

Predicting Effective Adaptation to Breast Cancer to Help Women to **BOUNCE** Back

CONTENTS

Predicting Effective Adaptation to Breast Cancer to Help Women to BOUNCE Back	1
Defining Resilience	2
Resilience as Potential	2
Resilience as an Adaptation Process	2
Resilience as Outcomes	3
Resilience and Breast Cancer	3
Coping with Resilience	3
Implementing a prospective clinical study to model resilience growth	4
Resilience monitoring through an electronic platform (the adapted Noona tool)	6
Using adaptive algorithms to achieve individualized models of resilience	6
BOUNCE dissemination events	7
Events that took place:	8
Event in Helsinki	8
Forthcoming events:	8
Event in Jerusalem	8
BOUNCE PARTNERS	8
Social Media	8

PROJECT COORDINATOR

Paula Poikonen-Saksela

Contact Information

Helsinki University Hospital
Comprehensive Cancer Center (HUS)

Address
Stenbäckinkatu 9 PO BOX 100,
FI-00029 HUS,
Finland

e-mail
info@bounce-project.eu

BOUNCE NEWSLETTER



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

PREDICTING EFFECTIVE ADAPTATION TO BREAST CANCER TO HELP WOMEN TO **BOUNCE** BACK

By Dr Paula Poikonen-Saksela, MD, Helsinki University Hospital Comprehensive Cancer Center, Helsinki, Finland, BOUNCE Project Coordinator

Breast cancer is the most common cancer in women worldwide accounting for 28% of the total cancer cases in the WHO European Region. According to the WHO, despite all advances in medicine and preventive strategies, the incidence of breast cancer in developing countries is still rising. In spite of this devastating fact, the mortality of breast cancer in the developing world seems to be decreasing, with five-year relative survival rate for female invasive breast cancer patients rising from 75% in the mid-1970s to 90% today and in cases of localized breast cancer even reaching 98.5%. As a result, there is a dramatic rise in the number of breast cancer survivors in Europe, posing new challenges to the healthcare system. Coping with breast cancer becomes a major socio-economic challenge calling for novel strategies for understanding, predicting and increasing the resilience of women with breast cancer to all the stressful challenges and experiences and ensuring better and faster recovery.

In this context, an interdisciplinary consortium of experts was formed in 2017 in response to a HORIZON 2020 call for Personalized Medicine research and innovation solutions. The product of this collaboration was BOUNCE a funded project developed to explore factors that influence breast cancer patients' long-term psychological resilience and their capacity to resume a normal everyday life and work following breast cancer treatments.

Resilience experts have developed a working model of resilience to breast cancer, taking into consideration also related clinical, biological, social, and psychological factors. This model is tested in a prospective multicenter study that recruits large numbers of early-phase breast cancer patients from specialized cancer treatment centers in Finland, Israel, Italy, and Portugal. This patient information will be largely registered through an innovative, interactive mobile app designed by Noona Healthcare. Information technology experts will then apply innovative computational tools to identify key factors involved in building and maintaining resilience in these women.

The BOUNCE Consortium includes experts from the field of oncology, computer modeling, psychology, and social medicine from Finland, Greece, Italy, Portugal, and Israel. Helsinki University Hospital (HUU) Comprehensive Cancer Center has been chosen to coordinate the multicenter study on how to support breast cancer

patients and improve their resilience. Consortium members are: *Helsinki University Hospital Comprehensive Cancer Center (Finland)*, *Foundation for Research and Technology -Hellas (Greece)*, *European Institute of Oncology (Italy)*, *Institute of Communication and Computer Systems (Greece)*, *NHG Consulting (Finland)*, *Hebrew University School of Social Work and Social Welfare (Israel)*, *Singular Logic (Greece)*, *Champalimaud Clinical Center & Foundation (Portugal)*, *Noona Healthcare (Finland)*.



Coping with breast cancer is a major challenge. Thus, it is necessary for health professionals to help patients increase their psychological resilience toward better and faster recovery.

The BOUNCE project will explore the factors that influence breast cancer patients' resilience and their ability to resume a normal everyday life through cost-efficient clinical tools for patient empowerment.

BOUNCE develops and deploys advanced computational tools to validate indices of patients' capacity to bounce back during the highly stressful treatment and recovery period following diagnosis of breast cancer. Elements of a dynamic, predictive model of patient outcomes are incorporated in building a decision-support system to be used in routine clinical practice providing oncologists and other health professionals with concrete, personalized recommendations regarding optimal psychosocial support strategies.

