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THE USABILITY, ACCEPTABILITY, AND SATISFACTION OF A DIGITAL MENTAL HEALTH TOOL FOR PATIENTS WITH BREAST AND PROSTATE CANCER

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THE USABILITY, ACCEPTABILITY, AND SATISFACTION OF A DIGITAL MENTAL HEALTH TOOL FOR PATIENTS WITH BREAST AND PROSTATE CANCER

Thesis for Doctoral Degree (Ph.D.)

By

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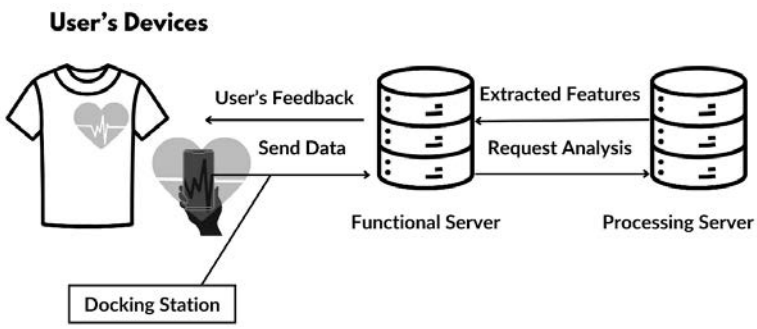
To my family,

Popular science summary of the thesis

One in four patients diagnosed with breast and prostate cancer suffer from depressive symptoms. The increased risk of depression in these patients can be attributed to a combination of factors, including the emotional burden of a cancer diagnosis, the physical impact of the disease and its treatment, feelings of loneliness, lifestyle changes, and a complex interplay of biochemical changes in the body. Despite this increased strain on cancer patients, they do not always receive full psychiatric support and care from hospitals to manage their mental health.

So, the NEVERMIND system, illustrated as the user's device in the figure below, comprised of a mobile app and a shirt with a sensor, was developed for patients with physical illnesses, such as cancer, to reduce depressive symptoms that are often associated with their physical diagnosis. The NEVERMIND system, utilizing mood assessment questionnaires via the mobile app and collecting physiological data through the shirt, provides personalised feedback, such as lifestyle changes, mindfulness practices, and cognitive behavioural therapy and guidance based on the severity of mental health symptoms. The NEVERMIND system was effective in reducing depressive symptoms in a randomized controlled trial of 425 patients diagnosed with breast and prostate cancer, kidney failure, myocardial infarction, and leg amputation. Patients who used the NEVERMIND system for 12 weeks had a significant reduction in depressive symptoms compared to those who only received treatment as usual.



Through four studies, this Ph.D. thesis examined the usability, acceptability, satisfaction, and clinical effectiveness of the NEVERMIND system in breast and prostate cancer patients. The aim was to understand different factors associated with usability, acceptability, and satisfaction and how these dimensions interact.

The first study found that the NEVERMIND system had above-average usability, with no differences across sex, age, education level, marital status, and cohabitation. Our findings also showed that women (breast cancer patients) rated the mobile app higher in terms of quality and content than men (prostate cancer patients) did, despite men

using the NEVERMIND system more. The second study found that patients were more likely to continue using the system if they perceived it as useful and engaged with it in the first two weeks. The findings of the second study were crucial, as the third study found that those who used the system for over six weeks showed a higher reduction in their depressive and stress symptoms compared to those who only used it for two weeks or less.

Study four looked at user satisfaction by analysing user responses to open-ended questions. Users were satisfied with the NEVERMIND system because it fostered personal agency and motivation alongside providing holistic well-being and supportive connections. Users also highlighted the need for user-friendly interfaces to enhance engagement and interaction experiences while addressing technical, interface, and comfort challenges that they experienced. Finally, users expressed the need for improved quality and breadth of content provided, ensuring that it is diverse and relevant to their needs and experiences. Interestingly, women valued the emotional support provided by the NEVERMIND system, while men appreciated the self-awareness and introspection the system provided.

The NEVERMIND system, when used consistently and perceived as beneficial, could have a positive impact on mental health among patients with breast and prostate cancer. Additionally, personalisation is crucial in digital health tools, revealing that more than a one-size-fits-all approach in digital health tools may be needed. Differences in usability and preference between genders highlight the necessity for a personalised touch, addressing individual needs and preferences. Digital health tools such as the NEVERMIND system offer great promise for managing mental health issues among patients with cancer. By focusing on the usefulness and informing patients about their benefits early on, we can promote their adoption for better patient outcomes.

Abstract

The impact and use of digital health tools vary considerably among individuals dealing with somatic illnesses, such as cancer. This variability can be attributed to several factors, such as sociodemographic characteristics, baseline mental health, perception of the intervention's usefulness, ease of use, and early engagement with the system. In this thesis, we aimed to examine the influence and interaction among these indicators on the usability, acceptability, satisfaction, and clinical effectiveness of a digital health tool in individuals with breast and prostate cancer.

All studies were based on data from the NEVERMIND trial, a clinical randomized controlled trial that included patients with five different somatic illnesses. Our study included 255 participants (at baseline) who were diagnosed with breast or prostate cancer. Half of the participants (n=129) were allocated to the NEVERMIND system, whereas the other half (n=125) were allocated to the treatment as usual (control) group. Those in the NEVERMIND system group were involved in the use of the NEVERMIND digital health tool, comprising a mobile app and sensorized shirt (shirt), over a 12-week period. Data from baseline assessments and follow-ups at four and 12 weeks were used. The aim was to assess the usability, acceptability, and satisfaction of the NEVERMIND system, as well as the factors associated with these dimensions. This Ph.D. project also examined how usability and acceptability impacted the clinical effectiveness of the NEVERMIND system on depressive and stress symptoms.

Study I. We investigated the association between baseline sociodemographic characteristics and usability assessed at four and 12 weeks of using the NEVERMIND system among 108 patients with breast and prostate cancer who received and used the system. The NEVERMIND system had good usability according to the usability questionnaires. Higher favourability of the mobile app was observed among women (breast cancer patients) compared to men (prostate cancer patients); however, men had significantly higher use of the overall system.

Study II. The relationships between sex, education, baseline depressive and stress symptoms, perceived ease of use, perceived usefulness, and system usage at various stages were examined using Bayesian Structural Equation Modelling in a path analysis of 129 patients with breast and prostate cancer. Higher perceived usefulness and initial usage were associated with a higher level of usage at 12 weeks. The results indicated that a better understanding of the system's benefits and early engagement were key drivers of its sustained use and clinical effectiveness in improving mental health outcomes.

Study III. In a sample of 255 patients with breast and prostate cancer, we examined the relationship between the clinical effectiveness, usability, and acceptability of the

NEVERMIND system when treating depressive and stress symptoms in patients with breast and prostate cancer. The results showed that patients in the NEVERMIND group had a greater reduction in depressive symptoms than those in the control group at the 12-week follow-up. The findings also showed that users who utilized the system for more than six weeks experienced a statistically significant decrease in both depressive symptoms and stress symptoms compared to those who used it for less than two weeks.

Study IV. This study looked at the overall satisfaction of users (68 with breast cancer and 39 with prostate cancer) with the NEVERMIND system. Satisfaction was measured at four and 12 weeks using a one-item questionnaire with two open-ended follow-up questions about user experiences. An inductive and deductive thematic analysis was conducted by using the NEVERMIND system's components as a sensitizing concept which was then refined and interpreted through the lens of Information Systems (IS) success model. The findings show that 68.24% of users rated the system as good or excellent at four weeks, with a slight decrease to 65.42% at 12 weeks. Three themes emerged from the thematic analysis: (1) Fostering Personal Agency and Motivation, (2) Engagement and Interaction Experiences, and (3) Content Quality and Relevance. Gender differences emerged in the prioritization of emotional support among female users and self-awareness among male users. The satisfaction and challenges faced by users underscore the importance of a user-centric approach that focuses on holistic well-being, user engagement, personalized content, and technical stability. This study also contributes to the broader literature by utilizing IS success model as a framework for interpreting user satisfaction.

Conclusions. Higher levels of usability, acceptability, and satisfaction in the NEVERMIND system may contribute to improving the mental health outcomes of patients with breast and prostate cancer, both independently from each other, and even more so when high levels of engagement, acceptance, use, and satisfaction coexist. They emphasize the importance of perceived usefulness, initial engagement, and user-centric design in different components of the NEVERMIND system and confirms the multidimensionality of successful digital health tools implementation. Moreover, the notable differences in usability and preference between genders indicate that tailored and personalized strategies might serve as effective means to address diverse user needs. Taken together, these insights strengthen scientific evidence for healthcare experts and digital health innovators and developers, guiding them towards creating and designing digital health tools through user-centric and multi-domain approaches.

Keywords: digital health tool, eHealth, usability, acceptability, satisfaction, technology acceptance model, mental health, cancer patients

Sammanfattning

Användandet och effekten av digitala hälsoverktyg varierar avsevärt bland individer som hanterar somatiska sjukdomar, såsom cancer. Denna variabilitet kan tillskrivas flera faktorer, såsom sociodemografiska egenskaper, grundläggande psykisk hälsa, uppfattning om interventionens användbarhet, användarvänlighet och tidig interaktion med systemet. I denna avhandling ämnade vi att undersöka inflytandet och samspelet mellan dessa indikatorer på användbarhet, acceptans, tillfredsställelse och klinisk effektivitet av ett digitalt hälsoverktyg hos individer med bröst- och prostatacancer.

Alla studier baserades på data från NEVERMIND-studien, en klinisk randomiserad kontrollerad studie som inkluderade patienter med fem olika somatiska sjukdomar. Vår studie omfattade 255 deltagare (vid baslinjen) som hade diagnostiserats med bröst- eller prostatacancer. Hälften av deltagarna (n=129) tilldelades NEVERMIND-systemet, medan den andra hälften (n=125) tilldelades kontrollgruppen (treatment-as-usual). Deltagarna i NEVERMIND-systemgruppen var involverade i användningen av det digitala hälsoverktyget NEVERMIND, som består av en mobilapp och en sensoriserad skjorta (skjorta), under en 12-veckorsperiod. Data från baslinjemätningar och uppföljningar vid fyra och 12 veckor användes. Syftet var att bedöma användbarheten, acceptansen och tillfredsställelsen med NEVERMIND-systemet, samt de faktorer som är förknippade med dessa dimensioner. Detta doktorandprojekt undersökte också hur användbarhet och acceptans påverkade den kliniska effektiviteten hos NEVERMIND-systemet.

Studie I. Vi undersökte sambandet mellan sociodemografiska egenskaper vid baslinjen och användbarhet som bedömdes efter fyra och 12 veckors användning av NEVERMIND-systemet bland 108 patienter med bröst- och prostatacancer som fick och använde systemet. NEVERMIND-systemet hade god användbarhet enligt frågeformulären om användbarhet. En högre grad av positiv inställning till mobilappen observerades bland kvinnor (bröstcancerpatienter) jämfört med män (prostatacancerpatienter); män hade dock en betydligt högre grad av användande av det övergripande systemet.

Studie II. Sambanden mellan kön, utbildning, depressions- och stressymtom vid baslinjen, upplevd användarvänlighet, upplevd nytta och systemanvändning i olika stadier undersöktes med hjälp av Bayesian Structural Equation Modelling i en path-analys av 129 patienter med bröst- och prostatacancer. Högre upplevd användbarhet och högre initial användning var förknippade med en högre användningsnivå efter 12 veckor. Resultaten visade att en bättre förståelse av systemets fördelar och tidigt engagemang var viktiga drivkrafter för dess fortsatta användande och kliniska effektivitet när det gäller att förbättra resultaten för psykisk hälsa.

Studie III. I ett urval av 255 patienter med bröst- och prostatacancer undersökte vi hur förhållandet mellan NEVERMIND-systemets kliniska effektivitet, användbarhet och

acceptans vid behandling av depressions- och stressymtom hos patienter med bröst- och prostatacancer. Resultaten visade att patienterna i NEVERMIND-gruppen hade en större minskning av depressiva symtom än de i kontrollgruppen vid 12-veckorsuppföljningen. Vidare visade undersökningen att användare som använt systemet i mer än sex veckor upplevde en statistiskt signifikant minskning av både depressiva symtom och stressymtom jämfört med dem som använt det i mindre än två veckor.

Studie IV. Denna studie undersökte den övergripande tillfredsställelsen hos användare (68 med bröstcancer och 39 med prostatacancer) med NEVERMIND-systemet. Tillfredsställelse mättes vid fyra och 12 veckor med hjälp av ett enpunkts frågeformulär med två öppna uppföljningsfrågor om användares erfarenheter. En induktiv och deduktiv tematisk analys genomfördes med NEVERMIND-systemets komponenter som ett känsliggörande koncept och finslipades och tolkades genom Information Systems (IS) framgångsmodellens lins. Resultaten visar att 68,24% av användarna bedömde systemet som bra eller utmärkt efter fyra veckor, med en liten minskning till 65,42% efter 12 veckor. Tre teman framkom från den tematiska analysen: (1) Främja Personligt Ansvar och Motivation, (2) Engagemang och Interaktionsupplevelser, och (3) Innehållskvalitet och Relevans. Könsskillnader framträdde i prioriteringen av emotionellt stöd bland kvinnliga användare och självmedvetenhet bland manliga användare. Användarnas tillfredsställelse och utmaningar betonar vikten av ett användarcentrerat tillvägagångssätt som fokuserar på holistiskt välbefinnande, användarengagemang, personligt innehåll och teknisk stabilitet. Denna studie bidrar också till den bredare litteraturen genom att använda IS success model som ett ramverk för att tolka användartillfredsställelse.

Slutsatser. Högre nivåer av användbarhet, acceptabilitet och tillfredsställelse i NEVERMIND-systemet kan bidra till att förbättra de mentala hälsoutfallen för patienter med bröst- och prostatacancer, både oberoende av varandra, och ännu mer när höga nivåer av engagemang, acceptans, användning och tillfredsställelse samexisterar. De betonar vikten av upplevd nytta, initialt engagemang och användarcentrerad design inom olika komponenter av NEVERMIND-systemet och bekräftar den flerdimensionella karaktären av framgångsrik implementering av digitala hälsorelaterade verktyg. Dessutom indikerar de märkbara skillnaderna i användbarhet och preferens mellan könen att skräddarsydda och personliga strategier kan fungera som effektiva medel för att möta varierande användarbehov. Sammantaget stärker dessa insikter den vetenskapliga bevisningen för vårdexperter och digitala hälsoutvecklare och guidar dem mot att skapa och utforma digitala hälsorelaterade verktyg genom användarcentrerade och flerdomänsmetoder.

Nyckelord: digitalt hälsoverktyg, e-hälsa, användbarhet, acceptans, tillfredsställelse, teknikacceptansmodell, mental hälsa, cancerpatienter

List of scientific papers

The doctoral thesis is based on the following original papers, which will be referred to in the text as Studies I, II, III, and IV.

Petros NG, Hadlaczky G, Carletto S, Martinez SG, Ostacoli L, Ottaviano M, Meyer B, Scilingo EP, Carli V. Sociodemographic Characteristics Associated With an eHealth System Designed to Reduce Depressive Symptoms Among Patients With Breast or Prostate Cancer: Prospective Study. JMIR Formative Research. 2022 Jun 8;6(6):e33734.

