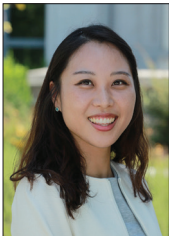


# Understanding the Associations between Caregiver Characteristics and Cognitive Function of Adults with Cancer: A Scoping Review

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## ABSTRACT

Cognitive impairment (CI) is one of symptoms that adults with cancer frequently report. Although there are known factors that contribute to a patient's CI, these factors did not sufficiently explain its variability. Several studies conducted in patients with neurocognitive disorders have reported relationships between patients' cognitive function and caregiver characteristics, which are poorly understood in the context of cancer. This scoping review aims to map the literature on caregiver characteristics associated with CI in adults with cancer. We used the framework proposed by Arksey and O'Malley and PRISMA-Sc. Studies published in English by 2019 were searched through seven electronic databases. All retrieved citations were independently

screened and eligibility for inclusion was determined by two independent authors. Ten studies met inclusion for this review with all of them showing significant associations between a patient's cognitive function and caregiver characteristics. Caregiver's mental health was the most commonly associated with a patient's cognitive function followed by family functioning, adaptation to illness, attitude toward disclosure of the illness, burden, coping and resilience, and demographic characteristics. These review findings suggest that enhanced information about CI in relation to caregiver characteristics will eventually provide the foundation for multifocal interventions for patients with impaired cognitive function. This scoping review identified

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caregiver characteristics that are associated with patients CI. These characteristics should be also assessed when health providers assess and treat CI of adults with cancer.

**Key words:** Caregivers, cognitive function, cognitive impairment, neoplasms, oncology, scoping review

## Introduction

Adults with cancer need support from their informal caregivers (e.g., family or close others) to cope with their illness.<sup>[1-3]</sup> Caregivers of adults with cancer engaged in caregiving tasks approximately 33 h/week, which is 1.3 times higher than the number of hours spent by noncancer caregivers.<sup>[4]</sup> Caregivers of cancer patients provide a wide variety of assistance, ranging from simply providing transportation to more complex tasks such as managing medications and cancer-related symptoms.<sup>[5,6]</sup> Given the wide variety of tasks and time commitment, caregiving can be demanding, and there are many reports about caregiving consequences such as burden.<sup>[7]</sup> Despite the negative consequences reported to be associated with cancer caregiving, caregivers are often essential for patients with cancer to manage their care and symptoms at home.<sup>[8]</sup>

## Background

Of many cancer-related symptoms, impaired cognitive function is a symptom frequently reported by adults with cancer. Cognitive symptoms manifest as a decline in at least one area of cognitive function: attention, concentration, information processing speed, memory, language, executive function, spatial ability, or psychomotor ability.<sup>[9]</sup> Patients with cognitive impairment (CI) often experience challenges in their social relationships with family or friends,<sup>[10,11]</sup> quality of life,<sup>[12]</sup> and adherence to treatment.<sup>[13]</sup> Researchers have reported that CI in cancer has been associated with the disease itself, adverse effects from cancer treatments (e.g., fatigue or emotional distress), patients' age, menopause status, genetic variation, and/or level of education.<sup>[14]</sup> However, these factors do not fully explain the clinical variability of CI among cancer patients. Some patients have reported that cognitive changes that occurred during chemotherapy persisted more than a year following cancer treatments.<sup>[15]</sup>

Caregiver characteristics may provide some explanation on the clinical variability in cognitive function in adults with cancer. In studies of those with neurocognitive disorders, caregiver characteristics such as burden,<sup>[16-18]</sup> personality,<sup>[19]</sup> type of coping strategies they used,<sup>[20,21]</sup> and closeness of relationship<sup>[22]</sup> with the patient are reciprocally associated with their patients' level of cognitive function. In their theory of dyadic illness management, Lyons and Lee<sup>[23]</sup> stated that caregiver characteristics (for examples,

relationship with patient and how caregivers appraise and cope with patients' illness) are associated with the patient health outcomes.<sup>[23]</sup> In addition, evidence suggests that the degree to which caregivers have negative or positive reactions toward the care situations can affect the quality of patient care and influence the patient health outcomes<sup>[24-26]</sup> such as physical and psychological distress.

Several cancer studies in cancer patients have also identified the interdependence of patients and caregivers and often assessed a patient-caregiver dyad as a unit of care.<sup>[23,27]</sup> More emotional and physical problems were noted among cancer patients when they received care from their caregivers with more emotional and physical problems.<sup>[25,28,29]</sup> Although researchers have acknowledged the importance of the interrelationship of patient-caregiver as a dyad, no consensus exists regarding if (and how) caregiver characteristics are associated with cognitive function in adults with cancer.

For our scoping review, we adopted the model that explained reciprocal relationship between patients' and caregivers' emotional distress, which was developed by Northouse *et al.*<sup>[29]</sup> This model was created based on two meta-analyses<sup>[27,30]</sup> showing a positive association between patients' and caregivers' emotional distress. Although this model primarily focused on emotional distress of both groups, we modified this model to explore the associations between caregiver characteristics and cognitive function of adults with cancer.

The aim of this scoping review is to address the question what caregiver characteristics are associated with cognitive function of adults with cancer? This will lay the foundation for studies that explicate the mechanism of CI in adults with cancer. Understanding the mechanism of CI in adults with cancer will also allow clinicians to more precisely identify patients at risk for CI associated with caregiver characteristics and will contribute toward the development of dyadic intervention for both patient and caregiver.

## Methods

A literature search was conducted in June 2019 using seven databases, PubMed (MEDLINE), CINAHL, Embase, PsycINFO, Scopus, Sociological Abstracts, and ProQuest dissertation abstracts. Prospero, PubMed (MEDLINE), CINAHL, Embase, PsycINFO, Scopus, Sociological Abstracts, and ProQuest dissertation abstracts were searched for existing review articles and we determined

that no reviews articles currently exist on a given topic. We followed the five methodological stages of scoping review developed by Arksey and O'Malley.<sup>[31]</sup> This review was conducted based on the following stages: (1) identifying the research question, (2) identifying relevant studies, (3) selecting studies, (4) charting the data, and (5) collating, summarizing, and reporting the results. A detailed methodology of this scoping review was reported in the published protocol.<sup>[32]</sup> Furthermore, the protocol was registered with Open Science Framework.<sup>[33]</sup>

We identified a research question using the PCO model:<sup>[34]</sup> "What caregiver characteristics ("C", concept) are associated with cognitive function ("O", outcome) of adults with cancer ("P", population)?" Inclusion criteria were the studies that (1) assessed one or more cognitive domains of adults with cancer (e.g., attention, concentration, information processing speed, memory, language, executive function, spatial ability, and/or psychomotor ability); (2) examined the associations between caregiver characteristics and cognitive function of adults with cancer; and (3) were conducted on both adults with cancer and their caregivers aged 18 years and above. Studies that focused on individuals with CI attributed to noncancer causes such as psychiatric or neurological illness, dementia, stroke, brain injury, or delirium were excluded. The search strategy can be found in Appendix A.

