



# Caregivers burden in palliative care patients: a problem to tackle

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## Purpose of review

To revise the family caregiver's burden concept and to understand the implications for the patient, family and healthcare system. We analyzed recent literature in three main areas: the role of family caregiver at the end of life, the family caregiver's burden and the involvement of social care networks.

## Recent findings

The family caregiver often accepts the caring as a natural action, presumably imposed by the society. A recent review described seven main roles of care which, according to family system and society, consist of different tasks and activities. To assume this role is not stress free. It is likely to develop a 'burden' by the assumed task.

## Summary

Family members who are close to the patient may play the role of caregiver, well-being enhancer, diversity of tasks fulfiller, minimizer and managing suffering, palliative care facilitator and responsible for the continuity of care, apprentice and participant of health teams. The family caregiver often gives priority to the problems of his dependent family member, becoming almost 'invisible' to the health system. It should also be considered the relevance of this issue into future bereavement process. Considering all these aspects, the family caregiver is often considered by the healthcare teams as 'overall tasks' performers'.

## Keywords

burden, family caregivers, palliative care

## INTRODUCTION

The inclusion of relatives and family caregivers into an integrated care approach represents a basic feature of palliative care. The family caregiver's perspective on the patient's symptom burden is usually integrated in symptom assessment and palliative care treatment decisions [1].

However, many palliative care professionals are still not prepared to implement strategies for effective interventions in this field. This might be because of lack of training and research on interventions focused on family caregivers, as well as the fact that working families who simultaneously assume the role of providing informal care are still not seen as a priority [2<sup>\*\*\*</sup>]. Moreover, studies in this area are mostly focused on cancer patient's caregivers and little information is known about non-cancer patient's family caregiver.

It is universally admitted that patients have three basic needs: security, integrity and sense of life; sense of belonging. Most parts of these needs can be satisfied by the family caregiver, especially because of the intimacy in the relationship shared

with the patient [2<sup>\*\*\*</sup>]. Nevertheless, to assume the role of a family caregiver is not stress free. It is likely to develop a 'burden' by the assumed task. In addition, the family caregiver often gives priority to the problems of his dependent family member, becoming almost 'invisible' to the health system. The relevance of this issue into future bereavement process should also be considered [3<sup>\*\*\*</sup>].

Much work remains to be done in the area of family caregiver empowerment. Palliative care teams can take an essential role as it is the primary objective of their work to promote suffering relief to patients and family caregivers [2<sup>\*\*\*</sup>]. Few studies have examined the associations between family caregiver

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## KEY POINTS

- The role of family caregiver is still poorly supported by society, health teams and family systems.
- To assume the role of family caregiver is not stress free, and it is likely to develop a 'burden' by the assumed task; generally, they are women, who are negatively affected in their QoL becoming almost 'invisible' to the health system.
- Becoming the family caregiver is fortuitous, caring tasks are gradually assumed, without programming and sometimes with lack of information.
- The family caregiver was associated with decision-making, assuming the role of 'Decider at the end-of-life'.
- Integrated knowledge about the family caregiver can facilitate good clinical and psychosocial practices, particularly in palliative care settings in which the family provides and receives healthcare at the same time.

emotional situation and length of stay in palliative care including grief prevention [4<sup>22</sup>]. Integrated knowledge about family caregivers can facilitate good clinical and psychosocial practices, particularly in palliative care settings in which the family provides and receives healthcare at the same time [2<sup>22</sup>].

The purpose of this review is to look into the family caregiver burden concept to enlighten the implications for the patient, family and healthcare system. The analysis of the recent literature is separated into three main areas: the role of family caregiver at end of life, the family caregiver's burden and the involvement of social care networks.

### The role of family caregiver at the end of life

The role of 'responsible' caregiver within the patient's family is assumed more prominence by a member of the social-family network, being identified as the 'primary caregiver'. We considered this concept and family caregiver as synonymous regarding their characteristics, even though, it could be played by many different people. This point of view amplifies the caregiver's concept as a social care network.

