MEANING-CENTERED GROUP PSYCHOTHERAPY FOR CANCER SURVIVORS

DEVELOPMENT, EFFICACY AND COST-UTILITY

NADIA VAN DER SPEK

Meaning-centered group psychotherapy for cancer survivors: development, efficacy and cost-utility

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In loving memory of my dear friend Tom Schmidt (1986-2007)

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“He who has a why to live for, can bear almost any how”

~Friedrich Nietzsche~

“We are self-determined by the meanings that we give to our experiences. Meanings are not determined by situations, but we determine ourselves by the meanings that we give to situations”

~Aaron T. Beck~

Chapter 1

General introduction

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INTRODUCTION

Although cancer is still a leading cause of death worldwide, increasing numbers of people can be treated successfully [1–3]. Nowadays, more than half of the cancer patients in developed countries recover from cancer and become long-term survivors [3]. Cancer survivors are at increased risk for psychological distress [4] and often struggle with unmet psychosocial needs [5].

For many patients, a cancer diagnosis composes an intense confrontation with their own mortality [6]. One realizes that life is in fact ending, and that one might not live long enough to participate in important, meaningful life events in the future, such as the graduation or marriage of one's child, or the birth of grandchildren. Some cancer survivors derive meaning from the cancer experience, feel more resilient, experience life more fully in the present, or reprioritize their lives. However, cancer survivors can also struggle with existential issues like fear of death, isolation, rejection, meaninglessness, life questions, or threats to self-identity [7–11].

According to Lee [6], existential distress is the experience of life with little or no meaning. Meaning is considered to be a crucial element in the adjustment to life after cancer. Absence of meaning is associated with more distress, despair, demoralization and difficulties with adjustment to cancer, while experiencing meaning in life correlates positively with psychological well-being and quality of life [12–15]. Meaning-centered group psychotherapy was developed to help advanced cancer patients in the palliative phase of the disease to enhance or sustain a sense of meaning in their lives, in order to cope with the consequences of cancer [16, 17].

This introduction provides background information on the role of meaning in cancer patients, and, more specifically in cancer survivors. Firstly, general theories and perspectives on meaning are briefly introduced, followed by theories and empirical studies on meaning in cancer patients. Subsequently, an overview of meaning-focused psychotherapies for cancer patients is presented, followed by a description of meaning-centered group psychotherapy. Finally, the aim and outline of this thesis are described.

Theories and perspectives on the concept of meaning

Meaning has been equated with purpose in life, life satisfaction, and positively valued life goals [18]. Definitions of meaning vary throughout the psychological and philosophical field, ranging from goal directedness or purposefulness [19] , to coherence in one's life [20, 21], to the personal significance of a particular life circumstance [18]. Reker and Wong [21] integrated these diverse definitions and conceptualizations, by defining meaning as: "the cognizance of order, coherence, and purpose in one's existence, the pursuit and attainment of worthwhile goals, and an accompanying sense of fulfillment". Tengan [22] defines meaning as "a goal, a reason, a 'certain why', an ideal, orientation toward a goal to spend your energy and time on".

Regardless of differences in definitions, meaning is considered a crucial aspect in human life, and psychological well-being. According to Frankl [23, 24] life has meaning under all circumstances, even the most miserable ones. He has suggested that the "will to meaning" is the primary and basic motivation of human beings, and that failure to achieve meaning results in psychological distress. Yalom [25] describes meaning as something that does not pre-exists, but is created by individuals. Steger [26] suggests that meaning must be created through the pursuit of important goals or the development of a coherent life narrative. According to others, meaning is created through self-transcendence [27]. Baumeister [28] proposes that one can experience meaning, by first meeting needs for value, purpose, efficacy, and self-worth. Frankl states in his book "Man's search for meaning" [24] that "The meaning of life differs from man to man, from day to day, and from hour to hour. What matters, therefore, is not the meaning of life in general but rather the specific meaning of a person's life at a given moment" (p. 110).

In the past decades, there has been growing attention for the role of sense of meaning in psychological well-being and the importance of meaning in coping with adversities in life, like cancer [6, 12, 16, 29–32]. The next paragraph describes the role of meaning related to psychological well-being and coping with cancer in cancer patients and, more specifically, in cancer survivors.

The role of meaning in cancer patients

Receiving a cancer diagnosis, can threaten the basic human assumption that life is meaningful [33, 34]. The diagnosis turns a patients world upside down, and often evokes existential questions, like "Why me?" "What is the purpose of my life?" "Who am I?" "What is fundamentally important to me?"

Many cancer patients seem to experience the diagnosis of cancer as a challenge to experiencing life as meaningful, for instance due to shifted priorities in life, or physical hindrances in achieving goals. For some people, the diagnosis of cancer can lead to the experience of life with little or no meaning. Lee [6] refers to the so called "existential plight of cancer" as the "search for meaning" following the cancer experience.

Park and Folkman [34] proposed an integrated framework, "the Meaning Making Model", which was recently further adjusted by Park [35] (*see Figure 1*), to explain how people find meaning in response to stressful events. This framework differentiates between *global meaning* and *situational meaning*. *Global meaning* encompasses a person's enduring beliefs and valued goals. According to Park and Folkman, *global meaning* refers to the most abstract and generalized level of meaning: people's basic goals and fundamental assumptions, beliefs, and expectations about the world. *Global meaning* influences people's understanding of the past and the present, and influences their expectations regarding the future. *Situational meaning* is defined as the meaning that is formed in the interaction between a person's *global meaning* and the circumstances of a particular person-environment transaction. *Situational meaning* encompasses an initial appraisal of the meaning of this particular event and the search for meaning, which may in turn affect *global meaning*. In terms of *situational meaning*, meaning refers to the significance of a particular occurrence in terms of its relevance.

The Meaning Making Model [35] proposes that people's perception of discrepancies between their appraised meaning of a particular situation and their *global meaning* (i.e., what they believe and desire) creates distress, which in turn gives rise to efforts to reduce the discrepancy and resultant distress, resulting in what is called a meaning-making process or search for meaning. This process appears to be only beneficial when meaning is found.

Several studies among cancer patients show that finding meaning is associated with psychological well-being, greater adjustment, and less distress, while a continued search for meaning (without finding meaning) is negatively related to well-being, leads to higher levels of distress and is maladaptive [32, 36–38].

Meaning in cancer survivorship

Meaning-making may be at the core of adequate adjustment to cancer: cancer patients who experience their life as meaningful are better adjusted, have better quality of life and psychological functioning [4, 7]. Up until now, the literature on meaning in cancer patients focuses for a large part on patients with advanced cancer in the palliative phase of the disease, who face meaning-related existential issues like demoralization and desire for hastened death [31, 39, 40]. However, sense of meaning is also an important issue in survivorship [36, 41].

Cancer survivors encounter fundamental uncertainties that they have to deal with, like possible recurrence and negative effects of treatment. Also, the diagnosis is often accompanied by losses in different domains in life (e.g. physical, work, relationships), which can challenge the experience of meaning in life [6]. Among cancer survivors, meaning is strongly related to successful adjustment and better quality of life up until years after cancer diagnosis [13, 36, 42–44]. In total, 24% of cancer survivors express a need for help regarding existential issues and meaning [45]. Psychological interventions that focus on enhancing meaning, can be beneficial for cancer survivors to increase adequate adjustment to life after cancer and prevent and decrease psychological distress [12, 17, 46].

Meaning-focused psychotherapies for cancer patients

Meaning is an existential concern, like death, responsibility and isolation [25], and meaning-focused therapies are therefore seen as existential psychotherapies. Research on existential interventions is still in a rather early stage, and much is unknown about meaning-making and the possibilities of facilitating this process. A meta-analysis on existential interventions shows that overall, there is particular support for interventions which are structured, focus directly on meaning, and incorporate psycho-education and exercises [47]. Several interventions for cancer patients, focusing at least partly on experiencing meaning in life, have been developed and evaluated. The outcomes of most of these studies are promising with improved self-esteem, optimism, mood, sense of meaning, spiritual well-being and decreased suffering after intervention [17, 46, 48–52]. However, many of these studies are hampered by methodological limitations, like high dropout rates, no control for the effects of attention, insufficient information on the treatment protocol, and short periods of follow up [46].

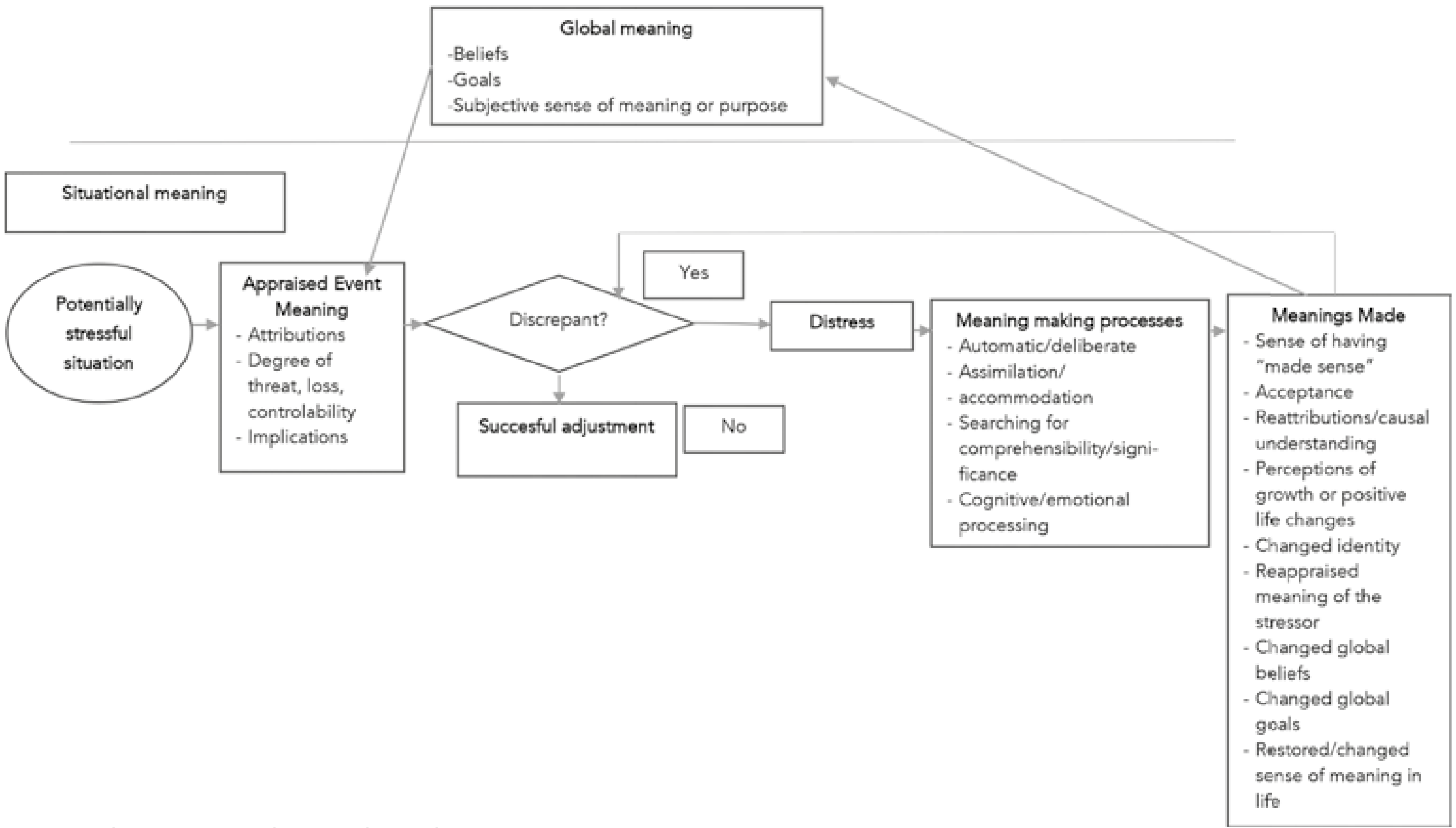

Figure 1 The Meaning Making Model (Park, 2010)

A few recent studies have described short-term interventions with meaning components for cancer patients. Chochinov *et al.* [52, 53] developed 'Dignity therapy', an individualized existential intervention that focuses on enhancing dignity for the purpose of relieving distress and enhancing end-of-life experiences of terminally ill patients. They randomly assigned 165 patients to dignity therapy, 140 to standard palliative care, and 136 to client-centered care. No significant differences were found on the primary outcome measure, level of distress, post-intervention. It remains unclear whether this finding is caused by floor effects, because of paucity of distress in the study population. However, they did find positive results on the secondary outcome measures, with improved quality of life, and sense of dignity. Kissane and colleagues [54] designed 'Cognitive-Existential Group Psychotherapy' for women with early stage breast cancer, focusing on cognitive reframing, problem solving, fostering hope and examining priorities for the future. A total of 303 women were randomly assigned to this 20-session intervention plus 3 'relaxation classes' or the 3 relaxation classes alone (control group); assessments were at 6 and 12 months after baseline. No significant differences in improved psychological distress were found between the intervention and control group.

Lee *et al.* [12] developed the 'Meaning-Making intervention (MMi)' which addresses existential issues through the use of meaning-making coping strategies on psychological adjustment to cancer. Eighty-two breast cancer and colon cancer patients were randomly assigned to the 4-session MMi arm or a care as usual arm. Following treatment, they found significant differences in optimism, self-esteem and self-efficacy. However, the investigators did not study sense of meaning, hopelessness, depression and anxiety as outcomes, and also did not investigate long-term effects. A pilot randomized controlled trial on MMi for patients with stage III and IV ovarian cancer showed promising results with enhanced sense of meaning at 1 and 3 months after intervention, however the sample size of this pilot study was very small (N=24).

'Meaning-centered group psychotherapy'(MCGP) was developed by Breitbart *et al.* for patients with advanced cancer. A recent randomized controlled trial provided support for the effectiveness of MCGP [55]. The next paragraph provides an overview of the theoretical background, content and research until now on MCGP.

Meaning-centered group psychotherapy

This thesis concerns the adaptation and evaluation of meaning-centered group psychotherapy (MCGP) targeting cancer survivors (MCGP-CS). MCGP was initially developed for patients with advanced cancer, by Breitbart and colleagues [17]. MCGP is a group intervention based on meaning-centered psychotherapy (MCP), and is grounded in Frankl's work. Frankl developed a meaning-focused approach in psychotherapy, called *logotherapy*[11], that concentrates on assisting people to find their individual meaning or purpose in life [23, 24].

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[1] The Greek word λόγος (logos) means reason or meaning

The main purpose of MCP is to help patients with advanced cancer to sustain or enhance a sense of meaning, peace and purpose in their lives, despite the confrontation with near death [18], in order to cope better with the consequences of cancer.

MCGP is a manualized 8-week intervention that makes use of didactics, group discussion and experiential exercises that focus around themes related to meaning [16, 56]. The 90 minute sessions are held weekly and participants complete homework assignments every week. Each session addresses a specific theme that is related to the concepts and sources of meaning, the impact of cancer on one's sense of meaning and identity, and placing one's life in a historical and personal context. *Table 1* gives an overview of the themes of each session.

There are four sources of meaning distinguished, based on the work of Frankl. The *historical source* concerns "our lasting legacy"; examples include personal story, family history, the history of one's name, one's accomplishments and whatever one wants to leave behind. The *creative source* concerns work, deeds, artistic endeavours, hobbies; examples include ones career/job, volunteer work, involvement in church or political issues, writing and painting. The *attitudinal source* turning personal tragedy into triumph, things one achieved despite adversities, rising above difficult circumstances; examples include overcoming grief/loss, persevering trough cancer, achieving an education despite personal challenges.

The *experiential source* concerns connecting with life through relationships, nature, art and humour; examples include one's family, loved ones, enjoying the sunset, gardening, museum visits, going out.

Table 1 Session topics covered in Meaning-centered group psychotherapy (MCGP)

Session	MCGP
1	Concept and sources of meaning
2	Meaning before and after cancer
3	The story of our life as a source of meaning: what made us who we are today
4	The story of our life as a source of meaning: things we have done and want to do in the future
5	Attitudinal sources of meaning: encountering life's limitations
6	Creative sources of meaning: responsibility, courage and creativity
7	Experiental sources of meaning
8	Termination: presentations of our life lessons and goodbyes

MCGP was first evaluated in a pilot randomized controlled trial, which showed that MCGP is potentially beneficial for advanced cancer patients for decreasing emotional and spiritual suffering [11]. Subsequently, a large randomized controlled trial with 253 participants was conducted, comparing MCGP with supportive group psychotherapy, post-treatment and two months after intervention [55]. This study showed strong support for the effectiveness of MCGP for patients with advanced cancer. Patients receiving MCGP showed significantly greater improvement in spiritual well-being and quality of life, and significantly greater reductions in depression, hopelessness, desire for hastened death and physical symptom distress, compared with patients who received SGP.

These results show that MCGP is effective for advanced cancer patients, who are approaching the end of life. As demonstrated in the paragraph above, cancer survivors face different challenges in life, but can also struggle with meaning-making issues until years after diagnosis. Therefore it is important to investigate whether this successful intervention might be beneficial for cancer survivors as well. In this population it is also relevant to look at long-term effects. Subsequently, from a health care policy point of view, it would be useful to know more about the cost-utility of this intervention. Up until now, there are no randomized controlled trials on the efficacy and cost-utility of meaning-focused psychological interventions specifically targeting cancer survivors.

AIM OF THIS THESIS

The aim of this thesis was to obtain insight into meaning-making processes in cancer survivors, to adapt meaning-centered group psychotherapy for a cancer survivor population, and to evaluate the efficacy and cost-utility of the adapted intervention, called "meaning-centered group psychotherapy for cancer survivors" (MCGP-CS).

OUTLINE OF THIS THESIS

Chapter 2 describes a focus group study that was carried out to gain more insight in the meaning-making process, and the perceived need for help with meaning-making in a Dutch cancer survivor population. The results of this study were used to adapt the meaning-centered group psychotherapy to a Dutch cancer survivor population, the adapted manual is called meaning-centered group psychotherapy for cancer survivors (MCGP-CS). *Chapter 3* reports the results from a feasibility study on MCGP-CS, that was conducted in preparation of the randomized controlled trial. *Chapter 4* presents a study protocol which describes how the randomized controlled trial to assess the efficacy and cost-utility of MCGP-CS will be conducted. *Chapter 5* reports the results of the randomized controlled trial, comparing MCGP-CS, with supportive group psychotherapy (SGP) and a care as usual (CAU) condition for cancer survivors. In *Chapter 6*, the cost-utility of MCGP-CS, compared to SGP and CAU, is examined. Finally, *Chapter 7* reports on the main findings of this thesis and provides a discussion of these findings, their clinical implications, and directions for future research.

REFERENCES

1. Brenner H. *Long-term survival rates of cancer patients achieved by the end of 20th century: a period analysis.* Lancet 2002:1131–1135.
2. Richards MA, D S, P B, MP C. *How many deaths have been avoided through improvements in cancer survival?* Br Med J 2000:895–898.
3. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA Cancer J Clin* 2013, **63**:11–30.
4. Hoffman KE, McCarthy EP, Recklitis CJ, Ng A.: Psychological Distress in Long-term Survivors of Adult-Onset Cancer Results From a National Survey. *Arch Intern Med* 2009, **14**:1274–1281.
5. Thewes B, Butow P, Girgis A, Pendlebury S. The psychosocial needs of breast cancer survivors; A qualitative study of the shared and unique needs of younger versus older survivors. *Psychooncology* 2004, **13**:177–189.
6. Lee V. The existential plight of cancer: meaning making as a concrete approach to the intangible search for meaning. *Support Care Cancer* 2008**, 16**:779–785.
7. Henoch I, Danielson E. Existential concerns among patients with cancer and interventions to meet them: an integrative literature review. *Psychooncology* 2009**, 18**:225–236.
8. Tedeschi RG, Calhoun LG. Posttraumatic growth: Conceptual foundations and empirical evidence. *Psychol Inq* 2004, **15**:1–18.
9. Thornton AA. Perceiving benefits in the cancer experience. *J Clin Psychol Med Settings* 2002, **9**:153–165.
10. Helgeson VS, Snyder P, Seltman H. Psychological and physical adjustment to breast cancer over 4 years: Identifying distinct trajectories of change. *Health Psychol* 2004, **23**:3–15.
11. Tomich PL, Helgeson VS, Vache EJN. Perceived growth and decline following breast cancer: a comparison to age-mathced controls. 5-years later. *Psychooncology* 2005, **14**: 1018-1029
12. Lee V, Cohen SR, Edgar L, Laizner AM, Gagnon AJ. Meaning-making intervention during breast or colorectal cancer treatment improves self-esteem, optimism, and self-efficacy. *Soc Sci Med* 2006, **62**:3133–3145.
13. Lee V, Cohen SR, Edgar L, Laizner AM, Gagnon AJ. Clarifying “meaning” in the context of cancer research: a systematic literature review. *Palliat Support Care* 2004, **2**:291–303.
14. Giese-Davis J, Koopman C, Butler LD, Classen C, Cordova M, Fobair D, et. al. Change in emotion-regulation strategy for women with metastatic breast cancer following supportive-expressive group therapy. *J Consult Clin Psychol* 2002, **70:**916–925.
15. Davis CG, Wortman CB, Lehman DR, Cohen Silver R. Searching for meaning in loss: are clinical assumptions correct? *Death studies* 2000, **24**: 497-540.
16. Breitbart W. Spirituality and meaning in supportive care: spirituality- and meaning-centered group psychotherapy interventions in advanced cancer. *Support Care Cancer* 2002, **10**:272–280.
17. Breitbart W, Rosenfeld B, Gibson C, Pessin H, Poppito S, Nelson C, Tomarken A, Timm AK, Berg A, Jacobson C, Sorger B, Abbey J, Olden M. Meaning-centered group psychotherapy for patients with advanced cancer: a pilot randomized controlled trial. *Psychooncology* 2010, **19**:21–28.

18. Jim HS, Purnell JQ, Richardson SA, Golden-Kreutz D, Andersen BL. Measuring meaning in life following cancer. *Qual Life Res* 2006, **15**:1355–1371.
19. Kafka GJ, Kozma A. The construct validity of Ryff's Scales of Psychological Well-Being (SPWB) and their relationship to measures of subjective well-being. *Soc Indic Res* 2002, **57**:171–190.
20. Battista J, Almond R. The development of meaning in life. *Psychiatry* 1973, **36**:409–427.
21. Reker GT, Wong PTP. *Aging as an individual process: Toward a theory of personal meaning. In Emergent theories of aging*; 1988:214–246.
22. Tengan A. *Search for Meaning as the Basic Human Motivation A Critical Examination of Viktor Emil Frankl's Logotherapeutic Concept of Man*. Frankfurt/M., Berlin, Bern, New York, Paris, Wien: Peter Lang; 1999.
23. Frankl V. *The Doctor and the Soul. From Psychotherapy to Logotherapy.* London; 1986.
24. Frankl V. *Man's Search for Meaning: An Introduction to Logotherapy.* British paperback edition: random House, London; 1998.
25. Yalom ID. *Existential Psychotherapy. Volume 1 edition.* Basic Books; 1980.
26. Steger MF, Mann JR, Michels P, Cooper TC. Meaning in life, anxiety, depression, and general health among smoking cessation patients. *J Psychosom Res* 2009**, 67**:353–8.
27. Seligman MEP. *Authentic Happiness.* New York: Free press; 2002.
28. Baumeister RF. *Meanings of Life.* New York: Guilford Publications: New York.; 1991.
29. Janoff-Bulman R. *Shattered Assumptions: Towards a New Psychology of Trauma*. The Free PressL New York.; 1992.
30. Breitbart W. Spirituality and meaning in cancer. *Rev Fr Psycho-Oncologie* 2005, **4**:237–240.
31. Nelson CJ, Rosenfeld B, Breitbart W, Galietta M. Spirituality, religion, and depression in the terminally ill. *Psychosomatics* 2002, **43**:213–220.
32. Park CL, Edomondson D, Fenster JR, Blank TO. Meaning Making and Psychological Adjustment Following Cancer: The Mediating Roles of Growth, Life Meaning, and Restored Just-World Beliefs. *J Consult Clin Psychol* 2008:863–875.
33. Janoff-Bulman R. Assumptive Worlds and the Stress of Traumatic Events - Applications of the Schema Construct. *Soc Cogn* 1989, **7**:113–136.
34. Park CL, Folkman S. Meaning in the context of stress and coping. *Rev Gen Psychol* 1997, **1**:115–144.
35. Park CL. Making sense of the meaning literature: an integrative review of meaning making and its effects on adjustment to stressful life events. *Psychol Bull* 2010, **136**:257–301.
36. Tomich PL, Helgeson VS. Five years later: A cross-sectional comparison of breast cancer survivors with healthy women. *Psychooncology* 2002, **11**:154–169.
37. Thompson SC, Pitts J. *Factors relating to a person's ability to find meaning after a diagnosis of cancer.* J Psychosoc Oncol 1994, 11.
38. Jaarsma TA, Pool G, Ranchor A V, Sanderman R. The concept and measurement of meaning in life in Dutch cancer patients. *Psychooncology* 2007, **16**:241–248.
39. McClain CS, Rosenfeld B, Breitbart W. Effect of spiritual well-being on end-of-life despair in terminally-ill cancer patients. *Lancet* 2003, **361**:1603–1607.

40. Lethborg C, Aranda S, Cox S, Kissane D. To what extent does meaning mediate adaptation to cancer? The relationship between physical suffering, meaning in life, and connection to others in adjustment to cancer. *Palliat Support Care* 2007, **5**:377–388.

41. van der Spek N, Vos J, van Uden-Kraan CF, Breitbart W, Tollenaar R a. EM, Cuijpers P, Verdonck-de Leeuw IM. Meaning Making in Cancer Survivors: A Focus Group Study. *PLoS One* 2013, **8**:e76089.

42. Bower JE, Meyerowitz BE, Desmond K a, Bernaards C a, Rowland JH, Ganz P a. Perceptions of positive meaning and vulnerability following breast cancer: predictors and outcomes among long-term breast cancer survivors. *Ann Behav Med* 2005, **29**:236–45.

43. Zika S, Chamberlain K. On the relation between meaning in life and psychological well-being. *Br J Psychol* 1992, **83**:133–145.

44. Debats DL. Sources of meaning an investigation of significant commitments in life. *J Humanist Psychol* 1999, **39**:30–57.

45. Jansen F, Van Uden-Kraan CF, Van Zwieten V, Witte BI, Leemans CR, Verdonck-de Leeuw IM. *Cancer survivors' perceived need for supportive care and their attitude towards self-management and e health.* Support Care Cancer 2014, 1):S203.

46. LeMay K, Wilson KG. Treatment of existential distress in life threatening illness: A review of manualized interventions. *Clin Psychol Rev* 2008, **28**:472–493.

47. Vos J, Craig M, Cooper M. *Journal of Consulting and Clinical Psychology Existential Therapies : A Meta-Analysis of Their Effects on Psychological Outcomes Existential Therapies : A Meta-Analysis of Their Effects on*. 2014.

48. Lee CH. Effects of Logotherapy with Exercise on meaning of life, ego integrity and IADL in the elderly (summary only). *Taehan Kanho Hakhoe Chi* 2006, **36**:701–709.

49. Coward DD. Facilitation of self-transcendence in a breast cancer support group: *II. Onc Nurs Forum* 2003, **30**:291–300.

50. Kissane DW, Bloch S, Smith GC, Miach P, Clarke DM, Ikin J, Love A, Ranieri N, McKenzie D. Cognitive-Existential Group Psychotherapy for Women with Primary Breast Cancer: A Randomised Controlled Trial. *Psychooncology* 2003, **12**:532–546.

51. Spiegel D, Spira J. *Supportive-Expressive Group Therapy: A treatment manual of psychosocial intervention for women with recurrent breast cancer.* Stanford, CA Stanford Univ Sch Med 1991.

52. Chochinov HM, Kristjanson LJ, Breitbart W, McClement S, Hack TF, Hassard T, Harlos M. Effect of dignity therapy on distress and end-of-life experience in terminally ill patients: a randomised controlled trial. *Lancet Oncol* 2011, **12**:753–62.

53. Chochinov HM, Hack TF, Hassard T, Kristjanson LJ, McClement S, Harlos M. *Dignity Therapy: A Novel Psychotherapeutic Intervention for Patients Near the End of Life.* J Clin Oncol 2005, 23.

54. Kissane DW, Love A, Hatton A, Bloch S, Smith G, Clarke DM, Miach P, Ikin J, Ranieri N, Snyder RD. Effect of cognitive-existential group therapy on survival in early-stage breast cancer. *J Clin Oncol* 2004, **22**:4255–4260.

55. Breitbart W, Rosenfeld B, Pessin H, Applebaum A, Kulikowski J, Lichtenthal WG. Meaning-Centered Group Psychotherapy: An Effective Intervention for Improving Psychological Well-Being in Patients With Advanced Cancer. *J Clin Oncol* 2015, **33**:749–754.

56. Breitbart WS, Poppito S. *Meaning-Centered Group Psychotherapy for Patients with Advanced Cancer.* New York: Oxford University Press; 2014.

Chapter 2

Meaning-making in cancer survivors: a focus group study

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ABSTRACT

Background. Confrontation with a life-threatening disease like cancer can evoke existential distress, which can trigger a search for meaning in people after having survived this disease.

Methods. In an effort to gain more insight in the meaning making process, we conducted four focus groups with 23 cancer survivors on this topic. Participants responded to questions about experienced meaning making, perceived changes in meaning making after cancer and the perceived need for help in this area.

Results. Most frequently mentioned meaning making themes were *relationships* and *experiences*. We found that, in general, cancer survivors experienced enhanced meaning after cancer through *relationships, experiences, resilience, goal-orientation* and *leaving a legacy*. Some participants, however, also said to have (also) experienced a loss of meaning in their lives through *experiences, social roles, relationships* and *uncertainties about the future*.

Conclusions. The results indicated that there is a group of cancer survivors that has succeeded in meaning making efforts, and experienced sometimes even more meaning in life than before diagnosis, while there is also a considerable group of survivors that struggled with meaning making and has an unmet need for help with that. The results of this study contribute to develop a meaning centered intervention for cancer survivors.

Key issues: meaning making, cancer survivors, focus groups

INTRODUCTION

Although cancer is still a leading cause of death worldwide, increasing numbers of people are being treated successfully [1-2]. About half of the cancer patients in developed countries recover from cancer and become long-term survivors [3-4]. Cancer survivors are at increased risk for serious psychological distress [5-6] and often struggle with unmet psychosocial needs [7]. Given that there will be more and more cancer survivors, a different approach in psycho-oncology will be needed to serve a novel target group: people who survive cancer and then deal with the sequelae that threaten their psychological well-being.

While some cancer survivors find it hard to cope with the psychosocial consequences of cancer and deal with existential issues like fear of death, isolation, rejection, meaninglessness, life questions and threats to self-identity, others experience hardly any problems in dealing with the aftermath of their disease. Some even report improved psychological well-being after cancer: they derive meaning from the cancer experience, feel more resilient, experience life more fully in the present or reprioritize their lives [8-13].

Confrontation with a life-threatening disease as cancer can evoke existential distress, which according to Lee [14], is the experience of life with little or no meaning. Lee [14] refers to the so called "existential plight of cancer" as the "search for meaning" following the cancer experience. Meaning in life is an important existential issue that is strongly related to psychological well-being and is liable to alteration after a negative experience like cancer [15-17]. The literature shows that some people clearly experience more meaning in life after they are confronted with cancer, whereas others adversely experience an absence or loss of meaning. Absence of meaning can lead to despair or demoralization and can trigger a search for meaning [18-21]. Several studies suggest that this search for meaning, or meaning making process, is only beneficial when meaning is found. Finding meaning is associated with psychological well-being, greater social adjustment, and less distress, while a continued search for meaning (without finding meaning) is negatively related to well-being, leads to higher levels of distress and is maladaptive [15, 22-26].

