



Predicting Effective Adaptation to
Breast Cancer to Help Women to

BOUNCE Back

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This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 777167

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BOUNCE NEWSLETTER



IS RESILIENCE OF WOMEN WITH BREAST CANCER PREDICTABLE: HOW CAN COMPUTATIONAL MODELS HELP HEALTH PROFESSIONALS OPTIMIZE PSYCHOLOGICAL INTERVENTIONS?

By **Konstantina Kourou** PhD, Unit of Medical Technology and Intelligence Information Systems, Institute of Molecular Biology & Biotechnology (IMBB), Foundation for Research & Technology – Hellas (FORTH), Ioannina, Greece and **Giorgos Manikis** PhD, Computational Bio-Medicine Laboratory, Institute of Computer Science, Foundation for Research and Technology-Hellas, Heraklion, Greece



Medical doctors and mental health professionals alike have long recognized that many patients show better recovery and capacity to bounce back following similar, serious illnesses than others. For some time, it was believed that **psychosocial resilience** is a relatively stable characteristic trait on which persons differ, in the same manner that people vary from each other on personality characteristics. In this context, self-rated psychological characteristics can serve as one of several indices of a patient's **trait resilience** (i.e., their perceived general ability to effectively deal with adversity, such as illness, or withstand its impact and consequences).

More recent conceptualizations of resilience highlight its multifaceted and dynamic nature. Thus, resilience can be viewed as a **process** (e.g., reflected in the trajectories of adverse psychological symptoms and subjective well-being measured over specific time windows during illness). These trajectories are expected to reveal patterns of stability (e.g., consistently high levels or consistently low levels of anxiety over time), lessening, or worsening of symptoms during the crucial months following diagnosis and during cancer treatments. Resilience as a process has been investigated in previous smaller-scale studies with solid theoretical models regarding trajectories. As more measurement waves (follow-up assessments) become available from the BOUNCE study, advanced statistical and computational models can be applied to explore the complex interplay of treatments side effects, life events, emotional, behavioral, and cognitive processes over time. Results of such models will be part of the next BOUNCE newsletter.

Current computational modeling of BOUNCE data, using supervised learning algorithms, has been applied to the definition of resilience as **outcome**.

Within this framework we have addressed two main **clinical** objectives:

- a) To achieve optimal prediction of one-year patient outcomes (in terms of symptoms of good mental health and good overall quality of life or subjective sense of well-being) using all available information aggregated over the first 3 months post diagnosis, and
- b) To identify potentially modifiable patient characteristics that determine one-year mental health and/or quality of life outcomes. The latter models did not include mental health and/or quality of life measurements obtained during the first three months post-diagnosis in order to enhance model sensitivity towards more clinically useful psychological characteristics (such as optimism and emotional self-regulation strategies) and behaviors (i.e., coping strategies such as exercise).

We have tested this machine learning framework on the fully annotated BOUNCE dataset that became available as of May 2021. This dataset

includes socio-demographic, lifestyle, medical and self-reported psychological characteristics of women recently diagnosed with breast cancer. Currently 12-month follow up data are available for 532 women aged 40-70 years.

The analysis pipeline employed to address these objectives entailed feature selection, model training, and model testing. Feature selection was conducted using a transformer built on Random Forest (RF) estimator which assigns weights to the most important features and ranks them according to their relative importance. The feature selection scheme was encapsulated with the classification algorithms into the ML-based pipeline in order to select only the relevant features to train the selected classifiers.

We took special care to avoid overfitting, which often results when model training and testing takes place on partially overlapping subsets of cases. To address this rather common problem in

machine learning applications in clinical research we adopted a cross-validation scheme with holdout data for final evaluation. In this manner, model testing was always performed on cases that were not considered during the training phase and, consequently, did not influence the feature selection process. This procedure helps to increase the generalizability of predictions and the accuracy of the final models when applied to new cases in the future. Specifically, a 3-Fold Split for Hyper-Parameters tuning and Model Evaluation (train, validation and test sets) were applied after splitting the dataset into training and test sets. A grid search procedure with an inner 5-fold cv was applied on the validation set for adjusting parameters and for selecting the best parameters of the trained models. Figure 1 illustrates the supervised learning analysis pipeline. Tree-based classifiers were applied within the ensemble methodology, such as Random Forest (RF), Decision Trees (DTs) and Gradient Boosting Machines (GBM) estimators.