DEFINING RESILIENCE

By Prof. Ruth Pat-Horenczyk, Hebrew University School of Social Work, Jerusalem, Israel

How do people deal with life-changing situations such as life-threatening illness, loss or trauma? Many people react to such circumstances with an initial flood of strong emotions and a sense of uncertainty. However, most people adapt well over time. What enables them to do so? The term “*Resilience*” is used to describe this common adaptive coping. How do people manifest resilience? What can explain the individual differences? Most importantly, can specific resilience skills—behaviours, thoughts and actions—be learned and developed? These are some of the many open questions regarding resilience in different contexts that BOUNCE has set out to address.

Being resilient does not mean that a person doesn't experience difficulty or distress. Emotional pain and sadness are part of the common experience of people who have suffered major difficult life events and trauma. In fact, the road to resilience, according to the APA (American Psychological Association) is likely to involve considerable emotional distress. Contrary to common belief, being resilient is not extraordinary, and as Ann Masten, one of the world's leading scholars in the field of resilience, coined it: “Resilience is ordinary magic.” To date, there is still a lack of clarity as to what resilience is and how it operates. Does being resilient relate to an individual's **potential** (capacity to engage in adaptive coping processes), **process** (adaptive reactions to adversity), or **outcome** (the final state achieved as the result of coping)?

Resilience as Potential

Some understand resilience to be a predisposition or an existing potential, before even facing an adverse situation. In this sense, *Resilience as Capacity* is the integration of the internal and external resources available to the individual facing adversity that may influence the effectiveness of the coping process, e.g., optimism, humor, cognitive flexibility, cognitive explanatory style and reappraisal, acceptance, religion/spirituality, altruism, social support, positive role models, flexible/healthy coping style, exercise, the capacity to recover from negative events, and stress inoculation.

Many studies show that the primary factor in resilience is having caring and supportive relationships within and outside of one's family. Relationships that create love and trust provide

What is the meaning of resilience since being resilient does not mean that a person simply doesn't experience difficulty or distress? There is a lack of clarity as to what resilience is and how it operates.

Resilient relates to an individual's potential (i.e., the capacity to engage in adaptive coping processes); it is a process (adaptive reactions to adversity) also an outcome (the final state achieved as the result of coping). An effort to reach a consensus definition was made by a panel of prominent resilience experts who agreed on the following definition (Southwick, 2014): “The concept of resilience includes healthy, adaptive, or integrated positive functioning over the passage of time in the aftermath of adversity”.

role models and offer encouragement and reassurance that help bolster a person's resilience. Several additional factors are associated with resilience, including:

- The capacity to make realistic plans and take steps to carry them out.
- A positive view of oneself and confidence in your strengths and abilities.
- Communication and problem-solving skills.
- The capacity to manage strong feelings and impulses.

Resilience as a potential is not a trait available solely to the individual—it can exist in groups as well. In a family, resilient characteristics may take the form of a sense of solidarity, involvement, warmth towards other family members, and cohesion among them. A resilient community would be one that offers supportive resources, and these may be based on a cultural context of resiliency reflected in the narratives, traditions or rituals of the individual or the community.

Resilience as an Adaptation Process

Resilience was defined by the American Psychological Association as “*the process of adapting well in the face of adversity, trauma, tragedy, threats or significant sources of stress—such as family and relationship problems, serious health problems or workplace and financial stressors.*” It posits that resilience is not a trait that

people either have or do not have, and can be considered as an adaptation process. Resilient individuals may experience transient perturbations in normal functioning (e.g., several weeks of sporadic preoccupation or restless sleep) but generally exhibit a steady reimplementation of healthy functioning across time, as well as the capacity for constructive experiences and positive emotions. In this sense, resilience is more common than generally accepted, and there may be multiple ways of achieving resilience (Bonanno, 2004).

Resilience as Outcomes

Resilience can also be defined as the outcome of coping with trauma or adversity in the form of relative satisfaction with one's quality of life and wellbeing. Resilience represents the ability to maintain a stable equilibrium, healthy functioning, subjective wellbeing, and satisfactory quality of life despite exposure to trauma. It means "bouncing back" from difficult experiences.