The family caregiver often accepts the caring as a natural action, presumably imposed by society and perceives to be fulfilling a moral obligation. The role that each caregiver has in society and in the family system consists of different tasks and activities. The analysis in a recent review originated seven main roles of care [2<sup>22</sup>]. Family members who are close to the patient may play the role of caregiver, well-being enhancer, diversity of tasks fulfiller, minimizer and

managing suffering (the patient and himself/herself), palliative care facilitator and responsible for the continuity of care, apprentice and participant of health teams. They also play a controlling role because they often have to make decisions about the sick person concerned that they cannot make themselves. In addition, becoming the family caregiver is something fortuitous, caring tasks are gradually assumed, without forward planning and sometimes with lack of information [5<sup>22</sup>].

It is well known that palliative care support promotes a sense of security and harmony in the continuity of care. To ensure that the family caregiver gives continuity at home, it is relevant that the families get timely information that will help them to participate in the care planning and provision, feeling part of the healthcare team. Some caregivers who were not supported by professionals often lost control of the situation, which was perceived as a negative experience [2<sup>22</sup>].

Moreover, the role of the family caregiver was associated with decision-making, assuming the role of 'Decider at the end-of-life'. This role incites a sense of obligation and at the same time, a feeling of anguish, particularly when these choices refer to medical decisions. Most articles describe that family caregivers are usually women, who are negatively affected in their quality of life (QoL) [2<sup>22</sup>-4,5<sup>22</sup>,6<sup>22</sup>,7]. Despite these findings, these researches do not emphasize enough on the implication of the feminization role of care. The three more relevant characteristics to outline the family caregiver profile in Latin context were female, informal and familiar [3<sup>22</sup>]. Also, female carers tend to have more burnout levels and receive less assistance from other family members [2<sup>22</sup>]. According to other authors, this category of feminization of the role should be framed into a socio-cultural process of the patriarchal mandate order, the inequitable distribution of power, social disparity and different forms of inequity, beyond sex [3<sup>22</sup>].

Most of the researches focused on the description of family caregiver's profiles, instead of concentrating on the development of interventions aiming to assist them to cope with their everyday emotions, instrumental and spiritual issues [2<sup>22</sup>]. In the same way, we pointed out four profiles which could be divided into three dimensions to evaluate: attitudes of the family caregiver toward treatment, perceptions of the family caregiver of the needs and wishes of the patient and evaluation of their own role as family caregiver [7]. The four family caregiver styles identified were: satisfied, potentially vulnerable, overwhelmed and isolated [7].

Previous studies have evaluated different patient's perspectives and their family caregivers,

or other related people. However, less information is known about the specific characteristics of the caregivers' perspective, the impact of frequency and intensity on patient's symptom burden and treatment requirements, as well as possible influential factors [1].

In other qualitative study about the ability of family members to give care, the authors assessed the factors influencing the capacity of a family to take care of an oncology patient in palliative care [8<sup>■</sup>]. Four axes could be identified: the practical, the relational, the internal experience and the health condition. The authors also identified many positive and negative factors that influenced as facilitators or barriers to the care ability [8<sup>■</sup>].

### Family caregiver's burden

It comprises a set of physical, mental and socio-economic problems faced by carers of sick people, affecting their leisure activities, social relationships, friendships, intimacy, freedom and emotional balance, becoming vulnerable from a health point of view [3<sup>■</sup>]. The multifactorial nature of caregiver burden involves social isolation, overload of activities both at home and outside, behavior alteration of family members receiving care, the idea of being exclusively 'responsible' for their family, financial difficulties and employment abandonment, among others [3<sup>■</sup>].

Regarding care of the elderly, it has been estimated as the caregiver's burden from objective and subjective points of view [9]. Subjective burden refers to perceptions and negative emotions, face to the experience of caring. The objective burden is defined as a set of demands and activities that caregivers must attend. The objective load is a parameter of damage of daily life caregivers. These Latin American authors also considered the caregiver's burden in close relation with the Burnout syndrome, which is usually associated with job conditions.