Of 4387 citations, 38 were identified after a title and abstract review, and eight were confirmed after a full-text review. Two additional citations were found from the reference lists of included articles [Figure 1]. A total of 10 studies were included in this scoping review. Each retrieved citation was reviewed at least twice by independent team members at title/abstract, full text, and abstraction. All discrepancies were discussed to reach consensus. The studies in the final sample were reported using the checklists of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR)<sup>[35]</sup> and tabulated based on caregiver characteristics (e.g., mental health). Studies were organized in chronological order, and data extraction included author information, publication year, study population, caregiver A chronological table was created and included the information on authors, years of publication, study population, caregiver characteristics (i.e., caregiver characteristics), cognitive measures, and its associations. At least two team members independently conducted the verification of data accuracy.

## Results

### Study characteristics

The studies reviewed were conducted in five countries; the majority were conducted in the in the US ( $n = 5$ ) and

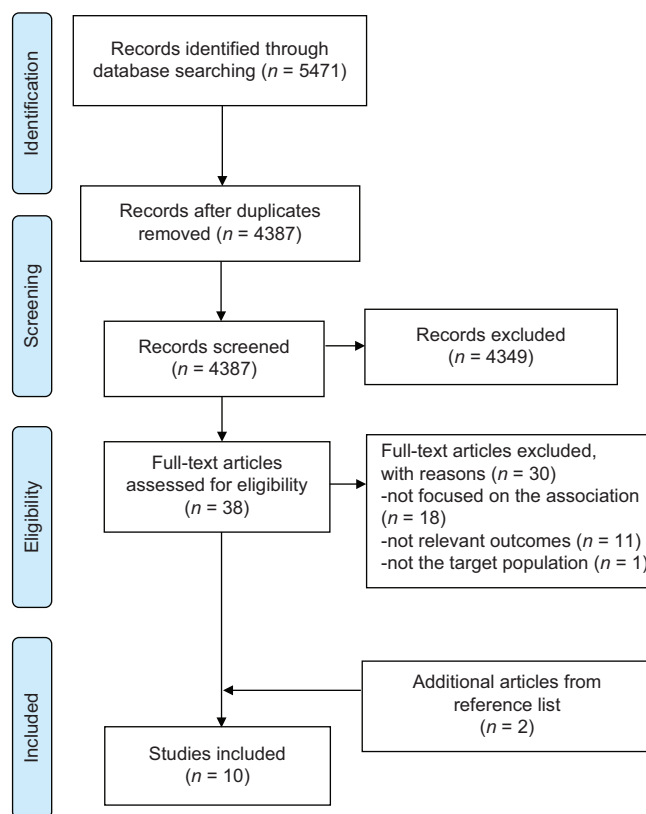


Figure 1: PRISMA-ScR flow diagram for the study selection process

Australia ( $n = 2$ ). Of 10 studies, six were cross-sectional, three were a secondary analysis from a multiple-institutional cohort study, and one was a multiple in-depth case study. Of those three secondary analysis studies, two used the same data set.<sup>[36,37]</sup> Sample sizes of all included studies ranged from 3 to 396 participants. The average age of patients reported in the studies ranged from 23.5 to 73 years of age. Of the included studies, five dealt with the group of patients with non-central nervous system (CNS) cancers followed by CNS cancer ( $n = 2$ ). The remaining of two studies included both groups of patients with CNS and non-CNS ( $n = 2$ ) cancers. The reported types of non-CNS cancers varied including the lung, hematologic, breast, gastrointestinal, and melanoma [Table 1].

### Caregiver characteristics and the associations with a patient's cognitive function

#### Mental health

Caregiver mental health is defined as an optimal level of emotional/psychological functioning, wherein caregivers report no caregiving-related stress.<sup>[38]</sup> Four studies examined the associations between a caregiver's mental health and a patient's cognitive function [Table 2]. These studies found that a caregiver's mental health was associated with cognitive function of adults with cancer.<sup>[36,38-40]</sup> Patients with nonbrain tumors (e.g., lung or breast) showed greater

Table 1: Study characteristics

Author (year), Country	Study design	Sample (n)	Patients			CG		
			Age, mean (SD)	Education level (%): Years, mean (SD)	Type of cancer	Age, mean (SD)	Variables	Relationship with patients (%)
Owensworth et al. (2009) <sup>[1]</sup> , Australia	Cross-sectional	(63) CG of patients with brain tumor and other cancers	≥ 18 years	NR	Brain tumor and other cancers	CG of patients with brain tumor: 56.93 (12.34) CG of patients with others: 62.47 (10.67)	Depression	CG of patients with brain tumor Spouse/partner: 85.2% Parent: 11.1% Child: 3.7% Sibling: 0% CG of patients with other cancer Spouse/partner: 91.7% Child: 5.5% Sibling: 2.8%
Owensworth et al. (2010) <sup>[2]</sup> , Australia	Cross-sectional	(63) CG of patients with brain tumor and other cancers	≥ 18 years	NR	Brain tumor and other cancers	60.1 (11.7)	Psychological well-being	Spouse/partner: 88.8%
Hocking et al. (2011) <sup>[3]</sup> , USA	Multiple, in-depth case study	(3) adults survivors with childhood brain tumors and mothers	19 years 24 years 26 years	NR; College graduate; specialized high school graduate	Brain tumor	NR	Family functioning, perceived demands, and QOL	Mother: 100%
Boele et al. (2013) <sup>[4]</sup> , Netherland	Secondary analysis	(396) CG of patients with LGG, NHL/CLL, HGG, and NSCLC	≥ 18 years	NR	LGG, NHL/CLL, HGG, and NSCLC	CG of patients with LGG: 45.27 (11.94) CG of patients with NHL/CLL: 52.96 (11.94) CG of patients with HGG: 53.31 (11.43) CG of patients with NSCLC: 57.23 (11.75)	Mental health	CG of patients with LGG Spouse/partner: 71.4% Parent: 11.3% Child: 2.3% Sibling: 1.4% Friend: 0.9% CG of patients with NHL/CLL Spouse/partner: 90.9% Sibling: 2.0% Parent: 1.0% Child: 1.0% Friend: 1.0% CG of patients with HGG Spouse/partner: 78.2% Friend: 10.9% Parent: 3.6% Sibling: 1.8% Child: 0% CG of patients with NSCLC Spouse/partner: 86.2% Child: 6.9% Sibling: 3.4% Friend: 0% Parent: 0%
Gao et al. (2013) <sup>[5]</sup> , USA	Secondary analysis	(221) patients with advanced cancer and their CG	59.5 (12.4)	12.4 (3.8)	Lung, colon, pancreatic, other gastrointestinal, breast, and other	51.4 (14.1)	Demographic: race/ethnicity and relationship with patients	Spouse/partner: 47.8% Child: 26.3% Other: 25.9%
Meyer et al. (2013) <sup>[6]</sup> , USA	Secondary analysis	(356) patients with advanced cancer and their CG	≥ 20 years	NR	Lung, colon, pancreatic, other gastrointestinal, breast, and other	NR	Preloss mental health	Spouse/partner and others
Kim et al. (2014) <sup>[7]</sup> , Korea	Cross-sectional	(136) patients with advanced cancer and their family CG	56 (median)	High school or less: 86.3% College or over: 13.7%	Lung, stomach, colon/rectum, breast, esophagus, and others	52 (median)	Attitude toward disclosure	Spouse/partner: 61.2% Parents or offspring: 29.8% Other family members: 9%
Hocking et al. (2015) <sup>[8]</sup> , USA	Cross-sectional	(34) brain tumor survivors and their mothers	23.53 (3.36)	NR	Brain tumor	53.74 (5.67)	Family functioning	Mother: 100%
Libert et al. (2017) <sup>[9]</sup> , Belgium	Cross-sectional	(166) patients with hematologic malignancies	≥ 65 years	Junior high school or less: 63% High school graduation or more: 37%	Hematologic malignancies	NR	Burden	NR

