Addressing Psychosocial and Lifestyle Risk Factors to Promote Primary Cancer Prevention: an integrated platform to promote behavioural change (IBeCHANGE)

Project Number: 101136840

D5.1 – iBC/PS protocol approval and registration

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Disclaimer

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List of Abbreviations

Abbreviation	Explanation
AI	Artificial intelligence
AUDIT	Alcohol Use Disorders Identification Test
BARD	Bayesian Adaptively Randomised Design
BC	Behavioural change
BMI	Body Mass Index
CG	Control group
COM-B	Capability-Opportunity-Motivation - Behaviour
CRF	Case Report Form
CrI	Credible intervals
CT-scan	Computerised Tomography scan
DPIA	Data Protection Impact Assessment
DMP	Data management plan
EC	Exclusion criteria
ECW	Exclusion criteria for the wearable sub-study
EG	Experimental group
EGw	Experimental group with wearable
EM	Emotional management
FOBT	Faecal Occult Blood Test
FTND	Fagerström test for Nicotine Dependence
GDPR	General Data Protection Regulation
GP	General Practitioner
GPAQ	Global Physical Activity Questionnaire
HAPA	Health Action Process Approach
HCP	Health care professional
HHS	Health Habit Score
iBC	iBeChange platform or group
IC	Inclusion criteria
ICF	Informed Consent Form
ICW	Inclusion criteria for the wearable sub-study
ICH GCP	International Council on Harmonisation Good Clinical Practice
ICO	Institut Català d'Oncologia
IEO	Istituto Europeo di Oncologia
IPAQ	International Physical Activity Questionnaire
IRB	Institutional Review Board
MCMC	Markov Chain Monte Carlo
MET	Metabolic equivalent of the task
MICE	Multivariate Imputations by Chained Equations
PHQ	Patient Health Questionnaire
PS	Pilot study
PSS	Perceived Stress Scale
QR code	Quick Response code
RCT	Randomised controlled trial
SMD	Standardised Mean Difference
SSI	Single-session intervention
TSC	Trial Supervision Committee
UMFCD	Universitatea de Medicina si Farmacie Carol Davila

UNIPA	Università di Palermo
UPR	Usual Practice Recommendations

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Executive Summary

The **iBeChange pilot study protocol** outlines the design and implementation of a 12-week digital health intervention aimed at promoting behavioural change for cancer prevention across five lifestyle and psychosocial health pillars: smoking, alcohol consumption, nutrition, physical activity, and emotional well-being. The pilot study will evaluate the feasibility, usability, and preliminary effectiveness and cost-effectiveness of the iBeChange platform prior to the launch of a randomised controlled trial (RCT).

This protocol includes the **wearable sub-study**, which forms part of the same **randomisation strategy** as the main pilot study. Participants in the intervention group will be further randomised to either receive or not receive a wearable device (Oura ring), enabling passive lifestyle data collection. This integrated design ensures consistency in participant allocation and adherence to methodological standards required for ethical approval. The Ethical approval for this pilot study protocol is expected to be obtained shortly. Deliverable 5.1 will be updated once approved by the Institutional Review Boards.

While the wearable sub-study is incorporated into this protocol submission to **facilitate joint ethical committee approval**, a **dedicated deliverable (D5.2: iBC/WS protocol approval and registration)** has been prepared, providing specific information regarding the wearable component, including procedures, data handling, and specific research objectives.

The outcomes of this pilot will inform the optimisation of the platform, recruitment strategy, and intervention delivery ahead of the full-scale RCT, ensuring scientific rigor and participant engagement are maintained.

1. Introduction

This deliverable presents the pilot study protocol for the iBeChange (iBC) project, developed under Work Package 5 (WP5) – Deployment of the Recommendation System to the Population. WP5 aims to design and implement prospective studies to evaluate the feasibility, usability, and preliminary impact of the iBeChange platform—a digital health solution promoting behavioural change for cancer prevention.

The pilot study (iBC/PS) represents the initial and critical phase of WP5. It is designed to test and refine all essential components related to participant recruitment, study management, intervention delivery, and data collection procedures across participating clinical sites. The findings of this pilot will directly inform the subsequent multicentre randomised controlled trial (iBC/CT), which will assess the long-term effectiveness, cost-effectiveness and implementation of the iBC platform.

This protocol was developed collaboratively by clinical, technical, statistical and data management partners in accordance with Task 5.1 – Pilot Preparation and supports the activities of Task 5.4 – Pilot Study and Data Management. It will also contribute to Task 5.2 – Study Management and Supervision, which includes oversight by the Trial Supervision Committee.

This protocol also includes the wearable sub-study, a nested component of the pilot trial. The wearable sub-study has been included as it is part of the same randomisation strategy as the main pilot. It aims to assess the feasibility of using digital devices (i.e., Oura Ring) to collect behavioural and psychosocial data passively. While included here for ethical submission purposes, additional details and procedures specific to the wearable component are described in a separate deliverable (D5.2 – iBC/WS Protocol Approval and Registration).

This document provides a detailed overview of the pilot's objectives, design, methodology, and ethical considerations, aligning with WP5's overarching goal of preparing for the scaled deployment and validation of the iBeChange recommendation system.

2. Protocol Summary

2.1. Synopsis

Table 1. iBeChange Pilot Study Synopsis

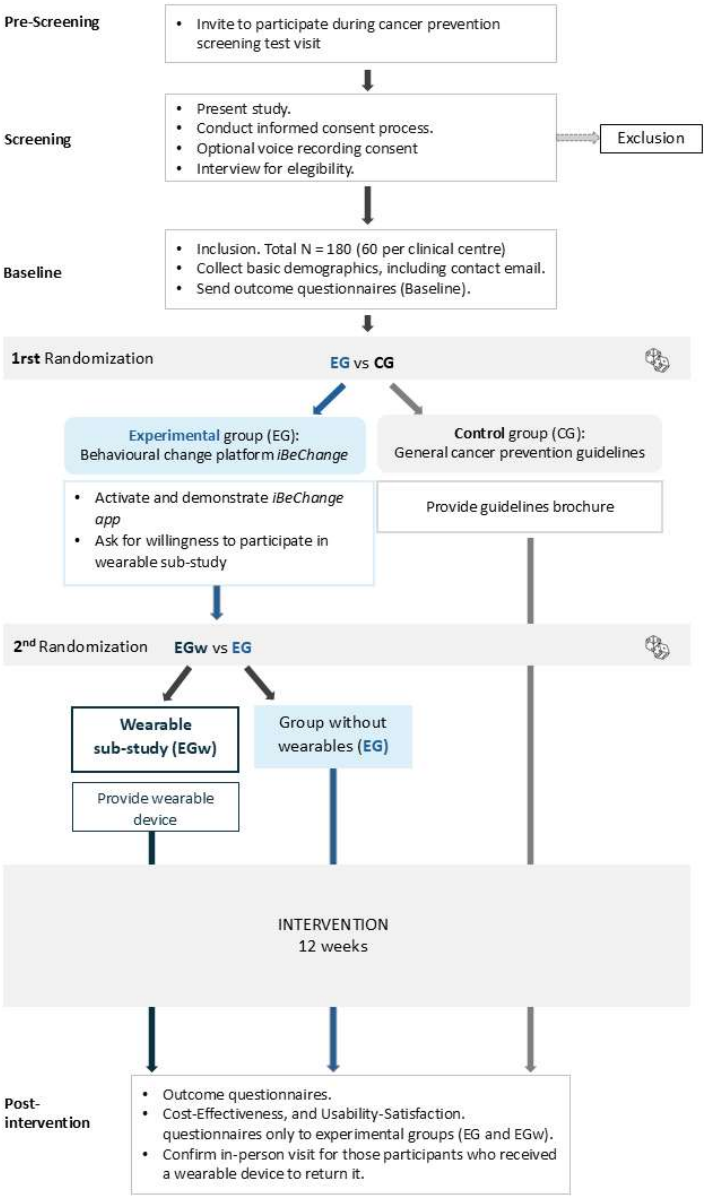
Title:	Behavioural change for cancer prevention: A pilot study protocol of a digital intervention
Grant Number:	Horizon Mission Cancer HORIZON-MISS-2023-CANCER-01 ID: 101136840
Study Description:	This pilot study will assess the feasibility of iBeChange, a digital platform designed to promote personalised behavioural change to address lifestyle and psychosocial risk factors associated with cancer risk. Twelve weeks of iBeChange intervention will be compared to treatment as usual, consisting of receiving general cancer prevention guidelines. A sub-group of participants in the iBeChange intervention group will receive an Oura ring wearable device to automatically and unobtrusively collect physiological data.
Objectives*:	The primary objective of this pilot study is to assess the feasibility of iBeChange in real-life settings. Additionally, preliminary data regarding the effectiveness and cost-effectiveness of iBeChange compared to general cancer prevention guidelines will be collected. Also, exploratory data from Oura smart rings will be collected from the allocated participants. Finally, usability and satisfaction will be assessed for the iBeChange platform and for the selected wearable devices.
Endpoints*:	The primary endpoints are the feasibility of the recruitment, data collection, and ability to manage and implement the study and intervention. The secondary endpoints are the effectiveness and cost-effectiveness of iBeChange in achieving a sustainable behavioural change in Smoking, Alcohol consumption, Nutrition, Physical activity habits, and Emotional Well-being symptoms.
Study Population:	This pilot study will enrol a total of 180 healthy individuals (60 per clinical centre), both men and women, aged 45-80 who undergo screening tests for breast, colorectal or lung cancer, from Spain, Italy and Romania.
Phase* or Stage:	Not Applicable (Behavioural Intervention)
Description of Sites/Facilities Enrolling Participants:	This pilot study is a European multicentric trial. It will be conducted in three centres: Institut Català d'Oncologia (ICO, Barcelona, Spain), Istituto Europeo di Oncologia (IEO, Milano, Italy), and Universitatea de Medicina si Farmacie Carol Davila (UMFCD, Bucarest, Romania).

Description of Study Intervention/Experimental Manipulation:	The study intervention consists of a digital platform promoting behavioural change towards healthier habits focused on primary cancer prevention. Individuals from the experimental group will have access to the iBeChange platform for 12 weeks, used as a smartphone application.
Study Duration*:	8 months
Participant Duration:	12 weeks

2.2. Schema

The following schema (Figure 1) indicates the activities to be accomplished at each time point for the iBeChange pilot study.

Figure 1. iBeChange Pilot Study Flow Diagram



2.3. Schedule of activities

The schedule on the next page indicates the procedures that will be accomplished at each study time (Table 2).