This is in line with the view of many existential psychotherapists, who consider meaning in life as a key concern in human existence, and assume that existential distress stems from failure in the search for meaning [27]. Frankl [28-30] states that the desire to find meaning is the primary and basic motivation of human beings. He developed *logotherapy*, an approach in psychotherapy that focuses on helping people to discover meaning or purpose in their lives and to overcome feelings of emptiness and despair.

Several studies have evaluated psychological interventions focusing on meaning making in cancer patients, mostly in the palliative phase. The majority of these studies show promising results with improved self esteem, optimism, mood, sense of meaning, spiritual well-being and decreased suffering after intervention [20, 31-36]. However, other studies did not report these improvements [37-38]. Research on this type of intervention is still in an early stage and much is unknown about meaning making and the possibilities of facilitating this process, especially in cancer *survivors*. A better understanding of meaning making after cancer can contribute to supporting cancer survivors more adequately in this process.

To obtain more insight in meaning making in cancer survivors, we conducted a focus group study. The study was designed to describe (1) the meaning making themes that play a role in cancer survivors, (2) the experienced changes in meaning making after cancer treatment and (3) the perceived needs for help in this particular area.

METHODS

Study design and sample

A focus group method was chosen, because of its group dynamics which can provide rich data, especially when there is little prior knowledge [39]. Focus group participants were recruited in three different ways: (1) Research nurses recruited eligible patients at the outpatient clinic of an academic hospital; (2) psychologists in a mental health care institution that specializes in cancer patients approached eligible patients and (3) online advertisements were placed at websites from cancer patient organizations. Eligible patients were 18 years or older, diagnosed with cancer up to 7 years ago, treated with curative intent and were able to speak Dutch.

For this study, 37 persons showed interest to participate. Ten people were not available to attend the focus groups at the scheduled dates, or did not meet inclusion criteria. Each enlisted person was contacted by the researcher (NS) to make sure the participant met the criteria and to explain how and where the group would be conducted. Those who provided written informed consent, were scheduled to participate. Four people did not show up. Eventually, four focus groups were conducted in the summer and fall of the year 2011; three groups of six persons and one group of five participants (N=23). The study has been approved by the Medical Ethical Committee of the Leiden University Medical Center, Leiden, the Netherlands. Characteristics of study participants are shown in *Table 1*.

Procedure

Participants were sent information about the goals of the study and were asked to think beforehand about meaningful aspects in their lives and about whether there were physical or personal changes after cancer. The focus groups took place at VUmc University Medical Center in Amsterdam and LUMC University Medical Center in Leiden, The Netherlands, and each focus group lasted two hours. The groups were led by two moderators, a psychologist and a theologian, both researchers with experience in focus group moderation. The moderators followed a semi-structured moderating guide; topics are shown in *Table 2*. It was determined beforehand that a maximum of four focus groups could be conducted. After these four focus groups, data saturation was reached; meaning that no new information of value was obtained. All focus groups were audio taped and transcribed verbatim.

Table 1 Characteristics of study participants (N=23)

Characteristic	Number	%
Sex		
Male	7	30
Female	16	70
Age		
Mean (SD)	56 (11)	
Range	33-73	
Type of cancer		
Breast	10	43.5
Colorectal	8	34.8
Other (skin-, bone-, nose-, Hodgkin- and oesophagus cancer)	5	21.7
Years since diagnosis[1]		
Mean (SD)	2 (1)	
Range	0.5-5	

[1] *There were no patients diagnosed longer than 5 years ago, who showed interest in participation*

Analysis

Three coders independently analyzed the data following the steps of the "framework approach" [40]. First, they read all the transcripts thoroughly (*familiarization*). Key issues and underlying emerging themes were identified drawing on research questions that were posed a priori as well as issues that were raised by participant responses (*identifying a thematic framework*). The thematic framework was applied to all the data (*indexing*) and the data was rearranged according to the appropriate part of the thematic framework to which they relate (*charting*). The coders met regularly with a fourth researcher to resolve disagreements in coding. All data was analyzed by hand by the coders separately. Inter-rater reliability was substantial (K = .72) [41]. After that, consensus was reached on all disagreements, concepts were defined and data was interpreted (*mapping and interpretation*). We closely followed the Consolidated criteria for reporting qualitative research (COREQ) criteria; to guard the rigor of this qualitative study.

Table 2 Focus group topics and key questions

Topics	Key questions
Meaning making	– What is meaningful in your life at the moment?
Changes in meaning making	– Did meaning in your life change after you were diagnosed with cancer? And if so, how did it change?
	– Have you ever had the feeling that you couldn't find meaning? And how did you deal with that?
	– What helps you to find meaning, despite possible problems in your life?
Need for help with meaning making	– Are there aspects of meaning making that you wish you received help with? And if so, what kind of help would you like to receive?

RESULTS

Table 3 Meaning making themes and key-issues and themes of perceived changes in meaning making and meaning related issues

Sources of meaning	Relationships (e.g. connection to friends and family) Experiences (e.g. enjoying nature, going out to dinner with friends) Creativity (e.g. painting, singing, writing) Work (e.g. being successful, working in a team, contributing to society)	
	KEY ISSUES	**THEMES**
Changes in meaning making	**Enhanced meaning (through…)**	
	Relationships	● Meaning something to others ● New or more intense relationships
	Experiences	- Experiencing life more intense ● Enjoying (little things in) life more ● Feeling more at ease
	Resilience	● Being more flexible towards uncertainties ● Seeing things more in perspective
	Goal orientation	● Better able to prioritize ● More balance in life ● More decisive
	Leaving a legacy	
	Loss of meaning (through)	
	Experiences	● Loss of meaningful activities ● Enjoying things less than before
	Social roles	● Unable to work anymore - Feeling incompetent as a parent or a partner
	Relationships	● Relationship problems with partner - Losing friendship
	Uncertainty about the future	- Hopelessness
	Searching for meaning	- Forced to shift to other sources of meaning - Still trying to find new meaning
	Meaninglessness	- Coping with meaninglessness through earlier experiences
Meaning related issues	● Isolation ● Threats to identity ● Physical limitations ● Confrontation with death ● Fear of passing cancer on to offspring ● Loss of freedom	

In this section we present the participants' experiences with meaning making and closely related themes that emerged from the analysis of the transcripts. *Table 3* presents an overview of meaning making themes, perceived changes in meaning making (enhanced meaning and loss of meaning) and meaning-related issues after cancer mentioned in the focus groups.

Sources of meaning

In the group discussions, it soon became clear that "meaning" is an abstract term that is not often used in daily Dutch language. Participants used other words for this experience, calling meaning *"a thrill"*, *"a sense of fulfillment"*, *"a kick",* or *"the important things in life"*. Participants mentioned several meaning making themes (*Table 3*): meaning through relationships (e.g. feel more connected to family members), experiences (e.g. enjoy nature more), creativity (e.g. painting) and work (e.g. being successful).

Changes in meaning making

Enhanced meaning

The majority of the participants mentioned to experience more meaning in life in certain specific areas. Many participants indicated to experience enhanced meaning through love and **relationships** with family and friends:

"*Meaning, you know….I just want* ***to be*** *there for people. How beautiful it is to be able to be there for someone. That has become my purpose."*

Others described to experience enhanced meaning through **experiences** like enjoying the little things in life, like the sound of a bird or a good meal:

"I enjoy the little things in life more and I live more in the present. I do not look as far ahead anymore, as it is of no use."

Most people noted to feel more **resilient** in dealing with adversities. Some people indicated that they became more **goal-oriented** live life more consciously and that they know better now what they find important in life.

"I used to be a true workaholic, working 60, 70 hours a week. But I don't do that anymore, it's not worth it. Really, there are so many things I want to do. So many things I could spend my precious time on."

Some participants felt the need to **leave a legacy**. A person started writing a book to pass on his knowledge to his younger co-workers, some people started making photo albums, and someone else started a blog, as a sort of diary, for family and friends.

Loss of meaning

Loss of meaning was named less frequently by participants. Some participants mentioned a loss of meaning through **experiences**, because they werenot be able to continue their meaningful activities due to physical impairments, for example not being able to work, not being able to have children or not being able to do specific recreational, enjoyable activities anymore:

"I have an invisible prosthesis in my leg, I can't run anymore and lift heavy things anymore. I cannot make long walks. The treatment left me with neuropathy. That's something you're confronted with for every minute of your life."

"I can't do my job anymore. I am a physiotherapist, but I don't have the strength to do my job anymore."

Some indicated that they do not enjoy some things less than they did before.

Other aspects participants named were not being able to fulfill certain important **social roles** in life (e.g. being a colleague or a good father) and loss of meaningful relationships.

"Of course, something changes, because some people let you down, because they can't or don't want to talk about it [cancer]*".*

Some people experienced feelings of hopelessness because of **uncertainties about the future**. They experienced difficulties with setting goals and planning meaningful activities for the future.

Searching for meaning

In general, participants tried to keep sources of meaning the same as they were before diagnosis, but in some cases they felt forced to search for other sources of meaning:

"I can do less things now, but the intensity has been shifted to other things. For example, things which used to give me satisfaction or purpose, it has been shifted from doings sports to…. To, like, enjoying the moment."

Others said they were still searching for a new meaning:

"I used to get ideas and then I would just start. I can't do that anymore. My artwork in the field, in the moment, that was where I got my thrill. And I don't have that back yet. I can't find it. I think I find it hard to accept that I can't do as much physically."

Meaninglessness

When dealing with feelings of meaninglessness, many drew from experiences with meaning making in the past. Some had learned a lot about searching for meaning from another stressful event earlier in their lives, which made it easier to cope with cancer and derive meaning from it:

"I had a burn out in 2008, which caused me to go into therapy for a year. That was more difficult than my cancer. That feeling returned for a while, but then you know: I can deal with this, but if you've never been in therapy, I can imagine that it hits you harder."

Meaning related issues

Besides meaning making, several other existential issues were noted in the focus groups (*Table 3*). Of these other issues, isolation (loneliness) was most frequently named by the participants. Most mentioned that they had felt abandoned or misunderstood by others and that cancer has separated them in a way from the rest of their environment:

"Yes, because after all the treatments, your hair starts growing and you carefully start working again. And the entire world goes: 'hurray, she's been cured'! And then it has to be finished."

"*People react so bluntly. 'Yes, your breasts, you can just have those removed, right?' Or 'Oo, it didn't get to your lymph nodes? O then it's not too bad.' Everyone has had enough of it. Your entire network has had enough of it, and you think: well I think it only just started now.".*

Some participants indicated that they did not feel a connection with their social environment anymore. They often felt like an outsider among friends or co-workers.

"Then you get back to work and people don't really know how they should deal with you and I found that difficult, they almost ignore you because they don't know what to say. It took me a year before I felt at ease again with others, before I could join in again. I'm still disappointed, but I do understand it."

Some struggled with **threats to their identity**. They felt that the new reality did not correspond to their self-image. This was mostly due to not being able to fulfill an old role (like parenting or working) in the same way anymore, or an experienced change in personal characteristics. One of the participants said:

"I find it shocking… I used to be a person who remembered everything about everyone and now suddenly, not at all anymore. I forget things completely, it's a total blank.".

Some felt that it is *other* people that view them differently:

"It's like you go to a party with people you don't know. But they do know your partner, then you are ' partner of…'. But you're not, you're just who you are. Before you know it, you are not 'boss of the lab' anymore, but 'that man with cancer'".

Others found it hard to deal with their **physical limitations**; especially with the feeling that their body had let them down, and might do that again in the future:

"*At a certain point you hear the diagnosis: you have cancer. Well, what you hear is: I will die. It takes a while before you pass that. And I am.. what I also found bothersome, you think you know your body. And you think your own body is tricking you. And it takes a while before you regain that trust."*

Most participants indicated to be confronted with death at some point after diagnosis:

"Recently I have experienced two funerals of two friends. So sometimes you realize that you're lucky for still being around. We had cancer at the same time and… yes, death is quite confrontational. Then it really gets close to you."

A few people claimed they had barely thought of dying since they were diagnosed. Most people felt more awareness of the fact that life is ending and that you have no control over it.

"I realized that I had always thought, without realizing,' I will be, like, 80 years old' that's different now."

To some people, the thought of death evoked some anxiety, others felt relieved in a way that they had 'gone through' this fear of death:

"*Because yes, I have seen death, so… I don't know how this was for you guys, but I have seen it. I absolutely don't have fear of death anymore."*

Some people indicated that they had a **fear of passing the cancer on to their offspring**.

One person mentioned that she experienced a **loss of freedom**, feeling like the cancer took control over her life and behavior.

"Your self-confidence is completely shattered by something you can't control. Cancer controls me, and I have no control over my life anymore."

Perceived need for help with meaning making issues in cancer survivors
The majority of the participants answered affirmative when asked if they needed help with meaning making. Most wanted help from a professional:

"Someone who is unbiased to speak with"

"Someone who explains to you which emotional process you're going through".

Others perceived a specific need for peer support, some specifically indicated that giving peer support to others is meaningful.

"Fellow sufferers can help each other. You can be a companion for others. I think that that gives meaning."

A few people noted they had only felt a need for professional help, immediately after the diagnosis. They mentioned that it is important that the help is quickly accessible. Others disagreed and said that help was better suited about one and a half year after diagnosis and after treatment:

"*Once the storm is over, you start thinking: what happened to me in the past year? Not during the treatment".*

Most participants agreed that when help with meaning making is offered, it should not be named as such. Many people felt offended by the link between meaning making and cancer, because they interpreted this as cancer being meaningful or that it should be considered as such. Some participants expressed a need for help for their partners, who according to most participants, do not get enough attention during the cancer process.

DISCUSSION

In this study, we investigated the perception of meaning making in cancer survivors. We found that, in general, cancer survivors experienced more meaning after cancer in at least one specific way, most frequently related to relationships and a newly found, more conscious way of living. Some participants, however, also mentioned to have (also) experienced a loss of meaning in their lives. These were mostly losses of meaning related to physical impairments or relational distress. In addition, it seemed that some people have an unmet need to fill a gap that arises from a loss of meaningful activities, for example not being able to work anymore.

The discrepancy in the literature between experiencing less or more meaning in life after cancer, was also shown in the outcomes of this study. Our results indicated that meaning making in cancer survivors is often a multifaceted process: in some specific areas (e.g. relationships) they experienced more meaning, while at the same time, meaning decreased in other areas (e.g. meaningful activities).

While this focus group study specifically aimed for more insight in meaning making processes in cancer survivors, also other related issues came up in the discussions. Many people stated that after they had been diagnosed with cancer they felt unacknowledged or abandoned in some way by most of their social environment, for example their co-workers, neighbors and other acquaintances. Some people seemed to miss a sense of belonging after having dealt with cancer, which can be seen as a characterization of the existential theme "isolation", a term explained by Yalom [27] as a feeling of "separation from the world". This finding corresponds with the theory of Ryff and Singer [42] that psychological well-being consists of two key dimensions: "leading a life of purpose" and "quality connections with others".

A quality connection with others seemed to play a crucial role in the perception of the cancer survivors in this study. Close relationships with others were often mentioned as one of the most important sources of meaning, while the strongly related concept of isolation often came up as the hardest thing to deal with after cancer. An explanation of this seeming discrepancy could be that people derived meaning from the intimate relations they have with their beloved ones, like family members and close friends, but simultaneously feel more excluded from the rest of their social environment.

When asked if they had a need for help with meaning making since their diagnosis, most people confirmed that they had, confirming previous research indicating that cancer survivors have indeed unmet existential needs [43]. Participants also expressed a need for peer support. Some people considered supporting other peers to be meaningful. This finding relates to the "helper therapy principle", a model by Riessman [43] that describes the therapeutic effect of giving and receiving support at the same time.

Also in line with previous studies [8-13], our results suggested that some people experience a satisfying, adaptive search for meaning, while others experience a continued, maladaptive search for meaning. Therefore, it is important to gain more knowledge on what the risk factors for meaning making problems are among cancer survivors, who may benefit from meaning making interventions and on how people with needs in this particular area can be screened and reached with interventions.

The results of this study did not only show that some people experience important shifts in meaning making, but also suggested that some meaning making needs are still unmet. Future psychological interventions should aim at these unmet needs.

Strengths and limitations

To our knowledge, there are no studies that used focus groups to investigate meaning making processes in cancer survivors. This study included a heterogeneous group of patients with various types of cancer to maximize the possibility of exploring a broad range of experiences and opinions from different perspectives. Although a valuable insight in patients' experiences with meaning making was obtained, a few limitations should be noted.

The results are based on a relatively small sample size, which may hamper the generalizability. However, typically between four and six focus groups involving 4-10 participants is considered adequate [44]. Based on this study, no conclusions can be drawn on whether there were actual changes in meaning making after cancer, but only on whether these changes were *perceived*. Since meaning making is a personal, subjective process, we consider perceived changes more relevant than actual changes.

In addition, there were relatively many people in our sample that had already sought psychological help for coping with cancer. These people might struggle more in general than other cancer survivors and therefore also more with meaning making. This may give a biased view on experienced meaning making issues, however, it also sheds a light on a potential target group that might be at risk for meaning making problems. In this study, detailed information on participant characteristics, like marital status, education level, stage of cancer or type of treatment, was lacking. It is likely that these characteristics influence ones reflection on meaning making. This study was not set up to establish relations between variables, but mostly to generate ideas and explore different experiences with meaning making that cancer survivors might have.

In this study, we specifically asked about participant's experiences and issues with meaning making. Without this specific asking, participants might not have mentioned these experiences, and this might have been influenced by the moderators, who were experts on this topic. The purpose of this study was not to objectively establish the themes that came to mind, but to gain more insight in the meaning making process specifically.

A critical point is that we did not obtain feedback of the participants on our findings to ensure the results are not curtailed by the researchers. However, the data was punctually transcribed verbatim, and coded and interpreted by three coders separately and discussed with a fourth researcher, to prevent curtailing.

The design of this study does not allow to draw conclusions about the prevalence of changes in meaning making in cancer survivors. Nevertheless, the results indicated that at least part of the cancer survivors clearly experience important shifts in meaning making after cancer.

In conclusion this qualitative study indicated that there is a group of cancer survivors that has succeeded in meaning making efforts, and experiences sometimes even more meaning than before diagnosis, while there is also a considerable group of survivors that struggles with meaning making and has an unmet need for help with that. These results may contribute to develop interventions targeting meaning in life in cancer survivors.

REFERENCES

1. Brenner H. Long-term survival rates of cancer patients achieved by the end of 20th century: a period analysis. *Lancet* 2000, 1131-1135.
2. Richards MA, Stockton D, Bapp P, Coleman MP. How many deaths have been avoided through improvements in cancer survival? *Brit Med Journal* 2000, 895–898.
3. Dutch Comprehensive Cancer Centres (2011) *Cijfers over kanker. Kanker in Nederland.* Availible: http://cijfersoverkanker.nl/. Accessed 12 March 2013.
4. Howlader N, Noone AM, Krapcho M, Neyman N, Aminou R, et al. (2012) *SEER Cancer Statistics Review, 1975-2009, National Cancer Institute.* Available: http://seer.cancer.gov/csr/1975_2009_pops09/. Accessed 9 April 2013.
5. Hoffman KE, McCarthy EP, Recklitis CJ, Ng AK. Psychological Distress in Long-term Survivors of Adult-Onset Cancer Results From a National Survey. *Arch Intern Med* 2009, **14**: 1274-1281.
6. Carlson LE, Groff SL, Maciejewski O, Bultz BD. Screening for distress in lung and breast cancer outpatients: a randomized controlled trial. *J of Clin Oncol* 2010, **28**: 4884-4891.
7. Thewes B, Butow P, Girgis A, Pendlebury S. Assessment of unmet needs among survivors of breast cancer. *J Psychosoc Oncol* 2004, **22**: 51-73.
8. Henoch I, Danielson E. Existential concerns among patients with cancer and interventions to meet them: an integrative literature review. *Psychooncology* 2009, **18**: 225-236.
9. Tedeschi RG, Calhoun LG. Posttraumatic growth: Conceptual foundations and empirical evidence. *Psychol Inq* 2004, **15**:1-18.
10. Thornton AA. Perceiving benefits in the cancer experience. *J Clin Psychol Med Settings* 2002, **9**: 153-165.
11. Tomich PL, Helgeson VS, Nowak Vache EJ. Perceived growth and decline following breast cancer: a comparison to age-matched controls 5-years later. *Psychooncology* 2005, **12**: 1018–1029.
12. Ferrell B, Smith SL, Cullinane CA, Melancon C. Psychological Well Being and Quality of Life in Ovarian Cancer Survivors. *Cancer* 2003**, 98**: 1061-1071.
13. Ussher J, Kirsten L, Butow P, Sandoval M. What do cancer support groups provide which other supportive relationships do not? The experience of peer support groups for people with cancer. *Soc Sci Med* 2005, **62**: 2565–2576.
14. Lee V. The existential plight of cancer: meaning making as a concrete approach to the intangible search for meaning. *Support Care Cancer*, 2008, **16**: 779-785.
15. Tomich PL, Helgeson VS. Five years later: A cross-sectional comparison of breast cancer survivors with healthy women. *Psychooncology* 2002, **11**: 154-169.
16. Zika S, Chaimberlain K. On the relation between meaning in life and well-being. *Brit J of Psychol* 1992, **83**: 133-145.
17. Debats DL. Meaning in life: Clinical relevance and predictive power. *Brit J of Clin Psychol* 1996, **35:** 503-516.

18. Lee CH. Effects of Logotherapy with Exercise on meaning of life, ego integrity and IADL in the elderly. *Taehan Kanho Hakhoe Chi* 2006, **36**: 701-709.

19. Lee V, Cohen SR, Edgar L, Laizner AM, Gagnon AJ. Clarifying "meaning" in the context of cancer research: a systematic literature review. *Palliat Support Care* 2004, **2**: 291-303.

20. Lee V, Cohen SR, Edgar L, Laizner AM, Gagnon AJ. Meaning-making intervention during breast or colorectal cancer treatment improves self-esteem, optimism, and self-efficacy. *Soc Sci Med* 2006, **62**: 3133-3145.

21. Davis CG, Wortman CB, Lehman DR, Silver RC. Searching for meaning in loss: Are clinical assumptions correct? *Death studies* 2000, **24***:* 497-540.

22. Park CL, Edmondson D, Fenster R, Blank TO. Meaning Making and Psychological Adjustment Following Cancer: The Mediating Roles of Growth, Life Meaning, and Restored Just-World Beliefs.*Cons and Clin Psy* 2008, **76**: 863-875.

23. Silver RL, Boon C, Stones MH. Searching for meaning in misfortune: Making sense of incest. *J of Soc Iss* 1983, **39**: 81-101.

24. Thompson SC, Pitts J. Factors relating to a person's ability to find meaning after a diagnosis of cancer. *J of Psychosoc Onc* 1994, **11**: 1-21.

25. Davis CG, Nolen-Hoeksema S, Larson J. Making sense of loss and benefiting from the experience: two construals of meaning. *J Pers Soc Psychol* 1998, **75**: 561-574.

26. Jaarsma TA, Pool G, Ranchor AV, Sanderman R. The concept and measurement of meaning in life in Dutch cancer patients. *Psychooncology* 2007, **16**: 241-248.

27. Yalom ID (1980) *Existential psychotherapy (*vol. 1 edn). Basic Books.

28. Frankl, V. (1986) *The doctor and the soul. From psychotherapy to logotherapy.* London: Random House.

29. Frankl V (1989) *The will to meaning: foundations and applications of logotherapy* (expanded edn). New York: Penguin Books.

30. Frankl V (1998) *Man's search for meaning: an introduction to logotherapy* (British paperback edition) London: Random House.

31. Chochinov HM, Hack TF, Hassard T, Kristjanson LJ, McClement S, et al. Dignity Therapy: A Novel Psychotherapeutic Intervention for Patients Near the End of Life. *J Clin Oncol* 2005, **23:** 5520-5525.

32. Breitbart W, Rosenfeld B, Gibson C, Pessin H, Poppito S, et al. Meaning-centered group psychotherapy for patients with advanced cancer: a pilot randomized controlled trial. *Psychooncology* 2010, **19**: 21-28.

33. Giese-Davis J, Koopman C, Butler LD, Classen C, Cordova M, et al. Change in emotion-regulation strategy for women with metastatic breast cancer following supportive-expressive group therapy. *Cons and Clin Psy* 2002, **70**: 916–925.

34. Bordeleau L, Szalai JP, Ennis M, Leszcz M, Speca M, et al. Quality of life in a randomized trial of group psychosocial support in metastatic breast cancer: overall effects of the intervention and an exploration of missing data. *J of Clin Oncol* 2003, **21**: 1944–1951.

35. Classen C, Butler LD, Koopman C, Miller E, DiMiceli S, et al. Supportive-expressive group therapy and distress in patients with metastatic breast cancer. *Arch of Gen Psychiatry* 2001, **28**: 494–501.

36. Spiegel D, Spira J. *Supportive-Expressive Group Therapy: A treatment manual of psychosocial intervention for women with recurrent breast cancer.* Stanford, CA: Stanford University School of Medicine. 2001.

37. Kissane DW, Bloch S, Smith GC, Miach P, Clarke DM, et al. Cognitive-Existential Group Psychotherapy for Women with Primary Breast Cancer: A Randomised Controlled Trial. *Psychooncology* 2003, **12**: 532–546.

38. Coward DD Facilitation of self-transcendence in a breast cancer support group: II. *Onc Nurs Forum* 2003, **30**: 291–300.

39. Rabiee F. Focus-group interview and data analysis. *Procof the NutSoc* 2004, **63**: 655.

40. Pope C, Ziebland S, Mays N. Analyzing qualitative data. *BMJ* 2000, 114-116.

41. Landis JR, Koch GG. An application of hierarchical kappa-type statistics in the assessment of majority agreement among multiple observers. *Biometrics* 1977, 363-374.

42. Ryff CD, Singer BH. Contours of positive human health. *Psychol Inq* 1998, 1-18.

43. Hodgkinson K, Butow P, Hunt GE, Pendlebury S, Hobbs KM, Wain G. Breast cancer survivors' supportive care needs 2–10 years after diagnosis. *Support Care Cancer* 2007, **15**: 515–523.

44. Litosseliti L. *Using focus groups in reserach.* London: Continuum. 2007.

Chapter 3

Meaning-centered group psychotherapy in cancer survivors: a feasibility study

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KEY POINTS

- We adjusted the Meaning-Centered Group Psychotherapy (MCGP) manual for advanced cancer patients, to make it applicable for cancer survivors.
- We performed the adjusted MCGP twice, 11 cancer survivors participated.
- This feasibility study proved good acceptability, compliance, client satisfaction, and recruitment strategies of MCGP in a cancer survivor population.
- Improvements among participants after intervention were measured.
- Meaning-Centered Group Psychotherapy seems beneficial for cancer survivors, but an RCT on (cost-)effectiveness is warranted.

Keywords: cancer, psycho-oncology, meaning, cancer survivors, group psychotherapy, feasibility study

INTRODUCTION

Many cancer survivors experience psychological and social problems while encountering the limitations in their life that occur as a consequence of their disease[1]. Meaning-focused coping seems to be at the core of adequate adjustment to cancer: cancer patients who experience their life as meaningful are better adjusted, have better quality of life and psychological functioning[2-3]. Several studies on existential interventions for patients with advanced cancer show promising results [4]. Meaning-Centered Group Psychotherapy (MCGP) was designed to help patients to sustain or enhance a sense of meaning, peace and purpose in their lives, despite the confrontation with death. A pilot randomized trial showed that MCGP is potentially beneficial for patients with advanced cancer on emotional and spiritual suffering[5].

This study focuses on cancer survivors, who have been treated for cancer with curative intent. Worldwide, there are no studies that have investigated meaning-centered therapy for cancer survivors. Based on outcomes of a focus group study with cancer survivors[6] and on the expertise of psychotherapists with expertise in this specific area, we adapted the MCGP manual to make it compliant for cancer survivors (MCGP-CS). The themes were kept the same as in the original manual, but the way they are addressed was changed, e.g. in the MCGP, patients are asked to respond to questions like 'What would you consider a good or meaningful death?' In the MCGP-CS, they are asked to respond to questions like 'How can you carry on in life, despite these limitations?' We are planning to conduct a randomized controlled trial (RCT) investigating the cost-effectiveness of MCGP targeting cancer survivors (MCGP-CS). Before starting the RCT, we decided to test the adapted MCGP-CS manual and the research set up in a feasibility study. The goals of the present feasibility study are to examine 1) the recruitment strategy 2) MCGP-CS compliance, 3) patient satisfaction with MCGP-CS, and 4) to test the outcome assessment procedures. Also, we wanted to obtain preliminary insight into the expected efficacy of the intervention.

METHODS

Design

In this pilot study, participants were recruited during six months at the departments of Surgery, Clinical Oncology, and Clinical Genetics of Leiden University Medical Center (LUMC). Eligible patients were recruited by a research-nurse. The goal was to include 18-24 patients enabling three MCGP groups. After three months, the accrual was behind on schedule, because the face-to-face accrual appeared to be too time consuming and was only reaching a small amount of patients. We decided to extend recruitment with online advertisements, and via a center for psychosocial care in Amsterdam. Outcome measures were administered before (T0) and after (T1) the intervention, and at 3 months follow-up (T2). After the MCGP's were conducted, two expert meetings with the two group facilitators (psychologists) and two researchers (NS and IV) were organised to evaluate the intervention manual. The study protocol was approved by the Medical Ethics Committee of the LUMC. All patients gave written informed consent.

Setting and study sample

Inclusion criteria: a diagnosis of cancer in the last 5 years; treatment with curative intent; main treatment is completed (i.e. surgery, chemotherapy, radiation); ability to attend all therapy sessions; need for psychological help/support for a psychosocial problem (e.g. anxiety, depression, coping issues, life questions, meaning-making problems).

Exclusion criteria: severe cognitive impairment; current psychological treatment; insufficient mastery of Dutch language. The criteria were ascertained during a telephone interview.

Meaning-centered group psychotherapy (MCGP)

MCGP is a group intervention with 8 weekly sessions of 2 hours. The main purpose of MCGP is to sustain or enhance a sense of meaning or purpose in the patient's life, in order to cope better with the consequences of cancer. Each session addresses a specific theme that is related to the concepts and sources of meaning (i.e. creativity, legacy, experience and attitude). The MCGP manual was originally developed for advanced cancer patients [5, 7]. In the present study, groups were planned to consist of 6-8 cancer survivors and led by two facilitators. The facilitators were psychologists with experience in treating psychosocial problems in oncology patients.

Outcome measures

The outcome assessment included items on sociodemographic variables and clinical characteristics (type of cancer, cancer treatment, time since treatment). Patients could choose to complete the questionnaires online or via paper-and-pencil. At T1, participants evaluated the strengths and weaknesses of the group training that they received by filling out a patient satisfaction questionnaire, to rate the content, duration, and quality of the training and the trainers.