Contd...

Table 1: Contd...

Author (year), Country	Study design	Sample (n)	Patients			CG		
			Age, mean (SD)	Education level (%): Years, mean (SD)	Type of cancer	Age, mean (SD)	Variables	Relationship with patients (%)
Saria et al. (2017) <sup>[10]</sup> , USA	Cross-sectional	(56) CG of patients with brain metastases	> 18 years	NR	Breast, lung, melanoma, and other cancers	56.3 (14.9)	Coping and Resilience	Spouse: 67.9% Son/daughter: 16.1% Parent: 5.3% Brother/sister: 3.6% Son-in-law/daughter-in-law: 1.8%

LGG: Low-grade glioma, NHL/CLL: Non-Hodgkin lymphoma/chronic lymphatic leukemia, HGG: High-grade glioma, NSCLC: Non-small-cell lung cancer, QOL: Quality of life, SD: Standard deviation, NR: Not reported, CGs: Caregivers

CI when their caregivers had poorer overall psychological well-being ( $r = 0.46, P < 0.005$ ),<sup>[38]</sup> and were more depressed ( $r = -0.40, P < 0.005$ ).<sup>[39]</sup> However, among brain tumor patients, no associations were identified between a caregiver’s depression and cognitive function of a patient diagnosed with brain tumor.<sup>[39]</sup> In comparison, in the total caregiver sample (caregivers of patients with brain tumor and nonbrain cancers), greater CI was observed among patients who received care from caregivers with poorer overall psychological well-being ( $r = 0.38, P < 0.005$ ).<sup>[38]</sup>

Two studies supported the association between a caregiver’s mental health and cognitive function of adults with cancer.<sup>[36,40]</sup> Adults with high-grade glioma and non-small-cell lung cancer reported decline in their subjective cognitive functioning ( $r^2 = 0.050, P = 0.090$ ) and overall cognition ( $r^2 = 0.363, P = 0.019$ ), respectively, when their significant others (i.e., caregivers) exhibited poor mental health.<sup>[40]</sup> Consistent with this finding, cognitive function of adults with advanced cancer showed the associations between their caregivers’ preloss mental health.<sup>[36]</sup> For example, significant CI was found among the patients whose caregivers had major depressive disorder (MDD) (odds ratio [OR] 6.88,  $P = 0.02$ ). However, among those attending bereaved caregiver groups, no associations were found between a patient’s CI and a caregiver’s postloss MDD.

**Family functioning**

Family functioning is defined as mutuality/closeness of the relationship within a family environment.<sup>[41]</sup> The associations between a patient’s cognitive function and family functioning was described in two studies<sup>[42,43]</sup> [Table 2]. Hocking et al.<sup>[42]</sup> conducted an intensive case analysis using quantitative measures and qualitative interviews obtained from three dyads of adult survivors with childhood brain tumors and their mothers. Of these, one patient demonstrated intact cognition, but the other two did not. The patient with intact cognition reported good levels of family functioning and so did her mother. However, one of two patients with CI expressed conflicts among family, and her mother also endorsed negative family functioning.

Interestingly, this was contradicted by the last patient with CI. He showed significant CI across all domains, but data obtained from both the patient and his mother suggested positive family functioning.

Another study conducted on 34 patient-caregiver dyads also indicated that worse patient-reported family functioning was associated with their poorer processing speed ( $r = -0.42, P < 0.05$ ), working memory ( $r = -0.35, P < 0.05$ ), long-term verbal memory ( $r = -0.35, P < 0.05$ ), and executive function ( $r = -0.39, P < 0.05$ ), respectively.<sup>[43]</sup> A similar pattern of the associations was noted between a patient’s cognitive function and mother-reported family functioning. A poor family functioning reported by mothers was significantly associated with a patient’s poor processing speed ( $r = 0.55, P < 0.01$ ), working memory ( $r = 0.39, P < 0.01$ ), long-term verbal memory ( $r = 0.43, P < 0.01$ ), mental flexibility ( $r = 0.55, P < 0.01$ ), and executive function ( $r = 0.39, P < 0.01$ ).

**Family adaptation to the patient’s illness**

Family adaptation reflects the process of how family members adjust or accommodate their roles and responsibilities to various stressors such as the patient’s illness.<sup>[44]</sup> One study described a patient’s cognitive function and family adaptation to the patient’s illness by using data obtained from three dyads of brain tumor survivors and their mothers<sup>[42]</sup> [Table 2]. Two patients showed impairments in their cognitive function, although one patient had intact cognition. A mother of the patient with intact cognition indicated positive family adaptation and showed confidence that she could deal with the patient’s illness. This patient also described her family as “backbone and support.” In contrast, qualitative data obtained from a patient with impaired cognitive function and her mother showed that they have been struggling to adapt to the patient’s illness. Her mother also expressed regret regarding a previous decision about her daughter’s treatment and admitted negative family adaptation to her daughter’s illness. Contrary to this, the other patient who had significant CI reported positive family adaptation to his illness. His mother even expressed appreciation for the

Table 2: Characteristics of studies regarding caregiver variables in relation to the Patient's cognitive function

