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di Ferrara**

**DOTTORATO DI RICERCA IN  
"NEUROSCIENZE TRANSLAZIONALI E  
NEUROTECNOLOGIE"**

CICLOXXIII

Coordinatore: Prof. Luciano Fadiga

**Distress in Family Caregiver of Individuals Recently Diagnosed With Acute  
Leukemia: a Grounded Theory Study**

Settore Scientifico Disciplinare BIO/09

**Dottorando**

Dott. Malfitano Carmine

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Prof. Caruso Rosangela

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Anni 2017/2020

## Preface

As a Social worker in Research at the Princess Margaret Cancer Centre (PM), in Toronto (Ontario, Canada), one of the largest cancer centres worldwide, I work with individuals and families facing advanced or metastatic cancer. In this context, I had the opportunity to collaborate with and learn from internationally renowned clinicians and scientists such as Drs. Gary Rodin and Dr. Camilla Zimmermann, leaders of some of the most important programs of research shaping the field of modern palliative care. As part of their research team, I contributed to many national and international research studies, including large randomized controlled trials (RCTs), and learned about quantitative research methodologies. Concurrently, I completed requirements to become a psychotherapist under the Ontario College of Social Workers and Social Service Workers (in Canada, Social workers are authorized to perform the controlled Act of psychotherapy under specific conditions) and trained extensively under the supervision of Dr. Rodin. Over the past 3 years, I sought additional training and supervision in many non cancer-specific psychotherapeutic modalities, including Cognitive Behavioural Therapy and, more recently, Emotion-Focused Therapy. I had the opportunity to train with experts in the field of psychotherapy such as Dr. Les Greenberg.

Early in this journey, I discovered the importance of conducting practice-informed research and maintaining a research-informed practice. It became apparent that the ability to operate as a clinician with a researcher's mind and as a researcher with clinical field experience, provides an increased understanding of the clients we strive to help and the segment of reality we seek to explore. For this reason, I chose to pivot my doctoral activities on the integration of clinical and research tasks. My research interests stemmed from the work conducted on two trial psycho-social interventions developed in our department, to which I have contributed, at different stages in the program, as a researcher and a clinician: Managing Cancer and Living Meaningfully (CALM)<sup>1,2,3</sup> and Emotion And Symptom-Focused Engagement (EASE).<sup>4</sup> CALM is a brief, manualized, psychotherapeutic intervention for individuals and families facing advanced cancer. EASE consists of a novel integrated psychotherapeutic and early palliative care intervention targeting traumatic stress and physical symptom burden in individuals newly diagnosed with acute leukemia.

My doctoral thesis, formally structured into 3 distinct publications, includes:

- 1) An original manuscript reporting on findings from my doctoral research project, which will be submitted for publication upon completion of data collection and re-analysis;

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<sup>1</sup> Chris Lo, Sarah Hales, Aubrey Chiu, Tania Panday, **Carmine Malfitano**, Judy Jung, Anne Rydall et al. "Managing Cancer And Living Meaningfully (CALM): randomised feasibility trial in patients with advanced cancer." *BMJ supportive & palliative care* 9, no. 2 (2019): 209-218.

<sup>2</sup> Gary Rodin, Christopher Lo, Anne Rydall, Joanna Shnall, **Carmine Malfitano**, Aubrey Chiu, Tania Panday et al. "Managing cancer and living meaningfully (CALM): a randomized controlled trial of a psychological intervention for patients with advanced cancer." *Journal of Clinical Oncology* 36, no. 23 (2018): 2422.

<sup>3</sup> Rosangela Caruso, Maria Giulia Nanni, Gary Rodin, Sarah Hales, **Carmine Malfitano**, Silvia De Padova, Tatiana Bertelli et al. "Effectiveness of a brief manualized intervention, Managing Cancer and Living Meaningfully (CALM), adapted to the Italian cancer care setting: Study protocol for a single-blinded randomized controlled trial." *Contemporary Clinical Trials Communications* 20 (2020): 100661.

<sup>4</sup> Gary Rodin, **Carmine Malfitano**, Anne Rydall, Aaron Schimmer, Charles M. Marmar, Kenneth Mah, Christopher Lo, Rinat Nissim, and Camilla Zimmermann. "Emotion and Symptom-focused engagement (EASE): A randomized phase II trial of an integrated psychological and palliative care intervention for patients with acute leukemia." *Supportive Care in Cancer* 28, no. 1 (2020): 163-176.

- 2) A book chapter (under review by the editor) summarizing the current literature on family caregivers of patients with advanced cancer;
- 3) A published article reporting on the adaptation of CALM in an Italian setting, to which I have contributed as a researcher and clinical supervisor.

A detailed list of the research and clinical activities related to these 3 manuscripts and performed during the course of my doctoral work (Nov. 2017 – Jan. 2021) is enclosed below.

### **Publications in Peer-reviewed Journals (2017-2021)**

- 1) Vehling S, **Malfitano C**, Shnall J, Watt S, Panday T, Chiu A, Rydall A, Zimmerman C, Hales S, Rodin, G, Lo C. A concept map of death-related anxieties in patients with advanced cancer. *BMJ Supportive & Palliative Care*, 2017; 1:1-8. Doi: 10.1136/bmjspcare-2016-001287.
- 2) Nissim R, **Malfitano C**, Coleman M, Rodin G, Elliott M. A Qualitative Study of a Compassion, Presence, and Resilience Training for Oncology Healthcare Providers. *Journal of Holistic Nursing*. First Published March 29, 2018 DOI: 10.1177/0898010118765016
- 3) Rodin G, Lo C, Rydall A, Shnall J, **Malfitano C**, Chiu A, Panday T, Watt S, An E, Nissim R, Li M, Zimmermann C, Hales S. Managing Cancer And Living Meaningfully: A Randomised Controlled Trial of a Psychological Intervention for Patients with Advanced Cancer. *Journal of Clinical Oncology*, 2018; 36(23), 2422. Doi: 10.1200/JCO.2017.77.1097
- 4) Fraser B, Korenblum C, Mah K, Watt S, **Malfitano C**, Rydall A, Schimmer A, Zimmermann C, Rodin G. The Experience of Medical Communication in Adults with Acute Leukemia: Impact of age and attachment security. *Psychooncology*, 2019; 28(1), 122-130. Doi: doi.org/10.1002/pon.4919
- 5) Vehling S, Tian Y, **Malfitano C**, Shnall J, Watt S, Mehnert A, Rydall A, Zimmermann C, Hales S, Lo C, Rodin G. Attachment security and existential distress among patients with advanced cancer. *Journal of Psychosomatic Research*, 2019; 116, 93-99. Doi: 10.1016/j.jpsychores.2018.11.018
- 6) Rodin G, **Malfitano C**, Rydall A, Lo C, Marmar C, Schimmer A, Zimmermann C. Emotion And Symptom-focused Engagement (EASE): A randomized pilot trial of an integrated psychological and palliative care intervention for patients with acute leukemia. *Supportive Care in Cancer*. 2019 Apr 17. 10.1007/s00520-019-04723-2.
- 7) Mah K, Powell RA, **Malfitano C**, Gikaara N, Chalklin L, Hales S, Rydall A, Zimmermann C, Mwangi-Powell FN, Rodin G. Evaluation of the Quality of Dying and Death Questionnaire with Caregivers of Patients with Advanced Cancer in Kenya. *Journal of Global Oncology*. 2019; 1-15. doi.org/10.1200/JGO.18.00257

- 8) Rodin G, An E, Shnall J, **Malfitano C**. Psychological Interventions for Patients With Advanced Disease: Implications for Oncology and Palliative Care. 2020; *Journal of Clinical Oncology*, 38(9), 885-904
- 9) Mah K, Shapiro G, Hales S, Rydall A, **Malfitano C**, An E, Nissim R, Li M, Zimmermann C, Rodin G. The impact of attachment security on death preparation in advanced cancer: The role of couple communication. 2020; *Psychooncology*, 29(5), 833-840. doi: 10.1002/pon.5354.
- 10) Caruso R, Nanni MG, Rodin G, Lo C, Hales S, **Malfitano C**, De Padova S, Bertelli T, Belvedere-Murri M, Miniotti M, Bovero A, Sabato S, Grassi L. Effectiveness of a brief manualized intervention, Managing Cancer and Living Meaningfully (CALM), adapted to the Italian cancer care setting: Study protocol for a single-blinded randomized controlled trial. *Contemporary clinical trials*, 2020 October 10 [Epub ahead of print]. doi.org/10.1016/j.conctc.2020.100661

### **Invited Book Chapter**

**Malfitano C**. The Management of Terror. In *Managing Cancer and Living Meaningfully (CALM): a psychotherapeutic approach to advanced cancer*. (Rodin G and Hales S, ed.). In Press.

### **Manuscripts in Preparation (including thesis)**

- 1) **Malfitano C**, Caruso R, Grassi L, Rydall A, Zimmermann, C, Rodin G. Distress in family caregivers of individuals recently diagnosed with acute leukemia: A grounded theory study. Manuscript in preparation.
- 2) **Malfitano C**, Caruso R, Grassi L. Problemi psicosociali e psichiatrici della famiglia. In *Aspetti Psicosociali in Cure Palliative* (Grassi L, ed.), Manuscript in preparation.
- 3) **Malfitano C**, Nanos S, Caruso R, Grassi L, Rydall A, Zimmermann C, Rodin G. Caregiving styles in family caregivers soon after diagnosis of acute leukemia. Manuscript in preparation.
- 4) Tricou C, Rodin G, Mah K, **Malfitano C**, Patterson A, Rydall A, Zimmermann C. Validation of the Edmonton Symptom Assessment Scale (ESAS) modified for Acute Leukemia patients: ESAS-AL. Manuscript in preparation.
- 5) Mah K, Shapiro GJ, de Vries F, Hales S, Rydall A, **Malfitano C**, An E, Nissim R, Li M, Zimmermann C, and Rodin G. Investigating the factor structure of the Demoralization Scale in advanced cancer. Manuscript in preparation.

## **Awarded Research Grants (2017-2021).**

- 1) Funding Agency: Gateway for Cancer Research – Gateway Grant. Title: *The Online Adaptation of Managing Cancer and Living Meaningfully (iCALM): A Phase II Randomized Controlled Trial*. Principal Investigators: Gary Rodin, MD; Sarah Hales, PhD, MD; Alejandro Berlin, MD (Co-PIs). Co-applicants: **Carmine Malfitano, MSW**; Twinkle aurora, Msc.. Collaborators: Anne Rydall, MSc; Lesley Chalklin, MSc; Rinat Nissim, PhD; Harald Baumeister, PhD; Natalie Bauerei, MSc. Sheena Melwani, MSc HI; Kenneth Mah, PhD; Eryn Tong, MSc. Funding period: Dec. 11, 2020 – Dec. 10, 2022. **Amount awarded: \$338,795.77 (2 years)**
  
- 2) Funding Agency: Canadian Institutes of Health Research (CIHR) - Spring 2020 CIHR Project Grant. Title: *Traumatic stress symptoms in family caregivers of patients with acute leukemia: a longitudinal observational study*. Principal Investigators: Gary Rodin MD & Lindsay Jibb, PhD, RN, M.Sc. (Co-PIs). Co-applicants: Sarah Alexander MD; **Carmine Malfitano, MSW**; Collaborators: Aaron Schimmer MD, PhD, Sumit Gupta MD PhD, Rinat Nissim PhD, Camilla Zimmermann MD PhD, Sarah Hales MD PhD, Anne Rydall MSc. Funding period: Oct. 1, 2020-Sep. 30, 2024. Amount awarded: **\$855,000 (4 years)**.
  
