Predicting Effective Adaptation to Breast Cancer to Help Women to BOUNCE Back 1.11.2017-30.4.2022

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SC1-PM-17-2017: Personalised computer models and in-silico systems for well-being

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Disclosures

- One consultation fee from Phizer 2022

Content

- BOUNCE project
- Concept of resilience
- BOUNCE prospective pilot
- BOUNCE results, models and trajectories
- Clinical recommendations
- Exploitation
- BOUNCE substudies in HUS

Goal in early breast cancer

BOUNCE

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- **Predictive model** of resilience, **a decision-support tool to be** used in **routine clinical practice** to provide physicians and other health professionals with concrete, personalized recommendations regarding **optimal psychosocial support strategies at the correct time point.**

- Eventually **increase resilience** in breast cancer survivors and help them remain in the workforce and enjoy a **better quality of life.**

- To further develop the **operational model** and **the care path** for breast cancer patient

BOUNCE Consortium

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Representation in the Advisory Board

Local collaboration

PP	Short Name	Partner Full Name	Nationality
P1	HUS	Helsinki University Hospital Comprehensive Cancer Center (HUS) PI: Paula Poikonen-Saksela, Johanna Mattson	FI
P2	FORTH	Foundation for Research and Technology – Hellas (FORTH) PI: Panagiotis Simos	EL
P3	IEO	European Institute of Oncology (IEO) PI:Ketti Mazzocco	IT
P4	ICCS	Institute of Communication and Computer Systems (ICCS) PI: Georgios Stamatakos	EL
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P7	SiLo	SINGULARLOGIC ANONYMI ETAIREIA PLIROFORIAKON SYSTIMATON KAI EFARMOGON PLIROFORIKIS (SiLo) PI: Konstantinos Perakis	EL
P8	CHAMP	Fundação D. Anna de Sommer Champalimaud e Dr. Carlos Montez Champalimaud (Champalimaud Clinical Center - CCC) (CF) PI: Fatima Cardoso, co-PI Berta Sousa	PT
P9	NOONA	Varian, Siemens PI: Pasi Heiskanen	FIN, SWI, GER

Concept of resilience

Problems related to resilience are common among breast cancer patients -

- Patient reported emotional changes (50%)
- functional limity (50%)
- changes in everyday life (48%)
- sexual activity (40%)
- fysical well-being (40%)
- body image (30%)
- social life (18%)

Travado 2013

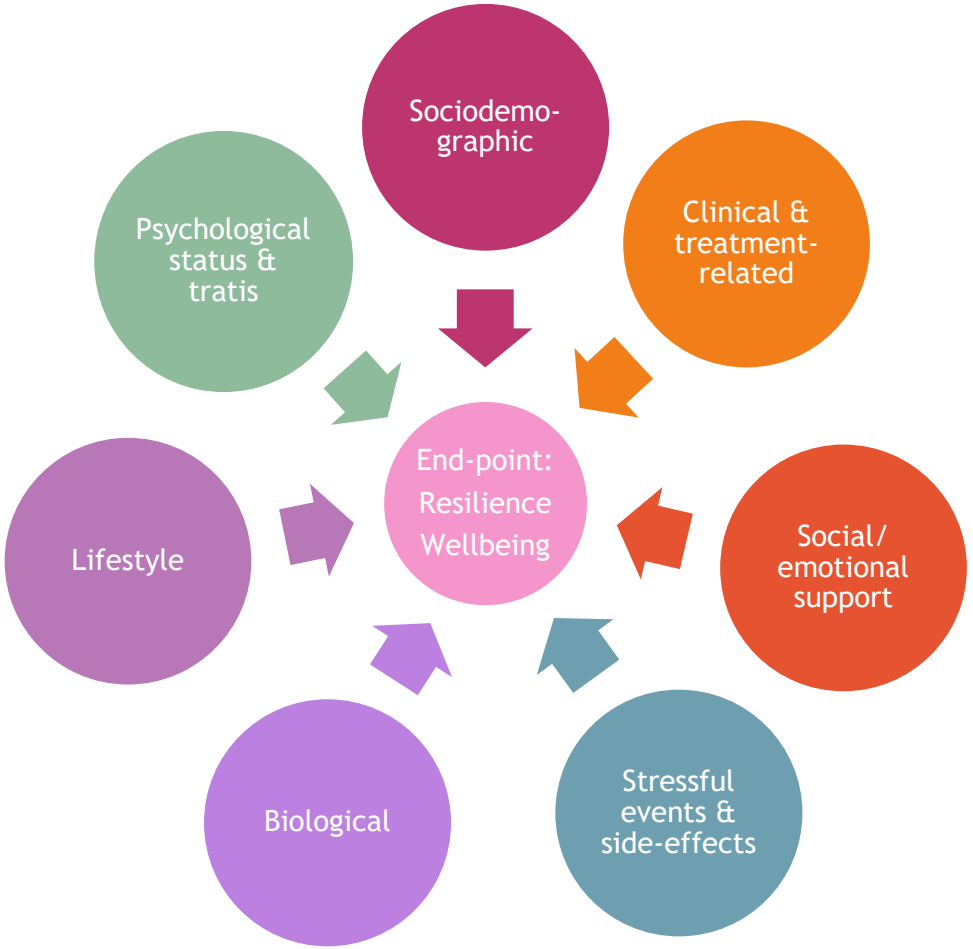
- Cancer is a traumatic stressor for many of the patients. In review of 13 studies regarding posttraumatic stress disorder (PTSD), mostly following breast cancer, reported that 5–19% of the cancer patients met full criteria for PTSD.