There are many validated tools to assess the family caregiver burden in palliative care. The Zarit scale caregiver burden considers the QoL domain, ability to self-care, social support network and skills to address behavioral and clinical patient care problems [10]. It allows identifying 'no burden' versus 'mild and intense burden', which could be very important to implement proactive interventions. Internationally, in everyday practice, the short version Zarit scale is the most used in palliative care settings. We found more similar outcomes using this tool than other Spanish speaker's authors: 43% intense burden, 24% mild burden and 33% no burden. Having validated tools becomes important allowing the family caregiver burden assessment.

The Zarit scale has been feasible to be implemented without obstacles [3<sup>■</sup>].

Ramirez *et al.* [5<sup>■</sup>] assessed the overall repercussions of caring and identified the impact on the Virginia Henderson 14 basic needs of the family caregiver of chronic and terminal patients. They concluded that in about 75% of the population studied, this role is an experience that leads to a general deterioration in the caregivers' lives, exposing them to suffer disturbances in their basic needs and damaging their integrity. The identified indicators, in a qualitative research, were of help in the holistic evaluation of the family by enabling an early detection of traits that may be of risk to their caring capacity, determining the continuity of the palliative care and/or a possible discharge [8<sup>■</sup>].

### BURDEN-RELATED FACTORS

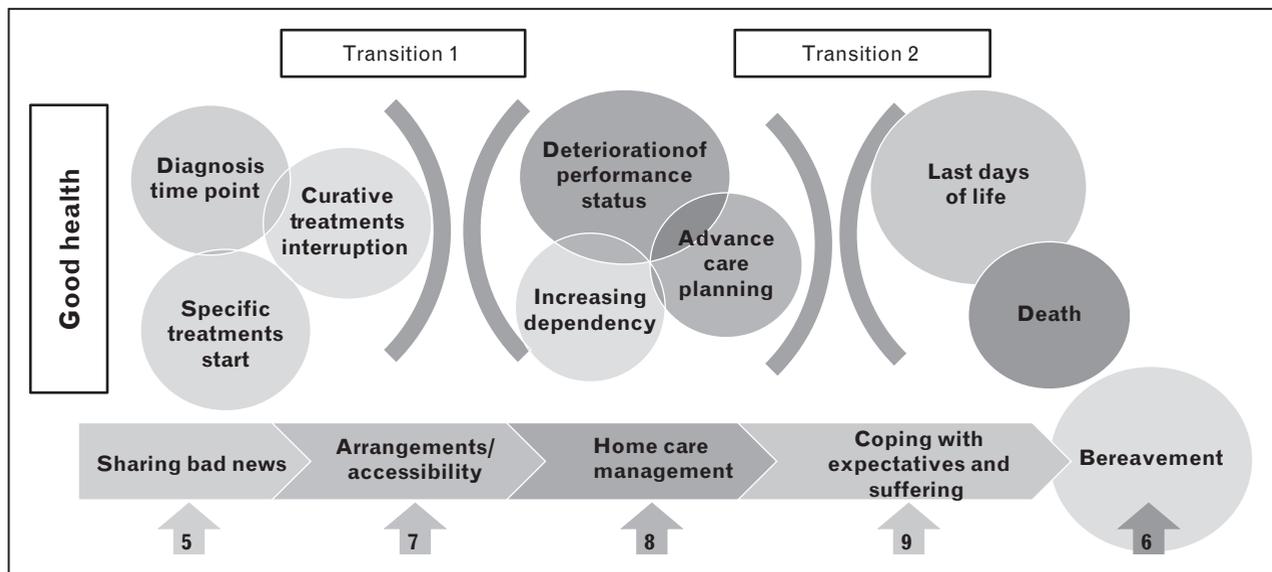
The unexpected presence of the disease within the family is responsible for the outbreak of new occupations and concerns that profoundly affect it [2<sup>■</sup>]. Furthermore, many governments, health schemes and social institutions just offer a little support to the family caregiver increasing the suffering and burden caused by such situations.