Primary outcome measures on meaning making

The *Dutch Personal Meaning Profile (PMP)* comprises 5 subscales: religion, dedication to life, fairness of life, goal-orientedness, relationships.[8]

The *Dutch Post Traumatic Growth Inventory* (PTGI) is for measuring posttraumatic growth and comprises 5 scales: relationships, viewing new possibilities, personal strength, spirituality, appreciation of life.[9]

The *Ryff's Scale of Psychological Well-being* (SPWB) assesses a person's level of positive functioning and well-being and comprises 6 scales: autonomy, environmental mastery, personal growth, positive relationships, purpose in life, self-acceptance.[10]

Secondary outcome measures

Secondary outcome measures were the 30-item EORTC QLQ-C30, (Quality of Life), the 14-item Hospital Anxiety and Depression Scale (HADS, Anxiety and Depression), the 20-item Dutch Beck Hopelessness Scale (BHS, Hopelessness), the 10-item Life Orientation Test-Revised (Optimism), and the 40-item Dutch Mental Adjustment to Cancer questionnaire (MAC, Adjustment to cancer).

Statistical analyses

Descriptive statistics were generated for the range of background and outcome variables. Free-text responses were used as illustrations for the quantitative data. Paired sample t-tests were used to analyse differences between patients before and after intervention, and between patients before intervention and at 3 months follow-up. Effect sizes were calculated regarding differences between outcome measures at T1 vs. T0 and at T2 vs. T0, by Cohen's d. Statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS) 20.0.

RESULTS

Recruitment

After six months, 11 (2 male, 9 female) participants were recruited and two MCGP-CS groups were conducted, one in Amsterdam (N=4) and one in Leiden (N=7). The mean age was 52 years, 7 participants were in a relationship, 4 were single, 8 participants were diagnosed with breast cancer, 3 with colorectal cancer and the average time since treatment was 16 months.

Compliance and patient satisfaction

The compliance rate of the MCGP sessions was good; all 11 patients finished the intervention. One patient missed one session. Ten patients completed a 12-item questionnaire on satisfaction with MCGP-CS post-intervention. Six patients reported to be 'very satisfied', three patients were 'satisfied' and one patients had 'mixed feelings'(*Table 1*). In total, nine patients indicated that they would recommend this intervention to others (one was not sure) and almost all patients were satisfied with the number of sessions and the duration of the sessions. One patient found that the sessions were too short. Two patients stated that they had preferred more sessions. Quotes from the free text-responses illustrate these findings:

"This training gave me new insights, a nice experience with meaningful conversations. I would not want to miss it."

"I feel that the end of the training came a little bit too soon. But I do believe I can go on with what I've learned."

Table 1 Patient satisfaction with MCGP

N = 10	Totally agree	Agree a little	Mixed feelings
The session themes were useful	80%	20%	-
The discussion topics were understandable	90%	10%	-
Discussing meaning making was useful for me	60%	40%	-
The workbook was easy to work with	40%	40%	20%
The homework assignments were helpful	60%	40%	-
This group training was very useful for me	60%	20%	20%
The facilitators were reliable	100%	-	-
I felt acknowledged by the facilitators	100%	-	-
The facilitators were experts	100%	-	-
There was enough room to tell my story	90%	10%	-
It was pleasant to share my experiences with others	100%	-	-
I have learned from the experiences of others	100%	-	-

*There were no scores in the categories 'disagree a little' and 'totally disagree', these categories are therefore not included in this table.

Evaluation by psychotherapists

In the expert meetings, the facilitators expressed that they were in general positive about the intervention manual. Most of their comments concerned the use of language. Based on the facilitators' experiences during this pilot study, the intervention manual was further adapted regarding the structure, order of topics, and rephrasing of expressions. Also, a short introspective exercise was added as a start of every exercise in the intervention manual.

Outcome evaluation

All patients preferred to complete the outcome measures online. Total scales and subscales could be calculated for 11 patients at baseline, 10 patients after the intervention (T1), and 9 patients at 3 months follow-up (T2). On several outcome measures, patients scored better post treatment and/or at follow up, with small, medium and large effect sizes (*Table 2*). Of course, these results should be handled with caution, because of the small sample size in this pilot study.

Table 2 Changes in primary and secondary outcome measures.

	Baseline, T0 Mean (sd)	Post, T1 Mean (sd)	Cohen's d	P value T1 vs. T0	Follow up, T2Mean (sd)	Cohen's d	P value T2 vs. T0
SPWB							
Psych. well-being							
Positive relations	**5.1** (.4)	**5.2** (.4)	-0.14	.678	**5.3** (.5)	-0.11	.747
Autonomy	**4.0** (.9)	**4.3** (.5)	-0.74	.044	**4.3** (.9)	-1.14	.008
Environmental mastery	**4.5** (.4)	**4.6** (.2)	-0.3	.363	**4.8** (.4)	-0.68	.065
Personal Growth	**4.7** (.5)	**5.1** (.3)	-0.93	.017	**5.1** (.3)	-0.91	.021
Purpose in life	**4.6** (.5)	**4.7** (.4)	-0.43	.204	**4.7** (.5)	-0.35	.300
Self acceptance	**4.5** (.6)	**4.6** (.4)	-0.21	.520	**4.7** (.5)	-0.55	.118
Spiritual well-being							
Inner strength	**4.4** (.7)	**4.8** (.5)	-0.66	.067	**4.8** (.7)	-0.46	.187
Higher Power	**3.6** (.4)	**3.7** (.4)	-0.21	.520	**3.7** (.5)	-0.55	.129
PMP							
Total Score	**66.2** (13.3)	**71.4** (10.0)	-0.69	.061	**70.0** (10.3)	-0.68	.084
Relation with God/ higher order	**26.5** (12.4)	**28.4** (11.4)	-0.34	.309	**25.6** (11.6)	-0.24	.456
Dedication to life	**68.9** (15.3)	**76.2** (11.2)	-0.65	.068	**74.7** (10.8)	-0.61	.090
Fairness of life	**54.6** (17.6)	**65.0** (15.9)	-0.98	.013	**64.3** (11.7)	-1.1	.009
Goal-orientedness	**72.8** (15.9)	**79.4** (10.4)	-0.62	.083	**73.4** (14.0)	-0.26	.430
Relations with others	**82.1** (14.9)	**82.1** (14.0)	0	1.00	**85.3** (12.3)	-0.28	.407
PTGI							
Total score	**75.6** (15.2)	**78.7** (19.1)	-0.36	.289	**76.1** (22.0)	-0.21	.534
Relating to others	**29.3** (6.7)	**29.4** (6.4)	-0.02	.945	**27.9** (6.9)	0.13	.682
New possibilities	**17.2** (5.1)	**17.0** (5.7)	0.05	.874	**16.3** (6.1)	0.05	.886
Personal strength	**13.8** (4.3)	**15.7** (5.0)	-0.68	.061	**15.0** (5.3)	-0.54	.128
Spiritual change	**3.8** (1.9)	**4.7** (2.3)	-0.49	.159	**4.6** (1.7)	-0.63	.081
Appreciation of life	**11.5** (3.2)	**11.9** (3.5)	-0.23	.479	**12.3** (4.3)	-0.39	.255
HADS							
Anxiety	**6.7** (4.4)	**4.7** (3.0)	0.63	.079	**4.1** (2.7)	0.89	.024
Depression	**2.9** (2.3)	**1.3** (1.2)	0.82	.127	**4.4** (0.9)	-0.55	.574
Total score	**9.6** (6.2)	**6.0** (3.9)		.043	**8.6** (2.7)		.353
EORTC QLQ-C30							
Function scales							
Emotional function	**71.7** (16.8)	**84.2** (10.0)	0.95	.015	**83.3** (11.8)	0.89	.023
Cognitive function	**56.7** (23.8)	**71.7** (19.3)	0.75	.041	**72.2** (20.4)	0.83	.030
Social function	**66.7** (19.2)	**81.7** (21.4)	0.82	.029	**74.1** (18.8)	0.73	.050

Continuation of Table 2

Symptom scales							
Fatigue	**50.0** (21.1)	**31.1** (17.2)	1.6	.001	**42.0** (24.1)	0.41	.227
Nausea/Vomiting	**10.0** (16.1)	**3.3** (10.5)	0.77	.037	**11.1** (16.7)	0.07	1.00
Pain	**26.7** (28.5)	**11.7** (22.3)	0.66	.068	**29.6** (21.7)	-0.11	.729
Dyspneu	**16.7** (23.6)	**20.0** (28.1)	-0.11	.726	**14.8** (24.0)	0.11	.729
Insomnia	**40.0** (34.4)	**23.3** (31.6)	0.71	.052	**25.9** (27.8)	0.47	.179
Loss of appetite	**10.0** (16.1)	**3.3** (10.5)	0.47	.168	**3.7** (11.1)	0.48	.169
Constipation	**10.0** (22.5)	**6.7** (14.1)	0.18	.591	**7.4** (14.7)	0.18	.594
Diarrhea	**13.3** (17.2)	**3.3** (10.5)	0.62	.081	**22.2** (33.3)	-.018	.594
Financial problems	**20.0** (32.2)	**10.0** (16.1)	0.44	.193	**18.5** (24.2)	0.18	.594
MAC							
Fighting spirit	**48.5** (4.1)	**49.0** (5.4)	-0.15	.647	**49.9** (5.6)	-0.3	.368
Helpless/Hopeless	**10.3** (2.8)	**8.6** (1.6)	0.68	.060	**9.7** (3.3)	0.21	.531
Anxious preoccupation	**24.1** (4.0)	**23.1** (2.9)	0.25	.443	**22.2** (1.8)	0.63	.082
Fatalism	**18.8** (3.7)	**17.6** (2.8)	0.37	.269	**17.3** (1.7)	0.24	.466
Avoidance	**1.3** (0.5)	**1.6** (1.0)	-0.36	.279	**1.3** (0.5)	-0.18	.594
LOT-R							
Optimism	**15.6** (3.7)	**16.3** (3.3)	-0.26	.428	**16.2** (2.7)	-0.17	.616
Becks Hopelessness							
Total score	**5.5** (4.6)	**3.4** (1.8)	0.46	.179	**3.7** (3.3)	0.41	.232

DISCUSSION AND CONCLUSION

The results of this feasibility study indicated that MCPG-CS is feasible and possibly effective. Patient satisfaction and compliance was high. The majority of the patients responded positively to the intervention and stated that they were very satisfied. All participants preferred to complete the outcome measures online. Participant's comments about the workbook and comments from the group facilitators on the intervention manual were processed.

The recruitment strategy appeared to be insufficient: during the inclusion period of 6 months, in total 11 patients were included instead of the planned 18-24. To ensure a better inclusion rate during the planned RCT, we decided to approach patients via multiple hospitals and advertisements in the public media.

In this feasibility study, we found improvements after the intervention in the expected direction regarding some aspects of meaning making, psychological distress, and quality of life, with medium to large effect sizes. The information from this feasibility study was valuable enabling further optimizing MCPG-CS.

Strengths and limitations

Based on the results of this uncontrolled study with a small sample size, no conclusions about the efficacy of MCGP can be drawn. Also, the majority of the sample were breast cancer patients, which might have caused a trend for this group that is known to respond well to psychotherapy. However, these preliminary findings are encouraging for starting an RCT. The study design and sample were suitable to predict problems that can undermine an evaluation on a large scale. The feasibility study was useful for examining key uncertainties in preparation of an RCT.

REFERENCES

1. Hoffman, K, McCarthy, E, Recklitis, C Ng, A. Psychological distress in long-term survivors of adult-onset cancer results from a national survey. *Archives of Internal Medicine*, 2009. **14**: p. 1274-1281.

2. Tomich, PL, Helgeson, VS. Five years later: A cross-sectional comparison of breast cancer survivors with healthy women. *Psycho-Oncology*, 2002. **11**(2): p. 154-169.

3. Park, CL, Edomondson, D, Fenster, JR Blank, TO. Meaning making and psychological adjustment following cancer: The mediating roles of growth, life meaning, and restored just-world beliefs. *Journal of Consulting and Clinical Psychology*, 2008. **76**(5): p. 863-875.

4. LeMay, K Wilson, KG. Treatment of existential distress in life threatening illness: A review of manualized interventions. *Clinical Psychological Review*, 2008. **28**: p. 472-493.

5. Breitbart, W, Rosenfeld, B, Gibson, C, Pessin, H, Poppito, S, Nelson, C, Tomarken, A, Timm, AK, Berg, A, Jacobson, C, Sorger, B, Abbey, J Olden, M. Meaning-centered group psychotherapy for patients with advanced cancer: A pilot randomized controlled trial. *Psycho-Oncology*, 2010. **19**(1): p. 21-28.

6. Van der Spek, N, Vos, J, Van Uden-Kraan, CF., Breitbart, W, Tollenaar, RAEM, Cuijpers, P Verdonck-de Leeuw, IM. Meaning making in cancer survivors: A focus group study. *PloS One*, 2013. **8**(9): p. 1-7.

7. Breitbart, W. Spirituality and meaning in supportive care: Spirituality- and meaning-centered group psychotherapy interventions in advanced cancer. *Supportive Care in Cancer*, 2002. **10**(4): p. 272-280.

8. Jaarsma, TA, Pool, G, Ranchor, AV Sanderman, R. The concept and measurement of meaning in life in dutch cancer patients. *Psycho-Oncology*, 2007. **16**(3): p. 241-248.

9. Jaarsma, TA, Pool, G. *Posttraumatic growth inventory: Dutch version.* Groningen: Noordelijk Centrum voor Gezondheidsvraagstukken, 2003.

10. Dierendonck, D. The construct validity of ryff's scales of psychological well-being and its extension with spiritual well-being. *Personality and Individual Differences*, 2005. **36**: p. 629-643.

Chapter 4

Efficacy and cost-utility of meaning-centered group psychotherapy in cancer survivors: protocol of a randomized controlled trial

This chapter is a modified version of the following publication:

van der Spek N, Vos J, van Uden-Kraan CF, Breitbart W, Cuijpers P, Knipscheer-Kuipers K, Willemsen V, Tollenaar RAEM, van Asperen CJ, and Verdonck-de Leeuw IM. (2014). Effectiveness and Cost Evaluation of Meaning-Centered Group Psychotherapy in Cancer Survivors: Protocol of a Randomized Controlled Trial. *BMC Psychiatry 14*(22): http://www.biomedcentral.com/1471-244X/14/22

ABSTRACT

Background. Meaning-focused coping may be at the core of adequate adjustment to life after cancer. Cancer survivors who experience their life as meaningful are better adjusted, have better quality of life and psychological functioning. Meaning-Centered Group Psychotherapy for Cancer Survivors (MCGP-CS) was designed to help patients to sustain or enhance a sense of meaning and purpose in their lives. The aim of the proposed study is to evaluate the effectiveness and cost-effectiveness of MCGP-CS.

Methods/design. Survivors diagnosed with cancer in the last 5 years and treated with curative intent, are recruited via several hospitals in the Netherlands. After screening, 168 survivors are randomly assigned to one of the three study arms: 1. Meaning-Centered Group Psychotherapy (MCGP-CS) 2. Supportive group psychotherapy (SGP) 3. Care as usual (CAU). Baseline assessment takes place before randomization, with follow up assessments post-intervention and at 3, 6 and 12 months follow-up. Primary outcome is meaning making (PMP, PTGI, SPWB). Secondary outcome measures address quality of life (EORTC-30), anxiety and depression (HADS), hopelessness (BHS), optimism (LOT-R), adjustment to cancer (MAC), and costs (TIC-P, EQ-5D, PRODISQ).

Discussion. Meaning-focused coping is key to adjustment to life after cancer, however, there is a lack of evidence based psychological interventions in this area. Many cancer survivors experience feelings of loneliness and alienation, and have a need for peer support, therefore a group method in particular, can be beneficial for sustaining or enhancing a sense of meaning. If this MCGP-CS is effective for cancer survivors, it can be implemented in the practice of psycho-oncology care.

BACKGROUND

In the past decade, life expectancies of cancer patients have increased significantly. Due to recent innovations in early detection and treatment, many patients have become cancer survivors and the population of cancer survivors is growing [1,2].

Many cancer patients seem to experience the diagnosis of cancer as a challenge to experiencing life as meaningful, for instance due to shifted priorities in life, or physical hindrances in achieving goals. For some people, the diagnosis of cancer can lead to the experience of life with little or no meaning [3]. Meaning in life is strongly associated to psychological well-being and is liable to alteration after a negative experience like cancer [4-6]. Meaning-focused coping may be at the core of adequate adjustment to cancer: cancer patients who experience their life as meaningful are better adjusted, have better quality of life and psychological functioning [4,7]. Therefore, a meaning-focused psychological intervention might be beneficial for cancer survivors to increase adequate adjustment to life after cancer and prevent and decrease psychological distress.

Several interventions for cancer patients focusing at least partly on experiencing meaning in life have been developed and evaluated. The outcomes of several evaluation studies are promising with improved self-esteem, optimism, mood, sense of meaning, spiritual well-being and decreased suffering after intervention. These studies are, however, hampered by methodological limitations, like high dropout rates, no control for the effects of attention, insufficient information on the treatment protocol and short periods of follow up [8-17]. Most of the studied interventions target cancer patients in the palliative phase. None of the described studies assess the cost-effectiveness. To our knowledge there are no randomized controlled trials on meaning-centered psychological interventions targeting cancer survivors.

In the proposed study, we aim to evaluate the effectiveness of a newly developed meaning-centered group psychotherapy for cancer survivors, based on the Meaning-Centered Group Psychotherapy (MCGP) [18]. MCGP, developed by Breitbart and colleagues, is grounded in Frankl's work and was designed to help patients with advanced cancer to sustain or enhance a sense of meaning, peace and purpose in their lives, despite the confrontation with death [18]. Frankl stated that the will to meaning is the primary motivation of humans [19-21]. He developed a meaning-centered approach in psychotherapy, called *logotherapy*, that focuses on assisting people to detect their individual meaning or purpose in life. A pilot randomized controlled trial showed that MCGP is potentially beneficial for advanced cancer patients for decreasing emotional and spiritual suffering [11].

In the present study, we adapted MCGP for cancer *survivors* (MCGP-CS). Based on outcome of a focus group study on 23 patients [22], and on the input of two psychotherapists with expertise in this specific area, we adjusted the MCGP manual to make it compliant for cancer survivors. Through this focus group study we obtained insight in how survivors experience and talk about meaning in life, and in their perceived need for help with meaning making.

In addition, the results indicated that some cancer survivors succeeded in meaning making efforts and experienced sometimes even more meaning in life than before diagnosis, while others struggled with meaning making and expressed an unmet need for help [22]. In preparation of the randomized controlled trial (RCT) studying effectiveness, the feasibility of the MCGP-CS protocol was tested in a feasibility study among 11 participants, divided over two groups. The outcomes of the feasibility study were positive: patient satisfaction and compliance were high [23].

Based on the results of these studies, the MCGP-CS manual and protocol were finalized. An example of an adjustment to Breitbart's original MCGP for palliative patients addresses attitudinal sources of meaning. In the advanced cancer patient protocol, patients are asked to respond to questions like 'What would you consider a good or meaningful death?' 'How can you imagine being remembered by your loved ones?' In the adjusted protocol for cancer survivors, they are asked to respond to questions like 'What are limitations in your life at the moment?' 'How can you carry on in life, despite these limitations?' 'What do you want to do *now*, that will make you happy and satisfied when you to die later?' Another change that has been made, based on expert advices, is that every experiential exercise starts with a brief meditation exercise, so feelings can be processed at a deeper level.

The main goal of the present study is to assess effectiveness and cost-effectiveness of MCGP-CS, compared to supportive group psychotherapy (SGP) and to care as usual (CAU) among cancer survivors with psychological or existential distress after treatment and a need for help.

METHODS/DESIGN

Design

This study is a prospective randomized controlled trial with three study arms: MCGP-CS, SGP and CAU. Cancer survivors are recruited in two different ways: via several hospitals in the Netherlands (region Leiden and Amsterdam) and via public media (i.e. advertisement on websites of patient societies, and in magazines and local newspapers). All cancer survivors who meet in- and exclusion criteria are asked to participate. Survivors are assigned through cluster randomization to one of the three study arms. The baseline assessment takes place before randomization, with follow up assessments one week post-intervention and at 3, 6 and 12 months follow-up. Reasons for dropout are registered. The study protocol, information brochure, questionnaires and informed consent form are approved as a multicenter study by the Medical Ethics Committee of the Leiden University Medical Center. The design is illustrated in Figure 1.

Study sample

Inclusion criteria: cancer diagnosis in the last 5 years, treated with curative intent, main treatment is completed (i.e. surgery, radiotherapy, chemotherapy), ability to attend all therapy sessions, expressed need for psychological help/support and at least one psychosocial complaint (e.g. depressed mood, anxiety, coping issues, life questions, meaning making problems, relationship problems).

Exclusion criteria: severe cognitive impairment, current psychological treatment and insufficient mastery of Dutch language.

The criteria are ascertained during a telephonic interview by a trained psychologist.

A study specific questionnaire comprises questions about sociodemographic (age, gender, religious background, marital status, family situation, education level, other important life events in the past 2 years) and clinical characteristics (type of cancer, cancer treatment, time since treatment) and will be filled out by participants at the first assessment, at baseline. Participants are asked which study-condition has their preference; this will not influence the assignment to the conditions.

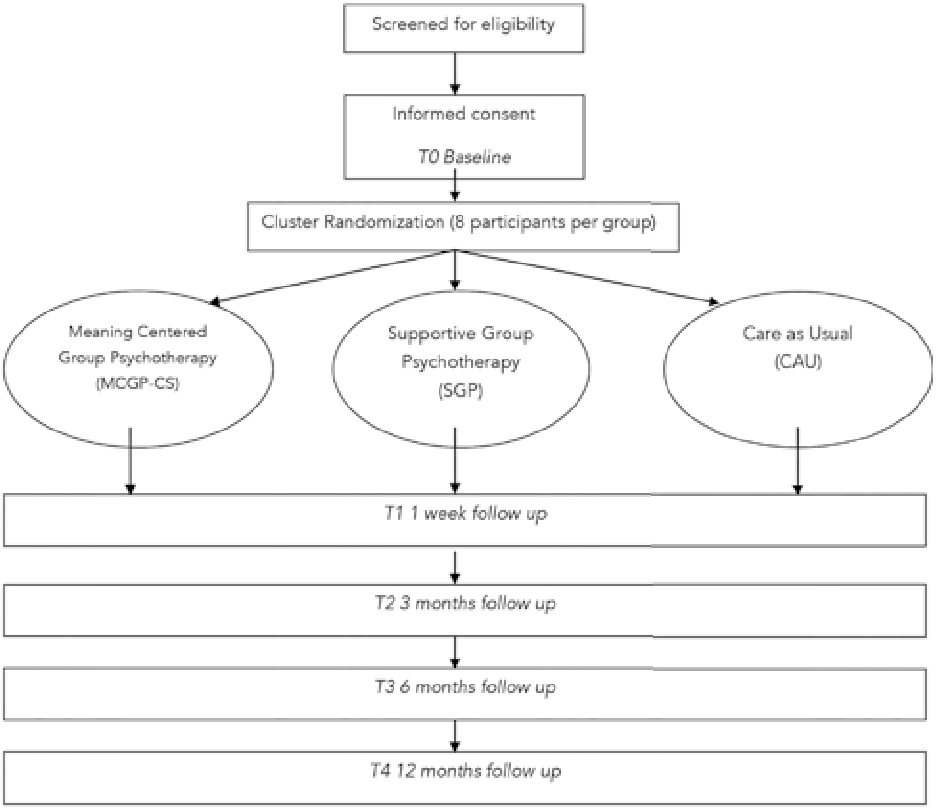

Figure 1 Design of the RCT

Randomization

Cancer survivors who meet the inclusion criteria and sign the informed consent, are allocated to a group. When the group counts 8 survivors, the group is randomly assigned by an independent researcher, through blocked randomization with randomly selected block sizes, to one of the three study arms.

Meaning-centered group psychotherapy targeting cancer survivors (MCGP-CS)

Cancer survivors in the experimental study arm participate in MCGP-CS. The main purpose of the MCGP-CS is to sustain or enhance a sense of meaning or purpose in the patient's life, in order to cope better with the consequences of cancer. MCGP-CS is a manualized 8-week intervention that makes us of didactics, group discussion and experiental exercises that focus around themes related to meaning and cancer survivorship. The sessions take two hours each and are held weekly. The participants use a workbook (called *Life lessons portfolio*) and get homework assignments every week. MCGP-CS is led by one psychotherapist with experience in treating patients with cancer. Each session addresses a specific theme that is related to the concepts and sources of meaning. The themes of the sessions are: 1. Concept and sources of meaning, 2. Meaning before and after cancer, 3. The story of our life as a source of meaning: what made us who we are today, 4. The story of our life as a source of meaning: things we have done and want to do in the future, 5. Attitudinal sources of meaning: encountering life's limitations, 6. Creative sources of meaning: responsibility, courage and creativity, 7. Experiental sources of meaning, 8. Termination: presentations of our life lessons and goodbyes. Table 1 gives an overview of the themes of each session.

Supportive group psychotherapy (SGP)

The control condition is an 8-week social support group following Payne et al. [24]. The sessions take two hours and are held weekly. Each group is supervised by a psychotherapist with experience in treating patients with cancer. The psychotherapist has an unconditionally positive regard and empathetic understanding, stimulates patients to actively share their experiences, and focuses on positive emotions, and expression of feelings.

Each of the 8 sessions has a different theme, which is mentioned at the beginning of the session. The themes of the sessions are: 1.group members' introductions, 2.need for support, 3.coping with medical tests and communicating with physicians, 4.coping with family and friends, 5.coping with work issues, 6.coping with body image and physical functioning, 7.coping with the future, 8.termination: where do we go from here? Table 1 gives an overview of the themes of each session.

Care as usual (CAU)

Cancer survivors assigned to the CAU study arm do not participate in one of the group interventions. If a patient in the CAU study arm asks the researcher for psychological help, he or she is referred to their General Practitioner (GP). Health care uptake is closely monitored, to enable detailed post-hoc description of what CAU entailed exactly.

Table 1 Session topics covered in MCGP-CS[1] and SGP[2]

Session	MCGP-CS	SGP
1	Concept and sources of meaning	Group member introductions
2	Meaning before and after cancer	The need for support
3	The story of our life as a source of meaning: what made us who we are today	Coping with the medical test and communicating with providers
4	The story of our life as a source of meaning: things we have done and want to do in the future	Coping with family and friends
5	Attitudinal sources of meaning: encountering life's limitations	Coping with vocational issues
6	Creative sources of meaning: responsibility, courage and creativity	Coping with body image and physical functioning
7	Experiental sources of meaning	Coping with the future
8	Termination: presentations of our life lessons and goodbyes	Termination: Goodbyes and how do we go from here?

[1]Meaning-Centered Group Psychotherapy for Cancer Survivors

[2]Supportive Group Psychotherapy

Treatment quality

In the MCGP-CS and the SGP study arms, after each session, the psychotherapist writes a short summary of the session where he/she notes whether the protocol was followed. All group sessions are audio taped and randomly selected audio fragments will be analysed by the researchers to establish whether the therapy protocol was followed correctly.

Outcome assessment

Outcomes measures include questionnaires on meaning, quality of life, anxiety and depression, hopelessness, optimism, mental adjustment to cancer, satisfaction with the intervention, and sociodemographic and clinical characteristics. Furthermore, a cost-evaluation will be carried out. Patients can choose to complete questionnaires online or via pen and paper. Primary outcomes are collected at all time points (baseline, after one week, 3, 6, and 12 months). Secondary outcome measures are collected at baseline, after one week, 3 and 6 months. Cost evaluation outcomes are collected at baseline, after 3, 6, and 12 months). A complete overview of the outcome measures is presented in Table 2.

Primary outcome measures

Meaning

The Dutch Personal Meaning Profile (PMP) is a 39-item self assessment scale for measuring meaning in life and comprises 5 subscales: religion, dedication to life, fairness of life, goal-orientedness, relationships. [25].

The Dutch Post Traumatic Growth Inventory (PTGI) is a 21 item self assessment scale for measuring posttraumatic growth and comprises 5 scales: relationships, viewing new possibilities, personal strength, spirituality, appreciation of life [26].

The Ryff's Scale of Psychological Well-being (SPWB) is a 49 item questionnaire to assess a person's level of positive functioning and well-being and comprises 6 scales: autonomy, environmental mastery, personal growth, positive relationships, purpose in life, self-acceptance [27].

Table 2 Outcome measures and instruments

Outcome measures	Instrument
Primary[1]	
Meaning	Personal Meaning Profile (PMP) [24]
Post Traumatic Growth	Post Traumatic Growth Inventory (PTGI) [25]
Positive psychological functioning and wellbeing	Ryff's Scale of Psychological Well-being (SPWB) [26]
Secondary[2]	
Quality of life	30-item EORTC QLQ-C30 (version 3.0) [27,28]
Anxiety and Depression	Hospital Anxiety and Depression Scale (HADS) [29]
Hopelessness	Beck Hopelessness Scale (BHS) [30,31]
Optimism	Life Orientation Test (LOT-R) [31,32]
Adjustment to cancer	Mental Adjustment to Cancer (MAC) [20]
Cost evaluation[3]	Trimbos and iMTA questionnaire on Costs associated with Psychiatric illness (TiC-P) [34,35]
	EQ-5D [36]
	PRODISQ [37]

[1] Assessment at T0, T1, T2, T3, T4

[2] Assessment at T0, T1, T2, and T3

[3] Assessment at T0, T2, T3 and T4

Secondary outcome measures

Quality of life

The 30-item EORTC QLQ-C30 (version 3.0) includes a global HRQOL scale (2 items) and comprises 5 functional scales: physical functioning (5 items), role functioning (2 items), emotional functioning (4 items), cognitive functioning (2 items) and social functioning (2 items). There are three symptom scales (nausea and vomiting (2 items), fatigue (3 items) and pain (2 items) and 6 single items relating to dyspnoea, insomnia, loss of appetite, constipation, diarrhoea and financial difficulties [28,29].

Anxiety and depression

A validated Dutch version of the Hospital Anxiety and Depression Scale (HADS) is used to assess emotional distress. The HADS is a 14-item self-assessment scale for measuring distress with two subscales, anxiety and depression. The HADS was specifically designed for use in the medically ill. The total HADS score ranges from 0 to 42, the subscales from 0 to 21. A score of >15 is used as an indicator of a high level of psychological distress [30].

Hopelessness

The Dutch Beck Hopelessness Scale (BHS) is a 20 item self-assessment scale for measuring hopelessness. The scale consists of 20 statements about oneself which are endorsed as true or false. The content of 11 statements is hopeless, the content of 9 statements is hopeful [31,32].

Optimism

The Dutch Life Orientation Test (LOT-R), is a 10-item self-assessment scale for measuring optimism. The scale consists of 10 statements about oneself which are endorsed on a 5-point likert scale (from 1 totally disagree to 5 totally agree) [33,34].

Adjustment to cancer

Cognitive and behavioural response to cancer diagnosis and treatment is determined by the Mental Adjustment to Cancer (MAC) questionnaire. The MAC scale comprises five subscales: Fighting Spirit, Helplessness/Hopelessness, Anxious Preoccupation, Fatalism and Avoidance [20].

Satisfaction with the intervention

At T1, cancer survivors in both the MCGP-CS and SGP study arms are asked to evaluate the strengths and weaknesses of the group training that they received and rate their satisfaction with the content, duration, and quality of the training and the trainers on a 15 item likert-scaled questionnaire and on free text responses. Participants in the MCGP-CS condition are asked three additional evaluation questions about the specific content of the MCGP-CS protocol (their opinion on talking about meaning, the homework assignments and the workbook).

Cost-evaluation

Direct medical and direct non-medical cost data are collected with the Trimbos and iMTA questionnaire on Costs associated with Psychiatric illness (TiC-P) [35,36]. Unit resource use (GP visits, hospital days, etc.) will be multiplied by their appropriate integral cost prices.

An economic evaluation regarding work (loss) and health care use will be conducted as a cost-utility analysis for (changes in) health-related quality of life as assessed with the EQ-5D [37].