Author (year)	Sample (n)	CG variables	Cognitive domains (measures)	Analysis adjust for	Key findings
<b>Mental health</b>					
Owensworth <i>et al.</i> (2009) <sup>[1]</sup>	63 CGs of patients with brain cancer (27) and other cancers (36)	Depression assessed by DASS	Subjective cognitive deficits (PCRS)	Patients' cancer type and CGs' gender	In other cancer groups, patients' cognitive function was significantly associated with the level of CGs' depression ( $r = -0.40, P < 0.05$ ), but no association in the brain cancer group
Owensworth <i>et al.</i> (2010) <sup>[2]</sup>	63 CGs of patients with brain cancer (27) and other cancers (36)	Psychological well-being assessed by WHOQOL-BREF	Subjective cognitive deficits (PCRS)	CGs' gender	In other cancer groups, patients' cognitive function was significantly associated with CGs' psychological well-being ( $r = 0.46, P < 0.005$ ) In brain cancer group, patients' cognitive function was not associated with CGs' psychological well-being In total CG sample, patients' cognitive function was significantly associated with CGs' psychological well-being ( $r = 0.38, P < 0.005$ )
Boele <i>et al.</i> (2013) <sup>[4]</sup>	396 significant others of patients with LGG (213), NHL/CLL (99), HGG (55), and NSCLC (29)	Mental health assessed by MCS of SF-36 health survey	Subjective cognitive functioning (MOS subjective cognitive scale) Overall cognitive function (assessed by both objective neuropsychological testing and self-report questionnaires)	CGs' age and education level	Patients' subjective cognitive functioning exhibited a significant association with mental health of significant others with HGG ( $r^2 = 0.050, P = 0.090$ ) Patients' cognition was associated with mental health of significant others with NSCLC ( $r^2 = -0.363, P = 0.019$ )
Meyer <i>et al.</i> (2013) <sup>[6]</sup>	356 patients with advanced cancer and their CGs	Mental health assessed by the structured clinical interview for DSM-IV disorders	Subjective cognitive functioning (SPMSQ)	Patients' white race and self-efficacy	Patients' cognitive deficits were significantly associated with their CGs' preloss MDD ( $OR = 6.88, P = 0.02$ )
<b>Family functioning</b>					
Hocking <i>et al.</i> (2011) <sup>[3]</sup>	3 adults survivors with childhood brain tumors and their mothers	Family functioning assessed by FAD GFS and semi-structured qualitative interviews	Working memory (digit span, letter-number sequencing) Processing speed (WAIS-IV) Verbal learning and memory (CVLT-II) Executive function (TMT, tower test from D-KEFS, and self-report version of the BRIEF-A)	N/A	Case 1: Patient's cognitive functioning is overall intact, and her mother also reported good levels of family functioning Case 2: Patient showed significant cognitive deficits, and both patient and her mother reported moderate difficulties related to family functioning Case 3: Patient showed cognitive deficits, and both patient and his mother reported positive family functioning
Hocking <i>et al.</i> (2015) <sup>[8]</sup>	34 pediatric brain tumor survivors and their mothers	Family functioning assessed by FAD and PEDS QL family impact module	Working memory (digit span, letter-number sequencing) Processing speed (WAIS-IV) Verbal learning and memory (CVLT-II) Executive function (TMT, D-KEFS)	NR	Poorer neurocognitive outcomes in brain tumor survivors were associated with worse survivor-reported family function ( $r = 0.35-0.53, P < 0.01$ ) Poorer neurocognitive outcomes in brain tumor survivors were associated with worse mother-reported family function ( $r = 0.39-0.55, P < 0.01$ )
<b>Adaptation to the patient's illness</b>					
Hocking <i>et al.</i> (2011) <sup>[3]</sup>	3 adults survivors with childhood brain tumors and their mothers	Adaptation to the patient's illness assessed by semi-structured qualitative interviews	Working memory (digit span, letter-number sequencing) Processing speed (WAIS-IV) Verbal learning and memory (CVLT-II) Executive function (TMT, tower test from D-KEFS, and self-report version of the BRIEF-A)	N/A	Case 1: Patient's neurocognitive functioning is overall intact, and her mother showed a positive adaptation to the patient's illness Case 2: Patient showed limited cognitive function, and her mother endorsed difficulties in adapting to the patient's illness Case 3: Patient demonstrated significant cognitive deficits but positive family adaptation to the illness was reported by his mother
<b>Attitude toward disclosure to the patient's illness</b>					
Kim <i>et al.</i> (2014) <sup>[7]</sup>	136 patients with advanced cancer and their family CGs	Family CGs' attitude toward disclosure assessed by asking questions authors developed	Subjective cognitive functioning (EORTC QLQ-C30)	NR	Patients' cognitive function was associated with family CGs' positive attitude toward disclosure of disease progression ( $P = 0.02$ )
<b>Burden</b>					
Libert <i>et al.</i> (2017) <sup>[9]</sup>	166 patients with hematologic malignancies	Burden assessed using a proxy measure of CG burden (100-mm VAS)	Subjective cognitive functioning (fact-cog)	NR	Patients' perceived cognitive impairment was associated with patient's self-perceived burden to their primary CGs ( $\beta = 0.211, P = 0.004$ )

Contd...

Table 2: Contd...

Author (year)	Sample (n)	CG variables	Cognitive domains (measures)	Analysis adjust for	Key findings
Coping and resilience					
Saria et al. (2017) <sup>[10]</sup>	56 CGs of patients with brain metastasis from solid tumors	Coping assessed by cope inventory Resilience assessed by resilience scale	Memory (RMBC)	NR	Less occurrence of memory problems was found in patients with cancer when their CGs used acceptance coping ( $r=0.31, P<0.05$ ) The occurrence of memory problems was negatively associated with CGs' resilience ( $r=-0.30, P<0.05$ )
Demographic characteristics					
Gao et al. (2013) <sup>[5]</sup>	221 patients with advanced cancer and their CGs	Demographic characteristics: Race/ethnicity and relationship with each patient	Subjective cognitive functioning (SPMSQ)	NR	Greater cognitive impairment was associated with patients who had nonwhite CGs (black: OR=2.06, $P<0.04$ ; Hispanic: OR=6.31, $P<0.001$ ) and CGs who were not a spouse/partner (child: OR=2.04, $P=0.04$ )
LGG: Low-grade glioma, NHL/CLL: Non-Hodgkin lymphoma/chronic lymphatic leukemia, HGG: High-grade glioma, NSCLC: Non-small-cell lung cancer, DASS: Depressive symptom anxiety stress scale, WHOQOL-BREF: World health organization quality-of-life scale, MCS: Mental component summary, SF-36: Short form-36, FAD GFS: General functioning scale from family assessment device, QOL: Quality of life, PEDS QL: Pediatric quality of life inventory, VAS: Visual analogue scale, PCRS: Patient competency rating scale, MOS: Medical outcome survey, SPMSQ: Short portable mental status questionnaire, CVLT-II: California verbal learning test-second edition, TMT: Trail making test, D-KEFS: Delis-Kaplan executive function, BRIEF-A: Behavior rating inventory of executive function - Adult, WAIS-IV: Wechsler adult intelligence scale-fourth edition, EORTC QLQ-C3: European organization for research and treatment of cancer QOL questionnaires, RMBC: Revised memory and behavioral problem checklist, N/A: Not applicable, NR: Not reported, MDD: Major depressive disorder, CGs: Caregivers, OR: Odds ratio, DSM-IV: Diagnostic and statistical manual of mental disorders-IV					
1. Ownsworth T, Henderson L, Chambers S, Shum D. Functional impairments and caregiver depressive symptoms in the context of brain tumour and other cancers: A mediating effect of strain. <i>Brain Impairment</i> 2009;10:149-61.					
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6. Meyer F, Zhang B, Gao X, Prigerson HG. Associations between cognitive impairment in advanced cancer patients and psychiatric disorders in their caregivers. <i>Psychooncology</i> 2013;22:952-5.					
7. Kim S, Ko Y, Kwon S, Shin DY, Kim CH, Yang SH, et al. Family caregivers' awareness of illness and attitude toward disclosure during chemotherapy for advanced cancer. <i>Psychooncology</i> 2014;23:1300-6.					
8. Hocking MC, Hobbie WL, Deatrick JA, Hardie TL, Barakat LP. Family functioning mediates the association between neurocognitive functioning and health-related quality of life in young adult survivors of childhood brain tumors. <i>J Adolesc Young Adult Oncol</i> 2015;4:18-25.					
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10. Saria MG, Courchesne N, Evangelista L, Carter J, MacManus DA, Gorman MK, et al. Cognitive dysfunction in patients with brain metastases: Influences on caregiver resilience and coping. <i>Support Care Cancer</i> 2017;25:1247-56.					

