

To the best of our knowledge, no pooled estimate on the prevalence of depression among patients with gastric cancer is published so far. The aim of this study was to provide valid estimates on the prevalence of depression in patients with gastric cancer in different regions by conducting a meta-analysis. Robust findings on this topic reveal the urgent need for well-defined social and psychological supportive care programmes for gastric cancer survivors.

MATERIAL AND METHOD

Protocol and registration

The present systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[14]

The aim of the present study was to determine the prevalence of depression among gastric cancer patients. The protocol of this study was approved and registered in the international prospective register of systematic reviews (PROSPERO registration code: CRD42020139836).

Search strategy and study selection criteria

To find relevant studies on the prevalence of depression in patients with gastric cancer, a comprehensive search was conducted in PubMed/MEDLINE, Web of Science (ISI), Embase, Scopus, Google Scholar and PsychINFO up to February 2020 without language restriction. To do this, three sets of related medical subject headings (MeSH) MeSH and non-MeSH terms in titles, abstracts or keywords were used: (1) 'gastric cancer' OR 'gastric carcinoma', (2) 'depression' OR 'depressive disorder' and (3) 'prevalence' OR 'occurrence'.

The search strategy was conducted with (AND, OR) operator. Two authors independently reviewed the articles (MK and HA) and discrepancies, if any, and resolved them by discussing with the third author (MD). The reference lists of related articles were also manually reviewed for other possibly relevant articles that were not found through the electronic search strategy.

Target population of the review

In line with the previous research, and to avoid biases related to the survival of cancer, we included studies on newly diagnosed patients with gastric cancer in any stage of disease (at the time of diagnosis) up to at least 2 years after diagnosis,[15] on the other hand, studies that performed on patients who had been newly diagnosed with stages I–IV stomach cancer were eligible to be included in the analysis.

Inclusion and exclusion criteria

To ensure that estimates could be compared across studies, depression was defined using standard diagnostic criteria, such as major depression from the Diagnostic and Statistical Manual of Mental Disorders (DSM) or depressive episode from the International Classification of Diseases.[16 17] We excluded studies that reported pooled means rather than proportions or raw numbers,[18] as well as studies that used indirect estimates of population depression or anxiety and studies reporting rates before diagnosis of cancer. We also

excluded duplicate publications, that is, two or more studies using the same sample.

Prospective cohorts and cross-sectional studies that investigated the prevalence of depression in gastric cancer patients were included. Also, encompassing both studies on newly diagnosed gastric cancer cases (incident cases) and prevalent cases of gastric cancer were included. For cohort studies, we reported depression prevalence at the first time point only. If studies assessed both current and previous depression, we reported current depression prevalence. If studies compared the prevalence of depression in patients with cancer with that in a healthy population, we used only the prevalence in the sample of patients.[15]

Prospective cohort studies and cross-sectional studies that did not report the prevalence of depression among patients, reported the prevalence of depression among other comorbidities of gastric cancer patients, reported the prevalence of depression among patients with other cancers (not relevant or modified data), review studies, editorials, letters to the editors, commentaries, expert opinions, case series, case studies, brief reports and book chapters or studies on gastric cancer recurrence were not included in our systematic review and meta-analysis.

Data extraction

Two independent authors (HAG and MK) extracted the following characteristics from the included studies: author's name, year of publication, study country, sample size (number of gastric cancer cases), the number of depressed patients, the prevalence of depression, study design and depression assessment tools. Any disagreement between the two reviewers was resolved through discussion with the third author (MD). Up to two attempts to contact the authors (or publishers) were made at 1 week intervals if the full text of any article was unavailable or if key information was missing from the reported data. Classification of regions was done according to the WHO region classification, including African, European, Eastern Mediterranean (EMRO), South-East Asia, Western Pacific region and region of Americas.