- 3) Funding Agency: Canadian Institutes of Health Research (CIHR) - Spring 2019 CIHR Project Grant. Title: *Emotion And Symptom-focused Engagement (EASE): A randomized controlled trial for individuals with acute leukemia*. Principal Investigators: Gary Rodin MD & Camilla Zimmermann MD, PhD (Co-PIs). Co-applicants: Aaron Schimmer MD, PhD; Jennifer White MD, MSc; Wendy Yeomans MD; **Carmine Malfitano, MSW**; Rinat Nissim PhD; Anne Rydall MSc. Collaborators: Charles Marmar MD; Kenneth Mah PhD; Chris Lo PhD. Funding period: Oct. 1, 2019-Sep. 30, 2024. Amount awarded: **\$761,176 (5 years)**.
  
- 4) Funding Agency: Ministry of Health and Long-Term Care (MOHLTC) and the Ontario Medical Association (OMA) - Academic Health Science Centre Alternative Funding Plan. Title: *A phase II randomized controlled trial (RCT) of an internet- and mobile-based intervention for individuals with advanced or metastatic cancer (iCALM)*. Principal Investigator: Gary Rodin, MD & Sarah Hales, MD, PhD (Co-PIs). Co-Investigators: Harald Baumeister, PhD; Natalie Bauerei, M.Sc.; Co-Applicants: **Carmine Malfitano, MSW**; Anne Rydall, MSc; Kenneth Mah, PhD. Funding period: January 2019 - January 2021. **Amount awarded: \$186,000 (2 years)**
  
- 5) Funding Agency: Canadian Cancer Society Research Institute (CCSRI) - Quality of Life Grant (February 2017). Title: *Emotion And Symptom-focused Engagement (EASE): A multi-site randomized controlled trial for individuals with acute leukemia*. Co-Principal Investigators: Gary Rodin, MD, and Camilla Zimmermann, MD, PhD. Co-Applicants: Rinat Nissim, PhD, Aaron Schimmer, MD, PhD, Sarah Sample, MSW, RSW. Additional Authors: Anne Rydall, MSc, **Carmine Malfitano, MSW**. Collaborators: Donna Hogge, MD, PhD, Wendy Yeomans, MD, Charles Marmar, MD, Christopher Lo, PhD. Funding period: February 2017-January 2020. **Amount awarded: \$294,000 (3 years)**

## Conference Presentation and Published Abstracts (2017-2021)

*\*Asterisk indicates when author is also presenter*

- 1) **Malfitano C\***, Caruso R, Nissim R, Rydall A, Patterson A, Zimmermann C, and Rodin G. Traumatic stress in family caregivers of individuals newly diagnosed with acute leukemia: a grounded theory study. The 22<sup>nd</sup> world congress of psycho-oncology and psychosocial academy. May 2021; Kyoto, Japan.
- 2) Benites AC, dos Santos MA, Pereira LF, **Malfitano C**, Rodin G. Psychological interventions for patients with advanced cancer and their family caregivers in Brazil: A scoping review and considerations for future implementation of CALM therapy. Palliative Care, Culture, and the Clinic Symposium. January 2021; Online
- 3) Chalklin L, Mah K, **Malfitano C**, Rodin G, Mwangi Powell F, Powell RA. Cross-cultural Evaluation of the Quality of Dying and Death Questionnaire with Caregivers of Advanced Cancer Patients in Kenya. 16TH world congress of the European Association for Palliative Care; May 2019; Berlin, Germany.
- 4) de Vries F, Hafkamp E, Aukema E, Reyners A, **Malfitano C**, Rodin G, van de Poll L. Implementation of CALM in Dutch Cancer Care settings. 21th World Congress of Psycho-Oncology; September 2019; Banff, Canada.
- 5) **Malfitano C\***, Mah K, Powell RA, Gikaara N, Chalklin L, Hales S, Rydall A, Zimmermann C, Mwangi-Powell FN, Rodin G. Evaluation of the Quality of Dying and Death Questionnaire in Kenya. Barrie Rose Research Day in Palliative Medicine; May 2019; Toronto, Canada.
- 6) Rodin G, **Malfitano C\***, Rydall A, Schimmer A, Marmar C, Mah K, Lo C, Nissim R, Zimmermann C. Barrie Rose Research Day in Palliative Medicine; Emotion and symptom focused engagement (EASE): an integrated psychosocial and palliative care intervention for individuals with acute leukemia. May 2019; Toronto, Canada.
- 7) Rodin G, **Malfitano C**, Rydall A, Schimmer A, Marmar C, Mah K, Lo C, Nissim R, Zimmermann C. Emotion And Symptom-focused Engagement (EASE): A randomized phase II trial of an integrated psychological and palliative care intervention for patients with acute leukemia. 16<sup>th</sup> world congress of the European Association for Palliative Care (EAPC); May 2019; Berlin, Germany.
- 8) Tricou C, Mah K, **Malfitano C**, Rydall A, Schimmer AD, Rodin G, Zimmermann C. Preliminary validation of the Edmonton Symptom Assessment Scale – Acute Leukemia (ESAS-AL) in patients with acute leukemia (AL). American Society of Clinical Oncology, Palliative and Supportive Care in Oncology Symposium; November 2018; San Diego, United States of America.
- 9) Bauereiß N, Rodin G, **Malfitano C**, Baumeister H. iCALM – Design einer randomisiert-kontrollierten Pilot studie zur Evaluation einer internet- und mobil-basierten Intervention für Menschen mit fortgeschrittener Tumorerkrankung. The 2018 European society for medical oncology congress; October 2018; Munich, Germany.

- 10) Rodin G, **Malfitano C\***, Rydall A, Schimmer A, Marmar CM, Lo C, Mah K, Nissim R, Zimmermann C. Emotion And Symptom-focused Engagement (EASE): proposed multi-center randomized controlled trial (RCT) of an integrated psychological and palliative care intervention for patients with acute leukemia (AL). Canadian Association of Psychosocial Oncology; May 2018; Toronto, Canada.
- 11) Krejcik V, **Malifitano C**, Shnall J, deGroot J. Relationships: an Antidote to Resident Disengagement from Academic Medicine. Canadian Conference on Medical Education; April 2018; Halifax, Canada.
- 12) Chalklin L, **Malfitano C**, Powell R, Gikaara N, Lee L, Doherty C, Fernandes S, Hales S, Zimmermann C and Rodin G. The Quality of Dying and Death in Hospice Care in Kenya. Toronto Global Cancer Control Conference; March 2018; Toronto, Canada.

### **Teaching Experience (2018-2021).**

- 1) **Supervisor, Global Institute of Psychosocial, Palliative and End-of-life Care (2019-2021).** Co-supervised a group of psychologists in Italy learning CALM, a brief psychotherapeutic intervention for patients with advanced or metastatic cancer.
- 2) **Teaching Assistant, University of Toronto (2018-2021).** Collaborative Specialization in Aging, Palliative and Supportive Care Across the Life Course, Academic year
  - a. AGE1500H - Advanced research methodologies in Palliative and Supportive Care. Academic year 2018/2019
  - b. AGE1500H - Advanced research methodologies in Palliative and Supportive Care. Academic year 2019/2020
  - c. AGE1000H - Multidisciplinary concepts in Palliative and Supportive Care Research: Investigating a global health priority. Academic year 2018/2019
  - d. AGE1000H - Multidisciplinary concepts in Palliative and Supportive Care Research: Investigating a global health priority. Academic year 2019/2020
  - e. AGE1000H - Multidisciplinary concepts in Palliative and Supportive Care Research: Investigating a global health priority. Academic year 2020/2021
- 3) **Seminar (6 hours), Università degli Studi di Ferrara, Italy (2018)**
  - a. Managing Cancer And Living Meaningfully (CALM). Two case studies for a brief psychotherapeutic intervention for patients with advanced or metastatic cancer. Audience: psychologists in supervised practice.

### **Modules in Professional Workshops (2018).**

- 1) Invited speaker: Managing Cancer and Living Meaningfully (CALM) International Workshops, Toronto (ON). June 2-3, 2018.
- 2) Facilitator: Responding to Distress and Anger in Cancer Patients - a Psychosocial Workshop for Nurses. Princess Margaret Cancer Centre, Toronto (ON). March, 2018

### **Certifications.**

Certified supervisor: Managing Cancer and Living Meaningfully (CALM). Institution: Global Institute of Psychosocial, Palliative, and End-of-life Care.

### **Appointments.**

Adjunct Lecturer (Field Instructor). Academic year 2017/2018. Institution: Factor-Inwentash Faculty of Social Work, University of Toronto.

### **Selected Clinical Training: Approaches in Advanced Cancer (2017-2021).**

- 1) International workshops: Twice yearly intensive workshops in Canada and additional workshops and seminars abroad. Institution: Princess Margaret Cancer Centre and collaborating institutions. Academic years: 2017/2018; 2018/2019.
- 2) Ongoing Training: Weekly clinical and research meetings with presentations and discussions with experts in the field. Institution: Princess Margaret Cancer Centre. Academic years: 2017/2018; 2018/2019; 2019/2020; 2020/2021

### **Selected Clinical Training: Cognitive Behavioural Therapy (2017-2018).**

- 1) Ongoing training: Twice weekly clinical rounds (assessment and treatment) with presentations and discussions with experts in the field. Institution: CBT Associates of Toronto. Academic years: 2017/2018; 2018/2019
- 2) Intensive Workshop: Cognitive Behavioural Therapy. Facilitator: Dr. C. Padesky. Academic Year: 2017/2018.

### **Selected Clinical Training: Emotion-Focused Therapy (2017-2021).**

- 1) Ongoing training: Weekly clinical rounds (individuals and couples) with presentations and discussions with experts in the field. Institution: Centre for Psychology and Emotional Health. Academic years: 2019/2020; 2020/2021
- 2) Intensive workshop: Emotion Focused Therapy (Level 2) - assistant. Facilitators: Dr. Les Greenberg and Dr. Serine Warwar. Institution: York University Psychology Clinic. August 2020
- 3) Intensive workshop: Emotion Focused Therapy (Level 1) - assistant. Facilitators: Dr. Les Greenberg and Dr. Serine Warwar. Institution: York University Psychology Clinic. August 2020



- 4) Intensive workshop: Emotion Focused Couples Therapy – observer. Facilitators: Dr. Les Greenberg and Dr. Serine Warwar. Institution: York University Psychology Clinic. October 2019
- 5) Intensive workshop: Emotion Focused Therapy (Level 2). Facilitators: Dr. Les Greenberg and Dr. Serine Warwar. Institution: York University Psychology Clinic. May 2019.
- 6) Intensive workshop: Emotion Focused Couples Therapy. Facilitator: Dr. Les Greenberg. Institution: York University Psychology Clinic. December 2017

### **Clinical Supervision (2017-2021)**

- 1) Psychotherapeutic approaches in advanced cancer. Individual supervision meetings. Supervisors: Dr. G. Rodin; Dr. S. Hales. Institution: Princess Margaret Cancer Centre, Toronto (ON). November 2017/December 2019.
- 2) Emotion Focused Therapy (individuals and couples). Weekly peer supervision meetings. Institution: Centre for Psychology and Emotional Health. October 2020/January 2021
- 3) Emotion Focused Therapy (individuals and couples). Weekly individual supervision meetings. Supervisor: Dr. S. Warwar. Institution: Centre for Psychology and Emotional Health, Toronto (ON). May 2019/January 2021
- 4) Cognitive Behavioural Therapy for Anxiety disorders. Individual supervision meetings. Supervisors: Dr. Daniel Pelusi; Dr. V. Velyvis. Institution: CBT Associates, Toronto (ON). November 2017/January 2019.