treatment that her son had received and reported that he and his family has been adapting well to his illness.

#### Attitude toward disclosure of the patient's illness

Attitude toward disclosure of the patient's illness refers to a caregiver's position on discussing an illness-related topic with the patient.<sup>[45]</sup> Some caregivers may show a positive attitude toward discussing disease progression with their patients, but others may not. A study conducted by Kim et al.<sup>[45]</sup> indicated that patients demonstrated better cognitive function when their family caregivers showed positive attitudes toward disclosure of the illness ( $P = 0.02$ ).

#### Burden

Caregiver burden occurs when caregivers feel overwhelmed as a result of providing care, and this feeling differs from depression, anxiety, and other emotional responses.<sup>[46]</sup> One study investigated a patient's guilt and concerns that caregiving may interfere with their primary caregivers' life and health (i.e., a patient's self-perceived

burden on primary caregiver [SPB-PC]) and its association with a patient's cognitive function. This study showed that a patient's cognitive function can be associated with SPB-PC<sup>[47]</sup> [Table 2]. For example, greater impairments in cognitive function were reported by patients when SPB-PC was higher ( $\beta = 0.211, P = 0.004$ ).

#### Coping and resilience

Coping is defined as the strategies that caregivers use when caring for their patients;<sup>[20]</sup> this is often classified as follows: problem-focused, emotion-focused, dysfunctional, or others. One study reported the associations between a patient's cognitive function and caregiver coping<sup>[48]</sup> [Table 2]. For example, lower incidence of memory problems was noted in patients with cancer when their caregivers used acceptance coping ( $r = 0.31, P < 0.05$ ). In the same study, authors also investigated a caregiver's resilience, a caregiver's ability to cope with stressors,<sup>[49]</sup> and examined their associations with a patient's cognitive function. Consistent with previous finding, lower incidence of

memory problems was noted when their caregivers were more resiliency ( $r = -0.30, P < 0.05$ ).

### Demographic characteristics

Gao *et al.*<sup>[37]</sup> examined the associations between cognitive function in patients with advanced cancer and the patients' and caregivers' preferences on the intensity of end-of-life care. In a subanalysis of data from their primary study, they showed a patient's cognitive function was associated with caregiver demographic characteristics, especially their race/ethnicity and relationship with the patient. Patients with advanced cancer tended to demonstrate greater CI when their caregivers were nonwhite [Table 2] (white: Ref, black: OR 2.06,  $P < 0.04$ ; Hispanic: OR 6.31,  $P < 0.001$ ) and not a spouse/partner (spouse/partner: Ref, child: OR 2.04,  $P = 0.04$ ).

## Discussion

A total of 10 studies met inclusion criteria and informed this review. Seven categories of caregiver characteristics were identified including mental health, family functioning, adaptation toward the illness, attitude toward disclosure of the illness, burden, coping and resilience, and demographic characteristics. Sixty percent of the studies ( $n = 6$ ) were designed as cross-sectional, followed by secondary analysis ( $n = 3$ ) and case study ( $n = 1$ ). Except for brain cancer group, the included studies ( $n = 10$ ) showed the significant associations between caregiver characteristics and a patient's cognitive function. This suggests the need to view the patient-caregiver dyad as a unit of care [Figure 2]. The model we adopted from Northouse *et al.*'s<sup>[29]</sup> provided a useful framework for understanding the associations between a patient's cognitive function and caregiver characteristics.

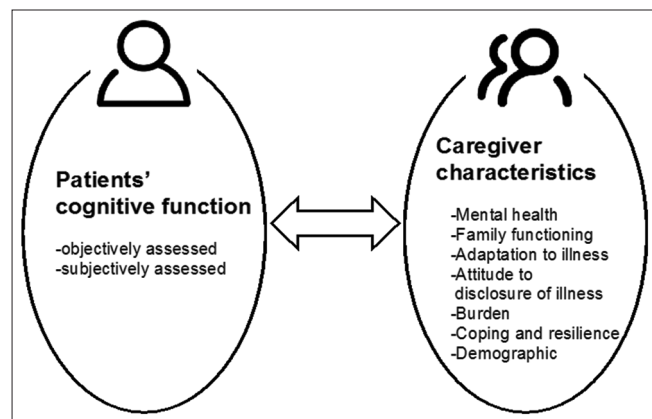
Mental health was the most studied caregiver characteristic that showed an association with a patient's

cognitive function. Since none of included studies reported the impact of caregiver mental health on a patient's cognitive function, mental health can be concluded as an associated factor, but not an influencing factor.<sup>[36,38-40]</sup> Family functioning reported by caregivers most frequently reported characteristic correlated with patients' cognitive function.<sup>[42,43]</sup> Poor cognitive function was noted when the patient's family members did not function well. Furthermore, caregivers' positive adaptation to the illness<sup>[42]</sup> and attitude toward disclosures to the patients' illness<sup>[45]</sup> were also found to be associated with a patient's positive cognitive function. Similarly, positive cognitive function was noted when caregivers were resilient and used certain types of caregiver coping strategies such as acceptance.<sup>[48]</sup> Conversely, greater patients' CI were found as caregiving burden was higher, which was assessed from the proxy perspective (i.e., patients' perspectives).<sup>[47]</sup> Finally, caregivers' race/ethnicity and their relationship with the patient (e.g., spouse) were also reported to associate with patients' cognitive function.<sup>[37]</sup>

In this review, the reporting of the results was summarized by associated caregiver characteristics of patients' cognitive function. This information is an essential component of developing dyadic interventions. We found that caregiver's mental health was found to be associated with a patient's cognitive function. This finding indicates that caregiver's mental health is a key characteristic which should be included in interventions offered to the patient-caregiver dyad to improve outcomes of dyads. Both patients with CI and their caregivers would benefit from the intervention to improve caregiver's mental health. These findings also suggest the need for clinicians to assess and monitor caregiver's mental health when they treat a patient's CI. Furthermore, this review paper includes relevant studies across multiple cancer groups and shows an association between a patient's cognitive function and caregiver characteristics. Reviewing caregiver characteristics in relation to cognitive function across a variety of cancer diagnosis allow the identification of a characteristic associated with a certain cancer group versus a characteristic associated across all cancer groups. In turn, this information can be used when creating interventions for each cancer group.