Several studies have focused on the possible emotional repercussions that could precipitate a crisis or threat to the family caregiver personal stability. In these cases, to care becomes a stressor whose negative impact is likely to overcharge the family caregiver, developing health problems, physical, mental, social and economic [5<sup>■</sup>].

Three typical illness trajectories and two transitions have been described for patients with progressive chronic illness: cancer, organ failure, the frail elderly and dementia trajectory [11,12<sup>■</sup>,13<sup>■</sup>]. Physical, social, psychological and spiritual needs of patients and their carers are likely to vary according to the trajectory they are following. Being aware of these trajectories may help clinicians plan care to meet their patient's multidimensional needs better, and help patients and carers cope with their situation. On the basis of this description, and the key transitions, we proposed in Fig. 1, five critical time points of care in accordance with these trajectories. It should be necessary to reflect and tackle family caregiver's different experiences and needs in order to prevent burden.

### BURDEN RELATED TO EMOTIONAL ISSUES

The clinical team should enhance the emotional stability of the family, understand the beliefs of each family member and devise appropriate and customized strategies when they want to transmit



**FIGURE 1.** This figure shows five burden critical points in the family caregiver pathway based on the patient's illness trajectory and key transitions.

information [2<sup>11</sup>]. The implementation of good practices and the involvement of the family in the care plan is a crucial reason why information and clarification of medical decisions should be done properly.

Other studies stated the 'primary caregiver syndrome' also known as 'stress in primary caregivers' [14<sup>12</sup>]. It is a syndrome of emotional exhaustion, depersonalization and low personal accomplishment, which can occur among people who work with patients in need of serious attention as in the case of cancer. The description of this syndrome is a combination of fatigue, loss of energy, exhaustion and tiredness.

Kim *et al.* [4<sup>13</sup>] affirm that there is no literature on the association between the palliative care services and the emotional status of the family caregiver. They hypothesize that the significant results for family caregiver emotional status could be partially explained by disparities between the preferences of the family caregiver and patient condition. Becoming aware that death may occur sooner than expected might evoke a feeling of anger or denial. Anxiety or depression might also be expressions indicating acceptance of death. The overall family caregiver's emotional status studied was likely to be a consequence of the delayed response to the deteriorating performance of the patients. A shorter length of stay reflected the relationship between delayed referrals and poorer performance status. Although growing evidence supports that early palliative care leads to greater satisfaction with high-quality care, the referral to palliative care often occurs too late in the cancer trajectory [4<sup>13</sup>].

Sometimes, the approach to the patient can generate the expression of emotions depending on the situation of chronicity or end of life, confronting death and the process of anticipatory grief. It leads to the consequent ambivalence of emotions in the family caregivers [5<sup>14</sup>].

Speaking of seriously ill children, very few authors investigated the psychological care needs of caregivers and their experience during the disease process [6<sup>15</sup>]. Martínez Llorente *et al.* [6<sup>15</sup>] concluded that care at home by a specialized palliative care team decreases the burden and the psychological parent's impact. It also increases the QoL in both parents and children.

## BURDEN RELATED TO SYMPTOMS MANAGEMENT

The first study analyzing three corresponding perspectives of palliative care patients, their family caregiver and their attending palliative care specialists on the patients' symptom burden and the resulting treatment requirement confirmed the high burden of distressing physical and psychological symptoms in patients with advanced cancer [1]. Treatment requirement seems to depend mainly on symptom distress than on intensity or frequency.

Physicians usually tended to underestimate the patients' symptoms, whereas the family caregivers tended toward overestimation. The awareness of these effects seems to be of significant relevance in daily clinical practice. Overall, adequate symptom treatment can only be successful in a close

dialog between patients, their family caregiver and the multidisciplinary palliative care team [1].