Resilience and Breast Cancer

Studies focusing on resilience in breast cancer patients show that women who maintained better body image had more positive future perspectives and reported less severe symptoms also reported higher resilience (Ristevska-Dimitrovska et al., 2015). In turn resilience may protect breast cancer patients against the development of psychological symptoms including depression and anxiety (Markovitz et al., 2015) and maintain high levels of subjective happiness after breast cancer. For the purposes of the BOUNCE project the consortium experts defined resilience in the context of coping with breast cancer as *"a conglomerate of dynamic self-regulatory capacities that allow an individual facing adversity to mobilize and use internal and external resources over time in order to maintain or promote wellbeing. The construct of resilience is used in three ways: (a) As a personal capacity or potential; (b) As a post-trauma adaptive process or trajectory; (c) As an outcome of maintaining healthy functioning and subjective well-being despite exposure to adversity"*

Coping with Resilience

When faced with such potentially life-threatening events each person engages coping strategies that can vary widely in their capacity to provide adaptive solutions and ensure optimal recovery with respect to the disease itself as well as to the patient's overall quality of life. Coping strategies frequently vary depending on the stage

and timing of illness (e.g. coping strategies when the person is diagnosed with breast cancer vs. after having received treatment). During the last decades, considerable progress has been made in the field of Health Psychology towards identifying factors that determine adoption of particular types of coping behaviors highlighting socio-demographic and cognitive-emotional (e.g., the persons own diverse perceptions of their illness), in constant interplay with ever-changing life circumstances. Moreover, it is recognized that intervention and/or prevention efforts should take into account both modifiable attributes as well as (constant) individual characteristics (such as sociodemographic, patient history, and cancer type) that may affect the person's dynamics.

What is the meaning of resilience since being resilient does not mean that a person simply doesn't experience difficulty or distress? There is a lack of clarity as to what resilience is and how it operates. Resilient relates to an individual's potential (i.e., the capacity to engage in adaptive coping processes); it is a process (adaptive reactions to adversity), but also an outcome (the final state achieved as the result of coping).

The overarching goal of BOUNCE is to incorporate elements of a dynamic, predictive model of patient outcomes in building a decision-support system used in routine clinical practice to provide physicians and other health professionals with concrete, personalized recommendations regarding psychosocial support strategies.

There is a growing need for novel strategies to improve understanding and capacity to predict the resilience of women to the variety of stressful experiences and practical challenges related to breast cancer. This is a necessary step toward efficient recovery through personalized interventions. BOUNCE will bring together modelling, medical, and social sciences experts to advance current knowledge regarding the dynamic nature of resilience, which relates to efficient recovery from breast cancer. BOUNCE will take into consideration clinical, cancer-related biological, lifestyle, and psychosocial parameters in order to predict individual resilience trajectories throughout the cancer continuum with the aim to eventually increase resilience in breast cancer survivors, help them remain in the workforce and improve their quality of life.



Modelled Psychological, Lifestyle and Socioeconomic Trajectory
Including Eventual Psychological Interventions <Machine Learning

Modulation of the mean probability for eventually surviving dormant tumour cells (residing in the G0 phase) to re-enter the cell cycle $P(G0 \rightarrow G1)$

Modulation of the psychological stress due to eventual tumour relapse

Initial Breast Cancer Treatment

Eventual Tumour Relapse

Modelled Biological and Clinical Trajectory Including Long Term Treatment <Multiscale Mechanistic and Machine Learning Modelling >

IMPLEMENTING A PROSPECTIVE CLINICAL STUDY TO MODEL RESILIENCE GROWTH

By Prof Ketti Mazzocco, Psycho-oncologist, European Institute of Oncology, Milan, Italy

The broad and general objective of the BOUNCE project is to build a quantitative mathematical model of factors associated with optimal adjustment capacity to cancer. Special emphasis is given to modifiable factors associated with optimal disease outcomes. At the core of the project is a prospective multi-centre clinical pilot at four major oncology centres: European Institute of Oncology in Italy, Helsinki University Hospital in Finland, Rabin Medical Center and Shaare Zedek Medical Center coordinated by the Hebrew University of Jerusalem in Israel, and Champalimaud Foundation in Portugal.

The study is currently recruiting over 660 breast cancer patients with stage I-III histologically confirmed diagnosis. There will be seven assessment waves over a period of 18 months: baseline, completed after the first visit to the oncologist, and Months 3, 6, 9, 12, 15, and 18. At baseline only non-cancer-specific measures are administered (such as optimism and self-efficacy).