Table 2. Schedule of activities for the iBeChange Pilot Study (next page)

	Pre-screening (Pre-consent)	**Screening** Day 0 In-person	**Time 1** Baseline Day 0	**Time 2** Post-intervention Day 90 ± 7
Phone call to review for eligibility and invitation to the study	X			
Informed Consent		X		
Demographics and contact information		X		
Randomisation		X		
Outcome Evaluation				
Primary - Feasibility outcomes: • Recruitment Capability and Resulting Sample Characteristics • Data Collection and Outcome Measures Answer Rate • Acceptability and Suitability of Intervention and Study Procedures • Resources and Ability to Manage and Implement the Study and Intervention	X	X	X	X
Secondary - Behavioural change and Psychosocial outcomes: • Seven-day point prevalence abstinence • Change in Smoking habits • Fagerström test for Nicotine Dependence (FTND) • Alcohol Use Disorders Identification Test (AUDIT)			X	X
Secondary - Behavioural change and Psychosocial outcomes (cont.): • iBeChange-Diet questionnaire on Cancer Nutritional factors • Height and Weight for BMI calculation			X	X

	Pre-screening (Pre-consent)	**Screening** Day 0 In-person	**Time 1** Baseline Day 0	**Time 2** Post-intervention Day 90 ± 7
• Global Physical Activity Questionnaire (GPAQ) • Perceived Stress Scale (PSS-4) • Patient Health Questionnaire (PHQ-4) • Perceived Social Support (F-SozU K-3)				
Secondary - Cost-effectiveness outcomes			X	X
Tertiary				
Voice analysis Informed Consent (optional)		X		
Wearable sub-study Informed Consent		X		
Wearable device delivery		X		
Wearable device return				X

3. Background

3.1. Study Rationale

Every year, 20 million citizens are diagnosed with cancer worldwide, a number that keeps increasing constantly.[1] Lung, colorectal and breast cancer are the three leading oncological diagnoses in terms of mortality, accounting for more than 40% of deaths, but also in terms of incidence, together with prostate cancer.[2]

Research has shown that certain risk factors increase a person's chances of developing a variety of cancers.[3] Such risk factors include those that cannot be controlled (e.g., age or family history), as well as those that could be modified, such as health behaviours and exposures to known environmental carcinogens.[4]

A recent study by Islami et al. (2018) estimated that 42% of all cancers diagnosed and 45% of all cancer deaths in the last years were attributable to modifiable behavioural factors, including tobacco use, alcohol consumption, unhealthy nutrition and obesity, and lack of physical activity.[5] Specifically, 90% of lung cancer cases, 55% of colorectal cancer cases, and 25% of breast cancer cases in Europe are related to modifiable factors, suggesting these diagnoses are, to some extent, preventable.[4]

The recent growing literature on modifiable cancer risk factors focuses on the interaction between health behaviours and psychosocial factors (e.g., depression, anxiety, recent loss events, social support, general distress), which could also be addressed.[6]

The process of intentionally altering a behaviour is known as behavioural change (BC). Behaviour change often has two primary objectives: starting or increasing healthy behaviours, such as exercising, or stopping or reducing unhealthy behaviours, like smoking. BC can involve setting goals, developing a plan of action, and tracking progress over time. Certain unhealthy behaviours such as smoking, drinking alcohol or eating junk food are often intertwined with emotional management (EM). EM is the ability to regulate one's emotions in response to different situations. Although BC and EM are distinct concepts, they strongly influence one another. For example, individuals experiencing anxiety may find it more challenging to quit drinking, as alcohol can provide short-term relief while ultimately increasing the risk of anxiety disorders.[7] Therefore, strengthening EM skills—such as coping strategies for anxiety—can significantly improve the likelihood of successfully adopting and maintaining healthier habits. Given the large number of cancer incidence and deaths worldwide caused by potentially modifiable behavioural, environmental, and psychosocial factors, widespread programs promoting BC and EM are necessary to reduce cancer incidence.

To improve the generally low accessibility of health care programs, delivering services depending on the person's needs could result in a sensible and compromised solution. Stepped-care interventions, designed to adjust to people's changing demands, enable to overcome the challenge of offering support with fewer health resources.[8,9] To do so, more and more digital platforms such as smartphone or web-based applications have been conceived to improve assessment and stepped intervention delivery.[10]

Digital health BC interventions are increasingly popular and widely accessible tools to foster and support BC for the maintenance and improvement of health.[11] Likewise, digital health (eHealth) interventions offer a promising and accessible option to promote mental health. Specifically, eHealth interventions for improving EM of healthy individuals through mindfulness and social support have shown effectiveness among psychologically distressed populations.[12]

Over the past few years, the field of mobile health (mHealth) has seen a rapid increase in the use of artificial intelligence (AI) to promote healthy behaviour change.[13] In particular, the integration of AI into mHealth interventions has shown great promise in facilitating the adoption of healthy lifestyle behaviours, such as regular physical activity, healthy eating habits, and tobacco or alcohol cessation. AI algorithms can be used to analyse data from an individual's behaviour, such as their activity levels and lifestyle habits, to develop personalised treatment plans that target their specific needs. Studies have demonstrated that mHealth interventions can be effective in promoting healthy behaviours by providing personalised feedback, reminders, and recommendations based on individual data. The AI component of the intervention has shown capacity to provide personalised feedback and suggestions for new lifestyle adoption (such as physical activity or promoting healthy eating habits)[14] tailored to each participant's individual needs and preferences, which likely contributed to the success of the intervention.[15] This can help individuals to better manage their mental health, improve their overall well-being and thus diminish their risk of cancer.

There is strong justification for developing an eHealth platform that monitors users' behaviours and delivers adaptive, automated recommendations to promote behavioural change. Additionally, the platform can offer targeted professional support, reserved as a higher intervention level for participants facing greater challenges in adopting healthier lifestyle habits. This structure pursues efficiency, leveraging to all users automatic personalised guidance and health advice, and allowing professionals to focus on cases that have not adhered or responded to this first level of care.

Moreover, digital platforms enable continuous monitoring of individuals' behaviour and health status. However, the key challenge lies in minimising intrusiveness to ensure ecological assessment, thus promoting user adoption. In this context, automatic voice analysis has been explored as a promising digital biomarker to detect emotional distress and depression. Anxiety and stress are often reflected in vocal tension and irregular prosody, characterised by a faster speech rate, higher pitch, greater pitch variability, and an increased presence of pauses and hesitation markers,[16] along with elevated fundamental frequency.[17,18] Depressive symptoms are typically associated with reduced speech expressivity, such as slower speech rate, lower pitch and increased pauses and hesitation.[19]

Altogether, the objective of this pilot study is to test the feasibility of delivering an accessible, usable, effective and efficient tool to the European population.

Additionally, wearable devices allow for the passive collection of a broad range of health indicators, including behavioural and psychosocial risk factors associated with cancer development. These technological tools provide a comprehensive, dynamic, and timely view of an individual’s physical and psychological state by measuring physiological data and seamlessly gathering information without disrupting daily routines.[20] Beyond enhancing data collection, wearable devices play a crucial role in promoting patient engagement and compliance, as many users find them empowering and effective in boosting self-awareness.[21] More importantly, they can support behavioural change and emotional management, which are key elements in the complex, multidisciplinary field of primary cancer prevention. Indeed, the continuous, timely data generated by these devices will not only strengthen the validity and reliability of our findings but, when integrated with traditional methods, can enable more accurate and less intrusive data gathering, monitoring, and potentially, in the future, the delivery of personalised interventions through the iBeChange platform.

Considering these advancements, a wearable sub-study has been included as part of this pilot study, involving a subsample of participants. The goal is to develop a passive and non-intrusive monitoring system that leverages wearable sensors to gather information about participants' health status, emotions, and lifestyle. This approach aims to enhance adherence and acceptance by potentially minimising the participants' burden in the future. Furthermore, the sub-study will assess the feasibility of integrating wearable devices to complement data already collected through questionnaires, allowing for more accurate detection and potential modification of risk factors. Ultimately, the sub-study will explore whether participants using wearables exhibit a higher degree of behavioural change and psychosocial adjustment compared to those not using these devices.

For this sub-study, smart rings will be used. Indeed, in recent years, the smart ring market has experienced significant growth due to increasing demand for discreet and non-invasive wearable devices. Smart rings represent an innovative category of wearables, standing out for their accuracy in biometric measurements, subtle design, and ease of use in daily life.[22,23] Compared to smartwatches, smart rings offer a crucial advantage for clinical studies: their compact size and minimal visibility enhance compatibility with participants' existing wearable devices while reducing the risk of study dropout by lowering the perceived intrusiveness.

Specifically, the Oura Ring[24] has been selected for this sub-study due to its unique combination of continuous health monitoring capabilities and user-friendly design. It offers cross-platform compatibility, connecting seamlessly with both iOS and Android devices, and includes an API that allows remote data access via an external app, as the one developed within the iBeChange project. The ring's availability in multiple sizes ensures a comfortable fit for a wide range of anatomical differences, accommodating most of the population. Additionally, its long battery life, lasting up to 8 days, supports uninterrupted data collection, minimising user inconvenience. Furthermore, the Oura Ring ensures robust data security and privacy by storing collected data on servers located in countries compliant with General Data Protection Regulations (GDPR). By choosing the Oura Ring, this sub-study aims to strike a balance between data accuracy and participant comfort, ultimately fostering higher adherence rates and maximising the reliability of the collected data.

3.2. Risk/Benefit Assessment

3.2.1. Known potential risks

Regarding known potential risks, this is a pilot study of minimum risk since administered questionnaires (behavioural and psychosocial factors) and the digital intervention do not have risk of complications. It must be considered that participants might feel triggered by some questions (for example, those related to emotional well-being). Also, the number of questions to be answered may overwhelm participants.

The wearable sub-study presents potential risks that must be carefully considered. In fact, participants may experience discomfort or irritation from wearing the device, although the availability of multiple sizes should minimise this risk. Moreover, some participants might feel increased anxiety or stress when confronted with health data, which could affect their emotional well-being. Finally, technical issues, such as connectivity problems or battery failures, may occasionally disrupt data collection.

3.2.2. Known potential benefits

Regarding known potential benefits, the participants will benefit from closer behavioural and psychosocial monitoring, along with professional support if needed, during the study.

Among the benefits of the wearable sub-study, the use of wearables like the Oura Ring allows for continuous and passive health monitoring,[25,26] providing real-time insights into participants' physiological and behavioural patterns. Additionally, the non-intrusive design of the Oura ring is expected to improve user compliance, contributing to more reliable data collection.

This will allow for the accuracy of health assessments, support the identification of risk factors, and potentially foster proactive behavioural changes by increasing participants' awareness of their risky health habits and health metrics.

4. Study Design

4.1. Study objectives and design

The main aim of this pilot study is to assess the **feasibility** and to obtain preliminary data on the **effectiveness of the iBeChange intervention** in achieving targeted behavioural change for primary cancer prevention. Preliminary data on the **cost-effectiveness** of the intervention in comparison to the standard practice recommendations will also be evaluated.

Participants will be randomly assigned to two different groups: the experimental group (EG), receiving a digital stepped-care intervention (i.e., iBeChange; iBC) and the control group (CG), receiving the usual practice recommendations (UPR). The experimental intervention will last 12 weeks. Outcomes will be obtained at baseline, and at the end of the intervention.

The overall study design is a Bayesian adaptive trial. It will use Bayesian methods to update intervention effect probabilities as data accumulate, allowing for trial modifications based on interim analyses.

The iBeChange intervention targets habits on five key health areas associated with behavioural and psychosocial factors that have been shown to increase or reduce cancer risk. These areas, referred to as **Health Pillars**, include:

- Smoking
- Alcohol consumption
- Nutrition and body weight
- Physical activity
- Emotional well-being (including stress, anxiety, depression, social support, and sleep)

As a result, the effectiveness outcomes of the study focus on changes in these health behaviours and psychological symptoms. Further details can be found in the following table and in Section 4.4: Effectiveness Data Collection.