Kangas 2002

Wellbeing in early BC

- Usually QOL improves gradually over the first year after dg after active treatments are over and side-effects go over
- Many patients cope well with the help of treating professionals, family, friends and peer support
- However, it is very important to recognize patient who are at risk for impaired well being and resilience and who would need more support

Resilience: ”coping with the change”



Connor Davidsson Resilience Scale
Measures resilience at one time point as a trait

1. Able to adapt to change
2. Can deal with whatever comes
3. Tries to see humorous side of problems
4. Coping with stress can strengthen me
5. Tends to bounce back after illness or hardship
6. Can achieve goals despite obstacles
7. Can stay focused under pressure
8. Not easily discouraged by failure
9. Thinks of self as strong person
10. Can handle unpleasant feelings

Broader perspective for resilience in BOUNCE

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Multifaceted concept: As defined in BOUNCE (2018) **A *conglomerate* of dynamic *self-regulatory capacities* that allow to mobilize and use internal and external resources over time *in the face of adversity* in order to maintain or promote wellbeing.**

- …a personality characteristic or personal capacity (trait)
  - Assessed in BOUNCE with CD-RISC at several time points
- …an adaptive process or change over time
  - E.g., as a specific trajectory over time
- …or an "outcome"
  - Less psychological symptoms, higher QOL

BOUNCE pilot 2019-2021

BOUNCE prospective pilot

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- Age 40-70
- Stage I-III BC patients receiving some type of medical therapy
- Without any major early onset mental illness
- Without any major disease or operation during past year
- Baseline = after first visit with oncologist

Questionnaires included in the study, divided by psychological domain and number of items at each time-point WP6

