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## Abstract

**Background:** Recently a great deal of attention has been focused on doctors' work related stress and the possibility of improving their quality of life. Several studies report that healthcare professionals, especially oncologists, are overloaded physically, emotionally and psychologically. They develop a confidential relationship with their patients through close contact and interpersonal communication. Previous studies in the field of healthcare have shown that communication skills training improves the sense of satisfaction and well-being of physicians and patients.

**Aims:** Our research investigates the relationship between Work Stress, Work Engagement and Personal Well-being in a sample of doctors working in Italian hospitals. Specifically, the study investigates some protective factors involved in this relationship.

**Materials and Methods:** The research included 176 physicians working in Italian healthcare units. Doctors filled out self-report questionnaires to evaluate Work Stress and Coping Strategies (*Health Professions Stress and Coping Scale*), Personal Well-being (*General Health Questionnaire*), Work Engagement (*Utrecht Work Engagement Scale*) and two purpose-built scales to measure the degree of perceived Organizational Support and the level of specific training on social and relational skills.

**Result:** The data seem to confirm our hypothesis. Positive and significant correlations were found between variables observed. Moreover, physicians who obtained higher levels of specific training on social and relational skills reported lower levels of stress. Finally, we examined the differences between oncologists and other specialists: oncologists experienced greater stress (particularly in problematic relationships with patients) than other physicians in terms of maladaptive coping (such as emotional distress), and they lack additional training.

**Conclusions:** The results presented seem to confirm that the well-being of physicians is mediated by typical aspects of the profession, such as social skills in relationships with patients. The possible implication of research will also be discussed: the training needs of physicians and planned learning opportunities.

## Introduction

Work takes up most of people's daily lives, so work-related stress may have consequences for a person's general health. In itself work doesn't cause suffering or stress, but work can become stressful or painful and impinge on a worker's quality of life. A stressful job environment may affect the person not only during working hours, but also during his private life, a phenomenon called the

“hallway syndrome.” Negative emotional effects may be carried over from the work environment to the home, resulting in psychological and physical overload (1). This problem is often found in people who work in unusually stressful environments, with psychological and physical damage (2,3). Jobs that are particularly stressful are the helping professions in general, and healthcare in particular, where workers carry the weight of important responsibilities every day, and are often subject to long hours and a fast pace.

The helping and health professions feature asymmetrical relationships: constant and continuing contact with the suffering of patients or clients and their families, in which the worker is expected to share their suffering. Such stressful conditions often lead to burnout, the probability increasing when the workplace isn't well-organized, and there is poor training or inadequate support (4,5). The phenomenon of burnout is a reaction to high levels of prolonged emotional stress, typical in the helping professions, and characterized by a group of symptoms expressed mentally, behaviorally and somatically (6,7). Doctors in general, and oncologists in particular, are in a high-risk category. Oncology is one of the medical fields with the greatest psychological demands (7,8,9,10). Factors such as constantly dealing with patients who have life-threatening diseases, the limited effectiveness of treatment, and other contributors to a high pressure environment, result in the emotional drain and exhaustion of staff, then depersonalization, and finally a sense of reduced professional satisfaction and lower self-esteem. All of these factors interact and reinforce each other in a vicious cycle that is difficult to break (11,12,13).

There are inconsistent findings on the frequency of this phenomenon in oncology (14,15,16), but it seems that 30% of workers in oncology have experienced the symptoms of stress and burnout during their professional lives (6,14,15); oncologists seem to be the most frequent victims, especially in terms of depersonalization. Working in oncology entails a certain amount of suffering, especially when an initial phase of enthusiasm is followed by a phase of stagnation in which the individual feels he can't achieve his original goals, with a subsequent phase of frustration resulting from a feeling of personal failure (5). According to some authors the origin of the stress and distress in the workplace is closely related to the motivations, often unconscious, for choosing that profession: the so-called calling that moves someone to choose this field as a kind of mission, with personal reasons such as the control of feared events (mental and physical decline), guilt feelings, repressed terror of death, omnipotence, rigidity, hyper-control, and above all a powerful need to cure in the widest sense of the word (4,5,6). All of that represents the main motive for the professional choice, which is more popularly known as the psychopathology of vocational self-healing, the basis for all helping professions (17). This absolute

need to cure that exists in the field of medicine, is constantly frustrated by the continuing disappointments of both the constant contact with patients and the lack of a well-organized workplace (4). The end result therefore is often tragic, the gap between the ideal expectations and the reality you have to face (5,12).

All of these factors qualify the profession of medicine as being among the highest risk categories for stress and burnout. In recent years the awareness is emerging that doctors are under a lot of stress in the workplace, and hence there is a need for support to improve their quality of life (18). Workplace stress refers to a set of emotional, behavioral, cognitive and physiological reactions related to toxic factors of the job and workplace (19). That concept clarifies the importance of aspects strictly related to the workplace, the typical stressors on the job, but also the subjective evaluation of those stressors and the specific individual's psychological reactions. Stress has been shown to play a crucial role in the deterioration of the physical and mental health of workers, and stress increases the economic costs of treating diseases, requests for transfers, and voluntarily resigning one's position. Work-related stress has also been found to be correlated with patient dissatisfaction and malpractice suits (20).

Some studies have indicated how situations with mental and physical danger and risk are closely related to how workplaces are organized and the consequent treatment choices made; other studies have highlighted the need to identify the factors that might lead to dissatisfaction and stress in the workplace, taking into consideration not only organizational and technical factors, but specific individual factors (21). Stress is always a subjective phenomenon, since everyone reacts to stressors –i.e. situations perceived as stressful and potentially dangerous– in different ways according to the individual's personality and life history (22).

Taylor's research has demonstrated how the main sources of stress (intrinsic factors of the job, factors related to workplace organization, relationships with other staff and the organizational climate, career factors, and the interface between work and private life) are closely related to individual factors (dysfunctional responses), and to organizational problems in causing distress in healthcare workers (23). However, high levels of stress don't always cause burnout, in the sense that under the same conditions not all doctors burn out. That suggests there are other important variables that mediate directly or indirectly between stress and burnout (24). Among the most important variables we may list:

- the degree and form of exposure to the stressor (environmental variable)
- the perception and evaluation of the stressful situation

- the individual's vulnerability to stress (previous experience)
- the physiological response to the stress
- the spontaneous ability to cope.

Among these variables the concept of coping is particularly important, understood as the combination of tactics, strategies, responses and attitudes or viewpoints that a person utilizes in attempting to manage a situation perceived as stressful and dangerous (25). Several studies have demonstrated the "pincushion" action derived from the use of effective coping strategies when confronting stressful events, and the conditioning effect on the level of well-being in the workplace experienced by the worker (26). In the literature active strategies to cope with stressful situations have been correlated with low levels of anxiety, high levels of perceived mental well-being, and high levels of perceived control over the environment (27). Other studies have confirmed that coping strategies aimed at concrete solutions are among the most effective and adaptive, while the strategies of denial and avoidance of problems are effective only if used for a short time, since they prevent strong emotional reactions but if used for prolonged periods they can result in difficulty in adapting to new situations (28).

Other studies have found that social support is a form of protection against stress. The perception of strong social support helps the worker feel esteemed, appreciated and part of a group in which there are reciprocal obligations and communication (29). Another factor has recently been recognized as a form of protection against stress: psychosocial training and the ability to communicate well, which all doctors should have (30). An important aspect of proper patient management is the relationship established between doctor and patient. In recent years the "paternal" model of the authoritarian doctor and obedient patient, the latter following the doctor's directions without question, is being replaced by a more egalitarian approach in which the patient makes specific requests and expects clear answers (31). For the new approach to work, the important role of communication must be acknowledged.

The ability to communicate with patients is often taken for granted, or considered a waste of time in a hectic environment. But several studies have recently demonstrated the advantages of effective communication for both doctors and patients (32). These studies have evaluated the impact of communication from both the doctor's and the patient's point of view. The patient's need for information in most cases is not satisfied. That aspect is most evident in regard to information about the prognosis (33). A recent article indicated the difficulty doctors have in informing patients that they have little time left to live, because the doctors are insufficiently trained, or they are afraid

of the patient's possible reaction, or because of the explicit request of the patient's relatives (34).

Although Gurmankin (2002) published an article on therapeutic decision-making in which he demonstrated that patients granting or withholding consent is more than 70% influenced by the doctor's opinion (35), communication courses are still not a part of doctor training in Italy today. As a consequence this fundamental part of medical practice is too often interpreted individually, according to each doctor's empathy, with all the weight and embarrassment of being professionally unprepared and forced to rely on one's own personal experience (36). However, information is only a small part of the communication between doctor and patient. Recently a group of Australian researchers demonstrated that the major needs of patients with advanced cancer are for psychological support and better communication (95%) with their oncologist (37).

Poor communication can leave the patient feeling uncertain about his diagnosis and prognosis, and confused about the results of diagnostic lab tests, with doubts about the further plans for management and intentions for treatment. We also know that communication problems may interfere with patients participating in clinical trials, and hence delay the potential benefits of new therapy in clinical practice. Hence, in a doctor's daily work he should not only know how to communicate but also how to interpret and manage the emotions of people in his work environment. That is because good communication and a good relationship between doctor and patient can improve the patient's satisfaction with the treatment offered, as well as improve the patient's understanding of the medical information, compliance with treatment protocols, adaptation to the disease, the quality of life, and general emotional state.

All of that requires significant effort on the part of the doctor, who isn't supported by appropriate training today (38). Oncologists themselves recognize that they haven't received adequate training, or even no training in communication, which may be correlated with high levels of stress, losing or resigning one's position, a sense of dissatisfaction, and emotional burnout (39). Hence, adequate training in communication and patient management not only offers proven benefits for the patient, but also contributes to the well-being of the doctor, offering a sense of long-term personal adequacy since the acquisition of communication skills lasts and becomes a regular part of clinical practice (39). According to Bandura (1977) people who strongly believe in their ability to achieve success are more likely to persevere even in the face of difficulties (40).

The literature reveals that the doctor's personal variables, style and communication skills are related to well-being as well as workplace stress, and that these factors reinforce and influence each other reciprocally. There are basically three ways to work on stress: 1) the primary level, by reducing the factors that cause stress; 2) the secondary level, stress management; and 3) the third level, programs to assist the doctor. According to the international literature, the second and third levels are the primary ways stress is handled, modifying the lifestyles and behavior considered responsible for injuring health, or training doctors to react positively and effectively to stressful situations. The first level approach, which is not utilized, in theory aims at prevention, attempting to abort the stress process in advance before it begins, or altering the factors considered to be possible causes of stress instead of acting on the consequences (41).

This research investigates the degree of well-being in the workplace, the stress, and the coping strategies in a sample of doctors who work in Italy, from a positive and protective perspective. Psychology is primarily considered a science related to suffering (42). It concentrates on repairing damage, relying on a model of human functioning based on disease, and the primary goal is to cure mental pathology. But psychology has always had other goals as well, such as helping people become more productive and satisfied through the identification and development of personal resources. Intervention in what isn't functioning isn't necessarily the same as promoting ideal functioning, just as the lack of distress isn't the same as the presence of well-being. The recognition of this fact has led to the creation of a new branch of psychological science: Positive Psychology (43). This new approach attempts to identify in each individual what works, what is right, and what is improving, and targets those abilities and competences that contribute to the individual's well-being. Positive Psychology doesn't deny pathology, suffering or distress, but attempts to find an alternative to the model of disease, by cultivating, improving and developing an individual's positive qualities (44). Prevention is fundamental to this new model, and hence the need to work on an individual's strengths and resilience rather than his weak points.