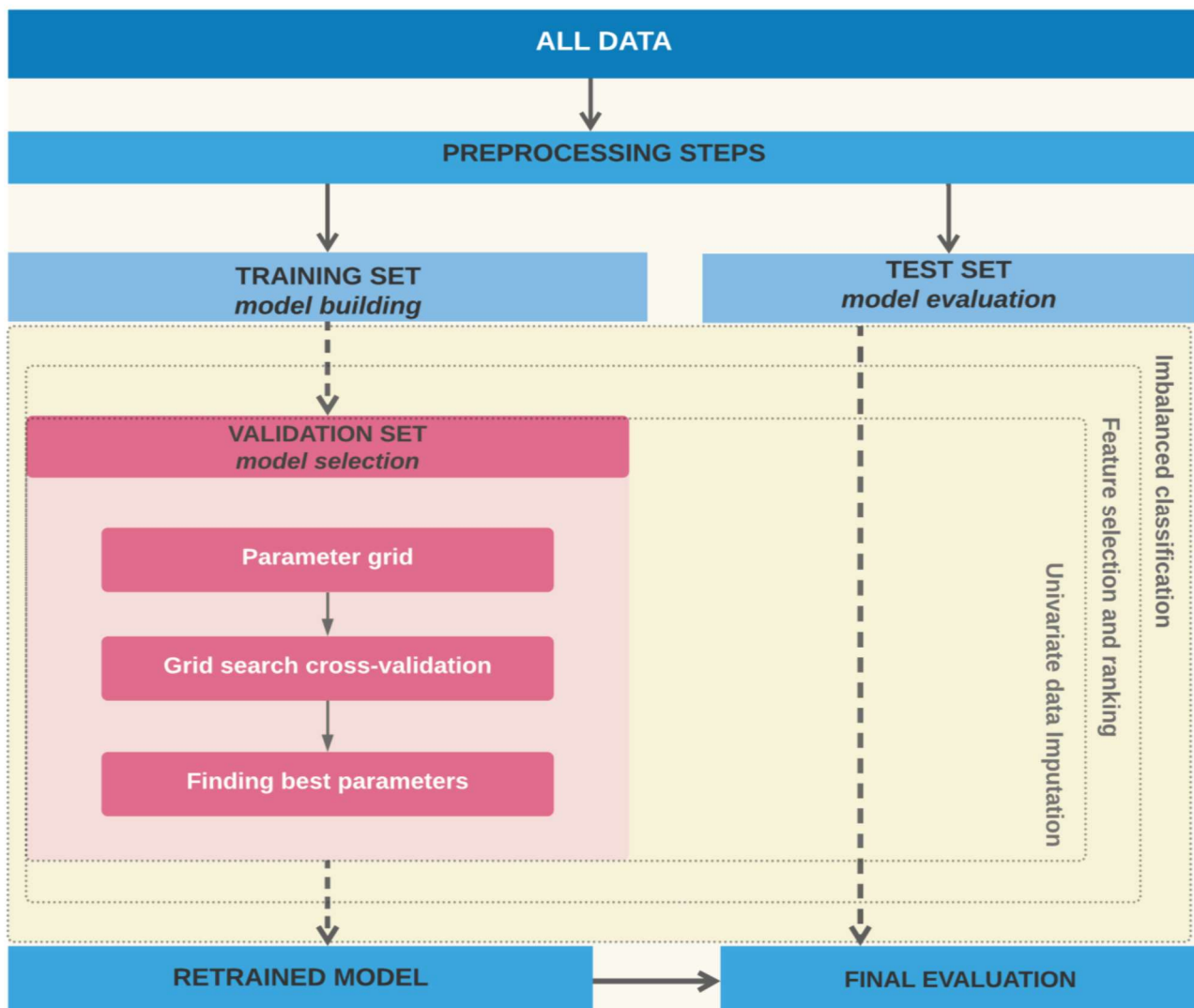


Figure 1. The data division scheme of the proposed supervised learning pipeline for training, testing and validation tests.

Initially, we assessed model accuracy for predicting who will show good resilience at one year post-diagnosis (in terms of anxiety and depression symptoms or overall well-being). All available medical, psychological, socio-demographic and lifestyle measurements, obtained immediately after diagnosis and shortly after (at the 3 months follow up), served as predictors in these models.