## **Acknowledgements**

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I am grateful to the Rodin Research Team for being a home away from home. Thank you to Ms. Anne Rydal for being a model of kindness, compassion, and integrity. Thank you to Dr. Sarah Hales, Dr. Chris Lo, and Dr. Rinat Nissim for providing guidance over the years.

I would like to thank my parents, for their unconditional love. My brother, who taught me how to fight and never give up. My chosen family, who has supported me through highs and lows. My partner, for teaching me love and acceptance.

Finally, I would like to thank the family caregivers who participated in this research and shared their experience with me so generously. Thank you, this work would not be possible without you.

## **MANUSCRIPT #1**

### **Distress in Family Caregiver of Individuals Recently Diagnosed with Acute Leukemia: A Grounded Theory Study**

To note: recruitment of study participants began in July 2019 and abruptly ended in February 2020 due to the SARS-CoV-2 pandemic and related social distancing restrictions at the University Health Network (UHN). UHN mandatory guidelines, in fact, stipulated that no unessential research activity could be carried on site, especially that involving vulnerable patients such as those diagnosed with acute leukemia. Research Ethics Board (REB) guidelines required direct contact with patients to obtain consent to approach their family members. Due to the nature of the inpatient unit where these patients are hosted and other REB procedural requirements, telephone or otherwise remote approach was rendered impossible. The health of our patients is of utmost importance and therefore it was our ethical responsibility to cease recruitment of family caregivers, which will resume in the foreseeable future. Given the limited data collected and the fact that saturation of themes was not reached, the results presented in this manuscript are to be considered preliminary in nature.

## Abstract

**Purpose.** The diagnosis, progression, or recurrence of advanced cancer can be traumatic events for family caregivers (FCs), who report substantial psychological and physical distress. Evidence indicates the presence of post-traumatic disorders in a significant proportion of FCs, yet there is a scarcity of research supporting early interventions to prevent it. The purpose of this study is to characterize the distress in FCs shortly after the diagnosis of acute leukemia (AL), which is a prototypical condition for the acute onset of a life-threatening disease with intensive treatment and severe physical symptoms. **Methods.** Nine FCs consented to participate in a qualitative interview about their experience with AL. A grounded theory approach was used to analyze the transcribed interviews. **Results.** Findings identified 3 phases in FCs' distress: anticipatory, acute, and post-acute. The anticipatory phase, which precedes the diagnosis, was characterized by concerns related to uncertainty. FCs' in the acute phase described overwhelming distress related to the diagnosis and the threat to life. Further analyses show an immediate response to this heightened distress in all FCs, who report a decrease in emotional arousal with intentional efforts to avoid thoughts and feelings to an unfavourable future. Only in the post-acute phase, FCs' begin to discuss themes related to difficult emotions. **Conclusions.** The decrease in distress observed soon after the diagnosis of AL is indicative of a dissociative response to overwhelming emotions. Underlying painful feelings seemed inaccessible during the acute phase and began to emerge later in the course of the treatment. Future research on targeted psychotherapeutic interventions should take into consideration the possible adaptive functions of this initial response.

**Obiettivo.** La diagnosi, la progressione o la recidiva di tumore avanzato possono essere degli eventi traumatici nella vita di caregiver primari (CP), che riportano notevole distress fisico e psicologico. Nonostante molti studi indichino la presenza di disturbi post-traumatici in una proporzione significativa di CP, esiste una carenza di ricerca scientifica che supporti lo sviluppo di interventi preventivi. L'obiettivo di questo studio è di caratterizzare il distress in CP subito dopo la diagnosi di leucemia acuta (LA), quest'ultima identificata come la condizione prototipica per malattie potenzialmente mortali ad insorgenza acuta, con trattamento intensivo e sintomi fisici severi. **Metodo.** Nove CP hanno dato il consenso a partecipare ad una intervista qualitativa riguardante la loro esperienza con la LA. Un approccio Grounded theory è stato utilizzato per l'analisi dei trascritti. **Risultati.** I risultati identificano 3 fasi nel distress dei CP: anticipatoria, acuta e post-acuta. La fase anticipatoria, che precede la diagnosi, è caratterizzata da preoccupazioni legate all'incertezza. CP nella fase acuta parlano di un'angoscia molto elevata e legata alla diagnosi ed alla possibilità di perdere una persona cara. Analisi successive mostrano un'immediata risposta a questa emozione in tutti i CP, che riportano una diminuzione dell'arousal emotivo in compresenza a sforzi intenzionali per evitare pensieri ed emozioni legati ad un futuro infausto. Solo nella fase post-acuta, i CP cominciano a discutere temi legati ad emozioni difficili. **Conclusioni.** La diminuzione di distress osservata subito dopo la diagnosi di LA è indicativa di una risposta dissociativa da emozioni difficili. Sentimenti più dolorosi sembrano inaccessibili durante la fase acuta e cominciano a ri-emergere più avanti nel corso del trattamento. Studi futuri su interventi psicoterapici mirati dovrebbero tenere in considerazione possibili funzioni adattive di questa risposta iniziale.

# **Distress in Family Caregivers of Individuals Recently Diagnosed with Acute Leukemia: A Grounded Theory Study**

## **1. Background**

### *1.1 Traumatic Stress in Cancer*

Traumatic stress has been observed and reported for over a century (under different names such as “shell shock” or “battle fatigue”).<sup>1,2</sup> However, only in the last 40 years it has been studied rigorously, with its first formal inclusion in the DSM-III in 1980 after the severe symptoms observed in soldiers returning from the war in Vietnam.<sup>2,3</sup> The Diagnostic and Statistical Manual of Mental Disorders – 5<sup>th</sup> Edition (DSM-5) defines a traumatic event as the “exposure to actual or threatened death.”<sup>4</sup> The cluster of distressing psychological symptoms that can occur in response to a traumatic event, been commonly referred to as *traumatic stress*, have been categorized in the DSM-5 under trauma- and stressor-related disorders.<sup>4</sup>

In its current DSM-5 classification, traumatic stress symptoms are categorized under 4 distinct clusters: 1) re-experiencing symptoms, which refers to the re-experience of intense distress in response to external (e.g. physical stimuli) and/or internal (e.g. dreams or flashbacks) reminders of the trauma; 2) avoidance symptoms, which are characterized by active efforts to avoid internal (e.g. thoughts) and/or external (e.g. situations or conversations) reminders of the trauma; 3) alteration in cognition and mood, such as the inability to remember aspects of the trauma or the presence of persistent and exaggerated negative thoughts, emotions, or feelings of detachment from others; and 4) arousal symptoms, which could manifest as excessive irritability and anger, hypervigilance, exaggerated startle response, reckless or destructive behaviours, decreased concentration, or perturbed sleep. The presence of some of these symptoms soon after the occurrence of a traumatic event may meet criteria for the diagnosis of acute stress disorder (ASD) or, if symptoms persists for over a month, of post-traumatic stress disorder (PTSD). The clinical relevance of screening for traumatic stress

symptoms in the days or weeks following a traumatic event is demonstrated by the severe impact of ASD on outcomes related to quality of life.<sup>5</sup> ASD has been shown to increase the risk for completed suicide, 10 times higher in affected individuals compared to the general population,<sup>6</sup> cardiac mortality,<sup>7</sup> and the development of subsequent PTSD.<sup>8</sup>

There is now a large body of research exploring the nature and course of traumatic stress in various populations, such as victims of physical or sexual assault, survivors of natural disasters, first responders to accidents, or those living in war zones.<sup>9,10</sup> In oncology, the communication of news about the diagnosis, progression, or recurrence of advanced cancer can be classified as a traumatic event under the DSM-5 definition.<sup>11</sup> Indeed, authors have demonstrated the presence of ASD and PTSD in a substantial proportion of individuals with various types of cancer.<sup>12-15</sup> While this work has included patients later in the course of the illness, very little research has studied individuals soon after the diagnosis, progression, or recurrence of advanced or life-threatening cancer. The scarcity of research at these stages of disease is partially due to the difficulty recruiting patients at a time of heightened psychological distress and demanding medical appointments and procedures.<sup>16</sup> Yet, the traumatic stress at these times may be related to the sense of inescapability from the threat, which is generated from within the body, or the repetitive exposure to traumatic stimuli such as invasive procedures, setbacks and bad news, or distressing physical symptoms.<sup>16</sup> Unfortunately, this paucity of research on traumatic stress in this circumstance has resulted in a lack of targeted, evidence-based interventions, leaving suffering individuals without structured psycho-social support.

### *1.2 Traumatic Stress in Acute Leukemia*

We identified acute leukemia (AL), a life-threatening cancer of the blood cells, as a prototypical traumatic stressor, due to its acute onset and requirement of urgent hospitalization for initiation of intensive chemotherapy. The admission to the hospital, which occurs soon after diagnosis and can last for weeks or even months, is a distressing event for patients and their families,<sup>17</sup>

although it offers the unique opportunity to explore the immediate impact of the illness and its treatment.<sup>16</sup>

The treatment of AL is associated with substantial toxicity and severe and potentially fatal side effects, including infection, bleeding, mucositis, graft failure, graft-versus-host disease, major organ toxicity, and multiple other drug-specific side effects.<sup>18</sup> While hematological settings are often characterized by a “culture of cure,”<sup>19</sup> acute myeloid leukemia, which accounts for about 80% of adult AL, has a median survival of only 11 months<sup>20,21</sup> and acute lymphocytic leukemia, accounting for most of the remaining 20%, has a median survival of approximately 2 years.<sup>22</sup> Despite the potential for physical and psychological distress in this population, referrals for specialized psycho-social support of palliative care, for management of physical symptoms, tend to occur only weeks before death.<sup>23,24</sup>

In a longitudinal study conducted at PM with over 350 individuals with newly-diagnosed or recently relapsed acute leukemia, one of the largest studies of this kind, about one third of respondents reported traumatic stress symptoms that met criteria for threshold or subthreshold ASD;<sup>25</sup> these symptoms persisted or recurred in over half of these patients over the 3-month follow-up period.<sup>26</sup> These rates are remarkably high compared to those reported in other trauma-exposed populations such as survivors of motor vehicle accidents (13-21%),<sup>27</sup> brain injury (14%),<sup>28</sup> or assault (19%).<sup>29</sup> In addition to the severe psychological distress, over 60% of the study participants reported more than 10 distressing, concurrent physical symptoms, and symptoms severity was higher in these individuals than observed in patients with solid tumour.<sup>23</sup> In parallel qualitative interviews, patients described the experience of the diagnosis and subsequent hospitalization and treatment as being “abducted by the illness.”<sup>30</sup>

