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BOUNCE

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

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0. Document Info

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1. Table of Contents

2. Introduction

2.1. About the project

Breast cancer accounts for 28% of all cancer cases in Europe ("WHO," 2018). Coping with breast cancer is becoming more a major socio-economic challenge not least due to its constantly increasing incidence in the developing world, which is occurring despite continuous advances in medicine. This said, mortality rate has decreased significantly as 5-year survival rate has risen from 75% to 90% ("Breast Cancer Research Foundation," 2016). For these reasons the number of cancer survivors has grown, with important effects on quality of life even years after the end of treatments.

The process of successful adaptation to breast cancer and the various accompanying stressors can be conceptually defined as the person's resilience. Resilience is a complex construct that can be defined on different levels: an individual's potential (capacity to engage in adaptive coping processes), a process (adaptive reactions to adversity), and an outcome (the final state achieved as the result of coping). An effort to reach a consensus definition was also made by Southwick and colleagues (2014), according to which resilience includes "healthy, adaptive, or integrated positive functioning over the passage of time in the aftermath of adversity". This definition highlights the two main components of resilience: the presence of an adversity and the positive adaptation to it (Cosco, Howse, & Brayne, 2017). When faced with such potentially life-threatening events each person engages coping strategies that can vary widely under 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. Another important consensus has been reached on the determinants of resilience and the approach to measure it: a multiple level of analysis perspective that includes biological, genetic, epigenetic, demographic, cultural, economic, psychological, and behavioural (e.g., life style) and social variables is needed (Southwick et al., 2014). As such, interest in the association between biological factors and resilience has increased. Some studies, not necessarily on humans, have shown an association between resilience and inflammation processes and immune system closely following similar pathways in aging (Tramontano, & De Amicis, 2018) and cancer process (Ben-Shaanan et al., 2018).

During the past decades, a considerable progress has been made on the study of resilience in the field of health psychology towards identifying factors that determine adoption of particular types of coping behaviours, highlighting how socio-demographic and cognitive-emotional in constant interplay with everchanging life circumstances (Deshields, Heiland, Kracen, & Dua, 2016). Indicators of resilience capacity can be stable or malleable. For example, age cannot be altered by intervention, while life style or coping strategies can be changed. Deshields and colleagues (2016) proposed a resilience model in adults with cancer on the basis of previous research and theories, suggesting that resilience is an array of variables that fall into specific categories. Within the baseline attributes, age, sex and socioeconomic status correlate with resilience; older adults and men seem to be more resilient (Bonanno, Galea, Bucciarelli, & Vlahov, 2007). Other baseline attributes are psychological aspects, such as presence of social support (Wills & Bantum, 2012). Zabalegui and colleagues (2013) for example have shown that perceived social support acts as a protective factor, allows for better adaptation and promotes positive coping strategies in breast

cancer patients. Marital status and initial optimism predicted 5-13-year follow-up adjustment, even when controlling for earlier adjustment, in breast cancer survivors (Carver et al., 2005). Another contributing factor for coping with cancer is self-efficacy, which is associated to higher levels of wellness, better quality of life and decreasing depression and anxiety even in 1-year follow-up (BorjAlilu, Kaviani, Helmi, Karbakhsh, & Mazaheri, 2017). Cognitive emotion regulation strategies, such as greater acceptance, positive refocusing, and positive reappraisal also seem to play an important role in patients' psychological wellbeing while rumination and catastrophizing were associated to negative affect (Hamama-Raz et al., 2016; Wang et al., 2014). While theoretical contributions regarding resilience models in medical settings have been advanced (Deshields et al., 2016), to date no one has tested the integrated contributing role of multiple psychological, biological and functional variables in predicting the patient's ability to bounce back from the stressful life event of being diagnosed with breast cancer. Resilience is going to be measured through a data-driven method (computation of resilience index on the basis of retrospective data) and through a psychometric method (various domains of resilience through questionnaires).

There is a growing need for novel strategies to improve understanding and capacity to predict 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, demographic, functional 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.

BOUNCE will deliver a unified clinical model of modifiable factors that could be associated with optimal disease outcomes. It will conduct a prospective multi-centre clinical pilot at five major oncology centres: European Institute of Oncology in Italy, Helsinki University Hospital in Finland, the Rabin Medical Center, Shaare Zedek Medical Center coordinated by the Hebrew University of Jerusalem in Israel and Champalimaud Foundation in Portugal. 660 women will be recruited in order to assess its clinical validity against crucial patient outcomes (illness progression, wellbeing, and functionality). The developed computational tools will validate indices of patients' capacity to bounce back during the highly stressful treatment and recovery period following a diagnosis of breast cancer. The overreaching 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.

2.2. About task 6.1

Task 6.1 (T6.1) undertakes the detailed description of the scope of the BOUNCE multicentre clinical pilots. Specifically T6.1 includes the following elements: refinement of inclusion/exclusion criteria, finalization of recruitment strategies and clinical interview protocol, approvals from Ethics Boards at the national and clinical site level, refinement of indices to be used for recording of clinical and biological variables, finalization of assessment tools (scales, questionnaires) to be used for measurement of sociodemographic, life style, personal, and cognitive-emotional variables, and specification and configuration of all patient data collection tools to be used in the pilots to collect patient reported data (including Noona; see section 5).

2.3. Purpose of the document

The main aim of this document is to provide a detail description of processes involved in the completion of T6.1 as part of the project, focussing on the construction of the study design and the methodology of the multicentre clinical pilot and its evaluation strategy.

2.4. Work methods

All clinical partners contributed, according to their expertise, first in the definition of resilience and then in the refinement of the relevant aspects regarding the multicentre clinical pilot.
In more detail, based on extensive review of the available literature, the panel of BOUNCE experts working on resilience suggested a working definition of resilience in the context of coping with breast cancer that integrates the various aspects (clinical, biological, functional, demographic and psycho-social) of the construct. Subsequently, all clinical partners collaborated to develop instruments for the multicentre clinical pilot.
The processes of defining the instruments for the BOUNCE study started with a list of about 50 relevant psychological constructs and their measures. This initial pool was determined basing on two sources: (1) The results of literature search; and (2) Preliminary proposals based on the research experience of the four national BOUNCE clinical teams, comprised of psycho-oncologists, health psychologists, social workers, and psychometricians.
The following criteria were taken into consideration for choosing the measures:

- Sound psychometric properties (reliability and construct validity).
- Divergent validity in context of the present research (low overlap with other measures).
- Ability to predict important outcomes in RCT's or in longitudinal studies (controlling for initial levels of the outcome measures).
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2.5. Main content of the document

The rest of this document has been structured as follows: Section 3 elaborates on the pilot scope definition, including endpoints of the project and the definition of resilience with a brief

description of prediction models. Section 4 contains information regarding patient selection and the refinement of inclusion and exclusion criteria. Section 5 explains the methods and study design, including a brief description of the Noona platform (used to electronically collect patients' data), the measures/questionnaires and the measurement time points. Finally, section 6 concludes this deliverable and presents the next plans.

3. Pilot scope definition

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. Within the multicentre clinical pilot, information relative to the macro-categories of the biomedical status (BMS), the psychosocial status (PSS) and the functional status (FUS) of breast cancer patients will be collected. To serve this overall goal the following primary and secondary endpoints were undertaken within T6.1.

3.1. Primary endpoint

Identifying factors and processes that may predict both interim and long-term patient resilience, their physical wellbeing and psychological outcomes of cancer and cancer treatment.

3.2. Secondary endpoint

Discriminating between trajectories of psychological adaptation to breast cancer.

- To 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.
- To develop a multi-dimensional index of resilience as a function of the biomedical status (BMS), the psychosocial status (PSS) and the functional status (FUS) of the patient.
- To deliver an advanced, more inclusive, and data-relevant definition of resilience, based on the findings of the study and the extracted prediction models.
- To perform a series of moderation, multiple mediation and moderate mediation analyses (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.
- To cross-validate the prediction models in order to assess the accuracy of their performance in practice and to enhance their generalization. This will take place through bootstrapping methods and, mainly, through data splitting. Specifically, through sophisticated sampling methods, the dataset will be split into two: one part of the dataset will be used so as to develop and train the model; the other part will be used to validate it. Proposed prediction models are detailed below.
- To develop a cost-benefit analysis in order to assess the strengths and limitations of the project outcomes and also determine the best approach to achieve the maximum benefits.

- To examine potential differences in the predictive and outcome variables across the four clinical sites of the BOUNCE Pilot Study.

3.3.Prediction models

In order to fulfil the main aim of the study, two prediction models are proposed: an overall model and a resilience-trajectory specific one.

3.3.1 The Overall Prediction Model

Based on the hypothesis that previous medical and psychological factors may determine or at least predict subsequent well-being and health outcomes, this overall model includes the following hypothesized significant relationships:

1. Outcomes may be predicted not only (1) by the variables (or their interactions) assessed at the immediately previous time-point, but also (2) by the factors (or their interactions) assessed at all previous time-points and baseline, as well as (3) by the interactions between variables assessed at different time-points.
2. Potential association between the medical and psychological variables of the study.

a) For example, it is possible for a medical event or changes in a significant biomedical index to lead to subsequent changes in illness self-regulation and psychological outcomes.

b) Likewise, it is possible and, therefore, should be examined whether there is an interaction between psychological variables, for example illness representations or self-efficacy, and crucial medical variables, for example therapy side effects, regarding their impact on health and psychological outcomes.