Petros NG, Alvarsson-Hjort J, Hadlaczky G, Wasserman D, Ottaviano M, Gonzalez-Martinez S, Carletto S, Scilingo EP, Valenza G, Carli V. Predictors of the Use of a Mental Health–Focused eHealth System in Patients With Breast and Prostate Cancer: Bayesian Structural Equation Modeling Analysis of a Prospective Study. JMIR cancer. 2023 Sep 12;9:e49775.

Petros NG, Alvarsson J, Hadlaczky G, Carletto S, Martinez SG, Ottaviano M, Malandrone F, Scilingo EP, Valenza G, Wasserman D, Ostacoli L, Carli V. Usage of the NEVERMIND eHealth system predicts treatment effectiveness of cancer patients' depression and stress symptoms. (Submitted).

Petros NG, Lögdberg U, Hadlaczky G, Alvarsson J, Wasserman D, Gonzalez-Martinez, S., Carletto, S, Scilingo EP, Valenza G, Carli V. Evaluating Cancer Patients' Experiences and Satisfaction in a Digital Mental Health Tool: A Mixed Methods Study (Manuscript).

Scientific papers not Included in the thesis

Carli V, **Petros NG**, Hadlaczky G, Vitcheva T, Berchialla P, Bianchi S, Carletto S, Christinaki E, Citi L, Dinis S, Gentili C. The NEVERMIND e-health system in the treatment of depressive symptoms among patients with severe somatic conditions: A multicentre, pragmatic randomised controlled trial. EClinicalMedicine. 2022 Jun 1;48:101423.

Carli V, Wasserman D, Hadlaczky G, **Petros NG**, Carletto S, Citi L, Dinis S, Gentili C, Gonzalez-Martinez S, De Leonibus A, Meyer B. A protocol for a multicentre, parallel-group, pragmatic randomised controlled trial to evaluate the NEVERMIND system in preventing and treating depression in patients with severe somatic conditions. BMC psychiatry. 2020 Dec;20(1):1-0.

CONTENTS

List of abbreviations

ASCO	American Society of Clinical Oncology
BDI-II	Beck-Depression Inventory-II
CBT	Cognitive behavioural therapy
CGP	Clinical Guideline Practice
DASS-21	Depression, Anxiety, Stress scale-21
DHT	Digital Health Technology/Tool
eHealth	Electronic health
ESMO	European Society for Medical Oncology
HCD	Human-centred design
iCBT	Internet cognitive behavioural therapy
ICC	Intraclass correlation coefficients
ICT	Information and communication technology
IS success model	Information Systems success model
ISO	International Organization for Standardization
LMM	Linear Mixed Model
LoC	Level of Care
mHealth	Mobile health
Mobile app	Mobile application
NEVERMIND	NEurobehavioural predictiVE and peRsonalised Modelling of depresslve symptoms duriNg primary somatic Diseases with ICT-enabled self-management procedures
PEOU	Perceived ease of use
PSSUQ	Post-Study System Usability Questionnaire
PU	Perceived usefulness
RCT	Randomized controlled trial
SD	Standard deviation
SEM	Structural Equation Model
SUS	System Usability Scale
TAM	Technology Acceptance Model
UCD	User-centred design
uMARS	The User version of the Mobile Application Rating Scale
UTAUT	Unified Theory of Acceptance and Use of Technology
VIF	Variance inflation factor

1 Introduction

1.1 Global depression and stress burden

Depression is a significant global health burden affecting over 280 million people (approximately 3.8%) worldwide, with a prevalence of between 7% and 10% in Europe (1, 2). As one of the preeminent causes of disability and a significant contributor to the global burden of disease, depression can undermine the overall sense of well-being and quality of life of affected individuals (1, 3). Among adults aged 60 years and above, the prevalence is approximately 5.7%, with a gender disparity, with women being approximately 50% more prone to depression than men (4). Depression manifests as persistent sadness, diminished interest or pleasure in activities, reduced energy, low self-esteem, disrupted sleep or eating patterns, and difficulty concentrating (5). These problems can become chronic or reoccur, significantly impairing an individual's ability to perform at work or school and affecting daily living, reducing the overall quality of life globally (3, 6). Depression can result in suicide, a fatality associated with the loss of over 700,000 lives annually (7-9). The burden of depression has increased over the past decade with the COVID-19 pandemic increasing isolation and loneliness (10).

Similarly, stress is a pervasive issue that has wide-ranging implications for mental health and overall well-being, including being a risk factor for Alzheimer's disease (11), tumour growth (12), and cellular damage (13). Stress manifests in many ways, from feeling overwhelmed and agitated, to physical symptoms such as headaches, digestive problems, sleep disturbances, and a weakened immune system (14). Furthermore, chronic stress is intricately linked to a spectrum of psychological disorders, particularly anxiety and depression (15-17). When these stresses become unmanageable, the risk of developing mood disorders, substance abuse, or suicidal ideation increases (8, 18).

The combined impact of stress and depression on physical health can be significantly more severe than their individual effects. Chronic stress can be both a precursor and a symptom of depression (17). When these conditions coexist, their combined physiological effects — such as elevated cortisol levels (19), sleep disturbances (20), and increased inflammation (21) — can further increase the risk of somatic illnesses (21).

1.2 Depression, stress, and cancer: An interwoven complex

There is a clear connection between mental well-being and physical health (11, 13, 14). People who have experienced trauma, significant losses, or other highly stressful events, including severe somatic illnesses, are at increased risk of developing depression (22). The connection is especially true when examining depression, stress, and cancer. While these can be understood separately, they often interact in complex ways, further accentuating

the connection between psychological and physiological well-being (23). The prevalence of depression in cancer patients is estimated to range from 11% to 30% depending on the type of cancer (e.g., lung, breast, prostate, and colorectal cancer), time elapsed since diagnosis (right after diagnosis, advanced stages, survivorship) and treatment setting (outpatient care, palliative care, inpatient care) (24-28). The increased prevalence of depression can be attributed to a combination of factors, including the emotional burden of a cancer diagnosis (29), the physical impact of the disease and its treatment (30), feelings of loneliness (31), lifestyle changes, and a complex interplay of biochemical changes in the body (32, 33). Consequently, depression in cancer patients can adversely affect their well-being (34), treatment adherence (35), as well as overall prognosis (36). In addition, the physiological stress response, marked by the release of cortisol, can weaken the immune system, and increase inflammation, potentially leading to cancer progression (21, 37, 38). Compared to the general population, this increased co-morbidity burden warrants more focused intervention in this group of patients (39, 40).

Finally, the co-occurrence of depression and stress with cancer has significant implications for public health (41), individual health outcomes (42), and the healthcare system (43). Patients with co-morbid depression and cancer face worse health outcomes and increased healthcare costs compared to those with good mental health (43).

1.2.1 Managing depression and stress in cancer patients

This Ph.D. thesis focuses on patients with breast and prostate cancer. Depression among patients with breast and prostate cancer, which are among the leading types of cancer in women and men, respectively, is of particular concern (44, 45). These cancers are life-altering diagnoses that profoundly impact the individual's self-image, sexuality, and life roles, thereby increasing vulnerability to depression (25, 44-46). Therefore, managing depression in these patients is essential to their overall care. Reis et al. reviewed neuroimaging studies with cancer patients, revealing that these patients had changes in pivotal brain regions, such as the prefrontal cortex, thalamus, and hippocampus, which are linked with heightened anxiety, depression, and distress (47).

Despite this increased strain on cancer patients, they do not always receive full psychiatric support and care from hospitals to manage their mental health (48). This disparity in mental health care among persons with cancer has been documented in different studies, citing the availability and accessibility of services (49, 50), stigma (51-53), and lack of adherence to behavioural lifestyle changes, such as physical activity (46).

In the 2023 Clinical Guideline Practice (CGP) update of the American Society of Clinical Oncology (ASCO) (27) and the European Society for Medical Oncology (ESMO) (26), both guidelines recognize the importance of addressing psychological and emotional well-being, especially depression and anxiety, in cancer patients. In both guidelines, screening

for different mental health symptoms among cancer patients remains a priority and one of the first crucial steps in bridging the gaps in mental health care for cancer patients (26, 27).

Due to the lack of screening, patients are not referred to psychiatrists or psycho-oncology services in due time (26, 27). One of the most effective depression management methods, apart from psychopharmacological treatments, is lifestyle changes, psychotherapy, cognitive behavioural therapy (CBT), and mindfulness-based therapies (26, 27). Though patients with breast and prostate cancer receive guidelines and recommendations to enhance their diet, physical activity, and mental health, many do not adhere to them due to the significant lifestyle changes required (54, 55), logistical difficulties (26, 56), and inability to follow-up. Compliance is challenging without proper guidance. Moreover, these lifestyle adjustments are particularly difficult for patients experiencing depressive symptoms, which can occur in any phase of the patient's life (26). The combination of a cancer diagnosis and feelings of inadequacy or self-stigmatization can worsen mental health, diminish the quality of life, and potentially worsen physical symptoms (39).

Thus, actions to improve mental well-being in patients with breast and prostate cancer have been implemented to bridge the gap in oncology. Different methods, including online educational programs, web-based interventions, mindfulness-related training, and educational and participatory sessions, are effective treatments (26, 57). Hence, integrating a technology-driven intervention within these patient populations could significantly improve mental health management and overall patient outcomes (40).

1.2.2 The need for integrated care models: A role for digital health technologies (DHTs)

Historically, mental health services have often been compartmentalized from other medical care services, leading to patients not receiving timely mental health support (58). The rising recognition of the interconnectedness of physical and mental health has led to a concerted push toward more integrated care models through liaison psychiatry and psychosomatic medicine (59, 60). In addition, digital health technologies/tools (DHTs) have emerged as significant catalysts.

1.2.2.1 What are Digital Health Technologies?

The U.S. Food and Drug Administration (FDA) refers to DHTs as "technologies that use computing platforms, software, sensors, or other devices for health care" (61). The FDA's definition includes mobile health, telehealth, wearable devices, personalized medicine, and health information technologies (61). The literature documents that various definitions of 'digital health' exist, and different terminologies are used interchangeably, notably electronic health (eHealth) and mobile health (mHealth) (62). In this Ph.D. thesis, we use

the term 'DHT' per the definition of the European Commission, which defines it as "tools and services that use information and communication technologies (ICTs) to improve prevention, diagnosis, treatment, monitoring, and management of health-related issues and to monitor and manage lifestyle-habits that impact health" (63).

Digital health technologies (DHTs), leveraging technologies such as mobile applications, wearable devices, telemedicine, and online therapy platforms, have demonstrated immense potential to bridge gaps in mental healthcare by improving mental health (26, 27, 64, 65), enhancing patient autonomy (66), and augmenting existing care systems (57, 67).

Digital health technologies are critical for individuals with prostate and breast cancer due to the demand for innovative solutions to address the challenges of depression and stress described above. They deliver therapeutic techniques based on CBT, interpersonal therapy, and other evidence-based approaches. In addition, DHTs provide resources for self-care, psychoeducation, peer support, and mood and symptom tracking, offering mental health support at convenient times and places (64).

> ***Key Definition 1***: Digital Health Technologies are tools and services that use information and communication technologies (ICTs) to improve prevention, diagnosis, treatment, monitoring, and management of health-related issues and to monitor and manage lifestyle habits that impact health.

2 Literature Review

2.1 Conceptual background

As DHTs have become an interest in mental health, one concept that has been integrated is the self-management of mental health symptoms. Barlo et al. (68) define self-management as "the individual's ability to manage the symptoms, treatment, physical and psychosocial consequences, and lifestyle changes inherent in living with a chronic condition", which aligns with this Ph.D. thesis. Although different definitions exist, all underscore individuals or patients' active roles in managing their health using support from healthcare providers, self-help tools, and available evidence-based resources.

In designing and developing DHTs, one of the best design approaches is user-centred design (UCD), also known as human-centred design (HCD). According to the International Organization for Standardization (ISO), UCD is defined as "an approach to interactive systems development that aims to make systems usable and useful by focusing on the users, their needs and requirements, and by applying human factors or ergonomics and usability knowledge and techniques" (69). User-centred design aims to create products or

services that are relevant to the user's needs by incorporating different principles that consider all aspects of the user's interaction with the system, supporting users in what they need to achieve, emphasizing the active participation of users in the design process, and adopting an iterative approach to refine the system based on user experience (69). According to UCD (ISO 9241-210-2010) (69), four steps are involved in making a system usable. The four steps include understanding and specifying the context of the use of the system, followed by specifying the user requirements that lead to the design of the product to meet the specified user requirements, and finally, the design is evaluated against usability requirements and refined until the solution meets user requirements (69) (Figure 1). This Ph.D. thesis focuses on the 'Evaluate the designs against Usability Criteria' step of the UCD (Figure 1).

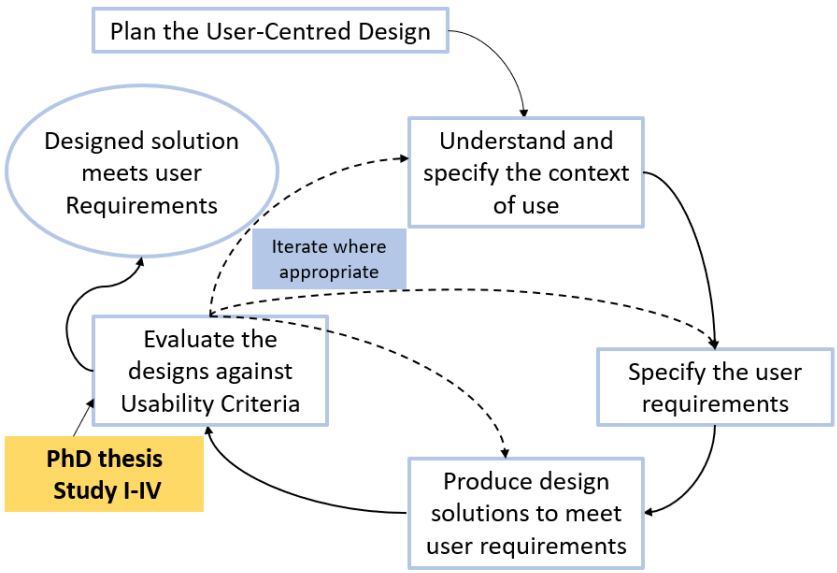


Figure 1. Modified figure of User-Centered Design according to the ISO 9241-210:2019 Ergonomics of human-system interaction–Part 210: Human Centered design for interactive systems (69).

Evaluating the design of a DHT against usability criteria involves understanding the different aspects of usability, acceptability, and satisfaction. The following section provides a comprehensive overview of the three dimensions: usability, acceptability, and satisfaction, starting with the definition of each.

2.1.1 Usability

Usability is rooted in the broader domain of UCD. It has been defined by the ISO as "the effectiveness (fulfilling a task), efficiency (as quickly as possible), and satisfaction (happy about it) with which specified users can achieve specified goals in a particular context of use (environments, equipment, task, user)" (69). Another widely used definition is Nielsen's model, coined in 1994 (70). Nielsen defined usability as the ease and pleasure of user interfaces, characterized by five dimensions (70). These key dimensions are (1) learnability: how easily the users learn the system's functionality and behaviour; (2) efficiency: the attainable productivity level users can achieve after they have learned the system; (3) memorability: how easily users can remember the system's functionality; (4) few errors: the capability of the system to support users in making fewer errors during use; and (5) satisfaction: the overall pleasantness of the design experience (70).

