BOUNCE

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

BOUNCE NEWSLETTER

PROJECT COORDINATOR

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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

Paula Poikonen-Saksela on the BOUNCE project

By **Paula Poikonen-Saksela**, MD, BOUNCE Coordinator

During the project, we have learned much about resilience in early breast cancer. Moreover, BOUNCE data is a rich and unique source for further research into various aspects of resilience. The BOUNCE consortium will actively continue this collaboration in the future, and already many BOUNCE partners have jointly participated in new research calls with proposals inspired by the BOUNCE study. Thus, the work aimed at improving the well-being of breast cancer patients will surely continue.

During the past four and half years, it has been my privilege as the coordinator of BOUNCE to work with a skillful group of professionals. Our consortium consists of clinicians including psychologists and oncologists, and a technical team of modelers and IT experts. The core data source of BOUNCE is a prospective pilot study that took place in four different countries, namely Finland, Portugal, Israel, and Italy. Data consist of psychological questionnaires and information on sociodemographic background, lifestyle, and medical records.

At the end of the project, we have reached our goal to build a decision support tool to predict the resilience of women with early breast cancer. We have generated models to predict patients´ mental health and global quality of life, as complementary resilience outcomes, and identified different trajectories of patient well-being during the 18-month follow-up period. Our results have been and will be further disseminated widely in the academic community and different stakeholders, including clinicians, patient organizations, and cancer societies. The first response from clinicians in participating hospitals has been enthusiastic, and BOUNCE results have been appreciated as an opportunity to further develop the care path and operational models. Relying on BOUNCE models we will be able to offer customized, interventions when women need them most.

A significant observation highlighted by BOUNCE concerns a sizeable group of patients who appear to be resilient at the time of diagnosis, but develop persistent signs of poor mental health thereafter. Systematic resilience prediction would help especially this group, as their problems might not be detected otherwise.

We have plans for possible commercial as well as for internal exploitation of the BOUNCE tool and BOUNCE will also provide information about resilience through ongoing scientific publication and dissemination activities.

The BOUNCE tool developed in this project is a digital instrument for professionals, but digital services to be used by patients have also been generated as a part of BOUNCE. Data collection in the prospective pilot was done mainly digitally through the Noona platform where BOUNCE data collection questionnaires were embedded. We have tested the first version of the BOUNCE tool in Helsinki and developed digital intervention paths for patients together with psychologists, physiotherapists, and nutrition therapists. Notably, the COVID-19 pandemic has further emphasized the importance of digital services during the last two years.

During the project, we have learned much about resilience in early breast cancer. Moreover, BOUNCE data is a rich and unique source for further research into various aspects of resilience. The BOUNCE consortium will actively continue this collaboration in the future, and already many BOUNCE partners have jointly participated in new research calls with proposals inspired by the BOUNCE study. Thus, the work aimed at improving the well-being of breast cancer patients will surely continue.

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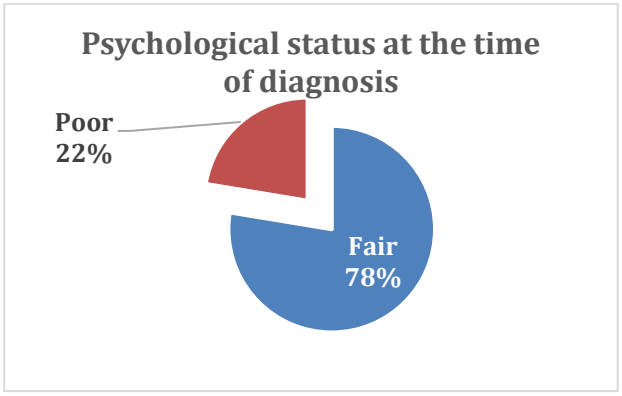
Predicting Psychological Resilience of Women Undergoing Treatment for Breast Cancer via Machine Learning Models

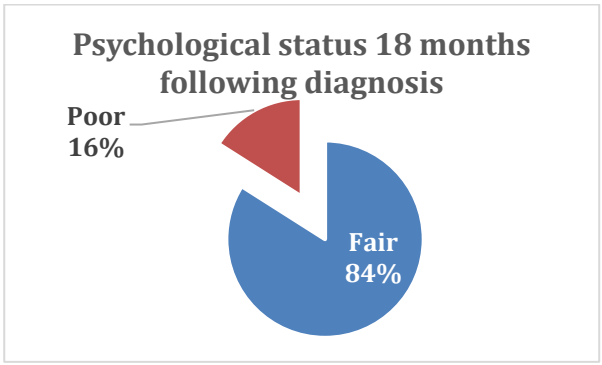
By **Panagiotis Simos, George Manikis, Konstantina Kourou, & Evangelos Karademas,** Computational Biomedicine Laboratory, Institute of Computer Science, Foundation for Research and Technology-Hellas

The overreaching goal of BOUNCE was to examine how women **adapt to breast cancer** and to illustrate paths to a successful recovery. To achieve this goal, we studied a wide range of variables related to the illness itself (clinical, biological, and treatment-related), patient family and social environment (actual and perceived), as well as social and psychological resources patients could rely upon to help them bounce back. The end product of these factors and processes defines the degree of **resilience (as an outcome and a process)** over the course of illness.