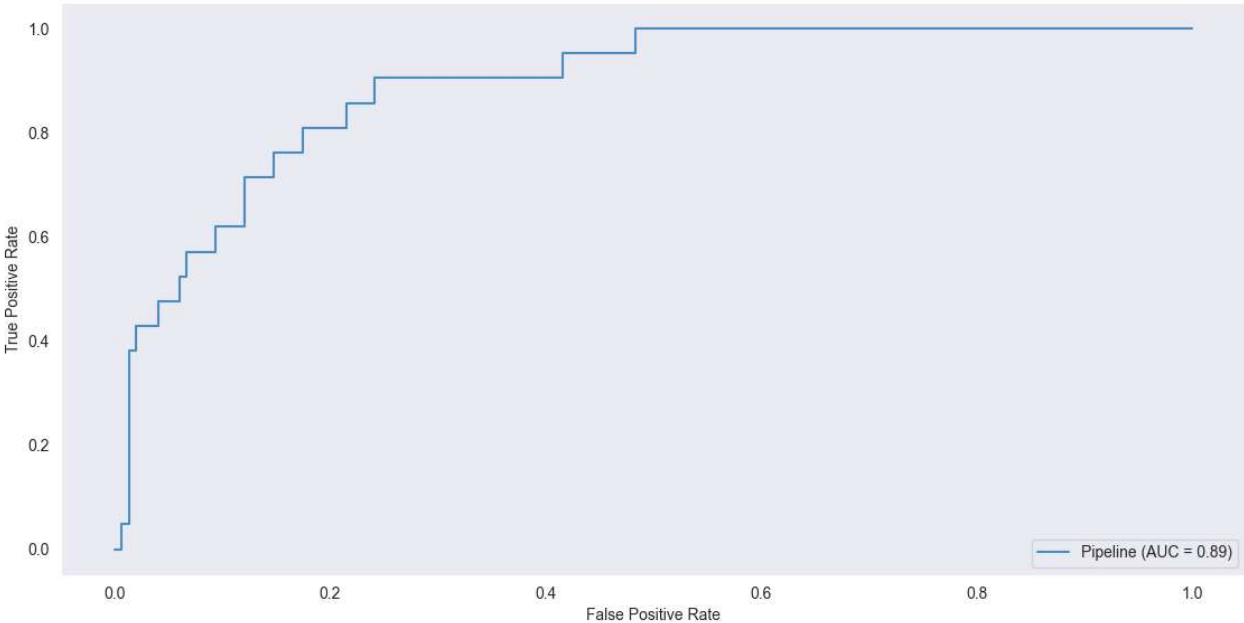
Predictors included overall mental health status and global QoL registered early during the course of the illness.

Table I. presents the classification performance of the two prediction models, revealing a fair balance between specificity and sensitivity metrics.

The shape of the Receiver Operating Characteristic Curve below supports this notion.

Table I. Performance of machine learning models in predicting one-year resilience as outcome (mean ± SD).

	Model 1	Model 2
Outcome	M12 Mental Health	M12 Global QoL
Accuracy	0.778 ± 0.05	0.670 ± 0.05
Sensitivity	0.785 ± 0.14	0.737 ± 0.10
Specificity	0.776 ± 0.06	0.654 ± 0.07



Overall, prediction of significant anxiety and/or depression symptoms was achieved in approximately 79% of cases (Model 1). Moreover, the model identified patients who develop such symptoms with approximately 78% certainty. Corresponding performance in predicting poor one-year well-being was somewhat lower (74% and 65%, respectively; Model 2).

In supplementary analyses, we sought to identify potentially modifiable behavioral and psychological characteristics that could inform clinicians regarding the needs of individual patients at the early phases of illness in order to maximize psychological resilience at later stages.

Model results related to the overall quality of life are presented here as one important instance of resilience-as-outcome. In view of the strong association between early and subsequent scores on the same self-report scales, scores on subjective quality of life obtained during the first 3 months of the course of the illness were excluded from the set of potential predictors of these variables as outcomes.

As shown in Table II, important predictors of 12-month quality of life included variables measured shortly after diagnosis, as well as variables, recorded three months into the course of the



illness. As expected, overall emotional state (negative affect) and the experience of physical side effects (illness- or treatment-related) during this period featured strongly among predictors. There were however additional variables corresponding to psychological characteristics that can become the focus of systematic psychological

interventions, such as ways of managing one's negative emotions in response to stressful events, and ways of thinking about the illness and what it represents in one's life. Lack of adaptive coping strategies is another characteristic that can be improved through intervention

Table II. The 10 most significant predictors of poor quality of life at one year after a breast cancer diagnosis.