Quality assessment

An standard eight-item checklist for the critical appraisal of studies of the prevalence/incidence of health problems[19] was used to examine the quality of the included studies by two independent investigators (MK and HAG). This tool defines eight criteria including: (1) whether a random sample or whole
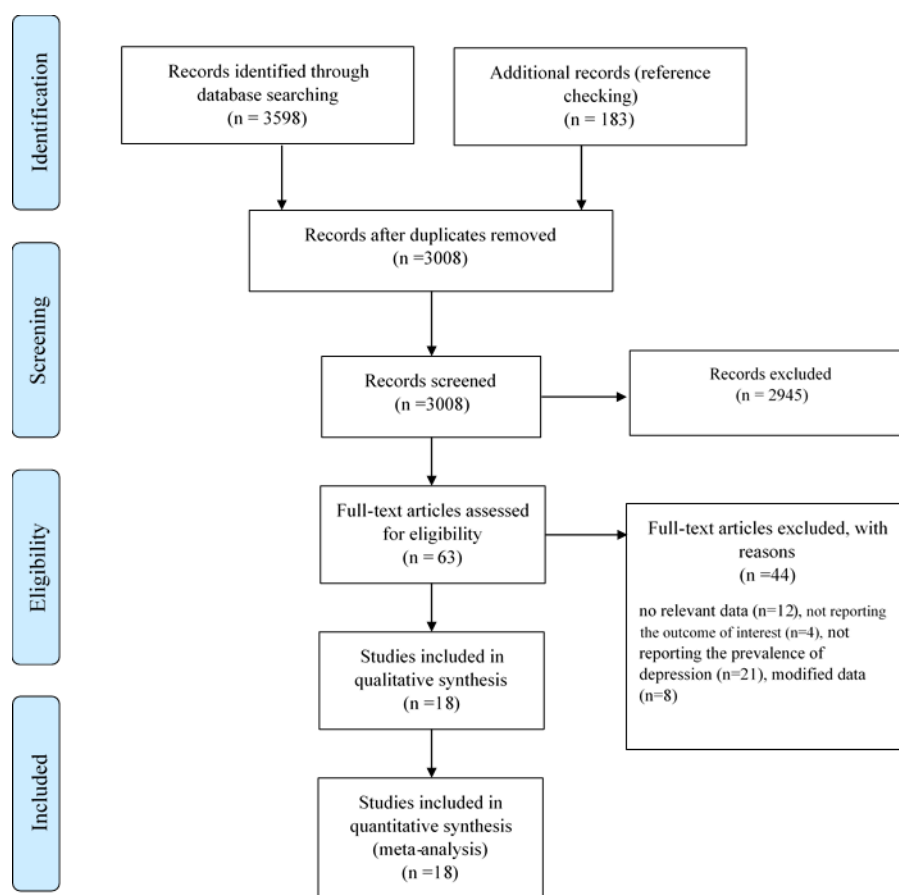
Figure 1 PRISMA flow diagram of studies included and excluded at each stage of screening. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

population was used, (2) if an unbiased sampling frame was used, (3) adequacy of the sample size, (4) the use of standard measures, (5) whether outcome measurements were made by unbiased assessors, (6) adequacy of the response rate, (7) CIs and subgroup analyses and (8) whether the study subjects were described. Each item was scored as 1 if a study met the criterion, and the scores were summed up. The range of the total score was from 0 (lowest possible quality) to 8 (highest possible quality). The studies quality is defined as high quality (score ≥7), medium quality (score between 4 and 6) or low quality (score <4). The quality assessment results were also checked by the third investigator (MD).

Statistical analysis

A random-effect model (REM) was use to investigate the pooled prevalence of depression with 95% CIs among gastric cancer patients. Subgroup analyses were performed based on the study quality and studies design. To evaluate the heterogeneity between the selected studies, I^2 test was used.[20] A value of 0% indicates no observed heterogeneity, and larger values show higher heterogeneity, with 0%–25% as low, 25%–50% as moderate and 50%–75% as high heterogeneity.

To find the heterogeneity of sources, meta-regression was used based on the design and quality of studies, sample size, country, the tool used to assess depression and publication year. Publication bias was assessed with Begg–Mazumdar and Egger tests. The Egger results and funnel plot[21] were used to show the severity of publication bias. Additionally, a sensitivity analysis was conducted to assess the stability of the results. The p values above 0.05 indicate that the total variance is due to variance within studies and not to variance between studies. Stata V.14 (Stata Corp.) was used for the statistical analysis.

Table 1 The main characteristics of the studies included in the present systematic review and meta-analysis