4.2. Study endpoints

Table 3 summarises the primary, secondary and tertiary objectives and endpoints of this pilot study:

Table 3. Objectives and endpoints in the iBeChange Pilot Study (next page)

Objectives	Endpoints	Justification for endpoints	Collected measures
Primary			

Objectives	Endpoints	Justification for endpoints	Collected measures
To assess the **feasibility** of the iBeChange intervention[27]	• Recruitment Capability and Resulting Sample Characteristics • Refinement of Data Collection Procedures and Outcome Measures • Acceptability and Suitability of Intervention and Study Procedures • Resources and Ability to Manage and Implement the Study and Intervention	The main goal of this pilot study is to assess whether the conduction of a clinical trial is feasible, to then potentially improve the critical points with mitigation strategies, and to conduct a randomised controlled trial with a recruitment size ten times bigger.	• Recruitment number and rate per centre and in total • Completion of study questionnaires at baseline and after 12 weeks for measuring the intervention's effectiveness • Potential difficulties in the recruitment process • System Usability Scale to assess the usability of the platform and participants' feedback collection • Feedback from study personnel on workload and areas for improvement
Secondary			
To preliminary assess the effectiveness and cost-effectiveness of the intervention	• Preliminary Responses to Intervention	We hypothesise that the iBeChange intervention will be effective in achieving BC towards habits more compliant with cancer prevention guidelines. To preliminary assess its effectiveness, measures on behavioural change habits and emotional well-being symptoms will be obtained before and after the intervention in the control and experimental groups. We also hypothesise that this solution will be cost-effective compared to standard healthcare. With the data collected, the iBeChange platform can be improved and tested in a randomised controlled trial with a recruitment size ten times bigger.	*Behavioural change outcomes:* • **Smoking**: Seven-day point prevalence abstinence; Change in Smoking habits; Fagerström test for Nicotine Dependence (FTND) • **Alcohol**: Alcohol Use Disorders Identification Test (AUDIT) • **Nutrition**: iBeChange-Diet questionnaire on Cancer Nutritional factors; Height and Weight for BMI calculation • **Physical activity**: Global Physical Activity Questionnaire (GPAQ) *Emotional well-being outcomes:*

Objectives	Endpoints	Justification for endpoints	Collected measures
			• **Perceived Stress**: Perceived Stress Scale (PSS-4) • **Anxiety and Depressive symptoms**: Patient Health Questionnaire (PHQ-4) • **Perceived Social Support**: Perceived Social Support (F-SozU K-3) *Cost-effectiveness:* • **Cost-effectiveness** PECUNIA Resource Use Measurement (PECUNIA RUM) Instrument • **EQ-5D-5L Quality of Life**
Tertiary/Exploratory			
Voice analysis			
To assess the feasibility of using voice biomarkers to derive information about emotional distress	• Preliminary concurrent validity (accuracy of machine learning algorithm on voice signals to automatically classify emotional distress)	Achieving a high accuracy of machine learning algorithms is essential to confirm that voice signals can be used as valid biomarkers of emotional distress.	• Voice recordings (raw data) • Emotional distress thermometer
Wearable Sub-study			
To test the feasibility and suitability of wearables to complement psychosocial and behavioural features in a health intervention. To assess the correlation between wearable data	• Feasibility assessed through the completion rate of wearable data collection and the percentage of successful data transmissions without technical issues. The times a ring size is not available at site for a participant	Assessing data completion rates and successful transmissions demonstrates whether wearables can reliably collect and transfer data to support the intervention. Data from wearables logistics will allow to adjust ring size purchases and distribution among clinical sites. Investigating participant satisfaction and perceived	• **Physical activity:** number of steps; metabolic equivalent of task (MET) (1-minute intervals); average MET minutes (average MET level sustained throughout the day, factoring in all activities and rest periods); high activity MET minutes and High activity time; low activity MET minutes and low activity time; medium activity MET minutes and

Objectives	Endpoints	Justification for endpoints	Collected measures
and self-reported measures. To assess whether wearable data can improve the effectiveness of personalised recommendations delivered by the recommender system in the intervention in future settings. To compare user's adherence and usability of the system between participants in the wearable sub-study and those in the standard iBeChange group.	will also be registered • Suitability evaluated via participant-reported satisfaction and perceived ease of use of wearables, measured through post-intervention questionnaires. • Preliminary concurrent validity (correlation between wearable data with self-reported outcome measures in domains such as physical activity and psychosocial health). • Changes in primary and secondary outcomes between participants in the wearable sub-study and the standard iBeChange group to evaluate the preliminary impact of the use of wearables on the intervention. • Changes in satisfaction and adherence rates between participants in the wearable	ease of use helps determine if wearables are suitable for complementing the monitoring of psychosocial and behavioural health. Validating the correlation between wearable data and self-reported measures is essential to confirm that wearables can assess psychosocial and behavioural constructs. Comparing changes between groups helps evaluate whether wearables, by providing objective and timely data, can enhance the personalisation and effectiveness of the iBeChange intervention. Analysing usability and adherence reveals whether the use of wearables increases participant engagement, positively impacting their involvement in the intervention.	medium activity time; sedentary MET minutes and sedentary time; inactivity alerts; active calories (calories burned during physical activity); total calories (total number of calories burned during the day) • **Psychosocial health:** ○ **Sleep data:** heart rate; heart rate variability; latency (time it takes to fall asleep from the moment the subject gets into bed); temperature deviation; restless period; average breath; efficiency (ratio of time actually spent sleeping to the total time spent in bed); sleep score; light, deep and REM sleep time; readiness score (body's recovery status and physical preparedness); start-end bed time. ○ **Stress Resilience:** daytime stress (in terms of heart rate, heart rate variability, motion and temperature throughout the day). • **Satisfaction and usability of smart ring use**

Objectives	Endpoints	Justification for endpoints	Collected measures
	sub-study and those in the standard iBeChange group.		

4.3. Demographic data collection

At baseline, socio-demographic data will be collected from participants at the initial in-person interview. The collected variables will be:

- Age
- Gender
- Sex
- City of origin
- City of residence (to know urbanisation and migration)
- Formal Education Level
- Employment/occupation status
- Digital literacy and Digital Health literacy[28]
- Height
- Weight

4.4. Effectiveness data collection

Effectiveness measurement time points will be at baseline and after 12 weeks.

Among secondary outcome measures to assess the iBeChange intervention effectiveness compared to the control group (described in Table 3), one main secondary measure has been selected per health habit or psychosocial measure according to those behaviours or symptoms with most evidence of cancer risk. These are the following:

- Smoking: Number of smoked cigarettes per day
- Body Weight: Body mass index calculation
- Alcohol: Weekly alcohol consumption
- Nutrition: Intake of processed food and red meat per week
- Physical activity: Minutes of moderate to vigorous physical activity per week
- Psychosocial: PSS-4 score for perceived stress.

4.4.1. iBeChange questionnaire on Cancer Nutritional factors

After a thorough literature review, there were some extensively used nutrition questionnaires assessing for adherence to the Mediterranean diet. However, this is not the scope of this pilot study: we aim to specifically assess the nutritional groups associated with increased or decreased risk of cancer. No validated scale assessing these specific constructs was found. Therefore, the iBeChange consortium is developing an iBeChange questionnaire on Cancer Nutritional factors. Questions will be selected and validated through experts' panels in an iterative manner. A paper-

format protocol detailing the development and validation of the scale will be attached to this pilot protocol submission for IRB approval.

4.5. Cost-effectiveness data collection

Cost-effectiveness measurement time points for the pilot study will be at baseline and after 12 weeks.

To evaluate the cost-effectiveness, variables such as household income, living situation, healthcare costs, medication, and diagnostic tests will be asked from participants. Sections B, C, H, D and F from the modular PECUNIA Resource Use Measurement (PECUNIA RUM) were selected to assess the cost-effectiveness of the iBeChange intervention compared to standard clinical practice. These target the following areas:

- **Section B**: Non-residential health and social care (7-13 items)
- **Section C**: Medication (2 items)
- **Section H**: Out-of-pocket and other expenses (4 items)
- **Section D**: Unpaid help (informal care) (1 item)
- **Section F**: Employment and productivity (1-5 items).

Additionally, the EQ-5D-5L questionnaire will assess quality of life at the same time points.

4.6. Wearable data collection

Through the Oura ring device, data related to Physical activity and psychosocial health will be collected. The specific variables collected per each group are the following:

Physical activity: number of steps; metabolic equivalent of the task (MET) (1-minute intervals); average MET minutes (average MET level sustained throughout the day, factoring in all activities and rest periods); high activity MET minutes and High activity time; low activity MET minutes and low activity time; medium activity MET minutes and medium activity time; sedentary MET minutes and sedentary time; inactivity alerts; active calories (calories burned during physical activity); total calories (total number of calories burned during the day).

Psychosocial health:

Sleep data: heart rate; heart rate variability; latency (time it takes to fall asleep from the moment the subject gets into bed); temperature deviation; restless period; average breath; efficiency (ratio of time actually spent sleeping to the total time spent in bed); sleep score; light, deep and REM sleep time; readiness score (body's recovery status and physical preparedness); start-end bed time.

Stress Resilience: daytime stress (in terms of heart rate, heart rate variability, motion and temperature throughout the day)

4.7. Future usability and human-computer interaction studies

Besides the satisfaction and usability measures collected in this pilot study of the use of the iBeChange app and of the Oura smart rings, additional studies will be conducted at the University of Palermo (UNIPA) to further investigate the acceptance, usability, and human-computer

interaction of the iBeChange mobile application. Each of these will be the subject of a dedicated research protocol to be submitted for approval to UNIPA's Institutional Review Board.

These studies will aim to provide deeper insights into user experience and engagement with the app and the wearable devices. They will focus on assessing the usability and acceptance of the application, human-machine interaction, including engagement and potential challenges in user interaction with the system. Both studies will examine key features such as integration with wearable devices and the voice recording function.

The UNIPA team, in collaboration with other partners within the iBeChange consortium, will define the objectives, methodologies, and procedures for both studies. Each study will involve a sample of at least 20-25 users, selected according to inclusion criteria similar to those established for the pilot study and the RCT. Participants will use the application for several weeks, during which their interactions with the system will be monitored. All participants recruited in these studies will be assigned an Oura ring for data collection.

At the end of the study periods, a mixed-methods approach will be employed to assess user experience. This will include semi-structured interviews or focus groups, self-report measures, and behavioural analysis tools such as eye tracking. By combining qualitative and quantitative data, these studies will provide a comprehensive understanding of usage patterns and the effectiveness of different app features.

5. Study Population

5.1. Inclusion and Exclusion criteria

Table 4. Inclusion and Exclusion criteria for the iBeChange Pilot Study

Inclusion criteria	✓ IC1. Ability to understand and voluntarily provide signed written informed consent approved by the study site's Institutional Review Board (IRB). ✓ IC2. Being at a high-risk age for breast (women between 45-70), colorectal (individuals between 50-70) or lung cancer (individuals aged 50-80 years). ✓ IC3. Having participated in a test for early detection of cancer (i.e., mammography or ultrasound for breast cancer, faecal occult blood test (FOBT) or colonoscopy for colorectal cancer, and CT-scan for lung cancer).
Exclusion criteria	- EC1. History of any prior or current personal cancer diagnosis. In the case of colorectal and breast cancer, this will be restricted to the pathology tested for screening. - EC2. Current severe disease that may significantly compromise the performance on the study according to the criteria of the investigator. - EC3. Not owning a smartphone. - EC4. For breast and colorectal cancer, participants undergoing screening for alert symptoms or family history of these cancer types (the latest are eligible for specific hereditary cancer programs).

Regarding EC2, the term "severe disease" is broadly defined to include conditions that would prevent participants from fully engaging in the study's activities. The criteria remain intentionally broad to allow flexibility in assessing potential participants. Specific examples may be refined as cases arise during the pilot study. Examples of excluded conditions:

Physical disabilities such as blindness or deafness, particularly in cases where the technology (e.g., mobile applications) is not adapted for these impairments, are examples of conditions that would prevent participation.

Participants with severe mental illness or cognitive impairments that hinder their ability to understand and navigate the app will be excluded from the study. Severe mental illness will not automatically lead to exclusion; instead, such cases will be referred to general practitioners for appropriate care.

