

Depression, Anxiety, and Other Mental Disorders in Patients With Cancer in Low- and Lower-Middle–Income Countries: A Systematic Review and Meta-Analysis

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PURPOSE Cancer is a growing public health issue in low- and lower-middle–income countries (LLMICs), but the mental health consequences in this setting have not been well-characterized. We aimed to systematically evaluate the available literature on the prevalence, associates, and treatment of mental disorders in patients with cancer in LLMICs.

METHODS We systematically searched Medline, PsycINFO, EMBASE, and CINAHL. We performed a random effects meta-analysis to determine the pooled prevalence of major depression or anxiety disorders in this population, defined by Diagnostic and Statistical Manual of Mental Disorders or International Classification of Diseases criteria. We qualitatively reviewed studies that examined the prevalence of depressive or anxiety disorders defined by self-report tools, the prevalence of other mental disorders, associated factors of depressive and anxiety symptoms, and the treatment of mental disorders in this population.

RESULTS Forty studies spanning a 15-year period were included in the review. The pooled prevalence defined by Diagnostic and Statistical Manual of Mental Disorders or International Classification of Diseases criteria was 21% for major depression (95% CI, 15 to 28) and 18% for anxiety disorders (95% CI, 8 to 30). Depressive and anxiety symptoms were most frequently associated with advanced disease and low levels of education. Among the four studies evaluating treatment, three evaluated the effectiveness of psychotherapy and one evaluated a yoga program.

CONCLUSION The prevalence of depression and anxiety in patients with cancer generally appears higher in LLMICs than in upper-income countries. Our findings demonstrate the existence of a significant and underappreciated disease burden. We suggest that clinicians remain vigilant to psychiatric symptoms. Improved screening and treatment are likely to improve quality of life and reduce both morbidity and mortality.

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INTRODUCTION

Cancer is currently the second leading cause of death worldwide, and the global burden continues to grow.¹ Between 2008 and 2030, the global incidence is expected to increase by more than 80%, with the greatest increases predicted to occur in less-developed countries.² Literature from developed countries clearly confirms that patients with cancer have higher rates of depression and anxiety than the general population³⁻⁵ and that cancer comorbidity with depression results in greater morbidity and poorer cancer-related outcomes.^{6,7}

Compared with upper-income countries, patients with cancer in low- and lower-middle–income countries (LLMICs) are generally diagnosed at a more advanced stage, have limited access to treatment, and face a poorer prognosis.^{8,9} Although almost half the world's population resides in LLMICs,¹⁰ the mental health burden among patients with cancer in LLMICs has not

been systematically evaluated. Many LLMICs are in the process of developing comprehensive cancer care programs. The International Federation of Psycho-Oncology Societies advocates for the integration of psychosocial support into routine cancer care.¹¹ Quantifying and characterizing the burden of mental disorders in this population may inform the development of cancer care services in LLMICs.

To our knowledge, no review has comprehensively examined the intersection between cancer and mental disorders in LLMICs. Thus, within this population, the aims were to

1. Systematically review the prevalence of depression, anxiety, and other mental disorders and perform a pooled prevalence meta-analysis where appropriate
2. Systematically review factors affecting mental disorder symptoms
3. Systematically review the effectiveness of treatment.

ASSOCIATED CONTENT

Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

To describe the intersection between cancer and mental disorders in low- and lower-middle-income countries, which has not been systematically evaluated previously.

Knowledge Generated

The prevalence of interview-defined major depression was 21%, and the prevalence of interview-defined anxiety disorder was 18%. Depressive and anxiety symptoms were most frequently associated with advanced disease and low levels of education.

Relevance

This review establishes the existence of a significant disease burden. It highlights the importance of mental disorder symptom recognition and treatment. It lends further support to the integration of mental health services within cancer care centers in LLMICs.

METHODS

Protocol and Registration

The meta-analysis followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. It was registered with PROSPERO (CRD42017057103), and the protocol was published.¹²

Search Strategy and Study Selection

The protocol contains a detailed description of the search strategy and the eligibility criteria for inclusion. In brief, the search used a comprehensive list of subject headings and keywords to link the broad concepts of (1) neoplasms, (2) LLMICs, and (3) mental disorders. The specific search strategies for MEDLINE, PsycInfo, EMBASE, and CINAHL are shown in the Data Supplement. MEDLINE, PsycInfo, EMBASE, and CINAHL were searched for all studies that met the inclusion criteria. The search was performed on March 31, 2017. Two additional searches were performed on July 16, 2017: one search to reflect the addition of three countries to the World Bank's 2018 fiscal year list of LLMICs, released on July 1, 2017, and another to capture eligible articles published since the initial search.

The target population was adults with cancer living in LLMICs, as defined by the World Bank's 2018 fiscal year list. Articles were included if they had been published in English after March 2002 and reported original peer-reviewed data on either the prevalence of mental disorders or the outcome of interventions addressing depression or anxiety in the target population. Validation studies and studies examining prevalence with fewer than 20 participants were excluded. Where necessary, study authors were contacted for data or clarification. Where there were multiple reports on the basis of the same study population, the results were taken from the study reporting the largest sample. The reference lists of included studies were also screened for any missed publications.

Data Management and Study Selection

The literature search results were uploaded to Endnote X8. Z.J.W. and M.P.J. independently screened the titles and

abstracts against the inclusion criteria and created a preliminary list of articles. The full text was retrieved, and Z.J.W. and M.P.J. jointly screened the full text of these articles. Disagreements were resolved through consensus. The reasons for exclusion were documented in the PRISMA flow diagram. Z.J.W. extracted the primary data from the included studies into both a Word document table and Excel spreadsheets. The data were cross-checked by S.X.

Risk of Bias

Z.J.W. and S.X. independently rated the quality of individual studies using the National Institute of Health's Study Quality Assessment Tools.¹³ Each study was rated as being good, fair, or poor, which equated to being at a low, medium, or high risk of bias, respectively. Disagreements were resolved by consensus. The quality assessment charts are given in the Data Supplement. Risk of publication bias across all studies was assessed using funnel plots. To minimize classification bias, studies were separated into two categories: those that defined major depression or anxiety according to either Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) or International Classification of Diseases 10th Revision (ICD-10) criteria using interview-based tools and those that defined depression or anxiety caseness using self-report tools. Both categories were analyzed and reviewed separately.