3. The process of adaptation to illness is probably characterized by a choreography of dynamic changes in specific aspects of this process. In other words, it is possible that changes in the basic self-regulatory spiral (illness representations, coping behaviors, reappraisals etc.) are associated with corresponding changes to the ways that facilitating factors (such as, self-efficacy) change over time, and for both of these patterns of change to be associated with variations in health outcomes (Leventhal 2016). Hence, the examination of the potential impact of the dynamic changes in different variables (or a set of the most important of them) on corresponding changes in health outcome scores is needed.

Some paradigmatic pathways are illustrated below:

- Clinical variables – (changes in) self-efficacy – (changes in) adherence to medical advice – (changes in) health outcomes
- Clinical variables – (changes in) optimism – (changes in) coping behavior (e.g., positive attitude) – (changes in) health outcomes
- Illness emotional representations – emotion regulation – social support – health outcomes
- Illness representation of treatment control – fear of recurrence – distress – health outcomes
- Sense of coherence – self-rated health – coping behavior – health outcomes

3.3.2 The Resilience Trajectory Prediction Model

This model is supplementary to the previous main one and aims to identify:

a. the (different types of) trajectory over time (i.e., months 1 to 18) for the main outcomes (or the composite outcome indexes) in order to detect the time-point(s) that is (are) critical for inclusion in (or exclusion from) a specific type of trajectory (specifically, the resilience trajectory);
b. the possible transitions from one specific type of trajectory to another;
c. The critical factors that precede inclusion in a specific type of trajectory (e.g., changes in important variables; significant events).

4. Patient selection: criteria for patient eligibility/ineligibility

Six hundred and sixty breast cancer patients with stage I-III histologically confirmed diagnosis will be recruited. HUJI, HUS and IEO will recruit 200 patients each, while CHAMP will recruit 60 participants.

4.1 Inclusion criteria

To be eligible for inclusion in the study, each patient must fulfill the criteria below:

- Presence of a devoted informed consent signed by the patient and the physician
- Female patients, 40-70 years of age at the time of recruitment of diagnosis
- Histologically confirmed invasive early or locally advanced operable breast cancer
- Tumor stage I, II and III
- Patients receiving surgery as part of the local treatment
- Patients receiving any type of systemic treatment for breast cancer regardless of treatment type

4.2 Exclusion criteria

Patients who meet any of the following criteria will be excluded:

- Refusal to sign informed consent
- Presence of distant metastases
- History of another malignancy or contralateral invasive breast cancer within the last five years except cured basal cell carcinoma of skin or carcinoma in situ of the uterine cervix
- History of early onset (i.e., before 40 years of age) mental disorder (i.e., schizophrenia, psychosis, bipolar disorder, diagnosis of major depression) or severe neurologic disorder (i.e., neurodegenerative disorder, dementia)
- Serious other diagnosed concomitant diseases such as clinically significant (i.e. active) cardiac disease (e.g. congestive heart failure, symptomatic coronary artery disease or cardiac arrhythmia not well controlled with medication) or myocardial infarction within the last 12 months.

- Major surgery for a severe disease or trauma which could affect patient's psychosocial wellbeing (for example, major heart or abdominal surgery) within 4 weeks prior to study entry or lack of complete recovery from the effects of surgery
- Treatment for invasive cancer
- Treatment for any major illness in the last half year
- Pregnancy or breastfeeding at time of recruitment

5. Methods and study design

Primary and secondary endpoints will be reached through a large-scale multi-pilot study, which will involve five clinical centers:

- European Institute of Oncology (IEO), Milan
- Rabin Medical Center and Shaare Zedek Medical Center – under the coordination of The Hebrew University of Jerusalem (HUJI), Israel
- Helsinki University Hospital (HUS), Finland
- Champalimaud Foundation (CHAMP), Portugal

Within each clinical center, research assistants, social workers and research nurses will undertake the same online training of the Noona platform in order to homogenize the interaction with patients while they complete the study questionnaires. In addition to this, all those involved in patient recruitment will follow a second training to optimize the fidelity of recruitment procedures.

5.1 The script for oncologist and researcher to introduce the pilot study to potential participants

ONCOLOGIST

"Mrs …
We are working on a project that can help us optimize the personalization of care provision and could help you and other women better manage your condition.

I would like to introduce you to a researcher who will explain the project in detail. This will allow you to freely decide whether you wish to participate or not."

RESEARCH NURSE/ASSISTANT

"Mrs …
I would like to present to you the project the oncologist mentioned earlier. Here is the document describing the project. It is important that you read it carefully. Please, feel free to ask for any information you need before deciding whether to participate to the project or not. If you decide to participate, you will be asked to sign a form (the informed consent) through which you accept to be included in the study.

[after reading the documents]
As you may have noticed in the Document, you will be asked to complete some questionnaires every three months for a period of a year and a half. That is, for 6 more times. This might seem difficult to you right now, but we assure you that most of these assessments will be shorter and, most importantly, they are

necessary in order to achieve the goals of the study. In this way, you will really help us change the way we assist breast cancer patients in their coping with illness."
As detailed in the informed consent, you are requested to fill in some questionnaires using an application on a tablet or smartphone.
[if the patient does not want/is not able to use an electronic device] Alternatively, you can fill the questionnaires using a printed copy.
Due to the complex nature of the cancer event there is quite a number of questions for you to answer. It looks long; however, it usually takes 30 to 45 minutes to answer all of them.
However, it is important for us to collect as much information as possible. This can help the medical team to better understand what women in your condition are experiencing, help future patients identify difficulties and limits that can impact their recovery or quality of life. Of course, you will be provided with feedback on some important parts of the questionnaire, such as your distress levels and how they change from time to time. Furthermore, through these questionnaires we can identify the personal characteristics of each patient that appear to support or impede the care-provision pathway.
Please, be as transparent as possible in responding to each question, so as to allow us to provide you with feedbacks that can support you in the coping process.
If you realize you are getting tired, feel free to have a 5-minute break to make sure that you can allocate the same attention to all questions."

5.1.2 Noona Platform

Noona mobile service was designed for cancer patient remote monitoring and as a support tool for communication between cancer patients and healthcare professionals.
In the US market area Noona is a medical device under exemption criteria for mobile medical devices (Mobile Medical Applications - Guidance for Industry and Food and Drug Administration Staff, issued on February 9, 2015) for which the U.S. Food and Drug Administration (FDA) exercises enforcement discretion.
In EU region Noona is a CE-marked class 1 medical device, in accordance with standards MEDDEV 2.1/6 January 2012, IEC 62304, and EU directive 93/42/EEC. The manufacturer of the service, Noona Healthcare, has carried out conformity assessment and classification according to class 1 requirements. The GMDN code for the service is 58884. The national regulative authority in Finland is Valvira, National Supervisory Authority for Welfare and Health.
The standard Noona tool includes the following functionalities. Patient side main functionalities are to report symptoms using cancer/treatment specific assisted question wizards that cover the clinically relevant questions and measurements for most common and relevant symptoms as well as a symptom diary to self-monitor on symptom progress and recovery status. Patients decide when they require clinical assistance regarding their symptoms and react by contacting clinic according to local guidelines of the pilot site in BOUNCE. Clinics may also send repetitive scheduled questionnaires to patients. Patients may also contact clinic regarding other topics than symptoms. This is done via an open question form. Further patient side functionalities include possibility to view notifications intended for all patients as well as patient specific messages from responsible nurses and doctors. Clinic side main functionality is a work queue to monitor new patients who have requested assistance or who have responded to a scheduled questionnaire, a view on patient information as well as symptom history and the possibility to communicate directly to patient. The possibility for a patient to contact the clinic directly and clinic to message back to patient is optional and configured based on clinic preferences.

In BOUNCE Noona will not be used for communication between 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 provides a web application-based service to the end user. It is a fully responsive web application usable with web browser and suitable device already available to each user including desktop, laptop, pad, and smart phone devices. Noona has two distinctive user groups, and corresponding user interfaces: cancer patients and cancer hospital care personnel (doctors and nurses). Patients are registered to Noona and begin use when treatments begin or after those are finalized and patient enters in the post-treatment recovery phase. During the treatment phase the intended use for Noona use is to evaluate patient symptoms and recovery progress based on the patient reported outcome data transmitted by the product. During the post-treatment recovery phase, the intended use is to monitor patient recovery from cancer and related symptoms and provide consultation & advice to support the recovery progress.

Noona is a cloud-based service and hence Noona can be used on most devices with a supported web-browser and internet connection. Thus, the technical requirements limit internet connectivity and users workstations:

- For care providers requirements are workstations or tablets with a web-browser and internet connection.
- For patient users requirements are smart phone, tablet, or computer with a web-browser and internet connection.