As for EC3, there is no feasible solution for providing smartphones to those without them due to logistical and financial constraints. Past studies attempted to loan devices, but it was not possible in this case.

Even though it may be challenging to address this issue in the current study, the team acknowledges it as a limitation. The percentage of excluded people is expected to decrease by the time the study is completed, but it remains an unavoidable problem.

Wearable sub-study

Participants to be enrolled in the wearable sub-study must fulfil the following additional criteria detailed in Table 5.

Table 5. Inclusion and Exclusion criteria for the iBeChange Wearable Sub-study

Inclusion criteria	✓ ICW1. Ability to understand and voluntarily provide signed written informed consent for the wearable sub-study approved by the study site's Institutional Review Board (IRB). ✓ ICW2. Being allocated by randomisation in the Experimental group of the iBeChange pilot study.
Exclusion criteria	- ECW1. History of any prior or current skin problems, such as allergic skin reactions, active eczema, or contagious skin conditions personal cancer diagnosis (restricted to the pathology tested for screening). - ECW2. Known allergies or previous reaction to titanium or medical-grade plastic.

5.2. Strategies for recruitment and retention

Three recruitment centres are participating in iBeChange. These are:

Table 6. Recruitment centres: characteristics and expected recruitment size for the iBeChange Pilot Study

Centre	City, Country	Ownership	Funding Type	Type of entity	N per cancer type (expected)
Institut Català d'Oncologia (**ICO**)	Hospitalet del Llobregat, Spain	Public	Catalan Health Service (CatSalut)	Hospital and comprehensive cancer centre integrated into the Catalan public health system	Breast = 20 Colorectal = 40
Istituto Europeo di Oncologia (**IEO**)	Milano, Italy	Private, Non-Profit	Private funding, with agreements for public healthcare services	Hospital and comprehensive cancer centre that collaborates with the Italian National Health Service for some publicly funded treatments	Lung = 10 Breast = 50
University of Medicine and Pharmacy Carol Davila (**UMFCD**)	Bucuresti, Romania	Public	Publicly funded as a state university hospital	General hospital ascribed to public university receiving funding through the Romanian Ministry of Education and Ministry of Health	Breast = 20 Colorectal = 40

Given their different nature, the recruitment strategy will be slightly different in each recruitment centre:

ICO, Spain (breast and colorectal)

Breast cancer:

Participants at ICO are recruited through the breast cancer screening program. Through a postal letter, women at **50-70** years old are invited to the program. Only those women attending a mammography test at ICO's radiology service are suitable for participation. Mammography technicians provide a brochure with a Quick Response (QR) code/phone to contact to chat.

Participants access a webpage with basic study information, where they can either directly contact the study personnel or provide their contact details and consent to be contacted. If they agree, participants will be contacted by telephone by a researcher to provide more information. If inclusion/exclusion criteria and willingness to participate are confirmed, then an in-person appointment for ICF signature is scheduled.

Colorectal cancer:

Participants at ICO are recruited through the colorectal cancer screening program. Through a postal letter, individuals at **50-70** years old are invited to the program. Only those individuals returning a faecal occult blood test (FOBT) sample to the pharmacies are suitable for participation. Pharmacies' personnel provide a brochure with a QR code/phone to contact to chat.

Participants access a webpage with basic study information, where they can either directly contact the study personnel or provide their contact details and consent to be contacted. If they agree, participants will be contacted by telephone by a researcher to provide more information. If inclusion/exclusion criteria and willingness to participate are confirmed, then an in-person appointment for ICF signature is scheduled.

IEO, Italy (breast and lung):

Breast cancer:

At IEO, women **aged 45-69** years old can participate in breast cancer screening by voluntarily booking, both privately and via national health care system. They are contacted by phone call to be introduced to the iBeChange study.

Interested people will receive via email an informative brochure with a study overview and a link directing to the project's website.

Signed informed consent will be collected at the cancer screening test appointment.

Lung cancer:

At IEO, individuals **aged 50-80** years with no clear signs of lung cancer (e.g., worsening cough, haemoptysis, unexplained weight loss) who are current smokers or former smokers that quit less than 15 years ago are eligible to participate in lung cancer screening by voluntarily booking if they have smoked at least (a) 10 cigarettes per day for 30 years, (b) 15 cigarettes per day for 25 years, or (c) 20 cigarettes per day for 20 years (> 20 packs/year). Individuals with history of cancer in the past 5 years are excluded. Since lung cancer screening is not usually available at IEO and is not offered by the Italian health care system, an *ad hoc* lung cancer screening program will be organised and promoted for this pilot study. Eligible participants will be able to access the screening with no additional costs. They are contacted by phone call to be introduced to the iBeChange study.

Interested people will receive via email an informative brochure with a study overview and a link directing to the project's website.

Signed informed consent will be collected at the cancer screening test appointment.

UMFCD, Romania (breast and colorectal):

Breast cancer:

Participants at UMFCD are recruited through general practitioners (GPs). At a GP visit, if inclusion/exclusion criteria and willingness to participate are confirmed, women **50-70** years old can be sent for screening in specialised centres (external, different centres, public or private). Only those women attending a mammography or an ultrasound test are suitable for participation. If inclusion/exclusion criteria and willingness to participate are confirmed, an in-person appointment for ICF signature is scheduled.

Colorectal cancer:

Participants at UMFCD are recruited through general practitioners (GPs). At a GP visit, if inclusion/exclusion criteria and willingness to participate are confirmed, individuals **50-70** years old can be sent for screening in specialised centres (external, different centres, public or private). Only those individuals attending a FOBT or a colonoscopy are suitable for participation. If inclusion/exclusion criteria and willingness to participate are confirmed, an in-person appointment for ICF signature is scheduled.

Common:

After ICF signature, participants are centrally randomised through REDCap,[29] and, if assigned to the experimental group (EG), the iBeChange app is downloaded together with a step-by-step demonstration on its functionalities by the researcher.

If assigned to the iBeChange group, the participant is asked for their willingness to use the study wearable. If yes, a specific ICF for wearables is signed and the participant is randomised to receive or not the wearable. If assigned to the wearable sub-group, and the needed size is available, the Oura smart ring is delivered (EGw).

The step-by-step demonstration of iBeChange will be detailed in a standardised protocol for welcoming and introducing the app to participants across all centres, considering age and other factors.

For enrolled participants of all groups, questionnaires will be sent by email through the REDCap platform. These will include demographic variables as well as questionnaires for assessing primary and secondary outcomes. These questionnaires are designed for the participant to answer at home, not in the recruitment centre.

Intervention for the iBeChange participants will start as soon as they provide enough information in the app for it to recommend a health pillar and deliver personalised interventions. For further details, please visit section 6.2.

Participants will also be asked for optional consent of voice recordings to analyse potential vocal stress markers. This will be registered and the option to record within the iBeChange app will only be displayed to those participants in the experimental group that have consented.

Regarding wearables, the ICF signature appointment and the introduction to the iBeChange app will also be used to deliver the device. The consumer-grade Oura ring has been selected. A stock of devices will be available at each recruitment centre. An Oura ring of the participant's size will be delivered and connected to the participant's iBeChange app account.

In case the needed size is not available at one centre, it will be requested at the other sites, and that participant will be excluded from the wearable sub-study so as not to delay the start of the intervention delivery.

5.3. Strategies to avoid missing data and increase adherence

To reduce missing data, the pilot study has been designed to minimise the number of questions, avoiding participants feeling overwhelmed, which could lead to incomplete responses.

Within the app, certain responses will be required for participants to progress to the next steps or level up. While this approach is intended to increase engagement, some missing data may still occur. Additionally, phone call or email follow-ups have been considered for non-responders; however, challenges may persist, as this study targets a preventive population rather than patients, and might be less motivated to engage.

The pilot study will serve as a test for retention and adherence. Based on its findings, adjustments and mitigation strategies will be designed and implemented for the subsequent randomised controlled trial (RCT) to optimise participation and data completeness.

6. Study intervention(s) or experimental manipulation(s)

6.1. Control group (CG) intervention

The control intervention consists of receiving an **informative leaflet** with a **summary of the clinical recommendations for cancer prevention**.

This document already exists in the ICO cancer screening program and will be adapted to Italian and Romanian for use in IEO and UMFCD, respectively. An English version can be found in Annex 10.1. To standardise this intervention, the translated informative leaflet will be delivered to control participants at each centre in their national language after randomisation.

6.2. Experimental group (EG) intervention: iBeChange platform

Participants allocated to the experimental group will have access to the **iBeChange platform**. This stepped-care app **provides personalised recommendations to promote behavioural change** according to participants' habits and needs.

In the beginning, participants will be asked for their **habits** regarding **Smoking, Alcohol consumption, Nutrition, and Physical activity,** and also for their Emotional well-being status, including **Perceived Stress, Anxiety and Depressive symptoms, Perceived Social support**, and **Insomnia** (Step 1). This health habit assessment will be transformed into scores according to compliance with clinical guidelines for cancer prevention (Health Habit Scores [HHS]) and displayed to the user. (Figure 2).

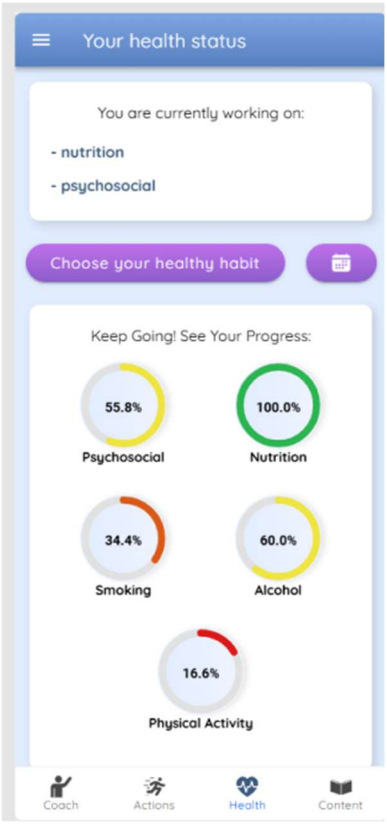
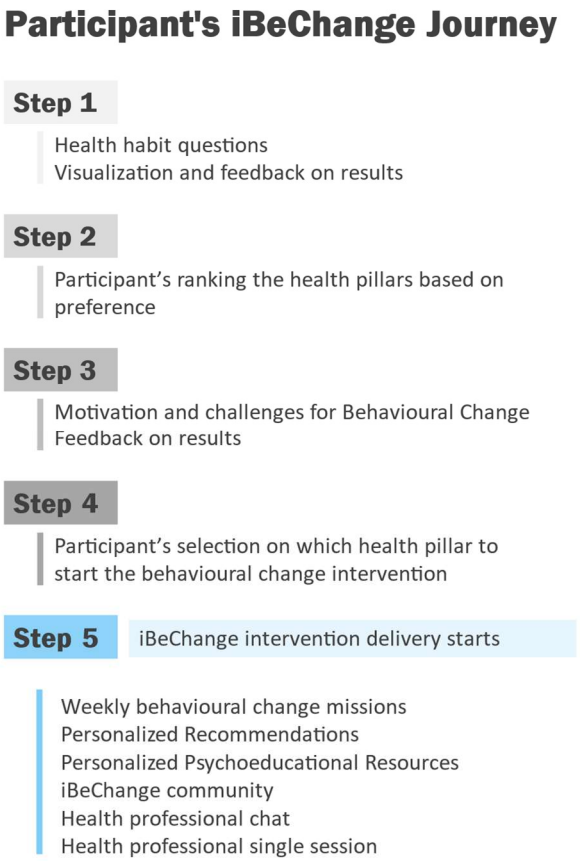


Figure 2. Participant's health habit status visualisation in the iBeChange platform

According to the participant's health habits, emotional status, and preferences (Step 2), further questions are administered to understand the motivational status of change and the main barrier/promoters of the target behaviours. This was designed based on **behavioural change models** such as the Health Action Process Approach (HAPA)[30] and the Capability-Opportunity-Motivation – Behaviour (COM-B) models[31,32] (Step 3).