The concept of resilience is strongly related to tension, stress and anxiety, i.e. to all those traumatic situations that may strike us. Resilience is a positive, adaptive process regardless of the presence of risks and difficulty, and is the result of a dynamic interaction between the individual and the environment (45). Individuals are no longer considered passive but active beings, able to choose, take risks, and assume responsibility. Seligman asserts that it's necessary to focus attention on the reinforcement of positive qualities to understand how to promote a program for individuals as well as the general population (46). That approach is fundamental especially in the sphere of promoting well-being in

workplaces. In recent years renewed interest in the concept of resilience and well-being has been noted on an international level, and has been applied to research on stress (47). Antonovsky has suggested that it's always possible to identify protective factors in individuals, and the primary goal of those in healthcare should be to cultivate those factors in individuals and society (48). This research was created and developed on the basis of the fundamental theory of the genesis of health, i.e. the study of the causes of health, in contrast to the causes of disease or distress. The perspective of stress on the genesis of health is fundamental to confront and intervene in work-related stress.

### **Aims of the thesis**

The goal of this research is to study the possible causes of stress in the workplace, in a sample of doctors working in various fields, considering some specific factors: extent of special training in managing relationships, coping strategies, perception of self-efficacy in social-relational competence, and structural supports in the organization. In addition, we propose to highlight some differences between oncologists and doctors working in other fields. Our hypotheses are:

**H1.** There are significant relationships between the observed variables in the sample, considering these specific factors:

H1a. Involvement in work will be positively correlated with the perception of general well-being, structural support in the organization, self-efficacy in social-relational competence; in contrast, it will be negatively correlated with the perception of workplace stress;

H1b. The perception of general well-being will be positively correlated with the perception of structural support in the organization and self-efficacy in social-relational competence, and with the use of adaptive coping strategies; in contrast, it will be negatively correlated with the use of maladaptive coping strategies;

H1c. The perception of structural support in the organization will be positively correlated with the use of adaptive coping strategies and with the perception of self-efficacy in social-relational competence; in contrast, it will be negatively correlated with the perception of workplace stress and the use of maladaptive coping strategies;



H1d. The perception of workplace stress will be positively correlated with maladaptive coping strategies; in contrast, it will be negatively correlated with the use of adaptive coping strategies and the perception of general well-being and self-efficacy in social-relational competence;

H1e. The extent of special training in managing relationships will be positively correlated with the perception of self-efficacy in social-relational competence, the structure of organizational support, general well-being, and the use of adaptive coping strategies; in contrast, it will be negatively correlated with the perception of workplace stress and the use of maladaptive coping strategies.

**H2.** The extent of special training (in terms of managing relationships, coping strategies, the perception of self-efficacy in social-relational competence, and structure of organizational support) predicts doctors' workplace stress.

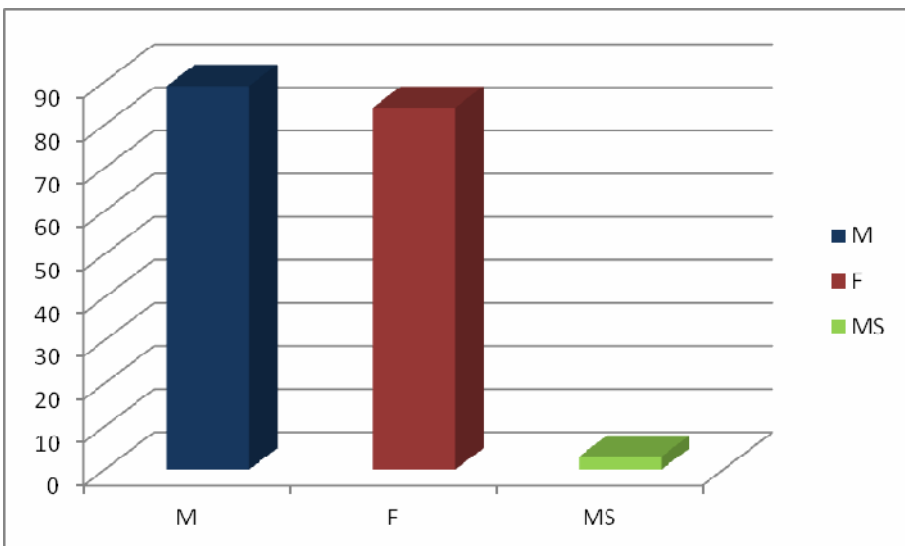
**H3.** The risk level of the disease predicts workplace stress in oncologists.

**H4.** There are significant differences between the scores of oncologists and doctors working in other fields.

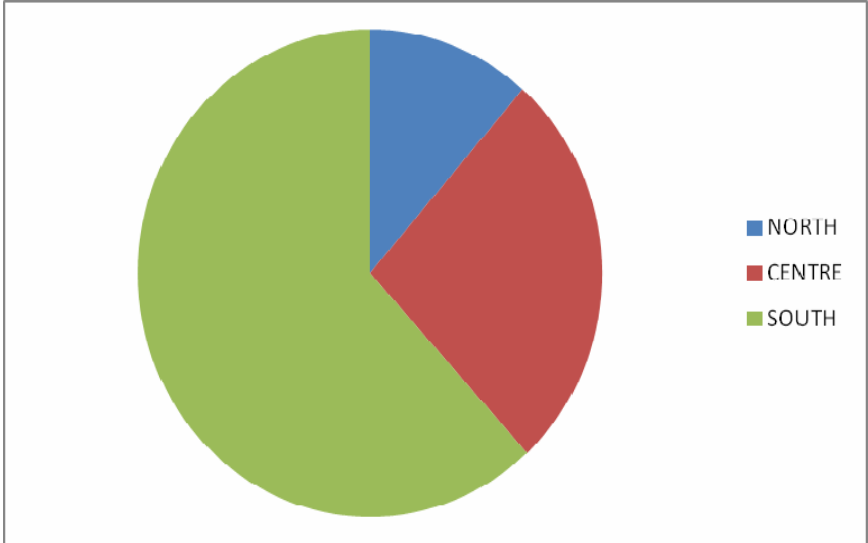
## Materials and Methods

This research studied 176 doctors (M = 89, F = 84, MS = 3), (Tab. 1) who work in various capacities in Italian hospitals (North = 11.4%, Centre = 26.8%, South = 61.8%), (Tab.2).

**Tab. 1**

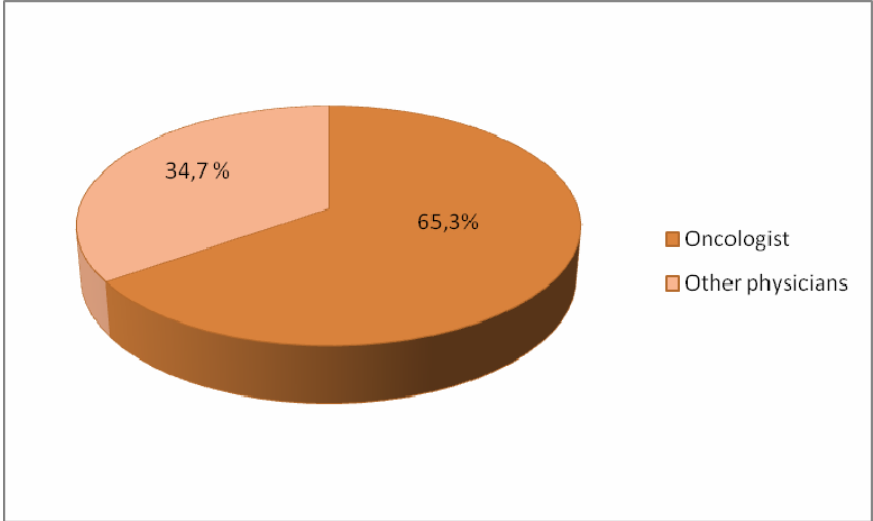


**Tab. 2**



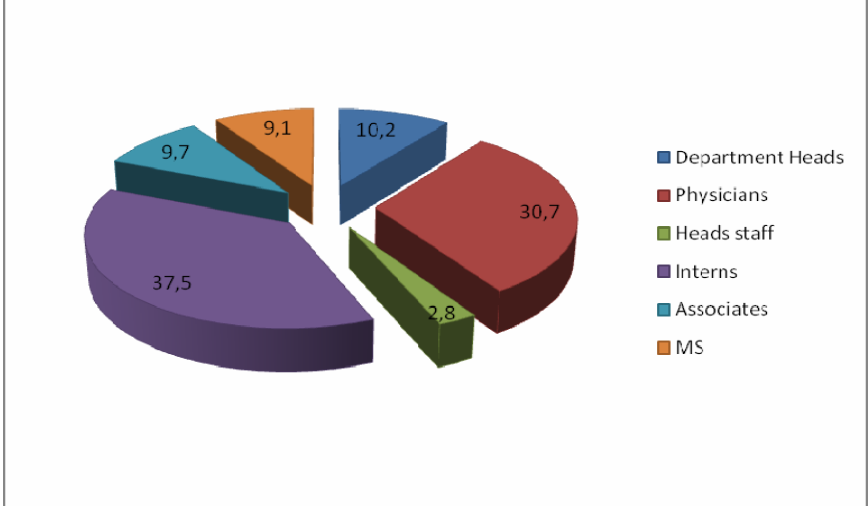
Age range from 25 to 70 years ( $M=38.56$ ,  $SD=11.48$ ). Oncologists make up 65.3% of the study subjects, and doctors working in other fields make up the remaining 34.7% (Tab.3)

**Tab. 3**



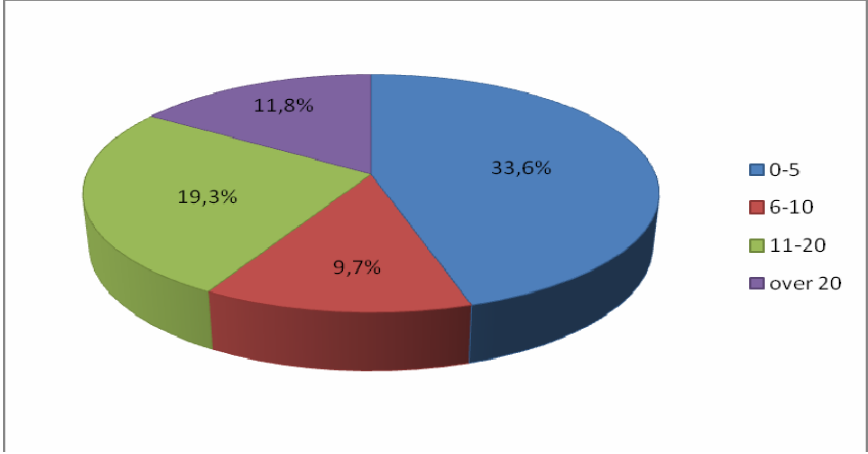
In detail, 10.2% of the doctors are department heads, 30.7% are physicians, 2.8% are heads staff, and 37.5% are interns (specialists in training, fellows), and 9.7% are medical associates (MS=9.1%) (Tab. 4).

