**Reconstruction of self-identity among immunotherapy cancer care patients, as a function of social support, resilience, and coping style: A mixed method longitudinal** **study**

**Scientific Background**

**Effect of Oncological Treatment on the Patient**

In recent years, oncological therapies for cancer have undergone dramatic changes. The most advanced treatments are based on immunotherapy, chemotherapy and biological drugs. The introduction of drugs from the family of immunotherapy treatments has changed the clinical treatment approach for most solid tumors. Modern immunotherapy enhances the body's natural immune response. These drugs do not fight cancer directly, but rather via a unique mechanism in which the human immune system attacks a tumor that has already formed in the body. At the basis of the mechanism is the process of binding an antibody to a receptor, following which the immune system identifies a cancerous cell as the target of attack and activates the system against it until it is eliminated. The most prevalent drugs are targeted against the following sites: CTLA-4, PDL-1, PD-1. Although they all have a similar mechanism, their side effect profiles differ (Kamata et al., 2017). The form of treatment involves an intravenous infusion once every 2-4 weeks, in the form of a single drug, a combination of drugs or in combination with chemotherapy.

Since immunotherapy is a new form of treatment there is a paucity of comprehensive information on long-term or post-treatment side effects. The side effects are usually mild and reversible and appear within a few weeks to three months from the start of treatment, but can also appear post-treatment. Any system in the body can develop an autoimmune inflammatory response and symptoms are most well-known in the skin, lungs, colon, liver and endocrine systems, for example, in pituitary and thyroid glands (June et al., 2017). The nervous system and brain are also exposed to this autoimmune response, albeit less frequently. The clinical manifestation is broad, ranging from muscle weakness, drowsiness and weakness to severe encephalopathy ("inflammation" in the brain tissue), respiratory muscle paralysis and more (Champiat et al., 2016). These drugs affect all body systems and it is not inconceivable that they also cause auto-immune–based mental health side effects.

Most patients treated with immunotherapy report non-serious physical side effects. As a result, the ability to cope with treatments for an extended period of time is comparable to that experienced under chemotherapy treatments, including at the level of mental health. Saghazadeh and Rezaei (2017) found that immunotherapy may induce a change in patients' mental state, including signs of depression, fatigue and anxiety; however, immunotherapy is associated with lower rates of depression when compared to chemotherapy (McFarland, 2019).

The adverse effects of chemotherapy on the mental state of cancer patients, their functioning during treatment and their quality of life are relatively well-known (Smith et al., 2013; Fagunde et al., 2012). Fears of exacerbation of the disease and its recurrence (Melchior et al., 2013), damage to self-image (Falk Dahl et al., 2011) and fear of changes at the personal and family level (Drageset et al., 2011) contribute to decreased self-worth, feelings of disappointment and hopelessness (Wong-Kim & Bloom, 2005; Levine et al., 2007), depression, decreased social interaction and even disease progression (Naeini et al., 2018). It has also been found that psychological stress in cancer patients is associated with a decrease in immune system function over a period of several years (Anderson et al., 1998). Knowledge about the effects of immunotherapy is limited; there is ongoing debate as to the relationship between treatment and patients’ mental state, and the question of whether, alongside the improved survival rates of immunotherapy patients, the treatment has unique psychological and sociological effects (Saghazadeh & Rezaei, 2017).

Sociology and psychology are distinct disciplines, even though there is substantial overlap between them. The discipline of social psychology stands alongside the sociological discipline, with the aim of developing a deeper understanding of the individual through sociological processes. Despite the potential overlap between the two disciplines, the fields of sociological and psychological research remain distinct. We argue that an integrative look at this phenomenon, relying on both disciplines, will provide a comprehensive and in-depth picture of the overlap, where the two disciplines intersect as well as the tension between the psychological and sociological aspects (Pfeffer et al.,[2016](https://link.springer.com/article/10.1007/s11199-017-0772-9#ref-CR51)). To the best of our knowledge, there have been almost no studies examining the effects of immunotherapy on cancer patients from a general psychosocial perspective, nor through the particular lens of self-identity formation.