### Limitations

Approximately half of included studies did not report confounding factors and did not adjust for these factors (e.g., sociodemographic).<sup>[37,43,45,47,48]</sup> This is an important limitation because the associations between caregiver characteristics and a patients' cognitive function could differ depending on confounding factors. Thus, it is important to report and adjust for confounding factors using statistical methods.



**Figure 2:** A model of the associations between a patient's cognitive function and caregiver characteristics, which was adapted Northouse *et al.*'s (2012)



The result of this review showed varying association between cognitive function and family adaptation to the patient's illness.<sup>[42]</sup> For example, one patient with intact cognition reported positive family adaptation, and another patient with impaired cognitive function reported negative family adaptation. However, other patients with CIs reported positive family adaptation, which was contradicted by two included cases. This inconsistency may be due to the characteristics of case study research aiming to collect a of variety cases that reflect complex aspects of a certain phenomenon.<sup>[50]</sup> Although this may limit the understanding of the associations between cognitive function and family caregiver characteristics, we included this study because it showed that they could be related.

Another limitation is that all included studies assessed the associations between caregiver characteristics and patient's cognitive function crosssectionally. To fully understand the impact of caregiver characteristics on a patient's cognitive function, alternative designs such as a longitudinal study are needed. We also included the study that assessed patients' self-perceived burden on their caregivers and considered it a substitute (proxy) for caregiver burden.<sup>[47]</sup> Using a proxy instead of a direct measure is not considered to provide an accurate assessment of a behavior (or concept).<sup>[51]</sup> However, as this scoping review aimed to explore potential caregiver characteristics associated with a patient's cognitive function, we included this article in our final sample.

### Implications

This study indicates that additional research is needed. Specifically, more comprehensive studies are needed to better examine the associations between a patient's cognitive function and caregiver characteristics to guide the development of interventions for adults with cancer who experience impaired cognitive function. CI has been assessed as a condition influenced by the patients themselves; however, this review suggests that patients' CI can also be associated with (or influenced by) outside sources, such as the caregiver's mental health or coping. Since no causal relationship has been identified, future research is warranted to investigate these associations longitudinally. A longitudinal study will provide insights into whether a caregiver's mental health influences the severity of a patient's CI. This understanding will advance the knowledge of cognitive function and be the foundation for more precise and effective dyadic interventions that will improve outcomes for both patients and their caregivers in the context of cognitive function.

### Conclusion

This scoping review summarized current evidence concerning caregiver characteristics that are associated

with a patient's cognitive function. Of the identified caregiver characteristics, caregivers' mental health was most identified, followed by family functioning, adaptation to the patients' illness, attitude toward disclosure to the patient's illness, burden, coping and resilience, and demographic characteristics. Given these review findings, future research needs to consider the type of measurements and statistical methodologies used when selecting studies. As the number of patients with CI rises, there is a need to concomitantly develop interventions for best practice to support the well-being of this patient population and their caregivers. Enhanced information about CI in relation to caregiver characteristics will eventually provide the foundation for multifocal interventions for patients with impaired cognitive function.

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### Conflicts of interest

There are no conflicts of interest.

