

## Caregiver Distress in the Early Phases of Cancer

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**Abstract.** *Background: Principal caregivers (PCs) of cancer patients experience high levels of stress that may significantly impact their quality of life (QoL). PCs' QoL during early phases of the disease (when patients were still on chemotherapy) were assessed. Patients and Methods: The PCs of all patients meeting the inclusion criteria (chemotherapy, performance status 0/1) treated at our institution between June 2007 and March 2008 were asked to answer a dedicated questionnaire. Results: One hundred and four PC-patient pairs participated in the study. Most of the caregivers (52%) spent more than 8 h daily caring for the patient, they also frequently reported the occurrence of new psychosomatic disorders, with the most reported symptoms being sleep disruption (24%), headaches (20%) and asthenia (16%). High levels of anxiety and depression were demonstrated in nearly a quarter of the study subjects. In nearly half of the cases, a substantial increase in monthly family expenses and restriction of recreation activities were reported. The overall gravity of the medical situation was perceived as severe by 86% of the PCs. Conclusion: Demonstrable PC QoL impairment occurs even at early phases of disease, therefore intervention strategies for caregivers should be considered early during cancer treatment.*

Approximately 2,800,000 new cancer cases are registered in Europe every year (1), with a prevalence of 7,300,000 individuals suffering from cancer. The occurrence of such disease in a person's life, similarly to other serious illnesses, determines an immediate impairment in quality of life (QoL) (2). Both relatives and friends, especially if actively involved in the management of the disease (principal caregivers, PCs), are considered to be a group similarly affected by such a tragic event, as they share a common experience that causes distress.

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Cancer, therefore, is able to invalidate not only the QoL of cancer patients, but also that of their closest caregivers (3-7). Previous studies have demonstrated that PCs may experience changes in their social roles, limitations of activities, psychological distress, and impaired physical health due to the burden of caring (8, 9). Moreover, cancer may perturb daily family life and its organisation and affect long-term personal projects (10, 11).

Nonetheless, studies with conflicting results have been published. In a paper by Kim *et al.* (12), significant levels of depressive symptoms in spouses of people with lung cancer were not demonstrated. Even more intriguing, an improvement in self-worth and personal satisfaction while providing care has been reported (13-15). In contrast, other authors assert that depression in PCs may be even more severe than that of the patients themselves. Wagner *et al.*, found that husbands of women with cancer more frequently experienced poorer mental health compared to husbands of women with chronic illnesses other than cancer (16).

QoL is a multidimensional concept, it is therefore reasonable to hypothesize that negative consequences of caregiving may manifest both as physical (*i.e.* pain, fatigue, sleep disturbance) and as psychological (*i.e.* depression, anxiety) symptoms and such symptoms may have a negative impact on the functional status and QoL of PCs, as well as on their ability to provide care. The burden of non-professional caregiving addressed to patients with cancer has been studied with regard to the effect on the physical (17, 18), psychological (17-21) and financial (22-26) well-being of PCs. Some of these studies have reported the mobilization of all family financial resources to pay for cancer treatment (24, 27) and this might be further complicated if a reduction in the income of PCs occurs (26). Moreover, a substantial reduction in social and leisure activities has been documented and, if the caregiver is a parent, childcaring can also be compromised (28).

It has been consistently reported that a high percentage of PCs dealing with patients in an advanced state of illness experience a variety of symptoms at a clinically meaningful level. Such symptoms may have a negative impact on the functional status and QoL of PCs. Few studies have investigated

the health disruption to PCs other than psychological distress. Data on physical functioning of PCs are scarce. Kiecolt-Glaser *et al.* (29) demonstrated that peripheral blood leucocytes from caregivers may produce significantly less interleukin-1 in response to lipopolysaccharide stimulation compared to controls. Previous studies have shown that the approach to patients with cancer cannot be separated from that to their families and PCs, especially considering that their QoL can be naturally influenced (30, 31).

Moreover it has been demonstrated that psychological support offered to cancer patients also has a beneficial effect on the respective caregiver and *vice versa* (32, 33) and studies on psychologically fragile caregivers showed that they may significantly hamper the patient's medical management (34, 35). Some studies have focused on patients in the 'acute' phase (within 2 years of diagnosis). Very little information is available on the QoL of PCs at the cancer onset when the patients' clinical characteristics are not impaired, as most published data refer to patients on palliative care or who are terminally ill with an ECOG performance status (PS) >2. The purpose of the present study was to assess caregivers QoL at the very beginning of the 'acute' phase (*i.e.* within three months of diagnosis) when the patients were still on chemotherapy, with a PS of 0/1, in order to investigate whether psychological distress at that time may precociously influence QoL of PCs.

