Feasibility and effectiveness of an EMDR psychotherapeutic intervention with additional procedures (EMDR Toolbox) in improving psychological well-being in patients diagnosed with oncological disease: a randomized study

Study Type:	Other Clinical Trial according to ClinO, Chapter 4
Risk Categorisation:	Risk category A
Study Registration:	to be registered on clinicaltrials.gov
Sponsor	Paola Arnaboldi c/o Lega cancro Ticino Piazza Nosetto, 3 6500 Bellinzona T. 091 820 64 20 E. paola.arnaboldi@legacancro-ti.ch
Principal Investigator	Paola Arnaboldi c/o Lega cancro Ticino Piazza Nosetto, 3 6500 Bellinzona T. 091 820 64 20 E. paola.arnaboldi@legacancro-ti.ch Dipartimento di Scienze Teoriche e Applicate (DiSTA) Università degli Studi eCampus Via Isimbardi, 10, 22100 Novedrate COMO I
Investigated Intervention:	Psicoterapia EMDR secondo le procedure addizionali (EMDR Toolbox) (Knipe, 2018; Spadoni, 2026)
Protocol ID	EMDRToolbox_001
Version and Date:	Versione 2 (05/02/2026)

CONFIDENTIALITY STATEMENT

PROTOCOL SIGNATURE FORM

Study Title	Feasibility and effectiveness of an EMDR psychotherapeutic intervention with additional procedures (EMDR Toolbox) in improving psychological well-being in patients diagnosed with oncological disease: a randomized study
Study ID	EMDRToolbox_001

The Sponsor-Investigator has approved the protocol version 1 (dated 30/11/2025) and confirm hereby to conduct the study according to the protocol, current version of the World Medical Association Declaration of Helsinki, and ICH-GCP guidelines as well as the local legally applicable requirements.

Sponsor:

Name: *Paola Arnaboldi*

Date: 05.02.2026 Signature: _____

GLOSSARY OF ABBREVATIONS

AE	*Adverse Event*
BASEC	*Business Administration System for Ethical Committees*
CORE OM	*Clinical Outcomes in Routine Evaluation*
CRF	*Case Report Form*
CTCAE	*Common Terminology Criteria for Adverse Events*
EMDR	*Eye Movement Desensitization and Reprocessing*
FADP	*Federal Act on Data Protection (in German: DSG, in French: LPD, in Italian: LPD)*
eCRF	*electronic Case Report Form*
FOPH	*Federal Office of Public Health*
GCP	*Good Clinical Practice*
HRA	*Human Research Act (in German: HFG, in French: LRH, in Italian: LRUm)*
ICH	*International Conference on Harmonisation*
ClinO	*Ordinance on Clinical Trials in Human Research (in German: KlinV, in French: OClin, in Italian: OSRUm)*
SAE	*Serious Adverse Event*

Sponsor / Sponsor-Investigator	Paola Arnaboldi c/o Lega cancro Ticino, Piazza Nosetto 3, 6500 Bellinzona T. 091 820 64 20 E paola.arnaboldi@legacancro-ti.ch
Study Title	Feasibility and effectiveness of an EMDR psychotherapeutic intervention with additional procedures (EMDR Toolbox) in improving psychological well-being in patients diagnosed with oncological disease: a randomized study
Short Title / Study ID	EMDR Toolbox in cancer patients
Protocol Version and Date	Version 2 (dated 05/02/2026)
Study Registration	To be registered on clinicaltrials.gov
Study Category and Rationale	Risk category: A (WHO, 2013)
Background and Rationale	Given the high prevalence of adverse childhood experiences (ACEs) among patients affected by somatic diseases, particularly in oncology, it is important to complement the usual triage and psychological distress screening interventions provided by psychologists working in liaison clinical psychology services with specialized, evidence-based psychotherapeutic treatments delivered by trained professionals. Among the range of currently available evidence-based psychotherapies, Eye Movement Desensitization and Reprocessing