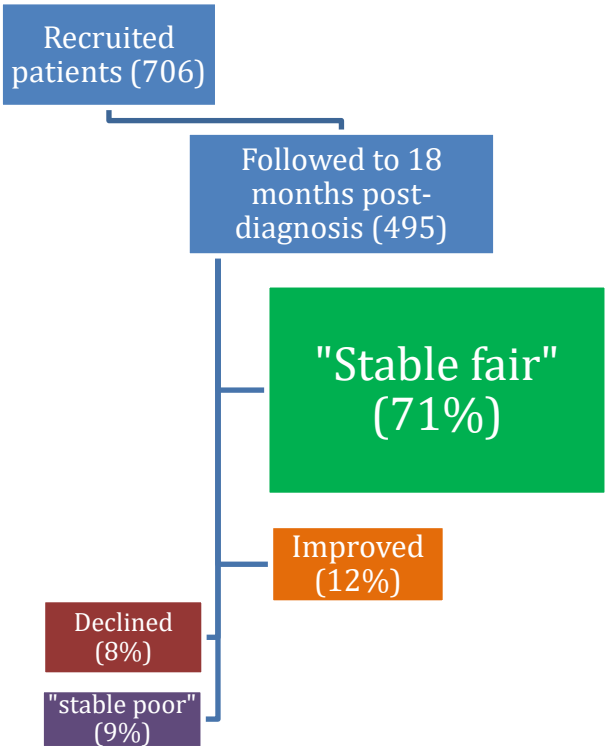
The baseline data collection of BOUNCE was designed to cover the psychological state of the patients as they take in, and attempt to mentally cope with the diagnosis of breast cancer. By design we studied women diagnosed with highly treatable breast cancers; that is to say, illnesses that may leave scars—both physical and psychological—although their threat to life itself is rather low. As expected only about one-fifth of the participating women reported significant symptoms of anxiety or depression at that time.



As time goes by, most women demonstrate successful adaptation, as indicated by the fact that fewer reported significant symptoms of anxiety or depression when queried again 18 months later.



These percentages, however, belie the diverse personal histories of adaptation known to take place during the critical first months of the illness. Among the most devastating manifestations during this period are negative emotional responses, ranging from fear and anxiety to anger, sadness, and hopelessness. These are also common symptoms of depression and are considered important determinants of well-being in the longer term. Fortunately, for most women, these emotional responses are temporary and subside within the first 6-9 months after diagnosis. For a relatively small minority, however, these responses persist longer (at least up to 18 months post-diagnosis). Others report fair emotional status early on, yet develop significant signs of poor well-being as time goes by, seemingly despite a positive medical prognosis, and after completion of cancer treatments.



So what set of factors predispose a woman who reports fair wellbeing when diagnosed with BC to later experience a significant increase in symptoms of anxiety and/or depression?

To address this problem in a flexible and sustainable manner, we developed and tested several Machine Learning (ML) models for optimal prediction of 12- and 18-month patient outcomes

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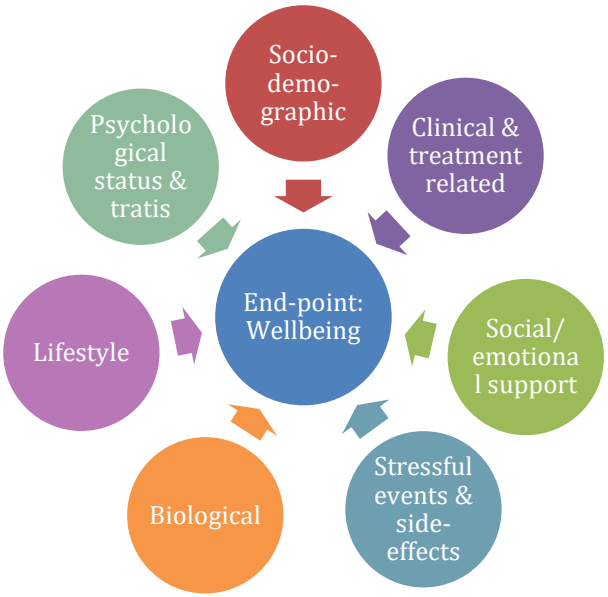
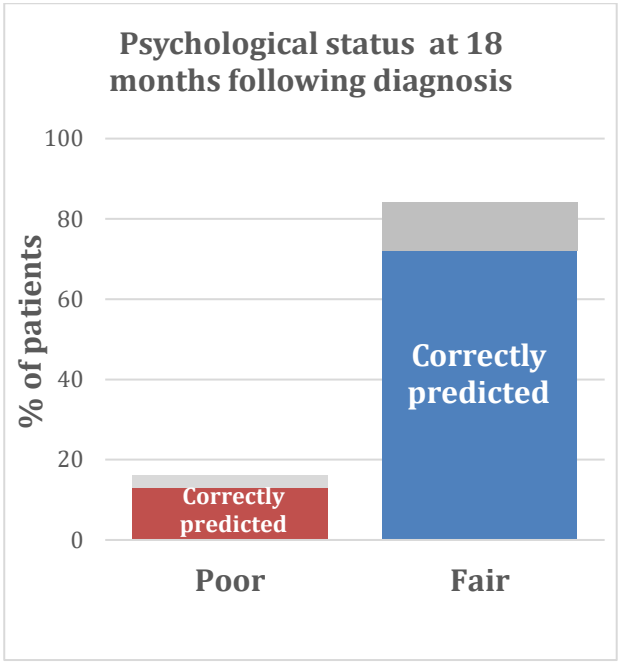
(in terms of symptoms of mental health and overall quality of life) by aggregating all available patient information from the early phase of illness (i.e., over the first 3 months following diagnosis).

