

THE IMPACT OF INFORMAL CANCER CAREGIVING: A LITERATURE REVIEW ON PSYCHOPHYSIOLOGICAL STUDIES

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Abstract

Objectives: Caregiving can be experienced as a stressful process, that can cause psychological and physical consequences. The combination of prolonged stress and the physical demands of caregiving may impair the physiological functioning of caregivers and increase the risk of health problems creating considerable stress in the life of caregivers regarding emotional, physical, social and financial areas.

Method: This literature review explored studies that used measures of the autonomic nervous system in caregivers of oncology patients such as electrodermal and cardiovascular (re)activity.

Results: The results revealed that caregivers had elevated stress levels and a serious autonomic imbalance that may, in the long term, trigger negative health consequences such as infectious diseases, cancer progression, cardiovascular disease, and even premature death.

Conclusions: The results showed the need to carry out preventive strategies in this population, in order to improve the autonomic profile of caregivers of cancer patients.

Keywords: Informal caregivers; Cancer; Peripheral Measures; Autonomic Nervous System.

INTRODUCTION

Since prehistoric times, the provision of informal care has been the main source of protection for individuals dealing with health problems (Lebel et al., 2001). Although caregivers have always had a socioeconomic value to society, in the future they will be even more important due to the growing number of elderly and the high prevalence of chronic diseases (Shilling, Matthews, Jenkins, & Fallowfield, 2016). The act of caring is based on personal and cultural values that give meaning to caregiving (Yamaguchi, Cohen, & Uza, 2016). For this reason, it is not uncommon for caregivers to report positive experiences, such as more intimate relationships, more empathy with others and greater appreciation of life (Mosher et al., 2017; Young & Snowden, 2017). However, caring for a family member with cancer is a challenging experience that requires an adjustment to change (Teskereci &

Kulakac, 2018), adaptation to daily care tasks and to a new lifestyle (Elis et al., 2017). Moreover, they usually need to establish a relationship and communicate with health professionals (Oh, 2017), understand medical information (Mosher, Ott, Hanna, Jalal & Champion, 2017) and, in cases of advanced cancer, suffer with the imminent loss of the loved one (Kuo et al., 2017).

Caregiving can be a stressful experience, with potentially negative consequences on both psychological and physical levels. In terms of psychological outcomes, several reviews and meta-analyses showed a higher prevalence of psychiatric disorders, particularly disorders of anxiety and depression, in caregivers, when compared to controls (Cochrane, Goering, & Rogers, 2007; Pruchno & Potashnik, 1989; Schulz, O'Brien, Bookwala, & Fleissner, 1995). In fact, compared to other contexts of care, the caregiving process in the oncology context presents distinct features. Despite the variability in the available studies in terms of caregivers' and patients' characteristics, cancer caregivers are usually younger, provide care for shorter periods of time (but in an intense way) and care for patients with a wide variety of physical and emotional symptoms as a consequence of multimodal therapies (Kent et al., 2016). For all of these reasons, the provision of care in oncology can create considerable stress in the lives of caregivers, affecting caregivers' physical health, immune function, health behaviors, mental health, social activities and relationships, finances and work (Lambert, Levesque, & Girgis, 2016). In the context of terminal illness, caregivers face the dual challenge of providing care and having to deal with anticipatory grief.

At a physiological level, research also suggests that the combination of prolonged stress and the physical demands of caregiving may impair the physiological functioning of caregivers and increase the risk of health problems (Kiecolt-Glaser, Glaser, Gravenstein, Malarkey, & Sheridan, 1996; Schulz et al., 1997). Therefore, caregiving can be considered a risk factor for impairing physical health, since it can trigger a cascade of stress responses through the activation of the hypothalamic-pituitary-adrenal and the sympathetic adrenal-medullary axes involving hormonal, immune, cardiovascular and metabolic disorders (Grant, 1999; Vitaliano et al., 2002).

Some studies have shown that caregivers tend to present a higher cardiovascular reactivity (Lee, Colditz, Berkman, & Kawachi 2003; Mausbach, Patterson, Rabinowitz, Grant, & Schulz, 2007). Also, caregivers tend to have a poorer immune response compared to non-caregivers that is not caused by nutritional factors, sleep or other health problems (Kiecolt-Glaser et al., 1996). Moreover, in the presence of mental or emotional strain, caregiving has been associated with an increased mortality risk (63% higher in comparison to non-caregiving controls) (Schulz & Beach, 1999). In addition, caregivers are much less likely to have time to rest when they are ill, time to practice exercise, or to get adequate sleep (Burton et al., 1997).