**Tab.4**



Almost all of the subjects (80.1%) are in clinical practice, while 3.4% are instructors or researchers (and MS=16.5%). In terms of experience, 33.6% of the subjects have from 0 to 5 years, 9.7% have 6-10 years, 19.3% have 11-20 years, and 11.8% have more than 20 years (MS=25.5%) (Tab. 5).

**Tab. 5**



The average number of work hours per day is 8.46 (DS=1.75); hours spent in contact with patients are from 3 to 60 weekly (M=31.67; DS=13.23). In 65.3% of the departments there is a psychologist present; out of these, 82.4% are oncological departments, and 17.6% are other fields.

Descriptive statistics were used to analyze the data, as well as correlation analysis (*r* Pearson), hierarchical regression analysis, (Enter *step*), analysis of variance (one way ANOVA); regression coefficients are indicated using non-standard beta confidence intervals; whenever both the upper and lower limit express the same sign we can accept the alternative hypothesis (with  $p < .05$ ) that the effect of the variable is statistically significant.

The “risk level” was determined by asking the doctors to label the mortality risk of the oncological disease as low, medium or high.

The subjects filled out a self-report questionnaire designed to measure perceived stress, coping (Health Professions Stress and Coping Scale), degree of personal well-being (GHQ-12), and degree of work involvement (UWES). In addition, an ad hoc scale was created to measure the degree of perceived support by the organization, and the subject’s degree of self-efficacy. In most cases the questionnaire was administered after a meeting with the subjects at their workplace, in which the subjects were provided with an explanation of the goals of the study. At the same time the subjects were encouraged to participate in the study.

The questionnaire distributed to the subjects is basically divided in three parts. The first part investigates the doctor’s perceived level of stress in the healthcare environment, and the coping strategies they usually employ. The second part investigates the subject’s psychological morbidity, work engagement, level of self-efficacy, and perceived level of organizational support. The third part records the subject’s socio-demographic data.

Socio-demographic data were recorded by 15 items, i.e. demographic variables, age, occupation, role in the department, daily work schedule, activities performed, experience, and quantity of time spent with patients. The questionnaire also recorded the level of training in managing some specific situations (communication of the diagnosis, handling the patient’s reaction, etc.). The level of training is examined both by questions about credentials and also by using an index (reported training level) obtained through seven questions about the topics covered during training and considered specific to medical practice. Five scales were used to investigate the following areas.

## *Perceived Stress and Coping Strategies*

The **Health Professions Stress and Coping Scale** (HPSCS) is a self-report questionnaire designed to measure perceived stress and coping strategies in healthcare (49). The scale presents a series of potentially stressful situations in the workplace that were identified in a careful analysis of the literature as well as a series of interviews of numerous doctors. The doctors were first asked to indicate the stress level for each of the situations presented, using a Likert 4-point scale (0=none to 4=high). Then the subjects were asked to indicate the frequency with which they utilized four coping strategies (same scale).

The HPSCS for doctors (in contrast to the HPSCS for nurses) consists of 23 items for stressful situations referring to five areas: personal attack and unexpected organizational events, clinical emergency, facing death, problematic relations with patients, personal criticism. The scale not only measures perceived stress but also offers the opportunity to evaluate coping strategies utilized. Those strategies are:

- Problem solving (focus on solving the problem);
- Request for assistance (focus on obtaining social support);
- Emotional focus (focus on emotional distress);
- Problem avoidance (focus on avoiding the situation).

## *Personal well-being*

The **General Health Questionnaire** (GHQ-12) developed by David Goldberg (1972), is one of the most widely used and studied indicators of minor psychiatric disorders (50). It has been extensively used in different settings and different cultures. The questionnaire was originally developed as a 60-item instrument but at present a range of shortened versions of the questionnaire, including the GHQ-30, the GHQ-28, the GHQ-20, as well as the GHQ-12, is available. The 12-item GHQ (GHQ-12) has recently become the most popular form of the scale because of its relatively good validity (51) as well as its space-saving properties in survey studies.

## *Work Engagement*

The **Utrecht Work Engagement Scale** (UWES) is a self-report questionnaire consisting of 17 items (UWES-17), which measure the three underlying dimensions of work engagement: vigor (six items), dedication (five items), and absorption (six items) (52,53,54). Vigor refers to high levels of energy and mental resilience while working, the willingness to invest effort in one's work, and persistence in the face of difficulties. Dedication is characterized by a sense

of significance, enthusiasm, inspiration, pride, and challenge. Absorption refers to being fully concentrated and deeply engrossed in one's work, and is characterized by time passing quickly and difficulties in detaching oneself from work.

According to a recent review, work engagement is positively associated, for instance, with mental and psychosomatic health, intrinsic motivation, efficacy beliefs, positive attitudes towards work and the organization, and high performance (52). The UWES was originally designed for the Dutch population, but has been adapted for many other countries (Australia, Canada, Finland, Greece, France, Germany, Norway, South Africa, and Spain. In addition, Schaufeli has translated the scale into other languages including Italian. There haven't been any definitive studies to validate the scale in Italy yet. According to the author's instructions the score should not be expressed in cumulative form, but the average should be calculated for scores of the items. The reliability of the scale, measured by Schaufeli et al. with the Cronbach Alpha (2003), was equal to an average of 0.90 (range 0.85 to 0.94). The same subscales (each of which is composed of three items in the nine-item version) achieve adequate levels of Cronbach Alpha: Vigor = 0.72, Absorption = 0.77, Dedication = 0.84 (55).

### *Self Efficacy*

A scale of 23 items was created ad hoc to measure the degree of self efficacy perceived by the doctors. They were asked how capable they felt in handling certain situations, e.g. "Try to see things from the other's point of view," and "Stay calm in stressful situations," etc. (56).

### *Organizational Support*

Another scale of seven items was created ad hoc to measure the degree of perceived support from the organizational structure, e.g. "You feel like part of a supportive team," and "You feel that there are clear roles, tasks, and duties," etc. (56).

## **Results**

Descriptive statistics were used to analyze the data, as well as correlation analysis (*r* Pearson), hierarchical regression analysis, (Enter *step*), analysis of variance (one way ANOVA); regression coefficients are indicated using non-standard beta confidence intervals; whenever both the upper and lower limit

express the same sign we can accept the alternative hypothesis (with  $p < .05$ ) that the effect of the variable is statistically significant.

The frequency distribution analysis shows that most variables have an asymmetrical and kurtosis index  $\geq [1]$ . This means that the distribution of the variables have an abnormal tendency. Even though the normality of the variable distribution is not assumed by the regression, that condition could threaten some of the assumptions such as the linearity of the relations.

### *Bivariate Correlation Analysis*

Table 6 presents the descriptive statistics (M and SD), and Table 7 presents the correlations between variables examined to further clarify the nature, intensity and direction of the existing relations between the constructs considered. As can be seen (Tab. 7), workplace involvement (UWES) shows significant positive correlations with the perception of general well-being (GHQ) ( $r = .32$ ;  $p < .01$ ), the perception of structural support in the organization ( $r = .29$ ;  $p < .01$ ), problem-solving ( $r = .29$ ;  $p < .01$ ), and self-efficacy in social-relational competence (SRC), specifically in empathy and listening ( $r = .23$ ;  $p < .01$ ), emotional control ( $r = .28$ ;  $p < .01$ ), perspective taking ( $r = .33$ ;  $p < .01$ ), trust and persistence ( $r = .24$ ;  $p < .01$ ). In contrast, there is a negative correlation with emotional focus ( $r = -.18$ ;  $p < .051$ ), and problem avoidance ( $r = -.26$ ;  $p < .01$ ).

The **perception of general well-being** has a positive correlation with organizational support ( $r = .23$ ;  $p < .01$ ), problem-solving ( $r = .23$ ;  $p < .01$ ), and a few variables related to self-efficacy in social-relational competence, in particular with emotional control ( $r = .18$ ;  $p < .05$ ), and the separation of borders ( $r = .15$ ;  $p < .05$ ). In contrast, there is a negative correlation with emotional focus ( $r = -.32$ ;  $p < .051$ ), and problem avoidance ( $r = -.19$ ;  $p < .05$ ).

The **perception of organizational support** correlates positively with self-efficacy in social-relational competence, specifically emotional control ( $r = .23$ ;  $p < .01$ ), perspective taking ( $r = .23$ ;  $p < .01$ ), trust and persistence ( $r = .18$ ;  $p < .05$ ), separation of borders ( $r = .23$ ;  $p < .01$ ).

The perception of total stress correlates positively and significantly with coping strategies related to requests for social support ( $r = .26$ ;  $p < .01$ ), and emotional distress ( $r = .31$ ;  $p < .01$ ); such reactions are also confirmed for the single stress scales. Specifically, problematic relations with patients correlate positively with the strategy of avoiding the problem ( $r = .18$ ;  $p < .05$ ), and negatively with competence in empathy and listening ( $r = -.22$ ;  $p < .01$ ).

The **extent of special training in managing relationships** correlates negatively and significantly with the perception of stress ( $r=-.26$ ;  $p<.01$ ), and with the single stress scales. That is even more evident regarding special training in psychosocial aspects ( $r=-.29$ ;  $p<.01$ ). The negative correlation is also evident for the coping strategy of emotional focus ( $r=-.16$ ;  $p<.05$ ).

**Tab. 6**

<b>Variables</b>	<b>Mean</b>	<b>SD</b>	<b>N</b>	<b>MS</b>
1. Additional training	4.2313	4.1613	147	29
2. Add. training (psychosocial aspect)	3.2313	3.0901	147	29
3. Stress	40.2	17.263	176	
4. Personal attack-unexpected organiz. events	12.89	5.751	175	1
5. Clinical emergency	7.06	3.242	176	
6. Facing death	8.38	4.118	176	
7. Problematic relations with patients	4.99	2.59	176	
8. Personal criticism	6.96	3.514	176	
9. Problem solving	52.01	9.829	176	
10. Request for assistance	30.22	13.295	176	
11. Emotional focus	19.78	10.729	176	
12. Problem avoidance	15.11	8.671	176	
13. UWES	77.2	18.051	176	
14. GHQ	35.43	5.672	176	
15. Organizational Support	13.49	6.413	176	
16. SRC empathy-listening	13.06	3.262	168	8
17. SRC emotional control	15.18	3.975	168	8
18. SRC perspective taking	10.71	2.701	168	8
19. SRC trust and persistence	7.7	2.078	171	5
20. SRC separation of borders	6.95	2.551	169	7