Statistical Analysis

A pooled prevalence meta-analysis was performed for major depression defined by interview-based tools and for anxiety disorders defined by interview-based tools. Raw counts were used in the analysis. In rare cases, when only proportions were available, they were converted into a raw count. For longitudinal studies, baseline prevalence values were used in the analysis. There were insufficient numbers for valid subgroup analyses on the basis of outcome measurement instrument, World Bank region, or country. All statistical analyses were programmed using the meta-prop command in Stata (version 14). Meta-analyses used

random effects modeling and Freeman-Tukey Double arcsine transformation. Sensitivity analyses were conducted, excluding studies that were identified as being at a high risk of bias.

Qualitative Review

A narrative synthesis was performed for the prevalence of depression and anxiety defined by self-report tools and the prevalence of other mental disorders. Statistically significant associated factors of depressive and anxiety symptoms identified by prevalence studies were also synthesized, as were those studies examining the effectiveness of interventions.

Role of the Funding Source

The NSWIOP had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

RESULTS

The literature search returned 2,371 records published in the English language between 2002 and 2017, with six additional reports found through other sources. Of the 116 full-text articles screened, 40 met the inclusion criteria. The PRISMA flowchart is shown in Figure 1. The majority (26 of 40) of studies were published after 2012. The articles contained data from 15 countries spanning four World Bank regions: East Asia and Pacific, South Asia, Middle

East and North Africa, and Sub-Saharan Africa. Nigeria and India had the most frequent representation with 10 and eight articles from these countries, respectively. Cancer type was often reported as mixed; however, 12 studies limited their study populations to patients diagnosed with breast cancer.

There were 36 studies identified reporting prevalence data on 32 separate study populations. The extracted study characteristics, prevalence data, study quality, and significantly associated factors are given in Table 1. Of these 36 studies, 30 contained data on associated factors. Four interventional studies were identified. The prevalence studies contained data on 9,195 participants in total, with 5,637 participants in studies of associated factors. Most studies were cross-sectional and defined depressive or anxiety disorders using clinical interviews or self-report tools. Four interventional studies were identified, involving a total of 217 participants. Overall, 13 prevalence studies were classified as being at low risk of bias, 18 at medium risk of bias, and five at high risk of bias, whereas two of the interventional studies were classified as being at a medium risk of bias and two at a high risk of bias. The most common study weaknesses are related to poor sampling methodology or poor reporting.

For major depression defined by interview-based tools on the basis of either DSM-IV or ICD-10 criteria, 12 studies

FIG 1. Preferred reporting items for systematic reviews and meta-analyses flowchart.

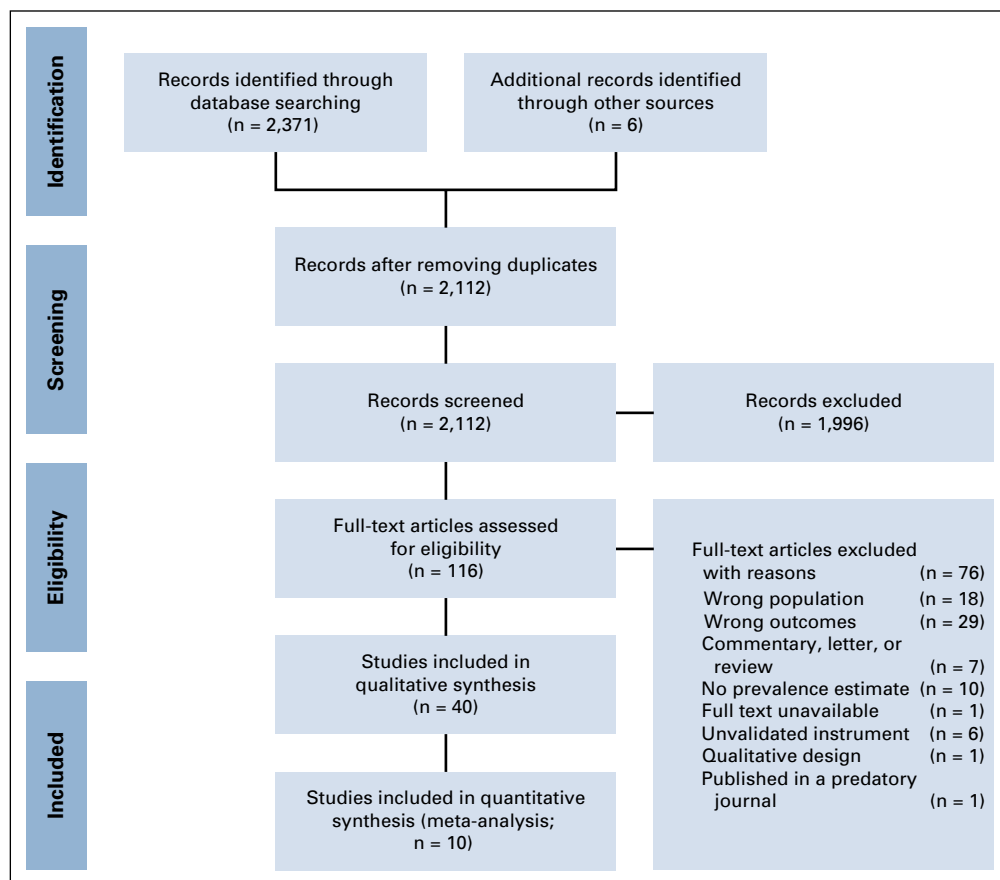


TABLE 1. Characteristics of Studies From Low-Income and Lower-Middle-Income Countries