The study of physical outcomes in the provision of informal care is limited essentially to the physiological functioning of caregivers of elderly and/or people with dementia (Etters, Goodall, & Harrison, 2008; Pinquart & Sörensen, 2003; Vitaliano, Zhang, & Scanlan, 2003). In a literature review carried out by Schulz, Visintainer, and Williamson (1990), only 11 of the 34 studies reviewed were focused on the physical health of the caregiver, and only one study included physiological measures. In other review that included 40 studies (Schulz et al., 1995), researchers found that caregivers had more chronic diseases and drug consumption than non-caregivers although other studies found no differences on these outcomes. These results highlighted the need of using physiological measures in the study of care providers. According to Vitaliano and colleagues (2003), physiological measures can certainly help to explain the associations between care and disease. Indeed, the physiological measures may show associations with the caregiver's experiences much earlier than chronic diseases.

Psychophysiology opened the doors for a deeper understanding and explanation of some human phenomena. Based on the organization of the nervous system, psychophysiological techniques may be divided into three broad categories (Stern, Ray, & Quigley, 2001): (1) those dealing with the activity of the central nervous system, such as electroencephalography, the evoked potentials, the electrical activity of the brain, the location of the source dipole, and based imaging methods (e.g., positron emission tomography, functional magnetic resonance imaging of the brain, regional cerebral

blood flow); (2) those measuring the activity of the somatic nervous system, such as electromyography, electro-oculogram, and the measurements of respiratory activity; and (3) those measuring the activity of the autonomic nervous system, which include techniques such as electrodermal activity, electrocardiography, plethysmography, and electrogastrography.

Considering the objectives of this paper, the measures that will be explored in more detail are two measures of the autonomic nervous system namely the electrodermal activity (skin conductance) and the cardiovascular activity (mainly heart rhythm). The electrodermal activity (EDA) is an important indicator of the activation of the autonomic nervous system (Dawson, Schell, & Filion, 2017), being sensitive to events with high emotional and cognitive impact (Sequeira, Hot, Silvert, & Delplanque, 2009). Specifically, skin conductance (SC) is highly associated with the activity of the sympathetic nervous system (Arangüena & Dorado, 2000), and it is a particularly useful measure in the evaluation of emotional reactivity (Orr & Kaloupek, 1997). Heart rate (HR) and blood pressure (BP) are two cardiovascular measures commonly used in psychophysiology (Berntson, Quigley, Norman, & Lozano, 2017; Orr & Kaloupek, 1997). Cardiovascular activity (CA) differs according to psychological aspects due to emotional changes, and it is therefore an important autonomic physiological variable (Arangüena & Dorado, 2000). An increasing body of evidence suggests that excessive cardiovascular reactivity to mental stress is a risk factor for the development of coronary artery disease and hypertension (Blascovich & Katkin, 1993; Treiber et al., 2003).

Electrodermal and cardiovascular reactivity have been recognized as being associated with atherosclerosis, hypertension, and other cardiovascular and immune disorders (e.g., Cacioppo et al., 1995; Jennings et al., 2004; Kronholm, Hyypä, Jla, & Toikka, 1996; Matthews, Salomon, Brady, & Allen, 2003; Powell et al., 2013). The use of these two measures has spread also due to their non-invasive characteristics and reduced cost when compared to measures of the central nervous system. In addition, these peripheral measures have the advantage of avoiding some of the common problems

in the interpretation of the results obtained, presented in other complex techniques of measurement of the central nervous system.

Having as background some of the principles, methods and practices of psychophysiology, this paper addresses the psychobiological stressors associated with the provision of care in caregivers of patients with cancer. Specifically, in this review we aimed to summarize the available evidence regarding the psychophysiological functioning (in terms of electrodermal and cardiovascular activity) among caregivers of patients with cancer in order to improve our knowledge regarding potential psychophysiological pathways through which cancer caregiving influences caregivers' illness outcomes.

Method

Eligibility criteria

Full-text research articles published in English or Portuguese that included at least one measure to assess psychophysiological functioning (in terms of electrodermal and cardiovascular activity) in adult caregivers of patients with cancer were eligible. Quantitative, qualitative, mixed-method studies, and reviews were eligible. Studies assessing other indicators of psychophysiological functioning (other than electrodermal and cardiovascular activity) and case-control or intervention studies (i.e., studies evaluating psychophysiological functioning after participation in a psychosocial intervention) were excluded.