Patient identity is encrypted and decryption keys are restricted to authorized users only. Data visibility is limited to individual patient on patient side and clinic level on clinic side. All clinic users have access to the data from all patients treated in their own clinic, with the possibility to configure nurse/doctor specific care teams for visibility filtering. Visibility to own clinic patients is enforced by access list mechanism.

Noona Healthcare customer service is responsible on the customers' key users. Other nurse and doctor user accounts are created by customers' own key users. All customer nursing staff is responsible and entitled on the patient user account management.

- Invitation link is sent to the clinic user via email
- Invitation link is sent to the patient via email.
- Patient sees in the system the information they submit and response messages from clinic staff.
- Users login to Noona with user name and password from the AWS cloud region specific login website
- According to our experience password authentication offers suitable level of protection for daily use from both perspectives of patient confidentiality and usability.
- Password policy is used to enforce strong passwords
- Patient using the native app from their personal smart phone will be asked to insert a pin code to access the platform.

Noona Healthcare does not offer direct end user support for patients. Instead as part of the patient on boarding, the Noona application gives a tutorial for the patient. Intuitive usability is also a design principle followed in Noona's product development process, which is ensured as part with continued usability testing on cancer patients. As part of the deployment, nursing staff is trained to give patients end user support. It mainly focuses on support in recovering an expired password

or change of password for some other reason as well as giving the initial introduction on what Noona is and how is it used in the customer hospital.

Bounce patients who agree to use Noona will receive feedback on their overall psycho-emotional status after filling out platform questionnaires. The patient will receive a graphic representation of her scores on "overall distress levels" together with a verbal message as described in the case scenario n. 1. She is further informed that this information will allow her to track her progress through treatment over the next 18 months and that these values are mere subjective estimates and may not necessarily indicate the presence or absence of a significant mental health problem. If values on two subscales from the Hospital Anxiety and Depression Scale (i.e., Anxiety and Depression) exceed 13 points indicating severe anxiety or depressive symptomatology, respectively, the patient is notified that she is probably experiencing considerable levels of distress and she may benefit from assistance by a mental health professional. She is further encouraged to discuss this with her oncologist at her next scheduled visit with her/him. If she feels that her mental/psychological status is poor and that she cannot cope at all with daily life then she should consider seeking immediate help at an Emergency Unit/Clinic. On subsequent "visits" to the electronic study platform the patient is provided with a qualitative comparison of her scores to the directly preceding visit on the same two subscales. Based on this measure and on the basis of responses to specific questions of the standardized questionnaires, the patient is provided with the following feedback categories:

- Stable high distress levels (encouraged to seek help from mental health professional and notify her oncologist on her next visit, or seek emergency mental health care),
- Significant increase in distress levels (encouraged to seek help from mental health professional and notify her oncologist on her next visit, or seek emergency mental health care)
- Significant reduction in distress levels (the patient is informed on her improving efforts to cope with her disease)
- Stable low distress levels (the patient is informed on her continuing success in coping with her disease).

5.1.3 Case scenario on feedback on patient's overall psycho-emotional status

CASE SCENARIO n. 1
FEEDBACK ALGORITHM RELATIVE TO THE HADS QUESTIONNAIRE PATIENT'S RESPONSES

M0
HADS questionnaire is filled by the patient

If HADS score equals or is higher than 13

Message to patient:
"You are probably experiencing considerable levels of distress and you may benefit from assistance from a mental health professional. You may want to discuss this with your oncologist at your next scheduled visit with her/him. If you feel that your mental/psychological status is so poor that you cannot cope at all with daily life then you should consider seeking immediate help at an Emergency Unit/Clinic."

If HADS score is greater than 7 and less than 13

Message to patient:
"It appears you are experiencing some distress which is expected when people are faced with a major (or non-negligible) health problem. Such changes in anxiety and/or mood are typically transient and part of the normal adaptive process"

HADS score is 7 or less

Message to patient:
"It appears you are coping very well with your current health problem."

M3, M6, M9, M12, M15, M18, M24
The patient enters the HADS questionnaire.
Case A.
If the patient's previous score was HIGH

Message to the patient:
"Have you visited a mental health professional since the previous time you answered to this questionnaire? Yes/No"

HADS Questionnaire is filled by the patient
Case A.1
If HADS score equals or is higher than 13 and the previous questionnaire score was higher than 13

Case A.1.1 – if the patient has visited a mental health professional
Message to the patient:
"You have been experiencing considerable levels of distress since you previously answered to this questionnaire. As you indicated you are currently being helped by a mental health professional and you should consider continuing this strategy and you should discuss your progress at the next scheduled visit with your oncologist. If, however, you feel that your mental/psychological status is so poor that you cannot cope at all with daily life then you should consider seeking immediate help at an Emergency Unit/Clinic."

Case A.1.2 – if the patient has not visited a mental health professional
Message to the patient:
"You have been experiencing considerable levels of distress since you previously answered to this questionnaire and you may benefit from assistance from a mental health professional. You may want to discuss this with your oncologist at your next scheduled visit with her/him. If you feel that your mental/psychological status is so poor that you cannot cope at all with daily life then you should consider seeking immediate help at an Emergency Unit/Clinic."

Case A.2
If HADS score is lower than 13 points and the previous questionnaire score was higher than 13

Message to the patient (message was missing from original spec, here is our suggestion):
"It seems that your distress levels (or mood accordingly) have eased over the past three months."

Case B.
If the patient's previous score was LOW

Case B.1
If HADS score equals or is greater than 13 and the previous questionnaire score was 13 or lower

Message to the patient:
"It seems that your distress levels (or mood accordingly) have worsened over the past three months. You may want to discuss this with your oncologist at your next scheduled visit with her/him. If you feel that your mental/psychological status is so poor that you cannot cope at all with daily life then you should consider seeking immediate help at an Emergency Unit/Clinic."

Case B.2
If HADS score is greater than 7 and equal or lower than 13

Message to the patient:
"You are experiencing some distress which is expected when people are faced with a major (or non-negligible) health problem. Such changes in anxiety and/or mood are typically transient and part of the normal adaptive process."

Case B.3
If HADS score is 7 or lower

Message to the patient:
"It appears you are coping very well with your current health problem."

5.2 Measures and measurement time points

5.2.1 Measurement time points

There will be seven assessment waves over a period of 18 months: baseline, which will occur after the first visit to the oncologist, Month 3 (M3), Month 6 (M6), Month 9 (M9), Month 12 (M12), Month 15 (M15), and Month 18 (M18).

During the baseline measurement wave, which will occur within three to four weeks from diagnosis, only non-cancer-specific measures are delivered (such as personality). Cancer-specific measures will be administered starting at M3, when the patient has already had some meaningful experience with the illness. Measurement sessions at baseline and at M12 will involve a face-to-face encounters with the researcher (administration of questionnaires will always be conducted through the Noona tool). During the first face-to-face encounter the researcher will demonstrate the Noona platform and give a short training, so that in the following time points the patient will be able to use Noona independently. For those patients that do not want or are unable to use Noona, paper-and-pencil mode will be available.

5.2.2 Psychological instruments

The validated questionnaires that have been considered for creating the comprehensive questionnaire are the following (see Appendix A for all the items):

- Ten item Personality measure (brief Big Five)
- PTSD Checklist
- Life Orientation Test Revised
- Sense of Coherence scale
- The Perceived Ability to Cope with Trauma
- Cognitive Emotion Regulation Questionnaire
- Mindful Attention Awareness Scale
- Modified Medical Outcomes Study Social Support Survey
- Connor Davidson Resilience Scale
- Illness Perception Questionnaire
- Mini-Mental Adjustment to Cancer Scale
- Cancer Behaviour Inventory
- Family Resilience Questionnaire
- MOS Adherence to Medical Advice Scale
- Post-Traumatic Growth Inventory
- EORTC Quality of Life questionnaire – General and Breast Cancer module
- Fear of Recurrence short form
- Hospital Anxiety and Depression Scale
- Positive and Negative Affect short form
- NCCN Distress Thermometer

For those questionnaires requiring permission to use in research, the developers of the measures where contacted to obtain permission to use the questionnaire within the BOUNCE pilot study. Following this, each clinical center contacted the authors that validated the measure in the language of the pilot center to request the measure, if it was not public.
In addition to standardized questionnaires, one-item questions on relevant psychological constructs were developed for the purposes of the study. Figure 1 shows all questionnaires and time-points administration.

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

Figure 1 Self-report instruments used in BOUNCE assessments by psychological domain, showing the measurement waves each instrument is administered and the number of questions it comprises.