**Tab. 7**

Variables	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
1. Additional training	1																		
2. Add. training (psychosocial aspect)	.965**	1																	
3. Stress	.265**	.290**	1																
4. Personal attack (...)	.263**	.283**	.931**	1															
5. Clinical emergency	.292**	.297**	.855**	.707**	1														
6. Facing death	.258**	.289**	.925**	.779**	.812**	1													
7. Problematic relations with patients	-.184*	-.195*	.847**	.734**	.677**	.805**	1												
8. Personal criticism	-.194*	.231**	.885**	.830**	.672**	.762**	.657**	1											
9. Problem solving	-.173*	-.193*	0.049	0.086	-0.045	0.042	-0.069	0.144	1										
10. Request for assistance	-0.098	-0.113	.262**	.249**	.212**	.276**	.215**	.240**	.181*	1									
11. Emotional focus	-.164*	-0.159	.317**	.287**	.263**	.311**	.319**	.239**	-0.122	.536**	1								
12. Problem avoidance	-0.005	0.009	0.097	0.066	0.052	0.116	.184*	0.061	-.192*	.409**	.581**	1							
13. UWES	0.127	0.07	0.099	0.122	0.005	0.088	0.062	0.12	.292**	-0.038	-.185*	.265**	1						
14. GHQ	0.049	0.048	-0.122	-0.073	-0.105	-0.121	-0.142	-0.113	.236**	-0.118	.328**	-.192*	.328**	1					
15. Organizational Support	0.138	0.127	-0.08	-0.06	-0.081	-0.037	-0.078	-0.081	.279**	0.132	-0.056	0.012	.296**	.234**	1				
16. SRC empathy-listening	-0.001	-0.016	-0.059	-0.055	-0.054	-0.032	-.221**	0.007	0.1	-.191*	-.175*	-.198*	.230**	-0.021	0.103	1			
17. SRC emotional control	-0.017	-0.063	-0.053	-0.079	-0.064	-0.014	-0.109	0.033	.183*	-0.141	.340**	-.173*	.289**	.184*	.235**	.621**	1		
18. SRC perspective taking	0.027	-0.013	-0.023	-0.03	-0.027	0.001	-0.135	0.053	.206**	-0.122	.314**	.242**	.337**	0.103	.235**	.669**	.765**	1	
19. SRC trust and persistence	-0.017	-0.055	-0.015	-0.016	-0.03	-0.004	-0.089	0.024	0.145	-0.143	.250**	.208**	.248**	0.083	.188*	.568**	.672**	.739**	1
20. SRC separation of borders	-0.002	0	-0.141	-0.141	-0.134	-0.102	-0.098	-0.127	0.074	-0.094	.208**	-0.029	0.139	.152*	.236**	.399**	.631**	.554**	.566**

\*\*p<.01; \*p<.05

*Regression analysis*

A hierarchical regression analysis was done to verify the hypothesis about the possible factors that influence workplace stress (Tab 8). The criterion used is the perception of workplace stress as indicator, and the predictors are the variables relative to the extent of special training in managing relationships, coping strategies, perception of self-efficacy in social-relational competence, and the structure of organizational support.

The insertion of several independent variables in the regression steps is as follows: first the control variables such as age, work experience, etc., and then the causes related to the individual followed by the causes related to the environment.

**Tab. 8**

	Beta	Confidence Interval (non-standard beta)	
		Below	Above
<i>Step 1</i>			
Age	-.327	-1.532	.475
Experience	.248	-.600	1.474
Role	.069	-2.501	4.355
R <sup>2</sup> Adjusted=-.001			
<i>Step 2</i>			
Age	-.129	-1.191	.775
Experience	.062	-.906	1.124
Role	.059	-2.489	4.079
Additional training	-.308**	-2.807	-.628
R <sup>2</sup> Adjusted = .082**			
Delta R <sup>2</sup> =.081**			
<i>Step 3</i>			
Age	.093	-.879	1.180
Experience	-.109	-1.204	.820
Role	.077	-2.115	4.207

Additional training	-.252*	-2.488	-.325
Problem solving	.109	-.206	.637
Request for assistance	.011	-.314	.342
Emotional focus	.377**	.201	1.067
Problem avoidance	-.041	-.595	.431
R <sup>2</sup> Adjusted = .164*			
Delta R <sup>2</sup> = .082*			

*Step 4*

Age	.234	-.695	1.451
Experience	-.189	-1.370	.702
Role	.122	-1.576	4.888
Additional training	-.229*	-2.364	-.189
Problem solving	.134	-.176	.704
Request for assistance	.032	-.288	.370
Emotional focus	.325*	.071	1.022
Problem avoidance	.005	-.515	.534
SRC empathy, listening	-.142	-2.352	.649
SRC emotional control	.111	-1.060	2.023
SRC perspective taking	.023	-2.191	2.513
SRC trust and persistence	.071	-1.874	3.144
SRC separation of borders	-.287*	-3.739	-.300
R <sup>2</sup> Adjusted = .183			
Delta R <sup>2</sup> = .019			

*Step 5*

Age	.216	-.727	1.425
Experience	-.198	-1.386	.689
Role	.098	-1.984	4.639
Additional training	-.212*	-2.290	-.077
Problem solving	.153	-.146	.750
Request for assistance	.032	-.289	.370
Emotional focus	.327*	.074	1.027
Problem avoidance	.008	-.510	.540
SRC empathy, listening	-.169	-2.557	.528
SRC emotional control	.136	-.968	2.156
SRC perspective taking	.038	-2.102	2.628

SRC trust and persistence	.062	-1.961	3.074
SRC separation of borders	-.264*	-3.616	-.107
Organizational Support	-.097	-.987	.360

R<sup>2</sup> Adjusted = .182

Delta R<sup>2</sup> = -.001

\*\*p<.01

\*p<.05

The hierarchical regression analysis of workplace stress highlights some significant evidence. In the first step of the regression there are no significant values. In the second step the variable of extent of special training has a negative correlation with stress (b = -.308, p<0.01). The variance explained by the inserted variable in this step is equal to 12% (p<0.01). In the third step there is a positive correlation between emotional focus and stress (b = .377, p<0.01), while the extent of special training has a negative correlation (b = -.252, p<0.05). The variance explained by the insertion of the variables in the third step is equal to 23% (p<0.05). In the fourth step there are negative correlations between stress and extent of special training (b = -.229, p<0.05), and perception of self-efficacy in the separation of borders (b = -.287, p<0.05), while there is a positive and significant correlation between stress and the coping strategy of emotional distress (b = .325, p<0.01). The variance explained by the variables inserted in the fourth step is equal to 29% (p=ns). In the fifth step the introduction of the perception of social support doesn't affect the values.

In the third step the change in significance of the beta weight of the extent of special training indicates a possible mediator: the relationship between stress and the extent of special training in managing relationships becomes less significant compared to the previous step. In other words, the predictor decreases significantly because of the effect of the introduction of the coping strategy. In order to confirm the hypothesis that the risks in oncological disease influence workplace stress, a regression analysis was done. The data aren't significant (Tab. 9).

**Tab. 9**

	R <sup>2</sup>	b	Sig
Risk Level	-.014	.054	ns

## Analysis of Variance

There are significant differences between oncologists and doctors in other fields (with  $p < .05$ ) in the scores obtained for request for assistance, organizational support, and problem avoidance (Tab. 10).

**Tab. 10**

	Other physicians		Oncologists		F	p
	M	SD	M	SD		
<b>Request for assistance</b>	27.44	13.67	31.70	12.91	4.15	0.04
<b>Problem avoidance</b>	16.90	9.77	14.16	7.91	4.07	0.04
<b>Organizational Support</b>	12.07	6.47	14.25	6.28	4.73	0.03

Other physicians (N=61); Oncologists (N=115)

## Discussion

The results of the analyses confirm some of the hypotheses. **H1a** postulated the existence of a significant correlation between **work involvement** and the variables we are interested in. Specifically, there are positive correlations with the perception of general well-being, organizational support, and self-efficacy in social-relational competence; those results indicate that to increase work involvement it is necessary to increase parallel aspects such as self-confidence in one's ability to handle difficult situations, as well as offer adequate support to co-workers. In contrast, no correlation was found between work involvement and the perception of stress; for that reason our first hypothesis is only partially confirmed.

Similarly, **H1b** postulated that the perception of **general well-being** would be correlated with the observed variables. Specifically, there are positive correlations with the perception of organizational support, self-efficacy in social-relational competence (emotional control and separation of borders), and the use of problem-solving as an adaptive coping strategy. There were negative correlations with the use of non-adaptive coping strategies, fully confirming our hypothesis.

Those results indicate that if the worker has great confidence in his own ability to stay calm and peaceful when confronting dangerous situations, and to separate emotionally his professional from private life, as well as being able to utilize resources and personal experience to confront workplace problems, he will

experience a greater sense of general well-being. Along with personal variables, a fundamental role is also played by organizational variables.

**H1c** postulated the existence of a significant correlation between the perception of **organizational support** and workplace stress, along with some personal variables. There are positive correlations with the perception of self-efficacy in social-relational competence, and the use of adaptive problem-solving as a coping strategy. In contrast, no correlation was found with the perception of stress nor with non-adaptive coping strategies; for that reason our hypothesis is only partially confirmed. That evidence indicates that great self-confidence in one's own social-relational competence increases the perception of organizational support, presumably by enabling the individual to be more assertive when facing input from the organization.

**H1d** postulates the existence of significant correlations between the perception of **workplace stress** and some personal variables. There is a positive correlation with the use of emotional focus as a non-adaptive coping strategy, but no correlation with other variables, hence our hypothesis is only partially confirmed. Those results indicate that doctors who use a coping strategy focused on an emotional response to events perceive even more workplace stress, presumably because of little ability to adequately manage one's own emotions.

**H1e** postulates the existence of a significant correlation between the extent of **special training in managing relationships** with all the variables considered. There are negative correlations with the perception of workplace stress and the use of emotional focus as a non-adaptive coping strategy. In contrast, there are no positive correlations with other personal and organizational variables. Hence, our hypothesis is only partially confirmed.

Those results indicate that having adequate training, especially in managing relationships, will have a positive impact on the perception of stress. Hence, it seems evident that to reduce the perception of workplace stress it would be useful to add specific training in managing relationships alongside traditional medical training.

**H2** relied on hierarchical regression analysis to examine some variables such as the extent of special training in managing relationships, coping strategies, the perception of self-efficacy in social-relational competence, the perception of organizational support, all of which may be considered predictors of the perception of stress in the medical workplace.

Me may confirm that little special training in managing relationships can cause stress. Or rather, those who spend little time in special training to improve their ability to manage relationships are more stressed. Conversely, those with more training in managing relationships are less stressed than other doctors.

In addition, some coping strategies may be considered a cause of workplace stress, specifically: the tendency to react emotionally when confronting problems, and the inability to manage one's own emotions. It possible that the use of dysfunctional coping strategies such as Emotional Focus might mediate the relationship between extent of special training and workplace stress. In other words, feeling unable to manage one's own emotions despite special training, might be a risk factor for stress. That possible relationship may be hypothesized from our data, but further study is needed.

A lack of self-confidence in one's ability to maintain a natural balance of tensions in the workplace in the helping professions may also be considered a source of workplace stress. We did not confirm that a lack of organizational support is a cause of workplace stress

**H3** postulated that the risk of mortality in oncology is a source of stress for doctors, and this hypothesis was not confirmed. Or more specifically, the data did not confirm that oncologists who work with patients at high risk of mortality were more stressed than doctors with patients having a more positive prognosis.

**H4** postulated the existence of significant differences between the scores of oncologists and doctors in other fields. The data show significant differences between these groups of variables: request for assistance, problem avoidance, and organizational support. Specifically, oncologists utilize counseling and help from others as an adaptive coping strategy more than other doctors, while the latter utilize reactive avoidance of problem situations as a coping strategy. Oncologists also perceive that they receive more help from the organization.