## Patients and Methods

**Participants and setting.** Patients and their PCs referred to the Medical Oncology Unit, 'Tor Vergata' Clinical Center, University of Rome between June 2007 and March 2008 were evaluated for study eligibility. The inclusion criteria were: patients on an active antineoplastic treatment; interval between cancer diagnosis and study enrolment not greater than three months and patients ECOG PS ≤1. All patients were required to identify their PC at study entry and signed written informed consent. Eligible PCs criteria were identified as: age ≥18 years; ability to read and ability to understand and sign a specific informed consent written in Italian.

For both the patients and PCs basic demographics were recorded (age, sex, education level, type of family relationship). Data on the tumour primary site and type of treatment were also collected.

All the study procedures were in accordance with the Helsinki Declaration (2000) of the World Medical Association.

**Procedure.** All the PCs were asked to complete a self-report (36) questionnaire developed to investigate QoL of caregivers of terminally ill patients. The questionnaire consisted of two investigational areas: QoL of PCs and the impact of the cancer diagnosis on the family's economic stability (PCs roughly rated the percentage increase of family monthly expenses caused by the 'cancer event' as compared to 'pre-cancer' era). The first section was further expanded as: the physical and functional area of PCs (investigating: time spent caregiving the patient and the occurrence of new psychosomatic symptoms); the psychological-emotional area (PCs were asked to 'monitor their mood' during the study and register the number of episodes a week of 'intense' anxiety, depression, fear and irritability)

and the social-relational area (PCs were asked to grade on a 4-point Likert scale the extent of restrictions [1, no restriction; 2, considerable restriction; 3, very considerable restriction; 4, total restriction] of ten major daily life activities/interests: personal care, aesthetic care, relaxation, entertainment, vacations, time spent with friends, amusements, social events, time spent with partner, time spent with family.

Questionnaires were completed within three months of diagnosis.

**Statistics.** Statistical Package for Social Science (SPSS) software v13.0 was used for both descriptive and inferential statistical analyses. Multiple Pearson correlation was used to analyse correlation between categorical variables, and the Mann-Whitney test was applied to investigate PCs categories at risk of developing mood alteration.

## Results

**PC and patient characteristics.** Among 203 screened patients, 150 met the inclusion criteria. Out of the 150 patient/PC subject pairs contacted for study participation, 104 agreed to participate in the present trial. Twenty-two percent of the patients were receiving adjuvant and 14% neoadjuvant treatment and 64% were being treated for metastatic disease.

Most of the enrolled patients and PCs were women (24% males and 76% females for patients, 43% males and 57% females for PCs), with a median age of 60 years (range 31-76) and 45 years (range 21-75) for patients and PCs, respectively (the characteristics are summarized in Table Ia and Ib). The PCs included in the study were mostly women (57%) and took care of predominantly female patients (88%); also the female PCs took care mostly of female patients but in a lower percentage (64%).

With respect to the type of family relationship, most of the PCs were offspring or spouses (80% of the total), almost all the PCs (96% of cases) had a medium-high education level (at least secondary school).

The most represented tumour primary sites were breast, lung and colorectum, and 64% of the patients were treated for metastatic disease.

**QoL of PCs.** Physical-functional area: As depicted in Figure 1, most of the PCs fell into the extreme classes of "time spent caring for the patient", *i.e.* 37% in the group spending less than 4 hours a day and 44% in the group spending more than 12 hours a day, suggesting a dichotomous distribution (either a lot of time or little time spent in caregiving). The results were comparable when the gender and age (> and <45 years) of PCs were analysed separately (*p*-values not statistically significant, data not shown). Interestingly, the type of relationship between the patient and the PC significantly influenced this distribution, with 68% of spouses spending more than 12 hours as compared to 32% of the other types of PC (*p*<0.001).