Similar to the Nielen's model, Shackel's Usability framework, based on Bennet (71, 72), and Eason (73) frameworks, defines usability as "the capability in human functional terms to be used easily and effectively by the specified range of users, given specified training and user support, to fulfil the specified range of tasks, within the specified range of environmental scenarios" and explained it using four attributes (1) Effectiveness: defining tasks that must be accomplished with some required level of performance by assessing, for example, speed and errors within the range of usage environment; (2) Learnability: how effectively users can grasp the system within a set time frame, alongside the provided training and user support; (3) Flexibility: allowing time to adapt tasks of the system beyond the predetermined boundaries; (4) Attitude: ensuring users experience minimal level of tiredness, discomfort, frustration, and minimizing personal effort to increase satisfaction and sustained use of the system (74).

> ***Key Definition 2***: Usability is a multifaceted concept that encompasses the extent to which a product can be used by specified users to achieve specific goals with effectiveness, efficiency, ease of use, and learnability, all while ensuring user satisfaction in a specified context of use.

2.1.2 Acceptability

Another crucial construct for evaluating the design of DHTs is acceptability. As Nadal et al. highlighted, the definition of acceptability in DHTs is inconsistent in the literature (75). The most commonly accepted definition of acceptability is "individual's affective attitudes toward a new digital health intervention, usage intentions (e.g., willingness to engage with the intervention), actual usage (frequent interaction with the intervention), and satisfaction after engaging with the intervention" (76). Consequently, acceptability can be measured at

different points, including (a) perception acceptability, which is the pre-use acceptability after hearing about the intervention but before engaging with it; (b) initial use of acceptance, which is the level of acceptance during engagement; and (c) sustained use acceptance measured after engagement with the system (75).

One of the most commonly used technology implementation approaches is the Technology Acceptance Model (TAM) (77). In the TAM, the two constructs that makeup acceptability are perceived ease of use (PEOU) and perceived usefulness (PU). Perceived ease of use (PEOU) is defined as "the degree to which a person believes that using a particular system would be free of effort" (77), p.320), and PU is defined as "the degree to which an individual believes that using a particular technology would be beneficial" (77). The TAM has been described in detail in section 2.2.1.

> ***Key Definition 3***: Acceptability is a crucial factor in digital health research and practice. It is related to the perceived ease of use and usefulness of technology, and it predicts user engagement, intervention effectiveness, and widespread adoption.

2.1.3 Satisfaction

User satisfaction is another vital indicator of the overall success of DHTs. User-centred design (UCD) stipulates that products should be developed by encapsulating every facet of a user's interaction with the system (69). Satisfaction, a construct within usability and acceptability, reflects how a system aligns with a user's needs, expectations, and preferences (78, 79). Within the context of this Ph.D. thesis, evaluating user satisfaction involves understanding to what extent users are content and happy with the DHT and whether it meets the unique needs, preferences, and expectations, that breast and prostate cancer patients, face in managing their mental health. Thus, when looking at satisfaction, we try to understand: *'Does the DHT provide the kind of information, features, and help that users like?*' , *'Does the DHT meet users' expectations?*', and *'Are the users happy with the DHT*?'. Gaining such insights into the user experience is crucial to comprehend the degree of contentment or fulfilment of users, which is influenced by their expectations, perceived usefulness, ease of use, accessibility, and perceived quality of support.

> ***Key Definition 4***: Satisfaction reflects the extent to which users are content and fulfilled with a system and whether the system aligns with their needs, expectations, and preferences.

Figure 2 summarizes various usability, acceptability, and satisfaction aspects, drawing upon the key models and definitions described in the previous sections. This includes Nielsen's definition of usability (70), Shackel's model (74), Davis's TAM (77), and the ISO guidelines (69), each contributing different perspectives and definitions.

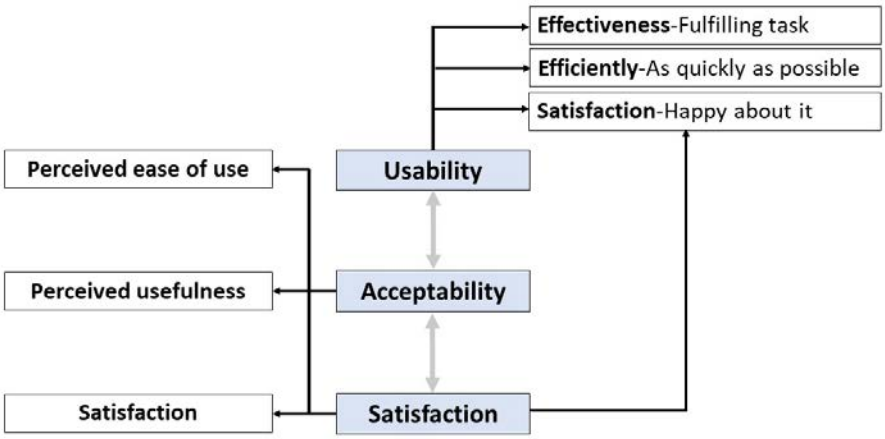


Figure 2. Conceptual framework for the Ph.D. thesis, adopted and modified from Nielson (70), Shackel (74), TAM (77), and ISO 9241-11 (69).

2.1.4 Digital health tools and cancer patients: Why usability, acceptability, and satisfaction matter

A plethora of research supports the effectiveness of digital health tools (DHTs) in managing mental health in many chronic conditions, including breast and prostate cancer (80-83). However, although these tools remain effective, engagement and acceptability among users tend to be suboptimal (76). These challenges are also observed in patients with cancer, especially in the self-management of mental health symptoms (84). In DHTs designed to help cancer patients self-manage mental health symptoms, usability, acceptability, and satisfaction have emerged as critical factors. In a pilot study, Chow et al. evaluated the IntelliCare platform (72). Initially developed for the general population, the IntelliCare platform comprises of a collection of mobile apps that cater to depression and anxiety, employing different strategies, such as mindfulness and healthy sleeping habits, to equip users with long-term coping and management tools (73). Chow et al. evaluated the platform in breast cancer patients and identified areas of improvement (72). They underscored the need to increase the relevance of the IntelliCare platform to cancer patients, compared to the general population, and its perceived usefulness and satisfaction levels for breast cancer patients, thereby increasing user engagement (72). In a systematic review and meta-analysis of RCTs, Singleton et al. examined 32 studies to assess the efficacy of eHealth interventions, patient engagement, and acceptability among

patients with breast cancer (74). They found that eHealth interventions significantly increased quality of life (74). In addition, they noted that these positive outcomes were linked to patient satisfaction, perceived usefulness, and levels of engagement (74). Moreover, Singleton et al. highlighted that interventions that provide disease-relevant information and incorporate interactive support are instrumental in increasing patient engagement (74).

Previous studies have examined both implementation barriers and facilitators of DHTs. In a systematic review of 48 studies by Vis et al., the most frequent determinants of the implementation of eHealth for mood disorders included acceptance of the intervention, including expectations and the appropriateness of the intervention in addressing patients' mental health (85). Similarly, Agochukwu et al. analysed 358 studies in a narrative review (86). They found that older patients with prostate cancer were more inclined to accept and adopt telemedicine when they perceived its potential to enhance their quality of life, that is, perceived usefulness (PU) (86).

2.1.5 Factors influencing usability, acceptability, and satisfaction in DHTs

Several factors influence usability, acceptability, and satisfaction. While healthcare settings and organizational structures significantly shape user experiences, this Ph.D. thesis focuses on individual user factors and DHT characteristics, as discussed in the following sections.

2.1.5.1 Individual factors

Sociodemographic characteristics and digital literacy

Individual factors, such as sex, age, educational level, marital status, ethnicity, and employment status, are associated with the usability, acceptability, and satisfaction of DHTs. In addition, factors such as varied digital literacy and cognitive and emotional states must also be considered in cancer patients. Consequently, UCD highlights the importance of involving end users early in product design (69). However, designing a DHT with high usability, acceptability, and satisfaction across all user groups might not always be achieved.

A literature review by Reiners et al. found that higher age, lower income, and lower education levels were associated with lower eHealth use among patients with chronic conditions (87). A qualitative study by Marklund et al. investigated the differences between the factors found in non-users or seldom users and users (88). Their study found that the level of motivation, how comfortable users were with information technology (IT) tools, and their level of health literacy, impacted how much users used the self-management eHealth tool to manage their chronic disease (88). It is also the case that some individual characteristics are confounded. In a systematic review by Zhang et al.,

several factors, such as older age, female sex, higher education level, living in an urban area, and high social support, were positively associated with high digital literacy among cancer survivors (89). Digital literacy, defined as "an individual's ability to seek, find, understand, and appraise health information from electronic sources and apply that knowledge to address or solve a health problem," is another critical factor in eHealth use, acceptance, and satisfaction (90).

Concurrently, it is evident that an individual's digital literacy and habitual engagement with technology are closely associated with their acceptance, use, and satisfaction with specific DHTs (91). For example, Eshet-Alkatli and Chajut investigated the factors that influenced changes in digital literacy over time (91). They explored how individuals' digital literacy skills can be improved, and whether age plays a role in this process, and found that, regardless of age, older adults can learn new digital skills and adapt to technological advancements, and that adequate training can lead to positive attitudes towards technology and improved digital literacy skills (91). Therefore, identifying how these individual characteristics play a role in the usability and acceptance of DHTs is crucial, so that they can be better tailored to end-users, or interventions can be improved to serve other demographics.

A qualitative systematic review and meta-synthesis by Patel et al. also suggested that users' initial beliefs about DHTs influence how they engage with these tools (92). In addition, environmental factors and personal support are associated with higher engagement, thus leading to the success of DHTs and satisfaction (92).

Mental health status

The use of DHTs among patients with different mental health symptoms has also been partially investigated. Moreover, individuals with poor mental health have different usage patterns and profiles than the general population (93). In a recent usability study, Cillessen et al. examined the predictors of an online mindfulness intervention in cancer patients who experienced distress (93). Patients were categorized as non-users, minimal users, and active users based on the number of practices and completed number of practices. Overall, patients with conscientiousness, which reflects a low ability to follow through with practices, were more likely to be non-users or minimal users (93). More importantly, Cillessen et al. reinforced the need for adopting and tailoring eHealth interventions for cancer patients, taking into account their mental capability (93).

2.1.5.2 Design, content, and user's perceptions

One of the cornerstones in designing DHTs is the design, content, and users' perception, which affects the usability, acceptability, and satisfaction of these tools, especially what aspects are valued by users and how they might be improved. Baumal and Kane analysed

product design quality using available data to predict how users engage with self-guided eHealth interventions on mobile and web platforms (94). They found that user engagement was correlated with how successfully an intervention can engage users in goal setting, encouraging them to complete goals, and the extent to which users feel accepted and supported by the intervention (94). Another important aspect of mobile app engagement is the visual design and content provided (94).

In a study by Gomersall et al. (95), the acceptability of a text message-enhanced clinical exercise rehabilitation program for patients with cancer was evaluated. Their findings showed that the content and design of the text messages played a crucial role in the acceptability of the intervention. However, while most participants reported high satisfaction levels and perceived usefulness of the text messages, a subset found them unnecessary and unhelpful, leading to dropouts (95). The importance of customizing the relevancy (96), content (94, 95, 97), and design (94, 98) of DHTs with individual preferences to optimize usability, acceptability, and engagement has been noted. Beyond the technical aspects of DHT functions, perceived ease of use (96, 99) and usefulness (99, 100) emerged as significant factors driving acceptability.

2.1.6 Evaluating usability, acceptability, and satisfaction in DHTs

Several metrics measure systems' usability, acceptability, and satisfaction depending on which dimensions are being studied, the stage of the UCD, the type of technology or product used, and the context of use (101). To evaluate DHTs, both formative and summative evaluations are conducted. Formative evaluations assess an eHealth intervention to improve the product and ensure the right goals are met (102). In contrast, summative evaluations focus on benchmarking the 'final' product (102). These evaluations involve quantitative and qualitative approaches, with formative usability evaluations heavily using qualitative methods. Formative evaluations include think-aloud protocols (103), cognitive walkthroughs (104), and heuristic evaluations (105). Here, we first describe the three widely used measures for summative evaluations, which the Ph.D. thesis focuses on, and then describe one widely used formative evaluation.

Standardized questionnaires

Klaasen et al. reviewed 127 publications that evaluated telemedicine systems and found that 80 of the 127 identified publications (69%) used questionnaires to assess usability (106). Some standardized questionnaires include the Post-Study System Usability Questionnaire (PSSUQ) (107), Software Usability Measurement Inventory (SUMI) (108), and System Usability Scale (SUS) (109). Among these questionnaires, the SUS is one of the most used usability scales to assess the attributes of learnability and satisfaction dimension of usability (109, 110). The SUS is a ten-item subjective scale that quantifies how well users interact and use the product covering, the ease of using different functionalities,

assessing any technical issues during usage, and the user's impression and benefits of using the system (109). Each item's score ranges from 0 to 4, and the sum of the items is multiplied by 2.5 to give a transformed composite scale ranging from 0 to 100, and a score of 68 is considered above average (111). By comparing the SUS with other methods, such as task metrics, Broekhuis et al. recommended that the SUS should be complemented with other usability metrics for the best indication of the usability of a DHT (101). The SUS is important when conducting summative evaluations, which is the focus of this Ph.D. thesis.

Task performance metrics

In addition to scales, task performance is a metric for gauging acceptability and usability (101, 112). Objective evaluations, such as usage logs and the number of completed practices, sessions, or tasks, are considered, by some, to be superior to questionnaires (101).

Qualitative questionnaires

While Maramba et al. acknowledged that quantitative questionnaires and scales are the most commonly used methods to assess usability, open-ended questionnaires (qualitative methods) are also used (112). Qualitative methods that include open-ended questions can help pinpoint usability or acceptability problems from the end-users' point of view. Satisfaction can also be assessed using interviews, which inquire about user experiences, expectations, and perceived benefits. These critical questions can be addressed by analysing user feedback and conducting qualitative interviews to capture the depth of the user experiences.

Heuristics evaluation

In the field of usability engineering, Nielsen proposed a usability inspection method called heuristic evaluation (113). Heuristic evaluation involves expert evaluators assessing the user interface against a set of ten heuristics covering the various facets of usability (105, 113). These ten heuristics emphasize the importance of (1) clear feedback to users about system status; (2) the use of familiar phrases and concepts by the user; (3) allowing users freedom and control in navigation; (4) maintaining consistency and standards across the interface; (5) prioritizing error prevention; (6) minimizing cognitive load by eliminating the need for recall; (7) flexibility and efficiency of use, catering to both novice and expert users; (8) maintaining a clean and minimalistic design; (9) providing clear error messages and suggesting a solution; and (10) offering accessible help and documentation when necessary (113, 114). These evaluations are used as formative evaluations to determine design problems early in the design phase (115).

In conclusion, although each evaluation method discussed has distinct advantages, employing diverse approaches to assess usability, acceptability, and satisfaction is more

advantageous (112). This multiplicity of methods allows for a more thorough and nuanced understanding, capturing various facets and dimensions of user experience with the DHT.

2.2 Theoretical background

Considering the specific DHT assessed in this thesis and its specific context of use, two theoretical models were employed to place the research in context. This approach ensures the research is grounded in existing theory, providing a framework for exploring and understanding the variables influencing usability, acceptability, and satisfaction.