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Appendix A: Search strategy

Set number	Query
<b>Database: PubMed</b>	
1	"Neoplasms"[Mesh] OR Cancer[tiab] OR cancers[tiab] OR cancerous[tiab] OR neoplasm[tiab] OR neoplasms[tiab]
2	"Caregivers"[Mesh] OR caregiver[tiab] OR caregivers[tiab] OR caregiving[tiab] OR "care giver"[tiab] OR "care givers"[tiab] OR "care giving"[tiab] OR carer[tiab] OR carers[tiab]
3	"Cognitive Dysfunction"[Mesh] OR "Cognition"[Mesh] OR "Neurodevelopmental Disorders"[Mesh] OR "Executive Function"[Mesh] OR "Cognition Disorders"[Mesh] OR "Attention"[Mesh] OR "Executive Function"[Mesh] OR "Mental Processes"[Mesh] OR "Memory"[Mesh] OR "Spatial Behavior"[Mesh] OR "Psychomotor Performance"[Mesh] OR ((cognition[tiab] OR cognitive[tiab] OR neurocognition[tiab] OR neurocognitive[tiab] OR Neuropsychological[tiab]) AND (disorder[tiab] OR disorders[tiab] OR disability[tiab] OR disabilities[tiab] OR deficiency[tiab] OR deficit[tiab] OR deficits[tiab] OR deficiencies[tiab] OR dysfunction[tiab] OR dysfunctions[tiab] OR impairment[tiab] OR impairments[tiab] OR function[tiab] OR functioning[tiab] OR functions[tiab] OR deterioration[tiab] OR attention[tiab] OR attentions[tiab] OR concentration[tiab] OR concentrations[tiab])) OR "executive function"[tiab] OR "executive functions"[tiab] OR "executive functioning"[tiab] OR "executive control"[tiab] OR "mental processes"[tiab] OR "information processing"[tiab] OR memory[tiab] OR "spatial behavior"[tiab] OR "spatial behaviors"[tiab] OR "spatial learning"[tiab] OR "spatial processing"[tiab] OR "spatial ability"[tiab] OR "spatial abilities"[tiab] OR "psychomotor performance"[tiab] OR "psychomotor ability"[tiab] OR "psychomotor abilities"[tiab] OR "visual motor coordination"[tiab] OR "motor skills"[tiab]
4	# 1 AND #2 AND #3
5	#4 AND English[lang] NOT (animals[mh] NOT humans[mh]) NOT (("Adolescent"[Mesh] OR "Child"[Mesh] OR "Infant"[Mesh]) NOT "Adult"[Mesh])
<b>Database: CINHAL</b>	
1	(MH "Neoplasms+") OR TI (Cancer OR cancers OR cancerous OR neoplasm OR neoplasms) OR AB (Cancer OR cancers OR cancerous OR neoplasms OR carcinoma OR carcinomas OR Oncology OR oncologic)
2	(MH "Caregivers") OR (MH "Caregiver Attitudes") OR (MH "Caregiver Burden") OR (MH "Caregiver Support") OR TI (caregiver OR caregivers OR caregiving OR "care giver" OR "care givers" OR "care giving" OR carer OR carers) OR AB (caregiver OR caregivers OR caregiving OR "care giver" OR "care givers" OR "care giving" OR carer OR carers)
3	(MH "Cognition+") OR (MH "Cognition Disorders+") OR (MH "Attention+") OR (MH "Mental Processes+") OR (MH "Memory+") OR (MH "Spatial Behavior+") OR (MH "Psychomotor Performance+") OR (MH "Executive Function") OR TI(((cognition OR cognitive OR neurocognition OR neurocognitive OR Neuropsychological) AND (disorder OR disorders OR disability OR disabilities OR deficiency OR deficit OR deficits OR deficiencies OR dysfunction OR dysfunctions OR impairment OR impairments OR function OR functioning OR functions OR deterioration)) OR "executive function" OR "executive functions" OR "executive functioning" OR "executive control" OR "mental processes" OR "information processing" OR memory OR "spatial behavior" OR "spatial behaviors" OR "spatial learning" OR "spatial processing" OR "spatial ability" OR "spatial abilities" OR "psychomotor performance" OR "psychomotor ability" OR "psychomotor abilities" OR "visual motor coordination" OR "motor skills") OR AB(((cognition OR cognitive OR neurocognition OR neurocognitive OR Neuropsychological) AND (disorder OR disorders OR disability OR disabilities OR deficiency OR deficit OR deficits OR deficiencies OR dysfunction OR dysfunctions OR impairment OR impairments OR function OR functioning OR functions OR deterioration)) OR "executive function" OR "executive functions" OR "executive functioning" OR "executive control" OR "mental processes" OR "information processing" OR memory OR "spatial behavior" OR "spatial behaviors" OR "spatial learning" OR "spatial processing" OR "spatial ability" OR "spatial abilities" OR "psychomotor performance" OR "psychomotor ability" OR "psychomotor abilities" OR "visual motor coordination" OR "motor skills")
4	# 1 AND #2 AND #3
5	#4 AND LA English and limited to all adult
<b>Database: Embase</b>	
1	'neoplasm'/exp OR Cancer: ti, ab OR cancers: ti, ab OR cancerous: ti, ab OR neoplasm: ti, ab OR neoplasms: ti, ab
2	'caregiver'/exp OR caregiver: ti, ab OR caregivers: ti, ab OR caregiving: ti, ab OR 'care giver':ti, ab OR 'care givers':ti, ab OR 'care giving':ti, ab OR carer: ti, ab OR carers: ti, ab
3	'cognition'/de OR 'executive function'/de OR 'attention'/de OR 'mild cognitive impairment'/de OR 'mental function'/de OR 'memory'/de OR 'psychomotor performance'/de OR 'spatial behavior'/de OR 'executive function':ti, ab OR 'executive functions':ti, ab OR 'executive functioning':ti, ab OR 'executive control':ti, ab OR 'mental processes':ti, ab OR 'information processing':ti, ab OR memory: ti, ab OR 'spatial behavior':ti, ab OR 'spatial behaviors':ti, ab OR 'spatial learning':ti, ab OR 'spatial processing':ti, ab OR 'spatial ability':ti, ab OR 'spatial abilities':ti, ab OR 'psychomotor performance':ti, ab OR 'psychomotor ability':ti, ab OR 'psychomotor abilities':ti, ab OR 'visual motor coordination':ti, ab OR 'motor skills':ti, ab OR cognition: ti, ab OR ((cognitive: ti, ab OR neurocognition: ti, ab OR neurocognitive: ti, ab OR Neuropsychological: ti, ab) AND (disorder: ti, ab OR disorders: ti, ab OR disability: ti, ab OR disabilities: ti, ab OR deficiency: ti, ab OR deficit: ti, ab OR deficits: ti, ab OR deficiencies: ti, ab OR dysfunction: ti, ab OR dysfunctions: ti, ab OR impairment: ti, ab OR impairments: ti, ab OR function: ti, ab OR functioning: ti, ab OR functions: ti, ab OR deterioration: ti, ab OR attention: ti, ab OR attentions: ti, ab OR concentration: ti, ab OR concentrations: ti, ab))
4	# 1 AND #2 AND #3
5	#4 AND [english]/lim AND ((adult)/lim OR [aged]/lim OR [very elderly]/lim) AND [humans]/lim
<b>Database: PsycINFO</b>	
1	DE "Neoplasms" OR DE "Benign Neoplasms" OR DE "Breast Neoplasms" OR DE "Endocrine Neoplasms" OR DE "Leukemias" OR DE "Melanoma" OR DE "Metastasis" OR DE "Nervous System Neoplasms" OR DE "Terminal Cancer" OR TI (Cancer OR cancers OR cancerous OR neoplasm OR neoplasms) OR AB (Cancer OR cancers OR cancerous OR neoplasm OR neoplasms)
2	(DE "Caregivers") OR TI (caregiver OR caregivers OR caregiving OR "care giver" OR "care givers" OR "care giving" OR carer OR carers) OR AB (caregiver OR caregivers OR caregiving OR "care giver" OR "care givers" OR "care giving" OR carer OR carers)

Contd...

## Appendix A: Contd...

## Set number Query

## Database: PsycINFO

- 3 DE "Cognitive Impairment" OR DE "Cognition" OR DE "Cognitive Ability" OR DE "Spatial Ability" OR DE "Verbal Ability" OR DE "Neurodevelopmental Disorders" OR DE "Disruptive Behavior Disorders" OR DE "Emotional and Behavioral Disorders" OR DE "Learning Disorders" OR DE "Executive Function" OR DE "Cognitive Processes" OR DE "Attention" OR DE "Memory" OR DE "Forgetting" OR DE "Tip of the Tongue Phenomenon" OR DE "Long Term Memory" OR DE "Memory Decay" OR DE "Short Term Memory" OR DE "Spatial Memory" OR DE "Verbal Memory" OR DE "Visual Memory" OR DE "Motor Skills" OR TI(((cognition OR cognitive OR neurocognition OR neurocognitive OR Neuropsychological) AND (disorder OR disorders OR disability OR disabilities OR deficiency OR deficit OR deficits OR deficiencies OR dysfunction OR dysfunctions OR impairment OR impairments OR function OR functioning OR functions OR deterioration)) OR "executive function" OR "executive functions" OR "executive functioning" OR "executive control" OR "mental processes" OR "information processing" OR memory OR "spatial behavior" OR "spatial behaviors" OR "spatial learning" OR "spatial processing" OR "spatial ability" OR "spatial abilities" OR "psychomotor performance" OR "psychomotor ability" OR "psychomotor abilities" OR "visual motor coordination" OR "motor skills") OR AB(((cognition OR cognitive OR neurocognition OR neurocognitive OR Neuropsychological) AND (disorder OR disorders OR disability OR disabilities OR deficiency OR deficit OR deficits OR deficiencies OR dysfunction OR dysfunctions OR impairment OR impairments OR function OR functioning OR functions OR deterioration)) OR "executive function" OR "executive functions" OR "executive functioning" OR "executive control" OR "mental processes" OR "information processing" OR memory OR "spatial behavior" OR "spatial behaviors" OR "spatial learning" OR "spatial processing" OR "spatial ability" OR "spatial abilities" OR "psychomotor performance" OR "psychomotor ability" OR "psychomotor abilities" OR "visual motor coordination" OR "motor skills")
- 4 #1 AND #2 AND #3
- 5 #4 AND LA English and adult