Considering all previously gathered information and the participant's choice of the habit to start working on (Step 4), 12 weeks of stepped care tailored intervention will start (Step 5). It will be structured with **weekly Missions** – specific and measurable behaviours to be performed and monitored in one week. By achieving the weekly mission, the participant's habits will be closer to clinical recommendation guidelines for cancer prevention. For a personalised intervention, the iBeChange platform relies on a Recommender system based on Reinforcement learning, which will collect participant's interactions and accomplishments in the app to fine-tune which and when recommendations and resources are delivered (**Figure 3**).

Figure 3. Participant's journey in the iBeChange platform



6.2.1. Intervention levels

The stepped care intervention will contain the following intervention levels:

- **Level 0**: In this intervention level, **automatic** recommendations and resources will be delivered to support the achievement of the weekly missions. Among these, the possibility to enter a group chat for social support among participants named iBeChange community can also be assigned.

Once every 4 weeks, the full health habit assessment (for more detail, refer to section 6.2. on the page before) will be administered (at baseline, 4 weeks, and 8 weeks).

In addition to the weekly mission monitoring, the emotional distress thermometer in the visual analogue scale (0-10) form will be assessed every 2 weeks. In case the answer > 5, PSS-4 and PHQ-4 will be administered to detect stress, anxiety or depression levels. If any of these are moderate or high, participants will be escalated to Level 1.

If the participant agrees to voice recording, after the emotional distress thermometer assessment, the question "How stressed do you feel right now?" will be displayed asking users to speak and record the answer.

- **Level 1**: In this intervention level, participants will be able to contact a **healthcare professional via chat** to solve doubts about their behavioural change strategy or emotional well-being status. This interaction will be initiated by the participant.

- **Level 2**: Participants in this level will receive a **single-session healthcare professional intervention.** This will be a **one-hour online** session with a motivational interview structure, in which the participant's needs and potential barriers for behavioural change will be addressed.

Techniques and interventions with effective evidence will be administered according to the participant's symptom or situation.

To standardise intervention Level 2, a detailed professional single-session protocol has been developed. After the session, professionals will register the techniques used for proper monitoring of the intervention.

- **Level 3**: For those participants whose healthcare needs exceed the reach of iBeChange, a referral to specialised services will be required. This is the case when severe mental health problems or psychological emergencies are suspected. Participants receiving Level 3 intervention will be categorised as **high-risk** users. The time points and criteria for intervention level escalation of participants are summarised in the following table for each health pillar. Criteria for escalation to Level 3 are further detailed in Annex 10.2.

The criteria for escalation to Level 1, Level 2 and Level 3 for the different health pillars is described in Table 7 below.

Table 7. Criteria for intervention escalation to Level 1, Level 2 and Level 3 in the iBeChange platform for each health pillar

	Criteria for intervention escalation to:		
	Level 1 Chat with professional	**Level 2** Professional single-session intervention (SSI)	**Level 3** Referral to specialised services
Smoking	*Weekly:* If not achieving the weekly mission for **3 attempts** *At month 1 and at month 2:* If the participant increases **2 points or more** in the Smoking health habit score (HHS).	*After Level 1:* If not achieving the weekly mission after **3 attempts** *At month 2:* If the participant increases **2 points or more** in the Smoking health habit score (HHS).	*After scheduling* SSI, if participants do not attend to one SSI and do not accomplish a mission for two consecutive weeks. *At SSI,* if a major mental health problem that hinders smoking cessation is suspected.
Alcohol	*Weekly:* If not achieving the weekly mission for **3 attempts** *At month 1 and at month 2:* If the participant decreases **2 points or more** in the Alcohol health habit score (HHS).	*After Level 1:* If not achieving the weekly mission after 3 weeks *At month 2:* If the participant decreases **2 points or more** in the Alcohol consumption health habit score (HHS).	*After scheduling* SSI, if participants do not attend to one SSI and do not accomplish a mission for two consecutive weeks. *At SSI,* if a major mental health problem that might hinder alcohol consumption cessation is suspected.

Nutrition	*Weekly:* If not achieving the weekly mission after **3 attempts** *At month 1 and at month 2:* If the participant drops **2 points or more** in the Nutrition health habit score (HHS).	*After Level 1:* If not adherent to missions for 3 weeks *At month 2:* If the participant drops 2 points or more in the Nutrition HHS.	If partially or non-compliant HHS and BMI <18.5 or ≥40 kg/m^2.
Physical activity	*Weekly:* If not achieving the weekly mission for **3 attempts** *At month 1 and at month 2:* If the participant drops by **100 METs** in the Physical Activity health habit score (HHS).	*After Level 1:* If not achieving the weekly mission after 3 weeks *At month 2:* If the participant drops by **100 METs** or more in the Physical Activity health habit score (HHS).	*After scheduling* SSI, if participants do not attend to one SSI and do not accomplish a mission for two consecutive weeks. *At SSI,* if a major mental health problem or other potentially impairing aspect that might hinder physical activity is suspected.
Emotional Well-being	*At baseline:* If acting on Stress, Anxiety and Depression but still presenting symptoms *Weekly:* Not achieving the weekly mission	*At month 1 and at month 2:* If adherent to missions but shows no improvement in PSS-4 and PHQ-4.	*At SSI,* if a full major mental health problem is suspected, according to the developed List of Standardized criteria (Annex 10.2).

6.3. Experimental sub-group intervention: Wearable Sub-study (EGw)

Participants randomised to the experimental group will be offered the opportunity to join the wearable sub-sample until the required sample size is reached in each clinical centre. If participants agree, and after specific ICF signature, a second randomisation will take place to determine whether they are assigned to the wearable sub-sample or not. Participants assigned to the wearable sub-sample will be provided with an **Oura ring** of their size, and additional data will be collected from these participants.

A potential issue is that, despite purchasing ring sizes based on the most likely gender- and age-specific measurements of the recruited sample, there may still be instances where suitable sizes are not available for participants willing to join this subsample and assigned to the wearable sub-group. To address the potential unavailability of ring sizes for participants assigned to the wearable sub-group, several measures will be implemented. Firstly, the extra rings will be centrally stored at one clinical centre (i.e., IEO), enabling redistribution to other centres if needed. However, fingers other than the index finger may be used without compromising data collection. Furthermore, if a suitable ring size is unavailable for a participant, the enrolment can proceed with the next eligible participant included in the iBeChange intervention group if willing to and randomised to the wearable sub-group. Lastly, if one centre completes recruitment ahead of others, any surplus rings will be reallocated to centres still actively recruiting participants.

The study will provide clear instructions for device use, offer technical support if needed, and ensure participants are fully informed about data security measures by signing a specific informed consent form. In this pilot study, participants will be able to access the Oura ring app, where the visual progress tracking will be available. This can significantly enhance participant engagement and minimise the risk of non-adherence.

Participants will be enrolled across all three clinical centres involved in the pilot study (i.e., ICO, IEO, and UMFCD). 33% of the intervention group will receive a wearable device, corresponding to approximately 30 participants across all centres (180 participants is the total recruitment of the pilot study, 60 participants per centre).

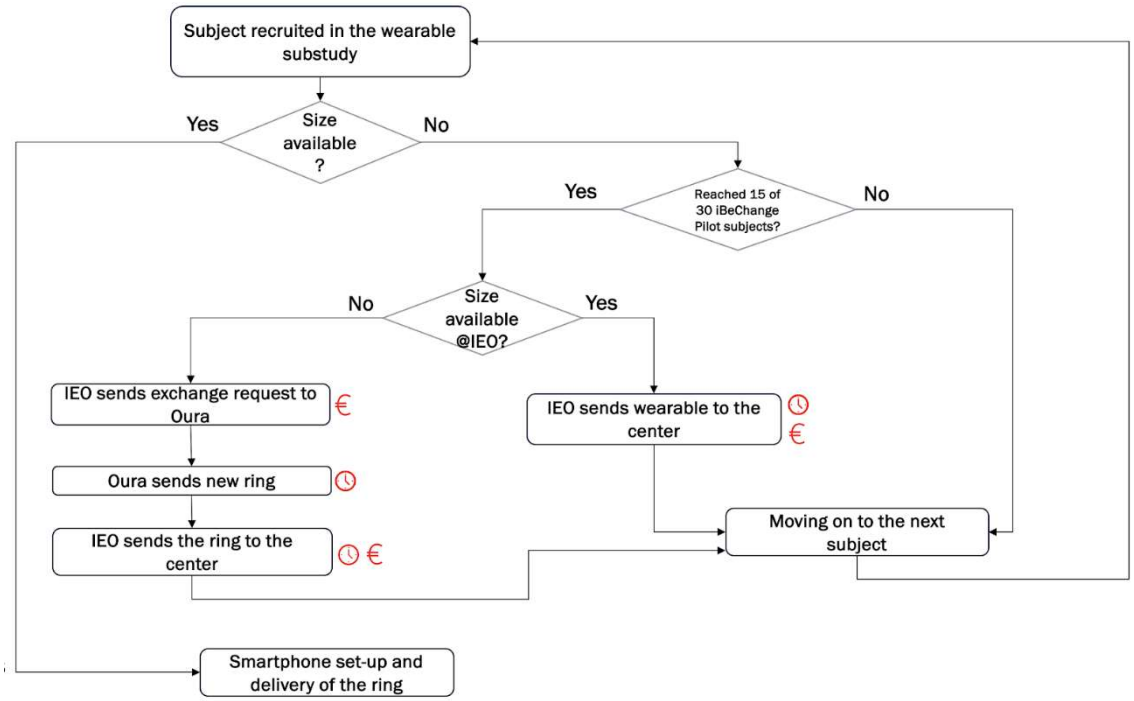
Based on the cancer screening type distribution observed in the pilot study, it is estimated that each clinical centre will have 10 participants with wearable devices, distributed as follows:

Table 8. Estimated recruitment per cancer screening type and clinical centre for the wearable sub-study

Cancer screening type	ICO	IEO	UMFCD
Breast *(females)*	7	8	7
Lung *(males/females)*	-	2	-
Colorectal *(males/females)*	3	-	3
TOTAL	10	10	10

If the ring is not available at the time of recruitment, the following workflow (**Figure 4**) will outline how the situation will be managed. The euro symbol means additional costs will be needed; the clock symbol means additional time, which results in the participants receiving the ring at a later stage.

Figure 4. Logistics workflow for wearable assignment depending on recruitment status and size availability



The intervention for participants assigned to the wearable sub-sample will be the same as in the experimental group, consisting of the behavioural change intervention through the iBeChange platform. Additionally, the Oura Ring will enable continuous and passive health monitoring, allowing accurate health assessments and, at future stages, potential support of the identification of risk factors and their targeting (adjusting the intervention if needed), and potentially encourage proactive behavioural changes by increasing participants' awareness of their health metrics.

6.4. Intervention training and supervision

To ensure standardised intervention across recruitment centres and healthcare professionals for the pilot study, the professional intervention has been written in a specific protocol. Summarised documents with key information will be prepared for health care professionals to review in case of doubt. Moreover, specific training sessions will be scheduled to properly prepare and kick off this multicentre pilot study, reviewing recruitment, platform use, and intervention.