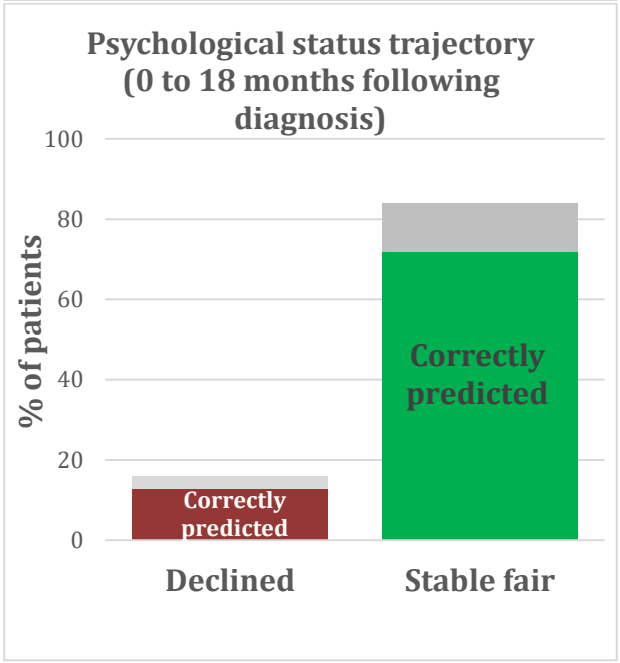
Potential predictors included:

- patient-reported outcomes (i.e., mental health, distress level, health- and global Quality of Life, and functionality),
- sociodemographic variables (i.e., education level, employment status) and perceived social or health-related support,
- potentially stressful events taking place during the follow-up period (including perceived side effects),
- psychological characteristics and coping reactions (i.e. perceptions of illness, optimism, emotional self-regulation strategies, etc.),
- lifestyle factors (i.e., diet and exercise),
- clinical variables (cancer stage, molecular tumor type, type, and timing of medical treatments), and
- biological indicators of systemic processes (e.g., anemia, creatinine and bilirubin, blood cell counts, etc.).



One of the best-performing Machine Learning models correctly predicted poor psychological status at 18 months following diagnosis for 71% of patients. The same model identified the patients who reported fair psychological status at that time with 76% certainty.





A second well-performing model correctly predicted a significant decline in psychological status for 76% of patients and correctly identified patients who maintained fair psychological status throughout the 18-month study period with approximately 77% certainty.

Most important predictors included variables measured shortly after the cancer diagnosis, as well as variables reported at the 3-month follow-up (that is, during treatment). They comprised lifestyle characteristics (at least moderate, regular exercise), trait resilience and other psychological characteristics presumed to be associated with illness adaptation, the emotional status of the patient (particularly on month 3), and specific, illness-related physical symptoms. In addition, two biological variables ranked among

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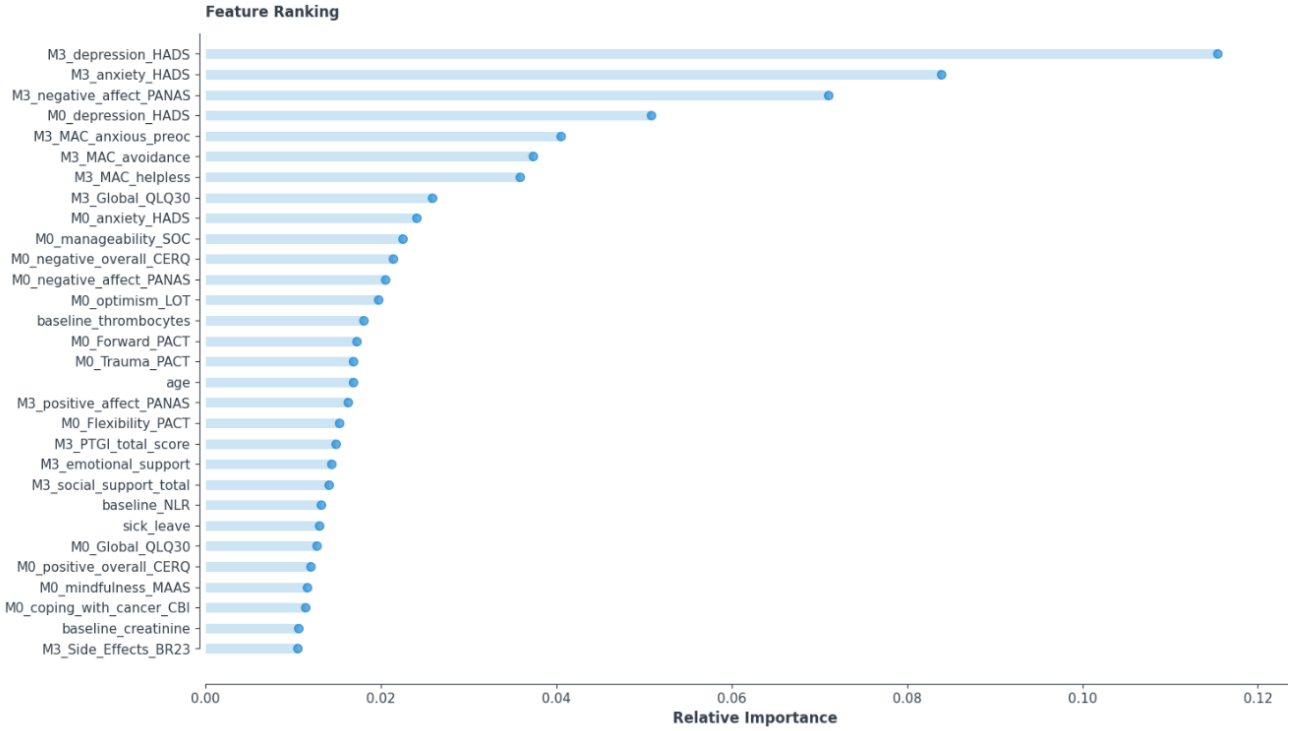
the important predictors: **low platelet count** (an index of the tendency of blood to coagulate and form clots), and **high neutrophil to leucocyte ratio** which reflects a predominance of one type of immune system cells (neutrophils). These variables are ranked according to their relative importance for model accuracy in the figure below.