Indirect non-medical cost data related to production losses through work loss days and work cutback days will be sampled with the appropriate PRODISQ modules [38]. Indicators of return to work (RTW) are: Time to partial and to full RTW, meaning number of calendar days between end of treatment and first day at work; Time to full RTW corrected for partial RTW.

Sample size

Based on a priori power analyses for hierarchical multiple regression, assuming a power of .80, Cohen's d of .80 and alpha of .05, each study condition will need at least 43 cancer survivors. We will anticipate for loss to follow-up of 30%, and will therefore need 56 cancer survivors per condition at baseline. In total, we will recruit 168 cancer survivors during an inclusion period of 2.5 years.

Statistical analyses

Descriptive statistics, t-tests and Chi^2 tests will be used to determine whether patient characteristics are similar across experimental conditions. Results will be reported on an intention-to-treat basis. The Linear Mixed Modeling (LMM) procedure will be used to estimate missing values. This procedure includes incomplete cases in the analysis and employs restricted maximum likelihood estimation to calculate parameter estimates. LMM assumes that missing data are missing at random. LMM will be used to investigate the longitudinal development of meaning making in the three groups. The effect of study condition will be tested using contrasts within the LMM. Mediation analyses [39,40] will be used to test as whether development in the patients' meaning making explains/mediates the expected improvement in psychological functioning in the MCGP condition.

Economic outcomes

For the economic evaluation we will make use of the pertinent guidelines [36,41-43]. The societal perspective will be taken encompassing intervention costs, direct non-medical costs and indirect costs. The latter is not expected to be very important in the studied population, which is characterised by unemployment, but the data on production losses will be collected anyway. Production losses will be economically valuated using the friction cost method [44]. Costs and effects will be analysed simultaneously, incremental cost-effectiveness ratios (ICERs) will be calculated and placed within 95% confidence intervals, 2,500 bootstrap replications of the ICERs will be projected on a cost-effectiveness plane, ICER acceptability curves will be plotted against different willingness-to-pay ceilings [44], and sensitivity analysis will be conducted as a matter of course focussing on uncertainty in the main cost-drivers. This will be done for the costs per QALY gained in a cost utility analysis.

Ethical considerations

This study is conducted in accordance with local laws and regulations. Eligible patients are fully informed about the study and asked to participate. The patients receive a patient information sheet and flyer and they are also informed by telephone about the implications of participation. Patients have ample opportunity to ask questions and to consider the implications of the study before deciding to participate. Patients provide written informed consent, compliant with the local and ethical regulations, before participation. Patients are allowed to withdraw from the study without giving a reason, at any time. The study protocol has been approved by the Medical Ethical Committee of Leiden University Medical Center, Leiden, The Netherlands.

DISCUSSION

The proposed study will assess the effectiveness of MCGP-CS, compared to SGP and to CAU in cancer survivors with psychological or existential distress after treatment. In addition, the cost-effectiveness of MCGP-CS will be determined.

There is a growing need for psychological interventions that target the issues that cancer survivors are dealing with in the aftermath of their disease. Meaning-focused coping is key to adjustment to life after cancer [7,46]. Many cancer survivors experience feelings of loneliness and alienation, and have a need for peer support, therefore a group method in particular, can be beneficial [47]. Group interventions may provide opportunities to cope with these problems. People who benefit from group interventions feel more comforted, less alone and have learned different ways to cope with their situation [47].

To our knowledge there are no RCT's that evaluate the effectiveness of meaning-centered psychotherapy for cancer survivors. Also, there is little known about who benefits from these types of interventions. Also, there is little known on who benefits from these types of interventions. We want to conduct an RCT that compares MCGP-CS with a SGP that focuses on other issues that cancer survivors deal with (see Table 2). This way, we hope to establish whether a meaning-centered approach is more effective compared to care as usual, than a non-meaning-centered approach. Secondary analyses will be conducted to assess the predictors of effectiveness on an individual level, in order to gain more knowledge on which people benefit the most from the meaning-centered intervention.

To our knowledge, there are no cost evaluations of meaning-centered interventions. Since the number of cancer survivors is increasing rapidly, cost efficient psychological care is, from an economic point of view, important to warrant the feasibility of implementation in mental health care settings.

This study evaluates if MCGP-CS is effective for cancer survivors and if so, whether this is a cost efficient method. If this MCGP-CS is effective for cancer survivors, it can be implemented in the practice of psycho-oncology care. The broad collaboration in this project with several hospitals and psycho-oncology organisations, facilitates possible implementation in practice after this evaluation. There are few evidence based group intervention manuals available for cancer patients. For meaning-centered group psychotherapy for cancer survivors, there are no evidence based intervention manuals yet. Therefore, if the results of this RCT are positive on effectiveness measures, the intervention protocol can be an important addition to the advancement of evidence based psychological care for cancer patients.

REFERENCES

1. Brenner H. Long-term survival rates of cancer patients achieved by the end of 20th century: a period analysis. *Lancet* 2002, **360:**1131–1135.
2. Richards M, Stockton D, Bapp P, Coleman MP. How many deaths have been avoided through improvements in cancer survival? *Brit Med Journal* 2000, **320:**895–898.
3. Lee V. The existential plight of cancer: meaning making as a concrete approach to the intangible search for meaning. *Support Care Cancer* 2008, **16:**779–785.
4. Tomich PL, Helgeson VS. Five years later: A cross-sectional comparison of breast cancer survivors with healthy women. *Psychooncology* 2002, **11:**154–169.
5. Zika S, Chaimberlain K. On the relation between meaning in life and well-being. *Br J Psychol* 1992, **83:**133–145.
6. Debats DL. Meaning in life: clinical relevance and predictive power. *Brit J of Clin Psychol* 1996, **35:**503–516.
7. Park CL, Edomondson D, Fenster JR, Blank TO. Meaning making and psychological adjustment following cancer: the mediating roles of growth, life meaning, and restored just-world beliefs. *Cons and Clin Psy* 2008, **76:**863–875.
8. Lee V, Cohen SR, Edgar L, Laizner AM, Gagnon AJ. Meaning-making intervention during breast or colorectal cancer treatment improves self-esteem, optimism, and self-efficacy. *Soc Sci Med* 2006, **62:**3133–3145.
9. Chochinov HM, Hack TF, Hassard T, Kristjanson LJ, McClement S, Harlos M. Dignity therapy: a novel psychotherapeutic intervention for patients near the end of life. *J Clin Oncol* 2005, **23:**5520–5525.
10. Giese-Davis J, Koopman C, Butler LD, Classen C, Cordova M, Fobair D, Benson J, Kraemer HC, Spiegel D. Change in emotion-regulation strategy for women with metastatic breast cancer following supportive-expressive group therapy. *Cons and Clin Psy* 2002, **70:**916–925.
11. Breitbart W, Rosenfeld B, Gibson C, Pessin H, Poppito S, Nelson C, Tomarken A, Kosinski Timm A, Berg A, Jacobson C, Sorger B, Abbey J, Olden M. Meaning-centered group psychotherapy for patients with advanced cancer: a pilot randomized controlled trial. *Psychooncology* 2010, **19:**21–28.
12. Classen C, Butler LD, Koopman C, Miller E, DiMiceli S, Giese-Davis J, Fobair P, Carlson RW, Kraemer HC, Spiegel D. Supportive-expressive group therapy and distress in patients with metastatic breast cancer. *Arch of Gen Psychiatry* 2001, **28:**494–501.
13. Spiegel D, Spira J. *Supportive-Expressive Group Therapy: A Treatment Manual of Psychosocial Intervention for Women with Recurrent Breast Cancer.* Stanford, CA: Stanford University School of Medicine; 1991.

14. Kissane DW, Bloch S, Smith GC, Miach P, Clarke DM, Ikin J, Love A, Ranieri N, McKenzie D. Cognitive-existential group psychotherapy for women with primary breast cancer: a randomised controlled trial. *Psychooncology* 2003, **12:**532–546.

15. Coward DD. Facilitation of self-transcendence in a breast cancer support group: II. *Onc Nurs Forum* 2003, **30:**291–300.

16. LeMay K, Wilson KG. Treatment of existential distress in life threatening illness: A review of manualized interventions. *Clin Psychol Rev* 2008, **28:**472–493.

17. Linn M, Linn B, Harris R. Effects of counseling for late-stage cancer patients. *Cancer* 1982, **49:**1048–1055.

18. Breitbart W. Spirituality and meaning in supportive care: spirituality- and meaning-centered group psychotherapy interventions in advanced cancer. *Support Care Cancer* 2002, **10:**272–280.

19. Frankl V. *The Doctor and the Soul. In From Psychotherapy to Logotherapy.* London: Random House; 1986.

20. Frankl V. *The Will to Meaning: Foundations and Applications of Logotherapy, ed. L.* New York: New American; 1989.

21. Frankl V. *Man’s Search for Meaning: An Introduction to Logotherapy.* London: British paperback edition: random House; 1998.

22. Van der Spek N, Vos J, Van Uden-Kraan CF, Breitbart W, Tollenaar RAEM, Cuijpers P, Verdonck-de Leeuw IM. Meaning making in cancer survivors: a focus group study. *PLoS One* 2013, **8:**1–7.

23. Van der Spek N, Van Uden-Kraan CF, Vos J, Breitbart W, Tollenaar RAEM, Van Asperen CJ, Cuijpers P, Verdonck-de Leeuw IM. Meaning-Centered Group Psychotherapy in Cancer Survivors: a Feasibility Study. *Psychooncology*, 2014 [E pub ahead of print].

24. Payne DK, Vroom P, Phil M. *Supportive Group Psychotherapy: A Group Intervention for Cancer Patients.* Memorial Sloan-Kettering Cancer Center: New York; 2009.

25. Jaarsma TA, et al. The concept and measurement of meaning in life in Dutch cancer patients. *Psychooncology* 2007, **16:**241–248.

26. Jaarsma TA, Pool G. *Posttraumatic Growth Inventory: Dutch Version.* Groningen: Noordelijk Centrum voor Gezondheidsvraagstukken; 2003.

27. Dierendonck D. The construct validity of Ryff’s scales of psychological well-being and its extension with spiritual well-being. *Pers Individ Dif* 2005, **36:**629–643.

28. Aaronson N, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993, **85:**365–376.

29. Fayers P, Bottomley A. Quality of life research within the EORTC-the EORTC QLQ - C30, European Organisation for Research and Treatment of Cancer. *Eur J Cancer* 2002, **38:**125–133.

30. Spinhoven P. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. *Psychol Med* 1997, **27:**363–370.

31. Young MA, et al. An item-response theory evaluation of the Beck Hopelessness Scale. *Cog Ther Res* 1992, **16:**579–587.

32. Beck AT, et al. Measurement of pessismism- hopelessness scale. *Cons and Clin Psy* 1974, **42:**861–865.

33. Scheier MF, Carver CS, Bridges MW. Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem) - a reevaluation of the life orientation test. *J Pers Soc Psychol* 1994, **67:**1063–1078.

34. ten Klooster PM, et al. Optimisme en/of pessimisme: factorstructuur van de Nederlandse Life Orientation Test-Revised. *Psychologie en Gezondheid* 2010, **38:**89–100.

35. Van Roijen LH, et al. Cost-utility of brief psychological treatment for depression and anxiety. *Br J Psychiatry* 2006, **188:**323–329.

36. Oostenbrink JB, Bouwmans CAM, Koopmanschap MA. *Manual for Costing: Methods and Standard Costs for Economic Evaluations in Health Care.* Diemen: Health Insurance Board; 2004.

37. Brooks R. EuroQol: the current state of play. *Health Pol* 1996, **37:**53–72.

38. Koopmanschap MA. PRODISQ: a modular questionnaire on productivity and disease for economic evaluation studies. *Expert Rev Pharmacoecon Outcomes Res* 2005, **5:**23–28.

39. Preacher KJ, Hayes AF. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behav Res Methods* 2008, **40:**879–889.

40. Kraemer HC, et al. Mediators and moderators of treatment effects in randomized clinical trials. *Arch of Gen Psychiatry* 2002, **59:**877–883.

41. Oostenbrink JB. Standardisation of costs: the Dutch Manual for Costing in economic evaluations. *Pharmacoeconomics* 2002, **20:**443–454.

42. Langley PC. The November 1995 revised Australian guidelines for the economic evaluation of pharmaceuticals**.** *Pharmacoeconomics* 1996, **9:**341–352.

43. Torrance GW, et al. Canadian guidelines for economic evaluation of pharmaceuticals. Canadian Collaborative Workshop for Pharmacoeconomics. *Pharmacoeconomics* 1996, **9:**535–559.

44. Brouwer WB, Koopmanschap MA, Rutten FF. Productivity losses without absence: measurement validation and empirical evidence. *Health Pol* 1999, **48:**13–27.

45. Van Hout BA, et al. Costs, effects and C/E-ratios alongside a clinical trial. *Health Econ* 1994, **3:**309–319.

46. Thompson SC, Pitts J. Factors relating to a person's ability to find meaning after a diagnosis of cancer. J *Psychosoc Oncol* 1994, **11:**1–21.

47. Gottlieb BH, Wachala ED. Cancer support groups: a critical review of empirical studies. *Psychooncology* 2006, **16:**379–400.

Chapter 5

Efficacy of meaning-centered group psychotherapy for cancer survivors: outcomes of a randomized trial

Submitted:

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ABSTRACT

Purpose. The aim of this study was to assess the efficacy of meaning-centered group psychotherapy for cancer survivors (MCGP-CS) to improve personal meaning, compared to supportive group psychotherapy (SGP) and care as usual (CAU). Furthermore, the effects of MCGP-CS on psychological well-being, posttraumatic growth, adjustment to cancer, optimism, hopelessness, psychological distress, and quality of life were explored.

Methods. A total of 170 cancer survivors were randomly assigned to one of the three study arms: MCGP-CS (n = 57), SGP (n = 56), CAU (n = 57). The primary outcome measure was the Personal Meaning Profile (total score PMP). The secondary outcome measures were subscales of the PMP, Scales of Psychological Well-Being (SPWB), Posttraumatic Growth Inventory (PTGI) Mental Adjustment to Cancer Scale (MAC), Life Orientation Test-Revised (LOT-R), Beck's Hopelessness Scale (BHS), Hospital Anxiety and Depression Scale (HADS), and EORTC QLQ-C30. Outcome measures were assessed before randomization, post-intervention, and after three and six months follow-up (FU).

Results. Linear mixed model analyses (intention-to-treat) showed significant differences between MCGP-CS, SGP and CAU on the course of the total PMP score, and on (sub) scales of the PMP, SPWB, MAC, and HADS. Post-hoc analyses showed significantly stronger treatment effects of MCGP-CS compared to CAU on personal meaning (d=0.81), goal-orientedness (d=1.07), positive relations (d=0.59), purpose in life (d=0.69), and fighting spirit (d=0.61) (post-intervention), helpless/hopeless (d=-0.87) (three months FU), and distress (d=-0.6) and depression (d=-0.38) (six months FU). Significantly stronger effects of MCGP-CS compared to SGP were found on personal growth (d=0.57) (three months FU), and environmental mastery (d=0.66) (six months FU).

Conclusion. MCGP-CS is an effective intervention for cancer survivors to improve personal meaning, psychological well-being and mental adjustment to cancer in the short term, and to reduce psychological distress in the long run.

INTRODUCTION

There is growing attention on the role of sense of meaning in improving psychological well-being, and preventing or reducing psychological distress among cancer patients [1]. Up until now, research on meaning in cancer patients focused mostly on patients with advanced cancer, who might face death and meaning-related existential issues like demoralization and the desire for hastened death [2, 3]. However, sense of meaning is also an important issue in cancer survivors [4, 5]. The cancer diagnosis and the treatment with curative intent often imply fundamental uncertainties that patients have to deal with. These include the possible recurrence of the cancer, or negative (long-term) side-effects of the treatment, and are often accompanied by losses in different domains of life (i.e. physical, social, personal), which can challenge the experience of meaning in life [5, 6]. Sense of meaning is positively related to psychological well-being, successful adjustment, better quality of life, and negatively to psychological distress after the cancer diagnosis [7–9].

Breitbart and colleagues [10] developed and evaluated meaning-centered group psychotherapy (MCGP), in order to meet the needs of patients with advanced cancer to help with meaning-making, improving spiritual well-being and reducing psychological distress. In a randomized controlled trial among 273 patients with advanced cancer, MCGP was compared to supportive group psychotherapy (SGP) [10]. After controlling for sex, social support, religiosity and cognitive functioning, intention-to-treat analyses showed significant positive effects of MCGP on spiritual well-being, quality of life, hopelessness, depression, and desire for hastened death immediately after the intervention and at two months follow-up, with small to moderate effect sizes (-0.27 to -0.67).

Besides MCGP there are several other interventions that focus, at least partly, on sense of meaning in advanced cancer patients and that show varying degrees of positive effects [1, 11–15]. To our knowledge there are no evidence based meaning-focused interventions specifically targeting cancer survivors treated with curative intent.

We adjusted the MCGP manual for cancer survivors (MCGP-CS) and subsequently conducted a feasibility study, which showed good acceptability, compliance, and satisfaction of MCGP among cancer survivors [16].

The aim of the present study was to assess the efficacy of MCGP-CS among cancer survivors to improve personal meaning. Based on earlier studies [1, 7, 8, 10, 13] we also expected a positive effect of MCGP-CS on psychological well-being, posttraumatic growth, adjustment to cancer, optimism, and quality of life. Moreover, we expected MCGP-CS to reduce hopelessness and psychological distress. In this randomized controlled trial (RCT), MCGP-CS was compared with SGP and with care as usual (CAU) to investigate the value of group psychotherapy, specifically focusing on personal meaning compared to regular supportive group psychotherapy and to standard care. Efficacy was evaluated post-intervention and at three and six months follow-up, to obtain insight into a possible decay of the effect.

METHODS

Study design and population

This study was a multi-center RCT with three study arms. The methods of this study have been described in a previously published study protocol [17]. The study protocol was approved by the Medical Ethics Committee of the Leiden University Medical Center and the trial was registered in the Netherlands Trial Register (NTR3571).

Eligible participants were adult cancer survivors who were diagnosed in the last five years, who were treated with curative intent, and who had completed their main treatment (i.e. surgery, radiotherapy, chemotherapy). Participants had to have an expressed need for psychological care and at least one psychosocial complaint (e.g. depressed mood, anxiety, coping issues, life questions, meaning-making problems, relationship problems).

Participants were excluded if they suffered from severe cognitive impairment, had current psychological treatment, or insufficient mastery of the Dutch language. The criteria were ascertained during a telephonic interview by a trained psychologist (KH).

Cancer survivors were recruited between August 2012 and September 2014 via four hospitals and via public media (i.e. advertisements on websites of patient societies, and in magazines and local newspapers). Cancer survivors were informed about the study, and asked to respond if they were interested in participating. The cancer survivors who signed the informed consent were randomized into one of the three study arms: MCGP-CS, SGP and CAU. All participants provided written informed consent.

Interventions

Meaning-centered group psychotherapy for cancer survivors (MCGP-CS)

The main purpose of MCGP-CS is to sustain or enhance a sense of meaning or purpose in a patient's life, in order to cope better with the consequences of cancer. MCGP-CS is an adaptation of meaning-centered group psychotherapy (MCGP) for advanced cancer patients. The adaptations concerned the use of different terminologies and topics more relevant for survivors. For instance, the topic "a good and meaningful death" was replaced by the topic "carrying on in life despite limitations". Also, brief mindfulness exercises were added. MCGP-CS is a manualized eight-week intervention that makes use of didactics, group discussions and experiental exercises that focus around themes related to meaning and cancer survivorship. The sessions lasted two hours each and were held weekly. The participants used a workbook (called *Life lessons portfolio*) and completed homework assignments every week. MCGP-CS was led by a psychotherapist with considerable experience in treating patients with cancer. The psychotherapists partaking in this study were trained in MCGP-CS during a pilot study [16]. Each session addressed a theme related to the concepts and sources of meaning (Table 1).

Supportive group psychotherapy (SGP)

SGP is an eight-week social supportive group therapy following Payne et al.[18] The sessions lasted two hours and were held weekly. Each group was supervised by a psychotherapist with considerable experience in treating patients with cancer. In SGP no specific attention is paid to meaning. The psychotherapists were trained to avoid group discussions on meaning-related topics. The psychotherapist has an unconditionally positive regard and empathetic understanding, stimulates patients to actively share their experiences, and focuses on positive emotions and expression of feelings. Each of the eight sessions had a different theme (Table 1).

Care as usual (CAU)

Cancer survivors assigned to the CAU study arm did not participate in one of the group interventions. If a patient in the CAU study arm asked the researcher for psychological care, he or she was referred to their general practitioner. Health care uptake was monitored, to enable detailed post-hoc description of what CAU entailed.

There were two psychotherapists involved in this study, who facilitated MCGP-CS as well as SGP. In both treatment arms, the psychotherapist wrote a short summary of each session and noted whether the protocol was followed. All sessions were audiotaped, and randomly selected audio fragments were analyzed by a researcher (NvdS) to establish whether the therapy protocol was followed correctly. During the trial, three evaluation sessions with the therapists were held in which they obtained feedback from each other and from the researchers (NvdS and IV) on conducting the therapies according to the manuals, based on the summaries of the sessions and the analysis of the audio fragments. The therapy protocols of both MCGP-CS and SGP were followed accurately and meaning was barely discussed in SGP. Based on these analyses and evaluation, we concluded that treatment integrity was good.

Table 1 Session topics covered in MCGP-CS[1] and SGP[2]

Session	MCGP-CS	SGP
1	Concept and sources of meaning	Group member introductions
2	Meaning before and after cancer	The need for support
3	The story of our life as a source of meaning: what made us who we are today	Coping with the medical test and communicating with providers
4	The story of our life as a source of meaning: things we have done and want to do in the future	Coping with family and friends
5	Attitudinal sources of meaning: encountering life's limitations	Coping with vocational issues
6	Creative sources of meaning: responsibility, courage and creativity	Coping with body image and physical functioning
7	Experiental sources of meaning	Coping with the future
8	Termination: presentations of our life lessons and goodbyes	Termination: goodbyes and how do we go on from here?

[1] Meaning-Centered Group Psychotherapy for Cancer Survivors

[2] Supportive Group Psychotherapy

Outcome measurement

The primary outcome was personal meaning, secondary outcomes were psychological well-being, posttraumatic growth, adjustment to cancer, optimism, hopelessness, psychological distress (anxiety and depression), and global quality of life. Outcome measures were collected at baseline before the intervention was scheduled and before randomization (t0), with follow-up assessments one week post-intervention (t1) and after three (t2) and six (t3) months follow-up (FU).

The primary outcome measure was Personal Meaning Profile-Dutch Version (PMP-DV) (total score)[7].

Secondary outcome measures were: subscales of PMP (relation to God/higher order, dedication to life, fairness of life, goal-orientedness, and relations with others), Ryff's Scales of Psychological Well-being (SPWB) (no total score available; eight subscales positive relations, autonomy, environmental mastery, personal growth, purpose in life, self-acceptance, inner strength, and higher power) [19]; Posttraumatic Growth Inventory (PTGI) (total score)[20]; Mental Adjustment to Cancer (MAC) (no total score available; five subscales fighting spirit, helpless/hopeless, anxious preoccupation, fatalism, and avoidance) [21]; Life Orientation Test-Revised (LOT-R) (total score) [22]; Beck's Hopelessness Scale (BHS) (total score) [23], Hospital Anxiety and Depression Scale (HADS) (total score, and subscales anxiety and depression) [24]; and EORTC QLQ-C30 version 3.0 (global quality of life subscale)[25].

A study specific questionnaire at baseline comprised questions about sociodemographic factors (i.e. age, gender, religious background, marital status, household composition, education level, history of psychological treatment, other important negative life events in the past two years). Clinical characteristics (i.e. type of cancer, cancer treatment, time since diagnosis) of the patients recruited in hospitals were retrieved from the hospital information system, the clinical characteristics of patients recruited via public media were obtained from self-reports.

Sample size

Based on a priori power analyses for hierarchical multiple regression, assuming a power of .80, Cohen's d of .80 and alpha of .05, each study condition needed at least 43 cancer survivors. We anticipated a 30% loss for the follow-up, and therefore included 56 cancer survivors per condition at baseline.

Randomization and blinding

This was a three-arm RCT study with block randomization. A computer-generated randomization table with random block sizes was prepared by an independent researcher not involved in the study. Participants were allocated to a group. When the group counted between seven and ten survivors, the group was randomly assigned by the independent researcher, using a list of sequentially numbered allocations, to one of the three study arms. Participants and psychotherapists were aware of the allocated arm, whereas data managers were blinded to the allocation.

Statistical analyses

Descriptive statistics, ANOVAs, independent samples t-tests, Kruskal-Wallis tests, and χ^2 tests were used to determine whether patient characteristics (sociodemographic and clinical) were similar across experimental conditions. Missing values were excluded analysis by analysis. Results were reported on an intention-to-treat basis. Linear mixed models (LMM), with fixed effects for group, assessment and their two-way interaction, as well as a random intercept for randomization group and subjects (nested within the randomization group), were used to investigate differences in the course of the outcome measures between the three groups. Potential confounders were added as fixed effects as well, in case they differed between experimental conditions. Post-hoc analyses were performed to assess which two groups differed significantly (via LMM) and at which points in time (via independent sample t-tests). Post-hoc analyses were corrected for multiple testing by Bonferroni's correction, and for the potential confounders that differed significantly between conditions. Effect sizes (Cohen's d) were calculated by dividing the difference in change since the baseline between groups by the pooled standard deviation, at the separate points in time (post-intervention, three months FU and six months FU). Effect sizes of 0.2 were categorized as small, 0.5 as medium, and 0.8 as large [26]. For all analyses SPSS 20 was used; a *p*-value < 0.05 was considered to indicate statistical significance.

RESULTS

Study population

A total of 2192 cancer survivors were approached via their hospital to participate in this study. Of these patients 411 (19%) applied for participation in response to this mailing (Figure 1). Eight participants applied in response to the advertisement in public media. Of the 419 cancer survivors who were screened for eligibility, 148 were ineligible and 87 declined to participate. A total of 184 consented to participate. Of those, 170 participants (40 male, 130 female) completed the baseline questionnaire and were randomly assigned to MCGP-CS (n = 57), SGP (n = 56), or CAU (n = 57). Table 2 displays the sociodemographic and clinical characteristics of the study population. There was a significant difference with respect to gender between the three groups, with more males in the MCGP-CS condition. When comparing the outcome measures at baseline (means and SD in Table 3), there was a significant difference between the study arms on positive relations (MCGP-CS = 4.1, SGP = 4.5, CAU = 4.5, $\chi^2 = 6.685$, df = 2, $p = .035$).

In MCGP-CS, two participants (4%) never attended any group sessions, and in SGP seven participants (13%) never attended. In MCGP-CS, eight participants (14%) did not complete the intervention, mostly because the intervention differed from their expectations or because of medical reasons. In SGP, one participant discontinued (2%) due to lack of interest in the intervention. A total of 147 participants (86%) completed the assessment post-intervention, 136 (80%) the three-month follow-up, and 126 (74%) the six-month follow-up. In CAU, most participants received no additional psychosocial care during the study (93%), 7% received additional care (i.e. psychotherapy, self-help group, social work, or spiritual counseling).

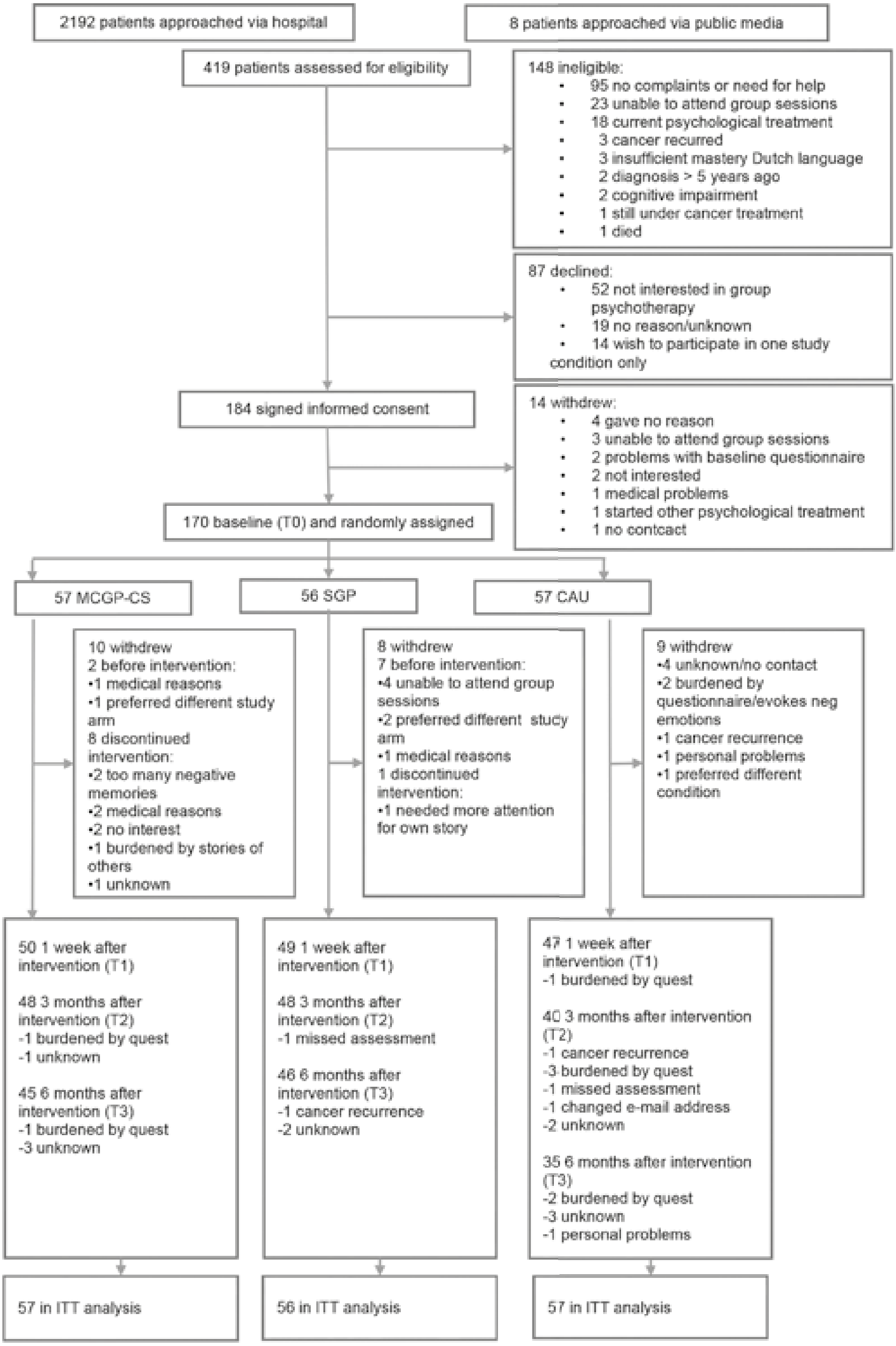

Figure 1 CONSORT diagram. Meaning-centered group psychotherapy for cancer survivors (MCGP-CS), supportive group psychotherapy (SGP), and care as usual (CAU).