## BURDEN RELATED TO ADVANCE CARE PLANNING

Reigada *et al.*'s [2<sup>o</sup>] review remarked the importance of sharing hard decisions as a relevant matter in this field, both for the healthcare teams and for the families. The role of 'decision-making', which is being assumed and/or assigned by the caregivers, results from daily tasks such as deciding when to contact the team, as well as when the family caregiver can refer to more complex and difficult situations such as those related to end of life treatments. The family caregiver can act as surrogates in the decision-making processes and support conversations and interactions between the patient and the physicians.

A qualitative study in neurodegenerative diseases concluded that strategies for effective communication, facilitating advance care planning among patients, their families and practitioners, were essential to improve end-of-life experience [15<sup>o</sup>]. In the absence of advance directives, the family caregiver may be asked to make end-of-life decisions on behalf of patients. Such decision-making has been shown to elicit distress in the family caregiver and does not always lead to decisions in agreement with patients' wishes [15<sup>o</sup>]. Existential distress is well documented among informal caregivers of patients with brain tumors and is a significant driving force of burden. Awareness and acknowledgment of this distress, as well as interventions to ameliorate this suffering, are needed [16<sup>o</sup>].

If the family caregiver is the partner or spouse of the patient, he/she can also help the patient to cope with the disease by addressing needs, maximizing the QoL of the patient, managing the complex care and contributing to decrease hospital/institutional admissions. Considering all these aspects, family caregivers are often considered by the healthcare teams as 'overall tasks' performers' [2<sup>o</sup>]. We also consider that the communication process reinforces the patient's autonomy helping family caregivers to prioritize their wishes when facing the palliative care team.

Advance care planning was also felt to be beneficial for the family caregiver, reducing the decisional burden during the illness and later feelings of regret. These findings are consistent with other qualitative studies on neuromuscular diseases caregivers [15<sup>o</sup>].

Furthermore, family caregivers have expressed the need for being more 'visible' to the healthcare system during consultations and to get their presence and expertise in caring for the patient acknowledgment, but these needs have not always

been met. Although family caregivers were involved in the treatment decision-making, the healthcare system failed to acknowledge their role. They were of great value as partners in patient care, and their effort should not be underestimated by the system [17<sup>o</sup>].

## Social care network

A systematic review has shown that although universally recognized, the role of the family caregiver is still poorly supported by society, health teams and family systems. The palliative care approach argued that the end-of-life care should be monitored and supported by specialized teams as they are trained and focused on pain relief, including the suffering of the family. However, and unintentionally, only material benefits at home (e.g. technical aids) are given to the family caregiver to support them, which can increase their suffering because of their social isolation [2<sup>o</sup>].

Concerning demographic dynamics and increased life expectancy, various forms of family organization and repeated economic crises have transformed the performance of families and intergenerational relationships [18<sup>o</sup>]. López *et al.* [18<sup>o</sup>] support the trajectories of family allowances considering intergenerational relationships. The main definitions of these relationships are reviewed, including moral, emotional and practical imperatives of each generation. The provision of care is organized through the figure of a 'diamond of care' whose four vertices are made up of the family, the state, the market and nongovernmental organizations, figure that seeks to balance resources among its four points and has implications for the caring and being cared for.

The level of perceived support that the family caregiver expressed with regard to hospice availability was necessary for relieving, partially, what is called the 'burden of care'. However, besides supporting the family caregiver, it should be stressed that addressing the responsibility of the health system for providing adequate alternatives to deal with end-of-life care at home is necessary. Otherwise, current end-of-life policies will keep maintaining and reproducing social and sex inequity, and delegating to nongovernmental organizations which they fail to provide [19].

It is important that care occupies a more prominent place on the public agenda, as by keeping it a private, domestic and family issue, any recognition of the rights of both dependents and those of their caregivers is prevented. This deeply affects the recognition of rights of both dependents and those of their caregivers [18<sup>o</sup>]. We strongly agree with the

right to be subject of care, both patients and family caregiver.