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Domain	Abbreviatio	Measure name	M0	M3	M6	M9	M12	M15	M18
Personality	TIPI	Ten Item Personality Measure (brief "Big Five")	10						
	LOT-R	Optimism/Pessimism	10						
Meaning	SOC-13	Sense of Coherence	13						
Trauma and PTSD	PCL-5	PTSD Check-List			20		20		20
		Recent negative life events	1	1	1	1	1	1	1
		Recent illness-related events		1	1	1	1	1	1
Coping	PACT	The Perceived Ability to Cope With Trauma (Flexibility in coping)	20			20		20	
	CERQ short	Cognitive Emotion Regulation Questionnaire	18			18		18	
		MAAS - Mindfulness	15				15		
		Spirituality coping - a visual bar		1		1		1	
Social Support	mMOS-SS	modified Medical Outcomes Study Social Support Survey		8		8		8	
	F.A.R.E.	1. Communication and cohesion; 2. Perceived family coping subscales		12		12		12	
		Instrumental/emotional perceived social support	1	1	1	1	1	1	1
Resilience	CD-RISC	Connor-Davidson Resilience Scale	10			10		10	
		How much are you back to yourself?			1	1	1	1	1
Illness Perception & b	IPQ	Illness Perception Questionnaire			56		56		56
	B-IPQ	Items no 3 and 4 from B-IPQ		2	2	2	2	2	2
	mini-MAC	Mental Adjustment to Cancer		29		29		29	
		Single item: what has done to cope (open question)		1	1	1	1	1	1
	CBI-B	Cancer Behavior Inventory (self-efficacy in coping with cancer)	14		14		14		
		A general self-efficacy item	1	1	1	1	1	1	1
		Adherence to medical advice: item 5 from the MOS Adherence to medical		1	1	1	1		1
	PTGI	The Posttraumatic Growth Inventory - short form		10			10		10
Quality of life	QLQ-C30	EORTC quality of life questionnaire	30	30	30	30	30	30	30
	QLQ-BR23	EORTC quality of life questionnaire breast cancer module	23	23	23	23	23	23	23
Distress	FCRI-SF	Fear of Recurrence - short form (severity scale of original FCRI)	9		9		9		9
	HADS	Hospital Anxiety and Depression Scale	14	14	14	14	14	14	14
	DT	NCCN Distress Thermometer	1	1	1	1	1	1	1
	PANAS	Positive and Negative affectivity - short form	10	10	10	10	10	10	10
Sociodemographics and lifestyle			22						22

- 23 Sociodemographic questions for the patient
- MO 268 questions

HADS alarm if score 13 or higher indicating severe anxiety

Medical and treatment information M0-18
Collected by the trial assistant

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- Tumour characteristics
- Treatment information
- Chronic illnesses
- Psychotropic medications
- ECOG performance status every 3 months
- Severe side-effects
- Biomarkers- hsCRP, blood cellcount (M0, M12)
- DFS, OS (M18)