## **Conclusions**

The data allow some conclusions. In general, the stress perceived by the doctors interviewed is not especially alarming. However, there are indications that workplace stress is related to specific causes that can compromise the performance and well-being of doctors over time, and that it's possible to improve the perception of well-being and hence quality of life.

Specifically, well-being in the workplace is closely related to having adequate social-relational competence and training in managing relationships. In addition, doctors who have more difficulty managing their own emotions are more at risk

of workplace stress. That finding highlights the importance of the quality of doctor-patient relationships during treatment. Doctors who have good relationships with patients feel more satisfaction and perceived well-being.

In clinical practice there must be technical competence and availability of adequate treatment, but also good relationships. A doctor must accompany the patient all the way from the first meeting to the diagnosis and treatment. Thanks to technological advances more and more diseases with a risk of imminent death have become “chronic diseases,” and the need to accompany the patient in good relations has become an essential part of treatment.

Helping people live with their disease and find a new balance in their lives, have become fundamental goals of modern medical practice rather than merely curing the disease, alongside the traditional goal of healing. These modern goals become even more important when the doctor-patient relationship entails deep trust over a period of possibly years, and often to the end of the patient’s life. A perception of little self-efficacy in social-relational competence is a cause of stress and distress for doctors. Those who report having received no special training in communication or in managing relationships with patients, perceive more workplace stress. We may say that the lack of such training is a source of stress. Hence, psychosocial training should play a central role in reducing the risks of workplace stress and promoting well-being among doctors and other workers in the helping professions who are in constant contact with serious suffering. Such training should focus on managing relationships and social-relational competence.

Courses in psychosocial training with specific attention to managing communication and relationships with patients are advisable in hospitals. Supervisory meetings with psychologists are advisable to express and share the doctor’s own emotions as well as the emotions of others, to better manage difficult and stressful periods. Adequate attention to the emotional life of individuals and groups is important to cultivate a sense of well-being in the workplace. It is also important to encourage effective strategies to manage stressful events. Departments and institutions, as well as individuals, must become aware and be willing to improve the quality of life in the workplace. There must be social, technical and psychosocial improvements in organizations (42). Social and technical improvements should focus primarily on structural changes in the workplace that are related to stress, health and satisfaction. Such improvements should address specific, objective factors and have measurable results. In contrast, psychosocial improvements should focus on the perceptions that workers have of their workplace, using strategies that increase workplace involvement, perceived social and organizational support and improved



communication. Finally, it is important to report that the workers interviewed were positive toward the research and its goals. Being asked to express their own opinions, and being listened to, were considered indications that others are interested in their problems, as well as being an opportunity to participate in a study that focused on some problems of their profession.

A limit of this study is that it's impossible to generalize from the geographically non-representative sample to the general population. Future studies should use a sample that is more representative of the national population, to replicate the findings and extend the analysis. Another limitation of this study is the exclusive use of self-reporting. Objective data sources would be more reliable. However, despite the limitations, this study contributes to our understanding of workplace stress in the health field, indicating some variables related to stress.

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- *“Protection from work stress and burnout in Italian oncologists”*, F.P. Guadagna, E. Foddai, V. Sanfratello, F. Pace, A. Russo (2011), Sezione Poster The 12<sup>th</sup> European Congress of Psychology, Istanbul.

## Publications

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### THE IMPACT ON THE PATIENT'S ADJUSTMENT TO BREAST CANCER OF THE CAREGIVER'S BURDEN AND DISTRESS

[L'impatto del carico emotivo e del distress del caregiver sull'adattamento alla malattia del paziente affetto da carcinoma della mammella]

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**Keywords:** Breast cancer; Caregiver; Distress; Adjustment

**Parole Chiave:** Carcinoma della mammilla; caregiver; Distress

**Abstract:** *Introduction:* Breast cancer involves continually stressful situation caused by the threat of the illness for both patient and caregiver. Impairment of coping and support processes can result in this context. The aim of the present study was to obtain further knowledge regarding the relationship between the breast cancer patient and the caregiver's psychological distress. *Methods:* Participants were recruited in an outpatient oncology clinic. Measures included *Impact of Events Scale* (IES), *Family Strain Questionnaire* (FSQ), *Mental Adjustment to Cancer* (MAC) and *Profile of Mood States* (POMS). Patients completed a measure of psychological adjustment to their cancer and caregivers underwent a measure of caregiver strain. *Results:* A sample of 56 patients with breast cancer and their respective caregivers was included in the study. Mean age of patients was 56 (range: 30-75). The IES-Avoidance scores of patients were significantly correlated with the IES-Intrusion of caregivers ( $p < .05$ ), the POMS-Anxiety ( $p < .01$ ), Depression ( $p < .01$ ) and Hostility ( $p < .01$ ) scores of their caregivers. The POMS-Confusion scores of caregivers were correlated with the IES-A scores of patients. *Conclusions:* Our findings indicated that the caregiver is as likely to experience psychological distress as the cancer patient, and lends weight to the assertion that both members of the dyad experience similar levels of distress. Moreover, we found that the hopelessness and the sense of the uncontrollability of cancer in the patients are predicted by the vigour and the emotional burden of the caregiver.

**Riassunto:** *Introduzione:* Il carcinoma della mammella frequentemente genera situazioni stressanti legate alla gravità della malattia, nel paziente così come nel caregiver. In questo contesto possono verificarsi alterazioni nel coping e nel processo di supporto. Lo scopo del presente studio è quello di investigare la relazione tra il distress psicologico del paziente affetto da carcinoma della mammella e il suo caregiver. *Metodi:* I partecipanti sono stati reclutati in un DH di oncologia. Come questionari sono stati somministrati l'*Impact of Events Scale* (IES), il *Family Strain Questionnaire* (FSQ), il *Mental Adjustment to Cancer* (MAC) e il *Profile of Mood States* (POMS). I pazienti hanno completato un questionario sull'adattamento psicologico alla loro malattia mentre al caregiver è stato proposto un questionario relativo al proprio malessere. *Risultati:* Il campione comprendeva 56 pazienti con carcinoma della mammella e i loro rispettivi caregiver. L'età media dei pazienti è stata di 56 anni (range: 30-75). Il punteggio dell'IES-evitamento dei pazienti è risultato significativamente correlato con l'IES-pensieri intrusivi dei caregiver ( $p < .05$ ), con i punteggi del POMS-Ansia ( $p$

< .01), Depressione ( $p < .01$ ) e ostilità ( $p < .01$ ) dei loro caregiver. I punteggi del POMS-Confusione dei caregiver è risultato correlato con i punteggi dell'IES-Evitamento dei pazienti. *Conclusioni:* I nostri risultati suggeriscono che il caregiver ha una probabilità di sperimentare un distress psicologico proporzionale a quella del paziente, e avvalorare la tesi secondo la quale entrambi i membri della diade sperimentano livelli simili di distress. Inoltre, abbiamo riscontrato che il senso di disperazione e di incontrollabilità della malattia da parte del paziente affetto da carcinoma può essere predetto dal vigore e dal carico emotivo del caregiver.

## Introduction

The experience of cancer may depend heavily on patients' interpersonal context and, notably, their primary caregivers. Caregivers of cancer patients may take an active role in key decisions concerning treatment options and provide emotional and instrumental support to the patient [1]. There is a general consensus that breast cancer poses a major stressor for patients as well as caregivers and that patients and partners are involved in each other's coping and support processes [2]. Significantly, an appropriate adjustment to cancer depends on the totality of the cognitive, emotional and behavioural responses to the diagnosis on the part of both the patient and the significant other.

Most studies concerning breast cancer has reported that this life-threatening illness produces high stress in both patients and families, and a number of studies have found a significant correlation between distress in patients and partners [3]. Moreover Hodges [4], in a meta-analytic investigation conducted on 21 independent samples regarding the relationship between the psychological distress of various types of cancer patients and their caregivers confirm the positive association between patients' and caregivers' psychological distress. Most studies of couples in which the woman has cancer have focused on breast cancer patients. Several studies indicates that the psychological distress of breast cancer patients is higher than that of their spouses [5, 6], while others found that spouses present more psychosocial problems than patients [7,8]. Northouse [9] described husbands' level of distress as similar to that of their wives and higher, up to 18 months after diagnosis, than that in non-patient populations. A recent meta-analysis has indicated that differences in distress within couples coping with cancer could clearly be ascribed to gender: women were found to report more distress than men, regardless of whether they were the individuals with cancer or the partners [10].

Several studies have documented that the primary caregiver of the cancer patient is in a continually stressful situation caused by the threat of the illness and, simultaneously, by the assumption of the role of main informal social support resource for the patient in the illness process. Previous research has consistently found that a good marital relationship predicts better emotional adaptation to breast cancer [11, 12]. In contrast, social constraints and unresponsiveness of family members in talking about the illness have been related to poor mental health among cancer patients [13]. Emotional distress and depres-



sion in the caregiver can have important consequences for the diagnosed patient and can negatively affect his/her adjustment and how the couple copes with challenges [14, 15].

Overall, it appears that perceived reactions of the patient's caregiver represent an important influence on the woman's response to the diagnosis and treatment of this disease [16]. Caregivers are at the center of the support network for the patient, and it is therefore extremely important to reach a detailed appreciation of their needs and experiences. Given this, it seems important to know more about how caregiver reactions relate to the patient's emotional well-being, whether the effect is an adverse one or a beneficial one. The aims of this study were to determine the correspondence between the psychological distress of cancer patients and their caregivers, and ascertain the nature of this relationship. The following specific questions were raised.

*Research Question 1:* Is there a significant positive correlation between breast cancer patient and caregiver psychological distress?

*Research Question 2:* Is the distress of the caregiver a predictor of the patient's poor adjustment to breast cancer ?

## **Patients and methods**

### *Participants*

For enrolment participants should be new and returning cancer patients seen at the medical oncology clinic at the University of Palermo (Italy), with their caregivers. As caregiver we considered a person indicated by the patient as the "primary informal caregiver."

### *Procedures*

Patients were approached in the medical oncology clinic before or after their treatment appointments and asked to participate in the study. If a patient was interested, the research assistant explained the informed consent form to the patient and asked for the patient's permission to contact his/her caregiver to request his/her participation. Exclusion criteria for patients were: prior history of psychiatric hospitalization (3 participants were excluded), and major concurrent disease (6 participants were excluded). Approximately 85% of the patients contacted who met eligibility criteria agreed to participate. Patients and caregivers who agreed to participate were separately interviewed before leaving the clinic.

### *Measures*

*Impact of Events Scale (IES)* [17]. Psychological distress was assessed using a short-

ened version of the Impact of Events Scale. This scale has been seen to offer a reliable assessment of intrusive thoughts related to stressful events and conscious avoidance of feelings and ideas about the events [18]. The shortened version of the scale includes eight items (four for each subscale). Patients and caregivers respond to statements about the frequency (0 = not at all, 1 = rarely, 3 = sometimes, 5 = often) in the prior 7 days of intrusive thoughts related to the patient's cancer (e.g. "I thought about the diagnosis when I didn't mean to") and to the frequency of avoidance behaviors (e.g. 'I kept away from reminders of the cancer'). In the present study, Cronbach's alphas for patients for the Intrusion and the Avoidance scale were .72 and .89, respectively, and .73 and .82 for caregivers.