Based on the findings of our longitudinal research, we developed a novel integrated psychotherapeutic and early palliative care intervention called Emotion And Symptom-focused Engagement (EASE).<sup>31</sup> EASE includes 2 components: 1) a brief individualized psychotherapy based on principles of relational support and empathic understanding, with trauma-focused, cognitive-behavioural strategies targeting traumatic stress symptoms; and 2) routine screening of physical symptoms, with triggered referral to early palliative care. EASE is delivered bed-

side to patients with newly diagnosed AL soon after admission to the hospital. In a phase II randomized controlled trial (RCT) of EASE versus usual care, we demonstrated its feasibility and preliminary efficacy in reducing psychological distress and physical symptom burden and increasing quality of life and satisfaction with care.<sup>32</sup> While the study was not powered to detect significant effects, we found statistically significant reductions in traumatic stress and in physical symptoms severity favouring the EASE group. A multi-centre phase III RCT is currently underway in 4 Canadian hospitals.<sup>33</sup>

### *1.3 Family Caregivers of Oncology Patients*

*(For more detailed information on the psychosocial and psychiatric needs of family caregivers of patients with advanced cancer please refer to Manuscript #2, p.35)*

Family caregivers (FCs) are commonly defined as those individuals who provide care to friends or family members suffering from a chronic or debilitating condition without receiving financial compensation.<sup>34</sup> Cancer caregiving has been rated as the most burdensome type of caregiving, with informal caregiver providing 70-80% of patient care.<sup>35,36</sup> FCs are often expected to assume key roles in complex clinical tasks such as coordination of care, symptom management, administration of various treatments, and direct personal care, while maintaining other ongoing responsibilities, such those related to employment or caring for other dependents.<sup>37-44</sup> The burden of cancer, which falls disproportionately on women,<sup>36</sup> has been amplified by the structural changes that have occurred in cancer centres across the world over the past 30 years, which have gradually shifted the delivery of care from inpatient to outpatient settings.<sup>38</sup> This has resulted in increased burden on FCs, particularly spouses,<sup>39-43</sup> for whom there has been a dramatic change in their role,<sup>45</sup> progressively becoming the primary source of practical, social, and emotional support for patients.<sup>39,46,47</sup> In response to the growing demands imposed by more complex treatments and more prolonged survival, caregiving has become a full-time job for many FCs, who must alter their schedule and decrease their work hours with consequential financial loss, narrowing of social interactions, and emerging feelings of isolation.<sup>48-52</sup>



Despite the demands and complexity of the caregiving tasks performed, little education or support is provided to FCs, who report feeling inadequately prepared for this role, especially during the earlier stages of the treatment trajectory.<sup>53,54</sup> The threat of mortality, the changes in roles in both patients and caregivers, the physical and psychological burden of caring, the financial strain caused by the illness, especially in Countries without universal health coverage, and the lack of preparation put FCs of patients with cancer at high risk for impaired mental health.<sup>55-59</sup> Further, witnessing a loved one suffer or fearing for her or his life constitute an additional threat to the mental and physical health of these individuals.<sup>60,61</sup>

The psychological distress observed in FCs is often equal to or even higher than that experienced by patients and tends to persist and even increase over time.<sup>46,62-66</sup> Between 13% and 20% of these individuals meet criteria for one or more psychiatric disorder and scores on quantitative measures of depression, hopelessness, and anxiety are higher than reported by non-caregivers.<sup>52,64,67</sup> Finally, oncology FCs have been shown to have poorer health status than non-caregivers and increased risk for coronary heart disease and stroke.<sup>68</sup> However, despite the burden of caregiving and threats to their own mental and physical health, FCs tend to focus exclusively on their loved one, denying their own distress, and not seeking help for themselves,<sup>67,69</sup> effectively increasing their risk for undiagnosed and untreated psychological and physical morbidity.

The World Health Organization, alongside other international organizations such as the American Society of Clinical Oncology, have emphasized the importance of early palliative care that included support for FCs.<sup>56,70</sup> Nonetheless, FCs frequently report a lack of dedicated support, indicating that the cancer care appears to them to be still largely patient-centred, rather than family-centred, especially during the first weeks following a cancer diagnosis.<sup>71-73</sup> FCs' distress is not systematically screened or addressed<sup>74</sup> in cancer care and the literature on interventions supporting this population is still very limited.<sup>75</sup> Of particular note, is the almost complete lack of research on the wellbeing of FCs following the trauma of diagnosis, which, to the authors' knowledge, is virtually inexistent. The specific objective of the present study is to explore the nature of distress over time of FCs caring for a patient with AL.

## **2. Methods**

The current study received approval on August 2018 from the oncology division of the Research Ethics Boards at the University Health Network (UHN), in Toronto (ON) as part of the pre-trial phase of a larger RCT testing the effectiveness of a novel, integrated psychotherapeutic and early palliative care intervention for patients newly diagnosed with AL, currently underway.<sup>31,33</sup> Patients in this phase of the RCT were not receiving any trial intervention and were only completing baseline questionnaires. Recruitment of study participants began in July 2019 and ended in February 2020.

### *2.1 Study Procedures*

A member of the research team planned to approach every English-speaking individual ( $\geq 18$  years of age) newly diagnosed with acute lymphoblastic leukemia and acute myeloid leukemia within 2 weeks from admission to the inpatient hematological unit at the Princess Margaret Cancer Centre. Patients were asked to identify a primary caregiver, who was approached in person or over the telephone to conduct the informed consent process. FCs were eligible to participate in the study if they were 18 years of age or older and spoke English fluently enough to comprehend the consent form. No purposeful sampling was employed in this study and all consenting caregivers were invited to participate in a qualitative interview conducted by the author (CM). Participants were informed that the intent of the interviews was to explore the experience of caring for an individual with AL. Interviews were arranged in person or over the telephone at the convenience of the participants and lasted approximately between 30 and 60 minutes, based on the willingness of the participants to share their experience. Interviews followed a semi-structured interview guide starting with an open-ended question (“how have you been doing these days?”) and were conversational in tone. The interviewer maintained a balance between following the narrative of the interviewees, directing the interviews towards themes that were included in the interview guide (if these themes did not emerge spontaneously) or that emerged in previous interviews, deepening new emerging themes, and

exploring underlying emotional experiences. The interviewer kept field notes and an audio reflection journal.

## *2.2 Data Analysis*

Interviews were audio-recorded, transcribed verbatim by volunteers, checked for accuracy by the author, and imported in NVivo 10. A grounded theory framework<sup>76,77</sup> was applied to produce an explanatory theory of the experience reported by FCs by mean of constant comparative analysis. The author firstly read the transcripts in their entirety to gain a global understanding of the interviews. Units of empirical data were structured into codes, which identified an initial framework of concepts. These units of data were compared within each code and codes were compared with other codes. Codes were finally structured into categories. New codes and categories were compared with previous codes and categories and data from subsequent interviews was compared with data previously analyzed. This was done in a constant iterative process. Hypotheses were formed, recorded in audio-journals, and subsequently proved or disproved throughout the analytic process.

## **3. Results**

### *3.1 Sample*

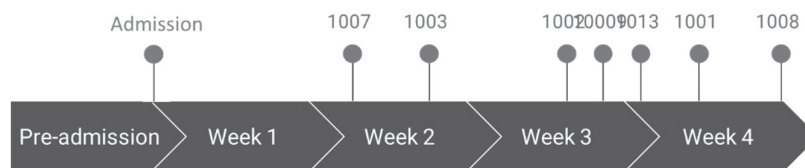
A total of 13 FCs were invited to participate in the study. Four FCs refused participation in the interview due to lack of time or interest. The demographic information of the final sample (N=9) is reported in Table 1. Unlike what is typically observed in cancer research,<sup>78</sup> or in research with caregivers,<sup>36</sup> FCs in this study reported low to average education and there was an even split between men and women. Additionally, the sample in this study was not fully represented by spouses.

**Table 1. Characteristics (N=9).**

Sample Characteristics	Description
Gender (female)	5/9 (56%)
Age (years) (mean [SD]; range)	59 [2.74]; 44-69
Relationship to patient	
Spouse	6/9 (67%)
Parent or adult child	3/9 (33%)
Marital Status	
Married/Common law	6/9 (67%)
Separated/Divorced/Single	3/9 (33%)
Canadian Born	8/9 (89%)
Education	
High School or less	3/9 (33%)
College/Trade	3/9 (33%)
Undergraduate	3/9 (33%)
Children (yes)	7/9 (78%)
Patient's diagnosis	
ALL	4/9 (44%)
AML	5/9 (56%)

### 3.2 Findings

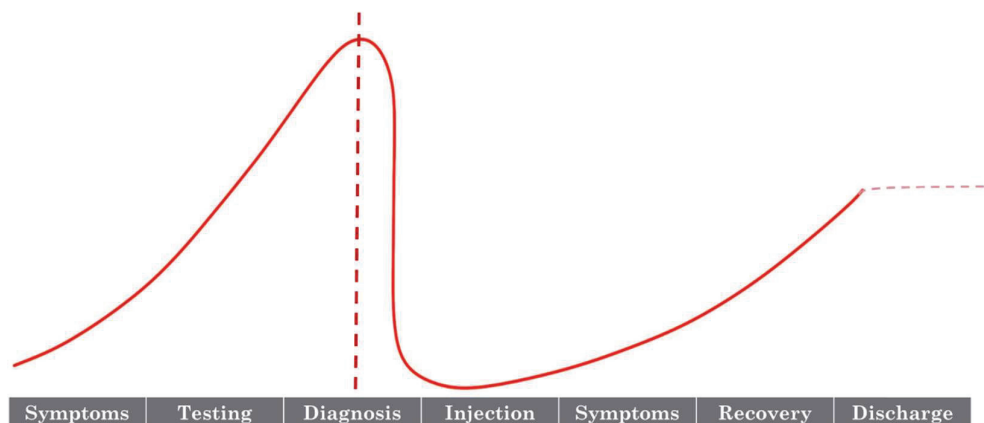
The focus of the results presented here is on the nature of the distress reported by FCs. Interviews were completed between 9 and 24 days (week 2 to week 4) from patients' admission to the hospital (see Figure 1).