BOUNCE platform

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noona

Preprocess & Pseudonymize

HUS Helsinki University Hospital

IEO

Fundação Champalimaud

האוניברסיטה העברית בירושלים
THE HEBREW UNIVERSITY OF JERUSALEM

Raw data upload

CBMLBox@FORTH

Data Cleanser

Cleaned data upload

Data Lake

Further clean data & calculate scales

Data Access APIs

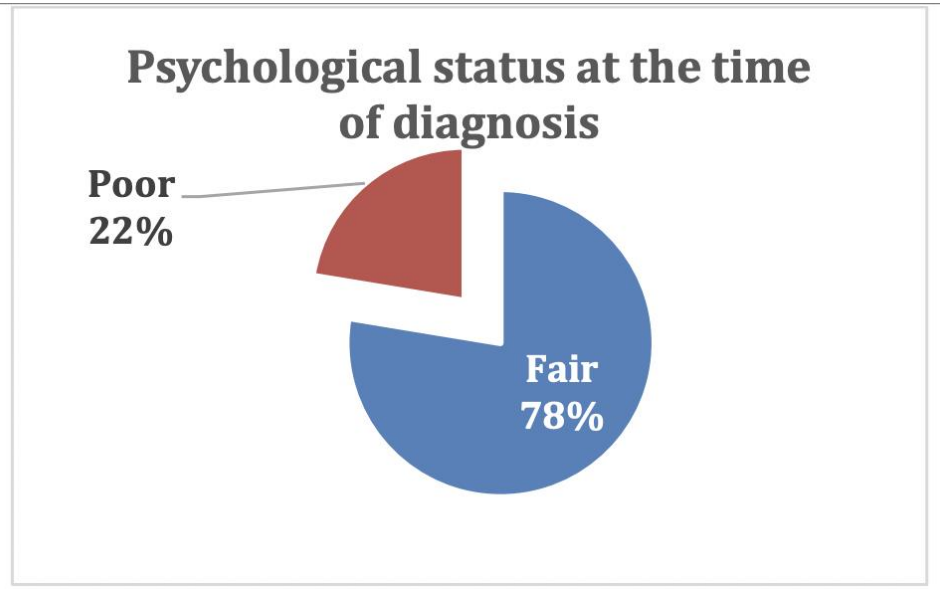
BOUNCE models& predictions

Bounce Ontology

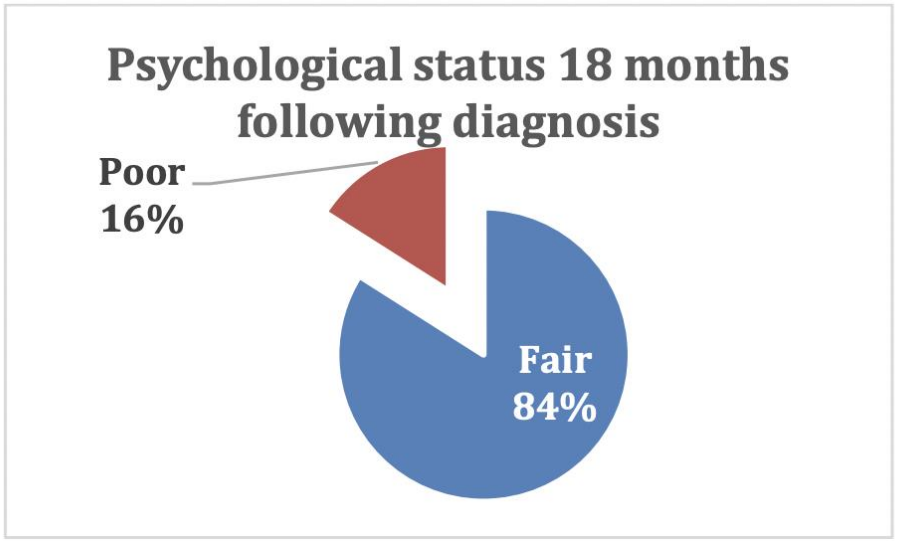
Kondylakis 2020

BOUNCE trajectories & models

Predicting Resilience of Women with Early Breast Cancer via Machine Learning Models