This pilot study will be coordinated by ICO team as the main responsible partner of clinical studies within the iBeChange consortium. Supervision of the pilot study will be ensured by regular meetings of a Trial Supervision Committee (TSC) and through the REDCap Platform. TSC includes partners from all recruitment centres, the technical leaders of the app development (i.e., Eurecat) and statistical partners (i.e., SporeData) of the consortium.

The TSC will meet regularly and according to Pilot timings to review its key aspects: recruitment, allocation, participant retention, data collection, discussion of controversial cases, protocol deviations, and technical issues, if needed.

6.5. Measures to minimise bias: randomisation and blinding

Participants will be randomised into either the control or the iBeChange group, with stratification based on recruitment centre and cancer screening type.

For those in the iBeChange group, participation in the wearable sub-study will be optional. To prevent selection bias, participants who opt in will undergo a second randomisation to determine whether they receive the wearable device or not.

Due to the nature of the intervention—where only the experimental group receives a digital behavioural change program—blinding is not feasible in this pilot study. However, to minimise bias in outcome assessment, all evaluations will be conducted remotely, ensuring that responses from participants in both groups are collected without direct influence from healthcare professionals.

7. Data Flow, management and protection

7.1. Description of Data Processing

This pilot study involves data collection through online questionnaires, via the iBeChange app, and with the use of wearable devices. This section addresses both the Pilot Study and anticipated RCT data flow requirements.

The data will be collected directly from participants in the form of questionnaire response data via REDCap forms. Data will also be collected from recruitment centres, including demographic data. The data items will be held within the REDCap platform hosted by ICO and to be used by all three clinical centres, and within the iBeChange app under development by SIMAVI and Eurecat (technical partners associated within the iBeChange European project consortium). Data collected from participants through the iBeChange app consists of questionnaires and voice recordings (raw data). These data will be collected during the periodic feedback that they will be invited to give, as outlined in Section 7.2 and Section 6. The voice raw data will be stored on Eurecat's server only for participants who provided their consent and managed in compliance with GDPR regulations to ensure data security. Wearable data will be collected through the Oura ring app in participants enrolled in the Wearable sub-study.

Data within the iBeChange platform will be accessed by technical teams within the consortium for the purposes of developing the platform and user interface, assessing and analysing the data for model generation and algorithm training, as well as the impacts and outcomes of the system. Data will be pseudonymised for access by the technical partners. Data will not be shared outside of the platform and REDCap server except for any analysis data used for publication. Access to data may be required by journal editors for results verification but will be limited strictly to what is necessary for their review and will not likely require access to identifiable data for this purpose.

The data collected through the Oura Ring will be stored on Oura's servers, located in Finland (EU), and managed in compliance with GDPR regulations to ensure data security. Data transfer will be explicitly agreed by the participants both in the informed consent and within the app.

Data collected through the Oura Ring will be retrieved from Oura server by using the Oura API and sent to iBeChange server managed by Eurecat. After wearable data have been stored in the iBeChange server, technical partners could access them to (1) compute meaningful indicators from time series (Politecnico di Milano) that will be stored in the iBeChange server, (2) incorporate them in the recommender system (Politecnico di Milano, Eindhoven University of Technology) in order to optimise the timing for sending recommendations.

The aggregated results of the analysis will be available to the Recruitment Centres and to SporeData, the statistical partner of the Consortium, for performing statistical analysis.

Data for the studies will be stored for at least 5 years for archiving purposes in line with regulatory requirements after the end of the pilot study and RCTs. The precise retention periods will be determined by the local jurisdiction's requirements in Italy, Romania and Spain in line with the recruitment centres' national regulations. This will be specified in the Joint Controller Agreement. Data will also be archived and retained under the same terms in the event that a participant withdraws from the Pilot Study or RCT. At the point of withdrawal, the data will be archived, and no further research will be conducted with it and it will be retained in line with national requirements as outlined earlier in this paragraph.

7.2. Data Processing Particulars and Data Flow Diagrams

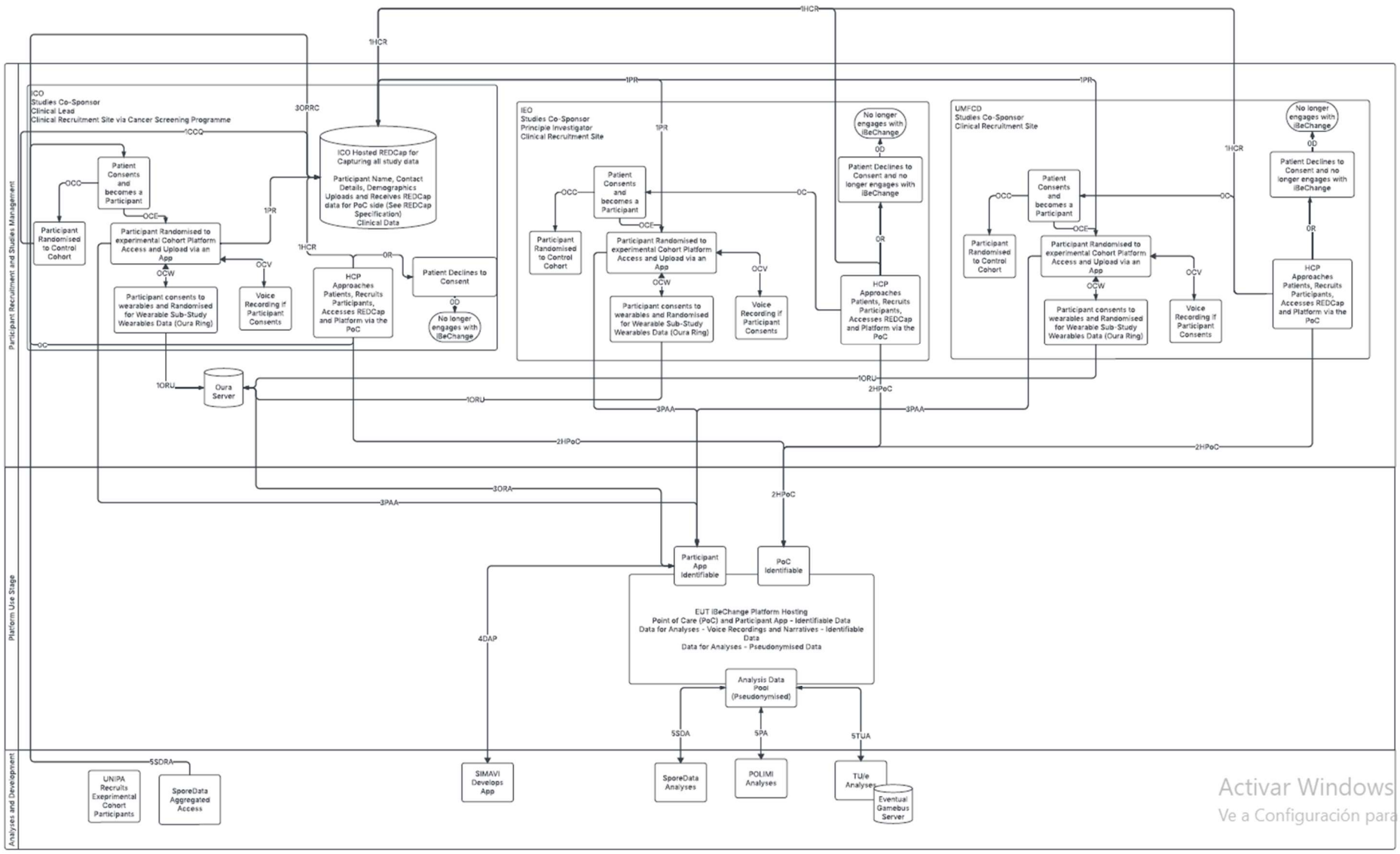
7.2.1. Participant Recruitment and Studies Management Stage

Please refer to Figure 5 below. The starting point for the data flows is contained within the Participant Recruitment and Study Management Phase and commences when the Health Care Professional (HCP) at each of the recruitment centres (ICO, IEO and UMFCD) approaches a patient during routine care/cancer screening and asks whether they would like to Participate in the iBeChange Study. The Patient will either consent as per steps 0C or decline as per steps 0D. On declining, that patient will no longer engage with iBeChange. Note that the steps listed in this section refer to each of the participating centres (ICO, IEO and UMFCD).

On consenting, the patient will become a Participant and will be randomised to be part of the Control Group at steps OCC or the Experimental Group at steps OCE. If randomised to the Experimental Group, Participants will be asked if they agree to being part of the wearables study, at which point they will be further randomised under steps 0CW to see if they form part of the Wearables sub-study. At steps 0CV, participants will also be asked if they consent to doing voice recordings for the voice recordings analysis and have the risks involved with this explained to them as part of the consenting process. These steps are also represented in the iBeChange pilot study diagram in Figure 1.

Their HCP will register each participant under the steps 1HCR according to the Group they are randomised to and whether they will form part of the Wearables sub-study and whether they have consented to voice analysis. The information will be gathered locally via the REDCap System available at each site and hosted by ICO as per steps 1HCR. The REDCap system has several functions where one is for HCPs to complete information entry.

Figure 5. Data Flow Diagram: Data processing for the iBeChange pilot study (next page)



REDCap will also manage study data and identifiable participant data and will also randomise participants. REDCap will also manage participant questionnaire responses which the participants in both control and experimental Groups will use. The data collected will be as per the REDCap Specification available in the iBeChange_variables_REDCap_20Mar25.doc. At the point of recruitment, a file will be opened on REDCap for each participant and a Study ID will be assigned (acting as the project PseudoID). Participants in the Control Group will fill out questionnaires at the outset and at 12 weeks into the pilot study (end of the intervention) as per steps 1CCQ. The Experimental Group will be asked to also complete questionnaires at the start and at the end of the study (additionally assessing satisfaction and usability of platform and smart rings use) as per steps 1PR.

If a Participant has been registered in the Wearables sub-study they will need to register for an Oura Ring Account on the Oura Servers that are not controlled by any iBeChange Partner as per steps 1ORU. This will be an arrangement between the participant and Oura directly, where Oura will be a controller of Personal Data in their own right as per their service agreement with the Participant. This will be explained to the Participants when approached to indicate their willingness to join the Wearables sub-study. Data will include a Username, an email account, and a Password, plus the processing of the wearables data as outlined in this protocol's section 3.6.

7.2.2. Platform Use Stage

As the pilot study continues, the Platform Use Stage commences with the HCPs at each site updating data on the PoC tool hosted by Eurecat on the Platform as per the steps 2HP0C. This involves registering the Participant on the PoC tool. It should be noted that at this stage, data will be identifiable, especially if voice recordings are uploaded via the iBeChange app. The data is collected and transferred to the Eurecat Platform in a Pseudonymised form using the Study ID assigned to each participant, with all identifiers taken out of the records submitted from REDCap, as per Step 2HPoC in the DFD. For the Pilot Study, this will be done manually from REDCap by the HCPs at each site, but the aim is to do this automatically for the RCT.