**Figure 1.** Family caregivers' interviews from the corresponding patient's admission to the hospital

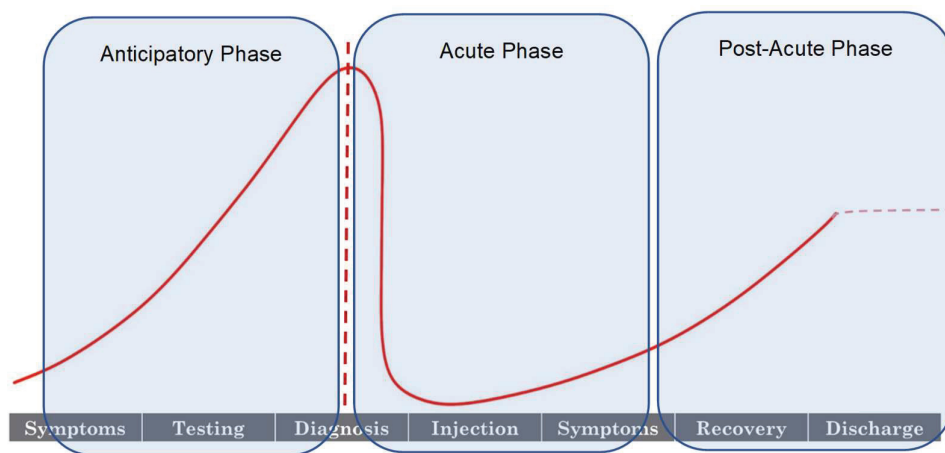
Given the closeness in time of the interviews with respect to the admission, time was not originally considered a relevant variable. However, preliminary analyses revealed differences among study participants in their description of distress at the time of the interview. Moreover, they reported fluctuations in the intensity of affect in the preceding weeks. Triangulation of data

(description of present state integrated with the recollection of previous states) showed a unique trajectory of distress that held true for all 9 study participants. FCs closely related this trajectory to the diagnostic and treatment phases of AL. These typically include: an initial period of time when the patients experienced mild to severe physical symptoms. It is possible that some patients could have reported no physical symptoms related to AL, with the illness being coincidentally discovered during routine medical tests. However, this was not the case in the study sample, all of whom experienced physical symptoms and who underwent tests until a diagnosis was reached. Admission to the cancer centre followed for induction chemotherapy, which frequently causes severe and distressing side effects,<sup>18</sup> and then a period of recovery leading to discharge. The latter typically takes place approximately 4 weeks after admission (with a range of 3 to 8 weeks), and all FCs in the sample were interviewed prior to it. The qualitative findings demonstrated an expected gradual increase in distress, occurring in parallel to the medical tests and procedures, peaking at the time of diagnosis. An unexpected finding in this sample was drastic decrease in emotional arousal reported by FCs soon after this event, which was followed by a gradual re-emergence as patients moved through recovery and toward discharge (see Figure 2).



**Figure 2.** Representation of the trajectory of distress in FCs (red line) mapped against diagnostic and treatment phases of AL incurred by patients

Further analyses categorized the distress trajectory in 3 sequential phases: anticipatory, acute, and post-acute (see figure 3). The anticipatory phase, which ends at diagnosis, includes the weeks leading to the discovery of AL. The acute phase covers the first weeks post-diagnosis, during which patients receive induction chemotherapy. The post-acute phase begins with the recovery of patients and comprises the days preceding discharge.



**Figure 3.** Representation of the phases of the trajectory of distress in FCs

### 3.3 Anticipatory Phase: *Sitting on the Fence*

In the anticipatory phase, FCs reported struggling with the various “unknowns” surrounding the patient’s condition in conjunction with a pervasive sense of powerlessness. The latter was aggravated in some participants by lengthy waiting times to complete tests and obtain results and by the severe physical symptoms in the patient:

*“The worst part was not being knowledgeable enough. I felt that I had to keep poking the doctors, I had to keep poking the nurses and nobody was saying anything. For me the unknown is more stressful than the known. I would rather know exactly what’s going on so I can wrap myself around it than just be sitting on the fence waiting to fall off”*  
(1022)

*“It was stressful because I’m just not used to seeing (patient) sick. That was something completely new to me and it was troubling because there was nothing I could do. She couldn’t eat anything, and she just continued to lose weight and I was thinking: ‘Man, something is happening here’” (1019)*

The moment of the communication of the diagnosis was uniformly described as shocking and accompanied by a sense of disbelief. Participants reported immediate thoughts and fears related to the future and the possibility of losing their loved ones:

*“[The day after the diagnosis], the worst fear was that we were going to walk into the assessment clinic here at Princess Margaret and they were going to say ‘there is nothing we can do’” (1001)*

*“My worst fear was that I was going to lose (patient)” (1022)*

#### *3.4 Acute Phase: Dialing it all back.*

The initial overwhelming fear of mortality was immediately followed in all study participants by intentional efforts to avoid negative thoughts and emotions related to a possible adverse future, even - in some cases - to the point of dismissing the severity of the prognosis:

*“I instantly went to what would my life be like without (patient) there. Like you go really far into the future. And then... oh fuck.. I’ve never thought about this before. I may not have a partner at some point. So, which is part of why, as soon as you go there... I dialed it all back [...] I don’t think that is constructive. I don’t know why go to a place like that. He is probably going to be fine” (1003)*

*“It’s passed my mind [that my spouse could die] but I try to remain positive. But as far as what might happen or how, I haven’t put a lot of thought into it. I try and stay away from that for now” (1013)*

The avoidance of distressing future-related thoughts was reported alongside a temporary decrease in emotional arousal, often described as “feeling numb,” or being in “autopilot.” Field notes and journal entries confirmed this finding in observations by the author, who described a “surprising lack of distress” (FN06.09.2019, 1003) in participants interviewed closer to the admission date, who were observed to be more “calm and composed” (FN18.09.2019, 1007) than FCs interviewed later in the treatment trajectory:

*“I probably would have expected myself to just fall apart... I didn’t... I just fell almost like a... numb. Numb is probably a good description [...] Almost feeling like an autopilot” (1001)*

*“[It is hard to see him sick] but I go into strong mode. I am there to take care of all he needs. I go into caregiver mode, which I like. That’s good for me [...] I just go into autopilot” (1003)*

Similarly to what was reported in patients by others (see Nissim, 2012),<sup>30</sup> FCs described keeping a focus on the present and the immediate future and maintaining a tunnel vision around manageable bits of information and actionable tasks, particularly those related to the medical treatment, tests, and results. Similarly to patients, this “present-focused”<sup>30</sup> agenda and the efforts to maintain an optimistic stance were co-constructed with the medical team, which encouraged a hopeful approach in the face of a poor prognosis:

*“We are just trying to just think about one step at a time. We can’t control anything in terms of [the] illness. We are trying not to look that*



*far ahead. Just focus on the next few weeks that we are [at the hospital], deal with at home once we are there. Just trying to get through each week at a time” (1003)*

*“They said: ‘it is treatable and curable.’ They used those words. I know [she may not survive], but at this point I am not going there and I don’t feel I need to [...] she got the big one, she got the jackpot [i.e. a severe cancer], but ‘treatable and curable’ are keeping us going” (1007)*

The present-focused approach was typically perturbed in the 2 weeks following induction chemotherapy in those FCs who witnessed distressing side effects in the patient. FCs witnessing their loved one suffering with severe physical symptoms described this experience as the most distressing part of their journey. One participant said:

*“It was exceptionally difficult the second week of chemo and he was very ill. I found it overwhelming to be here and watch him vomiting, have them tell us he’s fevered. And suddenly that move from, you know, sad, shocked, numb to terrified.” (1001)*

### *3.5 Post-Acute Phase: Living with Trauma*

In the typical course of the initial treatment of AL, patients begin to heal and recover as time progressed and to prepare to be discharged at home. The experience of witnessing a loved one regain strength provided FCs with a sense of relief.

*“[This week compared to the past month] I am little more calm. I guess it’s just a realization of what’s going on, what’s happening. [...] You can see the changes and she looks good today. So that makes you feel better” (1022)*

In an analysis of data from the interviews conducted close to the patient's discharge and those conducted earlier, the author found that the former more frequently included display of emotions [as noted in the transcript (e.g. "crying") or in field notes] and themes related to loss or the future. FCs in this later phase seemed more able to discuss difficult feelings and begin to reflect on the impact of the illness on their lives. An example is provided by this passage:

*Interviewer: As you are talking about [the future] I can see you are getting a little bit teary...*

*Caregiver: oh yeah, absolutely, yeah.*

*Interviewer: What is bringing the tears up?*

*Caregiver: Well, it was tough. It was tough (crying). And I think part of it, [...] is anger built in. There is anger, and anger comes with grief, right? [...] As much as this is happening to him, I also realized that this is happening to me and the life we had together (continues crying)" (1001)*

FCs in this phase also reported worries related to the length of the treatment post-discharge, the consequences of leaving the hospital, such as the exposure to germs, the home accommodations that would be required, the lack of continuous medical surveillance and support, and the practical limitations that would be imposed by the illness and the treatment. These findings were similar to those reported for patients by others (see Nissim, 2014):<sup>79</sup>

*"She's going to be vulnerable, her immune system could be weak, she's going to be, possibly getting on the train to come here, with sick people around her, there's so much public around. So this is what we're worried" (1013)*

*"As much as I am thrilled to have him home and happy for him that he is home, I do have anxiety about... There is no nurses watching for*

*his fever, it is me. There is no, you know, there is nobody making the call as to: do we go to the emergency or not?" (1001)*

#### **4. Discussion**

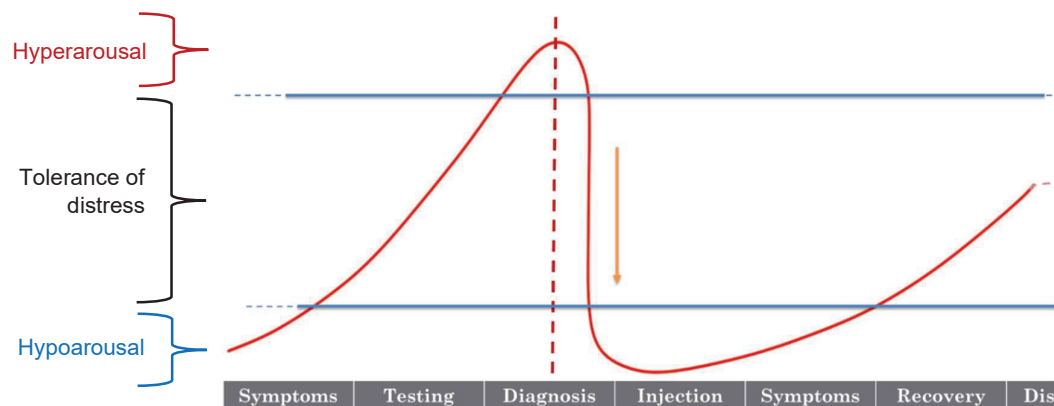
The diagnosis, progression, or recurrence of advanced cancer are traumatic events in the lives of affected individuals, which can trigger distressing psychological and physical consequences.<sup>4,11</sup> The fear of death, the sense of inescapability from the threat, the invasive medical procedures, and the presence of distressing physical symptoms can contribute to the emergence of traumatic stress symptoms in patients and their loved ones, and symptoms can persist or recur over time.<sup>16,25,26,68,80</sup> Many authors have demonstrated a significant prevalence of ASD and PTSD in various samples of cancer patients and primary caregivers later in the course of the illness.<sup>12–15,81</sup> However, despite the demonstrated psychological distress, the moment of the diagnosis and the weeks that follow its occurrence have received very little attention in patients and even less in their informal caregivers. This paucity of research has limited the development of specialized, targeted interventions that could alleviate distress in these individuals.