2.2.1 Technology Acceptance Model

The Technology Acceptance Model (TAM) has been described in previous sections as one of the conceptual frameworks used to understand acceptability through two key variables- Perceived usefulness (PU) and Perceived ease of use (PEOU) (77). This model, introduced by Davis in 1989 (77), was used to define these two constructs while conveying the underlying assumptions behind their effect on acceptability. As a theoretical framework, TAM provides a model that explains and predicts user behaviour through PU and PEOU, influencing users' decisions to accept and use technology. The TAM has been empirically validated across various contexts in health care for cancer patients, including acceptance and use of DHTs in palliative care (116), ambulatory care settings (117), mammography (118), self-management (119), and technologies including wearables (120) and mobile apps (117, 121), making it a reliable theory to explain and predict user behaviour towards new DHTs. While TAM is a widely used theory, it has not been devoid of criticism. For example, Holden and Karsh noted that several factors should be considered to enhance this model and thus increase its predictive power (122). One suggestion is integrating qualitative methods to enhance the understanding of users' perspectives further. Another is exploring factors that influence the long-term use of the technology, as the TAM might primarily indicate initial acceptance and use (122). The need to further refine the TAM was corroborated in a systematic review of TAM in health informatics by Rahimi et al. (123). Others have also pointed out that the initial model does not fully account for the complexity of technology acceptance and does not consider external factors that might influence technology adoption, such as organizational (124, 125), technological (124), and environmental contexts (126).

In this Ph.D. thesis, the TAM was modified to include individual characteristics influencing both PU and PEOU, as individual factors such as anxiety or stress (127) and sociodemographic characteristics (87, 89) have been shown to influence the acceptance and use of DHTs. Figure 3 shows the TAM adopted for this Ph.D. thesis.

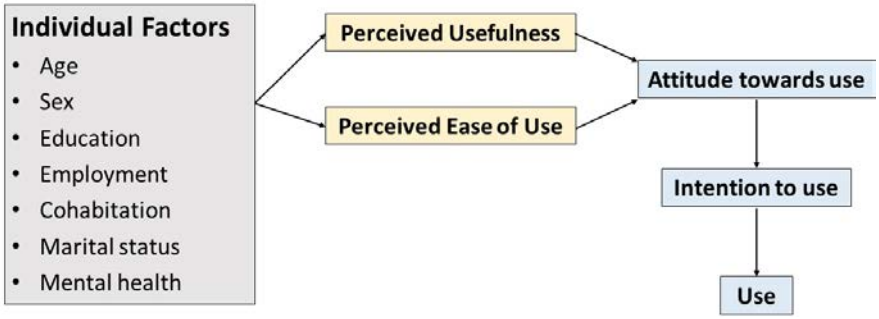


Figure 3. Theoretical framework for this Ph.D. thesis based on the TAM (77).

2.2.2 Information System success model

A second model was used to fully capture all three aspects, -usability, acceptability, and satisfaction. The information systems (IS) success model, also known as the DeLone and McLean IS success model, was introduced in 1992 by Deloe and McLean (79). The initial model identified six dimensions for assessing IS success: *System Quality*, *Information Quality, Use, User Satisfaction, Individual Impact, and Organizational Impact* (79). In their ten-year update, the dimension evolved into *Information Quality, System Quality, Service Quality, Intention to Use, Use, User Satisfaction, and Net Benefits*. (1) **System Quality** refers to the technical aspect of the system, evaluating its reliability, ease of use, and performance; (2) **Information Quality** focuses on the output of the IS, assessing its relevance, accuracy, and timeliness; (3) **Service Quality** centres on the support delivered to system users, examining the quality of service from personnel; (4) **Use/Intention to Use** looks into actual utilization or the intention to utilize the system; (5) **User Satisfaction** evaluates the users' contentment and overall satisfaction with the system; and (6) **Net Benefits** encompasses the tangible and intangible gains achieved through the use of the system at different levels (79). Thus, these dimensions seek to evaluate and determine the success of a system, providing a comprehensive lens through which the system can be further improved (79). Figure 4 shows how each dimension is interrelated.

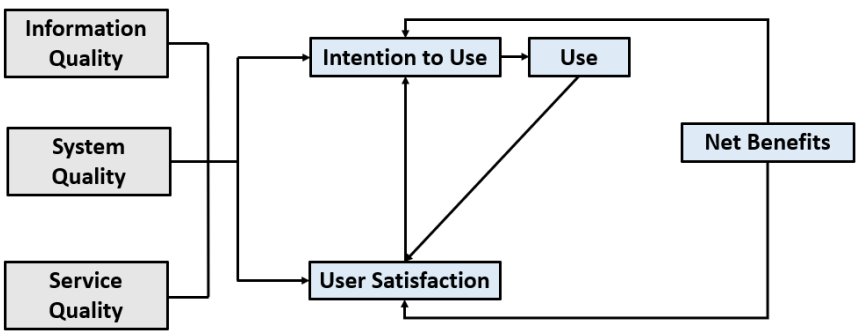


Figure 4. Information System (IS) Success Model (79).

Although the IS success model has been substantiated as a robust framework for assessing different facets of satisfaction, usability, and net benefits in non-health sectors (128), there is a limited number of studies applying the IS success model to DHTs. In one study, among those that used this theoretical model, the IS success model was used to examine how health information sites lead to user satisfaction and benefits by examining information, system, and service quality (129). Two additional studies used this model to evaluate a healthcare information system in a hospital setting (130, 131).

While the IS success model has not been predominantly utilized within the domain of DHTs, this Ph.D. thesis makes a case for its valuable use, harnessing its comprehensive framework to examine, evaluate, and enhance DHT adoption. The subsequent paragraph explains the implementation of the IS success model in this context. First, the model allows for a comprehensive assessment, enabling a meticulous examination of the various components of the DHT, spanning from system quality to tangible and intangible net benefits. Second, the IS success model encompasses technological facets, such as system and information quality, and user-oriented aspects, such as user satisfaction, providing a holistic evaluation. Third, analogous to the TAM, the IS success model acknowledges the importance of net benefits, which resemble PU in TAM, to ensure the efficacy of a DHT. Fourth, the nuanced distinctions between each dimension of the IS Model assist in accurately identifying the strengths and potential areas for enhancement across the multiple dimensions of the DHT. Lastly, the IS success model can be integrated with alternative models such as TAM, providing a more robust and context-specific theoretical framework.

2.3 Rationale of the thesis

In the context of the advancing landscape of digital healthcare, this Ph.D. thesis seeks to offer a relevant exploration. While the role of DHTs in the management of mental health has gained traction in the past decade, a noticeable gap remains: the increase in studies on DHT usability testing has lagged compared to those focused on effectiveness. This discrepancy is highlighted by Marmba et al., who demonstrated that under a third of studies, examining various DHTs, conducted usability testing (112). Given the roles of usability, acceptability, and satisfaction of DHTs in determining patient outcomes, evaluating these aspects becomes imperative.

This Ph.D. thesis follows the clinical evaluation of the NEVERMIND system, short for NEurobehavioural predictiVE and peRsonalised Modelling of depressIve symptoms duriNg primary somatic Diseases with ICT-enabled self-management procedures. The NEVERMIND system comprises a mobile app user interface and a sensorized shirt (shirt). The mobile app and shirt collect mental and physical parameters data through questionnaires and physiological data (e.g., heart rate variability and respiration),

respectively. Based on the severity of the patient's symptoms, patients are directed to personalized lifestyle behavioural advice, mindfulness, cognitive behavioural therapy, or referral to mental health care. These components embedded within the NEVERMIND system are designed to reduce and, secondarily, prevent mental health symptoms. The effectiveness of the NEVERMIND system in reducing mental health symptoms was evaluated in a real-world clinical setting, parallel-group, and pragmatic RCT in patients with myocardial infarction, kidney failure, amputation, and breast and prostate cancer. The NEVERMIND system was effective in reducing overall depressive symptoms in all patients (65).

While the NEVERMIND system has been shown to be effective as a proof of concept integrating diverse intervention components to reduce depressive symptoms, the focus of this Ph.D. thesis is to appraise its usability, acceptability, and satisfaction, specifically among patients with breast and prostate cancer. By examining these three dimensions and understanding their determinants and facilitators, this thesis provides valuable insights into the broader landscape of digital health tools (DHTs) and their potential to augment mental health management in holistic care for patients with both cancer and mental health problems. Beyond its immediate findings, this research can inform further development of the system and other analogous systems. Ultimately, this Ph.D. project focuses on the interplay among technology, mental health, and cancer management.

3 Aims and objectives

3.1 Overall Aim

The overarching aim of this Ph.D. project is to delve deeper into the usability, acceptability, and patient satisfaction of the NEVERMIND system among patients with breast and prostate cancer.

3.2 Specific Aims

This Ph.D. thesis aims to outline the NEVERMIND system's usability and acceptability concerning sociodemographic parameters, baseline mental well-being, user engagement, perceived usefulness, perceived ease of use and clinical effectiveness (Studies I-III). To better understand users' experiences and their satisfaction, we analysed user responses using qualitative methods in Study IV. The aims of each study included in this thesis are provided below.

Study I. To study the association between sociodemographic characteristics and different measures of the usability of the NEVERMIND system.

Study II. To examine the relationship between baseline depressive and stress symptoms, sex, education, usability, acceptability, and use of the NEVERMIND system.

Study III. To identify how the NEVERMIND system's usability, use, and acceptability relate to its clinical effectiveness.

Study IV. To investigate the overall satisfaction of prostate and breast cancer patients with the NEVERMIND system based on user experience.

4 Overview of the thesis

The four studies included in this thesis address a distinct facet of the user-centric experience and evaluation of the NEVERMIND system, aimed at understanding the intricacies of its usability, acceptability, and satisfaction among cancer patients.

Study I delves into sociodemographic variables associated with the usability of the NEVERMIND system. This study involves the analysis of factors such as age, gender, marital status, educational level, employment status, and cohabitation. By pinpointing these variables, this study sets the stage for understanding which demographic groups benefit most from the system and where further tailoring might be essential. It aims to answer the question, "Which sociodemographic characteristics are associated with the usability of the NEVERMIND system?"

Study II extends the analysis to baseline sociodemographic characteristics and baseline mental health status and their relationship with system usability and acceptability. Recognizing that different individual characteristics can shape both the perception and the frequency of interactions with the system, this study identifies if sociodemographic characteristics, depression, and stress levels influence the use of NEVERMIND for patients. In addition, the relationship between different usability and acceptability parameters and use of the NEVERMIND system is explored. The central query here is: "How do baseline mental health symptoms, sex, education, early engagement, and acceptability affect the use of the NEVERMIND system?"

Study III evaluates the relationship between the NEVERMIND system's usability, acceptability, and clinical efficacy. Here, the primary interest is determining whether those who find the system more user-friendly and acceptable gain more significant clinical benefits, evaluated as the reduction of depressive and stress symptoms from baseline to 12-week mark. The overarching question is: "How does the usability and acceptability of the NEVERMIND system influence its clinical effectiveness in reducing depressive and stress symptoms?"

Finally, Study IV delves into patients' overall satisfaction with the NEVERMIND system while concurrently examining how satisfaction differs between breast cancer (female) and prostate cancer (male) users. This study seeks to answer the following questions: (1) "What is the level of overall satisfaction among users of the NEVERMIND system?" (2) "Which elements of user experience contribute to user satisfaction or dissatisfaction with the NEVERMIND system?", and (3) "How does satisfaction with the NEVERMIND system differ between males (prostate cancer patients) and females (breast cancer patients), and what aspects of the system are valued or problematic for each gender?"

Figure 5 provides a summary of the four studies.

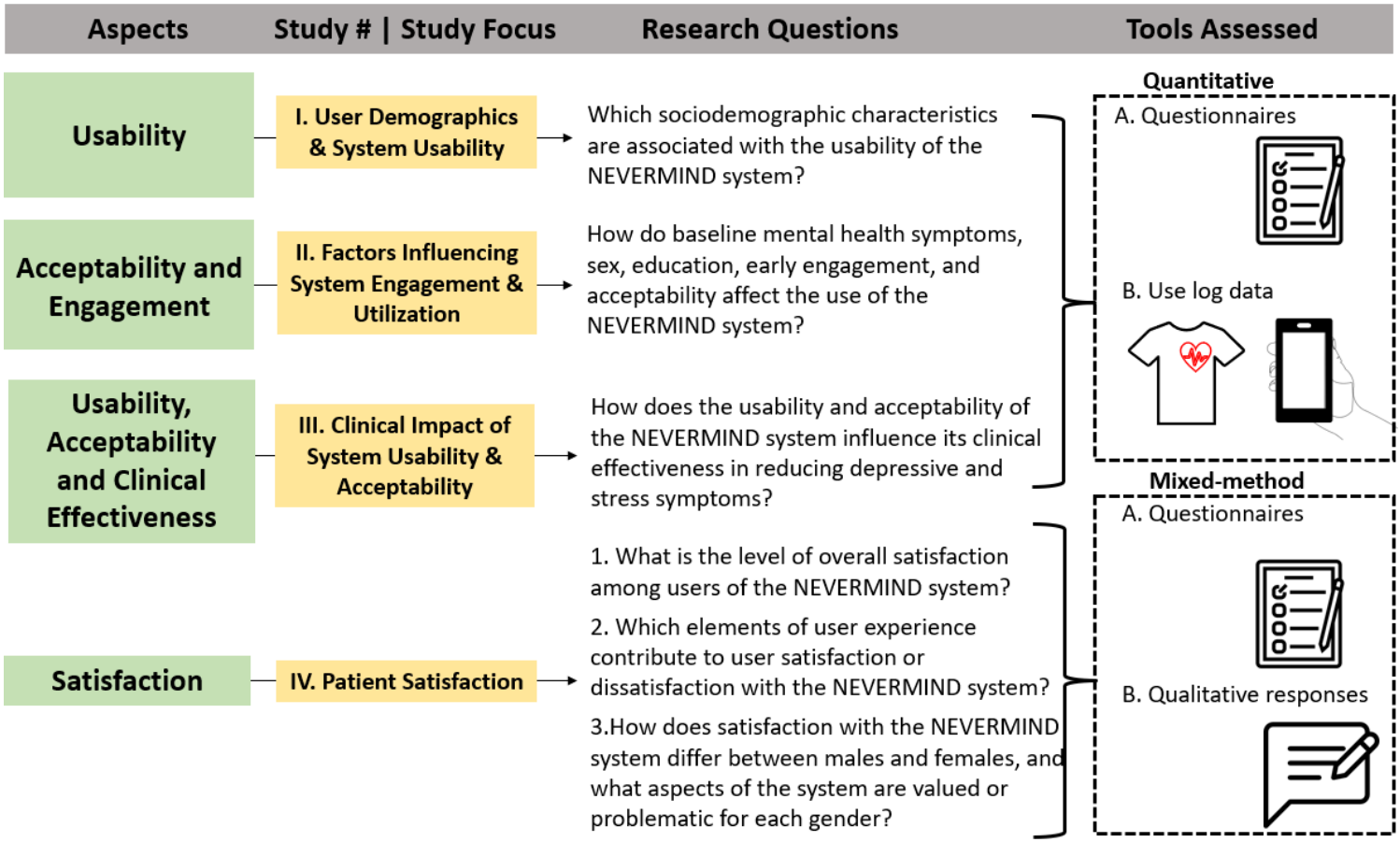


Figure 5. Schematic illustration of the four studies included in this Ph.D. thesis.

5 Materials and Methods

5.1 Study Design

A description of the NEVERMIND RCT is provided below to provide the context of the study design on which the Ph.D. project is based. After the description, the subsequent sections will focus only on parts that are within the scope of this Ph.D. thesis.