5.2.3 Socio-demographic and lifestyle variables

Socio-demographic and lifestyle variables will also be collected, particularly in reference to:

- Age
- Highest level of education
- Marital status
- Number of children
- Employment status and sick days
- Flexible arrangements at work
- Return to work
- Income

- Faith
- Smoking and alcohol consumption
- Drug use
- Weight and height
- Diet
- Exercise
- Number of support sessions
- Family reduced work/activities/services/domestic help

Sociodemographic and lifestyle variables	M0	M3	M6	M9	M12	M15	M18
Age	x						
Highest level of education	x						x
Marital status	x						x
Number of children	x						x
Employment status and sick days	x	x	x	x	x	x	x
Flexible arrangements at work					x		x
Return to work							x
Income	x						x
Faith	x						x
Smoking and alcohol consumption	x			x			x
Drug use	x		x		x		x
Weight and height	x		x		x		x
Diet	x			x			x
Exercise	x		x		x		x
Number of support sessions		x	x	x	x	x	
Family reduced work/activities/services/domestic help		x	x	x	x	x	x

Figure 2 A list of the questions of sociodemographic and lifestyle variables and the related time point assessment

Figure 2 shows the time-points for each socio-demographic area.
The exact questions related to the sociodemographic variables are listed in the Appendix B and will be embedded in Noona.

5.2.4 Clinical variables

Data on the following clinical variables (medical, treatment and patient care data - see Appendix C) will be collected:

- ICD-10 Classification
- Tumor biology: pT, pN, Histological type, Grade, Estrogen receptor, Progesteron receptor, HER- 2 receptor, Margins, Multifocality and multi-centricity, Lymphovascular invasion
- Surgery type and side
- Performance status
- Previous/ongoing oncological therapy
- Menopausal status (pre-menopausal, peri-menopasusal, post menopausal)
- Genetic risk factors
- Use of psychotropic medication
- Other chronic illnesses

- Number and dates of consultations with oncologists, nurses, psychiatrics, psychologists and other healthcare professionals in the oncology clinic
- Number and dates of treatment visits (chemotherapy and radiation therapy visits) in the oncology clinic
- Number and dates of inpatient days in the oncology clinic
- Number and dates of consultations (and phone consultation) with doctors, nurses, psychiatrics, psychologists and other healthcare professionals in other specialized care unit
- Number and dates of treatment visits and number of inpatient days in other specialized care unit
- Number and dates of consultations (and phone consultation) with doctors, nurses, psychiatrics, psychologists and other healthcare professionals in Primary care or Occupational Health Care or other
- Number and dates of inpatient days in Primary care or Occupational Health Care or other
- Number of visits with regards to emergency care, laboratory visits and imaging visits
- List of prescribed medication

All of the medical and tumor data will be collected at baseline, with the exception of treatment data, which will be filled out at M6, when chemotherapy is over and radiotherapy and antiHER2 endocrine therapy are ongoing, M12 and M18. Data from standard laboratory tests (blood cell counts, CRP) performed during the preceding months will be registered at baseline and M12.

5.3 Procedures to register a patient

The study informed consent form is included in appendix D, as prepared by IEO (Promoter of the multi-centre pilot). Each clinical centre will translate the form into their native languages and use it as is.
The patient will received the Informed Consent from the oncologist (or the experimental researcher) who oversees the clinical pilot at each site during a face-to-face interview. Patients will be informed of the voluntary participation in the pilot as well as about the possibility of withdrawing their participation at any time.

5.3.1 Data collection and storage

Data privacy and security obligations are implemented in Noona Healthcare procedures so that data processing is carried out according to statutory and regulatory requirements. Noona Healthcare has entered in written agreements with sub-processors regarding data privacy and security obligations in accordance with statutory and regulatory requirements. Appropriate process and technical controls are used in processing and storage of customer data according to information security risk assessment (ISO27001).
Security is part of Noona Service system architecture on all levels: software architecture, data center architecture and network architecture. Noona service is secured with application level controls, firewalls, application firewalls and denial of service protection mechanisms. Identity and

message information is encrypted on application level with rotating and patient specific symmetric encryption keys. Patient data audit log is collected and archived. All data is encrypted in rest and in transit. System components are segregated to dedicated subnets according to component security level. Noona Service is hosted in multitenant architecture. Access to customer data is restricted with authentication, authorization, cryptographic access controls, role access controls and customer user group access controls.
Noona Service system components are deployed in redundant configuration to ensure availability in case of system component failure. System data storages are backed up daily. In the event of storage failure customer data can be recovered from backups. Noona healthcare has disaster recovery procedure to recover from system wide technical failure or data corruption.
The following sub-contractors are used to provide Noona Service:

- Noona mobile service is hosted in Amazon AWS in Europe, Ireland.
- User Analytics are processed in Microsoft Azure in Europe, Ireland.
- Log processing services are provided by Sumologic in Europe

Data will be collected by Noona and stored centrally by FORTH, cleaned-homogenized, and shared with ICCS and NHG to jointly conduct analyses. Data will be extracted at different time phases during the project (i.e. after the M6 data is complete) to conduct interim analyses and quality checks. Requests for data sharing by other partners to perform additional analyses should be directed to the PCC.

6. Conclusions

This document elaborates on the main points regarding the structure of the multicentre clinical pilot, defining its method, objective and evaluation strategy. The next step is to obtain approval from all Ethical Committees at a national and clinical site level in order to start the recruitment at the beginning of year 2of the project.

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Appendix

1. Appendix A: Questions of the psychological instruments

	Measure name
TIPI	**Ten Item Personality Measure (brief "Big Five")**
I see myself as:	
1	Extraverted, enthusiastic
2	Critical, quarrelsome
3	Dependable, self-disciplined
4	Anxious, easily upset
5	Open to new experiences, complex
6	Reserved, quiet
7	Sympathetic, warm
8	Disorganized, careless
9	Calm, emotionally stable
10	Conventional, uncreative

LOT-R	**Optimism/Pessimism**
1	In uncertain times, I usually expect the best.
2	It's easy for me to relax.
3	If something can go wrong for me, it will.
4	I'm always optimistic about my future.
5	I enjoy my friends a lot.
6	It's important for me to keep busy.
7	I hardly ever expect things to go my way
8	I don't get upset too easily
9	I rarely count on good things happening to me
10	Overall, I expect more good things to happen to me than bad

SOC-13	**Sense of Coherence**
1	Do you have the feeling that you don’t really care about what goes on around you?
2	Have you ever been surprised by the behavior of people you thought you knew well?
3	Have people you counted on, disappointed you?
4	Until now your life has had
5	Do you have the feeling that you are being treated unfairly?
6	Do you have the feeling that you are in an unfamiliar situation and don’t know what to do?
7	The things you do every day are
8	How often are your feelings and ideas mixed-up?
9	Do you sometimes have feelings you would rather not have?
10	Many people - even those with a strong character - sometimes feel unlucky in certain situations. How often have you felt this way in the past?
11	When something happened, do you in your opinion usually

12 How often do you have the feeling that there's little meaning in the things you do in your daily life?
13 How often do you have feelings of which you're not sure if you can control them?

PCL-5 PTSD Check-List

1 Repeated, disturbing, and unwanted memories of the stressful experience?
2 Repeated, disturbing dreams of the stressful experience?
3 Suddenly feeling or acting as if the stressful experience were actually happening again (as if you were actually back there reliving it)?
4 Feeling very upset when something reminded you of the stressful experience?
5 Having strong physical reactions when something reminded you of the stressful experience (for example, heart pounding, trouble breathing, sweating)?

6 Avoiding memories, thoughts, or feelings related to the stressful experience?
7 Avoiding external reminders of the stressful experience (for example, people, places, conversations, activities, objects, or situations)?
8 Trouble remembering important parts of the stressful experience?
9 Having strong negative beliefs about yourself, other people, or the world (for example, having thoughts such as: I am bad, there is something seriously wrong with me, no one can be trusted, the world is completely dangerous)?

10 Blaming yourself or someone else for the stressful experience or what happened after it?
11 Having strong negative feelings such as fear, horror, anger, guilt, or shame?
12 Loss of interest in activities that you used to enjoy?
13 Feeling distant or cut off from other people?
14 Trouble experiencing positive feelings (for example, being unable to feel happiness or have loving feelings for people close to you)?

15 Irritable behavior, angry outbursts, or acting aggressively?
16 Taking too many risks or doing things that could cause you harm?
17 Being "superalert" or watchful or on guard?
18 Feeling jumpy or easily startled?
19 Having difficulty concentrating?
20 Trouble falling or staying asleep?

Recent illness-related events
During the last month, has any important illness-related event occurred to you?
If yes, please indicate it in the following list. You can indicate more than one event.