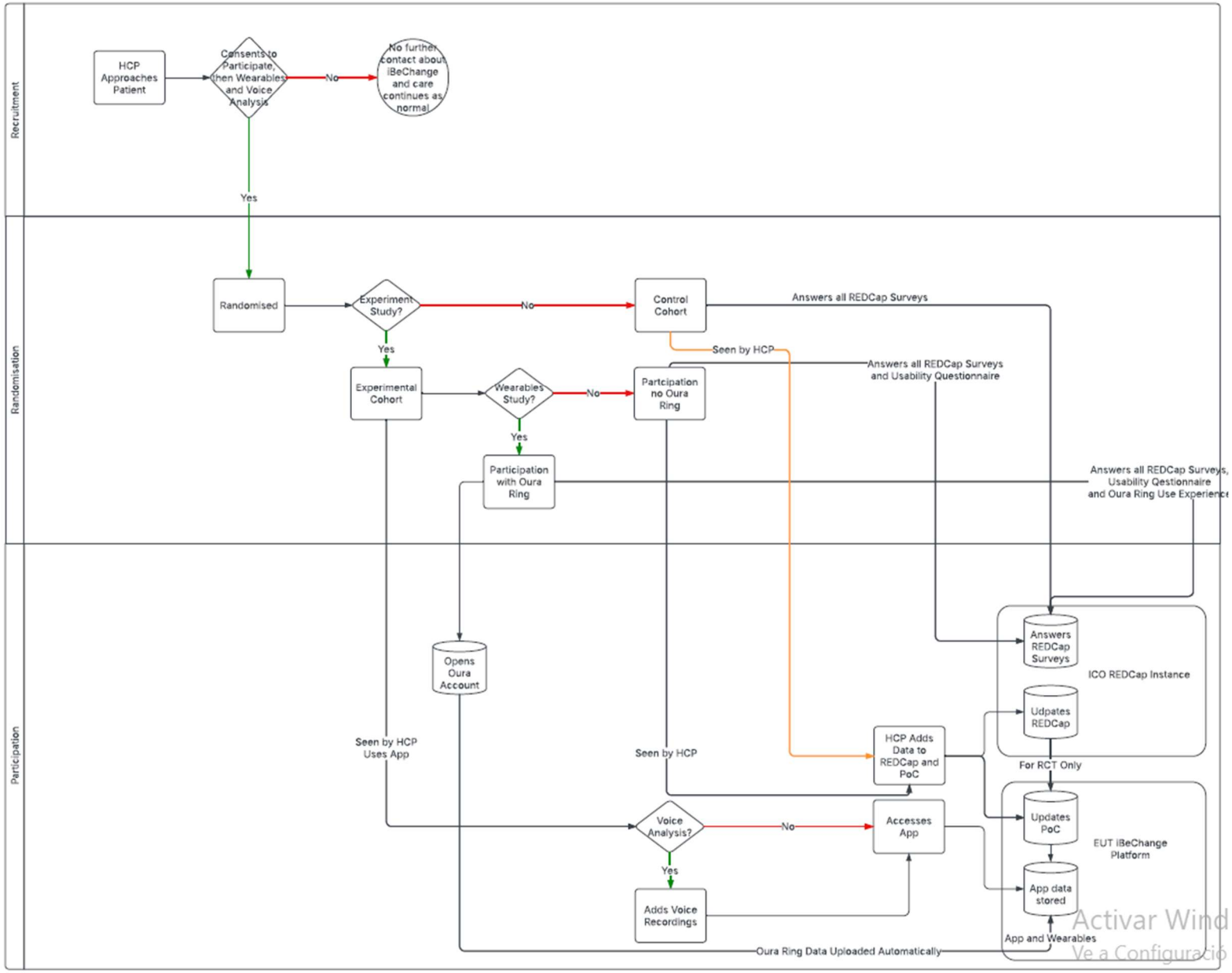
The Platform will host the Participant App and PoC system. This stage of the studies also relates to the data gathering from the participants via the Experimental Group App as per Steps 3PAA in Figure 5. Participants will be encouraged to use the App to add data, including voice recordings for emotion/stress analysis.

The Wearables data in the first instance via the Oura Ring via the Experimental Group app once the HCP has connected their accounts will also be uploaded to the Eurecat Platform. The Oura app will be automatically connected to the Platform through the app, redirecting to Oura server once the user account is already activated. The Oura Ring will also upload data to the Platform automatically under steps 3ORA for the RCT as per steps 3ORRC. Wearable data stored in the Oura server will be transferred periodically (ideally, at least once a day) through Rest API to the Eurecat's Platform (step 3ORA).

Voice recordings for the emotional/stress analysis will also be added via the App where Participants have consented to do so. Please see the Oura Ring Logistics Flow Diagram at Figure 4 and the App Specification Data Flow Diagram for the full details of data processing. The details of data collected are available at sections 4.3, 4.4 and 4.5.

Note that Figure 6, on the next page, outlines all steps to this point in more detail.

Figure 6. Participant recruitment and data flow diagram (next page)



7.2.3. Analysis Stage

Within the Analysis Stage, there are several points. SIMAVI will develop the app interface tool as per step 4DA and will need to process data on the platform to assist in their development and deployment. POLIMI will access the platform-held data as per step 5PZ and as described in Section 7.1. Within POLIMI, there are two groups, one focusing on wearables and the intervention wearables, where they need all the wearable data and the interventional/clinical data for correlation analysis. Another group will be running reinforced learning and will only require interventional/clinical data.

8. Statistics

8.1. Statistical hypotheses

The pilot study aims to assess the feasibility of a future larger RCT. It will also inform RCT planning, define the study protocol, and optimise the IBeChange intervention and study design.

Therefore, the statistical focus is on feasibility-related outcomes rather than formal hypothesis testing for clinical efficacy. The feasibility of the future RCT will be evaluated based on key metrics, including recruitment rates, completion rates, data completeness, and participant/staff feedback. The following feasibility hypotheses will guide our assessment

1. Recruitment Feasibility Hypotheses
   a. H_0 (Null Hypothesis): The recruitment rate will be insufficient for a future RCT, with an estimated rate below the predefined feasibility threshold (50% of eligible patients consent to participate).
   b. H_1 (Alternative Hypothesis): The recruitment rate will meet or exceed the feasibility threshold, indicating that the trial can recruit participants at an acceptable rate for an RCT.
2. Data Collection Feasibility Hypotheses
   a. H_0: The case report form (CRF) completion rate will be suboptimal, with excessive missing data (>10% missingness in primary outcomes).
   b. H_1: The CRF completion rate will be adequate, with minimal missing data, indicating good feasibility of data collection.
3. Acceptability and Usability Hypotheses
   a. H_0: Participants will report low usability and satisfaction scores, assessed through the one single 0-10 visual analogue scale item per construct (mean score < 7)
   b. H_1: Participants will report acceptable usability and satisfaction.
4. Operational Feasibility Hypotheses
   a. H_0: The time required to complete each trial step (e.g., participant recruitment, data entry, and data transfer) will exceed the predefined thresholds (recruit 100% of participants within the first 3 months and complete data entry and transfer within 1 month of the end of the pilot).
   b. H_1: The time required to complete each trial step will be within planned limits, supporting the feasibility of the future RCT.
5. Wearable usage Hypotheses
   a. H_0: Participants in the wearable sub-group will not consistently use the wearable device, with fewer than 80% of participants using the device at least 4 days per week.
   b. H_1: Participants in the wearable sub-group will consistently use the wearable device throughout the study.

8.2. Sample size determination

The sample size for the pilot study was determined as 10% of the total sample for the full RCT, which covers its feasibility nature. For the full RCT, assuming a 60% refusal rate, a significance level of 0.05, and a 5% difference between groups, a sample size of 900 participants per group would result in a power of 80%. Therefore, the estimated sample size for the pilot was 180 participants (90 per group).

8.3. Baseline Descriptive Statistics and Exploratory Analyses

Our exploratory analyses will use a comprehensive visual inspection of all variables. This process will include evaluating the frequency, percentage, and near-zero variance of categorical variables (e.g., gender and seven-day point prevalence abstinence), as well as analysing the distribution of numeric variables (e.g., age and scale scores) and their corresponding missing value patterns. Near-zero variance refers to situations where a categorical variable has few unique values compared to the sample size, making it almost constant. We will address near-zero variance by recategorising low-frequency categories. We will use univariate and bivariate plots, including histograms, bar plots, scatterplots, and pirate plots. We will also prepare tables with the frequency and percentage for categorical variables, as well as the mean and standard deviation for numeric variables. We will compare variables using a standardised mean difference (SMD), which is the difference in proportions or means divided by the pooled standard deviation. SMD magnitudes were interpreted according to the following criteria: SMD = 0.2 indicates a small effect, SMD = 0.5 indicates a medium effect, and SMD = 0.8 indicates a large effect. We will also present p-values for t-tests (for normally distributed numeric variables), Wilcoxon tests (for non-normally distributed numeric variables), and Chi-square tests (for categorical variables), considering p-values below 0.05 as statistically significant.

8.4. Statistical Analyses for Feasibility Metrics

We will use a line plot to assess the weekly cumulative recruitment rate for each participating institution, visualising trends over time and identifying recruitment bottlenecks. Additionally, we will analyse the proportion of eligible participants who consent, the dropout rate, and reasons for attrition to evaluate recruitment efficiency. To better understand recruitment efficiency, we will also measure the time from site initiation to the first participant recruitment at each centre.

To evaluate data collection quality, we will calculate the percentage of missing data for each variable and visualise missingness patterns to identify systematic issues. If the amount of missing data compromises further analyses, we will use imputation algorithms followed by sensitivity analyses to verify whether our results are stable with and without imputation.[33] Specifically, we will use the Multivariate Imputations by Chained Equations (MICE) algorithm,[34] which employs the fully conditional specification method,[35] where a separate model imputes each variable that contains missing data. We will use 100 multiple imputations and the predictive mean matching method for numeric variables, logistic regression imputation for binary variables, and polytomous regression imputation for categorical variables.

Furthermore, we will assess the mean time required to complete the Case Report Form (CRF) for both participants and staff, helping determine whether the data collection process imposes an undue burden.

8.5. Analysis of Primary and Secondary Endpoints

The pilot data will be analysed to determine the potential effectiveness of the iBeChange platform and to enhance the recommendation system. The analysis will account for confounding factors and

within-subject correlation over time, providing valuable information for the larger RCT and improving the accuracy of the feedback provided by the recommendation system.

Both the pilot and future RCT will involve a Bayesian Adaptively Randomised Design (BARD).

Compared to traditional frequentist trials, BARDs tend to be more efficient. They require smaller sample sizes as they allow multiple interim analyses without statistical penalties, enabling protocol refinements according to predefined rules. These designs can adapt allocation rules, sampling procedures, and the number of treatments tested, and they include a data-driven stopping rule to halt a treatment if it is effective, futile, or harmful.[36,37]

A Bayesian hierarchical modelling approach will be used to estimate intervention effects while accounting for site-level variability. We will use Bayesian multilevel models to evaluate the preliminary effectiveness of the IBeChange intervention on tobacco and alcohol consumption, nutrition, physical activity, and psychosocial outcomes while accounting for the grouping related to the longitudinal follow-up and the hierarchical structure of the data (i.e., multiple observations from the same participant over time as well as participants grouped in different institutions). When compared to single-level regression models, its Bayesian counterpart can assess the expected correlation between measurements of the same individual and individuals in the same group, accounting for the dependency of these observations. This is accomplished by dividing the total variance into variations associated with the groups (level-2) and individual participants (level-1). As a result, such models estimate the variance component for the second level (i.e., the variability of the participant-specific estimates) or higher levels, indicating that the findings are accurate and generalisable.[38,39]

Bayesian methods allow for the incorporation of existing knowledge about the probability of different model parameters (in the form of prior distributions) with observed data to generate updated knowledge about the parameters (in the form of posterior distributions).[38,40] Statistical inferences are then made based on these updated distributions. We will use weakly informative priors, defined a priori based on clinical assumptions and literature, to derive posterior distributions. Sensitivity analyses will assess the robustness of results to different prior assumptions. Bayesian multilevel modelling is particularly well-fit to handle multiple comparisons.[41] Under this framework, adjustment for multiple tests becomes unnecessary,[41] allowing us to explore hypotheses at a granular level while decreasing the risk of reaching spurious conclusions. Furthermore, Bayesian analyses allow for direct probability statements about parameters (population-level results), providing precise parameter estimates without the need for large samples and allowing the determination of zero effects. Finally, Bayesian models provide more intuitively interpretable uncertainty estimates around parameter values than those offered by their frequentist counterparts.