World Bank Region	Country	Author (year)	Study Design	No. of Patients With Cancer (percent of female)	Cancer Site	Cancer Duration	IP/OP	Previous Mental Illness	Caseness	Key Findings	Significant Associates	Risk of Bias
East Asia and Pacific	Cambodia Myanmar Vietnam	Peltzer and Pengpid ¹⁴	CS	72 (UNK)	UNK	Treated in the past 12 months	OP	UNK	HADS-D ≥ 11 HADS-A ≥ 11	Depression: 31.9% Anxiety: 45.8%	NA	Moderate
	Philippines	Que et al ¹⁵	CS	247 (UNK)	Mixed	Receiving treatment	Mixed	UNK	PHQ-8 ≥ 10	Depression: 21.5%	Depression Marital status (widowed) Metastatic cancer ECOG 4	Low
	Cambodia Indonesia Laos Myanmar Philippines Vietnam	The ACTION Study Group ¹⁶	LONG	3,044 (UNK)	Mixed	12 months after diagnosis	UNK	INCL	HADS-D ≥ 8 HADS-A ≥ 9	Depression: 38.5% Anxiety: 26.4%	NA	Low
	Vietnam	Yen et al ¹⁷	CS	695 (48)	Mixed	Receiving treatment	IP	EXCL (psychosis and addiction)	DASS-21 ≥ 4	Depression: 28.2%	Depression Lower income Lower educational level Occupation (farmers) Stage 4 cancer Cancer site (lung, otolaryngologic, and gynecologic)	Low
South Asia	India	Bhattacharyya et al ¹⁸	CS	174 (48.9)	Mixed	Receiving chemotherapy	OP	UNK	BEDS ≥ 6	Depression: 55.7%	Not significant	Low
	India	Chittem et al ¹⁹	CS	329 (62)	Mixed	Mixed	OP	EXCL	HADS-D ≥ 11 HADS-A ≥ 11	Depression: 24.9% Anxiety: 19.8%	Depression and anxiety Unaware of diagnosis	Low
	India	Gopalan et al ²⁰	CS	384 (63.5)	Carcinomas	Mixed	IP	INCL	MINI (UNK DSM-IV or ICD-10)	Major depressive disorder: 10.9% Adjustment disorder: 22.6% Hypomania: 1.6%	Any psychiatric disorder Female No. of chemotherapy cycles Previous psychiatric illness Family history of psychiatric illness Radiotherapy Surgery After multivariate analysis, only being female, radiotherapy, and surgery persist	Moderate
	India	Pandey et al ²¹	CS	123 (24.4)	Head and neck cancer	Receiving curative treatment	UNK	UNK	HADS-D ≥ 11 HADS-A ≥ 11	Depression: 9.8% Anxiety: 12.2%	Depression Higher stage Higher DIC scores Higher HADS-A score Lower educational level Less distance traveled Nonchewer of tobacco Anxiety Higher DIC scores Nonchewer of tobacco	High

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TABLE 1. Characteristics of Studies From Low-Income and Lower-Middle-Income Countries (Continued)

World Bank Region	Country	Author (year)	Study Design	No. of Patients With Cancer (percent of female)	Cancer Site	Cancer Duration	IP/OP	Previous Mental Illness	Caseness	Key Findings	Significant Associates	Risk of Bias
India	Shankar et al ²²	CS	534 (45.1)	Mixed	Attending oncology outpatient service	OP	EXCL	PHQ-9 \geq 10 GAD-7 \geq 8	Depression: 37.5% Generalized anxiety disorder: 35.8%	Depression and GAD Higher stage Blended family GAD Blended family Lower socioeconomic status	Moderate	
India	Singh et al ²³	CS	300 (44.7)	Mixed	Receiving chemotherapy	OP	EXCL	DASS-21 \geq moderate	Depression: 90% Anxiety: 56%	Anxiety Cancer duration No. of chemotherapy cycles	Moderate	
Nepal	Sharma and Zhang ²⁴	CS	120 (99)	Breast	Up to 6 years	Mixed	EXCL	HADS \geq 8	Depression: 93.3% Anxiety: 89.2%	Depression Illiteracy Occupation (housewife and agriculture) Moderate anxiety on HADS-A	Moderate	
Nepal	Thapa et al ²⁵	CS	50 (UNK)	UNK	UNK	UNK	UNK	HADS \geq 8 Clinical diagnosis using ICD-10	Depression (HADS): 28% Anxiety (HADS): 40% Depressive disorder (ICD-10): 6% Anxiety disorder (ICD-10): 2% Adjustment disorder (ICD-10): 10% Alcohol dependence (ICD-10): 8%	NA	High	
Pakistan	Dogar et al ²⁶	CS	60 (50)	Mixed	Receiving chemotherapy	OP	INCL	Clinical interview (DSM-IV) HADS \geq 8	Depression (interview): 28.3% Depression (HADS-D): 61.7% Anxiety (interview): 41.7% Anxiety (HADS-A): 43.3%	No significant associates	High	

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TABLE 1. Characteristics of Studies From Low-Income and Lower-Middle-Income Countries (Continued)

World Bank Region	Country	Author (year)	Study Design	No. of Patients With Cancer (percent of female)	Cancer Site	Cancer Duration	IP/OP	Previous Mental Illness	Caseness	Key Findings	Significant Associates	Risk of Bias
	Pakistan	Iqbal et al ²⁷ Iqbal ²⁸	CS	365 (48.5)	Mixed	Newly diagnosed	UNK	EXCL	SCID (DSM-IV)	Depression: 17.8% Anxiety disorders: 17.0% PTSD: 8% Anxiety disorder NOS: 6% Specific phobias: 3% Social phobias: 1% Agoraphobia without panic: 1% Adjustment disorders: 20.8% Delirium: 1.6% Somatoform disorder: 0.5%	Depression Age (45-55 years) Female Illiteracy Tense home atmosphere Poor family support Cancer site (genitourinary, head and neck, and multiple myeloma) Anxiety Age (below 25 years) Male Illiteracy Tense home atmosphere Poor family support Cancer site (bone and connective tissues, gastrointestinal, and lymphoma) Adjustment disorder Age (25-35 and 35-45 years highest) Female Illiteracy Tense home atmosphere Poor family support Multiple myeloma	Moderate
	Pakistan	Rashid et al ²⁹	CS	200 (74)	Mixed	Mixed	OP	UNK	Two-part screening: WHO-5 Scale (UNK cutoff) and then MDI	Depression: 36%	No significant associates	Low
Middle East and North Africa	Egypt	Gaballa et al ³⁰	CS	116 (59.5)	Solid and hematologic	UNK	UNK	UNK	HADS-D ≥ 11 HADS-A ≥ 11	Depression: 37.1% Anxiety: 37.9%	Depression Female Response (progressive plus stable disease) Receiving steroids Anxiety Female	High
	Egypt	El Missiry et al ³¹	CS	100 (100)	Breast	75 early postoperative and 25 with recurrence	OP	UNK	SCID (DSM-IV)	Major depression: 24% Anxiety plus adjustment disorder with anxious mood: 26% Minor depression (dysthymia and adjustment disorder with depressed mood): 8%	All diagnoses Higher stage	Moderate