*Family Strain Questionnaire (FSQ)* [19]. The FSQ consists of a semi-structured interview and questionnaire that can be administered in a total of about 20 min. The semi-structured interview was focused on the caregiver's knowledge of/beliefs about the disease and the way in which it is managed. The questionnaire consists of 35 dichotomous items (yes/no) covering five factors: Emotional Burden (EB); Problem of Social Involvement (SI); The Need for Knowledge of the Disease (KD); Quality of Family Relationships (FR); Thoughts about Death (TD). Nine non-factorial dichotomous items concern the caregiver's attribution of problems relating to social stigma. As the 'yes' answers are attributed a score of 1, the higher the score for each area, the greater the problems involved, with the exception of satisfaction of family relationships (in which a high score indicates good relationships). The FSQ has been validated in Italy and has good psychometric properties. In this study Cronbach's alpha ranged from .72 (TD) to .87 (EB).

*Mental Adjustment to Cancer (MAC)* [20]. The MAC is a 40 items scale which identifies four behavioral styles of coping: fighting spirit, fatalism, helplessness/hopelessness, and anxious preoccupation. Patients' responses were rated on a 4-point scale. *Fighting Spirit (FS)*: identifies the patient's tendency to see cancer as a challenge and to take an active role in therapy and recovery, and to adopt an optimistic attitude. *Helplessness (H)*: measures cognitive schema and corresponding behaviors characterized by a sense of the uncontrollability of cancer. *Stoic Acceptance/Fatalism (F)*: which indicates resignation and passive acceptance of the illness and the therapy, without personal involvement. *Anxious Preoccupation (AP)*: evaluates anxiety and diffuse worry about cancer and its possible recurrence, associated with excessive search for reassurance and information. In the present study, internal consistency (Cronbach's alpha) of the subscales of MAC were: FS=.76, H=.69, AP=.67, F=.62, respectively.

*Profile of Mood States (POMS)* [21]. Patients and caregivers were asked to rate the

Profile of Mood States (POMS), a 65-items measure designed to assess subjective mood states, including positive and negative affects. Responses were on a four-point scale, ranging from "Not at all like this" to "Very much like this". The POMS yields a score for total mood disturbance based on six subscales: Anxiety (A), Depression (D), Hostility (H), Confusion (C), Vigor (V), and Fatigue (F). In this study, all the alpha coefficients for the six POMS scales ranged from .84 (C) to .95 (D) (patients); the alpha coefficients ranged from .76 (F) to .89 (A) for caregivers.

*Statistical analyses*

Means and standard deviations were computed for demographic and medical information as well as for psychosocial variables. Paired-sample *t* tests were conducted to compare mean differences between patients and caregivers scores in IES and POMS. Pearson correlation coefficients were calculated to examine the bivariate associations among study variables. Six separate stepwise regressions were constructed to examine the role of family strain (FSQ) and mood states (POMS) of caregivers in predicting the patient adjustment to cancer (IES-I, -A; MAC-FS, -H/H, -AP, F). The equations had 2 steps: in step 1, we entered the age of the patient and caregiver as control variables, in step 2 we entered the independent variables with a stepwise procedure. The stepwise regression procedure describes how much more each independent or predictor variable has contributed to the prediction from the preceding predictor variables, and it is generally used in exploratory procedures. In this study, we adopted a more restrictive level of .01.

*Results*

Fifty-six patient-caregiver couples participated.

Demographic and medical characteristics of the sample are presented in **Table 1**. Patients had a mean age of 56 (range: 30-75). Eighty percent were married, and sixty-six percent had at least a high school diploma, and in terms of occupation, sixty-seven percent were unemployed. Eighty-five percent underwent surgical treatment or surgery and chemotherapy. Caregivers had a mean age of 48.8 (range: from 23 to 75), and 55.5% were female. Fifty-five percent were the patients' spouses, twenty-seven percent were the children, and eighteen percent had other relationships (parents, sisters). Only 44% were employed caregivers.

**Table 1. Demographic and medical characteristics**

Demographic and medical characteristics	Patients (N = 56)	Caregivers (N = 56)

Mean age	56,02 (11,36)	48,85 (13,92)
Sex		
male	12,5%	44,6%
female	87,5%	55,4%
Role		
partner	-	55,4%
son	-	26,8%
other	-	17,9%
Status		
single (or separated/widowed)	19,6%	23,2%
married	80,4	76,8%
Education		
less than high school	66,1%	58,9%
high school or more	32,1%	41,1%
Employment status		
Employed	32,2%	44,6%
Unemployed	67,8%	55,4%
Type of cancer		
breast	73,2%	
colon and other	26,8%	
Stage		
I	72,2%	
II and III	27,8%	
Range time since diagnosis	1 - 10 months	
Therapy		
surgery or surgery + chemio	85,7%	
palliative	14,3%	

A first step in the analysis was the comparison between patients and caregivers in terms of psychological distress (IES & POMS). Only the IES-Avoidant subscale was higher in cancer patients than caregivers ( $t = 2.02$   $p < .05$ ). **Table 2** shows zero-order correlations for the observed variables. The IES-Avoidance scores of patients were significantly correlated with the IES-Intrusion of caregivers ( $p < .05$ ), the POMS-Anxiety ( $p < .01$ ), Depression ( $p < .01$ ), and Hostility ( $p < .01$ ), scores of their caregivers. The IES-Intrusion of patients were correlated with the FSQ-Emotional Burden and KD scores of their caregivers ( $p < .05$ ;  $p < .01$ , respectively). The FSQ-Emotional Burden of caregivers was correlated

with the MAC-Helplessness ( $p < .05$ ). The POMS-Confusion scores of caregivers were correlated with the IES-A scores of patients.

**Table 2.** Zero-order correlations (Pearson's  $r$ ) between patients and caregivers

Patients	Caregiver													
	IES Intr	IES Av	POMS A	POMS D	POMS H	POMS V	POMS F	POMS C	FSQ EB	FSQ SI	FSQ KD	FSQ RF	FSQ KD	
POMS A	,034	,231	,095	,138	,180	-,225	,322(*)	,277*	,065	,189	,056	-,114	,108	
POMS D	,025	,214	,089	,176	,156	-,232	,212	,338*	,054	,150	-,006	-,060	,100	
POMS H	-,064	,188	,052	,091	,226	-,050	,246	,296*	,062	,147	,039	-,094	,048	
POMS V	-,080	-,129	,111	,057	,102	,407(**)	,104	-,095	-,182	-,196	-,212	-,155	-,076	
POMS F	,131	,180	,124	,174	,178	-,288(*)	,334(*)	,276*	-,013	,195	-,060	-,084	,057	
POMS C	-,013	,148	,098	,088	,113	-,062	,192	,211	-,081	,063	-,078	-,063	,015	
IES Intr	,128	,174	-,033	,038	,083	-,095	-,027	,104	,294*	,179	,408**	-,003	,208	
IES Av	,335*	,105	,346**	,433**	,362**	-,185	,216	,374**	,112	,184	,123	-,095	,232	
MAC FS	-,048	-,073	,113	,028	,076	,264*	,136	,052	-,180	,022	-,164	-,058	-,082	
MAC H/H	,160	,218	-,062	,042	-,105	-,398**	-,068	,062	,296*	,230	,232	,189	,243	
MAC AP	-,161	,170	-,122	-,072	-,129	-,152	,044	,059	,057	,070	,077	-,045	-,020	
MAC F	,087	,254	-,067	,087	-,167	-,110	-,170	,106	,016	,058	-,058	,083	,046	

\* Correlation is significant at the 0.05 level.

With regard to the regression analyses (see the statistical analyses section), the first block of equations (see Table 3) was conducted on the IES Intrusion and Avoidance scores of patients. The first final model was significant ( $F = 3.255, p < .01$ ), and revealed that the FSQ-KD ( $\beta = .40, p < .001$ ) was the only predictor of IES-Intrusion of patients. The second equation showed that age of the patient had quite a significant effect ( $p < .05$ ). A second block of multiple regression analyses was conducted on the MAC scores of patients as the dependent variables. In the final model both the POMS-Vigour and the age of patient were predictors of the MAC-Helplessness/Hopelessness ( $\beta = -.36, p < .01$ ;  $\beta = .42, p < .01$ , respectively). The FSQ-EB showed a low effect on MAC Helplessness/Hopelessness ( $p < .05$ ).

**Table 3.** Hierarchical multiple-regression analyses predicting patient's adjustment to cancer

	$\beta$	<i>p</i>	Adj <i>R</i> <sup>2</sup>	<i>F</i>	<i>p</i>	<i>p of R</i> <sup>2</sup> change
I – IES Intrusion			.14	3.26	.01	
FSQ – KD	-.40	.001				
I – IES Avoidance			.22	3.92	.01	
Age of patients	.29	.05				
POMS - C	-.52	.001				
II – MAC Helplessness/Hopelessness			.33	7.70	.00	
Age of patients	.42	.01				
POMS - V	-.36	.01				
FSQ - EB	.24	.05				

Only significant variables and those approaching significance are included in the table. The Table displays the standardised regression coefficients ( $\beta$ ), the significance of R squared increment provided at each step (*p of R<sup>2</sup> change*), and the overall Adjusted R squared (*Adj R<sup>2</sup>*).

IES Intrusion and Avoidance = subscales of Impact Event Scale; MAC Helplessness/Hopelessness = subscale from Mental Adjustment to Cancer; FSQ KD, EB = knowledge of disease, emotional burden, subscales of Family Strain Questionnaire; POMS – C = confusion, subscale of Profile of Mood States.

#### Discussion

In this study, the aim was to test if there exists a positive relationship between breast cancer patient and caregiver psychological distress, and if the caregiver's distress may be a predictor of the patient's poor adjustment to cancer. Our findings confirm a significant positive relationship between patient and caregiver psychological distress. Caregiver distress of (POMS-Confusion, Hostility, Depression, and Anxiety) is positively correlated with the patient's avoidance of feelings and ideas about the cancer (IES-AV). Interestingly, the Vigor (POMS) of the caregiver is positively correlated with the Vigor and Fighting Spirit, and negatively with the Fatigue and the Helplessness of the patient. These findings seem to indicate that the caregiver is as likely to experience psychological distress as the cancer patient, and lends weight to the assertion that both members of the dyad experience similar levels of distress [3]. In our study, only the IES-Avoidant scale is higher in breast cancer patients than their caregivers. A cursory review of the literature regarding distress in breast cancer patients and their caregivers suggests that it is not cumulative and that it is beset

by quite contradictory claims. Studies have reported that patients are as distressed as caregivers, that patients with cancer are more distressed than their partners, that caregivers are more distressed than patients. Our findings are consistent with previous research which has shown that the difference between patient and caregiver psychological distress appears to vary over time [4], and that from the 3-month assessment period onwards, no significant difference in distress between patient and caregiver levels exist. One critical issue in the interpretation of findings regarding distress in patients and caregivers appears to be gender. Studies that find greater distress among partners may have confounded the patient-partner role with gender.