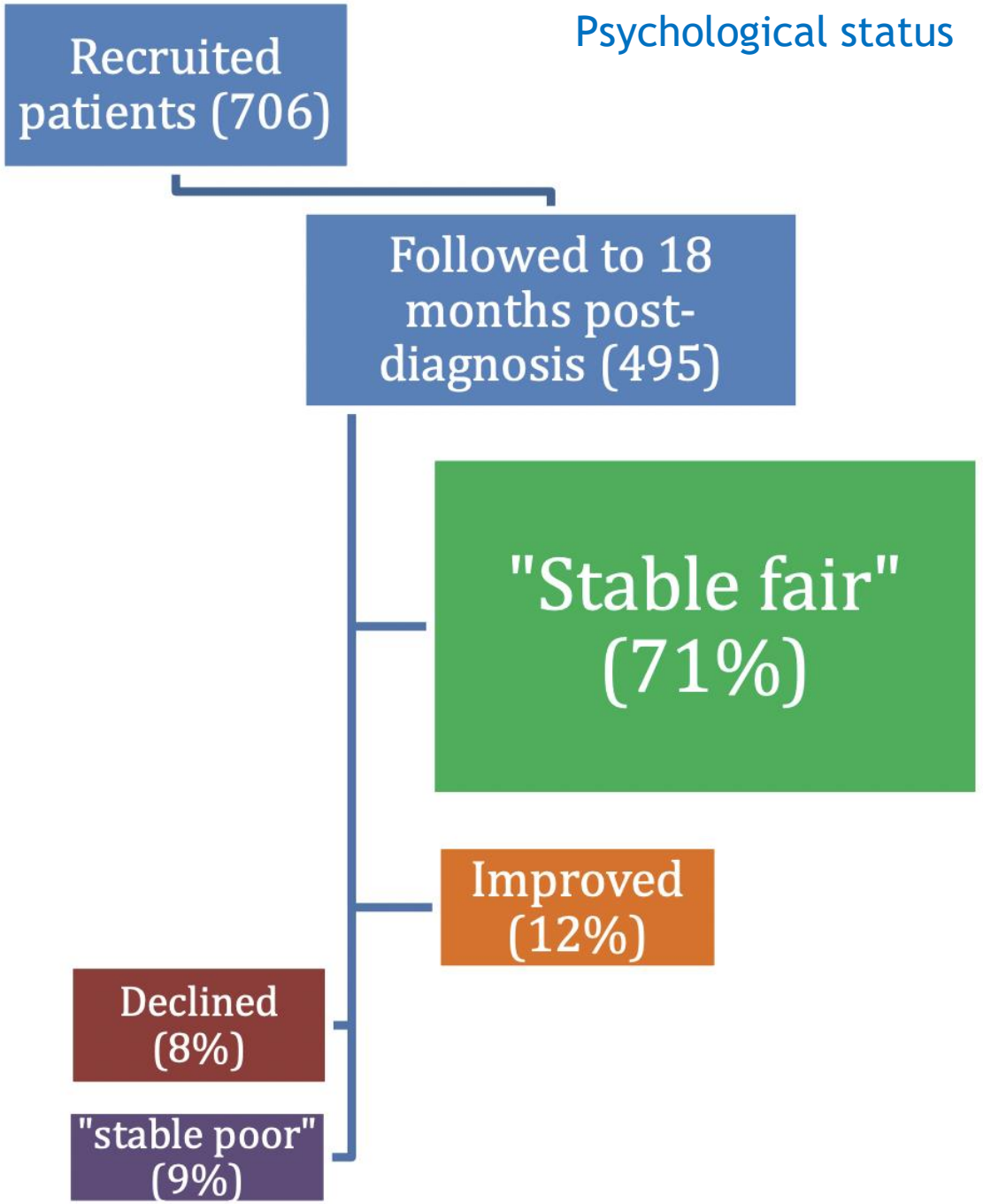


As time goes by, most women demonstrate successful adaptation, as indicated by the fact that fewer reported significant symptoms of anxiety or depression when queried again 18 months later.



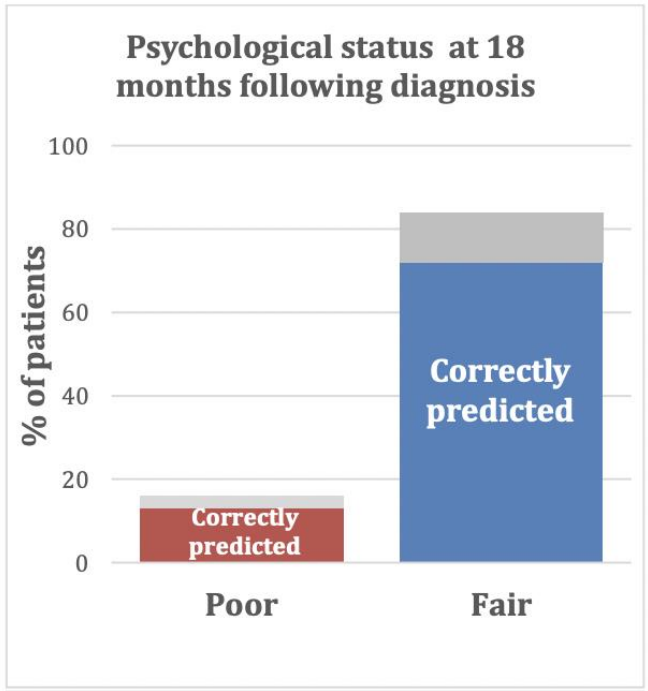
Simos FORTH 2022

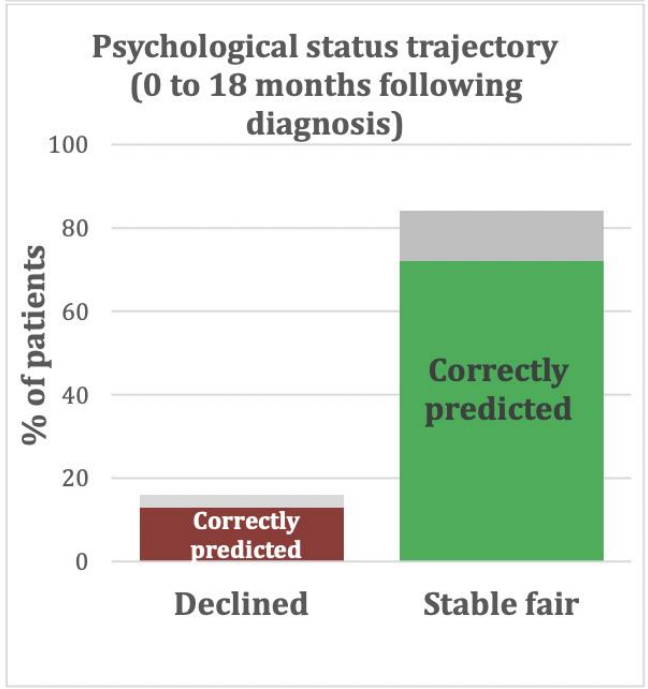
Psychological status



Simos FORTH 2022

Machine learning models correctly predicted one-year mental health deterioration for **71 & 76%** of patients.