The NEVERMIND RCT was conducted from December 2017 to December 2019, with the last follow-up conducted in June 2020, where 425 participants were recruited. This RCT study was a parallel-group and pragmatic trial conducted in Pisa and Turin in Italy and Lisbon in Portugal. Participants with kidney failure were recruited from clinical centres in Pisa and Turin, whereas patients with breast and prostate cancer were recruited from Turin. Patients with myocardial infarction and leg amputation were recruited from a clinical centre in Lisbon. The completed study design for the RCT is described in the study protocol (132).

The following section provides a detailed description of the NEVERMIND system, establishing a foundational understanding critical for successfully exploring its usability, acceptability, and satisfaction.

5.1.1 Description of the NEVERMIND system

5.1.1.1 The Mobile app

The mobile app features a user interface that consistently tracks patients' mental well-being and addresses mental health symptoms in real-time (Figure 6).

Figure 6. Screenshot of the Mobile app: The first component of the NEVERMIND system.

The mobile user interface is enhanced with an avatar and voice monitoring capability to articulate system notifications. Furthermore, the user interface can be customized to align with the patient's dietary needs, physical exercise abilities, and personal preferences, offering lifestyle advice designed to boost the users' physical well-being in relation to their cancer diagnosis. Below is an elaboration of the different modules within the mobile application.

Mood state monitoring platform (What's Up)

The Mood State Monitoring platform, named "What's Up" within the NEVERMIND app, aims to provide a detailed, real-time insight into the user's mental health through a sequence of daily questions and monitoring of mental health status. Below is a breakdown of the platform's components and functionalities.

I. *Daily check-ins*
   - **Objective**: To establish a baseline evaluation of a user's mental state using daily questions.
   - **Content**: Users were provided with three daily questions: Q1 *'How are you feeling today?'*, Q2 *'How was your sleep?'*, and Q3 *'How was your day?'*, where the responses were used to assess mental state.

II. *Advanced inquiry on mental state*
   - **Objective**: To obtain more information about mental health aspects based on responses to the three questions (described above).
   - **Content**: Depending on the initial responses, a second level of inquiry was triggered to examine users' levels of depression and anxiety. Q1 triggered three more questions: Q4 *'Do you feel sad, down, or uninterested in life?'*, Q5 *'Do you feel anxious or nervous?'*. Q3 triggered two additional questions: Q7. *'How would you rate the amount of stress today?'*, and Q8 *'How would you rate your ability to handle stress?'*

III. *Clinical assessment of mental state*
   - **Objective**: To clinically evaluate users' mental and emotional well-being based on responses to the three questions (described above).
   - **Content**: A third level of inquiry included clinically validated psychometric questionnaires, such as the 9-item Patient Health Questionnaire (PHQ-9), the Paykel Suicide Scale (PSS), the 7-item Generalized Anxiety Disorder Scale (AIS), and the 5-item World Health Organization Well-Being Index (WHO-5). After the first assessment, they are administered every 14 days.

IV. *Level of Care (LoC) assignment*
   - **Objective**: To direct users to an appropriate LoC based on user data.
   - **Content**: Users were guided to different LoCs depending on their depression, anxiety, or stress symptoms, as indicated by their psychometric scale scores (Figure 7).

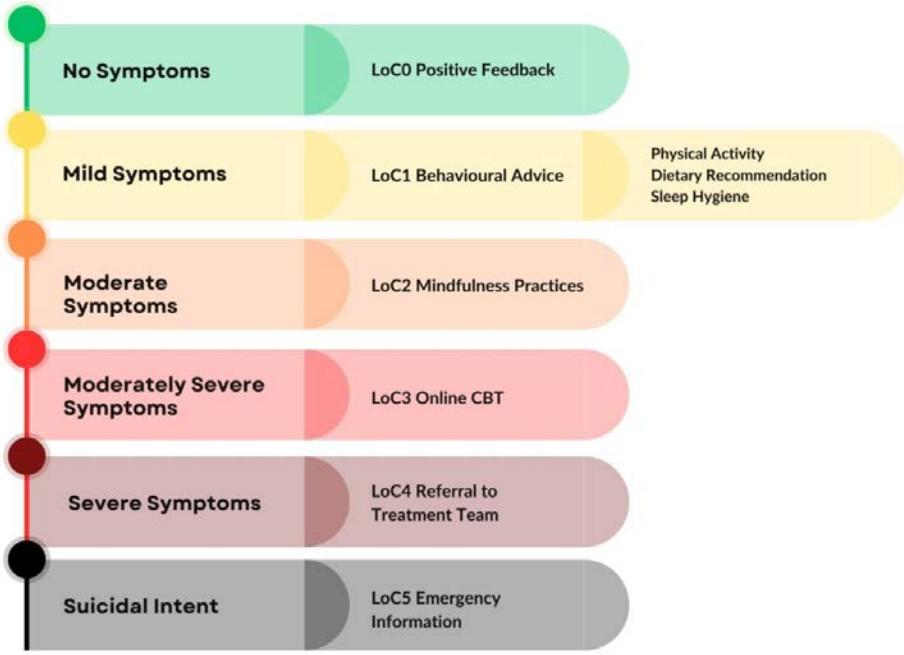


Figure 7. The Six Levels of Care (LoC) and their corresponding interventions.

Level of Care 0 (LoC0) caters to users managing their mental health; however, the app still positively reinforces everyday activities. In contrast, LoC1 provides personalized behavioural advice about sleep, physical activity, and diet to those exhibiting mild mental health symptoms. Further details about these modules are explained in the next section. Level of Care 2 (LoC2) and LoC3 recommend mindfulness and online CBT, respectively, for users exhibiting moderate-to-moderately severe symptoms. While the last two LoCs (referral to the treatment team and emergency information) fall beyond the scope of this Ph.D. thesis, they are illustrated in Figure 7 to provide a comprehensive overview of the interventions within the NEVERMIND system.

My Health module

The module tracks physiological data and provides educational content to users. Below is a breakdown of the educational content provided to users.

V. *Monitoring weight and blood pressure*
   - **Objective**: To provide users with a history of their weight and blood pressure.
   - **Content**: Users reported their weights and blood pressure to monitor their progress. A visual chart allowed users to observe the changes in every entry.

VI. *Educational content*:
   - **Objective**: To provide users with well-rounded, easy-to-understand, and in-depth information about their cancer diagnosis.

- **Content**: A total of 17 contents with disease-specific information, expert medical insights, a guide on managing life quality during treatment, personal narratives from cancer survivors, and a catalogue of additional resources and support networks.

Physical activity module

The physical activity module within the application features customized physical exercise programs tailored to align with the capacity and capabilities assessment of the user conducted during the enrolment process. A detailed outline of the physical exercise module is provided below.

I. *Assessment of individual capabilities*
   - **Objective**: To build a personalized plan based on a user's physical functionality, including any disabilities
   - **Content**: The clinician evaluated movement patterns and identified physical deficits to build a personalized plan to reinforce diaphragm mobility, resistance, balance, and aerobic exercises

II. *Exercises*
   - **Objective:** To set up specific modules based on the individual capabilities
   - **Content:** Physical activity module with a specific exercise program tailored to the physical capacity of the user. These programs included (according to difficulty level) diaphragm, core, leg stance, leg stance advanced, and aerobic exercises.

III. *Introduction and tutorial*
   - **Objective:** To introduce and familiarize users with the exercises
   - **Content:** A few textual introductions for users, along with a video tutorial for each exercise before the start of the exercise.

IV. *Exercise tips*
   - **Objective:** To have users perform the exercises proposed in the module
   - **Content:** Guide messages on how to continue after the introduction and tutorial. A timer was also included on the screen to support users in keeping track of each exercise.

V. *Feedback from users*
   - **Objective:** To progressively increase or decrease the difficult levels of consequent activities following each user's advancements and feedback.
   - **Content:** A questionnaire about the level of difficulty of the exercise performed.

Dietary recommendation module

The dietary recommendation (dietary) module utilizes a mechanism to enhance intrinsic motivation among patients. This interactive module allows users to select a specific

recommended diet based on ten categories available to be launched, including *breakfast like a king*, *the quality of protein*, *healthy routine, healthy meal, carbohydrates vs. sugar, fats and tastes, healthy chewing, alcohol, water vs. sugary drinks and vegetables and fruits* to focus on for improvement. Below is a refined breakdown of the dietary module.

I. *Initial setup and assessment*
   - **Objective**: To build a personalized plan according to clinician recommendations, user preferences, and priorities.
   - **Content**: Users are introduced to the ten categories, and a clinician sets up dietary recommendations, selecting categories of food recommendations coupled with users' priorities and preferences based on a questionnaire about their dietary habits.

II. *Educational content about dietary categories*
   - **Objective:** To help users adopt a healthy diet by providing educational content for each category.
   - **Content:** Description of each of the ten categories, and the user can see the 'read' status of the educational content once it is completed.

III. *User personalization and goal setting*
   - **Objective:** To set dietary goals for the users.
   - **Content:** Users prioritize the list of recommended categories by dragging items in the desired order, where they can alter their priorities at any time. In the chosen categories, users received a questionnaire to identify unhealthy dietary habits within each category. If an unhealthy habit is identified, then a corresponding goal is proposed to the user.

VI. Monitoring and progress tracking
   - **Objective**: To track the ongoing status of 'set' goals.
   - **Content**: The user interface shows the ongoing status, achievements, and goal completion percentage.

VII. *Recipes and tips*
   - **Objective:** To provide support to users in achieving goals.
   - **Content:** Recipes tailored to a user's condition, dietary predilections, and specific categories. These recipes also included images and video tutorials.

IV. *Continuous feedback*
   - **Objective:** To continuously track and adapt goals based on users' goals and progress and enhance performance on their 'set' goals subsequently.
   - **Content:** Users interacted with different diet categories and modules and provided feedback about their ongoing status to receive feedback.

Sleep module

The sleep module was designed to monitor sleep quality via a questionnaire and provides a wealth of educational content and calming practices. These resources aim to enhance sleep quality and provide strategies for managing insomnia and other sleep-related issues. By consistently tracking and analysing sleep patterns, the module offers personalized advice to help users develop healthy sleep habits and improve their overall well-being. A detailed outline of the sleep module is provided below.

I. *Initial interaction*
   - **Objective**: To familiarize users with the sleep module
   - **Content**: Introduction to the sleep module dashboard and guidance on how to perform sleep exercises.

II. *Dashboard Navigation and Exploration*
   - **Objective:** To provide users with a comprehensive list of support and interactive items to promote healthy sleep hygiene.
   - **Content:** A list of exercise recommendations for the current day where users can view historical responses to the question, 'How was your sleep?'. These data were provided in both text and graphical formats, representing analyses of previous quality of sleep and previous sleep practices. The dashboard also included tips on achieving higher quality sleep (e.g., positions during sleep and how to fall asleep quickly).

III. Sleep practice
   - **Objective**: To improve users' sleep quality.
   - **Content**: Users engage in practices such as 'self-contact' before sleeping. Users put on the shirt (described in Section 5.1.1.2) before sleeping. The practice was delivered through audio or video format 30 minutes before the intended sleeping time.

IV. *Daily Sleep Quality Assessment*
   - **Objective:** To assess users' sleep quality.
   - **Content:** Users were promoted with daily questions regarding sleep quality during the previous night. If the users completed a sleep exercise, they evaluated how much it helped them sleep.

V. *Continuous monitoring and feedback*
   - **Objective:** To offer supportive and applicable sleep practices.
   - **Content:** Users continually track their sleep quality over time, and receive tailored tips based on their responses to daily sleep and post-exercise questions.

Mindfulness module

The app's mindfulness module allowed users to participate in a mindfulness program built on smartphones and wearable technology. The comprehensive program includes audio sessions and video tutorials and introduces a progressive, personalized course that functions in accordance with a specific schedule. The following is a refined breakdown of the mindfulness module.

I. *Introduction to the mindfulness module*
   - **Objective**: To familiarize users with the mindfulness module.
   - **Content**: In the first phase, spanning 2-3 weeks, users are introduced to the mindfulness module dashboard through text and video tutorials on how to perform the practices and experiences it offers.

II. *Mindfulness Practices*
   - **Objective:** To engage users in mindfulness exercises.
   - **Content:** The mindfulness program offers sessions that are either 10 or 25 minutes long and include practices such as yoga and grounding exercises. Users had the option to perform the sessions while wearing or not wearing the shirt (described in Section 5.1.1.2).

III. Biofeedback during practices
   - **Objective**: To provide users with real-time physiological data and feedback during practice while wearing the shirt.
   - **Content**: Displayed physiological data (e.g., heart and respiratory rates) collected via the shirt. Users received feedback on changes, for example, in their heart rate during mindfulness practices, both in numbers and visually, showing percentage changes in heart rate and respiration rate.

IV. *Diary of Experiences*
   - **Objective:** To engage users in cognitive exercises related to their daily experiences based on situations presented (e.g., positive events, listening to nature, negative events, and welcoming emotions in the body).
   - **Content:** The concept and importance of recording experiences are explained to the users. Users can record, review, and access their experiences.

V. *Progress and Personalization*
   - **Objective:** To offer a personalized mindfulness journey based on user input and progress.
   - **Content:** Over 6-7 weeks, the app suggests practices that align with the user's personality, emotional style, and emotions reported throughout the day. Once users have done a mindfulness practice, a shorter version (1 min) of the practice is recommended daily. Users were also asked to provide problems with the experience, emotions, and feelings after each session.

Online CBT (Deprexis)

Below is a short description because only some users used the Deprexis module. Deprexis is an evidence-based online CBT (133) provided to patients at Level of Care 3 (LoC3). In this case, users are directed to log into a different system (Deprexis system) by registering with their email and password. Deprexis includes 11 tailored modules, ranging from 30 min to an hour. These modules, using interactive tools, are (1) psychoeducation and understanding of perceived causes of depression, (2) behavioural activation, (3) cognitive modification, (4) acceptance and mindfulness, (5) interpersonal skills, (6) relaxation, exercise, and lifestyle, (7) problem-solving techniques, (8) expressive writing and forgiveness, (9) positive psychology interventions, (10) emotion-focussed interventions, and (11) a summary/review module.

5.1.1.2 Shirt

The NEVERMIND wearable monitoring system consists of a shirt, a portable data logger, and a docking station (Figure 8).

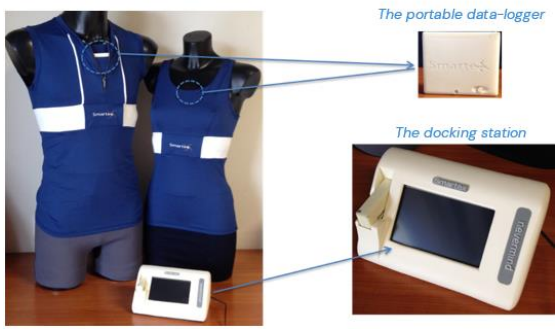


Figure 8. The Shirt: The second component of the NEVERMIND system.

This wearable monitoring platform has been designed to provide comfort and practical utility, and to be integrated into daily life while providing clinical monitoring. While users are free to wear the shirt as frequently as desired, they are instructed to wear it at least twice a week, especially when practicing mindfulness and sleep exercises. The app receives biofeedback on the user's respiratory and heart rates when the shirt is worn during mindfulness and sleep practices. This information is then displayed on the screen while the user is practicing.

Sensing platform

I. Shirt design

The shirt, designed for males and females (Figure 8), comes in cotton or a Meryl® Skinlife artificial fibre, chosen for their wearability and comfort. The shirts were made in different sizes to accommodate users and the data logger.