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TABLE 1. Characteristics of Studies From Low-Income and Lower-Middle–Income Countries (Continued)

World Bank Region	Country	Author (year)	Study Design	No. of Patients With Cancer (percent of female)	Cancer Site	Cancer Duration	IP/OP	Previous Mental Illness	Caseness	Key Findings	Significant Associates	Risk of Bias
Egypt	Egypt	El-Hadidy et al ³²	CS	54 (100)	Breast	Diagnosed within the past 6 months	OP	EXCL	MINI (DSM-IV) SCID II	Major depressive disorder: 38.9% Generalized anxiety disorder: 29.6% Panic disorder: 9.2% Manic episode: 0% Psychotic disorders: 0% Alcohol abuse: 0% Substance abuse: 0% Dysthymic disorder: 0% Agoraphobia: 0% Obsessive-compulsive disorder: 0% Anorexia nervosa: 0% Bulimia nervosa: 0% PTSD: 0% Personality disorder: 0%	Depression Greater marriage duration Higher BDI score (husband) Higher HAM-A score (patient or husband) Lower RSES score (patient or husband) Marriage type (love-based) Higher socioeconomic status Higher educational level (patient or husband) Anxiety Greater marriage duration Higher BDI score (patient or husband) Higher HAM-A score (husband) Lower RSES score (patient or husband) Marriage type (love-based) Higher socioeconomic status Higher educational level (patient or husband)	Moderate
Egypt	Egypt	Elsheshtawy et al ³³	CS	56 (100)	Breast	Before surgery	UNK	UNK	HADS-D ≥ 8 HADS-A ≥ 8	Depression: 71.4% Anxiety: 53.6%	Depression Brief COPE scale strategies (venting) Anxiety Brief COPE scale strategies (positive reframing, planning, and venting)	Moderate
Egypt	Egypt	Mansson et al ³⁴	LONG	32 (0)	Advanced bladder cancer	Undergoing radical cystectomy with orthotopic bladder substitution	NA	UNK	HADS-D ≥ 11 HADS-A ≥ 11	Depression 59.4% (preoperative) 46.9% (3 months postoperative) 28.1% (12 months postoperative) Anxiety 43.8% (preoperative) 25% (3 months postoperative) 28.1% (12 months)	Depression Timepoint (preoperative highest) Anxiety Timepoint (preoperative higher)	Moderate
Iraq	Iraq	Alkhyatt et al ³⁵	CS	100 (100)	Early breast (stage 1 or 2 node-negative)	Up to 20 months postdiagnosis	UNK	UNK	IES and BSI UNK cutoff	Cancer-related PTSD: 5% liberal criteria and 3% stringent criteria	NA	High

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TABLE 1. Characteristics of Studies From Low-Income and Lower-Middle-Income Countries (Continued)

World Bank Region	Country	Author (year)	Study Design	No. of Patients With Cancer (percent of female)	Cancer Site	Cancer Duration	IP/OP	Previous Mental Illness	Caseness	Key Findings	Significant Associates	Risk of Bias
Jordan		Abu-Helalah et al ³⁶	CS	236 (100)	Breast	12-36 months after diagnosis	UNK	INCL	HADS ≥ 8	Depression: 45% Anxiety: 53%	Depression Living with husband only Anxiety Higher stage Living with husband only Employment status Lower income Other social problems Age	Low
Jordan		Abu-Helalah et al ³⁷	CS	241 (47.7)	Colorectal	12-36 months after diagnosis	UNK	INCL	HADS ≥ 8	Depression: 22.9% Anxiety: 18.3%	Depression Stoma use Changing job after cancer diagnosis Smaller family Rural No health insurance Rheumatoid arthritis Diarrhoea symptoms HADS total score Mean ETORC QLQ-C30 emotional functioning score ETORC QLQ-CR29 anxiety scale Anxiety Extent of disease Other social problems Low back pain Other chronic diseases Diarrhea symptoms Hoarse voice HADS total score Mean ETORC QLQ-C30 fatigue score ETORC QLQ-CR29 embarrassment scale	Low
Jordan		Hamdan-Mansour et al ³⁸	CS	92 (57.6)	UNK	At least 6 months postdiagnosis	IN	EXCL	BDI-II ≥ 14	Depression: 77.2%	NA	Moderate
Jordan		Mhaidat et al, 2008 ³⁹	CS	208 (48)	Mixed	Mixed	Both	EXCL (previous psychologic treatment)	HADS ≥ 8	Depression: 51.9%	Reduced appetite Aware of diagnosis Higher stage	Moderate

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TABLE 1. Characteristics of Studies From Low-Income and Lower-Middle-Income Countries (Continued)

World Bank Region	Country	Author (year)	Study Design	No. of Patients With Cancer (percent of female)	Cancer Site	Cancer Duration	IP/OP	Previous Mental Illness	Caseness	Key Findings	Significant Associates	Risk of Bias
	Morocco	Berhili et al ⁴⁰	CS	446 (100)	Breast	Mixed	Both	UNK	HADS ≥ 11	Depression: 6.7% Anxiety: 5.6%	HADS global Younger age (under 50 years) Marital status (divorced) Other stressors (emotional and financial) Absence of family support Needing analgesics and/or anxiolytics Metastatic disease Treatment modality (chemotherapy or surgery)	Low
	Tunisia	Leila et al ⁴¹	CS	50 (100)	Breast, localized	Remission of > 3 months	OP	UNK	HADS-D ≥ 11 HADS-A ≥ 11	Depression: 44% Anxiety: 42%	Depression Poorer body image Anxiety Poorer sexual satisfaction Poorer body image	Low
Sub-Saharan Africa	Nigeria	Akin-Odanye et al ⁴²	CS	33 (UNK)	Breast	Currently undergoing chemotherapy	OP	UNK	BDI-II ≥ 14	Depression: 60.7%	Depression Better informed about breast cancer Higher stage Lower educational level	Moderate
		Fatiregun et al ⁴³ Fatiregun et al ⁴⁴	CS	200 (100)	Breast	Mixed stage of treatment	OP	INCL	SCAN (ICD-10)	Anxiety disorders: 19% Agoraphobia 1% Simple phobia 1.5% Social phobia 3.5% Mixed anxiety and depressive disorder 8.5% Panic disorder 2.5% Generalized anxiety disorder 2%	Anxiety Lower income Lower stage No previous history of breast cancer After logistical regression, only stage and history of breast cancer persists. Lower ETORC QLQ-C30 global health status, functional scale scores (physical, emotional, cognitive, and social functioning), and symptom scale scores (fatigue, pain, insomnia, appetite, diarrhea, and financial difficulties)	Low
		Nuhu et al ⁴⁵ Nuhu et al ⁴⁶ Nuhu et al ⁴⁷	CS	210 (70)	Mixed	Radiotherapy, surgery, or gynecology inpatient	IP	EXCL	SCID (DSM-IV)	Major depressive disorder: 29.5%	Depression Later stage Pain Family history of mental illness WHOQOL-Bref score	Moderate