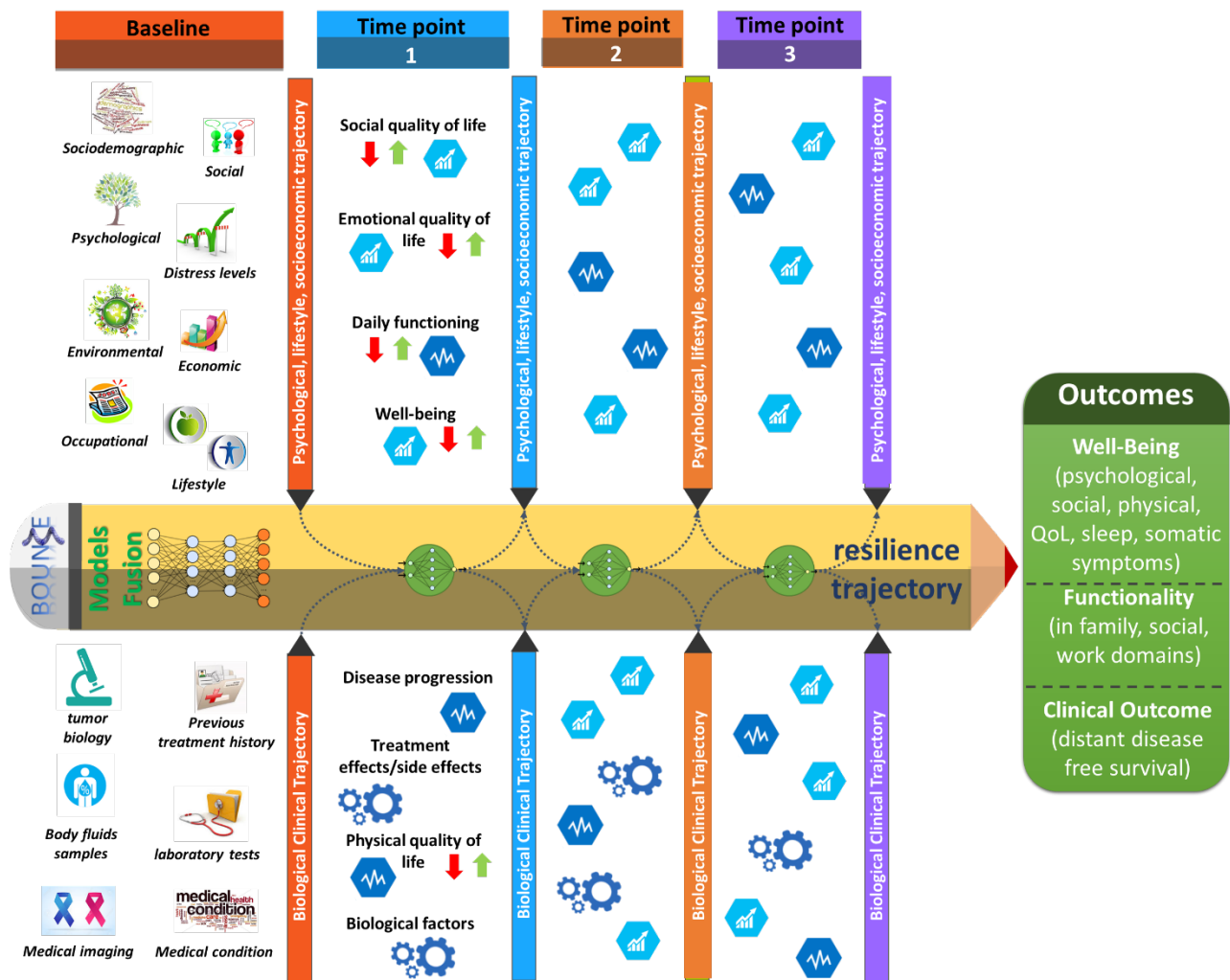
Cancer-specific measures are first administered at Month 3, when the patient has already had some meaningful experience with the illness. Measurement sessions at baseline and at Month 12 will involve face-to-face interviews with a health-care professional-researcher. During the first face-to-face encounter the researcher will demonstrate the electronic platform designed for BOUNCE to facilitate data collection as described below. For patients who find it difficult to use the electronic platform a paper-and-pencil version of the questionnaires is available.