Table 2 Participant characteristics

	MCGP-CS (n = 57)	SGP (n = 56)	CAU (n = 57)	P	χ^2
Age Mean (SD)	58.6 (10.7)	55.5 (9.6)	57.3(10.4)	.340	2.58
Sex Female N (%)	40 (70%)*	49 (88%)	51 (90%)	.012	8.83
Level of education				.156	6.65
Low	18 (32%)	9 (16%)	17 (30%)		
Medium	20 (35%)	25 (45%)	14 (26%)		
High	19 (33%)	22 (39%)	25 (44%)		
Religion				.181	3.42
Christian	23 (40%)	32 (57%)	30 (53%)		
No religion	34 (60%)	24 (43%)	27 (47%)		
Marital status Single N (%)	12 (21%)	9 (16%)	13 (23%)	.650	0.86
Household composition					
Lives alone	10 (18%)	11 (20%)	11 (19%)		
Lives with partner	28 (49%)	27 (48%)	21 (37%)		
Lives with children	2 (4%)	1 (2%)	3 (5%)		
Lives with partner and children	17 (30%)	17 (30%)	22 (39%)		
Type of cancer				.071	8.63
Breast	30 (53%)	40 (71%)	42 (74%)		
Colon	15 (26%)	12 (21%)	10 (18%)		
Other	12 (21%)	4 (7%)	5 (9%)		
Months since last cancer treatment Median (range)	19 (6-58)	16 (5-52)	18 (3-55)	.888	0.24[1]
Type of treatment					
Chemotherapy N (%)	26 (53%)	34 (61%)	36 (67%)	.124	4.18
Surgery N (%)	57 (100%)	56 (100%)	56 (98%)	.369	1.99
Radiation N (%)	31 (54%)	32 (57%)	33 (58%)	.924	0.16
Hormonal therapy N (%)	22 (30%)	28 (47%)	30 (47%)	.280	2.54
History psychological treatment N (%)				.724	3.65
Received psychological treatment in the last year	12 (21%)	11 (20%)	7 (13%)		
Received psychological treatment > 1 year ago	21 (37%)	21 (37%)	17 (31%)		
Never received psychological treatment before	24 (42%)	24 (43%)	31 (56%)		
Significant negative event in past 2 years other than cancer N (%)	27 (47%)	31 (54%)	33 (55%)		

[1] Kruskall Wallis

*significant difference between MCGP-CS and CAU

Efficacy of MCGP-CS

Table 3 shows the results of the LMM analyzing outcome measures per time assessment. In these models, the random slope for randomization group was removed as the estimated variance of randomization group was zero. Significant differences (corrected for sex) between MCGP-CS, SGP, and CAU were found on the course of personal meaning (total score PMP), and on secondary outcomes: subscale PMP (i.e. goal-orientedness), psychological well-being (SPWB) (i.e. positive relations, purpose in life, environmental mastery, personal growth), adjustment to cancer (MAC) (i.e. fighting spirit, helpless/hopeless), and psychological distress (HADS) (i.e. total score and depression). There were no significant differences between the three groups on the course of posttraumatic growth (PTGI), optimism (LOT-R), hopelessness (Beck's Hopelessness Scale) or global quality of life (EORTC QLQ-C30) (Table 3).

Post-hoc analyses showed significantly stronger treatment effects of MCGP-CS compared to CAU with respect to the course of personal meaning, goal-orientedness, positive relations, purpose in life, fighting spirit, helpless/hopeless, distress, depression, and significantly stronger effects of MCGP-CS compared to SGP for personal growth and environmental mastery (Table 4). Significantly stronger treatment effects of SGP compared to CAU were observed for goal-orientedness and fighting spirit.

Table 3 Linear Mixed Models analyzing treatment outcome

	Baseline, T0			***Post-intervention, T1***			***3-month follow-up, T2***			***6-month follow-up, T3***			
	MCGP-CS (n=57)	***SGP (n=56)***	***CAU (n=57)***	***MCGP-CS (n=50)***	***SGP (n=50)***	***CAU (n=47)***	***MCGP-CS (n=48)***	***SGP (n=48)***	***CAU (n=40)***	***MCGP-CS (n=45)***	***SGP (n=46)***	***CAU (n=35)***	
	Mean(SD)	**Mean(SD)**	**Mean(SD)**	**Mean(SD)**	**Mean(SD)**	**Mean(SD)**	**Mean(SD)**	**Mean(SD)**	**Mean(SD)**	**Mean(SD)**	**Mean(SD)**	**Mean(SD)**	**P**
PMP													
Total Score*	58.0(15.9)	60.2(13.3)	58.8(11.7)	61.0(16.2)	62.3(13.1)	56.3(13.1)	60.9(17.2)	61.5(14.8)	58.2(14.9)	60.4(16.6)	61.1(14.3)	58.7(13.2)	.019
Rel. God/higher order	31.9(25.0)	39.3(23.5)	29.8(20.0)	35.6(26.4)	40.4(25.7)	28.7(22.6)	36.0(27.2)	41.0(24.4)	30.6(21.7)	34.8(24.6)	39.3(22.6)	32.5(23.1)	.198
Dedication to life	67.1(18.8)	66.0(11.2)	67.7(10.5)	69.2(17.8)	67.4(10.4)	64.6(11.6)	69.7(18.6)	65.5(12.0)	66.9(11.8)	69.7(19.3)	67.0(11.6)	67.2(10.4)	.141
Fairness of life	55.7(15.9)	54.8(14.8)	54.7(15.3)	60.3(15.9)	59.4(16.7)	54.3(17.2)	59.8(18.4)	59.1(17.2)	55.6(17.3)	60.8(18.4)	58.7(17.7)	56.7(16.9)	.339
Goal-orientedness*	68.7(0.20)	71.0(16.9)	71.5(17.5)	73.6(19.7)	72.5(16.1)	63.0(23.3)	69.6(21.5)	71.1(18.4)	66.1(20.9)	67.2(21.7)	69.7(18.1)	67.2(20.1)	<.001
Relations with others	70.6(26.2)	73.9(25.3)	74.8(21.3)	70.4(25.3)	77.8(22.2)	73.7(21.6)	71.9(25.2)	76.3(22.1)	74.5(21.7)	70.1(27.5)	75.0(23.7)	71.1(23.2)	.344
SPWB													
Psych. well-being													
Positive relations*	4.1(1.0)	4.5(1.0)	4.5(0.83)	4.4(1.1)	4.7(0.95)	4.4(0.93)	4.3(1.0)	4.6(0.95)	4.5(0.86)	4.3(1.1)	4.6(1)	4.4(0.87)	.036
Autonomy[1]	4.2(0.85)	4.3(0.83)	4.3(0.72)	4.4(0.80)	4.5(0.76)	4.4(0.76)	4.4(0.76)	4.4(0.87)	4.4(0.62)	4.4(0.78)	4.4(0.93)	4.4(0.55)	.384
Environm. Mastery*	4.2(0.74)	4.3(0.71)	4.4(0.72)	4.5(0.75)	4.3(0.79)	4.4(0.67)	4.5(0.70)	4.3(0.67)	4.5(0.69)	4.5(0.80)	4.3(0.71)	4.5(0.69)	.012
Personal Growth*	4.2(0.75)	4.4(0.59)	4.3(0.60)	4.4(0.68)	4.4(0.56)	4.3(0.62)	4.4(0.63)	4.3(0.60)	4.3(0.66)	4.3(0.72)	4.4(0.60)	4.3(0.67)	.032
Purpose in life*	4.1(0.89)	4.3(0.77)	4.4(0.62)	4.4(0.89)	4.3(0.80)	4.3(0.65)	4.3(0.78)	4.3(0.84)	4.3(0.58)	4.3(0.85)	4.2(0.87)	4.4(0.61)	.007
Self-acceptance	4.0(0.87)	4.2(0.80)	4.3(0.64)	4.2(0.82)	4.3(0.83)	4.3(0.63)	4.3(0.77)	4.2(0.81)	4.4(0.57)	4.3(0.78)	4.2(0.88)	4.3(0.72)	.262
Spiritual well-being													
Inner strength	4.0(0.69)	4.1(0.80)	4.1(0.66)	4.2(0.80)	4.2(0.74)	4.1(0.78)	4.3(0.82)	4.2(0.83)	4.1(0.86)	4.2(0.91)	4.2(0.84)	4.2(0.60)	.245
Higher Power	2.8(1.4)	3.1(1.3)	2.8(1.3)	3.0(1.3)	3.2(1.3)	2.7(1.2)	3.0(1.4)	3.1(1.2)	2.7(1.2)	3.0(1.3)	3.2(1.2)	2.9(1.2)	.452

Continuation of Table 3

PTGI													
Total score	41.8(20.5)	48.2(17.4)	46.4(18.4)	48.1(20.5)	52.6(17.1)	49.1(19.5)	46.3(21.2)	52.1(17.1)	49.5(21.3)	45.8(23.3)	49.3(19.6)	51.4(19.3)	.453
MAC													
Fighting spirit*	46.0(5.4)	45.9(5.6)	47.3(4.3)	47.7(6)	45.5(5.1)	46.8(5.2)	47.0(4.9)	47.0(4.5)	46.5(5.8)	47.3(6)	46.9(46.5)	45.8(5.7)	.001
Helpless/Hopeless*	10.7(2.9)	10.7(2.9)	10.3(2.5)	9.6(3)	10.6(2.9)	10.2(2.7)	9.6 (2.9)	10.2(2.9)	11.0(2.7)	10.0(3.4)	10.4(2.9)	10.9(3.4)	.005
Anxious preoccupation	22.4(3.3)	23.1(3.3)	22.8(3.6)	21.7(3.2)	22.3(3.3)	22(3.2)	20.9(3.4)	22.4(3.9)	22.3(3.4)	21.1(3.9)	21.7(3.6)	22.4(3.8)	.231
Fatalism[1]	19.1(2.5)	18.6(3.1)	18.5(2.8)	19(3.1)	18.5(2.6)	18.2(3.0)	18.3(2.7)	18.8(2.5)	18.7(2.7)	18.6(2.8)	18.4(2.3)	18.7(2.7)	.113
Avoidance	1.7(0.70)	1.8(0.90)	1.6(0.78)	1.8(0.83)	1.7(0.65)	1.5(0.76)	1.7(0.71)	1.6(0.70)	1.7(0.85)	1.7(0.68)	1.7(0.80)	1.8(0.79)	.734
LOT-R													
Optimism[1]	12.2(3)	12.1(2.4)	12.1(3.5)	13.2(3.2)	11.8(2.5)	12.4(2.7)	12.8(3.2)	12.4(2.7)	12.4(3)	13(3.9)	12.2(2.9)	12.2(3.2)	.442
BHS													
Total score	6.6(4.9)	6.0(4.8)	5.8(3.8)	5.3(5)	5.6(4.7)	6.1(4.2)	5.0(4.7)	6.0(4.6)	5.9(5.2)	4.9(4.9)	5.7(5.0)	5.6(4.9)	.109
HADS													
Total score*	12.3(6.5)	12.4(6.5)	11.8(5.2)	9.8(6.2)	10.6(6.6)	11.1(6.8)	9.5(7.6)	10.9(7)	10.9(6.5)	8.8(7.0)	10.4(6.9)	12.3(8.1)	.025
Anxiety	7.2(3.9)	7.9(3.8)	7.4(2.8)	6.1(3.8)	6.8(3.7)	6.8(3.6)	5.6(4.0)	7.1(3.9)	6.5(3.6)	5.5(3.8)	6.8(3.7)	7.4(4.1)	.133
Depression*	5.1(3.5)	4.5(3.3)	4.4(3.3)	3.7(3.3)	3.8(3.4)	4.3(4.1)	3.9(3.8)	3.8(3.5)	4.3(3.8)	3.3(3.8)	3.6(3.7)	5.0(4.8)	.025
EORTC QLQ-C30													
Global quality of life	71.6(17.0)	70.2(17.3)	72.7(13.3)	72.6(18.1)	76.4(17.4)	74(17.1)	73.5(19.5)	76.6(17.5)	73.5(18.3)	73(22.1)	74.6(15.6)	68.5(22.4)	.263

[1] Corrected for gender

*= *p*<.05

Abbreviations: PMP, Personal Meaning Profile; SPWB, Ryff's Scale of Psychological Well-being; PTGI, Post Traumatic Growth Inventory; MAC, Mental Adjustment to Cancer Scale; LOT-R, Life Orientation Test-Revised; BHS, Beck's Hopelessness Scale; HADS, Hospital Anxiety and Depression Scale; EORTC QLQ-C30 quality of life questionnaire; MCGP-CS, Meaning-Centered Group Psychotherapy for Cancer Survivors; SGP, Supportive Group Psychotherapy; CAU, Care As Usual

Table 4 Linear Mixed Model analyses: differences between two study arms

	MCGP-CS- CAU	**MCGP-CS- SGP**	**SGP-CAU**
	***p*-value**	***p*-value**	***p*-value**
PMP			
Total Score	.027*	.73	.084
Goal-orientedness	<.001*	1.00	.009*
SPWB			
Positive relations	.033*	1.00	.56
Environmental mastery	.19	.006*	1.00
Personal Growth	.26	.021*	.24
Purpose in life	.021*	.057	.73
MAC			
Fighting spirit *	.021*	.072	.024*
Helpless/Hopeless*	.012*	.38	.084
HADS			
Total score*	.018*	1.00	.31
Depression *	.012*	1.00	.40

*p<.05

Abbreviations: PMP, Personal Meaning Profile; SPWB, Ryff's Scale of Psychological Well-being; PTGI, Post Traumatic Growth Inventory; HADS, Hospital Anxiety and Depression Scale; MAC, Mental Adjustment to Cancer Scale; MCGP-CS, Meaning-Centered Group Psychotherapy for Cancer Survivors; SGP, Supportive Group Psychotherapy; CAU, Care As Usual

Table 5 shows treatment effects post-intervention, and at the follow-up after three and six months. When comparing MGCP-CS with CAU post-intervention, large effect sizes were found on the primary outcome measure personal meaning and secondary outcome goal-orientedness, and medium effect sizes on positive relations, purpose in life, and fighting spirit. At the follow-up after three months, a large effect size was found on helpless/hopeless. At the follow-up after six months, a medium effect size was found on distress, and a small effect on depression (six months FU). When comparing MCGP-CS with SGP, a medium effect size was found for personal growth (three months FU), and environmental mastery (six months FU). When comparing SGP to CAU, a large effect was observed for goal-orientedness (post-intervention).

Table 5 Treatment effects post-intervention (T1), at 3-month (T2) and 6-month (T3) follow-up compared to baseline (T0)

	T1 vs T0			***T2 vs T0***			***T3 vs T0***		
	MCGP-CS -CAU	**MCGP-CS-SGP**	**SGP-CAU**	**MCGP-CS-CAU**	**MCGP-CS-SGP**	**SGP-CAU**	**MCGP-CS-CAU**	**MCGP-CS-SGP**	**SGP-CAU**
	d, *p*	**[1]d, *p***	**d, *p***	**d, *p***	**d, *p***	**d, *p***	**d, *p***	**d, *p***	**d, *p***
PMP									
Total Score	0.81, <.001	0.17, ns	0.66, ns	0.32, ns	0.17, ns	0.18, ns	0.19, ns	0.16, ns	0.03, ns
Goal-orientedness	1.07, <.001	0.23, ns	0.86, <.001	0.37, ns	0.02, ns	0.38, ns	0.08, ns	-0.03, ns	0.12, ns
SPWB									
Positive relations	0.59, .008	0.23, ns	0.41, ns	0.38, ns	0.21, ns	0.18, ns	0.51, ns	0.29, ns	0.27, ns
Environmental mastery	0.47, ns	0.65, .003	-0.22, ns	0.33, ns	0.57, .021	-0.24, ns	0.31, ns	0.66, 0.01	-0.34, ns
Personal growth	0.56, ns	0.58, .022	0.02, ns	0.31, ns	0.57, .031	-0.24, ns	0.16, ns	0.31, ns	-0.14, ns
Purpose in life	0.69, <.001	0.62, ns	0.09, ns	0.48, ns	0.34, ns	0.13, ns	0.12, ns	0.39, ns	-0.26, ns
MAC									
Fighting spirit	0.61, .012	0.54, ns	0.06, ns	0.51, ns	0.04, ns	0.47, ns	0.56, ns	0.04, ns	0.54, ns
Helpless/Hopeless	0.49, ns	0.43, ns	0.04, ns	-0.87, .001	-0.28, ns	-0.58, ns	-0.41, ns	-0.16, ns	-0.32, ns
HADS									
Total score	0.39, ns	0.1, ns	0.32, ns	-0.31, ns	-0.22, ns	-0.05, ns	-0.6, .014	-0.26, ns	-0.45, ns
Depression	-0.51, ns	-0.21, ns	-0.29, ns	-0.32, ns	-0.14, ns	-0.17, ns	-0.38, .017	-0.25, ns	-0.20, ns

Only those scales are shown with significant differences after LMM analysis

[1] d corresponds to between group difference score of Cohen's d

Abbreviations: PMP, Personal Meaning Profile; SPWB, Ryff's Scale of Psychological Well-being; PTGI, Post Traumatic Growth Inventory; HADS, Hospital Anxiety and Depression

Scale; MAC, Mental Adjustment to Cancer Scale; MCGP-CS, Meaning-Centered Group Psychotherapy for Cancer Survivors; SGP, Supportive Group Psychotherapy; CAU, Care As Usual

DISCUSSION

This randomized controlled trial provides evidence for the efficacy of MCGP-CS to improve personal meaning among cancer survivors. With respect to the secondary outcomes, support was found that MCGP-CS also improves goal-orientedness, psychological well-being and adjustment to cancer. Furthermore, that it reduces psychological distress and depressive symptoms in cancer survivors in the long run, at six months after intervention.

The results of this study are in line with the results of a previous study on MCGP for cancer patients in the palliative phase [10], showing that MCGP is not only beneficial for patients with advanced cancer, but also for survivors. Another new finding of the present study is that positive effects of MCGP-CS occurred not only shortly after the intervention but also in the longer term. Although the effect with respect to personal meaning, psychological well-being, and adjustment to cancer decayed, longer-term effects were found on environmental mastery, distress and depressive symptoms. Interestingly, the effect of MCGP-CS on distress and depressive symptoms did only occur at the long-term follow-up. An explanation may be that experiencing personal meaning or purpose after a search for meaning precedes a decrease in psychological distress, in accordance with Park's Meaning Making Model [27]. However, further research is needed to explore this finding.

MCGP-CS had no significant effect on posttraumatic growth (PTG). Growth is considered a part of psychological well-being [28], therefore it was hypothesized that MCGP-CS could improve PTG as well. However, recent empirical findings suggest that PTG is not related to psychological well-being [29]. This might explain why we did not find any effect on PTG. Interestingly, MCGP-CS did have an effect on *personal* growth. Whereas PTG entails growth that is specifically attributed to cancer as a traumatic event, narrowly focusing on the cancer experience, personal growth involves seeing oneself as developing through time and thereby realizing personal potential [19], unrelated to cancer. It may be that MCGP-CS focuses on sense of meaning placed in a broader context of one's personal narrative, and thus addressed personal growth rather than PTG. Further (qualitative) research is needed to examine this effect of MCGP-CS on personal growth.

When compared to CAU, it is clear that MCGP-CS is efficacious in improving personal meaning post-intervention. With respect to secondary outcomes, several improvements were measured until the six-month follow-up. MCGP-CS was equally effective compared to SGP on personal meaning, but more effective on personal growth and environmental mastery, also in the longer-term. When compared to CAU, SGP only had a positive effect on goal-orientedness, and only post-intervention. These findings indicate that in comparison to CAU, MCGP-CS is more efficacious than SGP, which implicates that a meaning-focused approach is more successful than traditional supportive group psychotherapy.

Important strengths of this study were the specific focus on cancer survivors, a large sample size with various types of cancer diagnoses, and high treatment adherence. Furthermore, a strength of MCGP-CS is that it was developed based on both theoretical and empirical knowledge, as well as on input from cancer survivors and clinical experts [17]. A limitation of this study was that no clear cut-off scores or minimal important difference (MID) criteria are available regarding the primary outcome measure personal meaning, and the secondary outcome measures psychological well-being and mental adjustment to cancer. Future research is needed to define cut-off scores and MIDs that may help to identify cancer survivors who might benefit most from MCGP-CS. Also, when interpreting the results of the linear mixed model analyses of the secondary outcome measures, it should be borne in mind that the use of multiple comparisons might only have led to significant results by chance. There is no clear consensus on whether this should be corrected, and a correction might have led to less efficient estimates. Therefore we did not perform a correction, and for every 20 true null hypotheses we expect one to be falsely rejected [30] However, with respect to the post-hoc analyses, Bonferroni corrections were applied. Another limitation is that patients and therapists in the study could not be blinded which may have caused bias. Also, MCGP-CS and SGP were supervised by the same therapists, this incorporates a risk of bleed across conditions; however, no indication for this was found in the evaluation of treatment integrity.

Despite the study limitations, this study provides evidence on the efficacy of MCGP-CS to improve personal meaning, psychological well-being, and mental adjustment to cancer, and to reduce psychological distress and depressive symptoms in the long run. Given that dealing with the aftermath of cancer is both a psychological and an existential challenge for many survivors, an evidence based intervention such as MCGP-CS, that addresses and successfully affects both these aspects, is an important addition to psycho-oncological health care.

REFERENCES

1. Treatment of existential distress in life threatening illness: A review of manualized interventions. *Clin Psychol Rev,* **28**:472–93, 2008
2. McClain CS, Rosenfeld B, Breitbart W. Effect of spiritual well-being on end-of-life despair in terminally-ill cancer patients. *Lancet* **361**:1603–1607, 2003
3. Lethborg C, Aranda S, Cox S, Kissane D. To what extent does meaning mediate adaptation to cancer? The relationship between physical suffering, meaning in life, and connection to others in adjustment to cancer. *Palliat Support Care* **5**:377–88, 2007
4. Tomich PL, Helgeson VS. Five years later: A cross-sectional comparison of breast cancer survivors with healthy women. *Psychooncology* **11**:154–69, 2002
5. Van der Spek N, Vos J, van Uden-Kraan CF, et al. *Meaning Making in Cancer Survivors: A Focus Group Study.* PLoS ONE 8:e76089. doi:10.1371/journal.pone.0076089, 2013
6. Lee V. The existential plight of cancer: meaning making as a concrete approach to the intangible search for meaning. *Support Care Cancer* **16**:779–85, 2008
7. Jaarsma TA, Pool G, Ranchor A V, Sanderman R. The concept and measurement of meaning in life in Dutch cancer patients. *Psychooncology* **16**:241–8, 2007
8. Zika S, Chamberlain K. On the relation between meaning in life and psychological well-being. *Br J Psychol* **83**:133–45, 1992
9. Park CL, Edomondson D, Fenster JR, Blank TO. Meaning Making and Psychological Adjustment Following Cancer: The Mediating Roles of Growth, Life Meaning, and Restored Just-World Beliefs. *J Consult Clin Psychol* **76**: 863–75, 2008.
10. Breitbart W, Rosenfeld B, Pessin H, et al. Meaning-Centered Group Psychotherapy: An Effective Intervention for Improving Psychological Well-Being in Patients With Advanced Cancer. *J Clin Oncol* **33**:749–754, 2015
11. Chochinov HM, Kristjanson LJ, Breitbart W, et al. Effect of dignity therapy on distress and end-of-life experience in terminally ill patients: a randomised controlled trial. *Lancet Oncol* **12**:753–762, 2011
12. Kissane DW, Bloch S, Smith GC, et al: Cognitive-Existential Group Psychotherapy for Women with Primary Breast Cancer: A Randomised Controlled Trial. *Psychooncology* **12**:532–546, 2003
13. Lee V, Cohen SR, Edgar L, et al: Meaning-making intervention during breast or colorectal cancer treatment improves self-esteem, optimism, and self-efficacy. *Soc Sci Med* **62**:3133–3145, 2006
14. Spiegel D, Bloom JR, Yalom I: Group support for patients with metastatic cancer. A randomized outcome study. *Arch Gen Psychiatry* **38**: 527-33, 1981

15. Yalom ID, Greaves C. Group therapy with the terminally ill. *Am J Psychiatry* **134**:396–400, 1977
16. Van der Spek N, van Uden-Kraan CF, Vos J, et al. Meaning-centered group psychotherapy in cancer survivors: a feasibility study. *Psychooncology* **23**: 827–831, 2014
17. Van der Spek N, Vos J, van Uden-Kraan CF, et al. Effectiveness and cost-effectiveness of meaning-centered group psychotherapy in cancer survivors: protocol of a randomized controlled trial. *BMC Psychiatry* **14**:22 doi:10.1186/1471-244X-14-22, 2014
18. Payne DK, Lundberg JC, Brennan MF, et al. A psychosocial intervention for patients with soft tissue sarcoma. *Psychooncology* **6**: 65-71, 1997
19. Dierendonck D. The construct validity of Ryff's Scales of Psychological Well-being and its extension with spiritual well-being. *Pers Individ Dif* **36**:629–643, 2004
20. Jaarsma TA, Pool G, Sanderman R, et al. Psychometric properties of the Dutch version of the posttraumatic growth inventory among cancer patients. *Psychooncology* **15**: 911-920, 2006
21. Watson M, Greer S, Young J, et al. Development of a questionnaire measure of adjustment to cancer: the MAC Scale. *Psychol Med* **18**:203–209, 1988
22. Ten Klooster PM, Weekers AM, Eggelmeijers F, et al. Optimisme en/of pessimisme: factorstructuur van de Nederlandse Life Orientation Test-Revised. *Psychol en Gezondheid*, **38**:89–100, 2010
23. Young MA, Halper IS, Clark DC, et al. An item-response theory evaluation of the Beck Hopelessness Scale. *Cognit Ther Res* **16**:579–87, 1992
24. Spinhoven P. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. *Psychol Med*. **27**: 363–70, 1997
25. Fayers P, Bottomley A. Quality of life research within the EORTC-the EORTC QLQ - C30. European Organisation for Research and Treatment of Cancer. *Eur J Cancer* **38**:125–133, 2002
26. Cohen J. *Statistical power analysis for the behavioral sciences.* London: Routledge; 1977
27. Park CL. Making sense of the meaning literature: an integrative review of meaning making and its effects on adjustment to stressful life events. *Psychol Bull* **136**: 257–301, 2010
28. Wong TP. *The human quest for meaning.* New York, USA, Routledge, Taylor & Francis Group, 2010, pp 235
29. Zoellner T, Rabe S, Karl A, et al. Post-traumatic growth as outcome of a cognitive-behavioural therapy trial for motor vehicle accident survivors with PTSD. *Psychol Psychother* **84**: 201–213, 2011
30. Gelman A, Hill J, Yajima M. Why We (Usually) Don't Have to Worry About Multiple Comparisons. *J Res Educ Eff* **5**:189–211, 2012

Chapter 6

Cost-utility analysis of meaning-centered group psychotherapy for cancer survivors

Submitted:

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ABSTRACT

Purpose. Meaning-centered group psychotherapy for cancer survivors (MCGP-CS) was found to be effective in improving meaning, psychological well-being, and mental adjustment to cancer and to reduce psychological distress. The present study aims to describe the cost-utility of MCGP-CS compared to supportive group psychotherapy (SGP) and care as usual (CAU), within the context of a randomized controlled trial.

Methods. A total of 170 patients were randomized to MCGP-CS, SGP, or CAU. Intervention costs, direct medical and non-medical costs, productivity losses and health related quality of life were measured until six months follow-up, using the TIC-P, PRODISQ, data from the hospital information system, and the EQ-5D. The cost-utility was calculated by comparing mean cumulative costs and quality adjusted life years (QALYs) of MCGP-CS, SGP, and CAU.

Results. After imputation of missing data, there were no significant differences in mean cumulative costs and mean number of QALYs between the three groups. MCGP-CS had a probability of 74% to be less costly and more effective than CAU, and 49% compared to SGP. Additional analyses assessing the robustness of these findings showed that, compared to CAU, MCGP-CS had a probability of 54-74% to be less costly and more effective. The probability that MCGP-CS is less costly and more effective compared to SGP was 48-55%. Comparing SGP to CAU, the probability that SGP is less costly and more effective was 22-49%. If society is willing to pay €0 for one gained QALY, MCGP-CS has a 78% probability of being cost-effective compared to care as usual. This increases to 85% and 92% at willingness-to-pay thresholds of €10000 and €30000, respectively.

Conclusion. MCGP-CS is likely to be more effective and less costly than CAU, while it is probably more effective and equally expensive when compared to SGP.

INTRODUCTION

Due to continuing innovations in the detection and treatment of cancer, more and more cancer patients become long-term survivors [1]. Although this is a positive development, often cancer survivorship comes with long-lasting hindrances in the patient's life, such as limitations of activities in daily living, functional and physical limitations, psychological problems, and work related problems [2]data from the National Health Interview Survey (years 1998-2000. Carlson and Bultz [3] argued that psychological treatment can lead to a decrease in health care use in cancer patients, and may be a corner stone in cost-effective cancer care, to meet the growing need for psychosocial care for cancer survivors. However, economic evaluations of psychosocial interventions for cancer patients altogether are scarce.

Meaning-centered group psychotherapy (MCGP) was developed to sustain or enhance a sense of meaning in cancer patients, and has shown to be effective in increasing spiritual well-being and quality of life, and reducing hopelessness, depression, and desire for hastened death in patients with advanced cancer [4]. Recently, a randomized controlled trial was conducted to evaluate the efficacy of meaning-centered group psychotherapy for cancer survivors (MCGP-CS) [5, 6]. The outcomes of this study showed that MCGP-CS, compared to supportive group psychotherapy (SGP) and care as usual (CAU), was effective in improving sense of meaning, psychological well-being, and mental adjustment to cancer, and to reduce psychological distress up until six months after intervention. The evidence of beneficial effects of meaning-focused interventions is thus growing [4, 7–11], yet no studies have been performed from an economical perspective. The aim of the present study was therefore to evaluate the cost-utility of MCGP-CS in comparison with SGP and CAU among cancer survivors, within the context of a randomized controlled trial.

METHODS

Setting and participants

The trial was performed in the Netherlands from August 2012 till May 2015. The study protocol was approved by the Medical Ethical Committee of the Leiden University Medical Center in Leiden. Cancer survivors were recruited via several hospitals and public media. Inclusion criteria were*:* cancer diagnosis in the last 5 years, treated with curative intent, main treatment completed (i.e. surgery, radiotherapy, chemotherapy), ability to attend all therapy sessions, expressed need for psychological help/support and at least one psychosocial complaint (e.g. depressed mood, anxiety, coping issues, life questions, meaning making problems, relationship problems). Exclusion criteria were*:* severe cognitive impairment, current psychological treatment and insufficient mastery of Dutch language. The study protocol and results on the clinical efficacy of MCGP-CS were published elsewhere [5, 6].

Design and randomization

Economic data was collected alongside the randomized controlled trial [5,6] at baseline, and at three and six months follow up. This study was a three-study arm randomized controlled trial with block randomization. A computer-generated randomization table with random block sizes, was prepared by an independent researcher not involved in the study. Participants were allocated to a group. When the group counted between seven and ten survivors, the group was randomly assigned by the independent researcher using a list of sequentially numbered allocations, to one of the three study arms. Participants and psychotherapists were aware of the allocated arm, whereas data managers were blinded to the allocation.

Meaning-centered group psychotherapy for cancer survivors (MCGP-CS)

Cancer survivors in the experimental study arm participated in MCGP-CS, a manualized 8-week intervention that makes use of didactics, group discussion and experiental exercises that focus around themes related to meaning and cancer survivorship. The sessions took two hours each and were held weekly. The participants used a workbook (called *Life lessons portfolio*) and received homework assignments every week. MCGP-CS was led by a psychotherapist with experience in treating patients with cancer. The main purpose of the MCGP-CS is to sustain or enhance a sense of meaning or purpose in the patient's life, in order to cope better with the consequences of cancer.