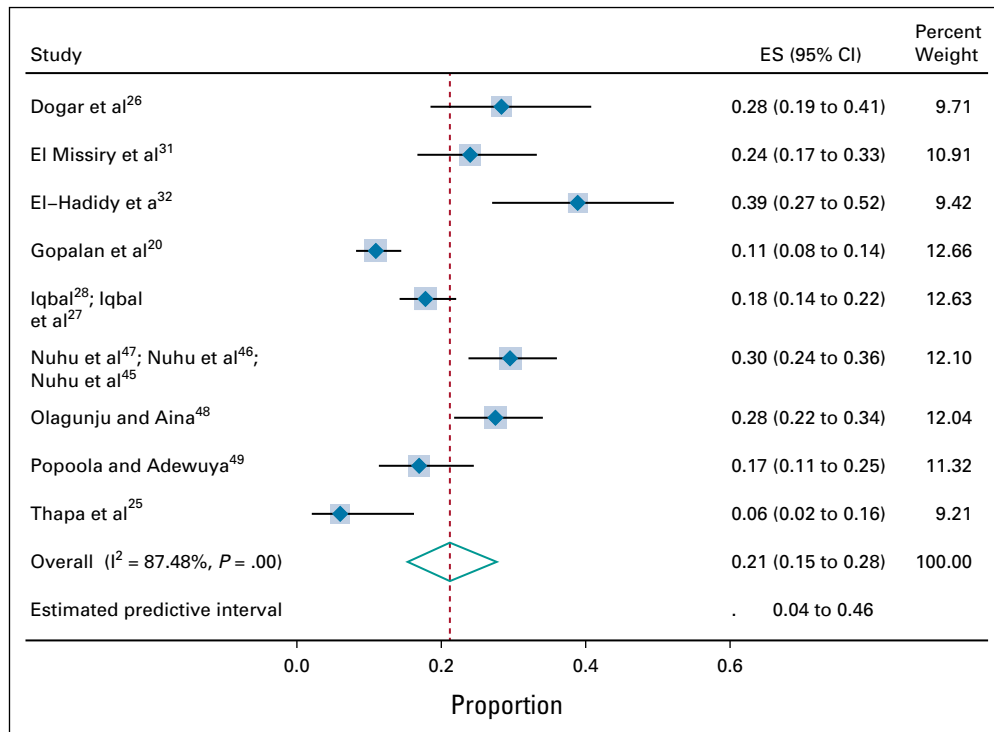
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TABLE 1. Characteristics of Studies From Low-Income and Lower-Middle-Income Countries (Continued)

World Bank Region	Country	Author (year)	Study Design	No. of Patients With Cancer (percent of female)	Cancer Site	Cancer Duration	IP/OP	Previous Mental Illness	Caseness	Key Findings	Significant Associates	Risk of Bias
		Olagunju and Aina ⁴⁸	CS	200 (85.3)	Mixed (breast, cervical, colon or rectal, and prostate)	Mixed	OP	UNK	SCAN (ICD-10) CES-DR ≥ 16	Depressive disorder (SCAN): 27.5% Depressive symptomology (CES-DR): 49%	NA	Moderate
		Popoola and Adewuya ⁴⁹	CS	124 (100)	Breast	More than 3 months	OP	UNK	MINI (DSM-IV)	Major depressive disorder: 16.9%	Depression Unmarried Greater amounts spent on treatment Poor social support Having a relative who died of breast cancer Higher stage Being diagnosed more than two years previously. After multivariate analysis, only marital status, poor social support, and higher stage persist	Low

Abbreviations: BDI, Beck Depression Inventory; BEDS, Brief Edinburgh Depression Scale; BSI, Brief Symptom Inventory; CES-DR, The Center for Epidemiologic Studies Depression Scale Revised; COPE, Coping Orientation to Problems Experienced; CS, cross-sectional; DASS-21, Depression, Anxiety, and Stress Scale 21-item; DIC, Distress Inventory for Cancer; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders Fourth Edition; ECOG, Eastern Cooperative Oncology Group Performance Status; EORTC QLQ-CR 29, EORTC Quality of Life Questionnaire—Colorectal Cancer Module; ETOC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; EXCL, excluded; GAD, generalized anxiety disorder; GAD-7, Generalized Anxiety Disorder 7-item scale; HADS-A, Hospital Anxiety and Depression Scale anxiety subscale; HADS-D, Hospital Anxiety and Depression Scale depression subscale; HAM-A, Hamilton Anxiety Rating Scale; ICD-10, International Classification of Diseases 10th Revision; IES, Impact of Event Scale; INCL, included; IP, inpatient; LONG, longitudinal; MDI, Major Depression Inventory; MINI, Mini International Neuropsychiatric Interview; NA, not applicable; NOS, not otherwise specified; OP, outpatient; PHQ-8, 8-item Patient Health Questionnaire; PHQ-9, 9-item Patient Health Questionnaire; PTSD, post-traumatic stress disorder; RSES, Rosenberg Self-Esteem Scale; SCAN, Schedules for Clinical Assessment in Neuropsychiatry; SCID, Structured Clinical Interview for DSM; UNK, unknown; WHO-5, 5-Item WHO Well-Being Index; WHOQOL-BREF, abbreviated version of the WHO Quality of Life assessment.

FIG 2. Prevalence of major depression (interview-based tools). ES, estimate.



reported prevalence estimates involving 1,547 participants drawn from nine separate study populations. The diagnostic criteria for major depression as per DSM-IV and ICD-10 are included in the Data Supplement. The pooled prevalence of major depression as defined by interview-based tools was 21% (95% CI, 15 to 28). The I-squared value was 87.5%, indicating a high degree of study heterogeneity (Fig 2). Sensitivity analysis yielded no substantial change. There was no evidence of publication bias.