Conclusions

The design of Machine Learning models implemented in BOUNCE was guided primarily by the potential future **clinical utility** of forthcoming results. Thus, the supervised learning models included **variables that can be readily available to practicing clinicians** at oncology centers in most European and North American countries, namely medical, sociodemographic, and lifestyle variables integrated with a select set of psychosocial patient characteristics. Importantly, we employed a rigorous analytic approach to mitigate some of the commonly observed pitfalls of machine learning approaches, namely overfitting and poor model generalizability.

Especially with regard to significant psychological predictors, these can be grouped into 6 major classes:

- negative affect at the time of diagnosis and soon after (i.e., when most women have undergone surgical treatments as indicated and most have already started chemotherapy and/or radiotherapy);
- available strategies for effective coping with cancer and the person's readiness to adapt;
- a sense of control over the illness and a general optimistic stance toward unforeseen life events;
- social and family support;
- certain lifestyle factors (i.e., exercise);
- the severity of certain physical symptoms and treatment side-effects.

These findings are in accordance with the major psychological theories about adaptation to severe illness, including BC, such as the Common Sense Model[1] or the Transactional Stress Model[2].

Our results highlight the **importance of early psychological responses** to cancer diagnosis and related treatments. The first few months following diagnosis can be considered as part of the acute phase of the disease, where pre-existing risk psychological traits can play a significant role in determining subsequent mental health. On the other hand, positive traits may be equally important in thwarting the impact of the disease on mental health. These may be even more important than negative traits because they could potentially be reinforced with the aid of health professionals at the first crucial visits of the patient.

The next step of our research was to develop analytic approaches toward specifying personalized profiles of "strong" and "weak" types of psychological and lifestyle resources which could be linked to appropriate clinical recommendations for health care professionals. This approach is outlined in the next article of this Newsletter.

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[1]*Leventhal, H., Halm, E., Horowitz, C., Leventhal, E.A., & Ozakinci, G. (2005). Living with chronic illness: A contextualized, self–regulation approach. In S. Sutton, A. Baum & M. Johnston (Eds.), The SAGE handbook of health psychology (pp. 197-240). London: Sage.*

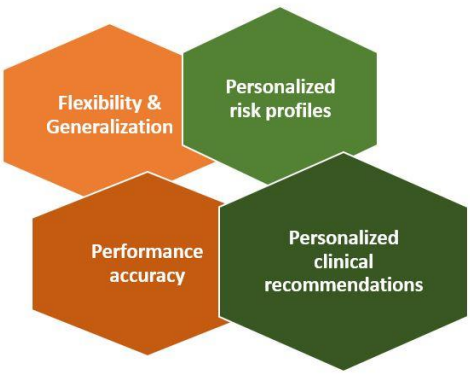
[2]*Lazarus, R., & Folkman, S. (1984). Stress, appraisal, and coping. New York: Springer.*

The BOUNCE Decision Support Tool: Linking Machine Learning Risk Assessment to Individualized Clinical Recommendations

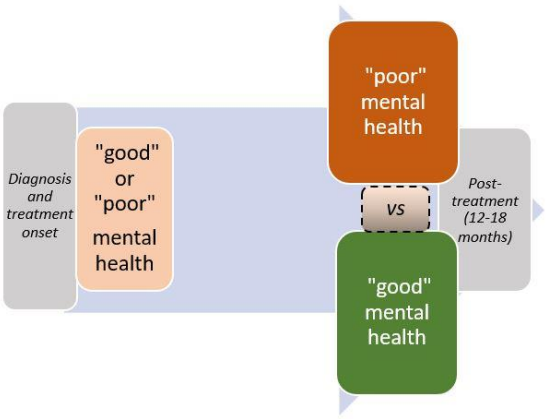
By **Panagiotis Simos, George Manikis, Konstantina Kourou, & Evangelos Karademas**, Computational Biomedicine Laboratory, Institute of Computer Science, Foundation for Research and Technology-Hellas

Extensive modeling work on the BOUNCE study dataset was instrumental in identifying key predictors of well-being trajectories during BC treatments and recovery. Machine Learning (ML) models displayed sufficient predictive accuracy regarding the probability that a given patient will show a successful recovery (i.e., achieve a fair level of well-being and escape the relatively infrequent possibility of a significant decline in well-being at the end of the arduous period of BC treatments).

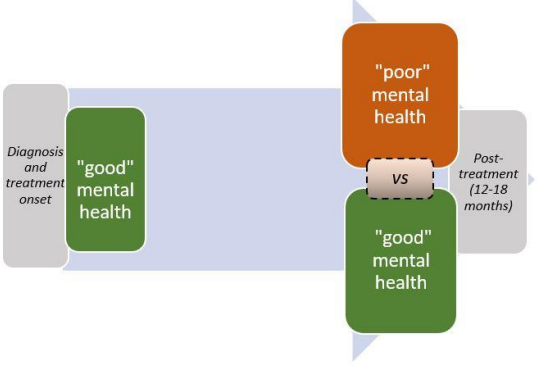
Yet, clinicians who are called in to support women likely to show poor illness adaptation are often challenged with the task of choosing therapeutic targets that can be directly and efficiently pursued in the context of relatively brief psychological interventions. In order to meet these clinical needs, the BOUNCE clinicians worked closely with the modeling team at FORTH to redesign the BOUNCE Decision Support Tool (DST) according to four principles: (i) flexibility toward future use in clinical settings, (ii) performance accuracy in predicting key aspects of patient well-being, (iii) robustness in formulating personalized risk profiles of potentially modifiable patient characteristics, and (iv) directly linking personalized needs assessment with concrete suggestions regarding psychological prevention strategies.