The present study represents one of the first attempts at characterizing the distress in informal caregivers shortly after the diagnosis of acute leukemia, which is a prototypical condition for the acute onset of a life-threatening disease with intensive treatment and severe physical symptoms. The experience of FCs that emerged from this research is remarkably complementary to that of patients identified in previous studies.<sup>30,79</sup> This is in line with our understanding that patients and caregivers respond to the illness as a “system of mutual influence,”<sup>66,82,83</sup> and this study particularly elucidates the psychological effects of witness suffering in a loved one. Additionally, it contributes to the existing body of knowledge by characterizing the immediate response to a traumatic event in the context of advanced cancer.

Interviewed FCs described what seemed to be an immediate dissociative response to the painful emotions related to the possibility of death. This was accompanied by intentional efforts

to avoid thoughts related to unfavourable outcomes, to engage in actionable issues, to process time-limited information, and to focus on the possibility of cure. As observed by others,<sup>30</sup> these coping mechanisms are supported by a treating team that encourages patients and family members to maintain a hopeful and positive outlook, despite the dire prognosis.<sup>19</sup>

The ability to process difficult emotions and to plan for a longer future begin to appear toward the patient’s discharge, indicating a weakening of the initial dissociative response and a greater access to underlying distressing feelings. Such model of functioning suggests that there is a “window of optimal tolerance” of distress,<sup>84,85</sup> reflecting the range of emotional arousal within which individuals can be aware of and reflect upon their emotional state (see figure 4). Hyperarousal in response to the communication of the diagnosis and the immediate threat to life, tend to trigger “fight-or-flight” responses, which include dissociation, with less awareness of internal states, or a heightened awareness or vigilance regarding external stimuli that constitute a potential threat.



**Figure 4.** Window of tolerance of distress

## 5. Future research and implications for clinical practice

Future research on targeted psychotherapeutic interventions should take into account the possible adaptive functions of the coping mechanisms of FCs that are directed to alleviate the distressing aspects of this response. Recommendations on the treatment of traumatic stress

symptoms soon after the exposure to a traumatic event discourage from exploring or deepening affect at this stage and recommend more supportive and stabilizing interventions.<sup>86</sup> Accessing underlying painful emotions such as overwhelming fear, attending to existential issues, or engaging in meaning-making may not be helpful in this moment.

At this stage, therapists may initially focus their efforts on building a strong therapeutic alliance through which they can validate and normalize the experience of trauma. A stage-based flexible approach will be fundamental for the effective therapist, who may begin more exploratory work in later phases, as FCs' affect begin to regain homeostasis. The ability of the therapist to switch from a supportive to an exploratory stance requires meticulous attention to the felt experience of FCs, with empathic attunement to their underlying emotional states. Supportive interventions may be assisted by present-oriented information and psychoeducation as well as by affect regulation techniques to down-regulate heightened arousal.

## **6. Limitations**

The findings of this study are limited to the experience of family caregivers of patients who have recently received a diagnosis of AL and may therefore not be generalizable to other traumatic events in the illness trajectory or to other types of cancer. Additionally, the sample was recruited from a large urban cancer centre of a major Canadian city and may not represent the experience of rural or underserved populations. Moreover, a bias could have been introduced by the recruitment procedures, which limited the results to patients who identified a FC, and to FC who consented to participate in the interview. Lastly, this grounded theory study lies on interpretations provided by the author, who may have introduced further bias, despite the employment of rigorous procedures in data analysis and collection. This is further limited by the absence of additional coders.

## **7. Conclusions**

The purpose of this doctoral study was to explore the experience of informal caregivers caring for individuals with newly-diagnosed acute leukemia. A grounded theory approach revealed three distinct phases: an anticipatory phase, that precedes the diagnosis, an acute phase that follows the diagnosis and includes the initiation of induction chemotherapy, and a post-acute phase that encompasses the days preceding the discharge from the hospital. FCs described an increase in distress that peaks at the time of diagnosis. Distress remarkably decreases soon after this moment, indicating a dissociative response from overwhelming emotions. This response was characterized by an optimistic stance and a focus on positive outcomes, present-oriented information, and actionable tasks. Underlying painful emotions seemed inaccessible during the acute phase and began to emerge later in the course of treatment. Future research on targeted psychotherapeutic interventions may take into consideration the adaptive function of this initial response.

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**MANUSCRIPT #2**

**Problemi psicosociali e psichiatrici della famiglia**

**Invited Book Chapter**

*In: Luigi Grassi (ed.) - Aspetti Psicosociali in Cure Palliative (Manuscript in Preparation)*

## **Problemi psicosociali e psichiatrici della famiglia**

### *Introduzione*

I caregiver familiari (o primari, o informali) sono quei membri della famiglia di un paziente - nell'accezione di famiglia più appropriata per ogni individuo - che più di altri provvedono alle cure fisiche ed al supporto psicologico dell'ammalato, senza percepire un corrispettivo economico. Nell'ambito delle cure palliative, il tema dell'assistenza ai caregiver arriva da una storia più civile che sanitaria, legata alle lotte sociali Nord-Americane centrate sulle differenze di genere in ambito lavorativo. In passato, infatti, il peso delle cure assistenziali veniva quasi esclusivamente sostenuto da donne, che ricoprivano questi ruoli per via di regole sociali oltre che per scelte individuali. Il prendersi cura di un ammalato era visto come un atto d'amore intrinseco dell'essere donna, e quindi un obbligo quasi identitario e fuori da ogni riflessione, riconoscimento, o supporto sociale. Con la seconda metà del ventesimo secolo, invece, le lotte civili sulla parità di genere e l'incremento nel numero dei malati cronici gravi porteranno ad una rivalutazione delle responsabilità assistenziali, spronando i primi studi scientifici sull'impatto sui curanti. Gli studi sul caregiving burden (dall'inglese "fardello" o "peso" della cura) si moltiplicarono così in diversi domini clinici: prima nel campo dell'assistenza agli anziani e ai bambini e poi nel settore delle malattie croniche a decorso lento, come nel morbo di Alzheimer, nella sindrome da immuno-deficienza acquisita (AIDS) o in alcune malattie cardiache. In tempi più recenti, l'attenzione sulla cura dei familiari ha trovato terreno molto fertile in oncologia, generando moltissimi studi demograficamente sovra-rappresentati da pazienti con tumore avanzato e dai loro caregiver.

In pazienti oncologici, la diagnosi, la progressione o la recidiva di tumore avanzato orientano il decorso del trattamento clinico verso interventi medici spesso più aggressivi e non sempre con chiari vantaggi prognostici. L'aggravarsi della malattia e l'evoluzione del trattamento si accompagnano in molti casi sia a sintomi fisici debilitanti, con effetti peggiorativi sulle funzioni fisiche e sull'autonomia del paziente, che a disturbi nella dimensione psico-sociale.

Questi ultimi sono caratterizzati principalmente dalla difficoltà nell'affrontare la malattia, dal bisogno crescente di dipendere dagli altri e dalla paura di morire. In sostanza, i pazienti con tumore avanzato affrontano la doppia sfida di vivere nel presente, complicato dalla neoplasia e dal trattamento oncologico, e di prepararsi al futuro e alla morte; un concetto definito da alcuni ricercatori nel nostro laboratorio come "double awareness". La difficoltà di alcuni pazienti nel sostenere questa "doppia consapevolezza" comporta un rischio elevato per la presenza di stati depressivi, demoralizzazione e una morte psicologica che si verifica anche molto prima della morte fisica, in cui i pazienti sembrano quasi rinunciare alla ricerca di ciò che da senso o significato alla loro vita. Nello specifico dei dati scientifici, molti studi riportano sintomi depressivi elevati in circa un quarto dei pazienti con tumore avanzato. Altri studi riportano un'aumento immediato del numero di suicidi, quasi il doppio in queste persone rispetto alla percentuale osservata nella popolazione generale. L'impatto del tumore non si circoscrive solo alla salute fisica e mentale degli individui che ne sono affetti, ma si dirama in diversi domini come quello sociale o economico, con ulteriori aggravamenti sul benessere psico-fisico del paziente. Non sorprende come un effetto così capillare si riverberi in maniera importante su tutto il sistema familiare, che reagisce alla malattia come una singola unità.

I caregiver primari di pazienti con tumore avanzato, come vedremo più avanti in questo capitolo, riportano livelli di distress psicologico uguali o addirittura più alti rispetto a quelli osservati nei loro congiunti, livelli di salute fisica molto bassi rispetto a non-caregiver di simile composizione demografica, e un deterioramento del funzionamento psico-fisico che persiste nel tempo anche fino a dopo la morte del paziente (per un approfondimento in merito si rimanda al capitolo 7g). Un impatto così robusto necessiterebbe quindi di una risposta proporzionata e tempestiva da parte del sistema sanitario, che tende invece a focalizzarsi principalmente sul trattamento delle masse tumorali. Questa carenza di attenzione ai bisogni psico-sociali della famiglia, tipica nel campo dell'oncologia in moltissime parti del mondo, rappresenta in parte una corrente di pensiero più ampia, che pone nei sintomi fisici un'urgenza maggiore che in quelli psicologici, spesso vittima di stereotipiche associazioni

con caratteristiche personali di debolezza o rassegnazione. Nel campo delle cure palliative, invece, l'assistenza al malato si impernia più saldamente che in altri settori della medicina su problematiche di salute mentale, e si estende fino a considerare il nucleo familiare del paziente come il destinatario primario delle cure psico-sociali. Una concezione olistica della cura così formulata, e supportata ormai da anni di ricerca, non si concretizza purtroppo sul territorio in maniera omogenea. Molte realtà ospedaliere, infatti, faticano ad offrire trattamenti psicoterapici specifici per la famiglia, che dovrebbero invece essere integrati organicamente nel trattamento oncologico standard. Il peso delle cure assistenziali, l'impatto della diagnosi e del decorso della malattia, la presenza di sofferenza fisica e mentale e la mancanza di supporto psicologico professionale, fanno così dei caregiver dei veri e propri pazienti invisibili.

### *L'impatto della diagnosi*

In tempi recenti, molti studi scientifici hanno cominciato ad esplorare i possibili effetti di tipo traumatico causati dal tumore o dal suo trattamento. Secondo la definizione del *Diagnostic and Statistical Manual of Mental Disorders – 5th edition (DSM-5)*, un evento viene considerato traumatico se questo espone alla morte o alla possibilità di morire, sia direttamente gli individui coinvolti sia le persone a loro vicine emotivamente. In ambito oncologico, questo corrisponde al momento della comunicazione della diagnosi o alla notizia della progressione o della recidiva della malattia. Più generalmente, il periodo di tempo che segue un evento traumatico può essere caratterizzato da gravi sintomi psicologici, reazioni fisiologiche o cambiamenti nel comportamento che vengono tipicamente definiti come *sintomi da stress traumatico*. Tra questi si registrano disturbi persistenti dell'umore, distorsioni cognitive e manifestazioni ansiose eccessive. In aggiunta, si osservano anche momenti di affettività piatta con stati dissociativi e sforzi nell'evitare stimoli fisici o psicologici legati all'evento traumatico (come ad esempio il rifiuto di guidare in persone che hanno subito un incidente stradale o lo sforzo di evitare pensieri o memorie legati allo stesso). Nel DSM-5, la persistenza nel tempo di questi sintomi può portare ad una diagnosi di *disturbo da*



*stress acuto* o di *disturbo da stress post-traumatico*. La risposta iniziale ad un evento traumatico è stata studiata approfonditamente in alcune popolazioni, come per esempio nei veterani in ritorno dalle missioni di guerra. La proliferazione scientifica in queste aree di ricerca ha portato ad uno sviluppo di interventi psico-sociali estremamente specializzati che, se mirati e tempestivi, aiutano a ridurre il rischio di sviluppare disturbi psichiatrici post-traumatici. In oncologia, esistono oggi pochissimi programmi di ricerca focalizzati sul periodo di tempo che segue la diagnosi di tumore avanzato. La carenza di studi scientifici in quest'area di ricerca corrisponde in pratica clinica ad una mancanza di interventi psico-sociali specifici ed è dovuta in larga parte alla difficoltà nel reclutare pazienti e familiari in un momento caratterizzato da stati emotivi intensi e impegni medici gravosi.