The PCs frequently reported the occurrence of new psychosomatic disorders, as shown in Figure 2. For the occurrence of a new psychosomatic disorder to be considered

Table I. Study subjects' characteristics.

| a. Principal caregivers (n=104) |                            |       |
|---------------------------------|----------------------------|-------|
| Age (years)                     | Median                     | 45    |
|                                 | Standard deviation         | 14.87 |
| Gender                          | Female                     | 57%   |
|                                 | Male                       | 43%   |
| Type of family relationship     | Parent                     | 4%    |
|                                 | Spouse                     | 44%   |
|                                 | Offspring                  | 36%   |
|                                 | Brother/sister             | 4%    |
|                                 | Friend                     | 5%    |
|                                 | Son-in-law/daughter-in-law | 8%    |
| Education level                 | Primary school             | 4%    |
|                                 | Secondary school           | 32%   |
|                                 | High school                | 36%   |
|                                 | University                 | 28%   |
| b. Patients (n=104)             |                            |       |
| Age (years)                     | Median                     | 60    |
|                                 | Standard deviation         | 14.87 |
| Gender                          | Female                     | 76%   |
|                                 | Male                       | 24%   |
| Primary cancer site             | Breast                     | 24%   |
|                                 | Lung                       | 14%   |
|                                 | Colorectum                 | 24%   |
|                                 | Pancreas                   | 11%   |
|                                 | Prostate cancer            | 3%    |
|                                 | Other**                    | 24%   |
| Type of chemotherapy            | Adjuvant                   | 22%   |
|                                 | Neoadjuvant                | 14%   |
|                                 | Metastatic disease         | 64%   |

\*Including biliary tract; \*\*including ovary, stomach and kidney.

as notable, an average of 2 or more 'acute' episodes a week had to be recorded (over a monitored period of at least 1 month). By this definition, 37% of the PCs reported the occurrence of at least one new psychosomatic disorder, with the most frequent being headaches, asthenia and sleep disruption. Interestingly, there was no statistically significant correlation between the occurrence of a new psychosomatic disorder and the time spent in caregiving (see Table II).

**Psychological-emotional area:** Frequent mood alterations were also observed in the study PCs, with half of them reporting at least one of the adverse emotional states investigated in the questionnaire (irritability, fear, depression, anxiety) at a significant level ( $\geq 2$  'acute' episodes/week). Anxiety, as shown in Figure 3, was the most frequently reported mood alteration (28% of cases). Multiple mood alterations (2 or more among irritability, fear, depression, anxiety) were reported by 17% of the PCs.

**Social-relational area:** A significant restriction (scores 3-4 on a 4-point Likert scale) in lifestyle was reported by the study

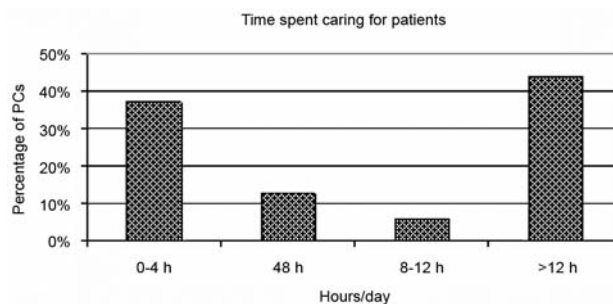


Figure 1. Time spent by principal caregivers (PCs) in daily care of the patients.

PCs. Overall more than 50% of the PCs reported a restriction of their usual lifestyle (see Figure 4) (at least one of the investigated life activities/interests restricted), with most sacrificed activities being vacations, amusements, participation in social events, time spent with friends and personal care. A less affected area was time spent with the family, that generally increased with the occurrence of the 'cancer event'.

**Evaluation of the overall gravity of the situation.** At the end of the questionnaire, the PCs were asked to rate the overall gravity of the situation using a 4-point Likert scale (from no gravity to severe gravity). Overall the situation was perceived as severe by 86% of the caregivers (Figure 5).

**Impact of cancer diagnosis on family economic stability.** An increase of 10% or more in family monthly expenses was reported by approximately half of the PCs (44%), with 8% reporting an increase greater than 50% (Figure 6). The main reported reasons for this expenditure increase were travelling costs for medical purposes (medical visits to hospital or other medical institutions) and costs of care drugs for side-effects of chemotherapy.

**Correlation analysis.** Correlation was investigated between different PC and patient subgroups taking into account: PC age, PC education level, patient age, hours spent by PCs in caregiving, psychosomatic symptoms reported by PCs, mood alterations of PCs and social-relational restrictions of PCs. According to the Pearson correlation analysis (Table II), the mood alterations of PCs significantly correlated with the hours spent in caregiving, the social-relational restrictions and the psychosomatic symptoms reported by the PCs. Furthermore, there was a statistically significant impact of age of both PCs and patients on the hours spent by the PCs in caregiving and the psychosomatic symptoms reported by the PCs, respectively. Spearman rank correlation analysis was used to analyse correlation between the type of relationship between the PC and the patient and reported mood alterations. A trend towards