## CONCLUSION

Family caregiver burden at end of life care is a complex situation influenced not only by the multiples task of care itself, but also by different kinds of socio-political and cultural issues, beyond the healthcare system limitations and family styles. We concluded that more research and education should be done on family caregiver burden regarding the impact on end of life care, for this right to be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

## REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. Oechsle K, Goerth K, Bokemeyer C, Mehnert A. Symptom burden in palliative care patients: perspectives of patients, their family caregivers, and their attending physicians. *Support Care Cancer* 2013; 21:1955–1962.

2. Reigada C, Pais-Ribeiro JL, Novella A, Gonçalves E. The caregiver role in palliative care: a systematic review of the literature. *Healthcare Curr Rev* 2015; 3:2.

This article is a systematic review of the literature published in English, Portuguese and Spanish between 2006 and 2014. A total of 13 studies were included and described seven major caregiver roles. Setting out the various carer tasks and roles will contribute for the 'family caregiver' agreement concept as well as will recognize their value as a person who needs to be cared too.

3. Tripodoro VA, Veloso V, Llanos V. Sobrecarga del cuidador principal de ■ pacientes en cuidados paliativos. Family caregiver's burden in palliative care patients. *Revista Argumentos*. Instituto de Investigaciones Gino Germani Facultad de Ciencias Sociales. Universidad de Buenos Aires 2015; 17:307–330; Accessed June 2016 <http://publicaciones.sociales.uba.ar/index.php/argumentos/article/view/1324>.

The stated goal of this research was to assess the level of overhead primary caregiver in palliative care patients assisted at a university hospital, using the 'Zarit Scale caregiver burden'. It introduced the concept of burden beyond the task list.

4. Kim SH, Hwang IC, Ko KD, *et al.* Association between the emotional status of ■ the family caregiver and length of stay in a palliative care unit: a retrospective study. *Palliat Support Care* 2015; 13:1695–1700.

This article is intended to address factors associated with referral time to hospice and/or palliative care services and association between these services and the emotional status of the family caregivers. It considers the relevance of family caregivers' emotional status when patients with terminal cancer are referred to palliative care.

5. Ramirez JFV, Grijalva MG, Avilés AGP. Repercusiones del cuidar en las ■ necesidades básicas del cuidador primario de pacientes crónicos y terminales. Repercussions on the primary caregivers' basic needs in chronic and terminal patients. *Medicina Paliativa* 2015; 22:146–151.

This Latin American research assessed the overall repercussions of caring and identified the impact on the 14 basic needs of the primary caregiver of chronic and terminal patients.

6. Martínez Llorente T, Serrano Gallardo P, Del Rincón Fernández C, Martino ■ Alba R. Consequences for the caregiver of a child hospitalized at home in paediatric palliative care. *Medicina Paliativa* 2016; 23:79–92.

This is a descriptive and cross-sectional study of main caregivers of patients treated successively in the pediatric palliative care unit. Caregivers evaluated in this study were overburdened, overload with an impact on quality of life, which, however, did not lead to giving up.

7. Luxardo N, Tripodoro V, Funes M, *et al.* Perfil de cuidadores de enfermos en cuidados paliativos. Caregivers of palliative care home patients. *Medicina (Buenos Aires)* 2009; 69:519–525.

8. Reigada C, Ribeiro E, Novellas A. Capacidades familiares para cuidar de ■ enfermos oncológicos paliativos: un estudio cualitativo. The ability of family members to care palliative cancer patients: A qualitative study. *Medicina Paliativa* 2015; 22:119–126.

This is a broad, qualitative and observational study. The aim of this study was to assess the factors that can influence the capability of a family to take care of an oncology patient in palliative care. The authors concluded that early detection of traits may be of risk to the caring capacity, determining the continuity of the palliative care and/or a possible discharge.

9. De Valle-Alonso MDJ, Hernández-López IE, Zúñiga-Vargas ML, Martínez-Aguilera P. Sobrecarga y Burnout en cuidadores informales del adulto mayor. *Enfermería Universitaria* 2015; 12:19–27.

10. Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: ■ correlates of feelings of burden. *Gerontologist* 1980; 20:649–655.