| Author | Country | WHO Region | Instrument | Study design | Gender% | | Depression Prevalence % | 95% CI | | Quality Assessment |
					Female	Male		lower	upper	
Nordin et al[28]	Sweden	European	HADS	Prospective cohort	ND	ND	22.00	12.00	38.00	Moderate
Brintzenhofe-Szoc et al[37]	USA	Americas	BSI	Cross-sectional	ND	ND	4.00	2.00	10.00	High
Wei et al[24]	China	Western pacific	HAMD	Prospective cohort	44.33	55.67	59.00	50.00	68.00	low
Palgi et al[27]	Israel	Eastern Mediterranean	SCES	Cross-sectional	43.10	56.90	56.00	47.00	65.00	Low
Tian et al[25]	China	western pacific	HADS	Cross-sectional	41.75	58.25	68.00	65.00	70.00	Moderate
Yu et al[13]	China	Western pacific	DSI	Prospective cohort	40.66	59.33	31.00	26.00	36.00	Low
Wi et al[23]	South Korea	Western pacific	HADS	Cross-sectional	23.33	76.66	24.00	17.00	33.00	High
Kim[31]	South Korea	Western pacific	CES -D5	Cross-sectional	27.18	72.82	35.00	26.00	45.00	High
Hong et al[33]	China	Western pacific	HADS	Cross-sectional	ND	ND	63.00	57.00	70.00	Moderate
Han et al[34]	South Korea	Western pacific	BDI	Cross-sectional	27.10	72.89	44.00	39.00	49.00	Moderate
Mashhadi et al[30]	Iran	Eastern Mediterranean	BDI	Prospective cohort	ND	ND	22.00	15.00	31.00	Moderate
Hwang et al[32]	South Korea	Western pacific	BDI	Cross-sectional	27.28	72.72	39.00	34.00	44.00	High
Nikbakhsh et al[29]	Iran	Eastern Mediterranean	HADS	Cross-sectional	ND	ND	47.00	33.00	63.00	Moderate
Duc et al[36]	France	European	GDS-15	Prospective cohort	ND	ND	32.00	19.00	49.00	Moderate
Goo et al[35]	South Korea	western pacific	PHQ-2	Cross-sectional	ND	ND	24.00	20.00	28.00	Moderate
Zhang et al[22]	China	Western pacific	HADS	Prospective cohort	46.50	53.50	12.00	10.00	14.00	Moderate
Kim et al[3]	South Korea	Western pacific	HADS	Cross-sectional	72.92	27.08	40.00	34.00	47.00	Low
Pan et al[26]	China	Western pacific	DSM-IV	Cross-sectional	66.66	33.33	42.00	32.00	52.00	Low

BSI, Brief Symptom Inventory; CES-D, Center for Epidemiological Studies Depression; DSI, Depression Status Inventory; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, 4th Ed; EMRO, Eastern Mediterranean; HADS, Hospital Anxiety and Depression Scale; HADS, Hospital Anxiety and Depression Scale; HAMD, Hamilton Depression Rating Scale; ND, no data; PHQ-2, Patient Health Questioner 2; SCES, Short Center for Epidemiological Studies Depression Scale.

Table 2 Subgroup analysis and heterogeneity assessment among the included studies

| Variable		Sample size	Pooled prevalence%	95% CI	I^2
WHO Regions	Western Pacific	4282	40	(26.00–54.00)	
	European	70	27	(16.00–37.00)	99.04
	Eastern Mediterranean	263	42	(18.00–65.00)	–
	Americas	94	4	(2.00–10.00)	–
Study design	Cross-sectional	3303	41	(27.00–54.00)	98.67
	Cohort	1406	30	(16.00–44.00)	96.30
Quality of study	High	680	26	(6.00–45.00)	97.61
	Moderate	3187	37	(18.00–56.00)	99.28
	Low	842	45	(35.00–56.00)	90.10
Depression measurement tools	HADS	2581	40	(15.00–64.00)	99.44
	BDI	865	36	(25.00–46.00)	–
	Other	1263	35	(22.00–48.00)	99.81