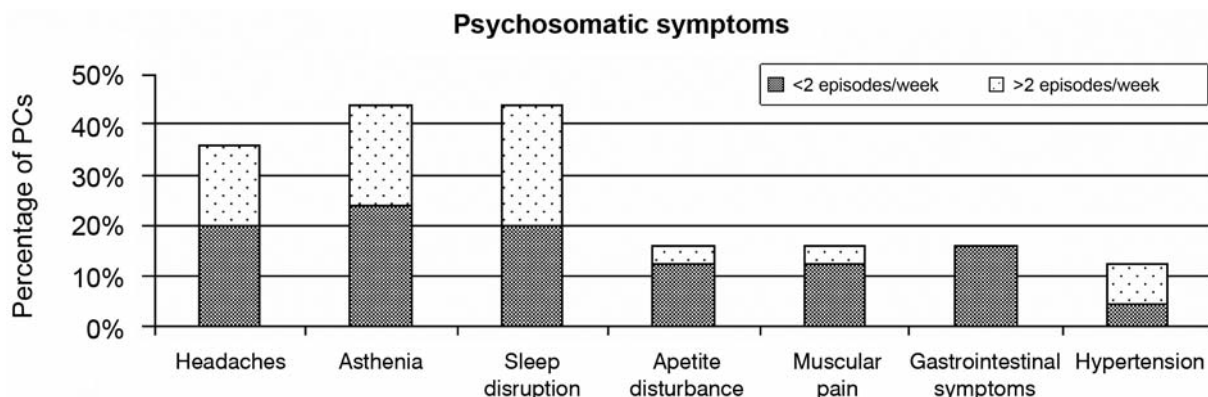


Figure 2. New psychosomatic disorders suffered by principal caregivers (PCs) during the caregiving.

an increased risk of developing mood deterioration was found in spouses compared to the other types of PCs, with borderline statistical significance ( $p=0.07$ ).

**Discussion**

In the present study, several particular aspects emerged in the profile of the PCs of cancer patients on chemotherapy. The male:female ratio was approximately unity, indicating that in spite of what is commonly believed, the probability of a PC being a male was approximately the same as of being a female. A typical PC profile was defined as female by Robinson *et al.* (37). This discrepancy could have been due to a cultural change in contemporary society. Historically caregiving was attributed to women, yet nowadays they are increasingly involved in demanding employment requiring an amount of time comparable to that spent by men. It was therefore not surprising that gender was evenly distributed between the PCs.

The median age (45 years; SD 14.87) of the PCs in the present dataset was not different from that reported in other studies (37), nor were the main types of family relationship between the PC and patient (44% spouse, 36% offspring), the latter confirming close relatives as having a central role in caregiving, with patients finding their main support within their families (37).

Considering that all the patients had a good PS and were at the beginning of their ‘cancer history’ as per the selection criteria, the hours spent in caregiving were expected to be relatively low. On the contrary, as many as 52% of the PCs spent more than 8 h in caregiving. This was obviously not on account of the patient’s ‘complicated’ clinical condition, but possibly because the ‘entrance’ of such a life-changing event (the cancer) into the lives of patients and PCs occasioned a disruption in the usual daily organisation of the family requiring a new ‘balance’ in life activities and individual family member roles.

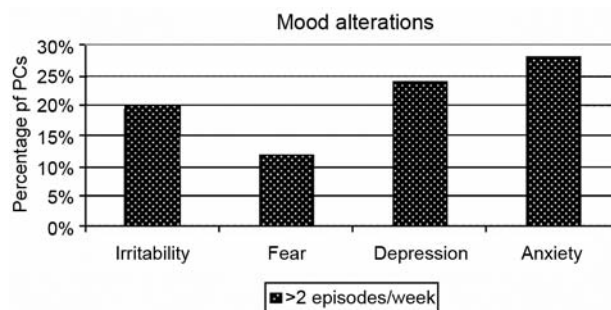


Figure 3. Adverse emotional states suffered by principal caregivers (PCs) during the caregiving.

While 52% of the PCs reported a limitation in at least one of their usual activities, with vacations, attendance at social events, friendships and personal care being the most sacrificed, in contrast the time spent with family members was not altered, in accordance with data reported by Sales (38) where family members were regarded as the main psychological support resource.