II. Data logger implementation

The data logger, attached to the shirt, collects physiological data. Utilizing signal processing techniques, the data logger extracts pertinent biomedical features from the gathered data. These features broadly fall into three domains: the intricacies of movement dynamics, the variability of heart rate as detected by electrocardiogram readings, and the patterns present in respiratory dynamics.

Docking station

The docking station serves as a charging station for the data logger and processes the collected physiological data. After a session with the shirt, the users placed the accompanying data logger into the docking station. The docking station was the central hub for data management. Data recording operations, including starting and stopping, were managed through the mobile app. The docking station automatically retrieves data from the embedded data logger and wirelessly sends the extracted data to the NEVERMIND server.

Integration of Decision Support System (DSS)

The DSS comprises of (1) a real-time module embedded within the NEVERMIND mobile app, providing immediate patient feedback, and (2) an updater module to continually refine prediction models for patient depressive symptoms and well-being based on observed patterns.

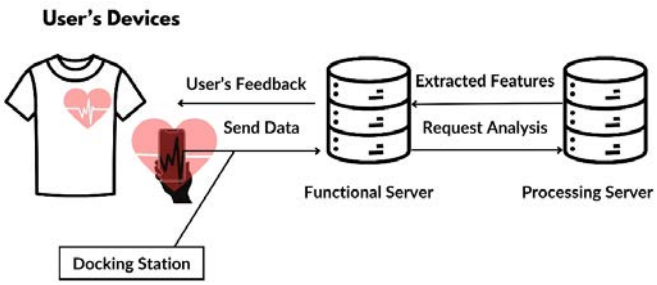


Figure 9. Schematic diagram illustrating the data flow within the NEVERMIND system.

In conclusion, utilizing the mobile app and shirt, the NEVERMIND system fosters data-driven mental health support interventions by providing comprehensive monitoring and personalized feedback tailored to the user's needs. Please refer to Figure 9 to visualize the data flow within the NEVERMIND system.

5.2 Overview of the study participants

Participants were recruited to the NEVERMIND RCT from December 2017 to December 2019. The RCT was designed to allocate half of the patients to receive the NEVERMIND system, and the other half to receive treatment as usual (control). This Ph.D. project uses cross-sectional data from the NEVERMIND RCT, focusing on patients with breast and

prostate cancers who used the NEVERMIND system for 12 weeks for studies I, II, and IV; Study III also includes participants in the control group to first evaluate the effectiveness of the NEVERMIND system in reducing depressive symptoms between those who were in the control group and those who were in the NEVERMIND system.

5.2.1.1 Selection criteria

Participants were recruited for the study according to the inclusion and exclusion criteria, detailed in Table 1. Patients with breast cancer were recruited from the Breast Unit-Oncology Department at Città della Salute e della Scienza di Torino University Hospital in Turin, Italy through the recommendations from oncologists (65). Those diagnosed with prostate cancer were recruited from San Luigia Gonzaga University Hospital and Città della Salute e della Scienza di Torino University Hospital in Turin, Italy from inpatient registers and through referrals from the Urology departments (65). Additionally, digital literacy was gauged in the NEVERMIND RCT study as 'Basic skills in using a smartphone' which inquired if users could send and receive emails on their phone.

Table 1. Participant Eligibility Criteria: Inclusions and Exclusions.

Inclusion Criteria	**Exclusion Criteria**
Adult individuals aged over 18 years	Patients diagnosed with stages of Breast and Prostate Cancer other than specified
Fluency in the Italian language	Major psychiatric disorder diagnosis (like bipolar disorder, psychosis, severe suicidality) except for depression, unless already receiving treatment
Diagnosed with advanced stage IV Prostate Cancer, having completed all treatments except for adjuvant androgen-deprivation therapy (ADT) at least a month prior.	Suicidal ideation within four weeks preceding study enrolment
Diagnosed with advanced stage III or IV Breast Cancer, having completed all treatments except for hormonal or trastuzumab therapy at least a month prior.	Suicidal ideation within four weeks preceding study enrolment
Basic skills in using a smartphone	Substance abuse disorders
	Undergoing psychological therapy involving mindfulness or similar relaxation methods or in psychotherapy for less than 6 months at the study enrolment time
	Pregnancy
	Conditions with the potential to influence short-term survival
	Inability to partake in study procedures, including giving informed consent
	Participation in any concurrent clinical trial that might conflict with the objectives or safety measures of this study

Figure 10 presents the CONSORT diagram detailing the participant flow through the various stages of the study.

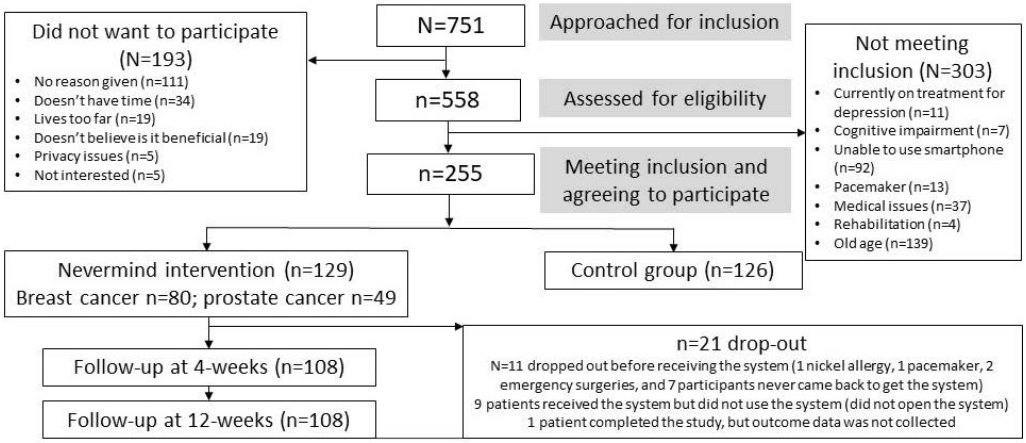


Figure 10. CONSORT Diagram illustrating participant flow.

A total of 751 patients with breast and prostate cancer were approached for inclusion, of which 558 (74.3%) were assessed for eligibility. Of the 558, 255 (45.7%) met the inclusion criteria and agreed to participate. Participants were then allocated to the NEVERMIND system (n=129) or the control group (n=126). Of the 21 who dropped out after being allocated to the NEVERMIND system, 11 (52%) dropped out before receiving the system due to various reasons, such as nickel allergy and emergency surgery (Figure 10). The remaining 10 (48%) participants either did not use the system or did not have any outcome data collected.

5.3 Data collection

The data for Studies I-IV were retrieved from the NEVERMIND RCT. All participants In the NEVERMIND trial underwent initial evaluations at baseline by a team of healthcare professionals, and researchers trained to standardize data collection procedures. The baseline questionnaires included questions about sociodemographic characteristics and mental health symptoms. The same mental health questionnaires were administered at 12 weeks. Participants in the NEVERMIND intervention group received additional follow-up questionnaires at four and 12 weeks. The following sections cover the questionnaires and assessments used in Studies I-IV.

5.3.1 Assessment of mental health symptoms

5.3.1.1 Depression

Depressive symptoms were measured using the BDI-II (134). The BDI-II is a widely used 21-item self-report inventory that measures the severity of depressive symptoms in adults and adolescents, with each item rated on a scale of 0 to 3 based on the intensity of the symptom (135, 136). The BDI-II score is calculated by adding the scores of its 21 items, with total scores ranging from 0 to 63, with higher scores signifying more severe depressive symptoms (135, 136).

5.3.1.2 Stress

Stress symptoms were measured using the DASS-21 (137). The Stress Scale of the DASS-21 is a 7-item subscale that assesses respondents' experience of stress symptoms over the past week (137). Each item is rated from 0 (did not apply to me at all over the last week) to 3 (applied to me very much or most of the time over the last week). The total is then doubled to align with the full version of the DASS-21, leading to a possible score ranging from 0 to 42, with higher scores indicating higher stress levels (136, 137).

5.3.2 Assessment of baseline sociodemographic variables

Sociodemographic information, including age, sex, marital status, educational level, employment status, and cohabitation, was recorded at baseline. Age was used as a continuous variable, and sex was (0) male or (1) female, which was confounded by cancer type. Marital status was coded into two variables: (0) Single (consolidating 'Single', 'Divorced', and 'Widowed' and (1) In a partnership (combining 'Married' and 'Domestic Partnership'). Education level, with original values ranging from 'No education' (0) to 'Postgraduate (5) was recoded into two groups: a reference group (0) 'Low levels of education' (including 'No education', 'Primary School', 'Secondary school', and (1) 'High levels of education (including 'College/Diploma', and above). Employment status, initially also comprising six values, was recoded into a reference group (0) 'Unemployed' (merging 'Retired', 'Unemployed', 'Not working due to health', and 'Other' and (1) 'Employed' (including 'Employed full time', and 'Employed Part-time'. Lastly, cohabitation was recoded into (0) 'Living Alone' (used as a reference group) and (1) 'With Someone' (combining living 'With Spouse', 'With spouse and children', 'With children' 'With other adults related to me', and 'With other adults not related to me'.

5.3.3 Assessment of usability

5.3.3.1 System Usability Scale (SUS)

After using the NEVERMIND system for four and 12 weeks, patients were asked to complete the SUS. Recognized as the most prevalent tool to assess usability, the SUS provides insights into user learnability and satisfaction within usability dimensions (109, 111, 138). This

ten-item scale serves as a subjective metric, offering a quantitative analysis of user interaction and use of the system, exploring the ease of use of different functionalities, addressing any technical challenges during usage, and examining users' perceptions about the advantages of system use (109, 111). The score for each 10 items ranges from 0 to 4, and the sum of the items is multiplied by 2.5, resulting in a score ranging from 0 to 100, where a score surpassing 68 is deemed above average (109). In a systematic review, Sousa et al. found the scale to have an interitem correlation between 0.34 and 0.69 and high reliability (Cronbach's α>0.80, with most studies having ≥0.90) (110). Thus, the SUS is an appropriate scale for evaluating the usability of DHTs (139).

5.3.3.2 The User Version Mobile Application Rating Scale (uMARS)

After 12 weeks of utilizing the NEVERMIND system, the participants were administered the uMARS. The uMARS, derived from the MARS initially intended for digital health specialists, has been developed and validated for end-users (140), as how users view an app significantly differs from experts building the app (141). The uMARS evaluates the calibration of mobile apps across different dimensions. It measures the quality of an app by appraising elements of engagement, functionality, aesthetics, and information (140). The global score of the uMARS global score and its four objective quality scales range from 0 to 5, where a score of 5 signifies optimal app quality (140). Furthermore, similar to the SUS, the uMARS has also been shown to have an overall high internal consistency (Cronbach's α=.90) and a good interrater reliability correlation coefficient (0.66-0.70) (140). The Italian translation of the uMARS used in this Ph.D. project, specifically Study I and II, has also been validated with a Cronbach's α of 0.945 and high reliability (Pearson's correlation coefficient higher than 0.7, $p<0.05$) and an Interclass Correlation Coefficient (ICC) between 0.75 and 0.94 (142).

5.3.4 Assessment of acceptability

5.3.4.1 Perceived Usefulness (PU)

The PU questionnaire, developed by the Polytechnic University of Madrid (UPM), comprises ten items rooted in the TAM (77). The questionnaire includes ten positively worded statements, such as *'NEVERMIND gives me more control over my health status.'*, for which patients rate their concordance on a scale of 1 (strongly disagree) to 5 (strongly agree) after using the NEVERMIND system for 12 weeks. The complete questionnaire can be found in Appendix A of Study II (136) and was used in Studies II and III as a continuous variable in the analysis.

5.3.4.2 Perceived Ease of Use (PEOU)

Patients were asked to complete a questionnaire regarding the PEOU after four weeks of utilizing the system and once more after 12 weeks of usage. The PEOU questionnaire serves as an acceptability metric and was developed by the UPM based on the TAM (77).

The questionnaire uses a 9-item Likert scale, ranging from 1 (very difficult) to 5 (very easy). For instance, participants evaluated the simplicity of reporting and managing dietary goals through the system. The questionnaire was applied in Studies II and III as a continuous scale in the analyses and can be found in Appendix B of Study II (136).

5.3.5 Assessment of satisfaction

5.3.5.1 Quantitative questionnaire

After using the NEVERMIND system for four weeks and subsequently after 12 weeks, patients were asked one question: "What is your Overall Satisfaction with the NEVERMIND system?" The response options ranged from poor (0), good (1), acceptable (2), and excellent (3) at both four and 12 weeks, respectively.

5.3.5.2 Qualitative questions

Patients were provided with a follow-up of two open-ended questions: (1) 'What did you like about the NEVERMIND system?' (2) 'What did you dislike about the NEVERMIND system?'. Only the responses from the 12-week mark were analysed.

5.3.6 Assessment of use

A simplistic approach was employed to evaluate the utilization of the NEVERMIND system, including the total days of use of the mobile app, shirt, or both by using log-in data. This assessment did not take frequency or duration of use into account. Regardless of whether a participant engaged with the components numerous times within a day or for extended periods, such metrics were not considered in the assessment. The sole focus was on whether they engaged with the system components. The use of the system was retrieved for two weeks and 12 weeks. An explanation of how these were computed and used in each of the studies is explained in the statistical analysis section below.

5.4 Statistical analyses

Three of the studies (I–III) primarily employed statistical methodologies. In contrast, Study IV used qualitative analysis. Traditional null hypothesis testing (NHT) was used to analyse data in Study I and III, while Study II employed a Bayesian framework. The studies using NHT used an alpha level of .05 to denote statistical significance, with the analyses executed in Stata 15.1 (StataCorp LP). The Bayesian model was done in R 3.6.1, while the qualitative analysis was done in Microsoft Excel. A comprehensive overview of these methods is presented in Table 2.

Table 2. Overview of analytical approaches and variables across the four studies.

Study	Participants	Predictors	Outcomes	Analysis
Study I	- NEVERMIND intervention group	- Sex, age, education level, marital status, employment status, cohabitation	- SUS - uMARS - Use of System	- Multivariate regression
Study II	- NEVERMIND intervention group - No missing data on any outcomes or predictors	- Sex, education level - BDI-II and DASS-21 score - Use of System at 2 weeks - PEOU at 4 weeks - PEOUS at 12 weeks - PU at 12 weeks	- Use of System at 2 weeks - PEOU at 4 weeks - PEOU at 12 weeks - PU at 12 weeks - Use of System at 12 weeks	- Bayesian Structural Equation Modelling - Bayesian Path Analysis
Study III	- NEVERMIND intervention and control group - No missing data on any predictors	- SUS, uMARS - PEOU at 12 weeks - PU at 4 weeks - Use of System at 12 weeks	- BDI-II and DASS-21 score at 12 weeks - Changes on BDI-II and DASS-21 score	- Multi-Level Linear Mixed Model (LMM)
Study IV	- NEVERMIND intervention group - No missing data on outcome	N/A	- Satisfaction	Abductive Thematic Analysis

Study abbreviations: SUS: System Usability Scale; uMARS: the User version of the Mobile Application Rating Scale; PEOU: Perceived Ease of USE; PU: Perceived Usefulness; BDI-II: Beck-Depression Inventory Scale-II; DASS-21: Depression, Anxiety, and Stress Scale (only the stress items used); N/A: Not applicable.