Six studies reported prevalence estimates of DSM-IV-defined or ICD-10-defined anxiety disorders identified

by interview-based tools. The six studies were drawn from four separate study populations involving 675 participants. The pooled prevalence of anxiety disorders defined by interview-based tools was 18% (95% CI, 8 to 30). The I-squared value was 90.6%, indicating high heterogeneity (Fig 3). Sensitivity analysis produced a marginal change. There was no evidence of publication bias.

Several studies defined depression and anxiety caseness using self-report tools. A range of self-report tools and cutoff scores were used, resulting in highly variable prevalence estimates. The Hospital Anxiety and Depression Scale (HADS) was the most frequently used instrument.

FIG 3. Prevalence of anxiety disorders (interview-based tools). ES, estimate.

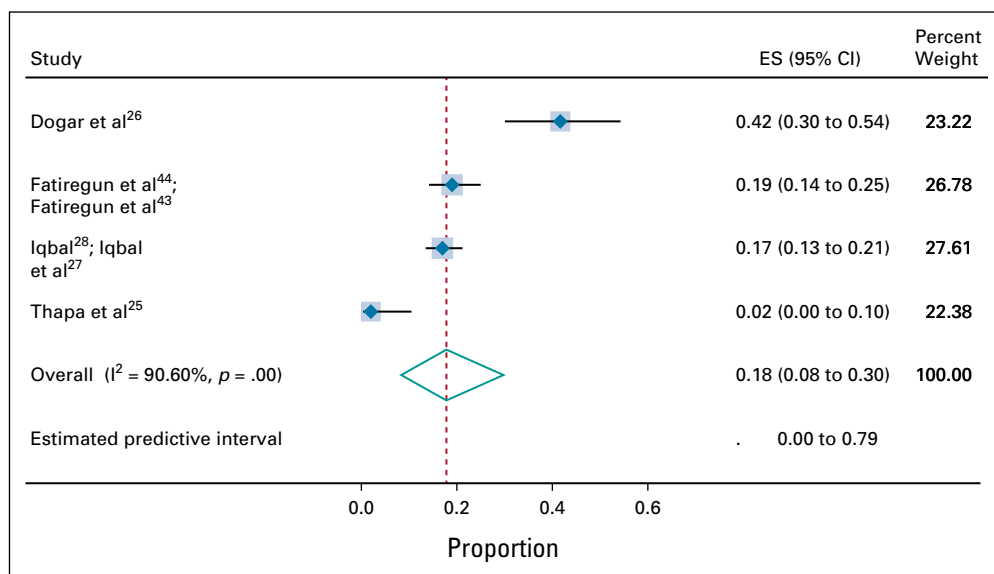


TABLE 2. Prevalence of Other Mental Disorders

Mental Disorder	Times Reported	Prevalence Range (%)
Adjustment disorder	3	10-22.6
Generalized anxiety disorder	3	2-35.8
Agoraphobia	3	0-1
PTSD	3	0-8
ETOH dependence	2	0-8
Panic disorder	2	2.5-9.3
Delirium	2	1.6-6.5
Specific or simple phobia	2	1.5-3
Social anxiety	2	1-3.5

NOTE. Reported only once: mixed anxiety and depression, anxiety plus adjustment disorder (with anxious mood), dysthymia plus adjustment disorder (with depressed mood), hypomania, somatoform disorder, social phobia, anxiety not otherwise specified, mania, psychosis, dysthymia, obsessive-compulsive disorder, anorexia nervosa, bulimia nervosa, substance abuse, and personality disorder.

Abbreviations: ETOH dependence, alcohol dependence; PTSD, post-traumatic stress disorder.

For depression defined by self-report tools, 24 studies reported prevalence estimates on 7,657 participants, with the range spanning 6.7%⁴⁰-93.3%.²⁴ Eight studies used a HADS subscale cutoff of ≥ 11 , whereas seven used an HADS subscale cutoff of ≥ 8 . Prevalence estimates of anxiety defined by self-report tools were reported by 15 studies involving 5,275 participants, with the range spanning 5.6%⁴⁰-89.2%.²⁴ Seven studies used an HADS subscale cutoff of ≥ 11 , and six used an HADS subscale cutoff of ≥ 8 , whereas one used an HADS subscale cutoff of ≥ 9 . For both depression and anxiety, the lowest estimates were reported in a Moroccan sample of women with breast cancer using an HADS subscale cutoff of ≥ 11 ,⁴⁰ whereas the highest estimates came from a Nepalese sample of women with breast cancer using an HADS subscale cutoff of ≥ 8 .²⁴

The prevalence of other mental disorders is summarized in Table 2. Generally, there were few reports, with Adjustment Disorder, Generalized Anxiety Disorder, Agoraphobia, and Post-Traumatic Stress Disorder (PTSD) each reported three times. A variety of interview-based tools and self-report tools were used.

Associated factors of depression and/or anxiety symptoms were examined by 30 studies, with 27 studies identifying statistically significant associated factors. These factors are listed in Table 1. In terms of biologic factors, 12 studies found a significant association between advanced cancer stage and mental disorders^{15,17,21,22,30,31,36,37,39,40,42,43,45,46,49} with an odds ratio as high as 14.42.⁴⁰ With regard to physical symptoms, cancer pain was found to increase the likelihood of depressive and anxiety symptoms.^{40,45,46} Higher rates of mental disorders or greater severity of symptoms were observed among a range of cancer sites

and cancer types,^{17,28} with none consistently predominating. There were significant sex differences referenced in several studies. Being female was found to correlate with an increased likelihood of experiencing depression,^{28,30} as well as any form of mental illness,^{20,31} but findings were mixed with regard to anxiety.^{28,30} Similarly, mixed findings were reported in the inter-relationship between age and symptoms of mental illness in patients with cancer.^{28,40}

There were several reports on the impact of marital relationships on the occurrence of emotional symptoms in patients with cancer. In both Nigeria and the Philippines, patients with cancer were more likely to report depression or depressive symptoms if they were unmarried or widowed.^{15,49} The inter-relationship between the home environment and overall emotional symptoms was also explored, with a tense home environment,²⁸ absence of family support,⁴⁰ and poor social support⁴⁹ leading to a significant likelihood of patients with cancer developing emotional symptoms.