ML-models identified the patients who had stable good mental health status at M12 with **76-77%%** certainty.

Simos FORTH 2022

Significant predictors of changes in mental health change over one year

- M0/M3 anxiety, depression, QOL
- negative affect
- coping with cancer, self-efficacy to cope with cancer, adjustment to cancer
- a sense of control/positive expectations (i.e., sense of coherence; optimism)
- social and family support
- lifestyle factors (i.e., exercise)
- symptoms (e.g., arm symptoms)

BOUNCE decision support tool

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- 1. Questionnaires in Noona for patients
- 2. Pseudomized data export from Noona to the BOUNCE platform with the prediction models
- 3. Platform provides predictions for individual patients
- 4. Platform provides clinical recommendations for interventions

Clinical recommendations

Clinical recommendations include

- Grouping predictors of resilience into intervention targets
- Suggestion for interventions based on the targets
- Interventions are planned locally according to local resources and practise

Grouping Psychological Predictors into General Concepts/Intervention Targets, evidence based

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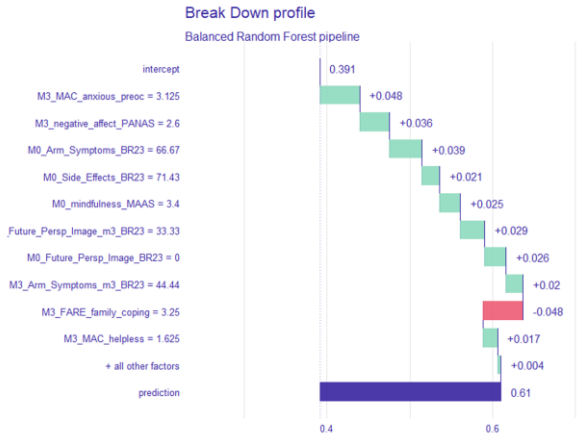
At baseline		
Predictors	***Matching concept/ Intervention Target***	***Validation / evidence for the grouping (example references)***
Negative affect Positive affect Overall positive emotion regulation Overall negative emotion regulation	*Emotion and emotion regulation*	https://doi.org/10.1177/1754073910380974 https://doi.org/10.1080/02699931.2010.544160 https://doi.org/10.1027/1015-5759/a000599
Self-efficacy to cope Ability to cope with trauma	*Perception of coping abilities*	https://doi.org/10.1080/08870446.2022.2038157 https://doi.org/10.4324/9781315800820 https://doi.org/10.1017/CBO9780511994791.005
Fear of recurrence Future perspective	*Representations of illness timeline*	https://doi.org/10.1007/s10865-016-9782-2 https://doi.org/10.1037/bul0000118 https://doi.org/10.1080/17437199.2019.1644189
Arm symptoms Breast symptoms Side effects	*Representations of illness symptoms / consequences*	https://doi.org/10.1002/pon.4213 https://doi.org/10.1007/978-1-4939-3486-7_7
Sense of coherence Optimism Resilience as trait Mindfulness	*Sense of control, resilience – as traits*	https://doi.org/10.1016/j.paid.2016.04.001 https://doi.org/10.1080/08870446.2010.484064 https://doi.org/10.1017/CBO9780511499784.020 https://doi.org/10.1046/j.1365-2648.1993.18111772.x