Poor health status has been reported in previous studies ranging from 0% to 40% of PCs and was mainly associated with older ages (37, 39). In the literature, the most reported disturbances among patients’ relatives have been depression, anxiety and other psychosomatic symptoms (38, 40). In a study by Ell and co-workers (40) 12% of PCs developed stress and anxiety during the first year of caregiving. In the present study, just a few months after disease diagnosis, a high percentage of the PCs had mood changes, especially an increase in anxiety and depression. Even though in the present study no new pathological conditions (ictus, MI *etc.*) were diagnosed in the PCs during the study period, in a high percentage of cases, a significant (*i.e.* >2 episodes a week) increase of psychosomatic symptoms was observed (headache, asthenia, sleep disruption,

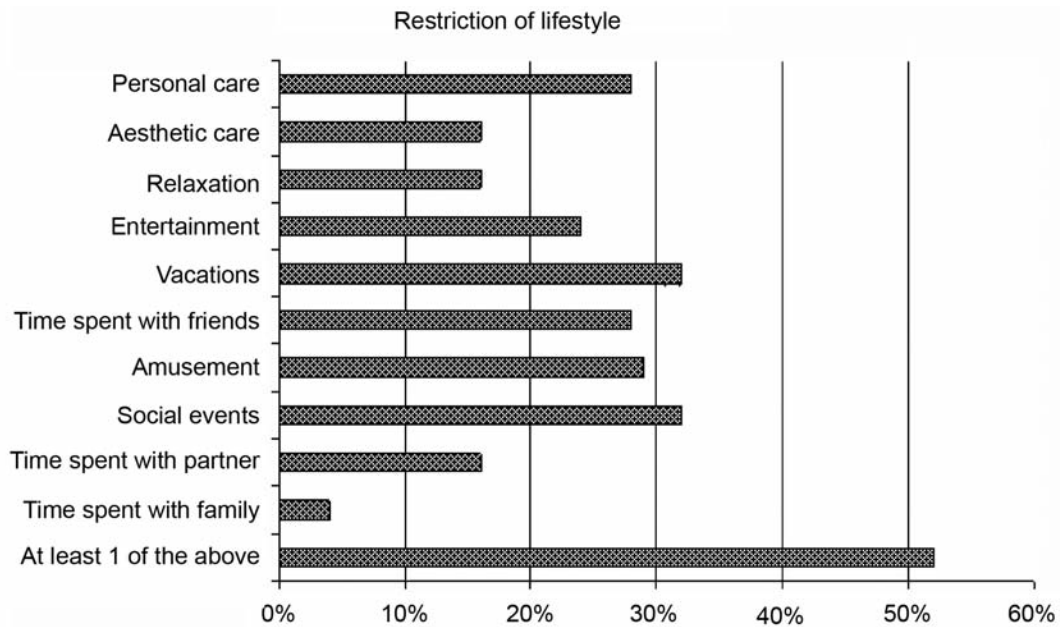


Figure 4. Perception of the principal caregivers as to the modification/reduction of some daily activities.

Table II. Multiple Pearson correlation analysis of subject characteristics and QoL.

|                                    | PC age | PC education level | Patient age | Hours spent in caregiving | Psychosomatic symptoms | Mood alteration | Social-relation restriction |
|------------------------------------|--------|--------------------|-------------|---------------------------|------------------------|-----------------|-----------------------------|
| PC age                             |        |                    |             |                           |                        |                 |                             |
| Correlation coefficient            |        | -0.25              | 0.28        | 0.58                      | -0.14                  | 0.12            | 0.09                        |
| Significance level <i>p</i> -value |        | 0.01               | 0.01        | 0.01                      | 0.14                   | 0.22            | 0.32                        |
| PC education level                 |        |                    |             |                           |                        |                 |                             |
| Correlation coefficient            | -0.25  |                    | 0.20        | -0.41                     | -0.05                  | -0.11           | 0.16                        |
| Significance level <i>p</i> -value | 0.01   |                    | 0.04        | 0.01                      | 0.58                   | 0.28            | 0.09                        |
| Patient age                        |        |                    |             |                           |                        |                 |                             |
| Correlation coefficient            | 0.28   | 0.20               |             | -0.15                     | -0.22                  | -0.09           | 0.02                        |
| Significance level <i>p</i> -value | 0.01   | 0.04               |             | 0.14                      | 0.03                   | 0.36            | 0.81                        |
| Hours spent in caregiving          |        |                    |             |                           |                        |                 |                             |
| Correlation coefficient            | 0.58   | -0.41              | -0.15       |                           | -0.09                  | 0.29            | -0.12                       |
| Significance level <i>p</i> -value | 0.01   | 0.01               | 0.14        |                           | 0.35                   | 0.01            | 0.24                        |
| Psychosomatic symptoms             |        |                    |             |                           |                        |                 |                             |
| Correlation coefficient            | -0.14  | -0.05              | -0.22       | -0.09                     |                        | 0.35            | 0.51                        |
| Significance level <i>p</i> -value | 0.14   | 0.58               | 0.03        | 0.35                      |                        | 0.01            | 2.15                        |
| Mood alteration                    |        |                    |             |                           |                        |                 |                             |
| Correlation coefficient            | 0.12   | -0.11              | -0.09       | 0.29                      | 0.35                   |                 | 0.21                        |
| Significance level <i>p</i> -value | 0.22   | 0.28               | 0.36        | 0.01                      | 0.01                   |                 | 0.03                        |
| Social-relation restriction        |        |                    |             |                           |                        |                 |                             |
| Correlation coefficient            | 0.09   | 0.16               | 0.02        | -0.12                     | 0.51                   | 0.21            |                             |
| Significance level <i>p</i> -value | 0.32   | 0.09               | 0.81        | 0.24                      | 2.15                   | 0.03            |                             |
| Number of patients                 | 104    | 104                | 104         | 104                       | 104                    | 104             |                             |