Several studies captured socioeconomic disadvantage as a risk factor for the development of emotional symptoms in cancer sufferers in LLMICs. Specifically, higher rates of depressive and anxiety symptoms were found among patients with cancer of a lower educational level.^{17,21,24,28,42} Higher levels of anxiety⁴³ and depressive symptoms¹⁷ were found among patients with lower incomes or with low socioeconomic status.²² Contradicting this, a single study reported higher rates of depression in patients with cancer of middle or high socioeconomic status or a higher level of education.³² Interestingly, two studies found agricultural workers suffering from cancer to experience higher levels of depressive symptoms compared with office workers with cancer.^{17,24}

Four studies examining the effectiveness of interventions addressing depression or anxiety among patients with cancer in LLMICs were identified. Two studies were based in India^{50,51} and two in Nigeria,⁵² with three of the four published since 2013.^{50,52,53} The study characteristics and findings are summarized in Table 3. Three randomized control trials^{50,51,53} and one open trial of interaction⁵² were conducted. The samples were highly heterogeneous with a range of cancer sites and stage of treatment. In one study, the presence of a current major mental disorder was an exclusion criterion.⁵¹

All four treatment studies were nonpharmacologic. Three studies measured the outcomes of psychotherapy treatments: four weeks of weekly counseling sessions compared with treatment as usual,⁵⁰ 10 sessions of rational emotive hospice care therapy compared with conventional counseling,⁵³ and seven sessions of cognitive restructuring therapy with no comparison group.⁵² A fourth study measured the outcome of a yoga program compared with supportive counseling.⁵¹

The four studies assessed the effect of the intervention on mean depression and/or anxiety symptoms as measured by

TABLE 3. Studies Examining the Treatment of Mental Disorders

World Bank Region	Author, Year	Country	Sample	Intervention and Control	Study Design	Target Outcomes	Outcome Measures	Key Findings	Risk of Bias
South Asia	Banerjee et al, 2007 ⁵¹	India	68 women undergoing radiotherapy Breast cancer Past psychiatric excluded	35 intervention 23 control Intervention: 6-week yoga program Control: 6 weeks of supportive counseling	Randomized controlled trial	Depression and anxiety	HADS-D = depression HADS-A = anxiety	Significant decrease in mean HADS-D and HADS-A scores in the intervention group and significant increase in mean HADS-D and HADS-A scores in the control group	High
	Pathak et al, 2013 ⁵⁰	India	100 inpatients receiving radiotherapy Mixed cancers Mixed duration of illness	50 intervention 50 control Intervention: 4 weeks of weekly 30- to 40-minute counseling sessions Control: treatment as usual	Pretest-post-test randomized controlled trial	Depression and anxiety	BDI-II = depression STAI = anxiety	Significant decrease in mean BDI-II and STAI scores in the intervention group and significant increase in mean BDI-II and STAI scores in the control group	Moderate
Sub-Saharan Africa	Asuzu et al, 2015 ⁵²	Nigeria	17 women Breast or cervical cancer	7 × 1 hour group-based sessions of cognitive restructuring therapy	Pilot single-arm pretest-post-test design	Depression	BDI-II = depression	Significant decrease in post-test mean BDI-II scores	High
	Onyechi et al, 2016 ⁵³	Nigeria	32 patients Terminal breast, cervical, or prostate cancer	16 intervention 16 control Intervention: 10 sessions of REHCT Control: usual care plus 10 sessions of conventional counseling	Pretest-post-test randomized controlled trial	Depression and anxiety	K10 = depression and anxiety	Significant decrease in mean K10 scores in the intervention group and no change in mean K10 scores in the control group	Moderate

Abbreviations: BDI, Beck Depression Inventory; HADS-A, Hospital Anxiety and Depression Scale anxiety subscale; HADS-D, Hospital Anxiety and Depression Scale depression subscale; REHCT, rational emotive hospice care therapy; STAI, State-Trait Anxiety Inventory.

the HADS, State-Trait Anxiety Inventory, Beck Depression Inventory II, or K10. No effect sizes were reported. Three studies used both depression and anxiety symptom rating scale scores,^{50,51,53} whereas one assessed the effect on depression symptom scale scores only.⁵² Following the psychotherapy intervention, three studies found a significant decrease in depression and anxiety symptom scale scores.^{50,52,53} The yoga program was found to be superior to the control group, which had received supportive counseling.⁵¹ The same study also found that the control group displayed an increase in depression and anxiety symptom scale scores.⁵¹

DISCUSSION

This meta-analysis produced pooled prevalence estimates of depressive and anxiety disorders among patients with cancer living in LLMICs. When interview-based tools were used, the prevalence of DSM-IV–defined or ICD-10–defined major depression and anxiety disorders was 22% and 18%, respectively. In general, the estimates are higher than those previously reported in meta-analyses of interview-based studies examining the prevalence of depression or anxiety among patients with cancer. Mitchell et al⁴ found a pooled prevalence of 16.3% for major depression and 10.3% for anxiety, whereas Krebber et al⁵ arrived at a pooled prevalence of 14% for major depression. The discrepancy in the prevalence rates could be explained in part by the fact that the majority of studies included in the meta-analyses by Mitchell et al⁴ and Krebber et al⁵ were conducted in upper-income countries. The meta-analysis by Yang et al⁵⁴ was restricted to studies based in China and spanned the period that China was classified as a lower-middle–income country and after its reclassification as an upper-middle–income country. Yang et al⁵⁴ identified prevalence rates for depression and anxiety, as defined by clinical diagnosis, of 47.49% and 44.93%, respectively.

When caseness was defined by self-report tools, this review found a crude pooled prevalence for depression and anxiety ranging between 6.7%–93.3% and 5.6%–89.2%, respectively. For the acute phase of illness, Krebber et al⁵ found a pooled prevalence of 27% for depression diagnosed by self-report instruments and Yang et al⁵⁴ found a pooled prevalence of 58.11% for depression and 51.74% for anxiety diagnosed by self-report instruments. However, both combined the results from disparate self-report instruments^{5,54} or identical self-report instruments but with disparate cutoffs, so comparisons are unable to be drawn.⁵⁴

With regard to the general population in LLMICs, data from the 2017 Global Burden of Disease Study indicate a 12-month prevalence estimate for DSM-IV–defined or ICD-10–defined depressive disorders, including dysthymia, of 2.87% in lower-income countries and 3.24% in LLMICs.⁵⁵ The 12-month prevalence of anxiety disorders was estimated to be 3.17% in lower-income countries and 3.36%

in LLMICs.⁵⁵ Both are substantially lower than the estimates identified in this meta-analysis.