Measured shortly after diagnosis
Greater reliance on maladaptive emotion regulation strategies and lesser reliance on adaptive strategies
Lack of sense of coherence
Lack of adaptive coping strategies
More severe anxiety symptoms
Measured at 3 months after diagnosis
Anxiety and depression symptoms, and weaker positive affect
More severe treatment side effects

Note: Variables pooled over several models using different subsamples of the BOUNCE cohort

Finally, the generalizability of the prediction models was assessed across the four clinical sites that contributed to the BOUNCE prospective study. In these analyses, feature selection and model training were conducted using data from three clinical sites, and the developed model was tested on unseen data from the fourth clinical site. Results revealed very similar classification performance across the four learning schemes. Importantly, predictor variables were largely overlapping across sites, despite notable cultural and sociodemographic differences across the four subcohorts. These results inspire optimism regarding the successful transfer of our prediction models to other clinical settings across Europe.

These findings are in accordance with the major psychological theories about adaptation to severe illness, including breast cancer, such as the Common Sense Model (Leventhal, Phillips, & Burns, 2016) or the Transactional Stress Model (Lazarus & Folkman, 1987). According to these models, adaptation to a severe health crisis is a complex process that is determined by (a) a variety of personal (and interpersonal) resources, which may buffer the negative impact of the situation and

facilitate adaptation; (b) cognitive-emotional processes (e.g., representations/perceptions of self and the condition) that guide behavior (e.g., coping behaviors); (c) contextual and specific

stressor-related factors that may impact adaptation (directly or indirectly).

Indeed, the variables that emerged as significant predictors of one-year mental health and quality of life (resilience-as-outcome) correspond to these "clusters" of factors. For example, sense of coherence, self-efficacy to cope with cancer, or optimism are key personal resources that refer to a sense of control. Emotion regulation and illness representations (e.g., representations of illness consequences) are forms of cognitive and emotional processes that typically guide emotions and actions/behaviors (e.g., anxious preoccupation). The experience of side effects or the previous levels of well-being are parts of the broader context that defines patients' experience (e.g., Hagger et al., 2017). In addition, the findings pinpoint those early factors (coming from a large array of sociopsychological, medical, and lifestyle variables) that are significant predictors of the final outcomes and, in this way, will guide our efforts to develop the clinical recommendations which may guide health professionals' and patients' informed decision making in order to achieve better adaptation and reinforce patient resilience.

Finally, it is worth noting that, besides side-effects (as perceived by the patient), the medical factors did not emerge as significant predictors of the M12 overall mental health and global quality of life. The most possible explanation might be that these



factors exert their influence on mental health and quality of life indirectly; that is, through the cognitive-emotional, behavioral, and situation-specific variables described above. Future analyses will examine the potential indirect impact of medical factors on the outcomes

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HOW THE BOUNCE PROJECT PROMOTES KNOWLEDGE ABOUT ADAPTATION TO BREAST CANCER

By **Evangelos Karademas**, PhD, University of Crete and Institute of Computer Science, Foundation for Research and Technology – Hellas (FORTH)

Although the main goals of the BOUNCE project are (a) to explore resilience in breast cancer patients and, (b) to develop a sophisticated prediction tool of resilience and key outcomes (e.g., psychological health and quality of life) that will facilitate health professionals’ and patients’ decision making, there is another parallel goal. Namely, the examination of the role of several important psychological factors with respect to adaptation to breast cancer. The rare occasion of a large longitudinal multi-center study provides the opportunity to study in-depth the relation of factors, including trait resilience, optimism, sense of coherence, family resilience, mindfulness, illness representations, coping behaviors, spirituality, positive and negative emotions, fear of recurrence, etc., to patients’ physical and psychological health and quality of life.

One of the factors that the BOUNCE research team has focused on so far is self-efficacy to cope with cancer or coping self-efficacy. Self-efficacy to cope with cancer refers to patients’ ability to perform those behaviors that may help them deal with the challenges caused by the disease, like diagnosis and treatment (Chirico et al., 2017). There is evidence that coping self-efficacy is related to several indicators of adaptation to breast cancer (e.g., pain management, distress, quality of life). Typically, higher levels of coping self-efficacy are linked to better adaptation to illness and enhanced well-being. Hence, its promotion is a frequent goal of psychological interventions for cancer patients (Merluzzi et al., 2019).