anxiety, depressive mood, fear and irritability). Further investigations revealed that the elderly, compared to the young PCs, spent more time in caregiving and complained more frequently and to a greater extent of mood changes. This was usually associated with an increase of reported somatic

disorders. The presence of emotional disorders was also significantly related to the reduction of usual life activities. Although not statistically significant, in this study, a higher risk of developing emotional disorders was shown when the PC was the spouse, in agreement with a previous report (41).

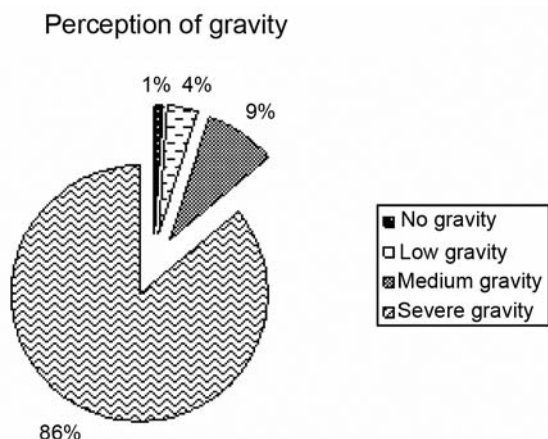


Figure 5. Perception of the principal caregivers of the gravity of the situation.

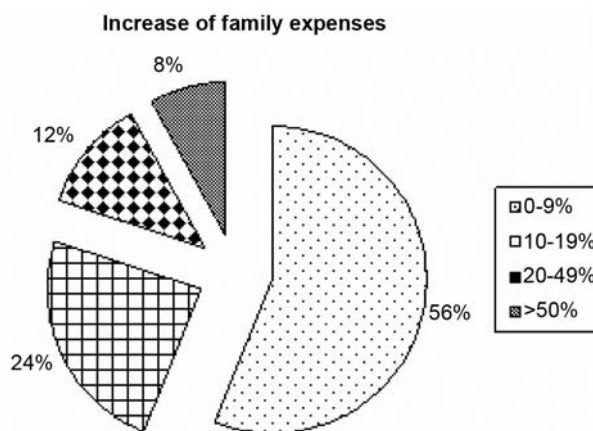


Figure 6. Percentage increase in family expenditure in the early phase of cancer treatment.

The present results, in keeping with previously reported data, may help provide an identikit of PCs at higher risk of health deterioration, *i.e.* female (42), spouse (43), with poor health (42-44), elderly (44) and able to face difficult situations (43, 45) who could be selected as candidates for targeted support programmes.

The present study confirmed that the approach to cancer patients cannot be separated from the approach to their families, and in particular to the PC, as their QoL is mutually influenced (30, 31).

Contrary to other studies (46-48), only a small percentage of the present subjects reported a relevant increase in additional medical expenses due to the disease, probably due to the Italian health system that broadly covers medical expenses.

In conclusion, a demonstrable reduction in PC QoL occurs even during the early phases of cancer and new psychosomatic symptoms and anxiety are reported as the most debilitating changes. Intervention strategies including psychological interventions for PCs should be considered earlier during cancer treatment in order to prevent psychological disturbances from arising and becoming chronic and less sensitive to therapies. Such interventions might provide PCs with adequate tools to face the 'cancer event' and help them adapt to new stressors.

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