Flexibility means that clinicians can adapt the DST to their clinical needs and to the availability of data for a given patient. Along these lines, we included models capable of assessing the risk for six distinct well-being outcomes (illustrated in the following diagram). Two models address the need to identify patients at risk of overall poor mental health at a particular end-time. These models were deemed more appropriate in terms of classification performance regardless of the **patient's reported mental health at the time of diagnosis** and at the beginning of cancer treatments. In other words, they can be applied to predict future mental health status regardless of how the patient felt initially.



Two alternative models address the need to identify patients at **risk of declining mental health** having displayed adequate classification performance in the subgroup of patients who reported good mental health at the time of diagnosis (and/or treatment onset).



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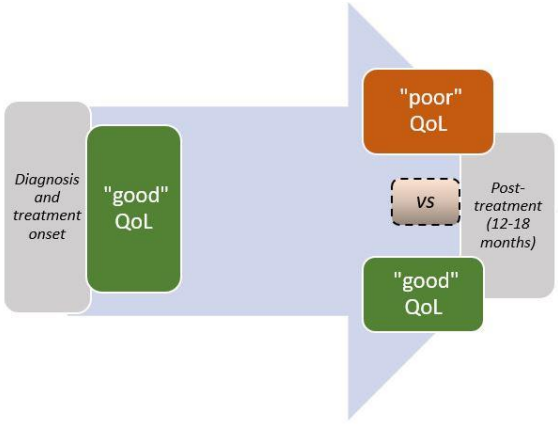
The DST provides the option to set the overall patient quality of life (QoL) as an alternative clinical outcome

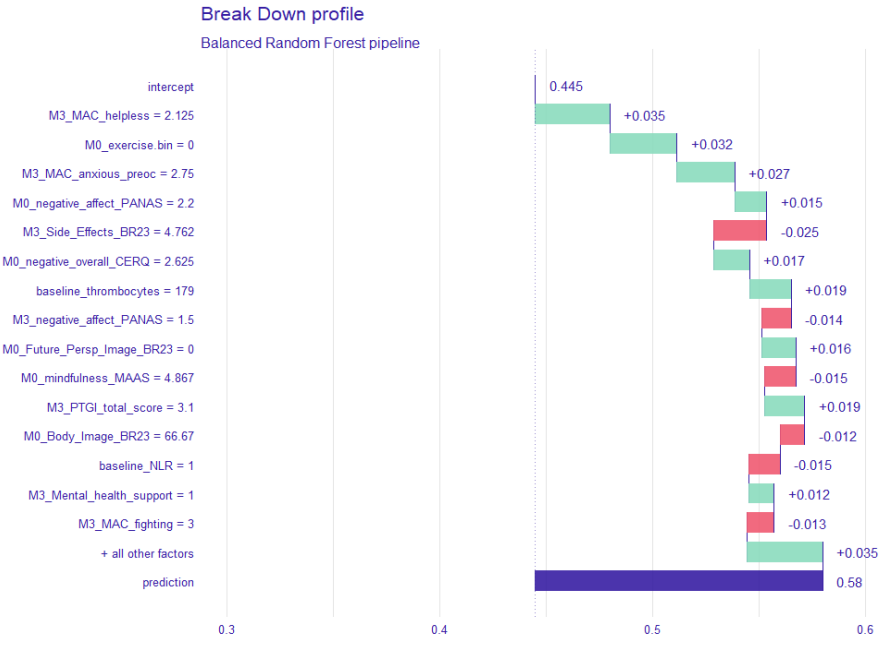


Additional clinical flexibility is afforded in terms of the available psychological and lifestyle measurements in mainstream clinical practice. Thus, it is possible to perform patient risk assessment under three alternative clinical scenarios in assessing risk for poor psychosocial recovery:

- Combining clinical and biological information with patient-reported psychological characteristics at the time of diagnosis and at 3 months later,
- Combining clinical and biological information with patient-reported psychological characteristics obtained at 6 months post-diagnosis, and
- Combining clinical and biological information with patient-reported psychological characteristics aggregated over the first 6 months post-diagnosis.

The **performance** principle means that the selected models were those that displayed adequate classification accuracy through extensive cross-validation schemes on the BOUNCE prospective clinical study. Personalized risk profiles can be obtained through a novel type of AI models, known as agnostic (or local explainability) analyses at the patient level[1,2]. This approach can pinpoint specific psychological or lifestyle characteristics, which appear to be underdeveloped in a given patient based on available and appropriately timed measurements. Model-agnostic analysis works by searching for predictor variables that contribute the most to the risk assessment for a given patient after statistically controlling for all other predictors in the model. An example of a personalized prediction of significant decline in overall mental health for a patient who at the time of diagnosis reported fair psychological status is given below

The 15 most highly ranked features selected by the Machine Learning model for this patient include 9 variables that appear to predominantly "facilitate" the adverse mental health outcome: relatively high negative affectivity, intense anxious preoccupation, and a sense of helplessness, combined with relatively low scores on Future Perspectives (that is, how worried patients are about their health in the future) and constitutional resilience. Conversely, the experience of only mild treatment side effects and negative affectivity, combined with high levels of a positive body image and mindfulness at the time of diagnosis, appear to exert a protective role for this patient by reducing the probability of an adverse mental health outcome.



Break-down profile of a patient who was correctly predicted by the ML model to display a substantial decline in overall mental health 12 months following diagnosis of breast cancer. Actual patient scores on each predictor variable are shown on the left-hand side

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Having extracted potentially crucial predictor variables, the DST then compares the patient's actual scores on these variables to the recorded scores of all patients in the BOUNCE prospective clinical study. Next, the DST identifies variables where the patient's score is either very high (for "risk" variables, such as anxious preoccupation) or very low (for "protective" variables, such as coping strategies). Variables that meet these criteria are "flagged" as potential targets of prevention strategies by mental health professionals.