In un programma di ricerca canadese attivo al Princess Margaret Cancer Centre di Toronto, alcuni studi del nostro team di ricerca sono riusciti a coinvolgere pazienti affetti da leucemia acuta ed i loro caregiver primari subito dopo la diagnosi di questo tipo di tumore avanzato. Questo è stato possibile in quanto i malati di leucemia acuta vengono ospedalizzati con urgenza per ricevere un trattamento chemioterapico immediato e molto intenso. La permanenza in ospedale, che può durare da diverse settimane ad alcuni mesi, offre quindi la possibilità di incontrare i pazienti e i loro familiari nei giorni successivi alla diagnosi. In uno studio con un campione di oltre 360 pazienti, ad oggi uno dei più ampi sul tema, più di un terzo dei partecipanti ha riportato sintomi da stress traumatico, confermando la presenza di un impatto di tipo traumatico in questa popolazione. La percentuale registrata in questo studio si dimostra più elevata rispetto a quelle riportate in altre popolazioni, come ad esempio per gli individui che hanno subito un trauma fisico severo. Uno studio qualitativo con i familiari di questi pazienti ha permesso di osservare l'impatto della diagnosi sui caregiver, identificando tre fasi distinte nell'esperienza di questi individui: una fase anticipatoria, una fase acuta, ed una fase post-acuta. La fase anticipatoria, che precede la diagnosi, contraddistinta da test medici e da giorni o settimane difficili in attesa dei risultati, sembra essere fondamentalmente caratterizzata dalla paura di una diagnosi nefasta. Il livello di distress psicologico in queste circostanze aumenta fino a raggiungere il picco nel momento

della diagnosi, che viene descritta come scioccante o sconvolgente. Inaspettatamente, nella fase successiva (quella acuta), che raccoglie le prime settimane che seguono il momento della diagnosi, tutti i caregiver intervistati in questo studio riportano una drastica riduzione del distress psicologico. Questa caduta dell'arousal affettivo viene descritta come una sensazione di intorpidimento emotivo ("numbness") o addirittura come un'assenza totale di emozioni. I caregiver parlano di sforzi intenzionali nel focalizzarsi sul presente, nel sopprimere pensieri negativi legati al futuro (per esempio riguardo alla lunghezza o alle diverse fasi del trattamento) o connessi alla possibilità di perdere il proprio caro, nel mantenere un'atteggiamento positivo, e nell'impegnarsi nei vari compiti pratici richiesti dall'ospedale o dal paziente. Solo nell'ultima fase, quella post-acuta, che corrisponde al miglioramento fisico nel paziente, cominciano a riemergere nei caregiver delle emozioni di rabbia, tristezza, o paura, che sembrano essere ora più accessibili. In questa fase, i caregiver sembrano cominciare elaborare gli eventi delle settimane precedenti, tentando di dare un significato all'accaduto.

I risultati riportati sembrerebbero descrivere un impatto immediato di tipo traumatico non solo sui pazienti, ma anche sui loro caregiver primari. La reazione iniziale dell'organismo dopo la diagnosi, che di certo necessita di maggiore ricerca e riflessione scientifica, sembrerebbe indicare la presenza di uno stato dissociativo in risposta all'emergenza di emozioni dolorose. Questa risposta potrebbe avere delle funzioni adattive organizzate intorno al bisogno di rispondere alle richieste dell'ambiente. Si osservano delle oscillazioni tra periodi in cui i caregiver sono in grado di accedere e processare delle emozioni difficili, e altri in cui sembrano innescarsi dei meccanismi protettivi di dissociazione dalle medesime. Per chiarire meglio questo concetto, potremmo immaginare la scena di una casa in fiamme con degli individui in essa intrappolati. Potremmo immaginare lo stato emotivo e cognitivo di queste persone, il cui immediato obiettivo è quello di trovare una via di uscita verso la salvezza. In simili circostanze, l'organismo si organizza intorno al bisogno di mettersi in salvo, ponendo attenzione solo a stimoli salienti e comportamenti necessari per raggiungere l'esterno della casa. L'accesso ad emozioni legate alla morte, all'impatto di questa sulla famiglia, alla

perdita di beni materiali, o all'elaborazione del significato dell'accaduto, viene reso difficile, in modo da permettere un'uso delle risorse cognitive ed emotive più adatto alla situazione immediata di pericolo. Nel caso della diagnosi di leucemia acuta, lo sviluppo di trattamenti di supporto specifici per questo periodo di tempo dovrebbero quindi tenere conto delle fluttuazioni osservate nello stato emotivo dei caregiver, della capacità di questi individui di affrontare tutti gli aspetti della realtà, e delle possibili funzioni adattive di una eventuale risposta dissociativa. Interventi mirati alla riflessione, all'approfondimento o all'espressione delle emozioni, dovrebbero alternarsi a momenti di sostegno, di validazione, e di normalizzazione dell'esperienza traumatica e di supporto delle funzioni adattive del corpo. Il lavoro del terapeuta richiederebbe così un'attenzione meticolosa all'esperienza affettiva degli utenti, una sintonizzazione emotiva accurata ed empatica, e la capacità di muoversi con flessibilità da una posizione più esplorativa ad una più supportiva.

#### *Disturbi psichiatrici e psico-sociali durante decorso della malattia*

Come menzionato nell'introduzione al capitolo, gli studi sul caregiving burden iniziarono negli anni '60 del secolo scorso, sulla scia delle lotte sociali centrate sul lavoro delle donne. All'epoca, la maggior parte degli studi scientifici misuravano il burden in maniera oggettiva, tenendo in considerazione ogni tipo di costo pratico per la famiglia. Con l'avanzare del tempo, alcuni ricercatori cominciarono a riconoscere la necessità di separare le varie attività fisiche da componenti più prettamente psicologiche, suddividendo così questo costrutto in due parti distinte e solo parzialmente interconnesse. Una parte, definita *objective burden* ("peso oggettivo"), indica tutti quei fattori obiettivi compresi nell'atto pratico della cura, come ad esempio il numero di ore spese in attività assistenziali in una settimana. L'altra, definita *subjective burden* ("peso soggettivo"), indica invece l'esperienza soggettiva dell'assistenza, così come viene vissuta dal caregiver. Quest'ultima, che viene oggi più largamente utilizzata in ricerca, sembra essere il fattore che più di altri correla con la presenza di disturbi psichiatrici e psico-sociali in questi individui. La percezione soggettiva del peso delle cure varia notevolmente tra individui con simile *objective burden*, e molti studi scientifici mostrano

come il subjective burden sia influenzato da caratteristiche individuali e sistemiche – ad esempio lo stato di salute del paziente, la percezione del supporto ricevuto da parenti e amici, la relazione tra caregiver e paziente, o lo stato finanziario della famiglia - piuttosto che dal numero o dal tipo di compiti assistenziali. È importante quindi sottolineare che caregiver in condizioni più vantaggiose rispetto a queste caratteristiche, magari migliorate da un supporto psico-sociale mirato ed efficace, possono avere un'esperienza del subjective burden meno travolgente, legata magari ad un distress psicologico più moderato o addirittura ad un aumento del benessere psico-sociale. In alcuni studi qualitativi, infatti, alcuni caregiver riportano esperienze di caregiving positive e un incremento nella vicinanza emotiva con il paziente. Altri caregiver parlano di lezioni personali significative emergenti da questa esperienza, che viene descritta anche come profonda, importante e soddisfacente e con effetti positivi sull'autostima.

Per quanto riguarda l'objective burden, l'impatto sui caregiver familiari si è aggravato negli ultimi 30 anni a causa dell'invecchiamento della popolazione mondiale e dell'avanzamento scientifico nelle cure mediche, con conseguente incremento del numero e dell'aspettativa di vita di pazienti oncologici gravi e dello spostamento di vari trattamenti anti-tumorali dal ricovero in ospedale all'ambulatorio. Il risultato fu un graduale trasferimento di molti compiti di natura assistenziale sui caregiver primari, i quali hanno assunto nel tempo ruoli sempre più impegnativi e che si estendono fino alla morte del paziente. Questi individui, ancora oggi purtroppo in grande maggioranza rappresentati da donne (spesso mogli, partner, o figlie adulte), modificano gradualmente il proprio ruolo in famiglia diventando la risorsa principale di supporto pratico, sociale ed emotivo per i pazienti, con effetti positivi sulla loro salute fisica e mentale ed addirittura sulla loro aspettativa di vita. Come mostrano alcuni studi naturalistici, con l'avanzare progressivo della malattia e delle esigenze del malato, l'impegno dei caregiver primari può estendersi fino ad occupare 40 ore settimanali, che vengono spese in compiti complessi quali il coordinamento dei vari appuntamenti medici o l'amministrazione di farmaci o in attività giornaliere più pratiche, come lavori domestici o assistenza nella cura dell'igiene personale. L'impegno dei caregiver tende a raggiungere il picco negli ultimi mesi

di vita del paziente, quando molti ricorrono al supporto personale medico specializzato o al ricovero in hospice. Alcuni studi mostrano come la maggior parte dei pazienti in questa fase preferisca ricevere assistenza e morire in casa propria. Questa scelta, che sembra migliorare la qualità della vita dei pazienti negli ultimi mesi di vita, allo stesso tempo comporta difficoltà aggiuntive per i caregiver primari, che in questo stadio della malattia affrontano sintomatologie nel paziente molto severe e bisogni fisici ingenti.