Search strategy

Database searches were conducted for articles published from inception up to 2018 in Medline, CINAHL, ERIC, and Psychology & Behavioral Sciences Collection. Searches in these databases were supplemented by additional manual searching in Google. The key search terms used were: "cancer",

“oncology”, “caregiver”, “caregiving”, “career”, “physiology”, “psychophysiology”. Titles and abstracts were assessed for eligibility by one researcher. Doubts were discussed with other researchers.

RESULTS

A total of 203 articles were identified. From these 27 were excluded because were duplicates and 169 because were not relevant to the current review topic (see Figure 1).

Insert Figure 1

The abstracts of the remaining 7 studies were screened and evaluated. From these 2 were excluded (1 was an intervention study and 1 did not include indicators of psychophysiological functioning assessed in this review). A total of 5 studies exploring the psychophysiological responses associated with informal cancer caregiving were included in this review. All studies examined cardiovascular reactivity (namely blood pressure and heart rate) and only one study examined electrodermal reactivity. Along with these measures, studies explored also psychological outcomes. Two studies explored the link between psychophysiological functioning and depression; anxiety, family functioning, perceptions of stress, quality of life, burden and post-traumatic stress disorder symptoms were also explored.

Since few studies were found, results from included studies were also related to studies from other caregiving contexts and from the broad psychophysiological literature to better understand the results. Results were divided into two groups: one focused on electrodermal (re)activity and other focused on cardiovascular (re)activity. The following information was extracted: author/study period, study objectives, participants, design/type of study, measure used to assess psychophysiological responses, variables associated, statistical analysis, and main findings (see Table 1).

Electrodermal (Re)Activity in Caregivers

Research studies exploring the EDA of cancer caregivers are extremely scarce. Only one cross-sectional experimental study conducted with caregivers of cancer patients was found (Teixeira & Pereira, 2014). In this study, psychological as well as psychophysiological measures were collected in order to explore differences on these measures among cancer caregiving and controls (controls included adult children without a chronically ill parent recruited at a university). Two matched groups, with 78 participants each (parental cancer vs. control) were used. EDA and cardiovascular (presented later) responses were recorded after pictures visualization. Physiological data were collected using the Physiolab software and the visual stimuli used were drawn from the International Affective Picture System. The authors found significant differences on skin conductance for all types of pictures. Specifically, the parental cancer group presented a higher skin conductance suggesting a higher arousal for this group, confirming the initial hypotheses that there were differences among the two groups in terms of psychophysiological reactivity.

Other studies with care providers within other contexts may be taken as a focus of interest. For example, although this is not a 'typical' study with care providers, Stampler, Wall, Cassisi, and Davis (1997) conducted a research on the premise that spouses may inadvertently contribute to the maintenance of the patient's pain behaviors. Based on existing literature, the authors hypothesized that individuals respond with physiological arousal when they see others in pain, and that the magnitude of these responses in spouses of patients with pain varies according to their level of marital satisfaction. To this end, the researchers collected data from 26 couples, in which one of the partners suffered from chronic low back pain. The authors examined marital satisfaction and care of the spouse (in terms of physiological responses) during marital interactions regarding the topic 'pain'. The strengthening of

the pain behavior by the spouse was named 'solicitude' that, in turn, seemed to have an impact on marital satisfaction. At the level of SC, the study showed that spouses less satisfied with their marital relationship showed higher SC in comparison to spouses more satisfied with it (Stamper et al., 1997).

Thompson and colleagues (2004) conducted a comparative study in terms of gender and emotional and biological responses of the caregiver spouses of patients with Alzheimer in terms of psychosocial, physiological and immunophenotypic parameters. Male spouses caregivers showed significantly lower levels of stress, depression, subjective burden, anxiety, anger-hostility and somatic symptoms, as well as higher levels of mental health, sense of coherence, number of NK cells, and better physical and social functioning. In turn, the wife's caregivers showed higher counts of T-helper cells (Th) and less NK cells than husbands' caregivers. Finally, men showed a less intense physiological response to stress, particularly at the HR level and skin temperature. However, at the level of changes in SC, significant differences between men and women were found, although men reported 'feeling' more relaxed than women.