	(EMDR) psychotherapy was recognized by the World Health Organization (WHO) in 2013 and again in 2024 as one of the treatments of choice for trauma and for the psychophysiological consequences of adverse events and stress. The standard eight-phase protocol, since its development by the American psychologist Francine Shapiro in 1987, has consistently represented the primary method for the application of EMDR; however, in hospital clinical practice and in liaison psychotherapy outpatient settings, difficulties are often encountered in administering standard EMDR procedures. These difficulties are often related to the complexity of patients' internal systems. Beginning in the early 1990s, the American psychologist Jim Knipe started to present to the EMDR community a series of insights aimed at extending the application of EMDR to complex patients, that is, individuals with a clinical history characterized by multiple stressful life events, as is frequently the case for patients affected by oncological disease who require psychotherapeutic psychological care. Subsequently, beginning in 2010, Manuela Spadoni further developed Knipe's insights by creating a toolbox with flashcards designed to facilitate the learning of specific EMDR tools (2023). This instrument is intended to guide clinicians in the use of a range of additional procedures for applying EMDR with complex patients characterized by high levels of psychological defenses and dissociative mechanisms. From 2015 to the present, Manuela Spadoni has systematized the available empirical evidence, theoretical concepts, the parts model, and the operational tools developed to date into a structured psychotherapeutic method known as the EMDR Toolbox Method (ETM) (Spadoni et al., 2026), drawing on Jim Knipe's 2018 book entitled *EMDR Toolbox: Theory and Treatment of Complex PTSD and Dissociation.* The present research project represents a first exploratory pilot study aimed at investigating the feasibility and effectiveness of an EMDR intervention with additional procedures (EMDR Toolbox) (Knipe, 2018; Spadoni, 2026) compared with standard EMDR procedures in improving emotional well-being in a consecutive sample of patients referred to the Clinical Psychology Outpatient Service of the Ticino Cancer League by general practitioners, treating specialists, or through self-referral.
Risk / Benefit Assessment	It is hypothesized that the present trial will be beneficial for patients receiving psychotherapeutic care while affected by a concomitant oncological somatic condition. No risks are anticipated in this study.
Objective(s)	To assess the feasibility and effectiveness of psychotherapy delivered according to additional EMDR procedures (EMDR Toolbox) within the Clinical Psychology Outpatient Service of a public-benefit organization, the Ticino Cancer League.
Endpoint(s)	Primary endpoints: - Feasibility outcome: completion rate of the 15 psychotherapy

	sessions in the two groups (Toolbox vs. standard). - Statistically significant difference in the improvement of global wellbeing in favor of the group receiving psychotherapy according to the additional procedures (EMDR Toolbox). - Statistically significant difference in the reduction of psychological symptoms in favor of the EMDR group using the additional procedures (EMDR Toolbox). Secondary endpoints: - Statistically significant difference in the improvement of Self-Compassion Scale scores in favor of the group receiving EMDR Toolbox psychotherapy. This psychological construct underlies well-being and a healthy attitude of the individual toward oneself (Zessin, 2015). - Statistically significant difference in perceived sleep quality in favor of the group receiving EMDR psychotherapy according to the additional procedures. Since dissociative mechanisms strongly influence the complexity of patients' internal systems and their ability to meta-reflect, thereby affecting their capacity to progress in the therapeutic process and benefit from it, a normal distribution of dissociative phenomena is assumed among the patients enrolled in the study.
Study Design	Open-label, parallel-group, randomized controlled trial.
Inclusion- / Exclusion Criteria	Patients diagnosed with cancer who are referred to the Clinical Psychology Outpatient Service of the Ticino Cancer League by their general practitioner, the treating oncologist, or nurses. Patients who self-refer to the service will also be included in the study. Inclusion criteria: - Clinical stage of cancer: stage I, II - Age 18 to 65 years - Conditions allowing proper participation in the proposed program (ability to complete questionnaires) - Written informed consent Exclusion criteria: - Psychiatric or other disorders that may prevent the provision of informed consent
Number of Participants with Rationale	This is a pilot, exploratory study. A total of 46 patients is expected to be enrolled. The sample size calculation is based on the comparison of means between independent samples. The most appropriate test is a one-tailed Student's t-test, anticipating a greater effect of EMDR Toolbox psychotherapy. The scientific literature on the effectiveness of EMDR in cancer patients for reducing PTSD symptoms, as well as