Recent negative life events
During the last three months, has any important problem (not directly related to your illness) happened to you that you had to spent time and effort to deal with it or it occupied your thoughts.
If yes, please indicate, in which area was this problem. You can indicate more than one area

PACT The Perceived Ability to Cope With Trauma (Flexibility in coping)
1 Keep my schedule and activities as constant as possible

2	Comfort other people
3	Look for a silver lining
4	Stay focused on my current goals and plans
5	Find activities to help me keep the event off my mind
6	Let myself fully experience some of the painful emotions linked with the event
7	Spend time alone
8	I would be able to laugh
9	Try to lessen the experience of painful emotions
10	Reduce my normal social obligations
11	Alter my daily routine
12	Reflect upon the meaning of the event
13	Distract myself to keep from thinking about event
14	Face the grim reality head on
15	Enjoy something that I would normally find funny or amusing
16	Focus my attention on or care for the needs of other people
17	Remind myself that things will get better
18	Keep myself serious and calm
19	Remember the details of the event
20	Pay attention to the distressing feelings that result from the event

CERQ short **Cognitive Emotion Regulation Questionnaire**

I feel that I am the one who is responsible for what has happened

I think that basically the cause must lie within myself

I think that I have to accept that this has happened
I think that I have to accept the situation
I often think about how I feel about what I have experienced
I am preoccupied with what I think and feel about what I have experienced
I think of pleasant things that have nothing to do with it
I think of something nice instead of what has happened
I think about how to change the situation
I think about a plan of what I can do best
I think I can learn something from the situation
I think that I can become a stronger person as a result of what has happened
I think that it hasn't been too bad compared to other things
I tell myself that there are worse things in life

I keep thinking about how terrible it is what I have experienced
I continually think how horrible the situation has been

I feel that others are responsible for what has happened
I feel that basically the cause lies with others

MAAS - Mindfulness

1 I could be experiencing some emotion and not be conscious of it until some time later.
2 I break or spill things because of carelessness, not paying attention, or thinking of something else.
3 I find it difficult to stay focused on what's happeningin the present.
4 I tend to walk quickly to get where I'm going without paying attention to what I experience along the way.
5 I tend not to notice feelings of physical tension or discomfort until they really grab my attention.
6 I forget a person's name almost as soon as I've been told it for the first time.
7 It seems I am "running on automatic," without much awareness of what I'm doing.
8 I rush through activities without being really attentive to them.
9 I get so focused on the goal I want to achieve that I lose touch with what I'm doing right now to get there.
10 I do jobs or tasks automatically, without being aware of what I'm doing.
11 I find myself listening to someone with one ear, doing something else at the same time.
12 I drive places on "automatic pilot" and then wonder why I went there.
13 I find myself preoccupied with the future or the past.
14 I find myself doing things without paying attention.
15 I snack without being aware that I'm eating.

Spirituality coping - a visual bar

"Please rate how much your faith (including religiosity)and spiritual values are helping you in coping with your illness."

mMOS-SS **modified Medical Outcomes Study Social Support Survey**

If you needed it, how often is someone available...

1 to help you if you were confined to bed?
2 to take you to the doctor if you need it?
3 to prepare your meals if you are unable to do it yourself?
4 to help with daily chores if you were sick?
5 to have a good time with?
6 to turn to for suggestions about how to deal with a personal problem?
7 who understands your problems?
8 to love and make you feel wanted?

F.A.R.E. Family Resilience Questionnaire

1 We understand each other about the illness experience that we are living
2 We believe that we can manage the illness
3 In our family we feel that we can talk about how to communicate between us
4 We can face this illness as a family
5 We can work out the significant difficulties in our life such as this illness
6 We think about the illness-related problems until we find a shared solution
7 Everyone in the family feels free to express their own opinion regarding the illness
8 We feel we are strong enough to face this illness
9 We are honest when talking about the illness between ourselves

10 Everyone in the family is open to listening other's opinions regarding the illness
11 We have the strength to solve our problems
12 The things we do for each other to face this illness make us feel part of the family

Instrumental/emotional perceived social support
"Please rate how much support (emotional and/or practical)have you been receiving from the people closest to you during the last month"

CDRISC Connor-Davidson Resilience Scale

1 I am able to adapt to change
2 I can deal with whatever comes
3 I see the humorous side of things
4 I cope with stress strengthens
5 I tend to bounce back after illness or hardship
6 I can achieve my goals
7 Under preassure, I can focus and think clearly
8 I am not easly discouraged by failure
9 I think about myself as a strong person
10 I can handle unpleasant feelings

How much are you back to yourself?
What extent did you bounce back to your ordinary life (before illness)? Can you,please, describe it in percentages (e.g., 20%, 50%, 80%)?

IPQ Illness Perception Questionnaire

IP1 My illness will last a short time
IP2 My illness is likely to be permanent rather than temporary
IP3 My illness will last for a long time
IP4 This illness will pass quickly
IP5 I expect to have this illness for the rest of my life
IP6 My illness is a serious condition
IP7 My illness has major consequences on my life
IP8 My illness does not have much effect on my life
IP9 My illness strongly affects the way others see me
IP10 My illness has serious financial consequences
IP11 My illness causes difficulties for those who are close to me
IP12 There is a lot which I can do to control my symptoms
IP13 What I do can determine whether my illness gets better or worse
IP14 The course of my illness depends on me
IP15 Nothing I do will affect my illness
IP16 I have the power to influence my illness
IP17 My actions will have no affect on the outcome of my illness
IP18 My illness will improve in time
IP19 There is very little that can be done to improve my illness
IP20 My treatment will be effective in curing my illness

IP21	The negative effects of my illness can be prevented (avoided) by my treatment
IP22	My treatment can control my illness
IP23	There is nothing which can help my condition
IP24	The symptoms of my condition are puzzling to me
IP25	My illness is a mystery to me
IP26	I don't understand my illness
IP27	My illness doesn't make any sense to me
IP28	I have a clear picture or understanding of my condition
IP29	The symptoms of my illness change a great deal from day to day
IP30	My symptoms come and go in cycles
IP31	My illness is very unpredictable
IP32	I go through cycles in which my illness gets better and worse.
IP33	I get depressed when I think about my illness
IP34	When I think about my illness I get upset
IP35	My illness makes me feel angry
IP36	My illness does not worry me
IP37	Having this illness makes me feel anxious
IP38	My illness makes me feel afraid
C1	Stress or worry
C2	Hereditary - it runs in my family
C3	A Germ or virus
C4	Diet or eating habits
C5	Chance or bad luck
C6	Poor medical care in my past
C7	Pollution in the environment
C8	My own behaviour
C9	My mental attitude e.g. thinking about life negatively
C10	Family problems or worries caused my illness
C11	Overwork
C12	My emotional state e.g. feeling down, lonely,anxious, empty
C13	Ageing
C14	Alcohol
C15	Smoking
C16	Accident or injury
C17	My personality
C18	Altered immunity

B-IPQ	**Illness Perception Questionaire - Brief form**
1	How much control do you feel you have over your illness?
2	How much do you think your treatment can help your illness?

mini-MAC	**mini-Mental Adjustment to Cancer**
1	At the moment I take one day at a time

2	I see my illness as a challenge
3	I've put myself in the hands of God
4	I feel like giving up
5	I feel very angry about what has happened to me
6	I feel completely at a loss about what to do
7	It is a devastating feeling
8	I count my blessings
9	I worry about the cancer returning or getting worse
10	I try to fight the illness
11	I distract myself when thoughts about my illness come into my head
12	I can't handle it
13	I am apprehensive
14	I am not very hopeful about the future
15	I feel there is nothing I can do to help myself
16	I think it is the end of the world
17	Not thinking about it helps me cope
18	I am very optimistic
19	I've had a good life what's left is a bonus
20	I feel that life is hopeless
21	I can't cope
22	I am upset about having cancer
23	I am determined to beat this disease
24	Since my cancer diagnosis I now realise how precious life is and I'm making the most of it
25	I have difficulty in believing that this happened to me
26	I make a positive effort not to think about my illness
27	I deliberately push all thoughts of cancer out of my mind
28	I suffer great anxiety about it
29	I am a little frightened

Single item: what has done to cope

1	During the last month, what specific actions have you taken in order to manage your experience with cancer? Please, circle how often have you used each of the following ways
2	Tried to relax (e.g., breath slowly, meditate, relax your muscles, yoga).
3	Distracted yourself (e.g., through housework)
4	Prayed, went to church/synagogue/mosque
5	Exercised or used physical activity (e.g., running, going to gym)
6	Tried to look at the more positive sides of your experience (e.g., the support from your family) or of your life
7	Burst to tears or lashed out
8	Talked to somebody important (e.g., partner, family members, close friends)
9	Asked for help somebody important (e.g., partner, family members, close friends)
10	Tried to see your experience rather as a challenge
11	Talked to your physician about your concerns

CBI-B Cancer Behavior Inventory (self-efficacy in coping with cancer)

1	Maintaining independence
2	Maintaining a positive attitude
3	Maintaining a sense of humor
4	Expressing negative feelings about cancer
5	Maintaining activities (work, home, hobbies, social)
6	Remaining relaxed throughout treatments and not allowing scary thoughts to upset me
7	Actively participating in treatment decisions
8	Asking physicians questions
9	Seeking consolation (support)
10	Sharing feelings of concern
11	Managing nausea and vomiting
12	Coping with physical changes

A general self-efficacy item

I am confident in my ability to successfully cope with the difficulties and needs related to my health problem.

the MOS Adherence to medical advice scale

5	Generally speaking, how often during the past 4 weeks were you able to do what the doctor told you?

PTGI	**The Posttraumatic Growth Inventory - short form**
1	I changed my priorities about what is important in life.
2	I have a greater appreciation for the value of my own life.
3	I am able to do better things with my life.
4	I have a better understanding of spiritual matters.
5	I have a greater sense of closeness with others.
6	I established a new path for my life.
7	I know better that I can handle difficulties.
8	I have a stronger religious faith.
9	I discovered that I'm stronger than I thought I was.
10	I learned a great deal about how wonderful people are.