**Self-Identity Formation Among Cancer Patients**

Self-identity consists of personal perceptions and attitudes toward the self. It is the integrated mental and physical system whose elements crystallize and guide an individual’s functioning, control and influence in his/her life and in the surrounding society (Cuzarinsky, 2003). Self-identity changes and is affected by various life situations, including states of illness (Charmaz, 1995). Cancer is a life-threatening disease that challenges one's familiar lifestyle, ways of communicating with the environment and perceptions of self. Intensive diagnosis and treatment lead to changes and a reformation of self-identity. During the treatment, questions arise regarding self-identity and decisions about coping methods are made. Previous perceptions about self-identity break down and thus the patient becomes more vulnerable (Charmaz, 2000).

Leite et al. (2015) found that cancer patients treated with chemotherapy experienced a negative change in self-identity, which included a decrease in self-esteem due to physical changes resulting from the treatment, difficulty in managing the treatment and its side effects, and readjustment at the end of treatment. Similarly, Adejoh et al. (2018) found that the maternal and female self-identity of cancer patients was impaired as a result of the severe side effects of treating the disease, however patients expressed preference for maintaining their family role despite the challenging illness. Soanes and Gibson (2018) examined changes in the self-identity of cancer-stricken adolescents, revealing three key themes expressed during coping with the disease and treatment: self-fragility, reconstruction versus self-preservation in the changing reality, and the need for social support.

Charmaz (1995) argues that most people coping with illness adapt and accept the changes and challenges presented by the disease and its treatment, in a process that includes a change in self-perception and attitudes about life itself, including adaptation to physiological changes. However, there are no findings regarding the effects of cancer immunotherapy on the reconstruction of self-identity patients. The reconstruction of a positive self-perception is crucial in coping with the illness, and even affects the perceptions of those in the patient’s environment and their support for him or her (Knapp et al., 2014).

**Social Support, Resilience, and Coping Strategies for Cancer Patients**

Social support is one of the most common tools for dealing with psychosocial stressors and is a valuable factor in coping with illness (Kubzansky, 2000) and in coming to terms with the severity of clinical symptoms (Taheri et al., 2014). Social support is defined as the degree to which an individual's social needs are met through his or her interaction with others. Thoits (1982) and Williams et al. (2019) found that 67% of 1460 adult cancer patients reported needing social support, half reported a need for emotional support, and 47% expressed the need for physical support. Nearly half reported that their need for such support went unmet. While the role of social support in the treatment of illness is irrefutable, its overall contribution to survival and recovery, or to abnormal outcomes, is not yet well understood. In the context of cancer research, most studies on social support focus on breast cancer patients and/or on a particular measurement of the level of social support, rather than on changing support needs throughout treatment (Jatoi et al., 2016; Leung et al., 2014; Lutgendorf et al., 2012). A recent review regarding the psychosocial needs of cancer patients found that many support needs are not adequately met (Barata, 2016). Unanswered psychosocial needs may adversely affect the patient's ability to cope and manage the illness, and may limit the patient's access to therapeutic resources (IOM, 2008). Environmental factors, especially social support, are responsible for psychological adaptation (Eicher, 2015) and for cancer patients' overall resilience (Somasundaram & Devamani, 2016).

Resilience describes an individual's ability to maintain stable physical and psychological functioning when dealing with an unusual life event (Bonanno et al., 2011). In the context of cancer treatment, resilience refers to the personal characteristics that promote successful adaptation to the disease and include, among others, optimism, self-esteem, self-efficacy, mental flexibility and coping style (Eicher et al., 2015; Helmreich et al., 2017). Resilience is dynamic and changes over time and may be influenced by life circumstances, environment and contextual factors (Mancini & Bonanno, 2009). In addition, resilience is associated with demographic variables, personality traits, social support, and coping styles, and in turn influences cancer recovery (Seiler & Jenewein, 2019). A study of 300 melanoma patients found that patients with high resilience tended to have greater social support and a more active coping style during the illness compared to patients with low resilience (Hamama-Raz, 2012).