	anxiety and depressive symptoms, reports effect sizes ranging from 0.5 to 1 (Capezzani et al., 2013; Dimitrov, 2019; Portigliatti Pomeri, 2021). Assuming an effect size of 0.8 in our study, a sample of 42 patients is sufficient to detect the expected improvement with a power greater than 80%, a type I error rate (alpha) of 5%, using a one-tailed test. Assuming a dropout rate of approximately 10–20%, we plan to enroll 46 patients. The sample size estimate was calculated using G*Power 3.1 software (Faul et al., 2009).
Study Intervention	The experimental group will receive EMDR psychotherapy according to the additional procedures (EMDR Toolbox) (Knipe, 2018; Spadoni, 2026) over 15 sessions.
Control Intervention	The control group will receive EMDR treatment according to the standard procedures (Shapiro, 2002) over 15 sessions.
Study procedures	At the time patients are referred to the Clinical Psychology Service of the Ticino Cancer League, participation in the study will be offered. Upon signing informed consent, they will be assigned to one of the two treatment arms (standard EMDR treatment vs. EMDR Toolbox treatment). At study enrollment (T0), all patients will complete: • A socio-demographic data form • A questionnaire assessing overall psychological well-being (CORE-OM, Palmieri, 2006) • A questionnaire assessing self-compassion (Self-Compassion Scale, Veneziani, 2017) • The Dissociative Experiences Scale (DES) for evaluating dissociative phenomena (Carlson, 1993) • A visual analog scale to assess perceived sleep quality Patients in the two groups will undergo psychotherapy according to either the additional EMDR procedures (EMDR Toolbox) or standard EMDR procedures for 15 sessions. The treatment schedule will be adapted to the specific needs of patients with oncological conditions, who are often engaged in multiple specialist visits and rehabilitative treatments, with a minimum frequency of two sessions per month. The 15 sessions represent the basic psychotherapy package covered by health insurance in the Swiss Confederation. After seven sessions, at mid-treatment (T1), patients will complete: • CORE-SF • Self-Compassion Scale (SCS)

	• A visual analog scale to assess sleep quality The mid-treatment assessment is intended to monitor the progress of the variables during the course of therapy. Patients will also be asked to report any critical events that have occurred since the start of the study in order to control for potential confounding variables (e.g., bereavements, separations, recurrence diagnoses, treatment complications, or other stressful events). At the end of treatment (T2, after 15 sessions), patients will complete: • CORE-SF • Self-Compassion Scale (SCS) • Dissociative Experiences Scale (DES) • A visual analog scale to assess perceived sleep quality Aware of the complexity of the psychological phenomena under study, it was decided to complement the quantitative data collection with qualitative data gathered through in-depth interviews aimed at exploring the therapeutic process from the patients' direct perspective after 15 treatment sessions (T2).
Study Duration and Schedule	Planned 03/2026 of First-Participant-In Planned 30/11/2027 of Last-Participant-Out
Investigator(s)	Paola Arnaboldi Lega cancro Ticino Piazza Nosetto 3, 6500 Bellinzona T. 091 820 64 20 E. paola.arnaboldi@legacancro-ti.ch
Study Center(s)	Lega cancro Ticino Piazza Nosetto 3 6500 Bellinzona T. 091 820 64 20
Statistical Considerations:	The present research project constitutes the focus of a doctoral thesis and has a primarily exploratory aim. It is a pilot study. Based on these premises, a statistically significant difference between the two groups is expected in CORE-OM scores at the end of the intervention, with a medium to large effect size (d). The statistical hypothesis to be tested using a one-tailed test is as follows: $H_0: \mu_{group1} = \mu_{group2}$ $H_1: \mu_{group1} \neq \mu_{group2}$