Lewis, Escamilla, and Novian (2008) conducted a study with cultural and gender implications on emotional responses of Mexican-American family caregivers of patients with Alzheimer compared to Caucasians caregivers (male and female) in terms of psychosocial, physiological and immunological variables. Caucasian male caregivers showed better outcomes in positive psychosocial health indicators (i.e., quality of life, sense of coherence, general health, social functioning and vitality), and lower results in negative indicators (i.e., stress, anxiety, depression, somatization and subjective burden). As for the physiological and immune measures, the results remained with Caucasians caregivers presenting a higher percentage of NK cells, and a smaller SC, before a cognitive stimulation.

More recently, Moya-Albiol and colleagues (2011) studied the reactivity to stress, in the laboratory, analyzing SC in caregivers (parents) of people with autism spectrum disorders, based on the assumption that these individuals may show a different physiological response due to their specific situation, characterized by a continuous state of alert. To such purposes, the authors compared a group

of 44 caregivers (i.e., parents of children with autism spectrum disorders) and 42 controls (i.e., parents of children without autism spectrum disorders) in performing a set of different mental tasks. They continuously recorded two indices of the SC: response and level. The results showed that caregivers showed a lower EDA reactivity to mental stress, when compared to controls, with a stronger effect for men. Although controversial, these results may reflect a lower reactivity to stressful situations from caregivers and, consequently, the loss of a potential adaptive stress response in this population. The authors concluded that the results reflected an idiosyncratic emotional situation of caregivers of individuals with an autistic spectrum disorder due to the special conditions they were subjected to (e.g., concerns about the future of their children and characteristics of the care, including number of hours providing care and caregiving being shared or not).

Cardiovascular (Re)Activity in Caregivers

The association between psychological morbidity and CA in adult children of cancer patients has received few attention from the investigation. Lucini and colleagues (2008) conducted an observational study aiming to explore if stress indicators and indices of CA would be altered in cancer caregivers. The study included 58 cancer caregivers and 60 matched-controls (i.e., healthy volunteers, who denied any kind of stressful condition). Blood pressure, electrocardiogram (ECG) and respiratory activity were recorded using a wireless radiotelemetry system and Finapres device. The results showed an increase in cardiac activity sympathetically. It is important to note that these caregivers were assessed at the early stage of the disease suggesting that caregiving may have a fast psychophysiological impact.

In the literature review performed by Sherwood and colleagues (2008) few studies examining the interaction between the bio-behavioral responses to stress and the caregiving were found. For these authors, the physiological responses are considered “adaptive” in the initial reaction to an acute stress situation (e.g., a diagnosis of primary malignant brain tumor and their initial treatments). However,

when it becomes a chronic situation (e.g., due to factors such as the prolonged treatment and disease progression), the production of hormones such as the cortisol can lead to changes in the cardiovascular and immune systems, compromising the overall physical health status of the individual. In this sense, the most frequent changes in the cardiovascular system were associated with an increased peripheral and vascular resistance hypertension. Weitzner, Haley and, Chen (2000) also found in their review that caregivers of older cancer patients usually reported an increase in BP associated with complex experiences in caregivers of cancer patients, in a context of constant concern, loss, grief, conflict, guilt and resentment, leading to an enhanced state of psychological morbidity.

More recently, the study of Corà, Partinico, Munafò, and Palomba (2012) aimed to examine psychological and cardiovascular responses in terminal cancer caregivers. Psychological variables (depression and mood disorders, anxiety and anger) and CA (i.e., cardiovascular risk, blood pressure, and heart rate) were assessed in 20 caregivers and compared with matched control group (healthy individuals similar in age and sex). Physiological measures were assessed using a validated automatic BP device at rest over 2 weeks (in order to deal with BP and HR variability). As expected, cancer caregivers reported higher levels of depression, state anxiety, and more sleep dysfunctions in comparison to controls. They also experienced heightened systolic and diastolic blood pressure. In this study, elevation of HR was associated with a longer duration of care. Although in this study BP and HR have been recorded at rest conditions, some extensive literature indicates that these parameters at rest, although not clinically relevant, are important cardiovascular risk precursors (Cook, Togni, Schaub, Wenaweser, & Hess, 2006; Cooney et al, 2010; Fox et al., 2007, Gu, Burt, Paulose-Ram, Yoon & Gillum, 2008; Palatini, 2009; Palatini & Julius, 1997). Finally, Teixeira and Pereira (2014) with a sample of 78 cancer caregivers found that this group of caregivers showed higher CA (in terms of HR) while visualizing standardized pictures with different emotional valences.