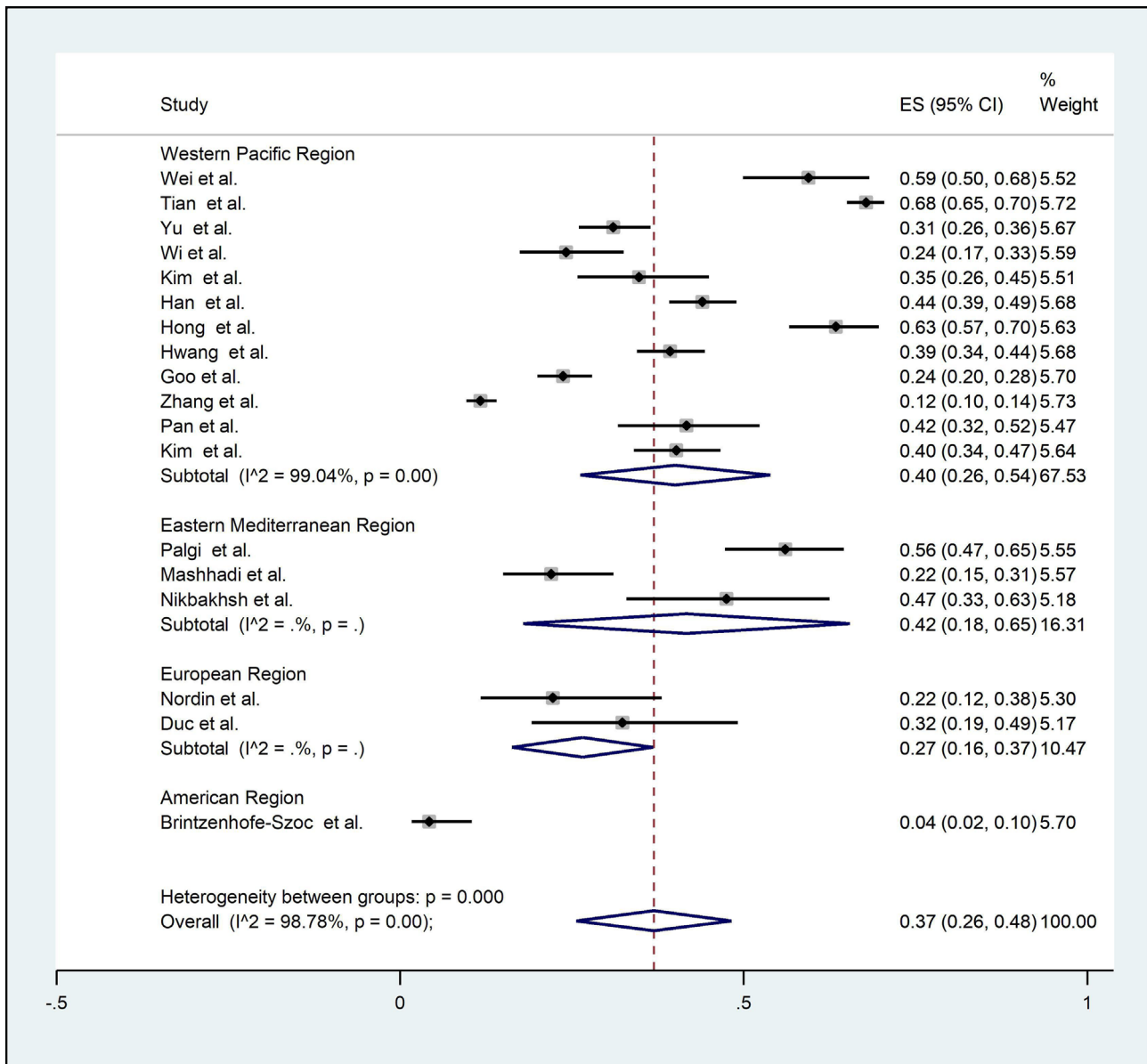HADS, Hospital Anxiety and Depression Scale.

RESULTS
Included studies
As described in figure 1, according to the PRISMA flow chart, totally 3781 studies were extracted by electronic and manual searching. Of these, 773 were excluded because of duplication. From the remaining 3008 articles, 2945 were excluded after titles and abstracts were assessed. Therefore, 63 studies remained to be carefully checked by examining the full texts. Of which 44 articles were excluded for the following reasons: no relevant data (n=12), did not report the outcome of interest (n=4), did not report the prevalence of depression (n=21) and using modified data (n=8). Finally, 18 studies[3] [13] [22–37] met our eligibility criteria and they were included in the systematic review and