11. Boyd K, Murray SA. Recognizing and managing key transitions in end of life care. *BMJ* 2010; 341:c4863.

12. Gómez-Batiste X, Martínez-Muñoz M, Blay C, *et al.* Prevalence and ■ characteristics of patients with advanced chronic conditions in need of palliative care in the general population: a cross-sectional study. *Palliat Med* 2014; 4:302–311.

This article points out that direct measurement of prevalence of palliative care needs on a population basis is feasible. Early identification and prevalence determination of these patients are likely to be the cornerstones of palliative care public health policies.

13. Tripodoro VA, De Vito EL. What does end stage in neuromuscular diseases ■ mean? Key approach-based transitions. *Curr Opin Support Palliat Care* 2015; 9:361–368.

This review revised the definition of end stage in the setting of neuromuscular disease (NMD), to understand the implications for the patient, family and health-care team. Also, it emphasized the relevance of an integrated approach through the whole trajectories of NMD patients considering key transitions.

14. Córdova MIP, Canales R, Krederdt S, *et al.* The relationship of the quality of life ■ and burden of informal caregivers of patients with cancer in Lima, Peru. *J Nurs Educ Pract* 2016; 6:36–42.

This study evaluated quality of life the informal cancer patients' caregivers offer to relatives suffering from cancer and determined their relation with the informal cancer work overload. The results described the caregivers group of people with cancer as a vulnerable group and in need of attention. The requirements described are referred to aspects, such as mental and social health.

15. Murray L, Butow PN, White K, *et al.* Advance care planning in motor neuron ■ disease: a qualitative study of caregiver perspectives. *Palliat Med* 2016; 30:471–478.

The authors aimed to investigate caregiver perspectives on the acceptability and impact of advance care planning for patients with motor neuron disease and caregivers. Advance care planning can assist patients to achieve a sense of control and 'peace of mind' and facilitates important family discussion. However, the timing and style of its introduction needs to be approached sensitively.

16. Applebaum AJ, Kryza-Lacombe M, Buthorn J, *et al.* Existential distress among ■ caregivers of patients with brain tumors: a review of the literature. *Neuro Oncol Pract* 2015. [Epub ahead of print]

This is a systematic review of 35 articles that examined any element of existential distress among informal caregivers of patients with brain tumors. Existential distress is well documented among informal caregivers of patients with brain tumors and is a significant driving force of burden. Awareness and acknowledgement of this distress, as well as interventions to ameliorate this suffering, are needed.

17. Lund L, Ross L, Petersen MA, Groenvold M. The interaction between informal ■ cancer caregivers and healthcare professionals: a survey of caregivers' experiences of problems and unmet needs. *Support Care Cancer* 2015; 23:1719–1733.

This study investigated to which extent the cancer caregivers' needs regarding the interaction with healthcare professionals are met and the associations between dissatisfaction with the interaction and socio-demographic and disease-related variables. Prominent problematic aspects included optimal involvement of the caregivers in the patients' disease, treatment and/or care, attention to the caregivers' well being and provision of enough information to the caregivers. The caregivers' dissatisfaction with the interaction with healthcare professionals was pronounced.

18. López E, Findling L, Lehner MP, *et al.* Los cuidados en las familias: Senderos ■ de la solidaridad intergeneracional. Care in families: solidarity paths between generations. *Revista Argumentos*. Publicación del Instituto de Investigaciones Gino Germani Facultad de Ciencias Sociales. Universidad de Buenos Aires 2015; 17:238–256; Accessed June 2016 at <http://publicaciones.sociales.uba.ar/index.php/argumentos/article/view/1321>.

The overall objective of this article was to collaborate with the construction of a theoretical frame and reflect on one of the current debates in the field of care approach: the trajectories of family allowances considering intergenerational relationships. The main definitions of these relationships are reviewed, moral and emotional and practical imperatives of each generation.

19. Luxardo N, Brage E, Alvarado C. An examination of advanced cancer ■ caregivers' support provided by staff interventions at hospices in Argentina. *E Cancer Medí Sci* 2012; 6:281.