So far, the research team has prepared (or are preparing) three scientific publications that focus on coping self-efficacy. The first one examines the factors that mediate the impact of coping self-

efficacy on patients’ psychological health and quality of life. The second one examines the potential interaction between coping self-efficacy and trait resilience. The third publication refers to the interplay between coping self-efficacy and coping with cancer behaviors.

Specifically, the first study (recently published in *Psycho-Oncology*; Karademas et al., 2021) showed that coping self-efficacy predicted psychological symptoms (i.e., anxiety and depression) and overall quality of life over a period of six months, through multiple cognitive, emotional, and behavioral pathways. Coping self-efficacy predicted positive and negative affect, perceptions about the effectiveness of the medical treatment to treat or control breast cancer, and coping behavior (that is, reacting with great anxiety), which in turn predicted psychological symptoms. Positive affect, perceptions of treatment effectiveness, sense of hopelessness, and the effort to directly confront/cope with illness mediated the impact of coping self-efficacy on the overall quality of life. It should be noted that all statistical analyses were performed after controlling for several medical and sociodemographic variables.

The findings of this study demonstrated that coping self-efficacy lies in the heart of the patient’s efforts to deal with breast cancer. Coping self-efficacy seems to impact patients’ ways of thinking about breast cancer, their emotional state, and their behavioral reactions towards the disease, which in turn impact well-being. The fact that these variables are also linked to several health-related outcomes showcases the central role of coping self-efficacy in achieving a better adaptation to illness and better well-being. Thus, the enhancement of coping self-efficacy should be a

central intervention goal for patients with breast cancer.

A second publication, which is currently under revision, refers to the potential interaction between self-efficacy to cope with cancer and trait resilience as far as their impact on a patient's psychological symptoms and quality of life is concerned. Trait resilience refers to a patient's general ability to adapt to a difficult situation and maintain good function despite the difficulty (Johnston et al., 2015).

The findings from this study showed that high trait resilience leads to higher levels of coping self-efficacy, which in turn results in better psychological health and quality of life. Moreover, it was found that the combination of higher levels of trait resilience and higher levels of coping self-efficacy predicts better psychological health and quality of life. Surprisingly, none of the examined relationships was affected by the participant's country of origin (BOUNCE is conducted in four different countries). At the beginning of patients' experience with illness, it is likely for their reactions to being mostly shaped by personal resources than contextual factors. Contextual factors (e.g., the health care system) may be more important later, as the condition becomes chronic.



The third publication focusing on coping self-efficacy is under preparation. It will be about the mutual determination of coping self-efficacy and cancer-related coping behaviors (e.g., avoidance, helplessness, fighting spirit), over a period of several months. The statistical analyses showed that probably there is no constant pattern regarding the relationships between coping self-efficacy and coping behaviors, as this may depend on the particular behavior and other factors. According to the results, in half of the cases, the

initial levels of coping self-efficacy predicted future coping behaviors, which in turn had an impact on subsequent levels of coping self-efficacy. In other cases, however, it was rather the coping behavior that guided coping self-efficacy, at least during the initial phases of illness. Thus, new theoretical models are needed in order to more accurately describe the many aspects of the link between these two major factors. Also, the findings suggest that addressing only coping self-efficacy in psychological interventions for breast cancer patients may not be sufficient in order to modify all dysfunctional coping behaviors. Addressing both coping self-efficacy and coping behaviors may facilitate adaptation to breast cancer more successfully.

Of course, each of these studies has its limitations (e.g., all variables were self-reported). Still, each one shed light on a particular aspect of coping self-efficacy and helped us gain a better understanding of the adaptation to the breast cancer process. Considering that the members of the BOUNCE research group are currently conducting more analyses and are preparing several publications focusing on different key factors (such as family resilience, fear or recurrence, mindfulness, the impact of the SARS-CoV-2 pandemic, illness representations, etc.), we are hopeful that, besides the main goals of the project, we will be able to offer the scientific community, stakeholders, and the patients new valuable knowledge that will bear significant implications for theory and practice.