meta-analysis. The main characteristics of included studies are described in table 1 (additional characteristics of the studies included in the present systematic review and meta-analysis are provided in online supplementary table 1). The 18 relevant articles were published from 2001 to 2017 and consisted 4709 gastric cancer patients, among which 1885 were diagnosed with depression. Most studies were performed in the South Korea (n=6)[3] [23] [31] [32] [34] [35] and China (n=6).[13] [22] [24–26] [33] Regarding the study regions, most studies were conducted in Western Pacific (n=12)[3] [13] [22–26] [31–35] and EMRO (n=3)[27] [29] [30] region. Of the included studies, 12 were cross-sectional[3] [23] [25–27] [29] [31–35] [37] and 6 were cohort[13] [22] [24] [28] [30] [36] in design. Totally, in the included
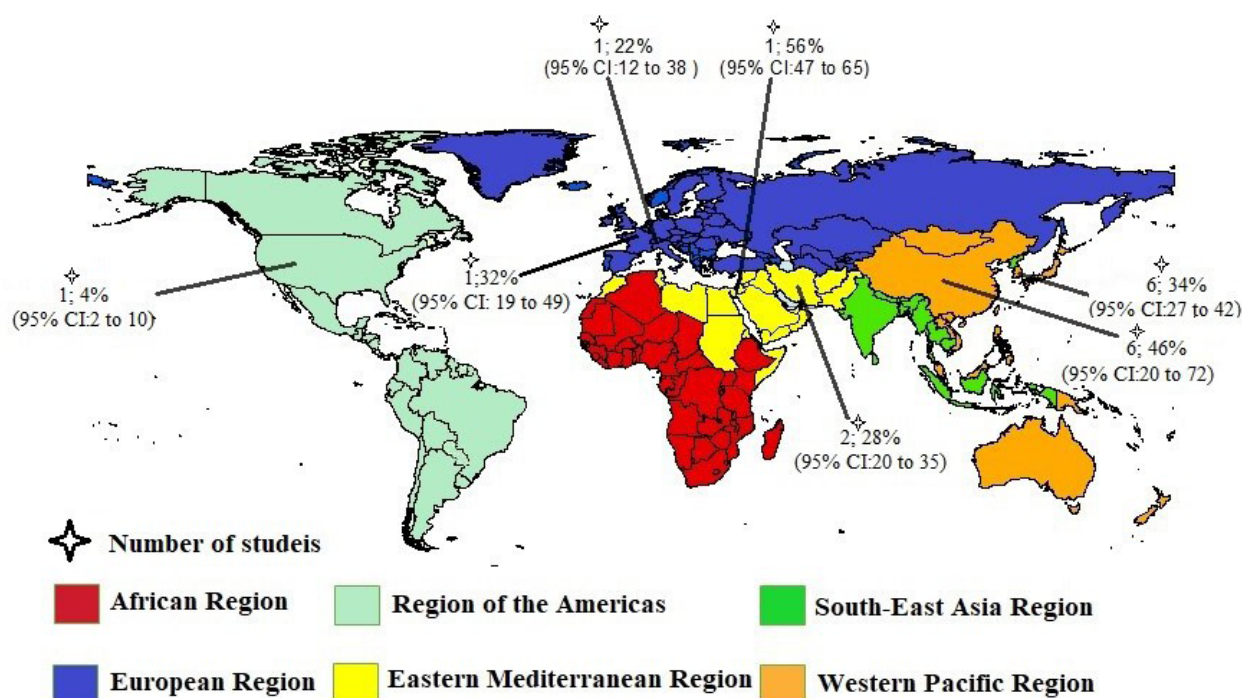
Figure 2 Number of studies and the pooled prevalence of depression (95% CI) according to WHO regions.

Figure 3 Forest plot of the included studies by WHO regions subgroup.

studies, 10 various tools were used to diagnose depression among gastric cancer patients. Eight studies used the Hospital Anxiety and Depression Scale (HADS),[3 22–25 28 29 33] three studies used Beck[30 32 34] questionnaire and other studies used different questionnaires such as Depression Status Inventory, HAMD, DSM-V, Center for Epidemiological Studies for Depression (CES-D), Brief Symptom Inventory (BSI), Patient Health Questioner 2 (PHQ2).[13 26 27 31 35–37]

Methodological quality assessment
According to critical appraisal of systematic reviews for prevalence/incidence studies,[19] 4 studies were assigned as 'high quality',[23 31 32 37] 9 studies as 'moderate quality',[22 25 28–30 33–36] and the rest 5 studies were grouped as 'low quality'.[3 13 24 26 27] The results

of methodological quality assessment are shown in online supplementary table 2.

Pooled prevalence of depression
The highest prevalence of depression among patients with gastric cancer was 68% (95% CI: 65% to 71%) which was reported by Tian *et al*[25] in China. The lowest rate was 4.0% (95% CI: 2% to 10%)) which was reported by Brintzenhofe-Szoc *et al*[37] in the USA. Based on REM, the pooled prevalence of depression was 37% (95 % CI: 26% to 48%). The included studies demonstrated a high heterogeneity ($I^2 = 98.78$ %, p=0<0.001).