As with a trait, coping style refers to an early tendency to deal with stressful events in a consistent manner (Prasertsri et al., 2011). This tendency affects both specific coping strategies when facing the stressor (disease) and responses to the stressor (increased pain or depression) (Gaston-Johansson et al., 1999). Many studies show that cancer patients with an adaptive coping style (positive reassessment, search for social support, problem-focused coping, and religious coping) reported decreased anxiety levels, while patients with a non-adaptive coping style (self-blame, addictive behaviors) suffered from high anxiety (Kramer et al., 2011; Manne et al., 2015; Pan et al., 2017). In addition, the use of an adaptive coping style of acceptance – as opposed to avoidance or denial – predicted higher levels of personal growth two to ten years after treatment (Nuray & Asli, 2007; Helgeson et al., 2004). A study of 95 cancer patients found that patients with a "helpless" coping style reported higher depression and anxiety one year after starting treatment, regardless of disease severity, and that this coping style was associated with lower survival rates (Johansson, 2011). A recent longitudinal study examined coping styles and their impact on outcomes among 248 breast cancer patients (Cheng et al., 2019). Patients who embraced an adaptive coping style expressed a lower level of disease-related feelings of stress, lower scores on anxiety and depression indices and higher quality of life metrics, compared with patients with a non-adaptive coping style. A study of 107 lung cancer patients found four coping styles during treatment of the disease: defensive, repressive, high anxiety, low anxiety. Patients with a repressive coping style were found to report lower levels of pain of various types and lower levels of depressive symptoms (Prasertsri et al., 2011). It is this very important to identify coping patterns, which constitute a risk factor, and examine their impact on patients.

**Objectives and significant of the study:**

Modern cancer treatment is based on cutting edge therapies, but does not yet provide satisfactory engagement with the psychological and sociological aspects associated with these innovations. There is a large gap in existing knowledge regarding the role that psychosocial factors play in innovative treatment processes such as immunotherapy. The literature is divided regarding the effect of immunotherapy on the patient's emotional world and on the side effects and psychological and sociological effects of this treatment. Despite the existence of a broad body of knowledge in the fields of sociology and psychology relating to the study of cancer and its impact on patients, only rarely is this research intentionally interdisciplinary. In the proposed study we seek to combine these two disciplines – despite the built-in tension between them – in our observations and interpretation of the findings. We aim to combine psychological and sociological approaches and tools with the goal of explaining the reconstruction of self-identity among cancer patients treated with immunotherapy, assuming that these factors cannot be isolated, as there is an interaction between the patient's personal and emotional aspects. Such a dialogue between disciplines and an integrative theoretical view of the phenomenon, combined with multiple methodological approaches, may provide a comprehensive and in-depth picture of how cancer patients undergoing alternative therapies, such as immunotherapy, reconstruct their sense of self-identity.

The effect of immunotherapy on the reconstruction of self-identity in various areas of life remains unknown. While many studies discuss the characteristics of self-identity in patients with chronic diseases or among those who recover from cancer (survivors), the effects of factors such as social support, resilience, and coping styles on rebuilding self-identity while dealing with cancer in immunotherapy patients have yet to be thoroughly investigated. An in-depth understanding of the processes involved in adapting and coping with immunotherapy over time may have implications for the duration of recovery and for treatment outcomes.

**The aims of this study** are to examine the process of self-identity reformation of cancer patients treated by immunotherapy, and to monitor changes in self-identity characteristics, social support needs, resilience and coping strategies from the beginning of treatment and over 12-18 months from its onset. Further, we examine the relationships between the study variables and whether there are changes in the strengths of the relationships over the period under question.