We will implement the Bayesian estimates using the R statistical language[42] with the rstanarm package,[43] which calls the stan package.[44] Our modelling strategy will use Markov Chain Monte Carlo (MCMC), repeated four times, i.e., four chains, with 1,000 warm-up iterations followed by 3,000 posterior sampling iterations per chain.

We will interpret model results as a point estimate representing the magnitude of each treatment effect (i.e., regression coefficient) and an interval estimate for the precision of that estimate. The median of the posterior distribution for each treatment effect constitutes the point estimate. We will

represent the posterior distribution of each treatment effect using 95% credible intervals (CrI). The 95% CrI is the smallest interval that contains the parameter values with the highest probability density (i.e., 95% credibility). Each interval estimate contains the range of the most reliable estimates for the magnitude of the treatment effect in light of the data, our model, the degree of random effect variability, and the sampling error. The posterior distribution's spread indicated the uncertainty of the estimate. Bayesian posterior probabilities will be employed to assess clinical effectiveness and futility for each primary outcome.

8.6. Planned Interim Analyses

Interim analyses will occur after 25%, 50%, and 75% of the planned sample size have completed their 12-week follow-up assessments, at the end of the intervention. Interim analyses will evaluate effectiveness and futility parameters, allowing for data-driven trial modifications while ensuring scientific standards. Efficacy will be evaluated through predefined posterior probability thresholds, where the trial may stop early if the probability that the treatment effect exceeds the clinically meaningful threshold reaches 95%. Futility will be assessed to prevent unnecessary exposure to an ineffective intervention, with stopping criteria set for scenarios where the probability of a clinically insignificant effect exceeds 90%.

8.7. Sub-group Analyses

The wearable data sub-group will be used to assess the feasibility, suitability, and added value of incorporating wearable devices into the study to complement psychosocial and behavioural features already captured through smartphone sensors. We will evaluate the quality of the data collected by wearables by assessing missingness and participant adherence to device usage over time. Specifically, we will track the percentage of missing data for each sensor (e.g., heart rate, sleep data, physical activity data, etc.) and assess adherence based on the number of days participants wore the device. To quantify feasibility, we will calculate the frequency of wearable device usage and assess any potential barriers to consistent engagement, such as device malfunction or participant non-compliance.

Additionally, we will investigate whether wearable data can provide more granular insights into psychosocial and behavioural risk factors. By correlating specific wearable metrics with corresponding outcome measures, we aim to determine whether these data can supplement or replace outcome assessments through questionnaires. For example, we will assess the relationship between heart rate, steps taken, and physical activity levels by comparing wearable data with the physical activity outcomes measured by the Global Physical Activity Questionnaire (GPAQ) or the International Physical Activity Questionnaire (IPAQ) assessed in the iBeChange app within the Health habit assessment. Pearson correlation coefficients (for continuous, normally distributed variables) or Spearman's rank correlation (for non-normally distributed variables) and visual correlation plots will be used to evaluate the strength and direction of these relationships. In addition, we will use Bayesian models to account for potential confounders such as baseline physical activity levels and demographic characteristics. Machine learning approaches will also be

explored to assess the concurrent validity between participant-reported outcomes and wearable data.

Alongside these evaluations, we will test whether participants using wearables demonstrate a higher degree of behavioural change compared to those who did not receive the devices. To assess this, we will compare smoking, alcohol, nutrition, physical activity, and psychosocial outcomes between the wearable and non- wearable groups. For these comparisons, we will use the same statistical methods described above, including Bayesian models and exploratory analysis techniques (e.g., t-tests for between-group comparisons). These analyses will help determine whether the use of wearables leads to more significant improvements in outcomes compared to conventional methods.

8.8. Full RCT design adaptation

The pilot data will help estimate the effect size and variability of the primary and secondary outcomes, both of which will be crucial for refining the required sample size and ensuring the power of the full RCT.

The pilot study will provide initial estimates of the intervention's effect size, which is the expected difference between the experimental and control groups for each primary and secondary outcome (e.g., smoking cessation rates, alcohol consumption, physical activity). By calculating the mean differences or standardised effect sizes (e.g., Cohen's d) based on the pilot data, we will be able to refine our hypothesis for the full RCT, ensuring that the study is powered to detect a meaningful difference. These estimates will be particularly useful if the observed effect size in the pilot study differs from initial assumptions, allowing for adjustments to the sample size calculation for the full trial.

The pilot study will also provide crucial information on the variability of the outcomes within each group, which directly influences the precision of effect size estimates and, consequently, the power calculation. By assessing the variance or standard deviation of outcomes, we can refine the estimate of variability that will be used in the power analysis for the full RCT. A better understanding of variability, including potential baseline differences or within-group heterogeneity, will allow for more accurate planning of the full RCT's sample size to achieve the desired statistical power.

With the pilot data informing both effect size and variability, the sample size calculation for the full RCT can be adjusted accordingly. For example, if the pilot data indicates a smaller effect size than initially anticipated, the sample size may need to be increased to maintain adequate power. Conversely, if the pilot data reveals lower-than-expected variability, a smaller sample size may suffice.

9. Regulatory, Ethical, and Study Oversight Considerations

The framing governance for the iBeChange studies, including this pilot study, is founded in the GDPR Data Protection by Design and Default recommendations. This has provided the project a basis to assess data protection requirements from the outset, incorporating a Data Protection Impact Assessment (DPIA) and a Data Management Plan (DMP) that has helped to define the data flows and management for the Project. These have helped to guide the development of a Joint Controller Agreement between partners that will govern the capture and sharing of data within the consortium to achieve the goals of the study.

These processes have also informed the application to local research ethics committees and/or independent review boards for local approvals prior to the studies’ commencement. These boards will also review the participant information brochures and consent forms provided to potential participants as part of recruitment.

The DPIA and DMP will be continuously updated and are currently being adapted to meet the requirements of the AI Act and expectations around trustworthy AI use and deployment. iBeChange as a Consortium will be making standard risk management around AI, focusing on transparency, data governance, security and privacy, system safety, traceability and explainability for the AI components that are being developed to make recommendations across the platform as the work progresses.

Assessments will be iterative, and activities will be adapted in accordance with the identification of any risks that may present themselves through the ongoing data governance work. These will be keyed towards supporting the validation of tooling approaches, data quality readiness assessments and documentation and record keeping for the platform development and operation.

10. Annex

10.1. Clinical Recommendations for Cancer Prevention for Control participants

Please include the text of the 2nd level.

This is an English version translated from the postal letter sent to participants from the Cancer Screening Program at ICO. It will be adapted to Italian and delivered to IEO participants, and adapted to Romanian and delivered to UMFCD participants.

Dear sir/madam,

We thank you for your participation in the cancer screening test.

Until your next screening, please consider these recommendations from the European Code Against Cancer:

- Do not smoke
- Keep a healthy weight
- Do daily physical activity
- Follow a healthy diet
- Avoid alcohol consumption
- Protect your skin from sunlight
- Get vaccinated against some infections
- Regularly undergo cancer screening tests

Prevention is also in your hands!

Adopting these practices contributes to a full and healthy life.

Thank you for participating in iBeChange!

iBeChange team

ICO/IEO/UMFCD team

10.2. List of Standardized Criteria for Level 3 intervention escalation

If any of the items listed below are suspected in a participant during the professional SSI, they will be referred to external professional assistance but keep the iBeChange support in parallel:

- Depressed mood most of the day, for at least 2 consecutive weeks, represents a difference from previous functioning.
- Important decrease in interest or pleasure in almost all activities most of the day, for at least 2 consecutive weeks, representing a difference from previous functioning.

NOTE: Ensure these two risk factors are not due to a recent bereavement process.

- Excessive worry about various events presents more than half the time for approximately 6 months.
- Other anxiety symptoms include: feeling restless, tense, panic, experiencing periods of increased heart rate, hyperventilation, sweating, trembling, or having trouble concentrating. These symptoms significantly interfere with the person's daily functionality.
- Indicators of Post-Traumatic Stress Disorder: 1) memories, nightmares, flashbacks; 2) persistent avoidance; 3) intense physiological reactions of hyper-arousal or other behaviours as if the traumatic event were occurring. These symptoms cause significant emotional distress and last more than 1 month.
- Risk behaviours or self-harm (including substance abuse and eating disorders).
- Recurrent thoughts of death or suicide.
- Significant cognitive impairment.
- Active psychotic symptomatology: disorientation (in time, place, or person), severely disorganised thinking and/or behaviour, hallucinations, and delusional ideas.
- Being a victim of psychological or physical abuse.
- Any other psychological symptom that generates significant functional impairment in any area of their life.

11. Conclusions

This deliverable presents the finalised protocol for the iBeChange pilot study, a foundational step within Work Package 5 aimed at evaluating the feasibility and usability of a digital behavioural change platform for cancer prevention. The protocol outlines the key procedures and methodological framework to be implemented across participating clinical sites, including recruitment, intervention delivery, assessment timelines, and data management. Importantly, this pilot study also integrates outcomes from Work Package 2 — Design of the integrated platform using Behaviour Change Techniques and a User-Centred Design approach. Specifically, the selection of representative outcomes related to lifestyle and psychosocial risk and protective factors, developed through Tasks 2.1 and 2.2, has directly informed the data collection strategy for T2.5 (Patient-Reported Outcome Measures, lifestyle, and psychosocial variables) and the development of the behavioural change and psychological support tool under T2.7.

This pilot also included the wearable sub-study, which is integrated into the same randomisation structure as the main study (as a second randomisation). This sub-study explores the potential of wearable technology to passively collect lifestyle and psychosocial data. While briefly described within this protocol for ethical submission purposes, further detail is provided in a separate deliverable (D5.2).

The pilot study will provide essential insights into the logistical and methodological aspects of deploying the iBeChange intervention, allowing for refinements before launching the full-scale randomised controlled trial (iBC/CT). Findings from the pilot will also help validate the tools and technologies used (such as REDCap and the Point of Care platform), and assess participant adherence, recruitment feasibility, and the suitability of outcome measures.

Future work includes the formal submission of this protocol to ethics committees across participating centres, its registration in relevant public repositories (WHO International Clinical Trials Registry Platform; ICTRP), and its publication in open-access, peer-reviewed scientific journals to promote transparency and facilitate knowledge sharing. Insights gathered from the pilot will inform adjustments to the intervention and study design ahead of the larger randomized controlled trial planned within WP5.

Other relevant future work will involve:

- Implementation and real-time monitoring of the pilot study across clinical sites.
- Evaluation of participant adherence and data quality.
- Refinement of the intervention and procedures based on pilot outcomes.
- Preparation and submission of ethical documents and protocols for the full RCT.
- Incorporation of learnings into the final version of the iBeChange platform.

The pilot study is a critical milestone to ensure the success of the iBeChange clinical validation, ultimately contributing to improved lifestyle-related cancer prevention across diverse European populations.

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Version history

Version	Description	Date completed
v1.0	First version drafted	03/03/2025
v1.1	Consortium revision (first)	28/03/2025
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v2.1	Consortium revision (second)	04/04/2025
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