Meta-regression and subgroup analysis results
A subgroup analysis was performed by study design, method of depression measurement, year of

Table 3 Heterogeneity among the selected studies based on meta-regression

	Beta	CI95% Lower	Upper	P-value
Quality of study	−0.09	−0.21	0.02	0.10
Design	−0.10	−0.29	0.08	0.24
WHO Regions	−0.04	−0.17	0.08	0.49
Year	0.002	−0.02	0.02	0.82
Sample size	−0.0001	−0.0002	0.0004	0.50
Tools	−0.02	−0.12	0.07	0.64
Country	0.002	−0.06	0.06	0.92

Table 4 Sensitivity analysis of the included studies in the meta-analysis

95% CI Upper	Lower	Estimate%	Study omitted
49.43	26.10	37.77	Nordin et al[28]
48.83	25.53	37.18	Duc et al[36]
47.23	29.99	35.61	Wei et al[24]
48.80	25.31	37.05	Kim et al[31]
48.61	24.86	36.74	Kim et al[3]
48.49	24.52	36.51	Han et al[34]
43.71	26.25	34.98	Tian et al[25]
49.35	27.58	38.47	Zhang et al[22]
46.86	23.83	35.35	Hong et al[33]
48.37	24.94	36.66	Pan et al[26]
49.94	25.52	37.73	Goo et al[35]
48.83	24.75	36.79	Hwang et al[32]
49.48	25.89	37.68	Wi et al[23]
49.31	25.26	37.29	Yu et al[13]
47.46	24.15	35.80	Palgi et al[27]
49.58	26.04	37.81	Mashhadi et al[30]
47.99	24.71	36.35	Nikbakhsh et al[29]
50.27	27.53	38.90	Brintzenhofe-Szoc et al[37]

publication, country, sample size, WHO regions and the quality of studies (table 2). Subgroup analysis by WHO regions showed that the lowest prevalence of depression was in the Americas 4% (95%CI: 2% to 10%) and the highest rate was in the Eastern Mediterranean 42 % (95% CI: 18% to 65%) (figure 2). Also, figure 3 shows the results of the included studies as forest plot by WHO regions subgroup. The prevalence of depression in Western Pacific, Europe, EMRO and America suggested that depression prevalence is the highest in Eastern Mediterranean and lowest in America 42% (95% CI: 18% to 65%) and 4% (95% CI: 2%to 10%) respectively (P=0.49).

Prevalence rates of depression by HADS, Beck and other instruments were 40% (95% CI: 15% to 64%), 36% (95% CI: 25% to 46%) and 35% (95% CI: 22% to 48 %)respectively) (P=0.64) (online supplementary figure 1).

The prevalence rate of depression by the studies' quality are provided in online supplementary figure 2. Accordingly, prevalence in low-quality, moderate-quality and high-quality studies were 45%(95% CI: 35% to 56%), 37% (95% CI: 18% to 56%) and 26 % (95 % CI: 6% to 45%),respectively (P=0.10).

Regarding the study design, the prevalence of depression was higher when the study used cross-sectional design 41%(95% CI: 27% to 54%) compared with the

cohort studies 30% (95% CI: 16% to 44%) (P=0.24). Moreover, the results were not heterogenic for all the previously mentioned results of subgroup analyses (table 2).

We performed univariate meta-regression analyses to identify possible variables associated with the rate of prevalence. The result of the meta-regression exploring the association between prevalence of depression and year of study is shown in table 3. Accordingly, the prevalence of depression shows a non-significant upward trend during the recent years (β= 0.002, p= 0.82).

Publication bias and sensitivity analysis
We used funnel plot and Egger test to assess publication bias. As presented in figure 4, a significant publication bias was found (t= 2.41, p-value=0.02). Also, the results of sensitivity analysis shown in table 4 suggest consistency with the result of pooled estimate of the prevalence.

DISCUSSION
The present systematic review and meta-analysis, which contained 18 observational studies and 4709 gastric cancer patients, provided a relatively high prevalence of depression among gastric cancer patients (37%). Therefore, the preventive measures to improve the outcome of disease treatment and QoL of the gastric cancer patients according to the recommended guidelines are highly suggested.[38 39] The development of depression among cancer patients has been linked with a higher risk of morbidity and mortality. Our findings are helpful in raising the awareness of the importance of depression in cancer patients as
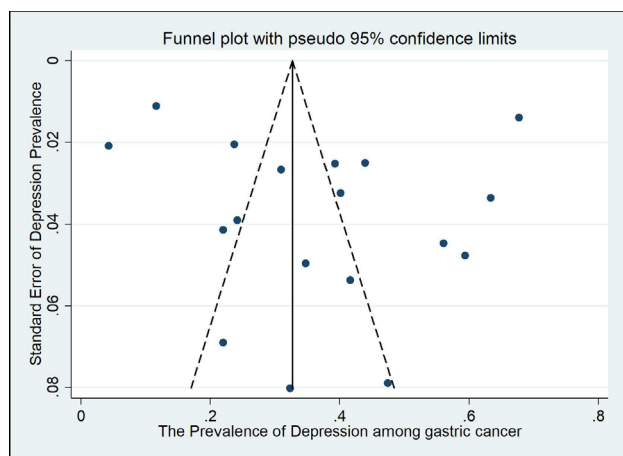
Figure 4 Funnel plot of studies included in the meta-analysis.