The importance of the study stems from its potential contribution to the psycho-oncological knowledge base. At the academic level, the research findings will bridge the knowledge gap and propose a data-based multivariate model which will link different psychological, sociological and clinical variables and their involvement in the coping and recovery processes of cancer patients treated with immunotherapy. At the practical level, the research findings will shed light on various factors that impact outcomes of innovative treatment processes and will enable the development of appropriate intervention programs to identify risk factors and support patients during immunotherapy treatments.

**Detailed description of the proposed study:**

**Working Hypothesis**

1. We anticipate the reformation of self-identity in different areas of life (self-esteem, functioning in relationships, parenting, employment) over time from the start of treatment (t1) in relation to treatment progress (t2, t3).
2. The more positive and stable the patient's resilience, social support and coping styles throughout the course of treatment, the less we expect changes in the patient's self-identity at each stage of treatment.
3. Coping strategies will moderate the relationship between resilience, social support and changes in the patient's self-identity. Thus, in patients with adaptive coping style we expect these variables to be positively correlated to self-identity, and in patients with non-adaptive coping styles, these variables will not be related to self-identity and/or the strength of these correlations will be lower.
4. Demographic variables and clinical indicators will have an impact on self-identity construction beyond psychosocial indicators.

**Work Plan and Methodology**

This study employs integrated research methods consisting of closed-ended questionnaires and semi-structured in-depth interviews with cancer patients undergoing immunotherapy. These two approaches complement and critique each other to allow a more comprehensive and deeper picture of the phenomenon under examination. Because the study deals with emotional issues, quantitative research alone is unable to reach an open and intimate inquiry. The qualitative element of this research will help identify the meanings hidden in the interviewee's discourse regarding his or her ability to cope with illness. Moreover, these mixed methods allow for triangulation (using different methods to investigate the same phenomenon, cross-referencing information from different angles and thus strengthening confidence in the conclusions, reliability and validity of the study) and complementarity (investigating different aspects or dimensions of the same phenomenon, to deepen and enrich the interpretations given).

Population and procedure: The study will involve approximately 80 cancer patients treated with immunotherapy at the oncology institutes at Wolfson and Barzilai Medical Centers (defined as mid-sized hospitals). The institutes offer services to all oncology patients in all diagnoses of cancer and operate according to international therapeutic standards and are affiliated with academic institutions (Tel Aviv and Ben Gurion Universities). Treatments at both institutions are outpatient and there are about 1200 new patients per year between them. After receiving approval from the ethics committees of both hospitals, patients will be recruited prior to treatment through an initial request from the relevant oncology institutes to the relevant patients. The general criteria for selection include: patients undergoing immunotherapy who are about to begin treatment (pre-treatment), are over the age of 18 and are Hebrew speakers. Patients who express a desire to participate in the study can contact the lead researchers and receive more in-depth information about the study and its various stages. Patients will be interviewed and respond to questionnaires at three points in time: at the beginning of treatment (t1), within 3 to 4 months from the start of treatment (t2), at the end of immunotherapy (t3). These stages are based on the principles of oncology treatment. The starting point is the baseline. Immunotherapy side effects appear in the first few months, so t2 is after 3-4 months. The end point will occur when the disease progresses or when the date of treatment approved according to the clinical studies expires and therefore it will have physical and/or mental significance for the patient. Measurement of response to treatments will be performed according to accepted criteria at the usual time intervals in oncology which are once every 3-4 months (depending on the patient, diagnosis and type of treatment). Measurement of side effects will be done clinically according to accepted medical criteria and performed consistently at the time of treatment.

The date of the in-depth interview and the completion of the questionnaires will be determined with the patient by a research assistant at a time and place that is convenient for the patient. Before completing the questionnaires, each patient will be given a unique code and explained that their participation is anonymous; questionnaires can be coded and cross-linked according to the code and subjects will not be identified by name. Patients will sign an informed consent form for the recording of the interview and its transcription, after being briefed that they do not have to answer all the questions and/or they may request to end the interview at any point. The interviews will be transcribed and analyzed in a theory-oriented approach using ATLAS.ti 8 software for qualitative analysis, looking for the elements of a sense of change in self-identity formation; social support or lack of support; positive emotions (e.g., optimism, hope, strength, resilience) versus negative ones (e.g., despair, sadness, anxiety, difficulty, pain, guilt, sacrifice), coping strategies, terms related to relationships and parenting, etc. We will examine both long-term changes among the same patient and differences between different patients. Quantitative questionnaire analysis will be done using SPSS v.26 software using correlations, paired-sample t-tests, one-way analysis of variance, and models of hierarchical linear regression.