QLQ-C30	**EORTC quality of life questionnaire**
1	Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?
2	Do you have any trouble taking a long walk?
3	Do you have any trouble taking a short walk outside of the house?
4	Do you need to stay in bed or a chair during the day?
5	Do you need help with eating, dressing, washing yourself or using the toilet?

During the past week:

6	Were you limited in doing either your work or other daily activities?
7	Were you limite dinpursuing your hobbies or otherleisure time activities?
8	Were you short of breath?
9	Have you had pain?

10	Did you need to rest?
11	Have you had trouble sleeping?
12	Have you felt weak?
13	Have you lacked appetite?
14	Have you felt nauseated?
15	Have you vomited?
16	Have you been constipated?
17	Have you had diarrhea?
18	Were you tired?
19	Did pain interfere with your daily activities?
20	Have you had difficulty in concentrating on things,like reading a newspaper or watching television?
21	Did you feel tense?
22	Did you worry?
23	Did you feel irritable?
24	Did you feel depressed?
25	Have you had difficulty remembering things?
26	Has your physical condition or medical treatment interfered with your family life?
27	Has your physical condition or medical treatment interfered with your social activities?
28	Has your physical condition or medical treatmentcaused you financial difficulties?
	For the following questions please circle the number between 1 and 7 that best applies to you:
29	How would you rate your overall health during the past week?
30	How would you rate your overall quality of life during the past week?

QLQ-BR23	**EORTC quality of life questionnaire breast cancer module**
	Durging the past week:
31	Did you have a dry mouth?
32	Did food and drink taste different than usual?
33	Were your eyes painful, irritated or watery?
34	Have you lost any hair?
35	Answer this question only if you had any hair loss: Were you upset by the loss of your hair?
36	Did you feel ill or unwell?
37	Did you have hot flushes?
38	Did you have headaches?
39	Have you felt physically less attractive as a result of your disease or treatment?
40	Have you been feeling less feminine as a result of your disease or treatment?
41	Did you find it difficult to look at yourself naked?
42	Have you been dissatisfied with your body?
43	Were you worried about your health in the future? 1
	During the past four weeks:
44	To what extent were you interested in sex?
45	To what extent were you sexually active? (with or without intercourse)
46	Answer this question only if you have been sexually active: To what extent was sex enjoyable for you?
	Durging the past week:

47	Did you have any pain in your arm or shoulder?
48	Did you have a swollen arm or hand?
49	Was it difficult to raise your arm or to move it sideways?
50	Have you had any pain in the area of your affected breast?
51	Was the area of your affected breast swollen?
52	Was the area of your affected breast oversensitive?
53	Have you had skin problems on or in the area of your affected breast (e.g., itchy, dry, flaky)?

FCRI-SF	**Fear of Recurrence - short form (severity scale of original FCRI)**
1	How long have you been thinking about the possibility of cancer recurrence (PCR)?
2	How many times per day do you spend thinking about the PCR?
3	How often do you think about the PCR?
4	In your opinion, what is your risk of having a cancer recurrence
5	I am afraid of a cancer recurrence
6	I am worried or anxious about the PCR
7	I believe that I am cured and the cancer will not come back
8	I think it's normal to be anxious or worried about the PCR
9	When I think about PCR, other unpleasant thoughts or images come to mind (death, suffering, consequences for my family)

HADS	**Hospital Anxiety and Depression Scale**
1	I feel tense or 'wound up':
2	I still enjoy the things I used to enjoy:
3	I get a sort of frightened feeling as if something awful is about to happen:
4	I can laugh and see the funny side of things:
5	Worrying thoughts go through my mind:
6	I feel cheerful :
7	I can sit at ease and feel relaxed:
8	I feel as if I am slowed down:
9	I get a sort of frightened feeling like 'butterflies' in the stomach:
10	I have lost interest in my appearance:
11	I feel restless as I have to be on the move:
12	I look forward with enjoyment to things:
13	I get sudden feelings of panic:
14	I can enjoy a good book or radio or TV program:

DT	**NCCN Distress Thermometer** Please circle the number (0-10) that best describes how much distress you have been experiencing in the past week including today.

PANAS	**Positive and Negative affectivity - short form**
	Thinking about yourself and how you normally feel, to what extent do you generally feel:
1	Upset

2 Hostile
3 Alert
4 Ashamed
5 Inspired
6 Nervous
7 Determined
8 Attentive
9 Afraid
10 Active

2. Appendix B: List of sociodemographic and lifestyle variables

1. Year of birth:	
2. What is the highest level of education you completed?	Primary school
	Secondary schol
	High school
	Vocational non-academic diploma
	Bachelor degree
	Postgraduate education (Master degree, PhD, Nba, specialization, etc.,)
3. What is your marital status?	Single
	Engaged
	Common-law partner
	Married
	Separated/divorced
	Widowed
4. Number of children	
5. What is your employment status?	Employed full time
	Employed part time
	Self-employed
	Unemployed
	Retired
	Housewife
6. What is your net monthly income?	0-500
	501-1,000
	1,001-1,500
	1,501-2,000
	2,001-2,500
	2,501-3,000
	3,001-3,500
	3,501-4,000
	4,001-4,500
	4,501 and up
7. During last three months, how many workdays did you miss because of illness or treatment?	

8. If you are employed, have you had support from your employer to better/more flexible work arrangements?	
9. Have you returned to work?	Yes, full-time. Please specify return date:
	Yes, part time. Please specify return date:
	No
10. If you quit working was it your decision or your employer's decision?	My decision to quit
	My employer's decision
11a. How would you describe the level of your religious faith?	ALL EXCEPT HUJI: Ateist Practicing believer Non-practicing believer HUJI: secular observing traditions religious ultra-religious/very-religious
11b. How would you describe the level of religious faith of your community?	ALL EXCEPT HUJI: Christian Muslim Jewish Other HUJI: Jewish/Muslim/Christian/Other
12. Do you smoke?	I only smoked in the past
	Yes/No
	If you smoke now or in the past: How many cigarettes do/did you smoke during the day?
13. a) How often do you drink wine or beer?	Never
	Less than once a month
	Once or twice a month
	About once a week
	Several times a week
	Every day
b) If you drink wine or beer, how many glasses do you usually have each time?	
c) How often do you drink spirits (such as vodka, gin, or whiskey)?	Never
	Less than once a month
	Once or twice a month
	About once a week
	Several times a week
	Every day
d) If you drink spirits, how many shots do you usually have each time?	
e) Do you drink now less / the same amount/ more than before the illness?	More
	Less
	The same amount
14. Do you use any drugs (please mark all that is applicable)? If you use any of these drugs, please mark near it whether you starting using it before or after the illness.	No
	Not medically-prescribed drugs (such as tranquilizers, Ritalin or strong pain-killers)
	Medically-prescribed cannabis
	Not medically-prescribed cannabis

	Other drugs (such as MDMA or cocaine)
15. What is your weight?	g
16. What is your height?	cm
17. Are you following a specific diet at the moment or have you followed a specific diet in the recent past?	Low-calories
	Low-carb
	Mediterranean
	Protein-only
	Vegan
	Vegeterian
	Gluten-free
	Dairy-free
	FODMAP-free
	Macrobiotic diet
	Other, please specify:
18. How much do you exercise? Please indicate all exercise you do in a week.	Moderate aerobic exercise (for example walking, cycling)_____min/week
	Heavy aerobic exercise (for example running, HIIT training)_____min/week
	Muscle training____times/week
	I do not exercise.
19. a) During the last three months have you seen a mental health professional inside and/or outside of the hospital?	No Yes
b) If yes, how many times?	
20. Has your partner or someone in your family reduced their work time to take care of you during the last three months?	No
	Yes. Please specify how many hours/days/months:
21. Do you do any activities to support your well-being (e.g. culture&arts, other hobbies, mindfulness/yoga, etc)?	No
	Yes. Please specify:
22. Have you used any services to support your well-being during the last three months (e.g. physiotherapy, peer support groups, etc)?	No
	Yes. Please specify:
23. Have you had any domestic help during the last three months? How many days?	No
	Yes. Please specify number of days:

3. Appendix C: Clinical variables

Medical information			**M0**	**M3**	**M6**	**M12**
Date of diagnosis						
Cancer stage: I II III IV						
Chronic illnesses	yes/no specification		x			
Genetic risk factors	family history positive genetic testing		x			
Menopausal status pretreatment	premenopausal perimenopausal postmenopausal		x			

Menopausal status posttreatment	premenopausal perimenopausal postmenopausal					x
Tumour pathology	pT	mm	x			
	pN	N1,N2,N3	x			
	histological type	ductal, lobular, other	x			
	ER	%	x			
	PR	%	x			
	Grade	I,II,III	x			
	HER2	positive (FISH, SISH/CISH) negative	x			
	molecular classification		x			
Performance status ECOG			x	x	x	x
Psychotropic medications	name		x	x	x	x
Hormone replacement therapy pretreatment	Yes/no		x			
lab	Hb, Leukocytes, thrombocytes, Neutrofiles, CRP		x			x

Treatment information		**M0**	**M3**	**M6**	**M12**	**M18**
Surgery	Date, type (breast conserving, mastectomy) axillary surgery (SNB, evacuation), reoperation date			x		
Radiotherapy	start date - end date faraction per day total dose intraoperative radiotherapy Area (breast, ablation area, nodal irradiation)			x		
Chemotherapy	Start date - end date Regimen (anthracyclin-docetaxel based anthracyclin -paclitaxel based paclitaxel docetaxel anthracyclin taxane-karboplatin FINXX type with capecitabine cyclophosphamide-docetaxel other)			x		
Endocrine	Start date and type (tamoxifen, letrotzole, exemestane, anastrotzole, ovarian suppression + tamoxifen, ovarian suppression + Al, oophorectomy)				x	x
Anti HER2 treatment	Start date – end date and type (trastutzumab, trastutzumab + pertutzumab)				x	x
side effects:	Osteoporosis (date of dg), cardiac failure (type asymptomatic decreaser of LVEF, heart failure, coronary sdr), neutropenic infection (date of dg), other sever side effect (type, date of dg)				x	

N.B.: It will be filled out only for the previous and ongoing treatment that the patient has undertaken.