Moreover, the findings of the multiple regression analyses show that different aspects of the caregiver's psychological distress may predict the adjustment to breast cancer and distress of the cancer patient. The need of hear the disease (FSQ-KD) of the caregiver predicts the patient's intrusive thoughts related to cancer (IES-Intrusion). The hopelessness and the sense of the uncontrollability of cancer in the patient are predicted by the vigour and the emotional burden of the caregiver. These findings seem to suggest the association between the psychological distress of caregiver and patient, and they might well be interpreted as support for the notion that patient-caregiver pairs react as an interdependent emotional system. These findings are also consistent with previous research on women with breast cancer, which shows that the family caregiver's vulnerability is heightened because he or she finds himself/herself in a double and conflictive role. As the primary supporter, he/she must assume new roles in the household and provide tangible as well as emotional support; and at the same time must cope with the distress emanating from the significance of the patient's diagnosis in terms of suffering and the threat to life [22]. Further research will be necessary to investigate how the distress of caregivers may influence the patient's distress. Moreover, some important variables, such as gender and role, need to be taken into account, in order to study the relationship between the breast cancer patient and his/her caregiver. A recent meta-analysis [4] which covered 21 studies of distress in people with cancer and their caregivers outlined that while these caregivers were mainly partners, they also included siblings, children, and close friends. In our sample, only 55% of the primary caregivers indicated by patients are the spouses. The available literature suggests caution about assuming that partners of people with breast cancer have substantial caregiving responsibilities, in terms of providing assistance with medical management or the activities of daily life. Rather than being accepted uncritically as a synonym for partners of people with cancer, use of the term "caregiver" requires justification with explicit reference to instrumental caregiving tasks or demands of home management or functional limitations of the person with cancer. Finally, attention needs to be directed toward factors other than breast cancer as direct influences of distress in these couples and to mediators

and moderators of the cancer experience.

A limitation of this study was the modest size and the heterogeneous characteristics of both the samples of patient and caregiver. Results should therefore be considered tentative and exploratory until confirmed by further research studies. Despite these limitations on generalizability, our findings seem to offer useful information in the attempt to reach a clearer understanding concerning the experiences of breast cancer patients.



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## What Are the Cancer Risks in BRCA Carriers Apart from Those Regarding the Breast and the Ovary?

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**Abstract:** Germline mutations in the tumor suppressor genes *BRCA1* and *BRCA2* predispose to familial breast and/or ovarian cancer. The lifetime risk of members of families with genetic predisposition depends on the mutations of susceptibility genes. *BRCA1* mutations seem to confer the highest risk of developing neoplastic diseases.

Apart from breast and ovarian cancer mutations in *BRCA*, related pathways are supposed to confer a smaller risk for additional cancers (colon, melanoma, pancreas, lymphoma, prostate, liver). All these tumors have an inherited component not necessarily associated with genetic susceptibility to *BRCA* genes.

To date he main focus of this review has been argued still with difficulty. Just a deeper and complete evaluation of the topic will allow to establish how much is the contribution of *BRCA* mutations in different types of cancers other than breast and ovary.

**Keywords:** *BRCA* genes, *BRCA* mutations, cancer risk.

### INTRODUCTION

Germline mutations in the tumor suppressor genes *BRCA1* and *BRCA2* predispose to familial breast and/or ovarian cancer [1-3]. The lifetime risk of members of families with genetic predisposition depends on the mutations of susceptibility genes. *BRCA1* mutations seem to confer the highest risk of developing neoplastic diseases.

*BRCA1* mutation carriers may develop breast cancer (BC) in 56–80% and ovarian cancer (OC) in 10–30% of cases up to the age of 70. In addition, women affected by breast cancer and carriers of a known *BRCA1* mutation show a 40–60% risk of developing a second breast tumor, while males with *BRCA1* mutations show a risk of less than 1% of developing BC. *BRCA1* mutations are associated with ovarian cancer risk from 28% to 44% compared to 1.6% in the general population.

Women who inherit a *BRCA2* mutation present a 25%–40% risk of developing a BC and a 10%–20% risk of an OC [4-6].

The Breast Cancer Linkage Consortium (BCLC) has established a lower cumulative risk of OC in families whose members are carriers of mutations in *BRCA2*, that is, of 0.4% under the age of 50 and 27% at the age of 70.

The presence of a mutation in the gene *BRCA2* in men leads to a risk of BC of 5%–10% and an increased risk of developing prostatic or pancreatic tumors, while there is a much lower risk in male carriers of *BRCA1* mutations [7, 8].

The incidence of mutation in high-risk families varies widely among different populations; some present a wide spectrum of different mutations, while in particular ethnic groups specific mutations show a high frequency due to a founder effect [9, 10].

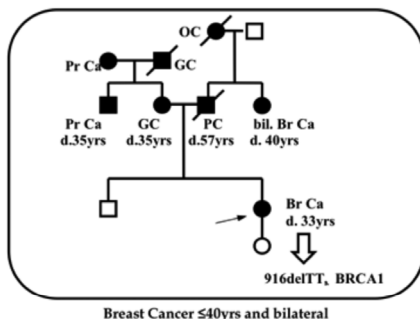
*BRCA1* and *BRCA2* proteins are involved in different pathways as DNA damage recognition, double strand break repair, checkpoint cellular control, transcription regulation and chromatin remodeling [11, 12]. These proteins are important for all cell types and in a large fraction of human cancers exist many *BRCA*-related pathways [13, 14]. Apart from breast and ovarian cancer mutations in *BRCA*, related pathways are supposed to confer a smaller risk for additional cancers (colon, melanoma, pancreas, lymphoma, prostate, liver). All these tumors have an inherited component not necessarily associated with genetic susceptibility to *BRCA* genes [15].

*BRCA* mutation carriers selected for BC and/or OC family risk may present a high risk of developing additional tumors not connected to familial breast or ovarian cancers.

Early reports from the BCLC and other family-based controls have suggested that families with deleterious *BRCA* mutations develop a larger number of prostate cancers compared with families without a known inherited

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**Fig. (1).** Genealogical tree of a family with a proband *BRCA1* mutation carrier and many members with different related tumors.  
 LEGEND: GC = Gastric Cancer; Pr Ca = Prostate cancer; PC = Pancreatic cancer; OC = Ovarian Cancer; Br Ca = Breast Cancer; Bil Br = bilateral Br.

predisposition [16-20]. Other types of cancer show wider variations, depending on population groups and cancer risks and larger populations may be needed in order to measure the effects on the development of other neoplasias (Fig. 1). Fig. (1) shows the genealogical tree of a family with a proband *BRCA1* mutation carrier and many members with different related tumors.

Results of meta-analyses show that the loss of *BRCA* gene function provides growth or survival advantages for a broader spectrum of tumors.

Rish *et al.* suggested that *BRCA1* and *BRCA2* mutations were associated with a significantly increased risk of cancers overall and sites other than breast and ovary in a recent population-based study from Canada [21].

In 2009, Mai *et al.* examined the effect of *BRCA* mutations on mortality apart from their known effects on cancer risk and observed an overall association between these alterations and reduced life expectancy with no deaths from cancers not associated with *BRCA* mutations.

#### ***BRCA* MUTATIONS AND PANCREATIC CANCER**

About 10% of pancreatic cancer patients may have an inherited form of the disease [22]. The term familial pancreatic cancer is applied to families with at least two first-degree relatives with pancreatic ductal adenocarcinoma but who do not fulfil the criteria for other familial cancer syndromes.

Familial pancreatic cancer marked by *BRCA2* mutations occurs 8 to 10 years sooner than sporadic disease [22, 23].

Some familial pancreatic cancers are caused by *BRCA2* germline mutations [22, 24]. Hahn *et al.* identified 12% of *BRCA2* mutations in 26 European families selected with familial pancreatic criteria. None of the families in this study met the criteria for familial breast or ovarian cancer. The risk for sporadic pancreatic cancer in *BRCA2* mutation carriers rises to 3.5 [22].

Pancreatic cancer is an established feature of the *BRCA2* phenotype. The association of mutations in *BRCA1* and susceptibility to pancreatic cancer is less strong [6].

Other biallelic *BRCA2*-mutations may cause Fanconi's anemia and are found in about 7% of pancreatic cancers [25].

A 6174delT-*BRCA2* mutation is found in about 1% of individuals of Ashkenazi Jewish descent, which may explain the higher rate of pancreas cancer observed in Jews as compared with that of non-Jewish populations [26].

#### ***BRCA* MUTATIONS AND MELANOMA**

The BCLC has reported approximately a 2.6-fold increase in the risk of malignant melanoma among *BRCA2* carrier families [17]. Nevertheless, a great many authors are not in accordance with this result since the case-control study curve had overestimated the risk [27, 28].

The Li-Fraumeni syndrome, associated with mutations in the p53 gene, has also been associated with both breast cancer and melanoma [29].

A number of studies devoted to identifying second cancers in women who have had breast cancer have noted an excess of melanomas [30-34]. Goggins *et al.* [33] specifically noted a 42% increased risk of melanoma in breast cancer patients following radiation [35]. Satram-Hoang *et al.* [36] observed an increase in melanoma as a second cancer in men who had had breast cancer.

Some authors [30, 31] noted an excess risk for melanoma in women with breast cancer. No excess risk for breast cancer was noted in the melanoma patients. Data from the Connecticut Tumor Registry found an increased occurrence of melanoma and breast cancer in the same patient. Data from the Swiss Cancer Registry demonstrated an increased incidence of melanomas.

Similar to its cutaneous counterpart, uveal melanomas seem to have a genetic predisposition [37, 38].

Some epidemiological studies have shown that this disease is associated with breast and ovarian cancers [39].

The *INK4A-ARF* locus encodes two alternative reading frame proteins P16 (INK4a) e P14(ARF), which mutations confer susceptibility to cutaneous melanomas. Other genes are germline mutations in *BRCA2* [40].

Hearle *et al.* didn't find these mutations in a systematically ascertained series of 385 patients with uveal melanoma [31].

Instead, Scott *et al.* estimated a prevalence at 3% of possible loss function changes in *BRCA2* in a group of 99 Australian patients with family history.

#### **BRCA MUTATIONS AND PROSTATE CANCER**

Many studies report that the evidence of cancers other than breast and ovarian are more elevated in *BRCA1/2* mutation carriers compared to individuals with no mutation [41, 42]. Of all these tumors, prostate cancer is the most frequent tumor associated with *BRCA1* and *BRCA2* mutations, as reported by different studies [41]. Various data have supported the evidence that this type of tumor is more often linked to the presence of ovarian cancer in *BRCA2* mutation carriers [42].

Moreover, BCLC family-based studies found that prostate cancer risk in *BRCA1/2* carriers depended on age and on mutation location. In fact, Streuwing *et al.* [18] estimated that the risk of prostate cancer at age 70 years was higher for *BRCA1* mutation carriers (25%) compared with *BRCA2* mutation carriers (5%). These data are confirmed by other studies which reported an increased risk of this tumor after age of 60 but not before (*OR* 3.7, 95% *C.I.*, 1.25–11.65, *P* = 0.01; *OR* 3.0, 95% *C.I.*, 0.56–10.72, *P* = 0.10) [43]. However, Giusti and colleagues reported that mutation carriers had twice the risk of prostate cancer and that the *BRCA1* 5382insC mutation was not associated with prostate cancer [44].