depression has adverse effects on disease progression and treatment process among gastric cancer patients.[3] For example, a previous study showed that adherence to treatment was less among those with depression and this association does not significantly differ by patient's age or length of follow-up period.[40] Another study provided a mechanism by which depression may increase mortality among cancer patients.[3] It is also suggested that early identification and management of even mild depression in cancer patients may contribute to better adherence to treatment and a higher QoL.[40] Similarly, it is suggested that prevalence of depression is highest during treatment of cancer, and among gastric cancer surgical resection, which is an invasive treatment strategy, is the mainstay of treatment and total gastrectomy is mandatory to achieve curative resection of tumours of the stomach. As a result, detrimental effects of total gastrectomy on emotional status and depression are inevitable among these patients. This finding indicates that when a person is diagnosed with gastric cancer, more attention on diagnosis and treatment of depression symptoms is required.[41]

In addition, the improvement in survival of cancer patients also comes with a higher prevalence of depression. The reports suggested that around 340 000 individuals in the UK and 2 million in the USA are living with both major depression and cancer.[41] However, most people with depression have no access to social, interpersonal or therapeutic needs.[38] At least half of those with cancer who have moderate-to-severe depression are willing to be provided with psychological help.[42] Knowing that 40% of patients with depression have suicidal thoughts gives to the problem another important aspect which needs serious attention.[41]

A previous meta-analysis suggested that prevalence of depression among cancer patients ranged from 3% in lung cancer patients to 31% in patients with cancer of the digestive tract.[41] Similarly, the results of another systematic review suggested that the prevalence of depression varies among patients with different cancers. As such, the prevalence of depression among patients was about 14.7% among those with prostate cancer,[43] 25% among those with ovarian cancer[44] and 32.2% among those with breast cancer.[45] The observed differences in the prevalence of depression among patients with different types of cancer are likely due to different factors including sex, marital status, psychiatric comorbidity, disease stage, alcohol drinking, treatment methods and annual income.[3] [10] The evidence also suggested that social and family support has a moderating role among patients diagnosed with cancer.[46] We found a higher prevalence rate of depression among gastric patients in comparison with the earlier mentioned figures. To justify the observed prevalence, it is suggested that, compared with other cancers, disabling symptoms such as persistent pain, nausea and vomiting and diarrhoea occurred more frequently in patients with gastric cancer, which results

in significant body weight loss during the first year of diagnosis.[7 8] Besides, total gastrectomy has detrimental effects on postoperative nutritional status, emotional status, depression and QoL, but it is often unavoidable in the treatment of gastric cancer.[8] Also, malnutrition has been widely recognised in gastric cancer patients because of the disease itself or because of the surgical and oncological treatments. Overall, these factors alone or together cause detrimental effects on mental health of gastric cancer patients, which prone patients to severe depression.

Additionally, it is believed that the higher rate of psychological problems among gastric cancer patients is due to the fact that the majority of patients are diagnosed at an advanced stage when the prognosis is poor and the treatment options are limited.[3] A previous meta-analysis reported that as the consequence of late diagnosis, patients face more aggressive tumours, require more aggressive treatment approaches and have a poorer prognosis.[46] Also, it has been suggested that patients who receive aggressive treatment or surgery are more prone to psychological problems, including depression.[46] Therefore, to provide an effective treatment to reduce psychological damage caused by depression among cancer patients, it is crucial that patients should be monitored for psychological changes and be treated to improve their survival and QoL.[4] Our results along with the previous reports provide robust support to the notion that screening for emotional disorders, especially for depression, is crucial.[41]