Patient care path data			M3	M6	M9	M12	M18
Oncology clinic	Number and dates of consultations of	oncologists	x	x	x	x	x
		nurses					
		psychiatrists					
		psychologists					
		other HC professionals					
	Number and dates of phone consultations of	oncologists	x	x	x	x	x
		nurses					
		psychiatrists					
		psychologists					
		other HC professionals					
	Number and dates of treatment visits	Chemotherapy visits	x	x	x	x	x
		Radiation therapy visits					
	Number and dates of inpatient days	Diagnosis/reason for stay	x	x	x	x	x
Other specialized care unit	Number and dates of consultations of	doctors	x	x	x	x	x
		nurses					
		psychiatrists					
		psychologists					
		other therapists					
	Number and dates of phone consultations of	doctors	x	x	x	x	x
		nurses					
		psychiatrists					
		psychologists					
		other therapists					
	Number and dates of treatment visits	Treatment type	x	x	x	x	x
	Number of inpatient days	Diagnosis/reason for stay	x	x	x	x	x
Primary care/Occupational HC/other	Number and dates of consultations of	doctors	x	x	x	x	x
		nurses					
		psychologists					
		other therapists					
	Number and dates of phone consultations of	doctors	x	x	x	x	x
		nurses					
		psychologists					
		other therapists					
	Number and dates of inpatient days	Diagnosis/reason for stay	x	x	x	x	x
Emergency care	Number of visits	Diagnosis/reason for visit	x	x	x	x	x
Laboratory visits	Number of visits	Test type	x	x	x	x	x
Imaging visits	Number of visits	Imaging type	X	x	x	x	x

Outpatient medication	List of prescribed medication		x	x	x	x	x

4. Appendix D: Information sheet and informed consent

As Promoter of the multi-centre pilot, IEO has prepared the informed consent sheet and consent to treatment of data. Each clinical centre will adopted the document, once translated into their native languages and adapted the document with the information needed.

INFORMATION SHEET AND INFORMED CONSENT

Assessment of psychological and biological aspects involved in effective adaptation in breast cancer patients: a multicentre pilot study

(… S___/____)"

INTRODUCTION

Dear Mrs,

The **(name of the clinical center)** is engaged in research aimed at improving disease management patient's quality of life.

In this regard, we ask you to participate in a Multicenter Pilot Study entitled "Predicting Effective Adaptation to Breast Cancer to Help Women to BOUNCE Back: a multicentre clinical pilot study".

This Multicenter Pilot Study is part of a wider project sponsored by the European Community entitled "Predicting Effective Adaptation to Breast Cancer to Help Women to BOUNCE Back" (Acronym BOUNCE, Call H2020-SC1-2016-2017).

The clinical centers involved in the Multicenter Pilot Study are: the European Institute of Oncology, Rabin Medical Center; Shaare Zedek, Medical Center, under the Hebrew University of Jerusalem (Israel), Helsinki University Hospital (Finland), and Champalimaud Foundation (Portugal).

RATIONALE AND PURPOSE OF THE PROJECT

The objective of the wider project sponsored by the European Community, and of the Multicenter Pilot Study as well, is to study the concept of resilience, i.e. the ability to manage complex events such as, for example, cancer diagnosis. In particular, the project aims to construct an instrument capable of describing as precisely as possible the degree of adaptation of the patient during illness and treatment, in order to provide a more personalized care that can respond to the specific needs of each patient.

Previous studies have shown that the ability to manage and adapt to the course of treatment depends not only on the type of cancer, but also on the patient's personal characteristics and the social environment in which she lives, such as work, social support, etc. It is important to be able to identify these characteristics in order to plan a care pathway that consider all the aspects involved in this process so as to understand and respond better to the needs of the patient themselves.

For this reason, the objective of the current Multicenter Pilot Study is to identify those personal and biological aspects that may predict your wellbeing in the short and in the long-term.

WHAT DO I HAVE TO DO IF I DECIDE TO PARTICIPATE IN THIS STUDY?

If you decide to participate, you will be asked to fill in some questionnaires that evaluate different aspects of your personality, quality of life, psychological functioning, and your way of coping with the disease, at seven different time points, each at a 3-month interval from one another, for a total of 18 months. To complete the questionnaires, at each time point you will need approximately from 30 to 45 minutes of your time.
We will also retrieve information about the biological characteristics of your illness, accessing your Personal Health Records. The researcher will collect this data and will not ask you medical questions about your illness.
The first meeting with the researcher will be face-to-face and you will see the researcher again after one year; in the other time points you will complete the questionnaires through a mobile service or in a paper-and-pencil mode, depending on your will.
During the first face-to-face meeting with the researcher, if you use electronic devices such as smartphone, tablet or computer, you will be shown the functioning of a web platform called Noona. Noona is an online centralized platform that is already predisposed to sending and receiving questionnaires from patients. To use the platform, you will need a Wifi or a mobile internet connection. You will be able to fill in the questionnaires at later points in time through this platform, which will alert you when you need to complete the questions and will provide you feedback on how you are doing.
If you do not use or you do not have an electronic device, unfortunately we are not able to provide you with one, but you will have the possibiliy to answer the questionnaires by completing a paper version of them. You will then be notified by the researcher when you have to complete the following step. In this latter case, you will be asked either to come by person to the hospital or send the questionnaires to the **(name of the clinical center)** through postal service and **(name of the clinical center)** will pay for the postal expenses.

WHO CAN PARTICIPATE IN THIS STUDY?
This multicentre pilot study will recruit a total of 660 female breast cancer patients in Israel, Finland, Portugal and Italy. **(name of the clinical center)** aims at recruiting 200 of patients, who come for their first visit with the oncologist to this Institute and who meet the following criteria:
1. Are 40 to 70 years of age at the time of diagnosis;
2. Have a histologically confirmed breast cancer diagnosis, who will receive some type of treatment and who do not have distant metastases;
3. Signed informed consent.

WILL THERE BE ANY COSTS ASSOCIATED TO PARTICIPATION?
You will not incur in any expenses related to participation in the study and will not receive any compensation for your participation.

WHAT ARE THE POSSIBLE BENEFITS RELATED TO PARTICIPATION TO THE STUDY?
There are currently no direct benefits related to participation in the study for the current participants. However, participation to the study can provide some psychological insights into the ways you cope with the illness In addition to this, it will help us to understand how to provide a better support to cancer patients during treatment or in the post-operative period, or during subsequent follow-up visits, as well as guidance to health professionals on how dealing with their patients. Therefore, the results will benefit future patients and could lead to the development of patient support tools. In any case, during the course of the study you will be provided with some feedbacks regarding specific aspects of the way you are coping with your disease that may help you to manage your disease in a more comprehensive manner.

POTENTIAL RISKS

There are no direct risks and/or distress related to participation in this study, as it does not involve the administration of any pharmacological compound nor does it subject patients to any intervention. There may be some indirect risks in terms of distress in filling in the questionnaires. However, the researchers involved in this study are at your disposal if anything makes you feel nervous, tense, or distressed and, if necessary, a healthcare professional will be available.

DO I HAVE TO PARTICIPATE TO THIS STUDY?

Your decision to participate to this study is completely free: you will be given the necessary time to read carefully this document that reports the information provided to you by the investigator responsible for the project or his delegate. You are given the opportunity, if you wish, to discuss it with people you trust, or with your general practitioner. Also, you can ask the investigator in charge of the study to explain to you anything that may seem unclear.

Once you have understood the procedures of the study, and you have decided to take part in it, you will be asked to sign this informed consent. A copy of this document, signed and dated, will be also given back to you.

If you decide not to participate in the project you will still be guaranteed the same attention that has been provided to you up until now.

Do not subscribe to this informed consent form if you are not sure you have fully understood the information contained in it.