Within the multicentre clinical pilot, information about the biomedical status, the psychosocial status and the functional status of breast cancer patients will be collected. The primary end-point of the BOUNCE clinical pilot is to identify factors and processes that may predict both interim and long-term patient resilience, their physical wellbeing and psychological outcomes of cancer and cancer treatment. The design of the

study will allow researchers to address several secondary aims: (i) Identify processes and interactions that can more accurately predict final (i.e., at 18 months) and intermediate (i.e., at 3, 6, 9, 12 and 15 months) psychological outcomes; (ii) Develop a multi-dimensional index of resilience as a function of the biomedical status, the psychosocial status and the functional status of the patient; (iii) Apply statistical models to understand complex interactions of variables both within and across measured domains (e.g., from personality traits to health outcomes, through health-related beliefs and behaviour, with socio-demographic and cultural variables as moderating conditions) in order to gain an enhanced understanding of the dynamic process of adaptation to breast cancer, and resilience-as-a-process; (iv) Perform cost-benefit analysis assessing the strengths and limitations of the project outcomes and also determine the best approach to achieve the maximum benefits.

The BOUNCE multicenter clinical pilot is currently recruiting over 660 breast cancer patients with stage I-III histologically confirmed diagnosis. Assessments of the biomedical, psychosocial and functional status of participating women are obtained at 7 time points over a period of 18 months. Among other goals the study aspires to allow researchers to:

- Develop a multi-dimensional index of resilience as a function of the biomedical, the psychosocial and the functional status of the patient,
- Enhance our understanding of the dynamic process of adaptation to breast cancer, and
- Assess the cost-benefit values of personalized clinical efforts to enhance resilience.



RESILIENCE MONITORING THROUGH AN ELECTRONIC PLATFORM (THE ADAPTED NOONA TOOL)

By Juja Salonen, Noona Healthcare, Helsinki, Finland

Electronic personalized medicine applications are rapidly gaining acceptance in clinical practice. One of the BOUNCE partners, Noona Healthcare is designing pioneering applications to help health care professionals and patients towards effective treatment and cancer recovery. The Noona mobile service permits remote monitoring and communication between cancer patients and healthcare professionals. In BOUNCE however, Noona will not be used for communication between the treatment team and patient but only for collection of study-relevant information, with the exception of HUS where Noona is integral part of their clinical practice. Noona is a smart cloud-based mobile solution, supported through a responsive web application, for all smart and standard devices. Noona app is GDPR compliant using encryption and decryption keys for all patient information and gives authorization rights according to user status.

Bounce patients who agree to use Noona receive feedback on their overall psycho-emotional status after filling out platform questionnaires.

They receive graphic representations of their scores on "overall distress levels" together with verbal messages. If responses indicate clinically significant levels of anxiety or depressive symptomatology, the patient is encouraged to contact a mental health professional as well as to discuss it with her oncologist.

The BOUNCE prospective clinical study utilizes Noona mobile service for the collection of study-relevant information.

It is a fully responsive web application for all devices, GDPR compliant and with authorization rights according to user status.

BOUNCE patients who agree to use Noona will receive feedback on their overall psycho-emotional status after filling out platform questionnaires. In case of high levels of distress, patients will be encouraged to seek help and discuss the issue with their oncologist.

USING ADAPTIVE ALGORITHMS TO ACHIEVE INDIVIDUALIZED MODELS OF RESILIENCE

By Prof. P. Simos and E. Karademas, University of Crete and FORTH, Herakleion, Greece

Statistical and/or computational models focusing on the well-being and functionality of breast cancer patients are limited. Modelling of psychological resilience requires building theoretically plausible, clinically useful, and computationally sound schemes describing: (i) the predominant mechanisms involved in the process of psychological adaptation to cancer and (ii) the most powerful longitudinal predictors of long-term psychosocial and functional outcomes following treatment for breast cancer. This goal could be effectively addressed using conventional multivariate statistical methods, such as structural equation modelling using latent constructs, logistic regression, and survival statistics, to name the most popular methods. Although these techniques could be adopted for modelling resilience over time as individual trajectories, they could not predict adaptation to illness as a dynamic process through a composite framework wherein the

contribution of each trajectory to the end-point outcomes is assessed and evaluated.

BOUNCE aspires to go further and develop a prediction tool that can be used at any point during breast cancer diagnosis and treatment to identify patients at risk for poor psychosocial and functional outcomes—i.e., patients who, at a given point in time, demonstrate poor psychological resilience. In its final form this tool should have the capacity to identify subgroups of persons defined on individual resilience levels (as a proxy for risk of adverse psychosocial outcome) using a limited number of validated predictors and moderators. The novelty of the BOUNCE computational approach is two-fold:

First, it takes full advantage of longitudinal measurements of potential predictors to test models that include both one-time measurements of each predictor (cross-sectional predictor



models) as well as individual trajectories of each predictor.