	To evaluate the comparative effectiveness of the two treatments, post-treatment (T2) mean scores will be compared between groups using an independent samples t-test (or, in the case of repeated measures, a repeated measures ANOVA). The test will be one-tailed, as a greater improvement is hypothesized a priori in the experimental group compared with the control group. The level of statistical significance is set at $p < 0.05$. Prior to analysis, assumptions of normality (Shapiro-Wilk test) and homogeneity of variances (Levene's test) will be checked. In case of violations, appropriate non-parametric tests will be applied. All analyses will be conducted using SPSS version 10.
Data privacy	All data collected in the study will be handled in accordance with the LPD (2023) and LRUm regulations on personal data protection. Participant information will be anonymized at the time of collection and stored securely. Patients' identities will not be disclosed under any circumstances, nor will it be possible to trace them in published results. Data will be used exclusively for scientific research purposes, with prior informed consent from each participant. There will be no transfer of data from the research site (Ticino Cancer League) to eCampus University. Data will be collected, analyzed, and stored at the same site.
Ethical consideration	This study aims to provide an initial contribution toward generating evidence of efficacy for patients undergoing psychotherapy while affected by a somatic illness. It seeks to extend the safety and benefit principles inherent to the medical discipline to the field of psychology. The anticipated benefits are considered to far outweigh the risks, which are estimated to be negligible.
GCP Statement	This study will be conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP, the HRA as well as other locally relevant legal and regulatory requirements.

11. REFERENCES

1. Common Terminology Criteria for Adverse Events (CTCAE): https://evs.nci.nih.gov/ftp1/CTCAE/

2. Declaration of Helsinki: https://www.wma.net

3. Federal Act on Data Protection (FADP): **https://www.fedlex.admin.ch/eli/cc/2022/491/en**

4. Human Research Act (HRA) https://www.fedlex.admin.ch/eli/cc/2013/617/en

5. International Conference on Harmonization (ICH) E6 Guideline for Good Clinical Practice (GCP): https://www.ich.org

6. International Conference on Harmonization (ICH) E2A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting: https://www.ich.org

7. Medical Device Ordinance (MeDO): https://www.fedlex.admin.ch/eli/cc/2020/552/en

8. Ordinance on Clinical Trials in Human Research (ClinO): https://www.fedlex.admin.ch/eli/cc/2013/643/en

9. Bremner J. Effects of traumatic stress on brain structure and function: Relevance to early responses to trauma. Journal of Trauma & Dissociation. 2005: 6(2), 51–68.

10. M. J. Brown, L. R. Thacker, & S. A. Cohen (2013). Association between adverse childhood experiences and diagnosis of cancer, Plos One, 8(6), e65524.

11. Carlson EB, Putnam FW, Ross CA, Torem M, Coons P, Dill DL, Loewenstein RJ, Braun BG. Validity of the Dissociative Experiences Scale in screening for multiple personality disorder: a multicenter study. Am J Psychiatry. 1993 Jul;150(7):1030-6. doi: 10.1176/ajp.150.7.1030. PMID: 8317572

12. Cocchi M, Girone N, Leonardi M, Achilli F, Benatti B, dell'Osso B. Evaluation of Adherence to Pharmacological Treatment in a Large Sample of Patients with Personality Disorder. Clin Neuropsychiatry. 2025 Aug;22(4):279-286. doi: 10.36131/cnfioritieditore20250402. PMID: 40989040; PMCID: PMC12453032.

13. Estrada, B., Angulo, B.D., Navarro, M.E., Jarero, I., & Sanchez-Armass, O. (2019). PTSD, Immunoglobulins, and Cortisol Changes after the Provision of the EMDR - PRECI to Females Patients with Cancer-Related PTSD Diagnosis. American Journal of Applied Psychology.