**Tools:**

The tools that will be used to measure the research variables are those found to be reliable and validated among cancer patients. Table 1, presented in Appendix H, summarizes the research variables and the tools that will be used.

**Preliminary results**

In November 2019, Dr. Bashkin, Dr. Dopelt, and Dr. Asana won a research grant from the National Institute for Health Services and Policy entitled "Innovative technologies for cancer treatment that are not covered by the healthcare basket: clinical, social, and ethical aspects for doctors, patients, and their families." Part of this funded research included interviews with, among others, with cancer patients. In-depth interviews with these 25 cancer patients revealed that there was a marked change in patients' self-identity from the status of a "healthy person" to a "patient with a potentially terminal illness." A number of salient issues emerged from the interviews, including the great significance of family members' support. Many patients reported that they relied on their family members, and that this had a significant effect on their mood. There seems to be a relationship between the degree of support a patient receives and his or her general feelings about and perception of the suffering he or she is experiencing. Patients who do not receive support tended to report more severe physical sensations and sound less optimistic. There is wide variety when it comes to the ways that patients cope with the physical and mental difficulties that accompany illness. There are patients who discussed the need for internal changes (emotional, spiritual) in order to cope with the disease, and patients who have taken the approach of "going to war" and invested themselves in various activities. On the other hand, there are patients who seem to deal more passively with their condition; they noted that they follow the doctors' instructions, but do not pursue care or support beyond these recommendations. A minority even took the approach of denying their illness and trying to conduct their lives as usual, as if they were not sick. The vast majority of patients testified that physicians did not address the emotional and mental aspects of treatment at all. Some added that they did not expect this and that in their opinion it is not the doctors' role to deal with these issues.

**Conditions available to the researcher for conducting the research**

The researchers are experts in the relevant fields of oncology medicine, health policy, public health, health systems management, quality, inequality, sociology of health and organizational and medical psychology. The researchers have at their disposal computers, software, a library and other research infrastructures through their affiliations with Ashkelon College, Barzilai University Medical Center, the Edith Wolfson Medical Center and Ben Gurion University, as well as working relationships with experts in the field in Israel and around the world.

**Expected obstacles (including alternatives to approaches and methods in case the method does not work as expected)**

1. Difficulty in recruiting patients to participate in the study: In order to overcome this challenge, patients will receive a comprehensive explanation about the importance of the study and will be encouraged to participate. Patients will also be fully briefed about the details of the research procedure and the maintenance of participant anonymity. Oncology institutes will be contacted at additional hospitals for the purpose of recruiting more participants, if needed.
2. Participants' potential fatigue from answering questionnaires and being interviewed in one session: Participants will be offered a meeting time and a meeting place according to their convenience, and there will also be a break between the in-depth interviews and filling out the questionnaires according to the participants' wishes. If the patient prefers, the research coordinator will read the questions of each Weissman tool aloud to him or her. If participants express a preference to complete the various research tools over the course of two meetings, this will be scheduled.
3. Dropout during the study (voluntary or in case of deterioration in the patients' condition): In order to deal with dropouts, we will try to maximize the initial number of participants on the assumption that a dropout rate of 10-20% of the participants is to be expected. Long-term studies among cancer patients report a typical 10% –30% dropout, depending on the level of commitment of the participants and the length of the study (Mantovani et al., 2010; Temel et al., 2016). Moreover, oncology institutes will be contacted at additional hospitals for the purpose of recruiting more participants.