Other reports showed a potential relationship between the increase of prostate cancer risk and mutations linked to specific ethnic populations. In fact, as reported by Agalliu *et al.* [45] the founder mutation 6174delT in the *BRCA2* gene gives a three-fold elevated risk of high-grade prostate cancer in such patients but not for those individuals who are carriers of the *BRCA1* 185delAG or 5382insC founder mutations in Ashkenazi Jews. The same study shows a strong association between founder mutations and prostate cancer in men with no first-degree family history of breast and/or ovarian cancer but affected by a family history of prostate cancer.

Furthermore, in the Icelandic population, a significant elevation in prostate cancer risk was reported for *BRCA2* mutation carriers [19, 46].

#### **BRCA MUTATIONS AND COLON CANCER**

Several studies have investigated the possibility of familial aggregation of breast cancer and colorectal cancer and have reported a positive association [47-49].

With the exception of the study by Risch *et al.* [41] which identifies an increased relative risk of colorectal cancer in first degree relatives of *BRCA2* mutation carriers, other studies have focused their attention on the risks of

cancers in *BRCA1* mutation carriers, [4, 50]. Thompson and Easton [50] reported a twofold increase in colon cancer risk (*RR* = 2.03, 95% *CI* = 1.45 to 2.85) but a significantly decreased risk of rectal cancer (*RR* = 0.23, 95% *CI* = 0.09 to 0.59) when *BRCA1* mutation carriers were compared with those without such a mutation. Other studies do not exclude a small increase in risk for colon cancer [43], although the statistical power of the two studies is not statistically significant, due to the small number of analyzed cases, suggesting that a larger number of mutation carriers is needed to demonstrate the increased risk.

Brose and colleagues estimated a cumulative age-adjusted risk of any cancer other than breast and ovarian of 13.8% (95% *CI* 10.7% to 16.9%) and in particular they found a cumulative age-adjusted risk of colon cancer in *BRCA1* mutation carriers of a two-fold increase compared to the general population (*p*<.05) [4].

A further distinction regarding the risk associated with developing other types of cancers in mutations carriers in *BRCA1* and *BRCA2* genes, is linked to the age of onset of the primary tumor (breast and/or ovarian cancer).

Harvey and Brinton [51] in a 1985 study, noted a significant relationship between breast and subsequent colon cancer. They found a significant downward trend for the risk of colon cancer (*RR*=1.6, 1.3, 1.1) and rectal cancer (*RR*=1.9, 1.1, 1.0) with age. This downward trend applied to ages <45, 45-54, and 55+ [51]. Similarly Teppo and colleagues [52] found that colon cancer in women whose breast cancer was diagnosed before age 50 occurred almost twice as often as it did in women diagnosed with breast cancer after age 70 [53]. In men under 65, the risk was significantly higher for cancer (21.4% vs. 4.4%;) and this was attributed largely to an excess of prostate, pancreatic, and colon cancers observed in male relatives of *BRCA2* carriers at that age.

Other studies have attempted to perform a stratification by sex revealing that female *BRCA1* mutation carriers had a twofold increased risk of colorectal cancer (*RR* = 1.94, 95% *CI* = 1.21 to 3.10), whereas male *BRCA1* mutation carriers had no increased risk of colorectal cancer (*RR* = 0.93, 95% *CI* = 0.6 to 1.44) [50].

#### **BRCA MUTATIONS AND HEMATOLOGICAL DISEASES**

Numerous studies evaluating *BRCA1/2* mutations in breast cancer families have noted an increased evidence of other cancers in sites other than the breast and ovary [16, 40, 54] suggesting that although breast and ovary are the primary component tumors of these cancer susceptibility syndromes, a generalized increased risk of developing a broad spectrum of malignancies may exist in association with mutations in these genes [55]. In particular leukemias were evidenced in the group of cases analyzed by Shih and colleagues [55] supporting the association between mutations in the *BRCA1/2* genes and this type of disease. Moreover Streuwing and colleagues [18] identified 120/3500 Jewish carriers of the three *BRCA* founder mutations of this ethnic group. These carriers were united by a common family history that included increased percentages of different cancers other than those involving the breast and ovary,

**Table 1. Epidemiological Studies that Include Data on the Risk of Other Cancers**

Authors	Base of Study	Number of Individuals Studied	Risk of Other Cancers
<i>Hahn et al.</i>	26 European families in which at least two first-degree relatives had a confirmed diagnosis of pancreatic ductal adenocarcinomas. Members of families carried BRCA2 mutations.	64	RR pancreatic cancer=3.5
<i>Murphy et al.</i>	31 samples of DNA from cancer patients in pancreatic cancer kindreds with 3 cases and at least 2 affected people first degree relatives	5 mutations carriers	17% of patients from familial pancreatic cancer had pathological BRCA2 mutations
<i>Goggins et al.</i>	the SEER public-use diskette that includes data from 9 SEER cancer registries. The cases included in this study were restricted to cancers that were malignant, microscopically confirmed.		Modest but statistically significant increased risk of cutaneous melanoma (CM) among female BC survivors and <i>vice versa</i> . Among young BC patients, they observed a 46% elevated risk of a second CM. Women who underwent radiation therapy exhibited a 42% increased risk for CM.
<i>Satram-Hoang et al.</i>	Data obtained from the California Cancer Registry included men aged 85 years and younger diagnosed with a first primary breast cancer.	1,926 men	Of the 1,926 male breast cancer cases, 221 (11.5%) developed a second primary cancer. The risk of a second site-specific cancer is elevated for cutaneous melanoma (SIR = 2.98, 95% CI = 1.63-5.00)
<i>Risch et al.</i>	A population-based series of 649 unselected incident cases of ovarian cancer diagnosed in Ontario, Canada, during 1995e1996 was screened for germline mutations in BRCA1 and BRCA2	Among the 515 women with invasive cancers, 60 mutations were identified, 39 in BRCA1 and 21 in BRCA2. No mutations were seen in the 134 women with borderline tumors	Prostate cancer risk 3.1 Risk of colorectal cancer was increased three-fold for relatives of cases carrying BRCA2 mutations (RR = 2.5)
<i>Aretini et al.</i>	Families with BRCA1/2 mutations ascertained in 6 Italian center	179 proband mutation carriers and 66 mutation carriers among relatives	Prostate cancer RR=1.91
<i>Struwing et al.</i>	Ashkenazi Jew population in Washington DC who filled up the epidemiologic questionnaires were analysed for BRCA mutation status	5318 subjects. (Risk of cancers were estimated by comparing the cancer histories of relatives of carriers of the mutations and on-carriers) 120 carriers of BRCA1/ BRCA2 mutation	By the age of 70 years, estimated risk 16% vs 1%; by age 80 years, estimated risk 39% vs <10% for BRCA1/BRCA2 mutation. Observed elevation in pancreatic cancer and lymphoma but were not statistically significant. Multiple myeloma, Hodgkin's disease and lung cancer were more common among mutation carriers but numbers were small.
<i>Thompson and Easton BCLC</i>	Family of BRCA1 mutation carriers. (The observed cancer incidence was compared with the expected cancer incidence-based on population cancer rates)	11,847 individuals from 699 families segregating a BRCA1 mutation that were ascertained in 30 centers across Europe and North America	Elevated risk of prostate cancer for BRCA mutation carrier younger than 65 years (RR=1.82), but not for those 65 years old or older, RR = 0.84. Colon cancer (RR= 2.03).
<i>Brose et al.</i>	483 patients (381 female, 102 male) from 147 families with documented BRCA1 mutations	316 (260 female: 56 male) tested positive for BRCA1 mutation: 167 presumed carrier	Colon cancer RR=2.0

Table 1. contd....

Authors	Base of Study	Number of Individuals Studied	Risk of Other Cancers
Bermejo and Hemminki	Families of the Swedish Family-Cancer Database with at least three generations	944,723 who eligible for BRCA1/BRCA2 test. Subgroup 2 bcs <50 years, 2 bcs one <50, bilateral bc <50, 1 bc <35, bc and oc.	Families with BC and OC presented increased incidences for stomach cancer before age of 70 years SIR 2.04. (SIR = standardized incidence ratio)
Shih et al.	Women with breast cancer reporting at least one other primary cancer in themselves or in a relative breast cancer.	98	Primary cancers included colorectal, cervical, thyroid, leukemia and lymphomas.
Harvey and Brinton	Primary cancers after diagnosis of initial breast cancer in females younger than 45 in Connecticut	About 7.3-12.2% based on Myriad tables, depending on percentage of Ashkenazi Jewish people.	Colon cancer (RR=1.6, 1.3, 1.1) and rectal cancer (RR=1.9, 1.1, 1.0) with age. This downward trend applied to ages <45, 45-54, and 55+.

among which multiple myeloma and Hodgkin's disease. These collected data reached enough statistical importance to warrant further investigations [18]. More recently an interesting study by Friedenson and colleagues proposed a theory in which not only inactivating mutations of *BRCA1/2* might increase the risk of developing lymphomas and leukemia, but that all the pathways connected with these two genes should also be considered, since any of the proteins involved in the DNA repair process might have an important impact on the genesis and evolution of such tumors [56]. All these previously mentioned data are supported by other epidemiologic studies showing an increased risk for leukemia/lymphoma in *BRCA* carriers [41]. On the contrary, others authors [41, 56] reported that a family history of BC increased the risk, due to a range of leukemia risk factors which are weak or non-consistent when considered alone, but combined with a family BC history and other factors as smoking and exposure to solvents were all associated with increased leukemia incidence.

#### BRCA MUTATIONS AND THYROID CANCER

Inherited mutations in genes predisposing for breast cancer (*BRCA1*, *BRCA2*, *PTEN*, *p53*) also increase the risk of other cancers and will therefore contribute to the relative risks of subsequent malignancies, particularly for breast cancer diagnosed at an early age [16, 17, 57]. Evans and colleagues report that a small percentage of their analyzed series of breast cancer patients showed increased risks for cancers of the lung, corpus uteri, ovary and thyroid. They identified several sites for which women diagnosed with breast cancer were at higher risk of developing cancer and speculate that associations with some sites might be due to known genes (ovary), shared environmental factors (corpus uteri), or the effects of therapy (myeloid leukaemia). Other associations, such as thyroid and stomach cancers, are more difficult to explain. They may be artifactual, or might be caused by more common but less penetrant genetic mutations causing only a moderately raised susceptibility to these cancers [58]. Other authors, for example Streuwing and colleagues, reported an increased percentage of cancers in sites other than the breast and ovary in Jewish families who

were mutation carriers, among which thyroid cancer, although the number of carriers was fairly low [18].

#### DISCUSSION

Germline mutations in *BRCA1* and *BRCA2* genes predispose to familial breast and/or ovarian cancer, but there is a increased risk of additional cancers (colon, pancreas, prostate, melanoma thyroid cancers and hematological diseases).

These tumors are present in families with a wider variation and so their evaluation need to be done by many population studies or large cases of *BRCA* carrier patients.

It seems that *BRCA* related pathway is probably associated with higher risk of cancers, but it is interesting to study not only patients eligible for the mutational testing but also those that are not eligible to it.

To date the main focus of this review have been argued still with difficulty. Table 1 summarize different epidemiological studies that include data on the risk of other cancers other breast and ovary (Table 1).

Just a deeper and complete evaluation of the topic will allow to establish how much is the contribution of *BRCA* mutations in different types of cancers other than breast and ovary.

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