CONTACT INFORMATION (to be adapted by each clinical center)

The principal investigator of the study is Dr. Ketti Mazzocco of the Applied Research Division for Cognitive and Psychological Science. The reference co-investigators of this study Dr. Greta Pettini, Dr. Flavia Faccio, and Dr. Marianna Masiero. You can contact the research unit by phone (02/94371083 or 02/94372099) or via email (unita.psicologia@ieo.it). If you would like to receive further information on this study, before deciding to participate or during the course of study if you have any doubts.

INFORMED CONSENT

I have read the informed consent form prepared by the **(name of the clinical center)**, I confirm that I was offered the opportunity to discuss every aspect of the study with the research, who was available for any further information regarding the study. I understood that my participation is voluntary. I have been sufficiently informed about the aims and methods of experimentation and are able to decide my free and voluntary participation in this study. I understand that I can freely decide to stop my participation in the study at any time.

I received a copy of the informed consent form.

NAME AND SURNAME OF THE PATIENT (in capital letters): _____
SIGNING OF THE PATIENT: _____ Date: _____

NAME AND SURNAME OF THE RESEARCHER (in capital letters) _____
SIGNATURE OF THE RESEARCHER _____ Date: _____

Privacy policy (pursuant to European Regulation No. 679/2016, "GDPR")

Dear Madam,
In accordance with current national and EU legislation on the protection of personal data, please, find below the information regarding the processing of the personal data collected in this study. The processing of personal data will be carried out in compliance with the fundamental rights and freedoms of the data subject in accordance with the principles of fairness, lawfulness and transparency.

Definitions
According to this legislation the following terms are used:
- Personal data: any information relating to an identified or identifiable natural person ('data subject'); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person (Article 4 No. 1 GDPR);
- Data controller: the natural or legal person, public authority, or other body which, alone or jointly with others, determines the purposes and means of the processing of personal data (Article 4 No. 7 GDPR);
- Data processor: natural or legal person, public authority, agency or other body which processes personal data on behalf of the controller (Article 4 No. 8 GDPR);
- Data concerning health: personal data related to the physical or mental health of a natural person, including the provision of health care services, which reveal information about his or her health status (Article 4 No. 15 GDPR).

Data controller
The Data Controller is:
- The European Institute of Oncology (IEO)
- Via Filodrammatici 10, 2012 Milan

Data Protection Officer (DPO)
The Data Controller has appointed a Data Protection Officer for the support in the application of national and European data protection legislation, working with the Supervisory Authority and acting as a reference of contact for data subjects. The Data Protection Officer can be contacted at the following address:
- Via Giuseppe Ripamonti n. 435, 20141 Milan
- Tel. 02.57489285
- Email: privacy@ieo.it / direzione.sanitaria@ieo.it
- PEC: direzionesanitariaieo@pec.it

Purpose and lawfulness condition of processing personal data
Personal data will be processed by the Data Controller only for the Multicentric Pilot Study: "Predicting Effective Adaptation to Breast Cancer to Help Women to BOUNCE back: a multicentre pilot study" according to the modalities and the potential risks and benefits related to this project and previously illustrated. More specifically, the processing of personal data will be carried out by the Data Controller in order to collect some information regarding patients belonging to different hospitals and countries, as well as companies specialized in data retention and analysis. Furthermore, the data collected could be used, within the limits of the provisions of Article 5 lett. b) and 89 paragraph 1 GDPR, for subsequent scientific research. However, the processing of personal data collected by Data Controller, including data relating to health, for the aforementioned purposes is carried out on the basis of your explicit consent.

Nature of the data provision
The consent for the purposes mentioned here is absolutely optional and refusal will not have any consequences on the provision of the services requested.

Modality of data collection

Personal data will be collected via the platform previously mentioned (Noona) and will be processed by authorized personnel in accordance with the current legislation on personal data protection. If the questionnaires are filled in on paper, the data will be entered manually in Noona by authorized personnel. The Data Controller will not make use of automated decision-making processes with respect to the personal data of the data subject.

Recipients/categories of recipients
The data collected will not be disseminated. In relation to the purposes set out in this statement, the data may be disclosed to:
Clinical centers (data will be collected in the following centers):
a) Helsinki University Hospital, Finland - Coordinator of the European Project and Responsible for data processing pursuant to art. 28 GDPR;
b) European Institute of Oncology, Italy - coordinator of the Multicentric Pilot Study and Responsible for data processing pursuant to art. 28 GDPR
c) HUJI, Israel - Responsible for data processing pursuant to art. 28 GDPR:
- Rabin Medical Center;
- Shaare Zedek Medical Center;
d) Champalimaud Foundation, Portugal - Responsible for data processing pursuant to art. 28 GDPR.

Technical partners (all the following partners are Data Processors under Article 28 of the GDPR, but their roles within the Multicentre Pilot Study vary):
e) FORTH, Greece - data analysis and archiving;
f) ICCS, Greece - data analysis and model development;
g) SiLo, Greece - data analysis and model development;
h) NHG, Finland - model development;
i) Noona, Finland - data storage.

The data will be processed using a coding system that allows identification of patients' identity only if and when necessary for the scientific purposes of this research project.
The Data Controller is classified by the Italian Ministry of Health among the scientific research institutes for which research is an integral part of its mission. All research, including the research project in question, is controlled and approved by the Ethics Committee of the Data Controller, which provides, in light of the current legislation, consent to the processing of personal data of patients.
The results of the research can be disseminated only in an aggregated manner (i.e. making it impossible to trace data back to the single patient) in scientific publications and/or presentations of conferences and/or scientific events in general.

Data transfer abroad
The involvement of third parties in the research project also involves transfer of personal data abroad. In the case of countries belonging to the European Union, as required by the current legislation, the same principles, the same rules, rights and protections in Italy will apply; in the case of countries not belonging to the European Union, the transfer can take place exclusively in compliance with the contractual clauses, which have to guarantee the same European safety and protection standards.

Data storage
The data will be kept for the necessary time to complete the purposes for which they were collected and in any case for a maximum of 10 years from the date of consent.
For future research, study reports or scientific presentations, data may be stored for up to 10 years.
The archived samples can be used in the future by the project partners to conduct further research in the field of resilience that could derive from the current project, in compliance with the provisions of art. 5 lett. b) and art. 89 paragraph 1 GDPR.

Rights of the interested party
At any time, the interested party may exercise her rights, listed below, in accordance with the EU Regulation 679/2016 regarding personal data protection:

- Right of access: the interested party has the right to obtain confirmation of whether or not personal data is being processed and, in this case, to obtain access to personal data. At any time, you can request access to the following information: the purposes of the processing, which data categories are being processed, the recipients to whom the personal data are or will be communicated, the period of storage, the existence of any rights in favour of the data subject, the origin of the data and whether or not there is an automated process.
- Right to rectification: the data subject has the right to obtain from the data controller the correction of inaccurate personal data concerning him without undue delay. Furthermore, he / she has the right to obtain the integration of incomplete personal data, also by providing an additional declaration. In this case, the data controller will be obliged to inform each recipient to whom the personal data concerning possible corrections have been transmitted.
- Right to erasure ("right to be forgotten"): the data subject has the right to obtain the erasure of his/her personal data without undue delay and to request erasure. In addition, if his/her data have been made public, the data controller will delete it and will take reasonable measures, including technical, to inform data controllers who are processing personal data of the request of the data subject to delete any copy of his personal data.
- Right to restriction of processing: if deemed appropriate, the data subject may request the limitation of the processing of his/her personal data and limit the processing of such data in the future. In this case, the data controller will inform each of the recipients to whom the personal data have been transmitted of any limitations to the processing of personal data, unless this proves impossible or involves a disproportionate effort.
- Right to data portability: the data subject has the right to receive personal data relating to him in a structured, commonly used and readable form by an automatic device and to request storage for further use for personal purposes. Furthermore, the participant has the right to request direct transmission of her data to another data controller without obstructions, where possible.
- Right to object to data processing: the data subject has the right to object at any time, for reasons connected with her particular situation, to the processing of her personal data.
- Right of withdraw the consent: in the case of a processing based on consent, the data subject may withdraw the consent given for the processing. However, that act does not affect the validity of the processing carried out by the data controller up to that moment.
- Right to lodge a complaint with a supervisory authority: if the data subject believes that his/her data has been processed unlawfully and that the rules and principles regarding the protection of personal data have been violated, he/she has the right to contact the Supervisory Authority to submit a complaint, in accordance with the procedures defined by the latter.

The rights referred to in this paragraph may be exercised by contacting alternatively:

- either the contact person at your clinic (each center must nominate a contact person and provide contact information)
- or the Data Protection Officer (DPO)

Consent and acknowledgment of the information

Based on the information acquired, I:

o Give consent o Deny consent

to the processing of personal data for the purposes set out in this statement

o Give consent o Deny consent

to the processing of data concerning health for the purposes referred to in this statement

I declare that I have read this privacy policy for the processing of personal data collected by the Data Controller and have understood the information provided by the Data Controller.

Date	Signature
_____ / _____ / _____	....