Supportive group psychotherapy (SGP)

The control condition is an 8-week social support group following Payne et al [12]. The sessions took two hours and were held weekly. Each group was supervised by a psychotherapist with experience in treating patients with cancer. The psychotherapist had an unconditionally positive regard and empathetic understanding, stimulated patients to actively share their experiences, and focused on positive emotions, and expression of feelings.

Care as usual (CAU)

Cancer survivors assigned to the CAU study arm did not participate in one of the group interventions. If a patient in the CAU study arm asked the researcher for psychological help after allocation, he or she was referred to their general practitioner (GP).

Outcome assessment

Patients could choose to complete questionnaires either online or via pencil-and-paper. The Patient Reported Outcome Measures (PROMs) were collected at all time points: baseline (T0), after one week (T1), 3 months (T2), and 6 months (T3). Cost evaluation outcomes were collected at T0, T2, and T3.

Direct medical and direct non-medical cost data were collected with the Trimbos and iMTA questionnaire on Costs associated with Psychiatric illness (TiC-P) [13]. The TiC-P measures the use of healthcare facilities (e.g. number of visits to the GP) and other facilities (e.g. participation in self-help groups or use of informal care) in the past four weeks, and medication use (i.e. antidepressants, painkiller, and sedative) in the past two weeks. In addition, healthcare utilization within the hospital during the study (i.e. visits to the medical specialist, day treatment, and hospital admission) was collected using the hospital information system. Unit resource use (GP visits, hospital days, etc.) was multiplied by their appropriate integral cost prices [14]. Direct non-medical traveling costs to health care services, including parking costs, were calculated by multiplying unit resource use by average distance to the location (e.g. GP or hospital) times the price per km. All prices were adjusted to 2014 prices using the consumer price index.

Productivity losses through lost workdays (absenteeism) and reduced quantity or quality of performed paid work (presenteeism) were sampled with the appropriate modules of The Productivity and Disease Questionnaire (PRODISQ) [17]. Productivity losses due to presenteeism were calculated by multiplying the days of less productivity at work by the estimated amount of lost quantity or quality of the performed work (ranging from 0-10 on a 10-point scale). Indirect non-medical costs due to absenteeism and presenteeism were calculated by multiplying productivity losses by respectively age and gender specific costs [14] using the human capital approach.

Health-related quality of life was assessed with the EuroQoL-5D (EQ-5D), the utility score was obtained using the Dutch index tariff [15, 16].

The primary outcome measures in the effectiveness study [5,6] on meaning were the Dutch Personal Meaning Profile (PMP-DV) [17], the Dutch Posttraumatic Growth Inventory (PTGI) [18] and the Ryff's Scale of Psychological Well-being (SPWB) [19]. Secondary outcome measures were adjustment to cancer (Mental Adjustment to Cancer, MAC) [20]; optimism (Life Orientation Test, LOT-R) [21]; hopelessness, (Beck Hopelessness Scale, BHS) [22]; distress (Hospital Anxiety and Depression Scale, HADS)[23]; and quality of life (the EORTC QLQ-C30 version 3.0) [24].

Intervention costs

Intervention costs were calculated using a bottom-up approach. The costs of MCGP-CS per patient consisted of costs for intake by a psychotherapist (€21.98), direct time of a psychotherapist for the provision of eight two-hour MCGP-CS sessions in groups of 8 (€175.87 per patient), indirect time of a psychotherapist of one hour per MCGP-CS session (€87.94 per patient) and costs of a workbook (€2,50). The costs of SGP were similar, except that no workbook was provided. Total costs per patient were consequently €288,- for patients in the MCGP-CS group and €286,- for patients in the SGP group.

Statistical analyses

All analyses were performed using the IBM Statistical Package for the Social Science (SPSS) version 22 (IBM Corp., Armonk, NY USA) and STATA version 12.1 (StataCorp LP, Texas, USA). Descriptive statistics were used to describe patient characteristics, costs in different resource use categories and EQ-5D utility scores per group at the different time points.

To assess the cost-utility of MCGP-CS compared to SGP and to CAU, and the cost-utility of SGP compared to CAU, a base case intention-to-treat cost-utility analysis was performed. In this base case analysis, all patients were included. Missing data were imputed as total costs or utility score. Imputation was done per time point per treatment arm using multiple imputation (predictive mean matching) by chained equations. Linear and logistic regression analyses were performed to investigate which variables (i.e. socio-demographic, clinical and several PROMs) were associated with missing data, observed costs or EQ-5D utility scores. Variables that were found to be associated with missing data (i.e. LOT-R total score), total cost (i.e. work situation, cancer type, time since last treatment, age and MAC fighting spirit), or EQ-5D utility score (i.e. work situation, history of psychological treatment, gender, and PMP total score) were included in the multiple imputation model. In addition, variables found to differ statistically between the treatment groups at baseline (i.e. gender, SPWB positive relations and spiritual change) were included in the multiple imputation model. Ten imputed datasets were created and analyzed separately. Results of the ten analyses were pooled using Rubin's (1987) rules.

Subsequently, cumulative costs and QALYs per patient per treatment group were calculated. Costs between T0 and T3, as measured using the TIC-P and PRODISQ, were calculated for the three groups using linear interpolation, by summing costs in the last 4 weeks at time point T0 and multiplying by 2 for the time period T0 to T1 (8 weeks), and summing the costs in the last 4 weeks at time point T2 and T3, multiplying by their corresponding time period of 3 months (respectively T1 to T2 and T2 to T3). Total cumulative costs per patient were calculated by summing costs measured using the TIC-P and PRODISQ with intervention costs and costs measured using the hospital information system. The number of QALYs per patient was calculated by multiplying the EQ-5D utility score by the appropriate time period it accounts for using linear interpolation, with the same calculation as the cumulative costs.

An incremental cost-utility ratio (ICUR) for each of the comparisons (MCGP-CS vs CAU; MCGP-CS vs SGP; SGP vs CAU) was calculated to obtain the costs per gained QALY by dividing the incremental costs by the incremental effects using the following formula: $(\text{mean Costs}_{\text{intervention}} - \text{mean Costs}_{\text{comparator}}) / (\text{mean QALYs}_{\text{intervention}} - \text{mean QALYs}_{\text{comparator}})$.

To study the impact of uncertainty on the cost and QALY estimates per treatment group, we used bootstrapping with 5,000 replications. The results were projected on a cost-utility plane. In the cost-utility plane, we depicted the incremental costs between conditions (MCGP-CS vs CAU; MCGP-CS vs SGP; SGP vs CAU), on the y-axis, while the incremental QALYs were presented on the x-axis, resulting in four different quadrants. The north-east quadrant indicates the intervention is more expensive and more effective compared to the control group, the south-east quadrant indicates the intervention is less expensive and more effective, the south-west quadrant indicates the intervention is less expensive and less effective and finally, the north-west quadrant indicates the intervention is more expensive and less effective. When the intervention is more effective but at additional costs (north-east quadrant), a trade-off has to be made between gained QALYs and additional costs (i.e. do the gained QALYs justify the additional costs). A cost-utility acceptability curve was therefore plotted, which presents the probability that the intervention is cost-effective compared to the control group for different willingness-to-pay values for one QALY gained.

To assess the robustness of the findings of the base case analysis, three additional analyses were performed: 1) a complete cases cost-utility analysis including only patients with complete data at all time points; 2) an intention to treat-analysis in which costs and quality of life measured at T2 were hypothesized to be representative for the time period T0-T2 (instead of the T0 measurement in the base case intention-to-treat analyses); and 3) an analysis in which we investigated whether adjusting for variables at baseline (i.e. total costs at baseline, EQ-5D score at baseline, gender, SPWB positive relations, spiritual change and employment status) had a major impact (i.e. a change of ≥ 20%) on incremental costs or incremental effects.

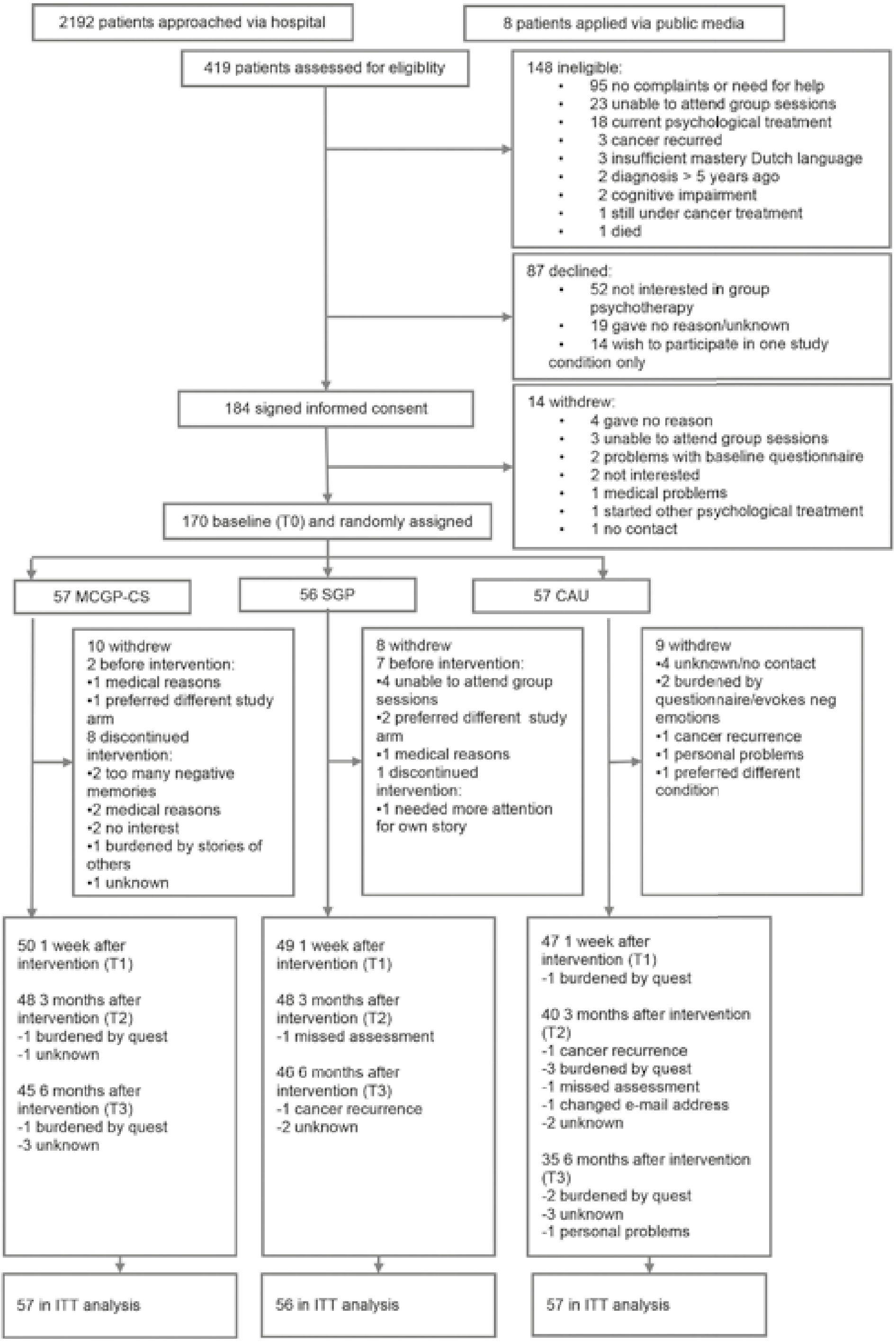

Figure 1 CONSORT diagram. Meaning-centered group psychotherapy for cancer survivors (MCGP-CS), supportive group psychotherapy (SGP), and care as usual (CAU).

RESULTS

The flow diagram of recruitment and inclusion of patients is shown in Figure 1. Of the 184 eligible participants, 170 (40 male, 130 female) completed the baseline questionnaire and were randomly assigned to MCGP-CS (n = 57), SGP (n = 56), or CAU (n = 57). Table 1 displays the sociodemographic and clinical characteristics of the total study population. There was a significant difference with respect to gender between the three groups, with more males in the MCGP-CS condition. In the SGP group, 1 patient deceased after randomization, but before the start of the intervention. A total of 110 participants (65%) completed the cost evaluation assessment at all time points (T0, T2, T3).

Direct and indirect medical costs and productivity costs

The mean costs per time point and per study arm of all 170 participants are presented in Table 2. In the four weeks prior to baseline assessment (T0), the total mean costs in the MCGP-CS group were €521 (SD = 1185), in the SGP group €478 (SD = 670) and in the CAU group € 550 (SD = 1007), these differences were not statistically different (*p* = .93). In all three groups, the productivity costs were the largest expense.

Health-related quality of life

Table 3 presents the mean EQ-5D utility scores per group and per time point. There was no statistically significant difference in the EQ-5D utility scores between the three conditions at baseline (*p* = .99)

Table 1 Participant characteristics

	MCGP-CS (n = 57)	**SGP (n = 56)**	**CAU (n = 57)**	**P**	**χ^2**
Age Mean (SD)	58.6 (10.7)	55.5 (9.6)	57.3(10.4)	.340	2.58
Sex Female N (%)	40 (70%)*	49 (88%)	51 (90%)	.012	8.83
Level of education				.156	6.65
Low	18 (32%)	9 (16%)	17 (30%)		
Medium	20 (35%)	25 (45%)	14 (26%)		
High	19 (33%)	22 (39%)	25 (44%)		
Religion				.181	3.42
Christian	23 (40%)	32 (57%)	30 (53%)		
No religion	34 (60%)	24 (43%)	27 (47%)		
Marital status Single N (%)	12 (21%)	9 (16%)	13 (23%)	.650	0.86
Work situation					
Paid job	26 (46%)	31 (57%)	31 (56%)	.441	1.64
No paid job/retired	30 (54%)	23 (43%)	24 (44%)		
Household composition					
Lives alone	10 (18%)	11 (20%)	11 (19%)		
Lives with partner	28 (49%)	27 (48%)	21 (37%)		
Lives with children	2 (4%)	1 (2%)	3 (5%)		
Lives with partner and children	17 (30%)	17 (30%)	22 (39%)		
Type of cancer				.071	8.63
Breast	30 (53%)	40 (71%)	42 (74%)		
Colon	15 (26%)	12 (21%)	10 (18%)		
Other	12 (21%)	4 (7%)	5 (9%)		
Months since last cancer treatment Median (range)	19 (6-58)	16 (5-52)	18 (3-55)	.888	0.24[1]
Type of treatment					
Chemotherapy N (%)	26 (53%)	34 (61%)	36 (67%)	.124	4.18
Surgery N (%)	57 (100%)	56 (100%)	56 (98%)	.369	1.99
Radiation N (%)	31 (54%)	32 (57%)	33 (58%)	.924	0.16
Hormonal therapy N (%)	22 (30%)	28 (47%)	30 (47%)	.280	2.54
History psychological treatment N (%)				.724	3.65
Received psychological treatment in the last year	12 (21%)	11 (20%)	7 (13%)		
Received psychological treatment > 1 year ago	21 (37%)	21 (37%)	17 (31%)		
Never received psychological treatment before	24 (42%)	24 (43%)	31 (56%)		
Significant negative event in past 2 years other than cancer N (%)	27 (47%)	31 (54%)	33 (55%)		

[1] Kruskall Wallis

*significant difference between MCGP-CS and CAU

Table 2 Mean costs in the past four weeks per time point Abbreviations: SD, standard deviation; DDD, defined daily dose; T0, baseline assessment; T2, assessment three months after intervention;T3, assessment six months after intervention.

		MCGP-CS				SGP				CAU			
	Reference price per unit index year 2014 (€)	**T0 (n=57) Mean(SD)**	**T2 (n = 47) Mean(SD)**	**T3 (n = 43) Mean(SD)**	**T0 to T3 Mean(SD)**	**T0 (n = 55) Mean(SD)**	**T2 (n = 47) Mean(SD)**	**T3 (n = 45) Mean(SD)**	**T0 to T3 Mean(SD)**	**T0 (n = 55) Mean(SD)**	**T2 (n = 37) Mean(SD)**	**T3 (n = 31) Mean(SD)**	**T0 to T3 Mean(SD)**
Total costs per time point		521 (1185)	374 (837)	389 (799)		478 (670)	344 (482)	450 (803)		550 (1007)	417 (859)	577 (964)	
Direct medical costs		127 (205)	114 (143)	105 (132)		160 (288)	105 (120)	177 (362)		127 (146)	100 (144)	177 (22)	
General practitioner	31	17 (22)	19 (24)	23 (30)		13 (28)	18 (29)	19 (27)		21 (29)	16 (31)	26 (30)	
Company doctor	68	12 (41)	7 (22)	0		9 (23)	3 (14)	5 (17)		11 (29)	2 (11)	7 (20)	
Social worker (company)	71	2 (13)	2 (10)	0		0	2 (10)	2 (11)		0	0	0	
Social worker (general)	71	0	3 (21)	5 (24)		8 (40)	3 (21)	6 (42)		4 (29)	0	5 (18)	
Physiotherapist	40	39 (83)	43 (88)	40 (74)		63 (92)	43 (86)	48 (79)		70 (122)	48 (88)	77 (100)	
Dietitian	30	3 (14)	2 (6)	3 (12)		6 (27)	6 (17)	1 (6)		1 (4)	0	1 (5)	
Psychological help (private practice)	85	12 (44)	5 (21)	2 (13)		0	4 (17)	2 (13)		3 (23)	9 (33)	3 (15)	
Psychological help (out-patient)	188	16 (74)	8 (55)	9 (57)		24 (136)	4 (27)	25 (118)		0	0	12 (47)	
Psychological help (addiction)	188	0	0	0		0	0	0		0	0	0	
Psychological help (mental hospital)	190	0	0	0		0	0	8 (40)		3 (26)	5 (31)	12 (68)	
Spiritual counsellor	129	11 (70)	8 (56)	9 (59)		12 (71)	0	3 (19)		0	7 (42)	4 (23)	
House cleaning	26	2 (14)	6 (27)	2 (16)		5 (25)	0	0		2 (13)	15 (66)	18 (72)	
Personal care	48	0	0	0		0	0	0		0	0	0	
Visiting nurse	71	0	0	0		9 (67)	9 (62)	44 (296)		0	0	0	

Continuation of Table 2

Medication	0.52 – 1.65 per DDD	11 (18)	11 (20)	11 (21)		11 (20)	14 (22)	13 (24)		12 (20)	9 (19)	12 (20)	
Specialist	79				521 (433)				617 (558)				730 (729)
Day treatment	276				82 (317)				61 (212)				161 (386)
Hospitalization	502				79 (422)				56 (252)				37 (132)
<u>Direct non-medical costs</u>		69 (136)	31 (62)	47 (121)		66 (129)	43 (117)	30 (72)		74 (210)	39 (104)	106 (206)	
Support groups	58	39 (105)	19 (59)	25 (95)		39 (99)	32 (112)	16 (66)		67 (208)	17 (49)	73 (163)	
Informal care	13	25 (83)	9 (26)	19 (65)		23 (82)	8 (28)	11 (45)		5 (14)	22 (96)	26 (95)	
Transport and parking costs	0.22 per km / 3.30 parking	4 (9)	3 (4)	2 (4)		4 (13)	2 (4)	3 (7)		3 (3)	3 (4)	7 (10)	
<u>Indirect non-medical costs</u>		325 (1069)	229 (993)	238 (731)		256 (605)	196 (445)	237 (587)		342 (880)	271 (794)	285 (705)	
Absenteeism paid work	9.30 – 41.93 per hour	228 (875)	112 (428)	170 (653)		178 (565)	99 (337)	177 (550)		287 (794)	262 (781)	225 (687)	
Presenteeism paid work	9.30 – 41.93 per hour	97 (258)	118 (387)	68 (231)		78 (199)	97 (261)	60 (168)		55 (252)	9 (33)	60 (232)	

Table 3 Mean EQ-5D utility score per time point (n=170)

Time point	MCGP-CS Mean (SD)	SGP Mean (SD)	CAU Mean (SD)
T0 Baseline	0.79 (0.17)	0.79 (0.18)	0.79 (0.18)
T1			
T2 (3 months after intervention)	0.82 (0.21)	0.77 (0.14)	0.79 (0.16)
T3 (6 months after intervention)	0.83 (0.21)	0.80 (0.17)	0.77 (0.21)

T0, baseline assessment; T2, assessment three months after intervention; T3, assessment six months after intervention

Table 4 Results of the different cost-utility analyses

	Costs (€) Mean (SEM)	QALYs Mean (SEM)	Incremental costs € [95% CI]			Incremental effect QALYs [95% CI]		
			MCGP–CAU	MCGP–SGP	SGP–CAU	MCGP–CAU	MCG–SGP	SGP–CAU
Base case analysis (n=170)			-812 [-2830-1350]	-53 [-1826-1979]	-759 [-2625-972]	.033 [-.007-.074]	.029 [-.012-.070]	.004 [-.036-.044]
- MCGP-CS (n=57)	4492 (778)	.540 (.016)						
- SGP (n=56)	4545 (580)	.511 (.014)						
- CAU (n=57)	5304 (722)	.507 (.014)						
Sensitivity analysis: complete case analysis (n=110)			-560 [-4146-2594]	-575 [-2774-2192]	15 [-3514-2635]	.024 [-.028-.072]	.030 [-.016-.071]	-.006 [-.049-.039]
- MCGP-CS (n=42)	4066 (1001)	.550 (.018)						
- SGP (n=41)	4641 (770)	.520 (.013)						
- CAU (n=27)	4626 (1371)	.526 (.018)						
Sensitivity analysis: unadjusted (n=170)			-843 [-2736-1168]	-139 [-1723-1726]	-704 [-2444-845]	.041 [-.004-.087]	.037 [-.007-.082]	.004 [-.041-.049]
- MCGP-CS (n=57)	4197 (725)	.544 (.018)						
- SGP (n=56)	4336 (499)	.507 (.015)						
- CAU (n=57)	5040 (678)	.503 (.018)						

* significant difference between the two groups (p<.05)

Cost-utility analyses

Table 4 shows the results of the base case intention-to-treat cost-utility analysis with imputed data (n = 170). There was no significant difference in costs and QALYs between the three conditions. When comparing MCGP-CS to CAU, the incremental costs were €812 [95% CI:-2830-1350], and the incremental effects were .033 [95% CI:-007-074]. The uncertainty surrounding this finding was assessed using bootstrapping and projected on a cost-utility plane (Figure 2). The same data were used to plot the acceptability curve (Figure 3), showing the probability that MCGP-CS was cost-effective compared to CAU, for a range of willingness-to-pay values. Of the bootstrapped cost-utility pairs when MCGP-CS was compared to CAU, 74% fell in the SE quadrant, representing the probability that MCGP-CS is more effective and less costly than CAU. The probability of MCGP-CS being more effective in gaining QALYs than CAU is 94%, and the probability that MCGP-CS is less costly compared to CAU is 78%. Figure 3 shows that MCGP-CS has a 78% probability of being cost-effective if society is willing to pay €0 for one gained QALY, this increases to 85% at €10000 and to 92% at €30000.

The incremental costs in the comparison of MCGP-CS to SGP, were €-53 [95% CI:-1826-1979], and the incremental effects were .029 [95% CI:-.012-.070]. Of the bootstrapped cost-utility pairs, 49% fell in the SE quadrant, representing the probability that MCGP-CS is more effective and less costly than SGP. The probability of MCGP-CS being more effective in gaining QALYs than SGP is 91%, and the probability that MCGP-CS is less costly compared to SGP is 53% (Figure 4). Figure 5 shows that MCGP-CS has a 52% probability of being cost-effective if society is willing to pay €0 for one gained QALY, this increases to 63% at €10000 and to 77% at €30000.

Between SGP and CAU, the incremental costs were €-759 [95% CI:-2625-972], and the incremental effects were -.004 [95% CI:-.036-.044]. Of the bootstrapped cost-utility pairs, 49% fell in the SE quadrant, representing the probability that SGP is more effective and less costly than CAU. The probability of SGP being more effective in gaining QALYs than CAU is 58%, and the probability that SGP is less costly compared to CAU is 79% (Figure 6). Figure 7 shows that SGP has a 80% probability of being cost-effective if society is willing to pay €0 for one gained QALY, this does not increase if society is willing to pay more.