Sarebbe forse impossibile assistere il numero odierno di pazienti affetti da malattie croniche senza il supporto dei loro familiari, che possono assumersi fino all'90% delle cure, con un cospicuo risparmio di risorse finanziarie per la comunità. Questo oneroso contributo alla vita dei pazienti e alla collettività manca di una risposta proporzionata da parte del sistema sanitario, che lascia moltissimi dei caregiver senza un supporto adeguato. Molti di loro, infatti, lamentano un'accesso a servizi dedicati lacunoso o insufficiente e segnalano una mancanza di preparazione per il ruolo che viene loro richiesto di assumere. Dal momento della diagnosi fino alla fine della vita del paziente, e anche oltre durante il periodo del lutto, una percentuale molto significativa di caregiver primari riporta disturbi in quattro domini fondamentali: quello psicologico, quello fisico, quello finanziario e quello legato alla sfera sociale. Molti studi scientifici riportano livelli di ansia e depressione elevati in circa il 50% dei caregiver primari. Studi comparativi (in cui vengono confrontate coppie di caregiver e pazienti appartenenti allo stesso nucleo familiare) hanno dimostrato come i livelli di distress nei caregiver eguagliano o addirittura sorpassino quelli dei pazienti. Altri studi riportano che tra il 15% ed il 30% dei caregiver primari di pazienti con tumore avanzato presentano sintomi psicologici che soddisfano i criteri diagnostici per uno o più disturbi psichiatrici. Tra questi compaiono più frequentemente il disturbo di panico, di depressione maggiore, di ansia generalizzata, e, come osservato nel paragrafo precedente, di stress post-traumatico. In aggiunta, alcuni studi medici riportano in caregiver primari funzioni immunitarie più basse, problemi cardiovascolari più severi e addirittura una mortalità più alta che in non-caregiver. Tra i sintomi fisici più ricorrenti, vengono riportati l'insonnia, la fatica, l'inappetenza e la perdita di peso. Nonostante ciò, i caregiver tendono a preoccuparsi quasi esclusivamente del

paziente e a sminuire il proprio bisogno di assistenza, contribuendo così al rischio che queste difficoltà non vengano rilevate dal sistema sanitario. Tra i fattori che influenzano l'esperienza soggettiva del burden, spicca prima degli altri quello legato allo stato di salute del paziente. Questo avviene non solo in risposta all'aumento fisico delle esigenze assistenziali, ma anche al vissuto angosciante nel vedere un proprio familiare procedere verso un declino fisico e cognitivo a volte inesorabile. Questo fenomeno, più presente durante trattamenti medici intensi, in compresenza con sintomi fisici severi, o verso la fine della vita del paziente, sembra essere mediato dalla presenza o meno di supporto sociale. Molti studi mostrano come i caregiver di pazienti oncologici tendano a riportare un senso di separazione dal loro network sociale, spesso dovuto proprio alle richieste ingenti dell'assistenza al malato. La valutazione dell'aiuto disponibile sembra essere però più legata all'esperienza soggettiva del caregiver piuttosto che alla presenza fisica di altre persone, indicando un'abilità intrinseca del singolo individuo di richiedere e fare uso del supporto altrui. Non ultimo deve essere considerato l'impatto finanziario della malattia, che dipende in parte del costo delle cure oncologiche (in quelle parti del mondo dove non tutti i trattamenti sono coperti dal sistema sanitario nazionale) e in parte dalla possibile perdita di guadagni della famiglia. Molti autori hanno mostrato, infatti, come l'assistenza ad un familiare possa diventare un vero e proprio lavoro full-time, soprattutto in quei casi in cui vi siano altri dipendenti come anziani malati o bambini. In questi casi, i caregiver primari sono spesso costretti a richiedere congedi lavorativi o addirittura a lasciare la propria occupazione per prendersi cura dei loro cari.

### *Conclusioni*

La paura di perdere un familiare, la modifica dei ruoli in famiglia, l'impatto fisico e psicologico delle cure assistenziali, le perdite economiche, l'isolamento sociale e l'essere testimone della sofferenza di una persona cara, rappresentano tutti fattori di rischio per malattie fisiche e disturbi psichiatrici e psico-sociali severi in caregiver primari di pazienti oncologici gravi. Il contributo di queste persone alla cura dei pazienti comporta dei costi enormi, che non sono

bilanciati da un supporto strutturato adeguato in moltissime aree geografiche nel mondo. Questo avviene a dispetto dei benefici apportati alla qualità e lunghezza della vita dei pazienti e al sistema sanitario, che si basa ormai quasi irreversibilmente sulle innumerevoli ore di lavoro gratuito apportate da questi individui. È quindi un dovere della comunità clinica, oltre che una necessità, quello di sostenere il diritto all'assistenza di questi individui, sia in termini di supporto pratico che psicologico. Anche nell'ambito scientifico che riguarda lo sviluppo di interventi di supporto specializzati, che solo nell'ultimo decennio ha beneficiato di un interesse accademico più nutrito, si regge su evidenze scientifiche ancora relativamente esigue. Anche i più importanti centri di cura al tumore nel mondo offrono supporto solo ai caregiver che ne fanno richiesta, lasciando moltissime persone in condizioni di sofferenza acuta. Un supporto ottimale a questi individui dovrebbe non solo essere integrato organicamente nel trattamento oncologico standard, ma dovrebbe partire da uno screening dei familiari coinvolti nella cura dei pazienti e basarsi su interventi psico-sociali basati su evidenze scientifiche rigorose.

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Mohammed S, Swami N, Pope A, Rodin G, Hannon B, Nissim R, et al: *"I didn't want to be in charge and yet I was": Bereaved caregivers' accounts of providing home care for family members with advanced cancer*. *Psycho-oncology*. 27(4):1229–36, 2018

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### MANUSCRIPT #3

#### PUBLISHED ARTICLE

Rosangela Caruso, Maria Giulia Nanni, Gary Rodin, Sarah Hales, **Carmine Malfitano**, Silvia De Padova, Tatiana Bertelli et al. "Effectiveness of a brief manualized intervention, Managing Cancer and Living Meaningfully (CALM), adapted to the Italian cancer care setting: Study protocol for a single-blinded randomized controlled trial." *Contemporary Clinical Trials Communications* 20 (2020): 100661.

# Application of Managing Cancer and Living Meaningfully (CALM) in Advanced Cancer Patients: An Italian Pilot Study

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Depression and anxiety occur in 25–30% of advanced cancer patients, as conditions arising from a final pathway of distress determined by the interaction of multiple factors [1]. Within the psychotherapeutic intervention developed to address these conditions, Managing Cancer and Living Meaningfully (CALM) [2] is an individual meaning and supportive-expressive intervention for patients with advanced cancer. In preliminary pilot studies, CALM was found to decrease depression and anxiety, and improve spirituality and attachment [3, 4], while in a randomized clinical trial, CALM reduced depression and improved end-of-life preparation [5].

We conducted a pilot study of CALM using a mixed method approach, in order to: (i) understand the possible application of CALM in a different cultural context (i.e., Italy) and examine the patients' subjective perception of CALM; and (ii) preliminarily explore, as already done in other countries (i.e., Germany) [6], the possible effects of CALM on a series of psychosocial outcomes.

The study was carried out on advanced cancer patients referred to the Program of Psycho-Oncology Psychiatry

in Palliative Care, University of Ferrara (Ferrara, Italy). Inclusion criteria were: age  $\geq 18$  years, a diagnosis of advanced cancer (expected survival of 12–18 months), no cognitive impairment, and a score  $\geq 10$  in the Patient Health Questionnaire-9 (PHQ-9) or  $\geq 20$  in the Death and Dying Distress Scale (DADDS). The study was approved by the Ethics Committee of the institution.

According to the CALM protocol, each patient was assessed at baseline (T0) and 3 months (T1) and 6 months later (T2) by using a battery of psychometric instruments, including: the PHQ-9 for depression, the DADDS for death anxiety, the Generalized Anxiety Disorders-7 (GAD-7) to screen for anxiety symptoms, the Posttraumatic Growth Inventory (PTGI), the Functional Assessment of Chronic Illness Therapy – Spiritual Well-Being Scale (FACIT-Sp) for spirituality and meaning, the Experiences in Close Relationships Inventory – Modified Short Form Version (ECR-M-16), and the Quality of Life at the End of Life – Cancer Scale (QUAL-EC). A 7-item tool, the Clinical Evaluation Questionnaire (CEQ) was used at 3 and 6 months (T1 and T2) to assess the subjec-

**Table 1.** Frequencies (%) of responses (much or very much) on the CEQ

CEQ	CALM		UC		p
	<i>much</i>	<i>very much</i>	<i>much</i>	<i>very much</i>	
<i>The intervention helped me to:</i>					
Freely discuss my concerns about cancer and my treatment options	16.7	75	22.2	22.2	0.04
Talk and feel understood about how cancer has affected my life	30.8	61.5	11.1	22.2	0.01
Deal with changes in my relationships as a result of cancer	54.5	27.3	22.2	22.2	ns
Explore better ways to communicate with my health care team, my family, and others	36.4	36.4	44.4	0	ns
Clarify my values and beliefs	45.5	18.2	11.1	0	0.01
Talk about my concerns about the future and be less frightened	41.7	41.7	11.1	11.1	0.01
Better express and manage my feelings	33.3	33.3	11.1	0	0.01

tive perception of both treatments and the insight patients have gained (online suppl. Document 1; see [www.karger.com/doi/10.1159/000505875](http://www.karger.com/doi/10.1159/000505875) for all online suppl. material).

Each patient, after random allocation to CALM intervention or usual care (UC) received 12 individual sessions (45–60 min each) delivered over 6 months on a 15-day basis. The CALM therapist, as in the original manual [7], explored meaning, preparation for death, symptom management, and interpersonal relationship domains. Participants in the UC received, from a different psychotherapist, unstructured psychological support. Also, in spite of the pilot nature of the study, preliminary statistical analysis on the quantitative data were carried out.

Of 50 eligible referred patients, complete data were available for 25 (mean age  $60 \pm 11.8$  years; education  $13.2 \pm 2.8$  years; breast cancer, 36%; gastrointestinal cancer, 28%, and lung cancer, 12%). Twenty-seven patients were allocated to CALM and 23 to UC. Thirteen subjects completed T1 and T2 in the CALM arm and 12 subjects in the UC arm. A greater satisfaction with care was found in the CALM group versus UC (Table 1). A significant series of themes, attributing value and meaning to the CALM experience emerged and were explored in terms of their content (online suppl. Document 2). A statistically significant improvement on PHQ-9, DADDS, GAD-7, and PTGI was found in CALM versus UC at T1 and T2, as well as on the same dimensions across time (T1–T2) in CALM, but not in the UC group (online suppl. Table 1).

This is the first CALM study in Italian cancer patients. In line with other CALM qualitative studies [8–10], CALM was also positively accepted by the patients,

as indicated by their general satisfaction and their comments, indicating the construction of a shared reflective space in which the therapist facilitated the patients in the discussion about death and dying, loss, spirituality, and aftermath concerns. In spite of the small number of participants, CALM was shown to be effective, both across time and with respect to UC, in reducing the levels of depression, death, and general anxiety, and in increasing the levels of posttraumatic growth at both T1 and T2. These results are in line with other CALM studies both in Canada and Germany and seem to confirm the role of this semi-structured intervention acting on meaning in ameliorating psychosocial parameters in advanced cancer patients. In contrast with the original Canadian study, CALM had no effect on attachment issues and quality of life issues.

The relevance of this pilot study is mainly linked to the possibility of further application of CALM, and other forms of meaning psychotherapy, in the Southern European cultural context, such as Italy. As limitations, the small number of patients indicates the need to expand the sample size. Also, since we compared CALM with UC, we cannot conclude that CALM is superior to or similar to other meaning-centered psychotherapy. A larger multicenter randomized clinical trial, in agreement with what in progress in other countries (e.g., Germany), is in a developing phase and the full study will address some of the limitations here underlined.

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## Statement of Ethics

The study was approved by the Ethics Committee of the institution.

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## Disclosure Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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