## Database: Scopus

- 1 TITLE-ABS-KEY (Cancer OR cancers OR cancerous OR neoplasm OR neoplasms)
- 2 TITLE-ABS-KEY (cargiver OR caregivers OR caregiving OR "care giver" OR "care givers" OR "care giving" OR carer OR carers)
- 3 TITLE-ABS-KEY ("executive function" OR "executive functions" OR "executive functioning" OR "executive control" OR "mental processes" OR "information processing" OR memory OR "spatial behavior" OR "spatial behaviors" OR "spatial learning" OR "spatial processing" OR "spatial ability" OR "spatial abilities" OR "psychomotor performance" OR "psychomotor ability" OR "psychomotor abilities" OR "visual motor coordination" OR "motor skills" OR ((cognition OR cognitive OR neurocognition OR neurocognitive OR Neuropsychological) AND (disorder OR disorders OR disability OR disabilities OR deficiency OR deficit OR deficits OR deficiencies OR dysfunction OR dysfunctions OR impairment OR impairments OR function OR functioning OR functions OR deterioration OR attention OR attentions OR concentration OR concentrations))
- 4 #1 AND #2 AND #3
- 5 #4 Limited to English language

## Database: Sociological Abstracts

- 1 MAINSUBJECT.EXACT.EXPLODE("Cancer") OR TI (Cancer OR cancers OR cancerous OR neoplasm OR neoplasms) OR AB (Cancer OR cancers OR cancerous OR neoplasm OR neoplasms)
- 2 TI (cargiver OR caregivers OR caregiving OR "care giver" OR "care givers" OR "care giving" OR carer OR carers) OR AB (cargiver OR caregivers OR caregiving OR "care giver" OR "care givers" OR "care giving" OR carer OR carers)
- 3 MAINSUBJECT.EXACT.EXPLODE("Cognition") OR MAINSUBJECT.EXACT.EXPLODE("Cognitive Functioning") OR MAINSUBJECT.EXACT.EXPLODE("Attention") OR MAINSUBJECT.EXACT.EXPLODE("Memory") OR MAINSUBJECT.EXACT.EXPLODE("Spatial Behavior") OR TI(((cognition OR cognitive OR neurocognition OR neurocognitive OR Neuropsychological) AND (disorder OR disorders OR disability OR disabilities OR deficiency OR deficit OR deficits OR deficiencies OR dysfunction OR dysfunctions OR impairment OR impairments OR function OR functioning OR functions OR deterioration)) OR "executive function" OR "executive functions" OR "executive functioning" OR "executive control" OR "mental processes" OR "information processing" OR memory OR "spatial behavior" OR "spatial behaviors" OR "spatial learning" OR "spatial processing" OR "spatial ability" OR "spatial abilities" OR "psychomotor performance" OR "psychomotor ability" OR "psychomotor abilities" OR "visual motor coordination" OR "motor skills") OR AB(((cognition OR cognitive OR neurocognition OR neurocognitive OR Neuropsychological) AND (disorder OR disorders OR disability OR disabilities OR deficiency OR deficit OR deficits OR deficiencies OR dysfunction OR dysfunctions OR impairment OR impairments OR function OR functioning OR functions OR deterioration)) OR "executive function" OR "executive functions" OR "executive functioning" OR "executive control" OR "mental processes" OR "information processing" OR memory OR "spatial behavior" OR "spatial behaviors" OR "spatial learning" OR "spatial processing" OR "spatial ability" OR "spatial abilities" OR "psychomotor performance" OR "psychomotor ability" OR "psychomotor abilities" OR "visual motor coordination" OR "motor skills")
- 4 #1 AND #2 AND #3
- 5 #4 AND LA English

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- 1 Exact("skin cancer" OR "colorectal cancer" OR "esophageal cancer" OR "ovarian cancer" OR "uterine cancer" OR "breast cancer" OR "thyroid cancer" OR "brain cancer" OR "cervical cancer" OR "genital cancers" OR "kidney cancer" OR "lung cancer" OR "testicular cancer" OR "pancreatic cancer" OR "prostate cancer" OR "bone cancer" OR "endometrial cancer" OR "cancer" OR "liver cancer" OR "oral cancer" OR "head & neck cancer") OR TI (Cancer OR cancers OR cancerous OR neoplasm OR neoplasms) OR AB (Cancer OR cancers OR cancerous OR neoplasm OR neoplasms)
- 2 TI (cargiver OR caregivers OR caregiving OR "care giver" OR "care givers" OR "care giving" OR carer OR carers) OR AB (cargiver OR caregivers OR caregiving OR "care giver" OR "care givers" OR "care giving" OR carer OR carers)

Contd...

Appendix A: Contd...

Set number Query

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3	Exact("memory" OR "cognition & reasoning" OR "recognition") OR TI(((cognition OR cognitive OR neurocognition OR neurocognitive OR Neuropsychological) AND (disorder OR disorders OR disability OR disabilities OR deficiency OR deficit OR deficits OR deficiencies OR dysfunction OR dysfunctions OR impairment OR impairments OR function OR functioning OR functions OR deterioration)) OR "executive function" OR "executive functions" OR "executive functioning" OR "executive control" OR "mental processes" OR "information processing" OR memory OR "spatial behavior" OR "spatial behaviors" OR "spatial learning" OR "spatial processing" OR "spatial ability" OR "spatial abilities" OR "psychomotor performance" OR "psychomotor ability" OR "psychomotor abilities" OR "visual motor coordination" OR "motor skills") OR AB(((cognition OR cognitive OR neurocognition OR neurocognitive OR Neuropsychological) AND (disorder OR disorders OR disability OR disabilities OR deficiency OR deficit OR deficits OR deficiencies OR dysfunction OR dysfunctions OR impairment OR impairments OR function OR functioning OR functions OR deterioration)) OR "executive function" OR "executive functions" OR "executive functioning" OR "executive control" OR "mental processes" OR "information processing" OR memory OR "spatial behavior" OR "spatial behaviors" OR "spatial learning" OR "spatial processing" OR "spatial ability" OR "spatial abilities" OR "psychomotor performance" OR "psychomotor ability" OR "psychomotor abilities" OR "visual motor coordination" OR "motor skills")
4	# 1 AND #2 AND #3
5	#4 AND LA English