Based on the personalized risk and vulnerability profiles, the DST provides specific **clinical recommendations** each targeting a specific underdeveloped or deficient psychological or lifestyle characteristic of the patient. The platform integrates appropriate recommendations for a given patient into a single document in two versions:

- One (abbreviated) version addressed to clinicians who come in direct contact with the patient but are not trained in administering systematic psychological support (such as physicians, nurses, and social workers).
- An extended version is also available for use by mental health professionals who have some training in psychological interventions.

In sum, the DST user will have several options based on their clinical needs—in terms of both prediction endpoints and capabilities to engage diverse prevention strategies—and also according to the timing of available psychological and lifestyle data. These features are expected to facilitate the applicability of the DS platform for a wider variety of clinical scenarios and settings.

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[1]Biecek, Przemysław. "DALEX: explainers for complex predictive models in R." The Journal of Machine Learning Research 19.1 (2018): 3245-3249.

[2]Baniecki, Hubert, et al. "dalex: Responsible Machine Learning with Interactive Explainability and Fairness in Python." arXiv preprint arXiv:2012.14406 (2020).

Transferring the BOUNCE predictive model into clinical practice: The IEO intervention testing pilot

By **Ketti Mazzocco** and **Diana Sala**, Department of Oncology and hemato-oncology, University of Milan and Applied Research, Division for Cognitive and Psychological Science, Istituto Europeo di Oncologia, Milan, Italy

George Manikis, Computational Biomedicine Laboratory, Institute of Computer Science, Foundation for Research and Technology-Hellas

The most interesting part of developing predicting models in health care is their application to clinical practice. Thanks to the H2020 European Project, the Bounce Consortium was able to develop models that can predict long-term breast cancer patients' resilience since the very beginning of the oncological treatment. Besides the identification of patients at high risk for developing long-term poor resilience, the Bounce Decision Support Tool (DST) guides health care professionals toward optimal psychological interventions by identifying the factors that are most likely to promote or, conversely, thwart resilience. The identification of resilience predictors and congruent personalized psychological interventions is crucial to support oncological treatments in ensuring satisfactory patient wellbeing in the long term.

In this perspective, an intervention study has been designed and received approval from the IEO Ethics Committee to test the Bounce Decision Support Tool on 60 breast cancer patients, aged 40 to 70 years. More specifically, before starting the systemic oncological treatments, just after the first visit with the medical oncologist, breast cancer patients' resilience-related factors are assessed using a short version of the original battery of questionnaires used in the Bounce prospective pilot study. The short version was established by retraining the predictive machine learning models on the IEO data obtained in the context of the Bounce Prospective Pilot Study. Highly ranked variables were identified as predictors of 6-month mental health outcomes. After the patient fills out the questionnaire, a risk profile is generated by the DST and available to the psychologists, detailing the level of risk and the specific factors that uniquely predicted mental health for that specific patient.

During the first meeting with the IEO psychologist, the patient is given feedback on the profile of her responses to the assessment questionnaires. Patients with a low-risk profile are then contacted after 3 and 6 months for a follow-up and to complete the same questionnaires as at baseline.

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Patients with a high-risk profile are assigned to two groups:

1) a group receiving conventional psychological intervention. In this group, the psychologist is blind to the DST-generated patient-specific risk profile and only knows that the patient is at risk of poor mental health; similarly, the patient knows only that she has a high risk of poor resilience and mental health;

2) a group receiving customized intervention based on the patient-specific risk profiles. With the support of the graphs generated by the DST patient-specific model, she is informed about the factors most likely to promote or thwart long-term mental health and how working on such factors can lower the risk. The psychologist then plans an intervention focused on the discussed factors.

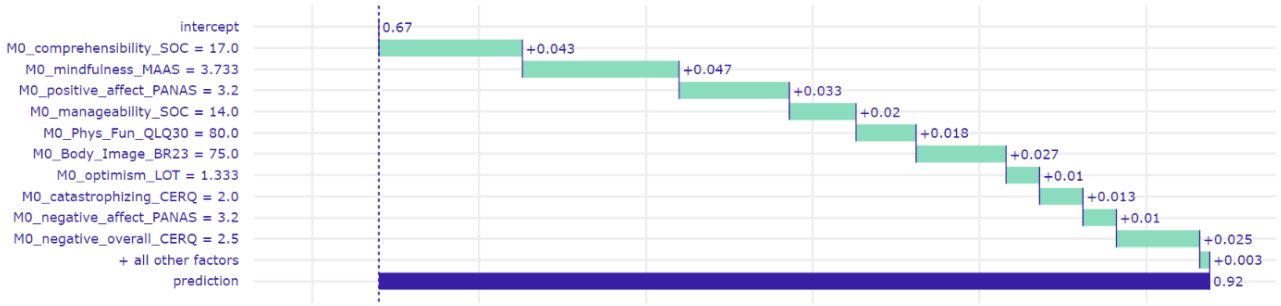
Both groups receive a total of ten psychological consultations.

Despite the testing pilot being still ongoing, the advantage of visualizing and discussing the patient-specific profile with the patient is already apparent. Not only the model confirms what patients often describe as crucial weaknesses and strong points in their initial interview but also it helps patients to better understand their psychological condition and facilitates their engagement in the psychological intervention.

After the analysis of the patient's profile, the psychologist discusses with her the results supported by a graph summarizing the overall risk profile. Additional graphs are presented as visual aids of the potential significance of specific predictive variables. When walked through the illustrations, patients showed a good understanding of the underlying concept and the need to work on significant predictors in order to lower the risk of poor outcome.