A high risk of cardiovascular disorders can be associated with sleep disorders (Mausbach et al., 2007; McCurry, Logsdon, Teri & Vitiello, 2007), and can be modulated by the emotional state of

the caregiver, the quality of the relationship between the caregiver and the receiver of care, the requirements of the care, as well as the perception of social support (Shaw et al., 2003; Uchino, Kiecolt-Glaser, & Cacioppo, 1992). Hypertensive caregivers also express an increased cardiovascular reactivity (BP and HR) before acute stressors (Vitaliano, Russian, Bailey, Young, & McCann, 1993).

Shaw and colleagues (1999), using a longitudinal design, evaluated the stress response in 144 spouses/caregivers of patients with Alzheimer's disease and a control group of 47 participants (i.e., demographically equivalent non-caregiving controls), in order to understand if belonging to the first group increased the probability of exceeding BP (in the beginning of the study, 33% of caregivers and 30% of controls were receiving antihypertensive treatment). Systolic and diastolic BP was assessed every six months during 2 to 6 years, so that researchers could determine in which group there was an increased risk of developing hypertension. Additionally, the authors intended to determine whether this increased risk was linked to variables such as the extent of assistance provided, patient problem behaviors, or caregiver distress. The results showed that the risk of reaching borderline hypertension values were higher in caregivers than in the control group.

Later, the same team conducted a new longitudinal study over seven years, where they semiannually recorded the BP levels in a sample of 111 caregivers of spouses of Alzheimer patients. Furthermore, they evaluated the requirements of care, emotional expressiveness, social desirability and hostility. The results showed that the risk of developing hypertension, in older caregivers, was linked to the perceived stress (intensified when they had to handle more dementia behavior and difficulties in carrying out daily activities) and to a lower emotional expression (Shaw et al., 2003).

Other authors have attempted to study the apparent relationship between cardiovascular comorbidity and the caregiver function of a family member with a chronic illness. Von Känel and colleagues (2006) studied this relationship through a high coagulation status (associated with the appearance of thrombosis) of blood as a physiological response to chronic stressors resulting from providing care for a family with Alzheimer's disease. The sample consisted of 54 spouses, and beyond

the physiological assessment associated with a pro- coagulant, the authors conducted a structured interview to identify stress factors not related to the act of caring. The results showed that the daily stress, combined with the chronic stress of providing care to a family with Alzheimer's disease, might cause a state of hypercoagulability, contributing to an increased likelihood of coronary heart disease and mortality in this population.

Mausbach and colleagues (2005) found that depressive symptoms may exaggerate the adrenergic response (elevated baseline plasma levels of noradrenaline) in caregivers of patients with Alzheimer's, possibly leading to an allostatic load (McEwen, 2006). This could lead to a predisposition to negative health consequences, including cardiovascular morbidity.

Some researches have also focused on possible differences in terms of physiological reactivity, considering the variable 'race'. For example, Knight and McCallum (1998) evaluated the cardiovascular reactivity to stress and indicators of depression, anxiety and two positive assessment measures on tension, in 110 Caucasian caregivers and 44 African-Americans caregivers. The latest have generally revealed a higher use of positive revaluations. Both groups showed an increased cardiac reactivity in a cognitive task related to the variable "history of care". In the Caucasian sample, the researchers found a positive association between depression and cardiac reactivity, in both stress inducing situations. However, in the African-American sample, this relationship was reversed in the variable 'history of care', leading researchers to conclude that there were cultural differences between caregivers, affecting the emotional and physical reactions to stressful situations. More recently, Wilcox, Bopp, Wilson, Fulk, and Hand (2005) also examined this variable in a sample of 28 women (16 Caucasian and 12 African-American) caregivers of a family member with dementia, in order to search for psychosocial and psychophysiological differences, considering the caregivers' race. The results showed a greater cardiac reactivity in African-American caregivers as well as higher levels of salivary cortisol and psychological distress, than in the Caucasian caregivers.

Schrag, Hovris, Morley, Quinn, and Jahanshahi (2006) studied the effect of caregiving in family members of patients with Parkinson in terms of physical and mental health. In a sample of 123 caregivers, they assessed depressive symptoms and factors associated with the burden. At the same time, BP values were also measured. The results indicated that 40% of caregivers (66% females) exhibited health changes (hypertension), as well as increased levels of depression and impairment of social life.

In another context, Soares (2009) investigated psychosocial variables and physiological reactivity in 120 caregivers of drug addicts and 36 controls (i.e., healthy non-caregivers), using visual stimuli with emotional content. The main results in physiological variables showed lower levels of HR in caregivers without burden. Caregivers with post-traumatic stress disorder (PTSD) showed higher levels of cortisol. In turn, the duration of caregiving (> 17 years) was associated with higher levels of HR and cortisol. However, the results for SC were not significant.