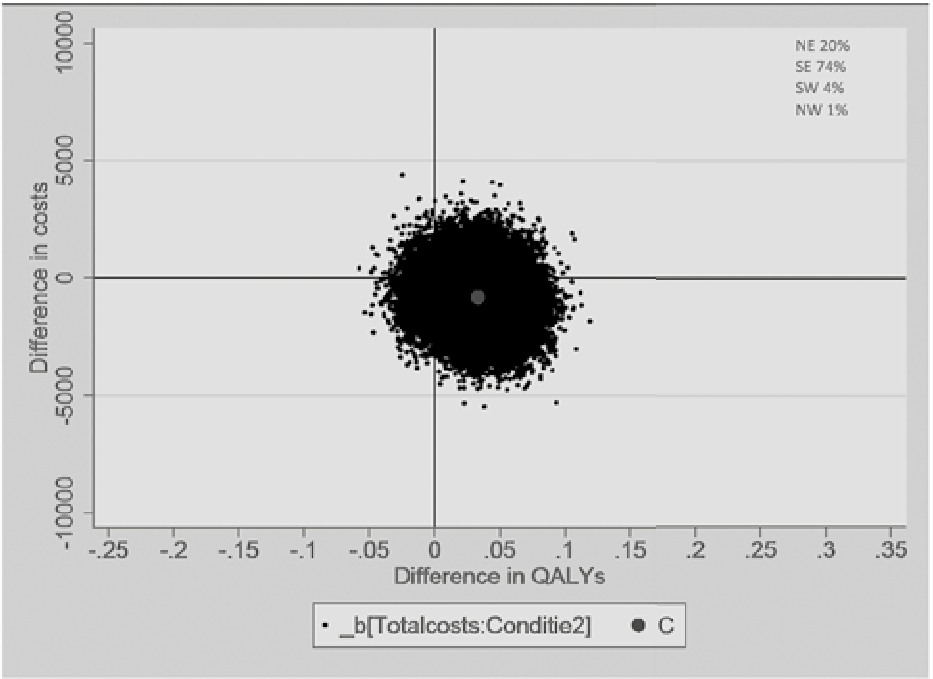

Figure 2 Cost-effectiveness plane of MCGP-CS compared to CAU

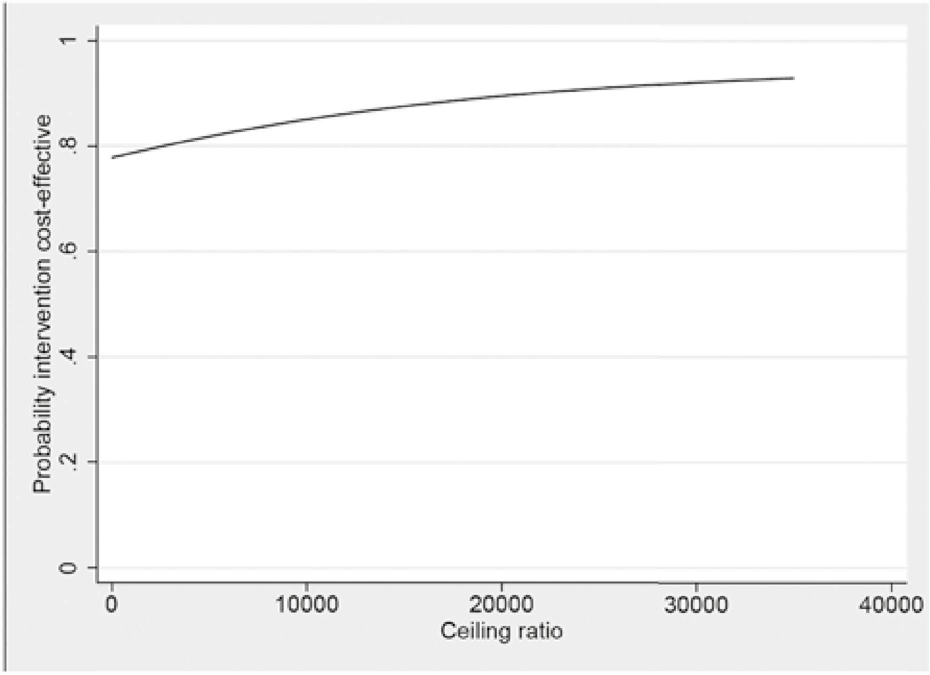

Figure 3 Cost-effectiveness acceptability curve of MCGP-CS compared to CAU

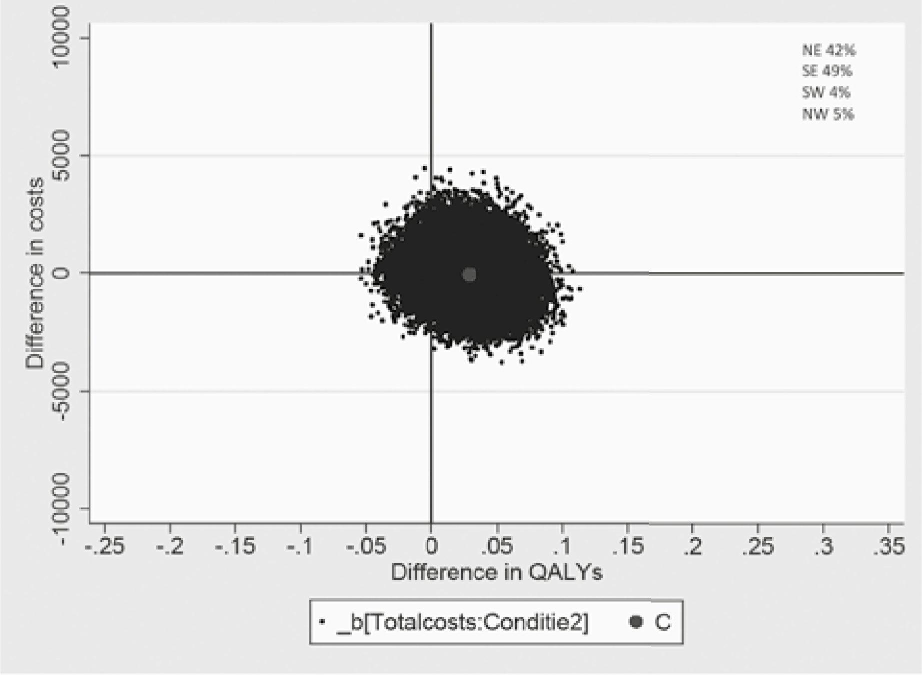

Figure 4 Cost-effectiveness plane of MCGP-CS compared to SGP

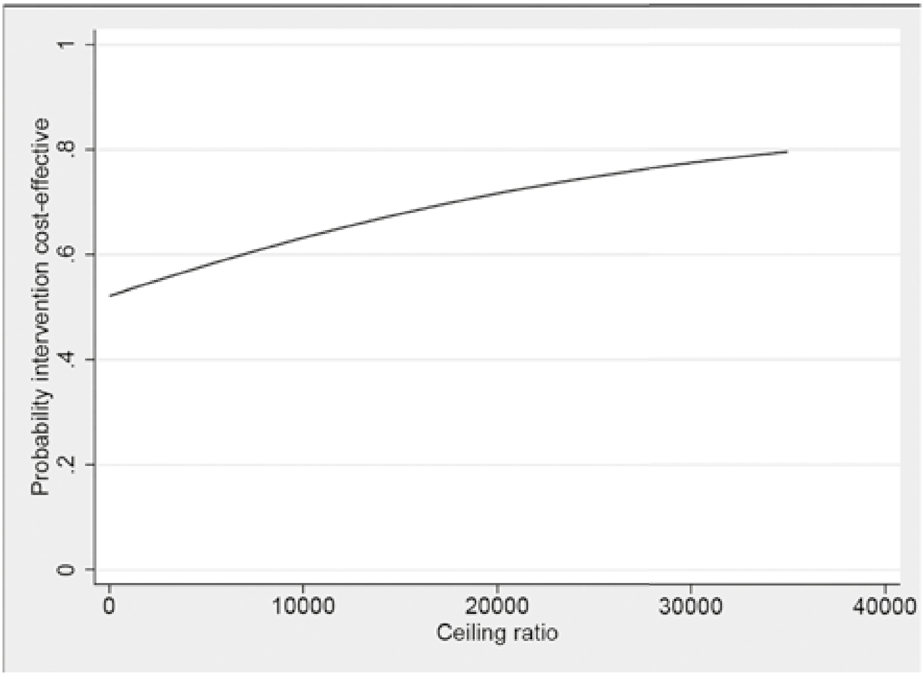

Figure 5 Cost-effectiveness acceptability curve of MCGP-CS compared to SGP

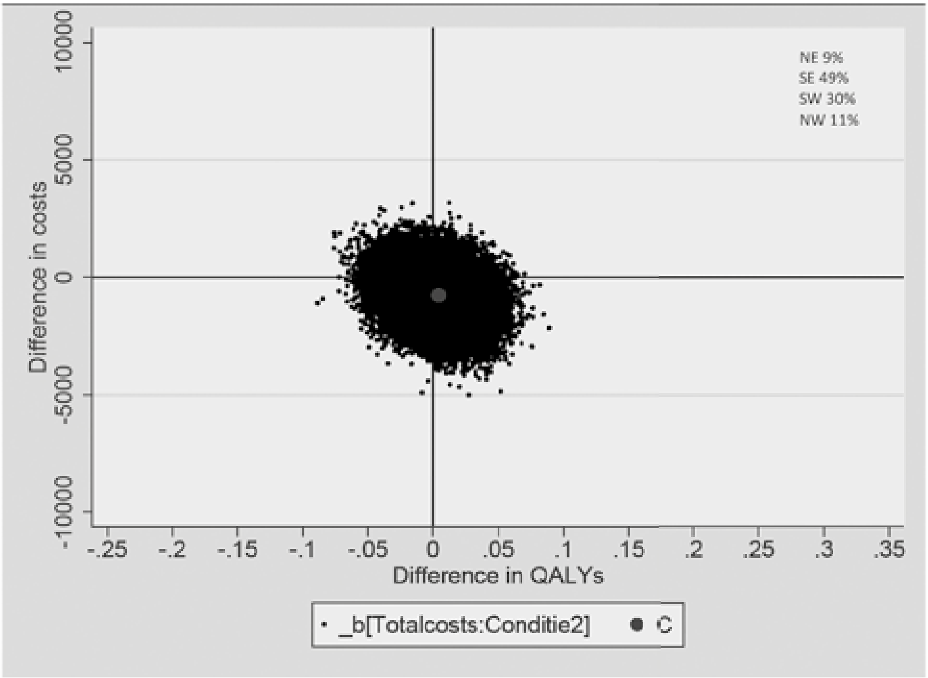

Figure 6 Cost-effectiveness plane of SGP compared to CAU

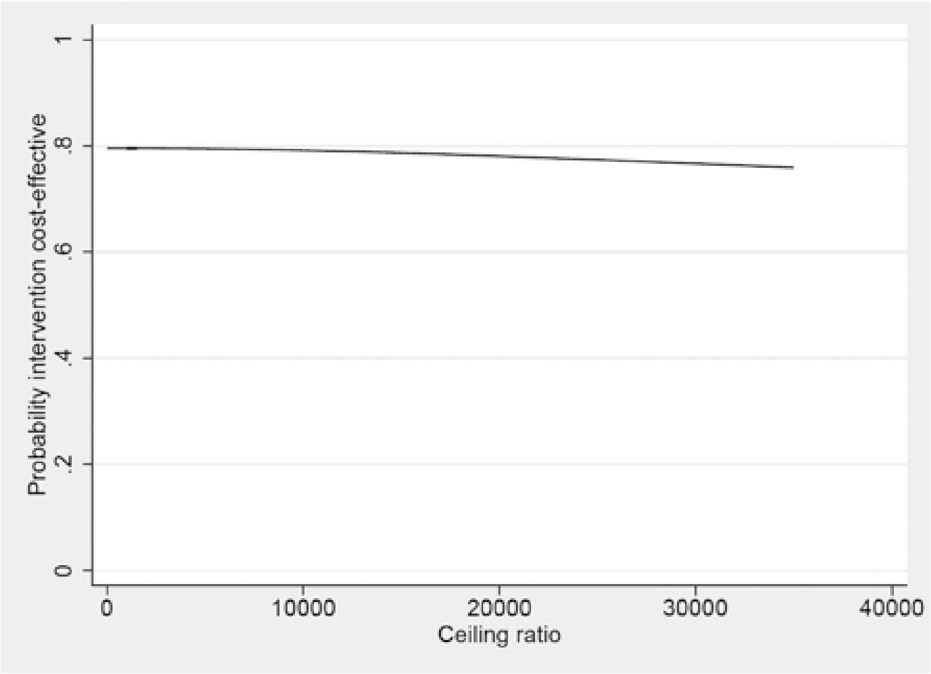

Figure 7 Cost-effectiveness acceptability curve of SGP compared to CAU

Sensitivity analyses

To assess the robustness of findings additional analyses were performed (Table 4). The complete case and intention-to-treat analyses showed that MCGP-CS had a probability of 54%-78% to be less costly and more effective compared to CAU, that MCGP-CS had a probability of 55%-64% to be less costly and more effective compared to SGP, and that SGP had a probability of 22%-47% to be less costly and more effective compared to CAU. In addition, adjusting for differences in variables at baseline did not influence incremental costs or incremental effects with more than 20%. These findings indicate that the results of the base case intention-to-treat cost-utility analysis are robust.

DISCUSSION

This is the first economic evaluation of a meaning-focused intervention for cancer patients from a societal perspective, incorporating both medical costs and non-medical costs (e.g. productivity losses and informal care costs). Evidence of the superiority of MCGP-CS over CAU and SGP, in terms of efficacy, was already found in a previous study [5]. The cost-utility analyses in the present study provided support to the hypothesis that the MCGP-CS is likely to be more cost-effective compared to CAU, and showed that MCGP-CS is probably more effective, but not less costly than SGP.

From a societal perspective, it can be concluded that compared to CAU, the probability is 83-97% that MCGP-CS is the most effective option and the probability is 63-81% that MCGP-CS leads to cost-savings. Compared to SGP, there is a probability of 91-95% that MCGP-CS is more effective, and it is probably comparably expensive (52-58%). However, further appropriately powered research is required to verify this finding. In addition, MCGP-CS has a 78% probability of being cost-effective, compared to CAU, if society is willing to pay €0 for one gained QALY, this increases to 85% at €10000/QALY and to 92% at €30000/QALY. Commonly accepted prevailing ceiling ratios are €20000 to €30000 for one QALY [25, 26].

Economic evaluations of psychosocial interventions for cancer patients up until now are scarce. Most of these studies find promising results, showing that psychosocial interventions for cancer patients can be cost-effective at potentially acceptable willingness-to-pay thresholds, and some interventions are even likely to be cost-effective at a willingness-to-pay threshold of zero [27–29], this is similar to our findings. However, this study is the first to assess the cost-utility of a meaning-focused group intervention for cancer survivors from a societal perspective, therefore we are not able to directly compare our findings with previous studies. One economic evaluation has been conducted on supportive-expressive group therapy (SEGT), which focuses on emotional expression, social support, coping, and also on existential issues, including meaning [30]. This study among patients with metastatic breast cancer, did not find evidence for lower costs in the intervention group, which is in contrast to our findings. A possible explanation is that our study used a broader scope of medical costs (i.e. not only hospital costs), and in addition, we included productivity costs and informal care costs. Also, our study targeted cancer survivors, while the SEGT-study targeted advanced cancer patients.

The present study has several limitations. First, the estimates of medical costs outside the hospital were based on self-report, which might be less accurate than data from public registers. However, there is empirical support that medical self-report data is comparable to register collected data [31]. Second, the assessments at all time points did not fully cover the actual costs made during the study period, so for the cost calculation we partly had to rely on estimates, which are less accurate. However, we conducted several sensitivity analyses around these estimates, showing that the findings were robust. Third, these results are based on the Dutch situation and costs, and are not necessarily valid in other countries. Finally, the results need to be interpreted with caution, because the differences in QALYs gained and total costs between the three conditions did not reach statistical significance, and the trial was under-powered to detect such differences. For this reason, a probabilistic approach to economic analyses alongside trials is applied, rather than reliance upon significance levels [32].

We have some recommendations for future studies. Economic evaluations are often underpowered, so this calls for more studies and moreover for systematic reviews on economic evaluations of psychosocial interventions, including meaning-focused treatments, to obtain more insight into what extend these interventions for cancer patients are economically beneficial. Furthermore, in this study we only took patient-related costs into account, while there might be an effect on costs made by caregivers as well (e.g. productivity losses due to caregiving, or increased health care use due to caregiving burden). Although we investigated informal care costs, this could further be explored. It would be interesting if future economic evaluations on psychosocial interventions would take costs made by caregivers into account, to give a more complete insight in the value for money of these interventions.

CONCLUSIONS

The results of this study show that MCGP-CS is more effective and less costly than CAU, while it is probably more effective and equally expensive, compared to SGP. More research on the economic benefits of psychosocial interventions in oncology, from a societal perspective are needed.

REFERENCES

1. *National Cancer Institute SEER Cancer Statistics Review* 1975-2009. 2010.
2. Hewitt M, Rowland JH, Yancik R. Cancer survivors in the United States: age, health, and disability. *J Gerontol A Biol Sci Med Sci* 2003, **58**:82–91.
3. Carlson LE, Bultz BD. Efficacy and medical cost offset of psychosocial interventions in cancer care: Making the case for economic analyses. *Psychooncology* 2004, **13**:837–849.
4. Breitbart W, Rosenfeld B, Pessin H, Applebaum a., Kulikowski J, Lichtenthal WG: Meaning-Centered Group Psychotherapy: An Effective Intervention for Improving Psychological Well-Being in Patients With Advanced Cancer. *J Clin Oncol* 2015, **33**:749–754.
5. van der Spek N, Vos J, van Uden-Kraan CF, Breitbart W, Holtmaat K, Witte BI, Tollenaar RA, Cuijpers P V, Verdonck-de Leeuw IM. *Efficacy of Meaning-Centered Group Psychotherapy for Cancer Survivors: a Randomized Controlled Trial.* Submitted .
6. van der Spek N, Vos J, van Uden-Kraan CF, Breitbart W, Cuijpers P, Knipscheer-Kuipers K, Willemsen V, Tollenaar RA, van Asperen CJ, Verdonck-de Leeuw IM. Effectiveness and cost-effectiveness of meaning-centered group psychotherapy in cancer survivors: protocol of a randomized controlled trial. *BMC Psychiatry* 2014, **14**:22.
7. Lee V, Cohen SR, Edgar L, Laizner AM, Gagnon AJ. Meaning-making intervention during breast or colorectal cancer treatment improves self-esteem, optimism, and self-efficacy. *Soc Sci Med* 2006, **62**:3133–3145.
8. LeMay K, Wilson KG. Treatment of existential distress in life threatening illness: A review of manualized interventions. *Clin Psychol Rev* 2008**, 28**:472–493.
9. Kissane DW, Love A, Hatton A, Bloch S, Smith G, Clarke DM, Miach P, Ikin J, Ranieri N, Snyder RD. Effect of cognitive-existential group therapy on survival in early-stage breast cancer. *J Clin Oncol* 2004, **22**:4255–4260.
10. Chochinov HM, Hack TF, Hassard T, Kristjanson LJ, McClement S, Harlos M. Dignity Therapy: A Novel Psychotherapeutic Intervention for Patients Near the End of Life. *J Clin Oncol* 2005, **23**.
11. Breitbart W, Poppito S, Rosenfeld B, Vickers AJ, Li Y, Abbey J, Olden M, Pessin H, Lichtenthal W, Sjoberg D, Cassileth BR. Pilot randomized controlled trial of individual meaning-centered psychotherapy for patients with advanced cancer. *J Clin Oncol* 2012, **30**:1304–9.
12. Payne DK, Vroom P, Phil M. *Supportive Group Psychotherapy: A Group Intervention for Cancer Patients.* 2009.
13. Bouwmans C, De Jong K, Timman R, Zijlstra-Vlasveld M, Van der Feltz-Cornelis C, Tan Swan S, Hakkaart-van Roijen L. Feasibility, reliability and validity of a questionnaire on healthcare consumption and productivity loss in patients with a psychiatric disorder (TiC-P). *BMC Health Serv Res* 2013, **13**:217.
14. Hakkaart-van Roijen L, Tan S, Bouwmans C. *Guideline for Cost Research. Methods and Standard Cost Prices for Economic Evaluations in Healthcare*. 2010.
15. Brooks R: EuroQol: the current state of play. *Heal Pol* 1996, **37**:53–72.

16. Lamers L, Stalmeier P, McDonnell J, Krabbe P, Van Busschbach J. Measuring the quality of life in economic evaluations: the Dutch EQ-5D tariff. *Ned Tijdschr Geneeskd* 2005, **149**:1574–1578.

17. Jaarsma TA, Pool G, Ranchor A V, Sanderman R.The concept and measurement of meaning in life in Dutch cancer patients. *Psychooncology* 2007, **16**:241–248.

18. Jaarsma TA, Pool G. *Posttraumatic Growth Inventory: Dutch Version.* Groningen Noord Cent voor Gezondheidsvraagstukken 2003.

19. Dierendonck D. The construct validity of Ryff's Scales of PsychologicalWell-being and its extension with spiritual well-being. *Pers Individ Dif* 2005, **36**:629–643.

20. Watson M, Greer S, Young J, Inayat Q, Burgess C, Robertson B. Development of a questionnaire measure of adjustment to cancer: the MAC Sca1e. *Psychol Med* 1988, **18**:203–209.

21. ten Klooster PM, Weekers AM, Eggelmeijers F, Van Woerkom JM, Drossaert CHC, Taal E, Baneke JJ, Rasker JJ. Optimisme en/of pessimisme: factorstructuur van de Nederlandse Life Orientation Test-Revised. *Psychol enGezondheid,* 2010, **38**:89–100.

22. Young MA, Halper IS, Clark DC, Scheftner W, Fawcett J. An item-response theory evaluation of the Beck Hopelessness Scale. *Cognit Ther Res* 1992, **16**:579–587.

23. Spinhoven P. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. *Psychol Med* 1997**, 27**:363–370.

24. Fayers P, Bottomley A. Quality of life research within the EORTC-the EORTC QLQ - C30. European Organisation for Research and Treatment of Cancer. . *Eur J Cancer* 2002, **38**:S125–S133.

25. *Raad Voor de Volksgezondheid En Zorg.* Zinnige En Duurzame Zorg. Zoetermeer. 2006.

26. Van Gils P, Schoemaker C, Polder J. How much should a gained life year cost? Study on the assessment of QALY. *Ned Tijdschr Geneeskd* 2013, **157**:A6507.

27. Sabariego C, Brach M, Herschbach P, Berg P, Stucki G. Cost-effectiveness of cognitive-behavioral group therapy for dysfunctional fear of progression in cancer patients. *Eur J Heal Econ* 2011, **12**:489–497.

28. Arving C, Brandberg Y, Feldman I, Johansson B, Glimelius B. Cost-utility analysis of individual psychosocial support interventions for breast cancer patients in a randomized controlled study . *Psycho-oncology* 2014, **23**(3):251–258.

29. Jansen F, Van Zwieten V, Coupe V, Leemans C, Verdonck-de Leeuw I. A review on cost-effectiveness and cost-utility of psychosocial care in cancer patients. *Asi-Pacific J Oncol Nurs* 2016, In press.

30. Lemieux J, Topp A, Chappell H, Ennis M, Goodwin PJ. Economic analysis of psychosocial group therapy in women with metastatic breast cancer. *Breast Cancer Res Treat* 2006, **100**:183–190.

31. Patel A, Rendu A, Moran P, Leese M, Mann A, Knapp M. A comparison of two methods of collecting economic data in primary care. *Fam Pract* 2005, **22**:323–327.

32. Drummond M, Sculpher M, Torrance G, O'Brien B, Stoddart G. *Methods for the Economic Evaluation of Health Care Programmes* (3rd ed.). Oxford Univ Press Oxford 2005.

Chapter 7

General discussion

A modified version of this chapter is in press:

Van der Spek, N. & Verdonck-de Leeuw, I.M. Meaning-Centered Group Psychotherapy for General Cancer Survivors. In: Breitbart, W., Holland, J.C. ed. Meaning-Centered Psychotherapy in the Cancer Setting: Finding Meaning and Hope in the Face of Suffering. Oxford University Press, New York

Meaning-making plays an important role in psychological well-being after a cancer diagnosis. The aim of this thesis was to obtain insight into meaning-making processes in cancer survivors, to adapt meaning-centered group psychotherapy for a cancer survivor population, and to evaluate the efficacy and cost-utility of the adapted intervention, called "meaning-centered group psychotherapy for cancer survivors" (MCGP-CS). This final chapter reports on the main findings of this thesis, and discusses these findings and the main limitations. Furthermore, clinical implications are addressed, and directions for future research are provided.

Meaning-making processes in cancer survivors

This thesis showed that cancer survivors, defined as cancer patients after treatment with curative intent, have to deal with a number of meaning-making and other existential issues. We found that many cancer survivors experienced an enhanced sense of meaning, compared to meaning before their diagnosis, and that they often switched to new sources of meaning, because the sources of meaning from before the diagnosis were no longer accessible (e.g. due to job loss or physical limitations). This is in line with the literature, reporting on the importance of meaning-making in cancer patients in relation to psychological well-being and successful adjustment to the disease [1–3] Park describes in the Meaning Making Model how a search for meaning occurs, when the appraised meaning to a negative event is in contrast with one's global meaning [4], and furthermore how meaning-making problems lead to psychological distress, while successful meaning-making is followed by successful adjustment (Chapter 1). Our findings are in accordance with the Meaning Making Model [4], describing that when, after a search for meaning, "meanings are made", patients give new meaning to their experiences and beliefs, and some report growth or positive life changes. However, a substantial group of survivors experienced problems with meaning-making and existential issues, and expressed a need for help with this (Chapter 2).

Meaning-centered group psychotherapy for cancer survivors

The goal of meaning-centered group psychotherapy for cancer survivors (MCGP-CS) was to enhance or maintain a sense of meaning, in order to cope better with the sequelae of their disease. Our pilot study showed that MCGP-CS was feasible, with good acceptability, adherence and client satisfaction (Chapter 3). A randomized controlled trial (RCT) was designed, comparing MCGP-CS with supportive group psychotherapy (SGP) and care as usual (CAU), with assessments at baseline, post-intervention, and after three and six months respectively (Chapter 4). We found support for the efficacy of MCGP-CS, showing positive effects on personal meaning in the short term, and on psychological well-being, distress, depression, and adjustment to cancer up until six months after participation in the intervention (Chapter 5).

According to previous studies, meaning and psychological distress are negatively related [5–7]. An interesting additional finding of this thesis is that among cancer survivors, improved meaning and psychological well-being are followed by a decrease of distress and depressive symptoms in the longer term.

It is remarkable that despite the beneficial effects of MCGP-CS on several aspects of psychosocial well-being, we found no effect on quality of life. This was in contrast to the findings of a previous study on the efficacy of MCGP for advanced cancer patients, showing effects on quality of life [8]. A possible explanation for this may be that the outcome measures for quality of life used in this study (EORTC-C30 and EQ-5D) measure health related quality of life, and have no existential domain. According to Cohen and colleagues [9], existential well-being plays an important role in determining the quality of life in cancer patients. In the previous study on MCGP, the McGill Quality of Life Questionnaire [10] was used to measure overall quality of life, which comprises an existential domain. This might be more relevant and suitable for measuring change in quality of life after an existential intervention such as MCGP-CS.

In addition, this thesis comprised an economic evaluation of MCGP-CS. The cost-utility analyses showed that compared to CAU, it is likely that MCGP-CS is more effective and less costly. Moreover, the results showed that MCGP-CS is probably more effective, and equally expensive compared to SGP (Chapter 6). Furthermore, this thesis provides evidence of the likelihood that MCGP-CS decreases health care use and productivity loss. There are only few cost-evaluations of psychosocial interventions for cancer patients until now, however, most of these studies find promising results showing that psychosocial interventions for cancer patients are good value for money [11–13] As far as we know, our cost-utility analysis was the first cost evaluation of a psychosocial intervention for cancer patients from a healthcare perspective (costs of the health care system) and also from a societal perspective, including productivity losses and costs of informal care.

This thesis showed that besides the struggle with meaning-making issues, cancer survivors can also deal with feelings of isolation and loneliness. Missing a sense of belonging, and feeling unacknowledged or abandoned were examples of isolation that were named in the focus group study. In addition, relationships and social roles came forth as important sources of meaning. This corresponds with the theory of Ryff and Singer, describing "quality connections with others" together with "leading a life of purpose" as the two key dimensions of psychological well-being [14]. MCGP-CS coins these two dimensions, focusing on both meaning and social support. Kissane [15] previously suggested that interventions that focus on those two aspects are likely to influence well-being and adjustment. This is in accordance with the results of our RCT.

Considering the above, the peer support element of MCGP-CS might be an important facilitator of the meaning-making process. It is possible that not only receiving support from peers plays a role in this, but merely being able to give support to peers is important in experiencing a sense of meaning, i.e. supporting others and feeling a sense of belonging to a group as a source of meaning. Riessman [16] calls this the therapeutic effect of giving and receiving support at the same time, the "helper therapy principle".

According to Cobb [17], human connectedness is important in dealing with suffering, and connection to others creates hope, meaning and adjustment. From this perspective, it is not surprising that group therapies are often effective [18–20], and have been popular in mental health care for cancer patients for decades [21–24]. However, in our study, MCGP-CS clearly performed better than SGP, which is also a peer support intervention, suggesting that the focus on meaning is an effective addition to peer support alone, for improving meaning-related outcomes like personal meaning and psychological well-being, but also for improving adjustment to cancer and decreasing distress. In addition, the results of the cost-utility analysis support the finding that MCGP-CS is more effective than SGP, and show that the costs of both interventions are probably comparable.

Strengths and limitations

A strength of this thesis was the thorough participatory design approach in the development and evaluation process, with participation of the target groups (i.e. cancer survivors and oncology psychologists) during several stages of the process. According to this widely used approach, stakeholders are actively involved in a design process, to help ensure the results meet their needs and are feasible. In addition, this thesis focused on both efficacy and cost-utility of MCGP-CS. However, there are also some limitations that should be borne in mind when interpreting the results of the conducted studies.

As described in the general introduction of this thesis, meaning is a complex theoretical concept, with many definitions. This is also reflected in the large number of available questionnaires operationalizing this concept [25, 26]. Personal meaning, psychological well-being and posttraumatic growth were expected to be closely related and to measure overlapping concepts of meaning [5], and were therefore selected as primary outcome measures in the study protocol (Chapter 4). However, to improve the statistical rigor when investigating the efficacy of MCGP-CS, and to avoid confusion of too many primary outcome subscales and comparisons, personal meaning was selected as primary outcome measure when reporting on the RCT in the final analyses of the randomized controlled trial, with the other outcomes as secondary outcomes (Chapter 5). Furthermore, it is difficult to establish what clinically relevant changes are, as no clear cut-off scores or minimal important difference (MID) criteria are available regarding the primary outcome measure personal meaning. Also, the study population in the RCT in this thesis had relatively low levels of distress, so these findings cannot be generalized to a more distressed population. Therefore, even though clear improvement on personal meaning after MCGP-CS was demonstrated, no firm conclusions can be drawn on the clinical impact of this change. However, in general, distressed cancer patients benefit more from group psychotherapies than non-distressed patients [28].

A surplus of the randomized controlled trial conducted in this thesis is that MCGP-CS was compared to an active control group (SGP), as well as care as usual (CAU). However, it should be noted that SGP is less structured than MCGP-CS and does not incorporate homework assignments. In addition, the psychotherapists played a less prominent role in the SGP condition, as the peer support element in this condition was much more central. Those elements may also (partly) explain the differences between MCGP-CS and SGP.

Finally, although there was sufficient power, according to the power calculation beforehand to detect differences on the primary outcome between conditions, this study was likely underpowered to detect significant differences in the cost-utility analysis. Therefore, for the cost-utility analysis a probabilistic approach was applied [29], and these results must be interpreted with more caution.

Clinical implications

Feasibility and implementation of MCGP-CS into clinical practice

Our findings showed that cancer survivors benefit from a meaning-focused approach, not only by enhancing personal meaning in the short term, but also by improving adjustment to cancer and decreasing distress in the longer term. Also, MCGP-CS is likely to reduce health care use and productivity loss compared to CAU.

This adds up to the already existing evidence of the effectiveness of MCGP for advanced cancer patients. Therefore, implementation of both MCGP and MCGP-CS in psycho-oncology health care settings is recommended, so that meaning-focused treatment becomes accessible for cancer survivors as well as for patients in the palliative phase.

The MCGP-CS manual was developed in cooperation with both cancer patients and health care providers in the psycho-oncology field. The results of our feasibility study showed good acceptability of MCGP-CS and high treatment satisfaction (Chapter 3). In the RCT (Chapter 4 and 5), MCGP-CS and SGP were also evaluated by the participants. We compared these results to participants who received SGP. In summary, the client satisfaction evaluation showed that in the MCGP-CS condition, 86% of the participants were (very) satisfied with the intervention, 10% had mixed feelings and 6% were dissatisfied. In the SGP condition, 94% were (very) satisfied, 4% had mixed feelings and 2% were very dissatisfied with the intervention. This difference was not significant ($\chi = 6.428$, df = 4, $p = .169$). In the MCGP-CS condition, 65% would definitely recommend the intervention to other patients, 31% were not sure and 4% would not recommend it. In the SGP condition, 94% would recommend the intervention, and 6% were not sure. The difference between both conditions was significant ($\chi = 12.513$, df = 2, $p = .002$). Participants in de MCGP-CS condition more often stayed in touch with the other group participants after the intervention (67%) than participants in the SGP condition (44%) ($\chi = 5.158$, df = 1, $p = .033$).

While the superiority of MCGP-CS compared to SGP was clearly demonstrated with more and larger effects on dependent variables, patients in the SGP condition were more inclined to recommend the treatment to others, which suggests they were more satisfied with the intervention. A possible reason for this is that MCGP-CS was much stricter protocolled, leaving less room for participants to discuss topics that they desired; furthermore, it also used weekly homework assignments. Interestingly, this did not influence the treatment effect. This is in line with previous findings of studies on support groups for cancer patients, which show highly satisfied participants, but often with little psychosocial benefit [24]. For clinicians it is important to know that higher satisfaction does not necessarily mean more treatment effect.

In summary, our results showed that MCGP-CS is feasible and acceptable, for patients as well as for health care providers. This is an important condition for implementation of MCGP-CS in psycho-oncology health care. Meanwhile, some steps for implementation of

MCGP(-CS) in Dutch health care settings have been taken. MCGP(-CS) has now been implemented into the health care offer of a center for psychosocial oncology in Amsterdam (Ingeborg Douwes Center). This center will ensure further implementation and will develop and offer training for oncology psychologists in the Netherlands, in order to upscale the implementation in psycho-oncology settings nationwide.

Recommendations for future research

Based on the results of this thesis, some recommendations and directions for future research can be offered. Our findings provide support for the efficacy and cost-effectiveness of MCGP-CS. However, insight into possible moderators and mediators is needed to predict which patients are most likely to benefit from MCGP-CS. Future research should focus on these aspects and contribute to analyzing for which patients MCGP-CS in particular provides added value. In our study, experiencing meaning-making issues was not an inclusion criterion, but it would be interesting to take into account if patients with meaning-making issues benefit more from MCGP-CS than patients with other types of psychological complaints.

Secondly, an interesting finding in this thesis was the improvement of patients on distress following improvements on meaning and psychological well-being, after MCGP-CS. It would be relevant to further study this course in a more distressed cancer survivor population.

Thirdly, since sense of meaning seems so important for successful adjustment after cancer, it would be interesting to investigate the role of meaning in individual psychotherapy for cancer survivors. The previous paragraph described the plausible benefit of delivering meaning-focused treatment in a support group setting, however, it would be useful to know if this is indeed more effective than individual meaning-centered psychotherapy (IMCP). Group interventions are not suitable for all patients, especially those who cannot attend group meetings due to physical limitations. A pilot RCT on IMCP [30], showed improvements on spiritual well-being, quality of life, symptom burden, and symptom-related distress, but, in contrast to MCGP, the effects were only observed post-intervention and were no longer significant at two months follow-up. However, more studies on a larger scale are needed to establish whether the group adaptation of MCP is more effective than the individual treatment.

Fourthly, a recent study by Tan and colleagues [31] showed that patients who are able to make meaning of their cancer illness exert a positive influence on their caregivers' well-being. This implies that interventions that help patients to facilitate a meaning-making process not only benefit patients, but are also beneficial for their caregivers. It would be interesting to investigate if MCGP-CS also indirectly impacts the well-being of caregivers, and additionally, if this impacts the cost-effectiveness of MCGP-CS, by decreasing the costs of health care use and productivity loss of caregivers.

Furthermore, it would be interesting to know what the long-term benefits of MCGP-CS are. Cancer survivors can struggle with adjustment and psychological distress for many years after their diagnosis [2, 31] and therefore longer-term treatment effects are important. Longer-term follow-up assessments (two years after the intervention) on the primary outcome measure and cost evaluation measures were added in the RCT on MCGP-CS. These results are expected to become available in 2017.

Conclusion

This thesis confirms the findings from previous studies that the experience of meaning can change after a cancer diagnosis, and adds to the growing evidence of beneficial effects of meaning-centered group psychotherapy (MCGP) for cancer patients, giving support for the efficacy of MCGP for a cancer survivor population (MCPG-CS). The results also offer some support for the theoretical assumption that experiencing meaning, adjustment to cancer, and less distress go hand in hand. Furthermore, this thesis contributes to the existing literature by reporting on the first cost-utility analysis of a meaning-focused intervention for cancer survivors, showing that MCGP-CS is likely to be more cost-effective than care as usual (CAU), and more likely to be effective than SGP, at comparable expense. Overall, the studies in this thesis showed that MCGP-CS is a beneficial addition to psychosocial cancer care to improve personal meaning and psychological well-being; it also reduces distress among cancer survivors, and probably even saves costs.