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PERSONAL EXPERIENCES WITH BREAST CANCER: FAMILY DYNAMICS

By **Chariklia Tziraki**, MD, PhD, Hebrew University of Jerusalem

In October 2020 the Eden Center and Beit Shemesh Municipality of Jerusalem, Israel organized an open, virtual event in order to raise awareness on breast cancer throughout Israel. The event was dedicated to the memory of a woman who was diagnosed with breast cancer at the age of 38. She was the mother of several children and one of her daughters, Nechama, participated in this conference to share her feeling and experience of how her mother's illness affected the family dynamic. The English summary of her talk was done with her permission.

In 2008, a woman by the name of Avigayil, aged 38, was discovered to have cancer. This discovery was only made after she conceded to go for testing, which she had protested for so long, insisting that she was too young to be affected by such illness. Until she finally agreed to go for an examination, she had no awareness of the disease or the need for treatment. Had she waited much longer the situation would have been far worse. Avigayil lived for 10 years after the disease was discovered, and Nechama gives a very open account of what those years were like for her mother, her extended family, and, of course, for herself

The three main points she tries to emphasize are the importance of awareness, the importance of maintaining as normal a life as much as possible under difficult circumstances, and her feelings under the circumstances of being a breast cancer survivor, mother and wife.

Avigayil became somewhat of a "crusader" to get other women to be checked for breast cancer. She felt it was important to speak to women individually rather than in large groups. So, she took it upon herself to find a way to have personal talks. What did she talk about? Two points that she made, are the gentle balancing act between maintaining the normalcy of a routine in life and accepting the fact that more help may be needed.

Nechama points out how hard it can be to concede the need to have someone shop or cook or just help a cancer patient with mobility problems. Acknowledging the fact that neighbors and friends may have to bring in meals, for example, is part of the acceptance of the new reality. Yet, at the same time, trying to continue running a family life as best as possible, is crucial. Nechama quotes her mother as once saying that although the meals from others may not be quite like her own cooking, the fact that she was relieved of this task, allowed her to

preserve her strength to continue to be a mother. Fulfilling her role as a mother was of utmost importance to Avigayil.




The Eden Center and Beit Shemesh Municipality invite you to a virtual event, for Breast Cancer Awareness month, In memory of Avigail Rock ז"ל

Knowledge Saves Lives

29.10.20
Thursday י' חשוון התשפ"א
20:00-21:30

ON PUBLICATION OF EDEN'S BREAST CANCER & MIKVEH GUIDE IN MEMORY OF AVIGAIL ROCK

Parallel programs in English & Hebrew

דברי זכרון ע"י קרובי משפחה של אביגיל	REFLECTIONS IN MEMORY OF AVIGAIL ROCK
לחיות עם נשאות למחלה BRCA בנים	WHAT YOU NEED TO KNOW ABOUT BREAST HEALTH & BRCA DR. SHARON GALPER GROSSMAN
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אורח חיים, בריאות ומודעות	WELLBEING, AWARENESS & SELF-CARE SARA SIEMIATYCKI, BISHVILACH HEALTH CENTER
יצי נבצקי, עמותת אחת מחשק	
שרית עם ד"ר שני פאלוך-שמון	Q&A WITH DR SHANI PALUCH-SHIMON
מנהלת, נאיהדה לעקרונותיה של רפואה, בית החולים מאכביסטי הרדסה	DIRECTOR, BREAST ONCOLOGY, HADASSAH UNIVERSITY HOSPITAL

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Register: bit.ly/bc-rock

Nechama touches on this point in a very moving way: she talks about her feelings vis-à-vis Avigayil's illness and role as a mother facing a major change in her own life – her entry into the Israeli army. Military service begins at age 18, and Nechama says that a few days before she was called up, she suddenly realized how sick her mother was. As she entered her basic training period—a tough time for any new young soldier—she kept asking herself: "what am I doing here?" People advised her to pretend as if everything was fine when she visited her mother at the hospital. But, in fact, she felt that her life had been turned upside down. In the army you are constantly being ordered around by other people, being told what to do at every moment, your life is no longer the same as before. On top of that, her mother was ill, so does that mean she is no longer her mother, the mother she knew before? This also brought back memories of how she dealt with the initial knowledge of Avigayil's illness: the

first question Nechama had asked her was whether she would lose her hair, meaning she would no longer be her "original" mother in some sense.

Nechama does not always provide answers or solutions to the feelings and questions she presents. Some of her thoughts leave the viewer, or listener, to try and find their resolutions.

In pursuing the theme of trying to maintain normalcy, Nechama points out the importance of a sense of humor in facing the burden of living with a cancer patient, but also the need to allow oneself to cry. By the way of example of humor, she talks about all kinds of humorous remarks that were written in the family WhatsApp group, even including subjects like blood transfusions. Nothing was hidden or masked.