Evidence based suggestion for interventions based on the targets

Emotion and emotion regulation	1. Explore patients' emotions. Encourage them to say more, if they wish. 2. Explore how they are dealing with these emotions. Do they find their methods helpful? If not, go to points 4 and 5. 3. Discuss what was helpful to them in previous distressing situations. Ask them to elaborate on that. Could these strategies be helpful in this occasion as well? If not, go to points 4 and 5. 4. Discuss/propose adaptive strategies – tailor to patient's needs and preferences. For example, • Expressive writing (write down your emotions, thoughts, images, reactions, etc.) • Physical exercise • Enjoy company/ talk to other persons (emphasize the role of social/family support) • Make plans for enjoyable and meaningful activities • Engage in pleasurable activities • Emphasize and discuss the role of sleep • *Participate in a support/patient group, if available*	https://www.cancer.gov/about-cancer/coping/feelings (emotions in cancer) https://www.cancercouncil.com.au/cancer-information/when-you-are-first-diagnosed/emotions-and-cancer/dealing-with-the-diagnosis/ (emotions in cancer, grief) https://www.who.int/publications/i/item/9789240003927?gclid (WHO for stress management) https://positivepsychology.com/stress-management-techniques-tips-burn-out/ (stress management) https://www.cdc.gov/mentalhealth/tools-resources/index.htm (stress management) https://positivepsychology.com/emotion-regulation/ (strategies for emotion regulation) https://doi.org/10.1007/s12671-020-01561-w (mindfulness, review) https://www.nhs.uk/mental-health/self-help/tips-and-support/mindfulness/ (social support tips)

General concept/ Intervention Target	Corresponding "Explore – Discuss – Suggest" procedure / BCS	Indicative online material – "how to" / online resources
Lifestyle factors	Present relevant guidelines. Help the patient: a) set relevant goals; b) anticipate potential obstacles, discuss ways to overcome these; c) track progress; d) discuss rewards; e) review and set new goals, if appropriate.	Physical exercise: https://doi.org/10.1249/MSS.0000000000002116 https://doi.org/10.1249/MSS.0b013e3181e0c112 https://www.cancer.org/treatment/survivorship-during-and-after-treatment/be-healthy-after-treatment/physical-activity-and-the-cancer-patient.html https://health.gov/our-work/nutrition-physical-activity/physical-activity-guidelines/previous-guidelines/2008-physical-activity-guidelines/advisory-report Alcohol consumption: https://www.cancer.gov/about-cancer/causes-prevention/risk/alcohol/alcohol-fact-sheet https://www.mdanderson.org/cancerwise/does-alcohol-cause-cancer.h00-159383523.html https://www.health.harvard.edu/diseases-and-conditions/11-ways-to-curb-your-drinking https://www.nhs.uk/conditions/alcohol-misuse/ Diet: https://doi.org/10.1111/obr.12591

Exploitation

Cost benefit analysis in BOUNCE

- Conclusion: It is cost-effective to utilize the in-silico predictor as a tool to aid the clinicians predict the patient's state of QoL and choose the intervention based on the prediction.
- The benefits depends on the intervetion type and strategy
- Main benefit to the society (sick leaves) and less to the service provider

Exploitation of the BOUNCE tool after the project

- Comercial exploitation
- Internal use in BOUNCE centers

Dissemination events

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1. Helsinki 2019: Opening event, Digitality
2. Jerusalem 2019: Cross cultural perspective
3. Milan 2020: From resilinece prediction to desicion making
4. Lisbon 2021: Patient centered care, cognitive function, biomarkers

Sub studies in Helsinki University Hospital

Testing pilot in HUS

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- 2021 recruited 101 participants with early breast cancer with BOUNCE inclusions/ exclusions
- **Prediction of the mental well being during following moths (first models)**
- **Exersice calculator, does patient exersice according to recommendations (150 minutes of moderate exersice plus two times muscle work per week)**
- **Patients under 55 years of age are offered nutrition intervention, because of the risk for early menopause**
- Based on prediction of mental health, age and amount of exersice patients are offered digital interventions in HUS Health Village platform

Intervention pilot

1. Empowerment path
2. Exercise path
3. Nutrition path

Paths include:

- Information, guidance
- detection
- self practices
- chat (paths 2, 3)
- walking in the forest (path 2)

Digital Interventions in The Health Village My Path in HUS

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Need and type of digital interventions

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79% exercise path
43 % nutrition path
32% empowerment path
13% no intervention

Same patients can take part to several paths

HUS retrospective BREX data

Trial was originally designed to test the value of exersice interventions. Results proved the benefit of physical activity in the whole population as the control group was also active.