Overall profile discussed with the patient

The patient is walked through the meaning of the graph, describing the variables that emerged as most significant in predicting her long-term mental health outcome. In the example presented below, the model predicts a poor six-month outcome with a probability of 92%. Highest-ranking predictors in the model as trained and tested in the total sample of IEO patients are listed by order of diminishing importance from top to bottom of the graph. However, not all highly-ranking variables appear to contribute strongly to the predicted mental health outcome of this particular patient. Let's consider for example physical functioning that despite in the top 5 variables, is not expected to facilitate long-term resilience even if it were to improve.



Variable-specific profiles: Focusing on optimal targets of intervention

After presenting the overall profile, the psychologist focuses on variables most likely to contribute to long-term mental health outcomes and therefore are worth working on. In this specific case, the model predicts a 10% decrease in the risk of poor mental health at 6 months, if the level of current **positive affect** would increase. Similarly, by increasing the level of **comprehensibility** (the capacity to understand the meaning of events), the risk of poor mental health at 6 months is predicted to decrease by 20%.

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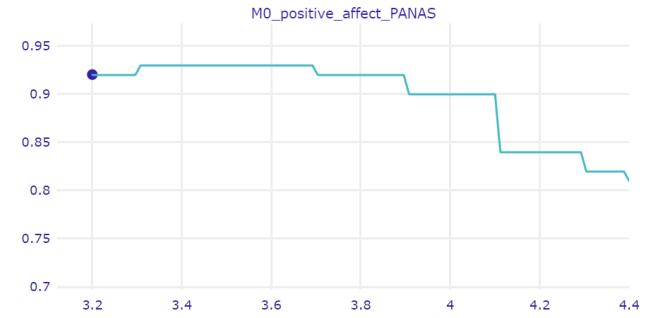
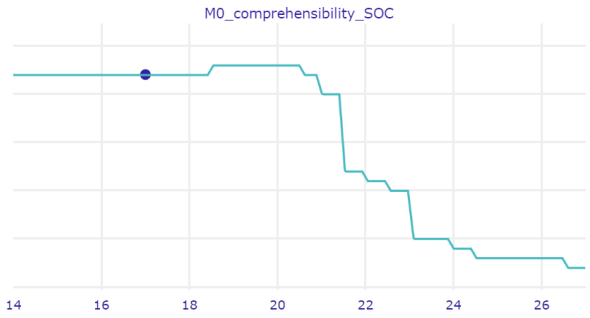
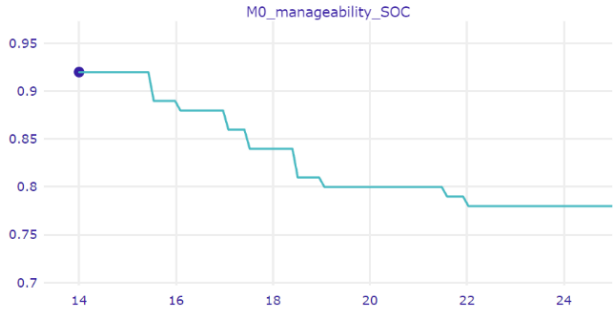
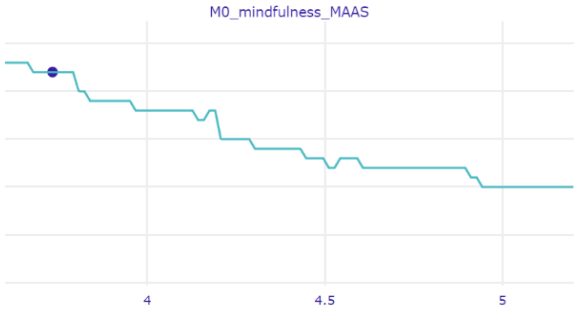




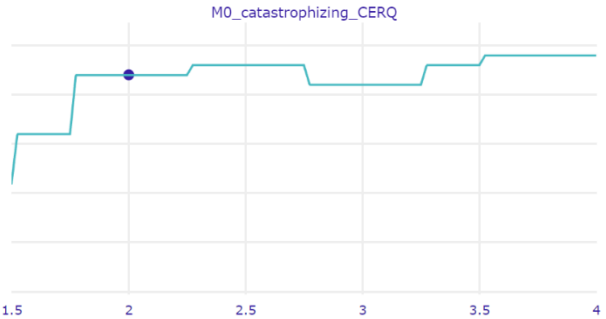
Additionally, the model estimated that working on **Mindfulness** (increasing the awareness and attention to the present moment and to what is happening and to associated feelings) and **Manageability** (increasing the perception of the available personal resources that respond to life demands) may further and significantly reduce the risk of an adverse mental health outcome for this patient.

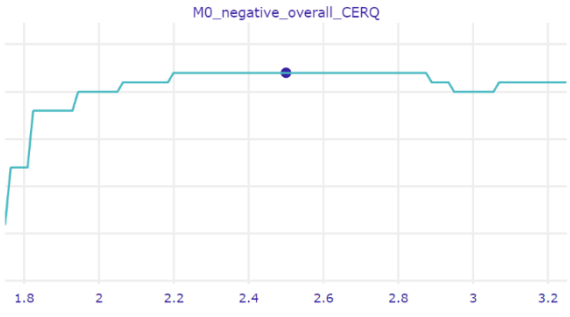




A smaller but still clinically relevant change toward reducing this risk is predicted if the patient manages to moderate her tendency to **catastrophize**, that is to see events as worse than they are; a similar result is predicted relative to the capacity to **cognitively regulate emotion**.

No significant changes in mental health outcome are predicted for the remaining variables. Therefore, the psychological intervention will not focus on them and for this reason, they are not discussed with the patient.