REFERENCES

1. Hoffman KE, McCarthy EP, Recklitis CJ, Ng AK. Psychological Distress in Long-term Survivors of Adult-Onset Cancer Results From a National Survey. *Arch Intern Med* 2009, **14**:1274–1281.
2. Lee V, Cohen SR, Edgar L, Laizner AM, Gagnon AJ. Clarifying "meaning" in the context of cancer research: a systematic literature review. *Palliat Support Care* 2004, **2**:291–303.
3. Tomich PL, Helgeson VS, Vache EJN. *Perceived growth and decline following breast cancer: a comparison to age-mathced controls 5-years later.* 2005, 1029(December 2004):1018–1029.
4. Park CL. Making sense of the meaning literature: an integrative review of meaning making and its effects on adjustment to stressful life events. *Psychol Bull* 2010, **136**:257–301.
5. Jaarsma TA, Pool G, Ranchor A V, Sanderman R. The concept and measurement of meaning in life in Dutch cancer patients. *Psychooncology* 2007, **16**:241–248.
6. Wong. *The Human Quest for Meaning*. 2nd edition. New York: Routledge, Taylor & Francis Group; 2010.
7. Vickberg SM, Bovbjerg DH, DuHamel CN, Curry V, Redd WH. Intrusive Thoughts and Psychological Distress Among Breast Cancer Survivors: Global Meaning as a Possible Protective Factor. *Behav Med* 2000, **25**:152–160.
8. Breitbart W, Rosenfeld B, Pessin H, Applebaum a., Kulikowski J, Lichtenthal WG. Meaning-Centered Group Psychotherapy: An Effective Intervention for Improving Psychological Well-Being in Patients With Advanced Cancer. *J Clin Oncol* 2015, **33**:749–754.
9. Cohen R, Mount BM, Tomas JJN, Mount LF. *Existential Well-Being Is an Important Determinant of Quality of Life.* 1996:576–586.
10. Cohen SR, Mount BM, Strobel MG, Bui F. The McGill Quality of Life Questionnaire: a measure of quality of life appropriate for people with advanced disease. A preliminary study of validity and acceptability. *Palliat Med* 1995, **9**:207–219.
11. Carlson LE, Bultz BD. Efficacy and medical cost offset of psychosocial interventions in cancer care: Making the case for economic analyses. *Psychooncology* 2004, **13**:837–849.
12. Arving C, Brandberg Y, Feldman I, Johansson B, Glimelius B. Cost-utility analysis of individual psychosocial support interventions for breast cancer patients in a randomized controlled study . *Psycho-oncology* 2014, **23**(3):251–258.
13. Jansen F, Van Zwieten V, Coupe V, Leemans C, Verdonck-de Leeuw I. A review on cost-effectiveness and cost-utility of psychosocial care in cancer patients. *Asi-Pacific J Oncol Nurs* 2016, In press.
14. Ryff CD, Singer B. Psychological well-being: meaning, measurement, and implications for psychotherapy research. *Psychother Psychosom* 1996, **65**:14–23.
15. Lethborg C, Aranda S, Cox S, Kissane D. To what extent does meaning mediate adaptation to cancer? The relationship between physical suffering, meaning in life, and connection to others in adjustment to cancer. *Palliat Support Care* 2007, **5**:377–388.
16. Riessman F. *The "Helper" Therapy Principle.* In Social work. Oxford University Press; 1965:27–32.

17. Cobb S. Social support as a moderator of life stress. *Psychosom Med* 1976, **38**:300–314.
18. Edelman S, Craig A, Kidman AD. Group interventions with cancer patients: Efficacy of psychoeducational versus supportive groups. *J Psychosoc Oncol* 2000, **181**:67–85.
19. Gottlieb BH, Wachala ED. Cancer support groups: a critical review of empirical studies. *Psychooncology* 2006, **16**:379–400.
20. Sherman AC, Mosier J, Leszcz M, Burlingame GM, Ulman KH, Cleary T, Simonton S, Latif U, Hazelton L, Strauss B. Group interventions for patients with Cancer and HIV disease: Part I: Effects on psychosocial and functional outcomes at different phases of illness. *Int J Group Psychother* 2004, **54**:29–82.
21. Spiegel D, Yalom ID. A support group for dying patients. *Int J Gr Psychother* 1978, **28** :245.
22. Kissane DW, Bloch S, Smith GC, Miach P, Clarke DM, Ikin J, Love A, Ranieri N, McKenzie D. Cognitive-Existential Group Psychotherapy for Women with Primary Breast Cancer: A Randomised Controlled Trial. *Psychooncology* 2003, **12**:532–546.
23. van der Meer CA, Wagner AW, Meijers-Heijboer EJMH, Seynaeve CMJC, Niermeijer MF. Perception of the need for support groups among carriers of a breast cancer gene mutation. *Psychooncology* 2000, **9**:457.
24. Hoey LM, Ieropoli SC, White VM, Jefford M. Systematic review of peer-support programs for people with cancer. *Patient Educ Couns* 2008, **70**:315–337.
25. White CA. Meaning and its measurement in psychosocial oncology. *Psychooncology* 2004, **13**:468–481.
26. Brandstätter M, Baumann U, Borasio GD, Fegg MJ. *Systematic review of meaning in life assessment instruments.* 2012, 1052(January):1034–1052.
27. Zoellner T, Rabe S, Karl A, Maercker A. Post-traumatic growth as outcome of a cognitive-behavioural therapy trial for motor vehicle accident survivors with PTSD. *Psychol Psychother* 2011, **84**:201–13.
28. Faller H, Schuler M, Richard M, Heckl U, Weis J, Kuffner R. Effects of psycho-oncologic interventions on emotional distress and quality of life in adult patients with cancer: Systematic review and meta-analysis. *J Clin Oncol* 2013, **31**:782–793.
29. Drummond M, Sculpher M, Torrance G, O'Brien B, Stoddart G. *Methods for the Economic Evaluation of Health Care Programmes* (3rd ed.). Oxford Univ Press Oxford 2005.
30. Breitbart W, Poppito S, Rosenfeld B, Vickers AJ, Li Y, Abbey J, Olden M, Pessin H, Lichtenthal W, Sjoberg D, Cassileth BR. Pilot randomized controlled trial of individual meaning-centered psychotherapy for patients with advanced cancer. *J Clin Oncol* 2012, **30**:1304–9.
31. Tan JYS, Lym HA, Kuek NMY, Heok Kua E, Mahendran R. Caring for the caregiver while caring for the patient: exploring the dyadic relationship between patient spirituality and caregiver quality of life. *Support Care Cancer* 2015, **23**:3403–3406.
32. Helgeson VS, Snyder P, Seltman H. Psychological and physical adjustment to breast cancer over 4 years: Identifying distinct trajectories of change. *Heal Psychol* 2004, **23**:3–15.
33. Tomich PL, Helgeson VS: Five years later: A cross-sectional comparison of breast cancer survivors with healthy women. *Psychooncology* 2002, **11**:154–169.

Summary

SUMMARY

Chapter 1 presents the general introduction of this thesis. First, this chapter explains the importance of meaning-making in cancer survivors' well-being, subsequently it provides a brief general overview of theoretical perspectives on meaning. Subsequently, the chapter elaborates further on the search for meaning in cancer patients, which Lee calls the "existential plight of cancer". Furthermore, the Meaning Making Model is described, explaining meaning-making processes, and the possible search for meaning, in response to adverse events. In this process, a discrepancy can occur between one's *global* and *situational* meaning, which, according to the model, leads to distress. In addition, specific attention is paid to the role of meaning in survivorship, describing that meaning is strongly related to successful adjustment and better quality of life up even years after cancer diagnosis. Moreover, this chapter gives an overview of meaning-focused therapies. Most of these interventions focus on advanced cancer patients and show promising, but inconclusive results. Furthermore, the content, design, and previous evaluations of meaning-centered group therapy, which was initially developed to enhance or sustain a sense of meaning in advanced cancer patients, are described. In addition, this chapter presents the aim of this thesis: to obtain insight in meaning-making processes in cancer survivors, adapt meaning-centered group psychotherapy for a cancer survivor population, and evaluate the efficacy and cost-utility of the adapted intervention, called "meaning-centered group psychotherapy for cancer survivors" (MCGP-CS). Finally, this chapter provides an outline of this thesis.

Chapter 2 includes the outcomes of a focus group study on meaning-making processes in cancer survivors. Four focus groups were conducted with 23 cancer survivors (< five years after their respective diagnosis), who were treated with curative intent. Participants responded to questions about experienced meaning-making, perceived changes in meaning-making after cancer, and the perceived need for help in this area. We found that most frequently mentioned meaning-making themes were *relationships* and *experiences*. In general, cancer survivors experienced enhanced meaning after cancer through *relationships, experiences, resilience, goal-orientation* and *leaving a legacy*. Some participants however also said to have (also) experienced a loss of meaning in their lives through *experiences, social roles, relationships* and *uncertainties about the future*. The results of this study indicated that there is a group of cancer survivors that has succeeded in meaning-making efforts, and sometimes even experienced more meaning in their lives than before the diagnosis, while there is also a considerable group of survivors that struggled with meaning-making and has an unmet need for help with that.

Chapter 3 describes a feasibility study on meaning-centered group psychotherapy for cancer survivors (MCGP-CS). Based on the focus group study presented in Chapter 2 and on expert input, the MCGP manual was adjusted for a Dutch cancer survivor population (MCGP-CS). We performed the adjusted MCGP-CS twice, a total 11 cancer survivors participated. The recruitment strategy was tested, improvements among participants after intervention were measured, and client satisfaction was evaluated. The results showed good acceptability, compliance and client satisfaction, and gave valuable information for improving the recruitment strategy. The results were encouraging to start a randomized controlled trial (RCT).

Chapter 4 includes a rationale and description of the study protocol of our RCT. Meaning-focused coping is key to adjustment to life after cancer, however, there is a lack of evidence based psychological interventions in this area. The aim of the proposed study was to evaluate the effectiveness and cost-effectiveness of MCGP-CS. Survivors diagnosed with cancer in the last five years and treated with curative intent were recruited via several hospitals in the Netherlands. After screening, it was planned to randomly assign 168 survivors to one of the three study arms: 1. Meaning-centered group psychotherapy (MCGP-CS) 2. Supportive group psychotherapy (SGP) 3. Care as usual (CAU). A baseline assessment was scheduled before randomization, with follow-up assessments post-intervention and after three, six and twelve months respectively. The primary outcome was meaning-making (PMP, PTGI, SPWB). The secondary outcome measures address quality of life (EORTC-30), anxiety and depression (HADS), hopelessness (BHS), optimism (LOT-R), adjustment to cancer (MAC), and costs (TIC-P, EQ-5D, PRODISQ). Because many cancer survivors experience feelings of loneliness and alienation and have a need for peer support, a group method can be particularly beneficial for sustaining or enhancing a sense of meaning. If this MCGP-CS is effective for cancer survivors, it can be implemented in the practice of psycho-oncology care.

Chapter 5 examines the efficacy of MCGP-CS, in the RCT as described in Chapter 4. A total of 170 cancer survivors were randomly assigned to one of the three study arms: MCGP-CS (n = 57), SGP (n = 56), CAU (n = 57). The primary outcome was the Personal Meaning Profile (PMP). Secondary outcomes were the subscales of PMP, Scales of Psychological Well-Being (SPWB), Posttraumatic Growth Inventory (PTGI), Mental Adjustment to Cancer Scale (MAC), Life Orientation Test-Revised (LOT-R), Beck's Hopelessness Scale (BHS), Hospital Anxiety and Depression Scale (HADS), and quality of life (EORTC QLQ-C30). Outcome measures were assessed before randomization, post-intervention, and after three and six months follow-up (FU). Linear mixed model analyses (intention-to-treat) showed significant differences on the course of the PMP, subscales of the SPWB and MAC, and the HADS, between MCGP-CS, SGP and CAU. Post-hoc analyses showed significantly stronger treatment effects of MCGP-CS compared to CAU on personal meaning (d=0.81), positive relations (d=0.59), purpose in life (d=0.69), goal-orientedness (d=1.07), and fighting spirit (d=0.61) (post-intervention), helpless/hopeless (d=-0.87) (three months FU), and distress (d=-0.6) and depression (d=-0.38) (six months FU). Significantly stronger effects of MCGP-CS compared to SGP were found on personal growth (d=0.57) (three months FU), and environmental mastery (d=0.66) (six months FU). This chapter concludes that MCGP-CS is an effective intervention for cancer survivors to improve meaning in the short term. Also, there are indications for improvements on psychological well-being, and mental adjustment to cancer and to reduced psychological distress in the longer-term.

Chapter 6 reports on the results of a cost-utility analysis of MCGP-CS, compared to SGP and CAU, within the context of the randomized controlled trial, as described in Chapter 4 and 5. Intervention costs, direct medical and non-medical costs, productivity losses and health related quality of life were measured until six months follow-up, using the TIC-P, PRODISQ data from the hospital information system, and the EQ-5D. The cost-utility was calculated by comparing mean cumulative costs and quality adjusted life years (QALYs) of MCGP-CS, SGP, and CAU.

After imputation of missing data, there were no significant differences in mean cumulative costs and mean number of QALYs between the three groups. A probabilistic approach was applied. MCGP-CS had a probability of 74% to be less costly and more effective than CAU, and 49% compared to SGP. Additional analyses assessing the robustness of these findings, showed that compared to CAU, MCGP-CS had a probability of 54-74% to be less costly and more effective. The probability that MCGP-CS is less costly and more effective compared to SGP was 48-55%. Comparing SGP to CAU, the probability that SGP is less costly and more effective was 22-49%. If society is willing to pay €0 for one gained QALY, MCGP-CS has a 78% probability of being cost-effective; this increases to 85% at €10,000 and to 92% at €30,000. This chapter concludes that MCGP-CS is likely to be more effective and less costly than CAU, while it is probably more effective and equally expensive compared to SGP.

Chapter 7 provides a general discussion, summarizing the main findings, limitations, and implications of the studies in this thesis. This thesis confirms the findings in previous studies that the experience of meaning can change after cancer, and adds to the growing evidence of beneficial effects of meaning-centered group psychotherapy (MCGP) for cancer patients, giving support for the efficacy of MCGP for a cancer survivor population. The economic evaluation shows that MCGP-CS is likely to be more cost-effective than care as usual (CAU), and more effective than SGP, but not less costly. Furthermore, this chapter elaborates on the role of peer support, suggesting this might be an important element in this meaning-centered psychotherapy. The main study limitations concern the use of outcome measures with no clear cut-off scores, and the relatively low levels of distress in this study population. Also, this section points out that the results of the cost-utility analysis should be interpreted with caution, as statistical significance was not reached; however, a probabilistic approach could be applied. Furthermore, this chapter provides clinical implications, recommending that MCGP-CS should be implemented in clinical settings, as the results of this thesis show that it is feasible and acceptable for patients as well as for health care providers. Recommendations for future research include further investigation of moderators and mediators of the effects, and research and application of MCP for different target groups (e.g. with higher levels of distress, individual therapy, caregivers). In conclusion, this thesis showed that MCGP-CS is a beneficial addition to psycho-oncology health care, improves meaning and psychological well-being of cancer survivors, and is likely to ensure good value for money.

Samenvatting

SAMENVATTING

Hoofdstuk 1 geeft een algemene inleiding van dit proefschrift. Ten eerste wordt het belang van zingeving voor het welzijn van overlevers van kanker uiteengezet en aanvullend wordt een kort algemeen overzicht geschetst van verschillende theoretische perspectieven op zingeving. Vervolgens wordt in dit hoofdstuk dieper ingegaan op de zoektocht naar zingeving bij mensen met kanker, die ook wel "de existentiële opgave bij kanker" wordt genoemd. Aan de hand van het "Meaning Making Model" (Zingevingsmodel) van Park, wordt beschreven hoe zingevingsprocessen en een eventuele zoektocht naar zingeving verlopen na ingrijpende negatieve levensgebeurtenissen. Hierbij kan discrepantie ontstaan tussen iemands *algemene zingeving* en iemands *situationele zingeving,* wat volgens het model leidt tot *distress.* Voorts wordt specifiek aandacht besteed aan de rol van zingeving bij overlevers van kanker en wordt beschreven dat zingeving sterk gerelateerd is aan het succesvol aanpassen aan het leven na kanker en betere kwaliteit van leven tot jaren na de diagnose. Verder volgt een overzicht van verschillende therapieën die zich op zingeving richten. Er wordt een beschrijving gegeven van de inhoud, ontwikkeling en eerdere onderzoeken naar "meaning-centered group psychotherapy" (MCGP), een therapie die oorspronkelijk is ontwikkeld om zingeving te behouden of te vergroten bij mensen met kanker in een vergevorderd stadium. Hierop volgend wordt de doelstelling van dit proefschrift geformuleerd: het verkrijgen van inzicht in zingevingsprocessen bij overlevers van kanker, het aanpassen van MCGP voor deze doelgroep en het onderzoeken van de effectiviteit (doeltreffendheid) en kosten-effectiviteit van de aangepaste interventie, genaamd "meaning-centered group psychotherapy for cancer survivors" (MCGP-CS; Zingevingsgerichte groepstherapie voor overlevers van kanker). Tot slot beschrijft dit hoofdstuk de verdere opbouw van dit proefschrift.

Hoofdstuk 2 beschrijft de resultaten van een focusgroep studie naar zingevingsprocessen bij overlevers van kanker. Er werden vier focusgroepen uitgevoerd met in totaal 23 overlevers van kanker die behandeld waren met curatieve intentie. De deelnemers beantwoordden vragen over hun ervaringen met zingeving, ervaren veranderingen met betrekking tot zingeving na kanker en hun hulpbehoefte op dit gebied. We vonden dat de meest genoemde thema's *relaties* en *ervaringen* waren. Over het algemeen, ervoeren de deelnemers meer zingeving na kanker op het gebied van *relaties, ervaringen, veerkracht, doelgerichtheid* en *nalatenschap*. Sommige deelnemers zeiden echter (ook) een verlies van zingeving te hebben ervaren op het gebied van *ervaringen, sociale rollen, relaties,* en *onzekerheid over de toekomst*. De resultaten van deze studie wijzen er op dat er een groep overlevers van kanker is die succesvol zingevingsprocessen doorloopt na kanker en soms zelfs meer zingeving ervaart dan voor diagnose, terwijl er ook een aanzienlijke groep overlevers is die worstelt met zingeving en behoefte heeft aan hulp bij dit proces.

Hoofdstuk 3 rapporteert de uitkomsten van een pilot studie naar de haalbaarheid van "meaning-centered group psychotherapy for cancer survivors" (MCGP-CS). Gebaseerd op de uitkomsten van de focusgroep studie zoals beschreven in Hoofdstuk 2 en gebaseerd op de inbreng van experts, is het MCGP protocol aangepast voor Nederlandse overlevers van kanker (MCGP-CS). De aangepaste interventie MCGP-CS, werd twee keer uitgevoerd, in totaal deden 11 patiënten mee. In deze studie werd de wervingsmethode getest, werden verbeteringen na interventie gemeten en werd de klanttevredenheid geëvalueerd. Uit de resultaten bleek dat MCGP-CS goed geaccepteerd werd, dat er hoge therapietrouw en klanttevredenheid was en er werd waardevolle kennis opgedaan om de wervingsstrategie te verbeteren. De resultaten waren bemoedigend om te starten met een studie op grotere schaal (een "randomized controlled trial", RCT).

Hoofdstuk 4 beschrijft de rationale en het onderzoeksprotocol van onze RCT. Zingevingsgerichte coping is zeer belangrijk bij de aanpassing aan het leven na kanker, er is echter een gebrek aan bewezen effectieve psychotherapieën die zich hier op richten. Het doel van deze studie was om de effectiviteit en kosteneffectiviteit van MCGP-CS te onderzoeken. Overlevers van kanker die korter dan 5 jaar geleden die diagnose kanker gekregen hadden en met curatieve intentie behandeld waren, werden geworven in verschillende ziekenhuizen in Nederland. De planning was om, na een screening, 168 patiënten at random toe te wijzen aan een van de drie studiecondities: 1. Meaning-centered group psychotherapy (MCGP-CS) 2. Supportive group psychotherapy (SGP, lotgenoten steungroep) 3. Care as usual (CAU, standaard zorg). De nulmeting was gepland voor randomisatie, met nametingen na de interventie, na 3, 6, en 12 maanden. De primaire uitkomstmaat was zingeving (PMP, PTGI, SPWB). De secundaire uitkomstmaten richtten zich op kwaliteit van leven (EORTC QLQ-C30), angst en depressie (HADS), hopeloosheid (BHS), optimisme (LOT-R), aanpassing aan kanker (MAC) en kosten (TIC-P, EQ-5D, PRODISQ). Veel overlevers van kanker ervaren gevoelens van eenzaamheid en vervreemding en hebben behoefte aan lotgenotencontact. Daarom zou juist een groepsinterventie geschikte interventie kunnen zijn om zingeving te behouden of te vergroten. Als MCGP-CS effectief blijkt te zijn voor overlevers van kanker, kan het geïmplementeerd worden in de psycho-oncologische zorg.

Hoofdstuk 5 beschrijft een onderzoek naar de effectiviteit van MCGP-CS, middels een RCT zoals beschreven is in Hoofdstuk 4. In totaal werden 170 patiënten at random verdeeld over de drie studiecondities: MCGP-CS (n = 57), SGP (n = 56), CAU (n = 57). Primaire uitkomstmaat was het Persoonlijke Zingevings Profiel (PMP). Secundaire uitkomstmaten waren de subschalen van de PMP, Schalen van Psychologisch Welzijn (SPWB), de Post traumatische Groei Vragenlijst (PTGI), de Mentale Aanpassing aan Kanker Schaal (MAC), de Levensoriëntatie Test (LOT-R), Beck's Hopeloosheid Schaal (BHS), Ziekenhuis Angst en Depressie Schaal (HADS) en de kwaliteit van leven vragenlijst EORTC QLQ-C30. De uitkomstmaten werden afgenomen voor randomisatie, na interventie, 3 maanden en 6 maanden later. Linear mixed model analyses (intention-to-treat) lieten significante verschillen tussen MCGP-CS, SGP en CAU zien over het verloop op de PMP, subschalen van de SPWB, de MAC en de HADS. Post-hoc analyses lieten significant grotere behandeleffecten zien van MCGP-CS vergeleken met CAU op persoonlijke zingeving (d=0.81), positieve relaties (d=0.59), doel in het leven (d=0.69), doelgerichtheid (d=1.07) en vechtlust (d=0.61) (na interventie), hulpeloosheid/hopeloosheid (d=-0.87) (3 maanden later), distress (d=-0.6) en depressie (d=-0.38) (6 maanden later). Significant sterkere effecten van MCGP-CS vergeleken met SGP werden gevonden op persoonlijke groei (d=0.57) (3 maanden later) en grip op de omgeving (d=0.66) (6 maanden later). Dit hoofdstuk concludeert dat MCGP-CS een effectieve interventie is voor overlevers van kanker in het verbeteren van zingeving op korte termijn. Ook zijn er aanwijzingen voor verbeteringen van psychologisch welzijn en mentale aanpassing aan kanker en vermindering van psychologische *distress* op langere termijn.

Hoofdstuk 6 beschrijft een studie naar de kostenutiliteit van MCGP-CS, vergeleken met SGP en CAU, uitgevoerd binnen de RCT zoals beschreven in hoofdstuk 4 en 6. Interventiekosten, directe medische en niet-medische kosten, productiviteitsverliezen en gezondheidsgerelateerde kwaliteit van leven zijn gemeten tot zes maanden na interventie, aan de hand van de TIC-P, PRODISQ, data uit het ziekenhuis informatiesysteem en de EQ-5D. De kostenutiliteit werd berekend door de gemiddelde cumulatieve kosten en "quality adjusted life years" (QALYs)[1] van MCGP-CS, SGP en CAU met elkaar te vergelijken. Na imputatie van ontbrekende data, werden geen significante verschillen gevonden in gemiddelde cumulatieve kosten en gemiddeld aantal QALYs, tussen de drie groepen. Vervolgens werd een "waarschijnlijkheidsbenadering" toegepast. MCGP-CS had een waarschijnlijkheid van 74% om meer kostenbesparend en meer effectief te zijn dan CAU en vergeleken met SGP was de waarschijnlijkheid 49%. Aanvullende analyses, om na te gaan of deze bevindingen robuust waren, toonden aan dat, vergeleken met CAU, MCGP-CS een waarschijnlijkheid had van 54-74% om meer kostenbesparend en meer effectief te zijn. De waarschijnlijkheid dat MCGP-CS meer kostenbesparend en meer effectief is vergeleken met SGP, was 48-55%. Wanneer SGP met CAU vergeleken werd, was de waarschijnlijkheid dat SGP meer kostenbesparend en meer effectief is 22-49%. Als de maatschappij bereid is om €0 voor een gewonnen QALY te betalen, heeft MCGP-CS een waarschijnlijkheid van 78% om kosteneffectief te zijn, dit neemt toe tot 85% bij €10000 tot 92% bij €30000. Dit hoofdstuk concludeert dat MCGP-CS waarschijnlijk effectiever en meer kostenbesparend is dan CAU, terwijl het waarschijnlijk effectiever en even kostenbesparend is als SGP.

Hoofdstuk 7 geeft een algemene discussie en beschrijft de belangrijkste bevindingen, beperkingen en implicaties van dit proefschrift. Dit proefschrift bevestigt bevindingen uit eerdere studies dat zingeving kan veranderen na kanker, vormt een toevoeging aan de groeiende evidentie voor de gunstige effecten van meaning-centered group psychotherapy (MCGP) voor mensen met kanker en vindt ondersteuning voor de effectiviteit van MCGP voor een populatie van overlevers van kanker. De economische evaluatie liet zien dat het aannemelijk is dat MCGP-CS kosteneffectiever is dan standaardzorg (CAU) en effectiever is dan SGP, tegen vergelijkbare kosten. Dit hoofdstuk gaat tevens dieper in op de rol van *peer support* en suggereert dat dit een belangrijk element van meaning-centered psychotherapy zou kunnen zijn. De belangrijkste beperkingen van dit proefschrift betreffen het gebruik van uitkomstmaten zonder duidelijke afkapwaarde en het relatief lage niveau van

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[1] Een QALY staat voor een extra levensjaar in goede gezondheid

distress in de studiepopulatie. Deze paragraaf wijst er tevens op dat de resultaten van de kostenutiliteitsstudie met terughoudendheid geïnterpreteerd moeten worden, aangezien de resultaten geen statistische significantie bereikten. Een "waarschijnlijkheidsbenadering" kon echter worden toegepast. Voorts wordt een aantal klinische implicaties beschreven, waaronder de aanbeveling dat MCGP-CS geïmplementeerd wordt in een klinische setting, aangezien de resultaten van dit proefschrift aantonen dat de interventie bruikbaar en acceptabel is voor zowel patiënten als hulpverleners. Aanbevelingen voor toekomstig onderzoek bevatten verder onderzoek naar moderatoren en mediatoren van de gevonden effecten en onderzoek naar andere toepassingen van MCP (bijvoorbeeld voor patiënten met meer *distress*, mantelzorgers of binnen individuele therapie). De conclusie van dit hoofdstuk is dat dit proefschrift aantoont dat MCGP-CS een waardevolle toevoeging is voor het psycho-oncologisch zorgaanbod, zingeving en psychologisch welzijn van overlevers van kanker verbetert en waarschijnlijk zelfs kosten besparend is.

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ABOUT THE AUTHOR

Nadia van der Spek was born in Amsterdam, the Netherlands on January 1st 1986. She graduated from secondary school in 2003 at Gemeentelijk Gymnasium in Hilversum. After graduation she studied psychology at the University of Amsterdam where she received her Master's degree in Clinical Psychology in November 2009. During the last years of her study, she started working at Jellinek Preventie (drug prevention), on the development and evaluation of a peer-education program for young cannabis users. In 2010 she started as a researcher/consultant at Rutgers WPF, working on several projects concerning sexual health and chronic diseases, and health education on contraception for adolescents with low health literacy. In April 2011 she started her PhD study on the evaluation and adaptation of meaning-centered group psychotherapy at the Vrije Universiteit Amsterdam. She combined her PhD-project with clinical work at the Ingeborg Douwes Centrum (psychosocial care for cancer patients and their families), where she started her education as a couples and family therapist in 2012, and her postdoctoral degree in health care psychology (GZ-opleiding) in April 2014. Currently, Nadia still works at the Ingeborg Douwes Centrum, combining clinical work with research projects (Academische Werkplaats), and since February 2016 she also works at Jellinek Preventie, focusing on research, quality, and policy-making.

LIST OF PUBLICATIONS

Asterisks indicate publications included in this thesis

Holtmaat, C.J.M, Van der Spek, N., Cuijpers, P., Leemans, C.R. & Verdonck-de Leeuw, I.M. (2016). Posttraumatic growth among head and neck cancer survivors with psychological distress. *Psycho-Oncology DOI: 10.1002/pon.4106*

Holtmaat, C.J.M., Van der Spek, N. Cuijpers, P., Verdonck-de Leeuw, I.M. Can meaning and positive psychological changes be empirically distinguished from psychological well-being in cancer patients? *In prep.*

Holtmaat, C.J.M., Van der Spek, N. Cuijpers, P., Verdonck-de Leeuw, I.M. Moderators of effects of meaning-centered group psychotherapy on psychological well-being and meaning in cancer survivors. *In prep.*

Noijen, J. & Van der Spek, N. (2009). Fa'waka? Handleiding voor het opzetten en uitvoeren van een peer educatie project. Utrecht: Forum.

Van der Spek, N. (2009). De Cannabisshow: jongeren zelf aan het woord over een effectieve interventie gericht op cannabisgebruik. *Maandblad Geestelijke Volksgezondheid*, *64*, 970-980.

Van der Spek, N. (2015). Zingevingsgerichte groepstherapie voor mensen die behandeld zijn voor kanker: uitkomsten van een pilot studie. *Tijdschrift Psychosociale Oncologie.*

*Van der Spek, N., Jansen, F., Holtmaat, K., Vos J., Breitbart W., van Uden-Kraan C.F., Tollenaar R.A.E.M., Cuijpers P. & Verdonck-de Leeuw I.M. Cost-Utility Analysis of Meaning-Centered Group Psychotherapy for Cancer Survivors. *Submitted.*

Van der Spek, N., Peters, G.J.Y., Noijen, J. & Jamin, J. (2010). De Cannabisshow. Een preventieve peer-education methode op het podium. *Tijdschrift Verslaving, 6* 22-36.

*Van der Spek, N., van Uden-Kraan C.F., Vos J., Breitbart W., Tollenaar R.A.E.M., Van Asperen C.J., Cuijpers P. & Verdonck-de Leeuw I.M. (2014). Meaning-Centered Group Psychotherapy for Cancer Survivors: a Feasibility Study. *Psycho-Oncology 23,* 827-821. doi:101002/pon3497.

*Van der Spek, N. & Verdonck-de Leeuw, I.M. Meaning-Centered Group Psychotherapy for General Cancer Survivors in Meaning-Centered Psychotherapy in the Cancer Setting: Finding Meaning and Hope in the Face of Suffering, Oxford University Press, New York. *In press.*

Van der Spek, N. & Verdonck-de Leeuw, I.M. (2016). Meaning-Centered Group Psychotherapy: zingevingsgerichte groepstherapie voor mensen met kanker. *Nederlands Tijdschrift voor Behavioral Medicine, 25*, 2-3.

*Van der Spek, N., Vos, J., van Uden-Kraan, C.F., Breitbart, W., Holtmaat, K., Witte. B.I., Tollenaar, R.A.E.M., Cuijpers, P., & Verdonck-de Leeuw, I.M. Efficacy of Meaning-Centered Group Psychotherapy for Cancer Survivors: a Randomized Controlled Trial. *Submitted*.

*Van der Spek, N., Vos J., van Uden-Kraan C.F., Breitbart W., Cuijpers P., Knipscheer, M., Willemsen V., Tollenaar R.A.E.M., Van Asperen C.J. & Verdonck-de Leeuw I.M. (2014). Effectiveness and Cost Effectiveness of Meaning-Centered Group Psychotherapy: Protocol of a Randomized Controlled Trial. *BMC Psychiatry,* 14(22) doi:10.1186/1471-244X-14-22

*Van der Spek, N., Vos J., van Uden-Kraan C.F., Breitbart W., Tollenaar R.A.E.M., Cuijpers P. & Verdonck-de Leeuw I.M. (2013) Meaning Making in Cancer Survivors: A Focus Group Study. *PLoS ONE* 8(9): e76089. doi:10.1371/journal.pone.0076089