14. Arnaboldi P, Massari I, Lombardi E, Cavallo M. Prevalence of Personality Disorders in Cancer Patients: A Systematic Literature Review in the Era of Personalized Cancer Care. Cancers (Basel). 2025 Dec 5;17(24):3901. doi: 10.3390/cancers17243901. PMID: 41463152; PMCID: PMC12730817.

15. Faretta, E., & Borsato, T. (2016). EMDR Therapy Protocol for Oncological Patients. Journal of EMDR Practice and Research, 10, 162-175. https://doi.org/10.1891/1933-3196.10.3.162

16. Faretta E., Civiclotti C. (2016). EMDR Therapy in Psycho-Oncology: A Bridge Between Mind and Body. Journal of EMDR Practice and Research Vol 10 Issue 3 , Jan 2016, DOI: 10.1891/1933-3196.10.3.138

17. Fernandez A, Askenazy F, Zeghari R, et al. Somatic and Posttraumatic Stress Symptoms in Children and Adolescents in France. JAMA Netw Open. 2024;7(4):e247193. doi:10.1001/jamanetworkopen.2024.7193

18. Grusnick JM, Garacci E, Eiler C, Williams JS, Egede LE. The Association between Adverse Childhood Experiences and Personality, Emotions and Affect: Does Number and Type of Experiences Matter? J Res Pers. 2020 Apr;85:103908. doi: 10.1016/j.jrp.2019.103908. Epub 2019 Dec 10. PMID: 32863469; PMCID: PMC7453784.

19. Hensley B (2015) An EMDR Therapy Primer, 2nd Edition. From Practicum to Practice

20. Hinnen, C., von Haeseler, E., Tijssens, F., & Mols, F. (2024). Adverse childhood events and mental health problems in cancer survivors: A systematic review. Supportive Care in Cancer, 32, Article 80. https://doi.org/10.1007/s00520-023-08280-7

21. Hughes K, Bellis MA, Hardcastle KA, Sethi D, Butchart A, Mikton C, Jones L, Dunne MP. The effect of multiple adverse childhood experiences on health: a systematic review and

meta-analysis. Lancet Public Health. 2017 Aug;2(8):e356-e366. doi: 10.1016/S2468-2667(17)30118-4. Epub 2017 Jul 31. PMID: 29253477

22. Inwood, E. and Ferrari, M. (2018), Mechanisms of Change in the Relationship between Self-Compassion, Emotion Regulation, and Mental Health: A Systematic Review. Appl Psychol Health Well-Being, 10: 215-235. https://doi.org/10.1111/aphw.12127

23. Knipe, J. (2018). EMDR Toolbox: Theory and Treatment of Complex PTSD and Dissociation (2nd ed.). Springer Publishing Company. DOI: 10.1891/9780826172563

24. FLASHCARDS (Manuela Spadoni, Jim Knipe, 2023) Edizione: Strumento di autoformazione per il terapeuta EMDR. Corso pratico in scatola. (ISBN-13 : 979-1221019483)

25. Küchler T, Bestmann B, Rappat S, Henne-Bruns D, Wood-Dauphinee S. Impact of psychotherapeutic support for patients with gastrointestinal cancer undergoing surgery: 10-year survival results of a randomized trial. J Clin Oncol. 2007 Jul 1;25(19):2702-8. doi: 10.1200/JCO.2006.08.2883. Erratum in: J Clin Oncol. 2007 Sep 20;25(27):4328. PMID: 17602075.

26. Lutgendorf SK, Weinrib AZ, Penedo F, Russell D, DeGeest K, Costanzo ES, Henderson PJ, Sephton SE, Rohleder N, Lucci JA 3rd, Cole S, Sood AK, Lubaroff DM. Interleukin-6, cortisol, and depressive symptoms in ovarian cancer patients. J Clin Oncol. 2008 Oct 10;26(29):4820-7. doi: 10.1200/JCO.2007.14.1978. Epub 2008 Sep 8. PMID: 18779606; PMCID: PMC2653140.