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"CHEMOBRAIN" How to deal with the cognitive changes during and after treatments?

By **Isabel Manica** and **Berta Sousa**, Champalimaud Research and Clinical Centre, Champalimaud Foundation, Lisbon, Portugal

Breast cancer survivors often experience cognitive changes during and after systemic treatments, mainly chemotherapy [6,7]. Even though this topic has been undervalued for some time, it has been gaining more focus by the scientific and medical communities, driven by the increasing awareness of survivorship issues [5]. The pathophysiology of these cognitive changes is not yet fully understood [4].

It is estimated that 30% to 70% of cancer patients undergoing systemic treatments experience some kind of cognitive change [1,7], with most studies being conducted on breast cancer patients. However, the experience of these cognitive changes can be very different for each individual patient not only for the severity of symptoms but also for their duration. In most cases, patients report mild changes that last for a few months, but others present long-term complaints that impact their daily functioning, and quality of life and can be even perceived by the one's around them [2,4,8].

The most frequent cognitive complaints[3] are:

- Difficulty concentrating or focusing on tasks;
- Slower thinking and more time needed to learn and understand new information;
- Difficulty with multitasking;
- Trouble recalling or remembering common words or names, especially during conversations;
- Increased reaction time;
- Forgetfulness.

The cause of these cognitive changes is multifactorial, involving medical and treatment-related factors (type of treatment, duration of the treatment), psychological factors such as anxiety and depression, sleep disturbances, fatigue, and individual risk factors, such as age, comorbidities, and cognitive reserve [1,2].

Are you dealing with this or do you know someone who is? What should you do?

First, you should inform your doctor or the care team about these complaints. A referral to a neuropsychological assessment can be organized after the assessment of these complaints. Additionally, you can also use some strategies in your daily life that will help you cope with these difficulties [9]:

- Use of compensatory strategies such as external memory aids [planners, lists, keep things in the same place];
- Do the most cognitively demanding tasks at the time of the day when energy levels are highest;
- Using relaxing and stress reduction strategies;
- Regular physical activity;
- Limit the use of alcohol or other substances that can affect cognition and sleep routine;
- Yoga and/or meditation;
- Exercise your brain by doing cognitively stimulating activities (e.g., reading books or magazines, practical activities like gardening, visiting places, playing musical instruments, and artistic activities, among others).
- Talk to somebody and alert them about how you are feeling.

In case of severe or persistent cognitive difficulties, confirmed by the neuropsychological assessment, a cognitive training program or psychotherapy can be offered to improve with proven efficacy [9].

Workshop 4th Dissemination Event BOUNCE

On the 8th of October 2021, the Champalimaud Foundation (CF) organized a scientific workshop for the fourth Bounce project dissemination event. A session was dedicated to Neurocognition in breast cancer patients. Kathleen Van Dyk (researcher UCLA Semel Institute & Comprehensive Cancer Center) presented the current evidence about neurocognitive deficits in this population and the emerging research on this topic was presented by Sanne Schangen (Cognition group leader; Netherlands Cancer Institute). A review was presented about cognitive changes experienced by breast cancer patients, including main symptoms presentation, how to use diagnostic testing methods, and most importantly, the intervention programs that are now being proposed and applied in this setting.

This project has received funding from the European Union's Horizon 2020 research and innovation programme

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Depression and Anxiety in patients with breast cancer: The impact of the Covid-19 pandemic

By **Sílvia Almeida, Berta Sousa** and **Albino Oliveira Maia**, Champalimaud Research and Clinical Centre, Champalimaud Foundation, Lisbon, Portugal

Patients with cancer frequently experience depressive and anxiety symptoms, which can negatively affect quality of life, adherence to treatment and health service use (1). The reported prevalence of depression and anxiety varies according to cancer-related variables (such as tumor type), their conceptualization and diagnostic methods that are used. In patients with breast cancer the prevalence of mood disorders ranges from 13% to 54% (2) since the time of diagnosis and most commonly in the first year. While there are some factors well known in the literature as having an impact on increasing psychological distress of patients with cancer, such as having a previous psychiatric diagnosis or having low social support (3), there is some evidence of a possible association between stressful life events and cancer (4).

The COVID 19 pandemic, declared by WHO on March 2020, is a global public and mental health crisis that, in addition to the measures adopted to control its spread, can be considered a stressful event and may cause a significant emotional burden, especially for vulnerable groups (5). These groups encompass patients with preexisting mental or physical health issues (including cancer) that may be at higher risk of becoming mentally unwell in response to the pandemic and its associated factors (6).

Thus, the aim of Covid-BOUNCE study being led by the Champalimaud partners is to assess the psychological impact of the COVID-19 pandemic in patients with early breast cancer by measuring associations between symptom severity and COVID-related parameters (e.g. incidence, death

rates, and containment measures). The data collection started at the beginning of the recruitment for the Bounce project in January 2019. The study was ongoing when the COVID 19 pandemic started in Europe and data collection has continued, allowing for measurements of psychological variables in five time points until April 2021. Currently, we are performing descriptive statistics and series of multilevel mixed-effects linear regression models to assess two main points:

- If there are differences between groups of patients with cancer (not exposed vs exposed to the pandemic) in the variation of psychological outcomes over the BOUNCE study period;
- If country-level pandemic-related parameters are associated with individual psychological

This project has received funding from the European Union's Horizon 2020 research and innovation programme

outcomes independently of other individual characteristics.

Preliminary results were presented at a poster session of ESMO Breast Cancer 2021 (7) and updated results will be presented at the EUROPA DONNA Session of the European Breast Cancer Conference (EBCC-13) that was postponed to 16-18 November 2022 and will take place in Barcelona.

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