5.4.1 Study I

The sample size was based on the number of patients with breast or prostate cancer in the NEVERMIND study who received the NEVERMIND system (n=129). However, participants who dropped out before receiving the NEVERMIND system and those with missing data on outcome measures were excluded, resulting in 108 participants. All outcomes, as described in Table 2, were measured on a continuous scale, and sociodemographic characteristics, except for age, were dichotomized. The use of the NEVERMIND system at 12 weeks, called the usage index in Study I (143), was computed as the total sum of days used divided by the number of days the participants were in the study. Normality tests were used to check the normality of the outcomes. A multivariate regression was used to examine the associations between sociodemographic characteristics and SUS, uMARS, and usage index.

5.4.2 Study II

This study included participants in the NEVERMIND intervention group (n=129). Descriptive statistics were calculated for all variables, including participants' demographic characteristics, baseline depressive and stress symptoms, acceptability parameters, and use of the NEVERMIND system. A path analysis through Bayesian Structural Equation Modelling (SEM) was used to investigate the relationships among these parameters in the study. Several factors influenced the choice of employing Bayesian SEM. Firstly, it provides more robust estimation with smaller sample sizes compared to frequentist methodologies by facilitating the incorporation of prior information about model parameters, hence enhancing estimate accuracy even in small sample sizes (144, 145); it can estimate intricate models involving several parameters, which might be overly complex for frequentist approaches like maximum likelihood, particularly relevant when investigating the relationship among a substantial number of variables through a path analysis (144). Thirdly, it allows for integrating prior information from previous research on model parameters, enhancing precision in estimating their posterior distribution (146).

Though Bayesian SEM can provide better estimates in small sample sizes, the sample size required for SEM analysis is influenced by expected effect size, the number of variables in the model, and the complexity of the model (147). A general guideline suggests 10 to 20 cases for each estimated parameter. In our model (Figure 11), nine variables were present: baseline depressive and stress symptoms, sex, educational level, use at two weeks, perceived ease of use (PEOU) at both four and 12 weeks, perceived usefulness (PU) at 12 weeks, use at 12 weeks (136). Given this guideline, our sample size should range between 90 and 180. Since all users needed to have data on each of the nine variables, our sample size was 100, within the range of the recommendation.

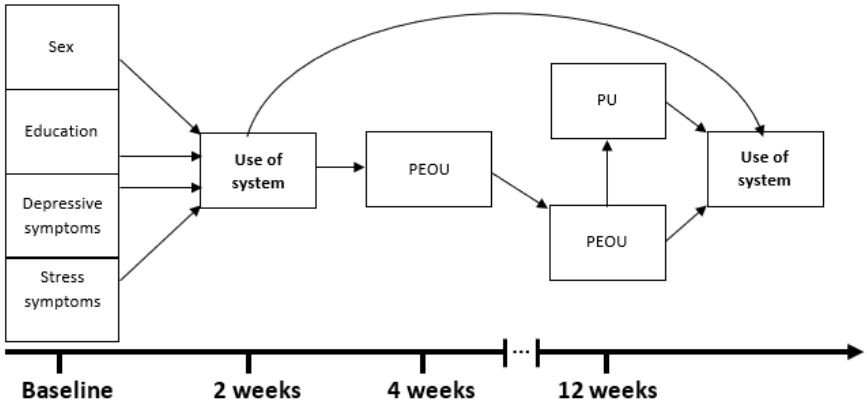


Figure 11. Model of the study. PEOU: perceived ease of use; PU; perceived usefulness.

The full statistical analyses and steps taken in this study can be found in the published article (136), but a summary of the analyses is described below.

Prior distributions for the model parameters were selected using three sources, prioritized in the following order: (1) previous research, (2) weakly informed priors gathered from the authors of the study, representing expert opinions, and (3) the default prior from the Blavaan package in R, which was adjusted during the prior convergence analysis to avoid model divergences, ensuring the model ran on prior assumptions. Expert opinions and default priors were only used in the absence of previous empirical findings. The prior information was then used to estimate the posterior distributions for these parameters based on the observed data.

A literature search was conducted on August 26, 2022, on PubMed to identify effect sizes found in previous research. The search included the words “user characteristics” AND “usability” OR “usage” AND “eHealth.” All effect sizes were then transformed and combined into means and standard deviation (SD) to align with the input criteria of the Blavaan package in R.

A Bayesian structural regression was conducted by leveraging prior knowledge of the observed data using the bsem function from the Blavaan package (148). This was conducted in R software (version 4.2.2; 2022-10-31 ucrt) through Rstudio graphical user interface (version 2023.03.0; Posit, PBC).

A sensitivity analysis was also conducted to understand how changes in sampling sizes and prior distributions influenced the model’s posterior parameters. To test that, different number of adaptation samples and burn-samples, as well as prior hyperparameters, were varied.

5.4.3 Study III

This study included two parts, described as follows.

Part 1. Clinical effectiveness of the NEVERMIND system

This part included participants in the control group (breast cancer, n=75 and prostate cancer, n=51) and the intervention group (breast cancer, n= 80 and prostate cancer, n=49). The goal was to assess the effectiveness of the NEVERMIND system in reducing depressive and stress symptoms in the intervention group compared to corresponding symptoms in the control group.

Because data was already collected (132), a post-hoc power test was used before conducting the LMMs. The power analysis was conducted using the observed mean difference between the intervention and control groups in depressive symptoms (primary outcome for the RCT), with an alpha of 0.05 and a sample size of 225 (comprising 129 in the intervention group and 126 in the control group). The results showed that, given the sample and effect size, the power was 96.3%.

Consequently, after the power was shown to be sufficient, two LMMs were conducted to examine the effects of the treatment on both depression and stress, adhering to the protocol of the RCT study (132). The analyses incorporated age, sex, cohabitation, group (intervention and control), time, and interaction between time and group as fixed factors at the first level. At the second level, individual variances in general depression and stress were constructed using random intercepts and slopes for each participant.

The proportion of variance ascribed to random variables was evaluated by calculating intraclass correlation coefficients (ICC). Additionally, to analyse the potential multicollinearity of each predictor variable, Variance Inflation Factors (VIF) were determined.

Part 2. Usability, acceptability, and clinical effectiveness of the NEVERMIND system

Similar to Part 1, two LMM were used to evaluate the connection between clinical efficacy of reducing depressive and stress symptoms and several factors: age, sex, cohabitation, corresponding usability (as measured by SUS and uMARS) and acceptability (as assessed by PEOU and PU), and usage, all of which were incorporated as fixed factors. At the second level, individualized random intercepts and slopes were calculated for each participant. The usage variable was formulated by leveraging the daily log data derived from the mobile app, as the most used component of the NEVERMIND system was the mobile app. Due to the asymmetrical distribution of the usage variable, a log transformation was undertaken utilizing the *'lnskew0'* in Stata. The ICC and VIF were also calculated.

After parts 1 and 2, additional analyses were done by categorizing participants into non-active, passive, and active users based on their engagement duration throughout the 12-

week study period. Active users were characterized as those engaging with the NEVERMIND system for a minimum of 42 days (half the study duration), while passive users interacted with the system between 16 and 42 days (approximately 20% to 50% of the study period). Non-active users were identified as those who engaged with the system for less than 16 days. This variable, 'user groups', was then used in a multiple regression model to predict changes in the BDI-II and DASS-21 (stress) scores, controlling for baseline depressive and stress symptoms, age, sex, cohabitation, SUS, uMARS, PEOU, and PU.

5.4.4 Study IV

The fourth and last study of the Ph.D. project covered *'Satisfaction'* and utilized cross-sectional with a mixed-method approach, using quantitative and qualitative data. Quantitative responses to the question 'What is your overall satisfaction with the NEVERMIND system?' were summarized. The second part included a thematic analysis of the open-ended responses, using both inductive and deductive thematic analysis based on Braun and Clarke (149).

The analyses started with the translation of responses from Italian to English using Google Translation, with ambiguous or longer phrases translated by a native Italian speaker and back-translated to Italian by a fluent English speaker. Following translation, an inductive approach, using the NEVERMIND system's components as a sensitizing concept to guide the preliminary understanding and scrutiny of the data, was used. Sensitizing concepts serve as a provisional starting point without being definitive, aligning with Charmaz's views (150). During the analysis, responses were carefully read to grasp the overall feedback and discern repetitive patterns. Using Microsoft Excel, responses were mapped to different components, such as the mindfulness module and physical activity. Responses were then categorized using codes related to the sensitizing concept, after which variations within each code were explored to identify categories and themes. Post inductive identification of the themes, the IS success model assisted in deductive analysis, aiding in interpreting and refining themes identified through the inductive approach. While the primary focus was on satisfaction through the IS success framework, it should be noted that other themes beyond satisfaction also emerged. Themes were examined within the IS success framework regarding content quality, information quality, use, satisfaction, and net benefits. To ensure a comprehensive analysis and reduced bias, all data, even if singularly mentioned, were coded by two research team members. Themes were collectively agreed upon through several consensus meetings held by two research team members. The findings were then systematically organized, starting with a broad summary followed by a detailed examination of specific, pertinent themes. The 21-item Standards for Reporting Qualitative Research (SRQR) (151), a set of guidelines that comprise 21 items that represent critical aspect of qualitative research reporting to increase clarity and transparency, was used to guide the reporting of this study.

5.5 Ethical Considerations

The Ph.D. thesis used data derived from the NEVERMIND study trial, which included five patient groups and focused on patients with breast and prostate cancer. The ethical permit for conducting the trial in patients with breast and prostate cancer was received from the Ethical Committee of Città della Salute e della Scienza di Torino University Hospital and Ethical Committee of San Luigi Gonzaga University Hospital, Orbassano (Reg nr. 185/2015); the main trial was registered in the German Clinical Trials Registry (DRKS00013391). An additional ethical permit was granted by the Regional Ethical Review Board of Stockholm (Reg nr. 2020-04175) for the analysis of pseudonymized patient data at Karolinska Institutet, including all the studies in this Ph.D. project.

5.5.1 Informed consent

The patients were selected by their own medical doctors, who explained the study's implementation and purpose. Written documentation detailing the study was provided to each patient for further analysis. If the patient agreed to participate in the study, an informed consent form was signed, and an alphanumeric code was assigned to that patient, under which all their documentation and data were catalogued.

5.5.2 Addressing participant inactivity and ensuring additional mental health support

Furthermore, during the NEVERMIND trial, if a patient remained inactive (not using the system) for seven consecutive days, the treatment team was notified to determine the cause of inactivity. If the inactivity stemmed from difficulties in managing their depressive symptoms, users were referred to further psychiatric treatment.

5.5.3 Ensuring participant anonymity in small sample sizes

We received pseudonymized patient data with codes and no names, ensuring patient privacy and confidentiality. Particular attention was dedicated during the translation phase in Study IV to ensure the accuracy and culturally sensitive representation of patients' expressions and experiences while maintaining ethical standards.

However, working with small sample sizes, especially those with unique characteristics (such as breast and prostate cancers and demographics), poses ethical challenges. Individuals are at risk of being identifiable even with pseudonymized data. This type of challenge has been noted more frequently in qualitative research (152) but also occurs in quantitative studies (153). This potential for re-identification raises significant ethical concerns regarding privacy and confidentiality, compromising the anonymity of participants and exposing them to potential social and psychological consequences. Therefore, in addition to following ethical guidelines, precautions in this Ph.D. thesis included using only aggregated data in studies, limiting data accessibility. For example, In Study III, only specific study data, as mandated by the journal, were uploaded to a data depository (DOI link: https://doi.org/10.48723/21y0-2g17). Moreover, the data for

Study III was uploaded employing randomly generated numbers as code for patients. When choosing quotes in Study IV, only those devoid of any deductive identification potential were selected, as those are better suited for anonymity (152).

6 Results

This section presents the principal findings of this Ph.D. thesis. For an in-depth exploration and additional details, please refer to the published papers and manuscripts incorporated within the thesis.

6.1 Characteristics of the study population

At baseline, the study population of the NEVERMIND trial comprised patients with breast and prostate cancer, totalling 255 participants. A total of 129 participants were allocated to the NEVERMIND intervention group on top of the treatment as usual, with an average age of 59.5 years (± 9.4), 80 (62.02%) patients with breast cancer and 49 (37.98%) patients with prostate cancer (Table 3).

Table 3. Baseline Sociodemographic and Clinical characteristics of cancer patient samples from the NEVERMIND study.

	Intervention	**Control**
Total population (n)	129	126
Sociodemographic characteristics		
Mean age (SD)	59·53 (9·37)	58·38 (9·70)
Cohabitation (%)	..	..
Alone	19 (14·73)	25 (19·84)
With someone	110 (85·27)	101 (80·16)
Education (%)	..	..
Low	27 (20·93)	29 (23·02)
High	102 (79·07)	97 (76·98)
Marital status (%)	..	..
Single	37 (28·68)	37 (29·37)
In a partnership	92 (71·32)	89 (70·63)
Employment (%)	..	..
Unemployed	70 (54·26)	65 (51·59)
Employed	59 (45·74)	61 (48·41)
Clinical characteristics		
Cancer Diagnosis (%)	..	..
Breast Cancer	80 (62·02)	75 (59·52)
Prostate Cancer	49 (37·98)	51 (40·48)
BDI-II[a] score (SD)	12·51 (8·84)	13·08 (7·50)
BDI-II Score (%)	..	..
Minimal depressive symptoms*	85 (65·89)	75 (59·52)
Depressive symptoms**	44 (34·11)	51 (40·48)
DASS-21[b] score (SD)	12 ·93 (9·37)	14 ·33 (8·47)

[a]BDI-II: Beck Depression Inventory-II
[b]DASS-21 score: Depression Anxiety Stress Scale-21
*BDI-II score≤13
**BDI-II score>14

A majority of the participants had attained at least a college-level education (n=102, 79.07%), lived with someone (n=110, 85.27%), and were unemployed (n=70, 54.26%). The control group comprised a total of 126 participants, with an average age of 58.4 (± 9.7), with 75 (59.52%) patients with breast cancer and 51 (40.48) patients with prostate cancer (Table 3).

Similar to the intervention group, the majority of participants had at least a college-level education (n=97, 76.98%), lived with someone (n=101, 80.16%), and were unemployed (n=65, 51.59%). Baseline sociodemographic and clinical characteristics are shown in Table 3. Specific exclusion criteria were applied to each study; therefore, the sample size for each study was different.

6.2 Sociodemographic characteristics, usability, and use of the NEVERMIND system (Study I)

The sample for this study included 129 patients initially allocated to the NEVERMIND system, among whom 108 (83.7%) completed the study and 21 (16.3%) withdrew post-baseline assessment. The mean age (SD) of the patients who completed the study was 58.6 (± 9.3) years, and the majority were women (n=68, 63%).

No significant baseline differences were observed between those who completed the study and those who dropped out before receiving the NEVERMIND system. Most completers cohabited (n=93, 86.1%), were highly educated (n=87, 80.6%), and had partners (n=78, 72.2%). The average usage duration of the NEVERMIND system was approximately six weeks, less than the recommended 12 weeks, with only 12 patients adhering to the advised period.

In terms of usability, SUS scores at the final time point, represented by a mean of 73.4 (± 12.5), were higher than the interim scores of 70.9 (±12.3) (Table 4), and both scores were normally distributed.

Table 4. Descriptive statistics for usability and acceptability metrics at multiple time points.