Secondly, given the inherent complexity of the longitudinal data, BOUNCE will develop and evaluate a **Machine Learning (ML) framework** to identify subgroups of patients that display distinct psychosocial profiles (at specific time points and over time) in adapting to breast cancer.

Cross-sectional and longitudinal data are exploited by unsupervised and supervised machine learning techniques aiming at identifying patterns of patients' symptoms and at predicting final and intermediate outcomes at each and across different time points, respectively. A model fusion computational framework is developed to enhance the predictive outcomes of the models. The BOUNCE trajectory predictor will exploit effectively factors measured in the multicenter clinical study. This set of factors consists of: (i) patient-reported outcomes (i.e. mental health, distress level, health- and overall Quality of Life (QoL), and functionality), (ii) illness-related self-regulation variables (i.e. self-rated health etc.), (iii) potentially stressful events taking place during the follow up period, (iv) moderators and facilitators (i.e. self-efficacy, resilience, social support etc.) and (v) lifestyle factors (i.e. health habits etc.).

The BOUNCE computational approach evolves along **four main axes** each serving crucial clinical scenarios.

Firstly, a cross-sectional clustering methodology aims to determine basic clusters of patients that at a given time point belong to a

BOUNCE aspires to develop a prediction tool that can be used at any point during the course of breast cancer diagnosis and treatment to identify patients at risk for poor psychosocial and functional outcomes (i.e., poor psychological resilience).

To this end BOUNCE will develop and evaluate a Machine Learning (ML) framework to identify subgroups of patients that display distinct psychosocial profiles (at specific time points and over time) in adapting to breast cancer.

specific 'level' of adaptation to illness. In this approach resilience is defined according to the observation of affective and functional status.

Secondly, longitudinal data are exploited through a clustering methodology aiming to distinguish patient profiles according to possible transitions from one resilience category to another due to changes in specific factors.

Thirdly, prediction of resilience is performed to determine factors or interactions among them that can more accurately predict final and intermediate outcomes as well as an overall resilience level.

Finally, all clinical predictive outcomes **will be entered into a decision-level fusion model** to investigate whether the ensemble of the decisions further improves prediction of resilience at a specific time point.

BOUNCE DISSEMINATION EVENTS

By Dr. Berta Sousa, MD, MSC, Champalimaud Cancer Center, Lisbon, Portugal

In order to make the BOUNCE results widely available, a number of dissemination activities will be initiated during the project, with the overall objective to target all levels of stakeholders and practitioners. The BOUNCE results will be disseminated to a broad audience including private and public organizations, pharmacy industries, academia and research institutions, as well as the general public and patient organizations, through activities such as conference attendance, journal publications, internet exposure, and social media. Other dissemination activities extend to standard contributions targeting stakeholders within the relevant research community and industry, participating in EC concentration meetings and clustering activities, as well as ensuring an outreach amongst related projects and researchers.

The first dissemination event of BOUNCE took place the day before HIMSS Europe 2019

conference. The event targeted health and social care professionals, breast cancer patients, patient organizations, researchers and media. The event had two independent sessions. The first session focused on resilience and breast cancer patient care in general, and the second session on digital tools in research and care.



Events that took place:

Event in Helsinki

At The Hebrew University of Jerusalem
September 18, 2019



The 1st BOUNCE Dissemination Event presenting the BOUNCE project took place at Helsinki on the 10th of July 2019 as an off-site event of HIMSS Europe 2019 & Health 2.0 2019 Event, providing opportunities for the researchers to engage with different stakeholders and general public. The event consisted of two independent sessions: one with orientation in patients' perspective, psychological adaptation in cancer and resilience as a concept, and the second session had more technical orientation, concentrating on digital tools in cancer care and research, and modelling the resilience with data.

Also on July 12th 2019, Director Johanna Mattson from HUS Comprehensive Cancer Center and one of the PIs of BOUNCE gave a keynote speech in session engaging all the stakeholders including patients and families at HIMSS.

Forthcoming events:

Event in Jerusalem

At The Hebrew University of Jerusalem
September 18, 2019



The 2nd BOUNCE Dissemination Event will take place in Jerusalem on September 18th, 2019. The event will focus on Cross-Cultural Perspective on Resilience In Breast Cancer.

More Information available at (Bounce site)

BOUNCE PARTNERS



Helsinki University Hospital
Comprehensive Cancer Center

HUS
www.hus.fi
Finland



Foundation for Research and
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FORTH
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