Transparency was the attitude that the family adopted. The concept of cancer, and its very name, were never hidden by euphemism. Nechama points out that in Israel it is often customary for people to refer to cancer as "the disease", in the manner of "Voldemort", whose name cannot be mentioned. Nechama would reply to people who said to her "I heard your mother has the disease", by saying "let's just call a spade a spade. Cancer is NOT a pink

elephant in the room, which people make believe isn't there".

Avigayil went through bouts of cancer. Nechama tells how the second time, when she went to see her in the hospital, she still wasn't sure how to behave towards her, and what to say, and how. Yet Avigayil, sensing this, stunned her by saying to Nechama that she may have gotten a "pass" from many difficult obligations in her life, but she didn't get a "pass" on being a mother. So many things had changed in her life—like being taken around in a wheelchair—but some things would never change. Avigayil said it was important to learn to accept, to embrace limitations, and to learn to live with this new reality.

Nechama reiterated a number of times that her family is a "crying family", this doesn't deny sadness; when one member of the family starts crying, the others join in. But you can't cry all the time—you also have to laugh, even at cancer.

Nechama summed up her talk by stressing things that characterized her mother: transparency, openness, and dialogue. She lived in this world. And above all, awareness, which became so important to her.

RECENT EVENTS

BOUNCE experts elaborated on important issues related to the cognitive and psychosocial quality of life of women recovering from breast cancer at a dedicated Symposium entitled: *"Interdisciplinary approaches to assess psychological resilience in breast cancer survivors"* organized by the Champalimaud Research & Clinical Centre within the International Congress of Psychology (ICP) virtual conference held in July 18-23 2021 ("ICP 2020").

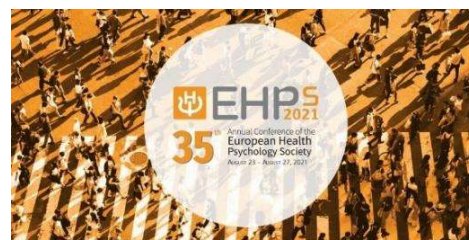


Specific topics included:

- Psychosocial adjustment and resilience in cancer patients from an interdisciplinary perspective by Prof. Ruth Pat-Horenczyk, Hebrew University of Jerusalem

- Bridging the gap between psychosocial care and oncology: The Bounce Project by Ketti Mazzocco, Istituto Europeo di Oncologia
- Neuropsychological changes associated with breast cancer patients: Current evidence by Berta Sousa, Champalimaud Research & Clinical Centre
- Online platforms to capture patient-reported outcomes and improve personalized cancer care by Paula Poikonen-Saksela, Helsinki University Hospital Comprehensive Cancer Center

Our work was presenting during the 35th Annual Conference of the European Health Psychology Society (EHPS2021) that was held online on August 23-27, 2021: *"The impact of cultural and health-care system differences on psychological adaptation to breast cancer"*



"The impact of cultural and health-care system differences on psychological adaptation to breast cancer"

BOUNCE

BOUNCE participated in a special session entitled: "Sensor-based behavioural informatics in support of health management and care" within the IEEE BHI – BSN 2021 virtual conference on July 27.



**Sensor-based behavioural informatics
in support of Health
management and Care**



The session highlighted recent patient – centered research using wearable sensing ecosystem and machine learning/AI to optimize interventions through monitoring, assessing, and modeling behavior. Health-related behaviors are significant determinants of health and quality of life. Modern mobile technologies, such as smartphones and wearables, offer opportunities to sense and intervene on patient health behaviors in real-time at enormous scale.

4th DISSEMINATION EVENT

The 4th BOUNCE Dissemination Event will be organized on October 8th, as a Special Session, by the Champalimaud Foundation on the Breast Unit Open Day and in combination with the 2021 Champalimaud Research Symposium (CRS21) under the topic "Dialogues on Neural and Machine Intelligence".

The Symposium will take place on 13-15 October 2021 probably in a mixed environment (face-to-face and virtual), and will be hosting expert speakers from EU and US research centers, focusing on recent findings regarding neural and cognitive implications of breast cancer.

Readers are cordially invited to the BOUNCE Dissemination Event where all advances and results of the project will be presented,

For more information about the event and registration, follow this link:

<https://www.bounce-project.eu/events/>

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