Discussion

The aim of this review was to summarize the available evidence about the psychophysiological functioning of caregivers of patients with cancer. Overall, the results of this review suggest that cancer caregivers, in comparison to controls, present higher electrodermal and cardiovascular reactivity (Corá et al., 2012; Lucini et al., 2008; Teixeira & Pereira, 2014). While few studies have been included in this review, this pattern of results is in line with previous research conducted with caregivers outside of the cancer context (e.g., Moya-Albiol et al., 2012).

Moreover, results seem to suggest that cancer caregiving may have detrimental consequences for the psychophysiological functioning not only during long-term care (Corá et al., 2012; Shaw et al., 1999) but also during short periods of care. Indeed, in the Lucini et al. study (2008), caregivers of patients with cancer an altered psychophysiological functioning in the early stage of the disease suggesting that caregiving may have a fast impact on psychophysiological functioning. However,

Sherwood and colleagues (2008) highlight the 'adaptive' nature of psychophysiological alterations during the initial reaction to an acute stress situation.

While the included studies did not control for the potential moderator or mediator role of sociodemographic and psychological variables on the link between caregiver stress and psychophysiological functioning, studies within other caregiving contexts (e.g., chronic pain or autism) suggested that gender (Moya-Albiol et al., 2012) or marital satisfaction (Stampller et al., 1997) may interfere with this link. These results seem to suggest that the impact of cancer caregiving on psychophysiological functioning may depend on contextual factors.

Conclusions, limitations and implications for practice and research

Caring for sick family members is a physically and psychologically stressful task engendering stress that might compromise the emotional health and endorse multiple risks to the body. Different studies with family caregivers, from different clinical settings (cancer, Alzheimer, Parkinson, autism) have found, through physiological measures, that stress reactivity is associated with an increased electrodermal and cardiovascular activity, thus contributing to the increased risk of cardiovascular disease and immune suppression.

It is important to keep in mind, however, that this review has some limitations. First, the sample of this review is small since only five studies were included and the design of the studies varied greatly. This evidences that the physiological impact of cancer caregiving remains understudied. Most studies were cross-sectional or reviews. For these reasons, caution is needed in interpreting results since causality cannot be derived. While all of the quantitative studies used a control group, they included small sample sizes, which limits our conclusions. Moreover, one of the studies employed an experimental task to examine physiological functioning among cancer caregivers, which means that these physiological functioning may not be true in a non-experimental environment. Second, only English and Portuguese published studies were included. This may lead to some reporting biases since

some relevant studies may be missed because they were not published or were not present in traditional outlets.

Despite these limitations, this review provides important research implications. First, it suggests that more studies are needed to examine the physiological impact of cancer caregiving since we only found 5 studies. Second, because studies suggest a heightened electrodermal and cardiovascular activity within this context, future studies should further explore not only these indicators, but also other physiological indicators (e.g., respiratory activity, temperature or neuronal activity). Also, longitudinal studies should be conducted in order to explore changes over time in the process of adaptation to the caregiving task and the long-term impact of caregiving related physiological changes for the physical health of caregivers.

Also, important clinical implications are identified to improve the care provided to family caregivers as second-order patients who also need and deserve care. While more studies are needed, findings suggest that cancer caregivers are at increased risk for physiological changes and, consequently, have a higher risk for developing chronic diseases and/or have their immune system functioning compromised. Thus, this paper shows how important is for health professionals to address the psychosocial needs of family caregivers to reduce caregivers' burden, prevent physical and mental illness, and improve their quality of life.

For these reasons, psychological and psychophysiological symptoms should be screened as part of the routine care provided by health care professionals. Moreover, from a prevention point of view, psychosocial support should be provided to cancer caregivers in an early phase of the caregiving process in order to avoid the development of psychophysiological symptoms. Gender performs an important role on caregiving, with females being more vulnerable to stress. This confirmation has also important clinical implications, so that female caregivers can warrant even greater attention from health professionals. Interventions should therefore be gender specific, such as self-help groups or psycho-educational stress management groups for female caregivers.

Finally, physiological variables in the context of other chronic illnesses should be explored targeting not only patients and caregivers, but also health professionals, particularly those with higher levels of burnout. From a heuristic point of view, this type of investigation would have important practical implications, regarding the design of interventions that could meet formal and informal caregivers' specific needs.

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Figure 1. Flowchart of literature search.

Author's Version