Our results based on regions of WHO suggested that the prevalence of depression was higher in Eastern Mediterranean (EMRO) (42%) compared with Western Pacific (40%), European (27%) and American (4%) studies. The evidence recommended that there is a geographical distribution for high incidence/prevalence areas for gastric cancer in Asia that extends from Japan, Korea and some parts of China to north of Iran.[47] The observed discrepancy is more likely because of individual, economic, social and cultural differences between regions.[48] Generally, the result of a systematic review and meta-analysis by Pilevarzadeh et al based on WHO regions showed that the pooled prevalence of depression was low in America, Europe and Western Pacific region and the highest rate was reported in the EMRO region, which is in line with our findings.[45] In the present study, the Eastern Mediterranean (EMRO) than that in Western Pacific and Europe, Americas regions, and the difference was statistically significant. However, the estimates that come from our subgroup analysis should be interoperated with caution, as most of the included studies in this meta-analysis were conducted in the Asian or Mediterranean countries with higher prevalence of mental health problems as compared with developed countries and since only one study was conducted in the region of America, generalisability of the results of this single study in this region

is under question. Additionally, depression in cancer patients was assessed using different questionnaires that may have provide different estimates.[49] The most frequent instrument used to screen depression was the HADS (n=8 studies), and this tool is one of the most common tools to investigate depression, especially among cancer patients[50], followed by the Beck (n=3 studies) and other instruments (n=7 studies). In several studies that used HADS scale, the prevalence of depression among gastric cancer patient was slightly higher (40%) than that what reported based on Beck scale (36%) or what estimated based on other scales (35%). In another study, the most frequent instrument used to investigate depression among breast cancer patients was the CES-D (n=11 studies), followed by the Beck Depression Inventory (BDI, n=6 studies) and the HADS (n=6 studies). CES-D returned about similar prevalence of depression (22%) with BDI (22%) but higher than HADS (10%).[49] In another study, depression was evaluated using the HADS and the CES-D (which are used to check levels of anxiety or depression). It seems that the differences between the instruments in the results should be acknowledged and the results should be compared with caution.[10]

Along with the previously discussed issues, the observed difference in the prevalence of depression reported by different studies can also be explained in terms of study design. In this systematic review, the prevalence of depression reported in cross-sectional studies (41%) was higher than that reported in prospective studies (30%). It is also to be noted that the definitions of prevalence used in different studies could slightly vary across studies, typically relying on cross-sectional assessment at different cancer stages and different times during the cancer trajectory, and occasionally used convenience sampling.[41] In line with this conclusion, another study reported that the prevalence of depression obtained in cross-sectional studies was higher than that in prospective studies. A possible reason for this discrepancy is that cross-sectional studies usually include both new and old cases of depression among cancer survivors.[46]

To the best of our knowledge, this is the first pooled analysis that the prevalence of depression was estimated based on the results of various studies that used various instruments. One strength of this study is the inclusion of both interview and self-administered diagnostic instruments. Another strength of this study was the assessment of bias in the selection of the studies and selection of medium-bias and low-bias-induced studies. Nonetheless, heterogeneity was high, and it remained high after subgroup analyses.

In the present meta-analysis, since heterogeneity was high, we used REM rather than fixed-effect approach for meta-analysis.[51] A key benefit of REM is the aggregation of information leading to a higher statistical power and more robust point estimate than is possible from the estimates derived from any individual study.

However, in performing a meta-analysis, an investigator must make choices that can affect the results, including deciding how to search for studies, selecting studies based on a set of objective criteria, dealing with incomplete data, analysing the data and accounting for or choosing not to account for publication bias.[52]

This study has its own limitations; first, we could not assess other psychosocial factors such as anxiety. Moreover, patients with gastric cancer entered at various stages and the impact of the disease stage on depression was not considered in the present study. However, previous studies showed little impact of stage on the prevalence of depression among patients.[3] Additionally, another important point that might affect the generalisability of our estimates is the imbalance in study location. Most studies were conducted in Asian countries which may limit the interpretation and generalisability of the results to particular countries with regard to culture and economic status. In total of the included studies, most of them were conducted in Asian countries, and only few were conducted in other countries in the region of America or Europe. So, discrepancy in the Asian or Mediterranean and Western countries is existing, which may influence the generalisability of our study results. Finally, it was impossible to investigate the impact of other demographic factors such as economic status or type of treatment on the estimated prevalence due to the unavailability of relevant information in most studies.

CONCLUSIONS

The results of this meta-analysis revealed a high prevalence of depression among patients with gastric cancer. Western Pacific countries need to take depression among cancer patients into account when planning diagnosis and treatment services for the patients. Further research is needed to identify effective strategies for preventing and treating depression among gastric cancer survivors. Early diagnosis and social and family emotional supports can help in management of depression, which will help in improving patient's QoL. Finally, our results provided evidence indicating the need for routine screening, assessment and management for emotional disorders, especially depression, among gastric cancer patients.

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