This review examined the prevalence of other mental disorders in patients with cancer in LLMICs. In the broader global literature, mental disorders among patients with cancer, other than major depression and anxiety, generally appear to be less well-studied. However, meta-analysis of interview-based studies by Mitchell et al⁴ found a pooled prevalence for adjustment disorder of 19.4%. Meta-analysis by Abbey et al⁵⁶ examined cancer-related PTSD and found that prevalence rates varied depending on assessment method, with prevalence rates ranging from 5.1% for interview-based PTSD to 11.2% for PTSD symptom clusters on the basis of self-report tools. A previous meta-analysis found that comorbid substance abuse rates in cancer ranged from 2% to 35%.⁵⁷

This systematic review identified a broad range of reported associated factors contributing to an increased likelihood of experiencing emotional symptoms. Among them, the most consistently noted were advanced disease followed by a low level of education. Both factors were also reported in the systematic review by Niedzwiedz et al,⁵⁸ which examined depression and anxiety among patients with cancer worldwide.

No published reports were found examining pharmacotherapy for the treatment of mental disorders among patients with cancer living in LLMICs. Multiple previous reviews have examined the evidence for this across the global literature. The findings are equivocal, with several meta-analyses finding some evidence of benefit,^{59–63} and others finding no clear evidence of benefit.^{64,65} Non-pharmacologic interventions evaluated in this review included psychologic therapies and yoga, a complementary therapy. In keeping with the current literature,^{59,66} this review found that psychologic interventions significantly improved depressive or anxiety symptoms. The superior outcomes of the group randomly assigned to yoga compared with counseling were consistent with the findings in the review by Cramer et al.⁶⁷

To our knowledge, this review is the first to evaluate studies of mental disorders in patients with cancer in LLMICs and to establish a benchmark pooled prevalence of depressive and anxiety disorders. The current review was conducted in line with PRISMA guidelines, used a registered protocol, involved a broad search strategy, and performed screening in duplicate. The risk of bias was assessed using a validated tool, and sensitivity analyses were conducted. These steps confirmed that most studies included were of a low to moderate risk of bias.

This investigation has several shortcomings, and the results should be interpreted with caution. The limits imposed on the search had the potential to introduce bias, although the funnel plots indicate that relevant studies were not overlooked. The number of studies included was relatively small

and used varying methodologies. The high heterogeneity of the pooled study populations further limits the generalizability of the results. The individual studies might have been prone to selection bias with most of the studies conducted in major cancer centers. Many LLMICs lack universal health coverage, and intracountry health inequalities can exist across socioeconomic, geographic, sex, racial, and ethnic lines. At least one study excluded participants with a prior mental disorder, and almost all the prevalence studies used a cross-sectional design. Finally, no causal relationship can be established between cancer morbidity and mental illnesses. Although previous literature has reported that rates of depression tend to peak in the acute period during treatment,⁵ it was noted that time since diagnosis of cancer and onset of emotional difficulties varied widely in the included studies. It is of note that the included treatment studies had relatively small numbers and the duration of follow-up was short with any sustained longer-term benefits not mentioned.

Several caveats should be noted around the process of diagnosis. Only a minority of studies used validated interview-based tools, which are considered the gold standard to identify depressive and anxiety disorders. Although measurement tools were previously validated in English, the translated versions often lacked local validation and cultural adaptation. It is possible that the frequent use of self-report tools to identify depressive and anxiety conditions might have led to an overestimation of prevalence rates. This flaw may explain the variation in rates when measured by observer-rated versus self-rated methods. We encourage future researchers to be selective in their choice and use of self-report tools, which are largely validated as screening, not diagnostic tools.

Of the 84 countries classified as LLMICs in 2018, only 15 were represented in our review. Many LLMICs, ethnic groups, and minority populations remain unrepresented. Future research could examine these populations or investigate broader psychologic distress in response to cancer among people living in LLMICs. Suicide was beyond the defined scope of this study and warrants exploration given the higher rate of suicide in patients with cancer.⁶⁸ The dearth of treatment studies identified in this review highlights opportunities for future research, such as assessing antidepressants from the WHO essential

medications list or exploring culturally appropriate psychosocial interventions. More broadly, there is a need for increased mental health research in LLMICs. Globally, mental health research is not funded proportional to the burden of disease⁶⁹; furthermore, the distribution of this research is inequitable, with negligible funding for central Asia, the Middle East, and Africa.⁶⁹

The International Psycho-Oncology Society International Standard on Quality Cancer Care, endorsed by International Psycho-Oncology Society and the Union for International Cancer Control, states that “*Psychosocial cancer care should be recognised as a universal human right; Quality cancer care must integrate the psychosocial domain into routine care; Distress should be measured as the 6th Vital Sign after temperature, blood pressure, pulse, respiratory rate and pain.*”⁷⁰ However, psychosocial care is often not an established part of cancer care. National Cancer Control Plans (NCCP) are government plans that guide cancer prevention and management for each country. At present, NCCPs are being developed and updated in individual LLMICs to address the growing cancer burden. Not all NCCPs include psychosocial cancer care,⁷¹ and some LLMICs do not yet have an NCCP.⁷² This review reveals the existence of a substantial burden of disease and the importance of the greater recognition of psychosocial needs by clinicians in LLMICs. Furthermore, it adds weight to the importance of psychosocial care being consistently included in the NCCPs of LLMICs, with the aim of psychosocial care becoming an integral part of routine care. Future research could examine models of delivery, as well as effective and culturally acceptable treatment options, which could be integrated into comprehensive cancer care.

Once previously overlooked, mental disorders are now acknowledged as common and affect culturally and ethnically diverse people across the globe. This review suggests that considerable levels of mental disorder exist among patients with cancer in LLMICs. With the development of national cancer care plans in LLMICs, there is the opportunity to embed and integrate mental health care into cancer care services. Although interventions that target cancer-related mortality are essential in resource-limited settings, addressing the unmet mental health burden could improve survival rates and may be critical for improving quality of life.

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