In BOUNCE the data was analyzed with graphical LASSO method

scientific reports

OPEN

A graphical LASSO analysis of global quality of life, sub scales of the EORTC QLQ-C30 instrument and depression in early breast cancer

Paula Poikonen-Saksela[1,5], Eleni Kolokotroni[2,5], Leena Vehmanen[1], Johanna Mattson[1], Georgios Stamatakos[2], Riikka Huovinen[3], Pirkko-Liisa Kellokumpu-Lehtinen[4], Carl Blomqvist[1] & Tiina Saarto[1]

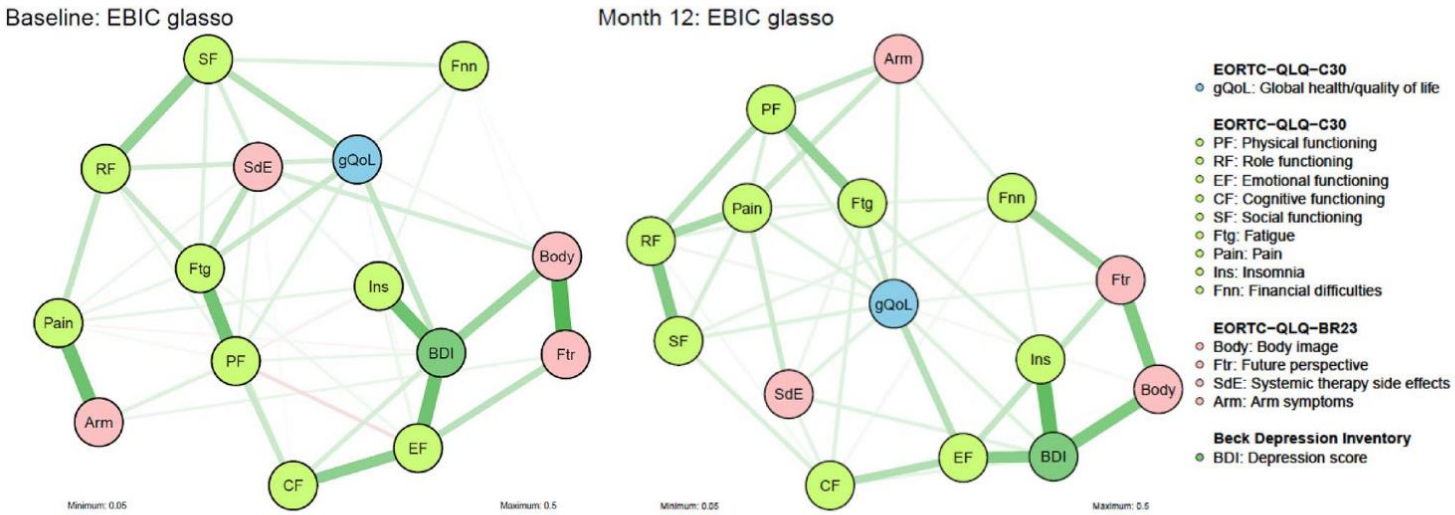

Figure 1. Networks constructed via graphical LASSO visualizing the regularized partial correlations between global health/QoL, symptoms, functioning and depression, measured by EORTC-QLQ C30, EORTC-QLQ B23 and BDI questionnaires, at baseline and 12-month follow up. Green edges represent positive partial correlations and red edges negative ones. Thicker and more saturated edges represent stronger partial correlations. Edges with absolute weight above 0.05 are displayed. The distance between two nodes reflects the absolute edge weight between them (Fruchterman–Reingold layout). All edge weights are reported in Supplement Table 3. The depression score and the symptom scores have been reversed to follow the functioning scales interpretation, i.e. higher score indicates a lower level of symptoms and a better state of the patient.

Summary

- Psychological factors are strongest predictors for resilience and most important targets for interventions in early BC
- BOUNCE models to predict mental health and QOL at M12-18 are ready
- BOUNCE decision support tool functionalities and structure are ready
- Digital support material from the testing pilot can be opened for all BC patients in Helsinki
- Bounce partners are working with exploitation plans of our tool
- BOUNCE increased understanding about resilience in breast cancer with 15 papers published/ submitted
- BOUNCE data is a rich and valuable data source for further studies.

HUS

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HUS Comprehensive Cancer Center

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BOUNCE Consortium meeting 2022 Heraklion

Thank You

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