27. McNair, D.M., Lorr, M. and Droppleman, L.F. (1971) Profile of Mood States. Educational and Industrial Testing Service.

28. Organizzazione Mondiale della Sanità (2024). Psychological interventions implementation manual. ISBN: 9789240087149

29. Prunas A, Sarno I, Preti E, Madeddu F, Perugini M. Psychometric properties of the Italian version of the SCL-90-R: a study on a large community sample. Eur Psychiatry. 2012 Nov;27(8):591-7. doi: 10.1016/j.eurpsy.2010.12.006. Epub 2011 Feb 21. PMID: 21334861

30. Ramallo-Machín A, Gómez-Salas FJ, Burgos-Julián F, Santed-Germán MA and Gonzalez-Vazquez AI (2024) Factors influencing quality of processing in EMDR therapy. Front. Psychol. 15:1432886. doi: 10.3389/fpsyg.2024.1432886

31. Renzi, C., Perinel, G., Arnaboldi, P. et al. Memories of paternal relations are associated with coping and defense mechanisms in breast cancer patients: an observational study. BMC Psychol 5, 37 (2017). https://doi.org/10.1186/s40359-017-0206-z

32. Riedl D, Lampe A, Exenberger S, Nolte T, Trawöger I, Beck T. Prevalence of adverse childhood experiences (ACEs) and associated physical and mental health problems amongst hospital patients: Results from a cross-sectional study. Gen Hosp Psychiatry. 2020 May-Jun;64:80-86. doi: 10.1016/j.genhosppsych.2020.03.005. Epub 2020 Mar 19. PMID: 32304934.

33. Shapiro F. EMDR. Il manuale. Principi fondamentali, protocolli e procedure. Nuova ediz. 18 aprile 2019.

34. Spadoni M. (2023) Flashcards: una guida all'utilizzo di alcuni strumenti per il lavoro EMDR con i pazienti complessi.

35. Zessin U, Dickhäuser O, Garbade S. The Relationship Between Self-Compassion and Well-Being: A Meta-Analysis. Appl Psychol Health Well Being. 2015 Nov;7(3):340-64. doi: 10.1111/aphw.12051. Epub 2015 Aug 26. PMID: 26311196

36. Portigliatti Pomeri A, La Salvia A, Carletto S, Oliva F, Ostacoli L. EMDR in Cancer Patients: A Systematic Review. Front Psychol. 2021 Jan 18;11:590204. doi: 10.3389/fpsyg.2020.590204. PMID: 33536968; PMCID: PMC7847844.

37. Dimitrov, L., Moschopoulou, E., and Korszun, A. (2019). Interventions for the treatment of cancer-related traumatic stress symptoms: a systematic review of the literature. *Psychooncology* 28, 970–979. doi: 10.1002/pon.5055

38. Capezzani, L., Ostacoli, L., Cavallo, M., Carletto, S., Fernandez, I., Solomon, R., et al. (2013). EMDR and CBT for cancer patients: comparative study of effects on PTSD, anxiety, and depression. *J. EMDR Pract. Res.* 7, 134–143. doi: 10.1891/1933-3196.7.3.134

39. Spadoni M, Arnaboldi P, Knipe J. The EMDR Toolbox Method (ETM): Expanding Jim Knipe's work and Enhancing the AIP Model. J EMDR Pract and Res. 0:DOI:10.34133/jemdr.0027

40. Arnaboldi P, Massari I, Lombardi E, Cavallo M. Prevalence of Personality Disorders in Cancer Patients: A Systematic Literature Review in the Era of Personalized Cancer Care. Cancers (Basel). 2025 Dec 5;17(24):3901. doi: 10.3390/cancers17243901. PMID: 41463152; PMCID: PMC12730817.