Variable	Mean (SD)	Median (range)
SUS[a] at 4 weeks	70.9 (12.3)	73.8 (37.5-97.5)
SUS at 12 weeks	73.4 (12.5)	75 (40-97.5)
UMARS[b] at 12 weeks	3.8 (0.3)	3.9 (3.1-4.7)
PEOU[c] at 4 weeks	32.6 (4.20)	33 (20-43)
PEOU at 12 weeks	32.6 (4.43)	33 (19-45)
PU[d] at 12 weeks	37.2 (6.09)	38 (20-50)
Use at 12 weeks (days)	45.3 (28.14)	42 (2-100)

[a]SUS: System Usability Scale
[b]uMARS: the User version of the Mobile Application Rating Scale
[c]PEOU: Perceived Ease of Use
[d]PU: Perceived Usefulness

No sociodemographic characteristics showed a significant association with SUS scores at either four weeks or final time point (12 weeks). Regarding the uMARS score at 12 weeks, the global score was 3.8 (±0.3), which is above the average score of the uMARS scale (3.0). The subscales for engagement, functionality, aesthetics, and information scored 3.5, 3.9, 3.6, and 4.2, respectively. The mean uMARS score was higher in women than in men. The only significant association found in sociodemographic characteristics was between gender and the uMARS score, particularly the engagement subscale, where women exhibited higher scores with a uMARS mean score of 3.9 (±0.3) compared to men (3.7 ± 0.3).

Usage data was available for 99.1% (107/108) of patients, with the mean usage index being 0.48 (range between 0 and 1). However, the data distribution was skewed, according to the Skewness and Kurtosis tests ($P<0.001$). The data distribution had a subset of patients having significantly higher usage indices that increased the overall mean. However, using non-parametric regression to accommodate the non-normality of the data yielded similar results to using parametric regression. The only significant sociodemographic association found with system use was gender, with women showing lower system usage than men.

The comprehensive results, including significant associations and variations in usability scores, are further elaborated in the published article (143). Table 4 above shows the values of all usability and acceptability questionnaires used in this Study and Study II.

6.3 Baseline mental health symptoms and usability, use, and acceptability of the NEVERMIND system (Study II)

This study included 100 participants, primarily women (66%) and highly educated individuals (81%). The system usage was, on average, 5.52 days in the initial two weeks and 45.3 days after 12 weeks. The participants rated the system highly regarding PEOU and PU.

Table 5. Descriptive statistics of variables in the structural equation modelling Bayesian path analysis model (N=100).

Variable	Mean (SD)	Median (range)
Depression (BDI-II[a])	12.23 (9.20)	10 (0-43)
Stress (DASS-21[b])	13.64 (9.56)	14 (0-38)
Use at 2 weeks (days)	5.52 (4.14)	6 (0-14)
PEOU[c] at 4 weeks	32.5 (4.22)	33 (20-43)
PEOU at 12 weeks	32.7 (4.33)	33 (24-45)
PU[d] at 12 weeks	37.1 (5.86)	38 (20-50)
Use at 12 weeks (days)	45.3 (28.14)	42 (2-100)

[a]BDI-II: Beck Depression Inventory-II
[b]DASS-21: Depression Anxiety Stress Scale-21
[c]PEOU: Perceived Ease of Use
[d]PU: Perceived Usefulness

A literature review informed the priors for the Bayesian SEM, with 12 articles fully screened and ten contributing to the study. The full list of included articles and the priors chosen can be found in the published article (136). The prior model underwent several modifications and assessments, leading to acceptable convergence indices and adequate sample sizes.

Figure 12 illustrates that four regression paths, highlighted in bold, exhibit more distinct associations. The credibility intervals of the highest posterior density, marked by an asterisk, maintain a consistent direction, either positive or negative, thereby not intersecting with zero. From these regression analyses, two primary paths were identified as predictors of the use of the NEVERMIND system at 12 weeks. The initial path stemming from PEOU at four weeks (β_{PEOU} at 12 weeks was predicted by PEOU at 4 weeks = .589), progressing through PU at 12 weeks (β_{PU} at 12 weeks is predicted by PEOU at 12 weeks = .581), culminating in system usage at 12 weeks (β_{use} at 12 weeks was predicted by PU at 12 weeks = .384). The secondary path highlights the relationship between system usage at 2 weeks and its subsequent use at 12 weeks (β_{use} at 12 weeks was predicted by use at 2 weeks = .239).

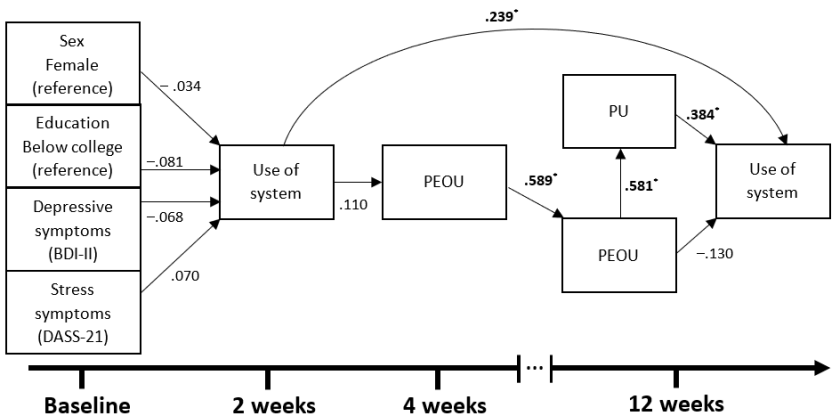


Figure 12. The Bayesian structural regression model results showing standardized regression coefficients (β) for all paths. Abbreviation: BDI-II: Beck Depression Inventory–II; DASS-21: Depression, Anxiety, and Stress Scale–21; PEOU: perceived ease of use; PU: perceived usefulness.

In terms of variance accounted by the model, the variable PEOU at 12 weeks was the most explain variance (r^2=0.358), closely followed by PU at 12 weeks (r^2=0.338). The variables for use at 2 weeks, PEOU at 4 weeks, and use at 12 weeks had a variance value of 0.010, 0.012, and 0.166, respectively. Consequently, the model effectively captures some variations, especially at 12 weeks, but it is less adept at explaining use and PEOU at 2 and 4 weeks, respectively.

Sensitivity analysis of prior settings revealed some variations in point estimates and distributional ranges, yet these did not significantly affect the directionality of the

regression coefficients. The model fit indices depicted a reasonable fit, although their interpretative values warrant caution.

6.4 NEVERMIND system's clinical effectiveness, usability, use, and acceptability (Study III)

A total of 129 patients (80 breast and 49 prostate cancer patients) assigned to the NEVERMIND intervention group, and 126 (75 breast and 51 prostate cancer patients) to the control group were included in this study. Baseline characteristics, including sociodemographic information and clinical features, showed no significant differences between the intervention and control groups ($p>0.05$). At baseline, participants in the intervention and control groups exhibited minimal depressive symptoms, with mean BDI-II scores of 12.51 (±8.84) and 13.08 (±7.50), respectively. Baseline sociodemographic and clinical characteristics are shown above in Table 3, and usability and acceptability are shown above in Table 4.

6.4.1 Clinical effectiveness

The LMM revealed that, at 12 weeks, the NEVERMIND group experienced a significant reduction in depressive symptoms compared to the control group (B=-3.32; 95% CI -5.24 to -1.39; p=0.001), while differences in stress symptoms were not significant. In both models, the "Female" fixed effect significantly impacted the results ($p<0.001$), revealing that, all other factors being equal, females exhibited higher BDI-II depression scores and DASS-21 stress scores. Females had BDI-II scores 6.54 points higher (B=6.54; 95% CI 4.50 to 8.58, $p<0.001$) and DASS-21 Stress scores 6.77 points higher (B=6.77; 95% CI 4.56 to 8.98, $p<0.001$) than their male counterparts. In the NEVERMIND group, males showed a reduction in mean BDI-II scores from 7.88 (SD 5.53) at the beginning to 5.4 (SD 6.87) at 12 weeks. Females in the same group also saw a decrease in mean depression scores from 15.35 (±9.31) to 9.67 (±8.58) over the same period. Conversely, in the control group, while males experienced a minor reduction in mean depression scores from 9.00 (±4.98) to 7.82 (±5.34) by the 12th week, females observed only a slight decrease from 15.85 (±7.68) to 15.24 (±9.35). The overall variance in depression and stress symptoms at 12 weeks was explained by 54% and 56% of random variations within the participant groups, respectively.

6.4.2 The association between usability, use, acceptability, and clinical effectiveness

At 12 weeks, the mean PEOU was 32.6 (±4.44), and the mean PU was 37.16 (±6.09). No significant associations were found between the SUS scores, uMARS, PEOU, PU, and use of the system as a continuous variable and changes in depressive or stress symptoms. The following figure (Figure 13) shows the extent to which users agreed with each item of the PU.

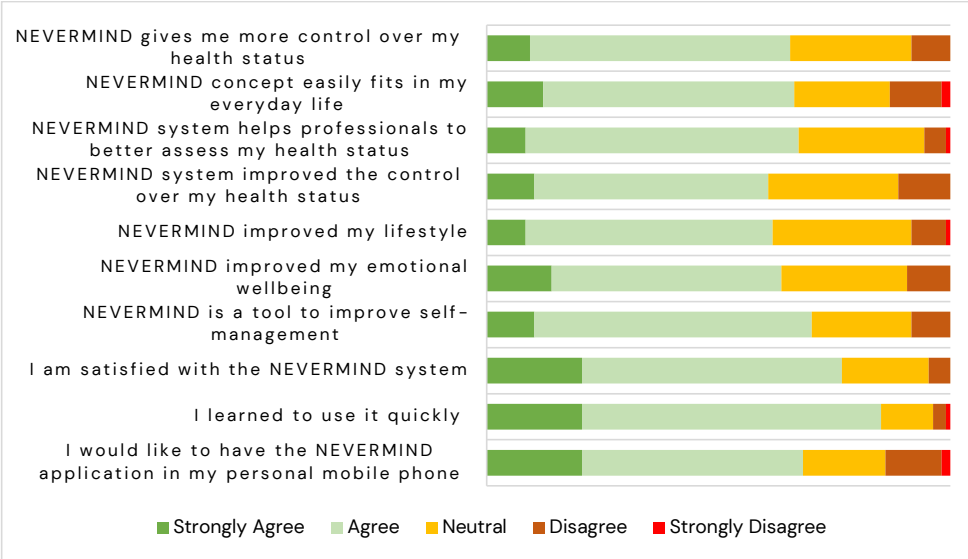


Figure 13. Patients' perceived usefulness of the NEVERMIND system at 12 weeks.

Figure 14 demonstrates the degree to which users found each item on PEOU easy. Most users expressed agreement or strong agreement regarding the usefulness of the NEVERMIND system across various aspects, with the most prominent consensus surrounding the ease with which they learned to use the system (Figure 14).

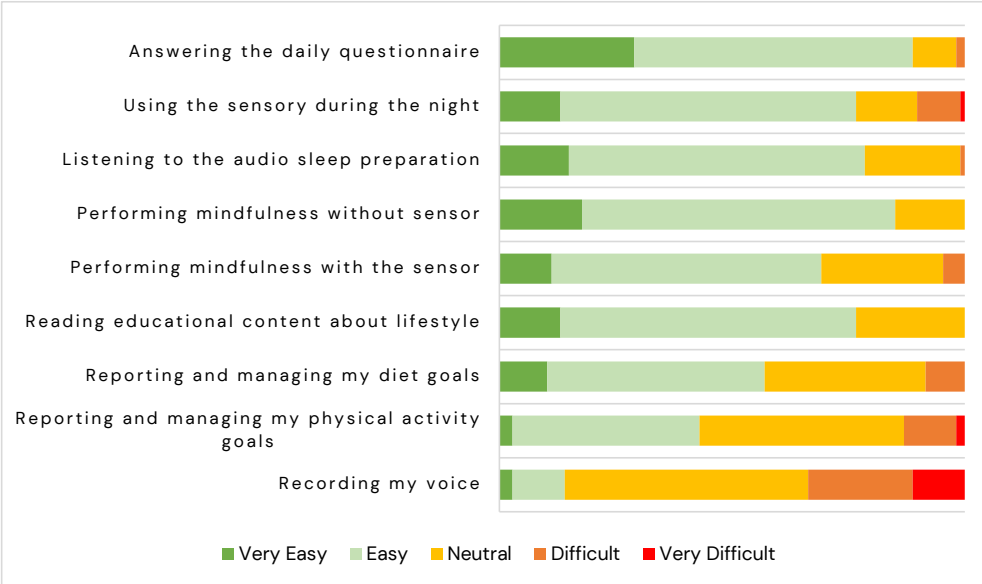


Figure 14. Patients' perceived ease of use of the functions of the NEVERMIND system at 12 weeks.

Users generally found it simpler to respond to the daily questionnaires and to utilize the sensory shirt during the night (Figure 14). However, voice recording, and the reporting

and management of physical activity goals were identified as the less user-friendly functionalities, with 36 users (34%) and 14 users (13%), respectively, rating them as difficult or very difficult (Figure 14). Interestingly, while no users reported difficulties conducting mindfulness practices without the shirt, five users experienced challenges when performing the practices with the shirt on.

6.4.3 User groups as predictors of clinical effectiveness

The observed trajectory of system use showed that only 13% (14/108) of the participants used the system on the first day. The use of the system was lowest during the first three days of the study. The mindfulness, physical activity, and sleep modules of the mobile app were the most frequently accessed. By the third week, around 80% of participants engaged in the mindfulness module, yet the system usage saw a decline starting on the 62nd day, after approximately nine weeks of usage.

The variable 'Use of system' was used as continuous in previous analyses in Study I-III, so to explore a potential non-linear association between the use of the system and the change in depressive and stress symptoms from baseline to 12 weeks, the variable was trichotomized, as described in the methods section. The user categories, non-active (n=38/108), passive (n=37/108), and active users (n=33/108) had nearly equal distribution. Notably, this categorization only considered the overall usage over the 12 weeks, not consistent use. However, there was a strong correlation ($p<0.001$) between weekly system usage and the usage category. For example, in week 9, 67% (n=22/33) of those classified as active users accessed the system at least three times, and all used it in week 8. Furthermore, there was also a gender difference ($p=0.035$) in using the system. While 45% of female users (n=30/68) were in the non-active category, only 20% of male users (8/40) were grouped as such.

Interestingly, the active user group showed a more significant decrease in BDI-II scores than the non-active group (B=-3.90; 95% CI -7.46 to -0.34, p=0.032) (Table 6). However, there was no significant difference in BDI-II scores between passive and non-active users. In contrast, a marked difference was identified in the change in stress symptoms between passive and non-active users (B= -4.57; 95% CI -7.71 to -1.44, p=0.005), and between active and non-active users (B= -5.81; 95% CI -9.27 to -2.35, p=0.001) (Table 6).

Table 6. Multiple regression of user groups as a predictor variable for change in score of BDI-II and DASS-21 (stress) score (N=104).

	Change on BDI-II score[a]			Change on DASS-21 score[b]		
Predictors	**B**	**95% CI**	**p**	**B**	**SE**	**p**
Baseline BDI-II	-0.49	-0.65 to -0.33	<0.001*		N/A	
Baseline DASS-21[a]		N/A		-0.47	-0.62 to -0.34	<0.001*
SUS[c] at 12 weeks	0.03	-0.11 to -.18	0.636	0.06	-0.08 to 0.21	0.364
uMARS[d] at 12 weeks	-1.66	-6.95 to 3.63	0.536	-2.33	-7.47 to 2.81	0.371
PEOU[e] at 12-weeks	-0.31	-0.70 to 0.08	0.114	-0.22	-0.60 to 0.16	0.245
PU[f] at 12-weeks	-0.30	0.36 to 0.31	0.866	-0.02	-0.35 to 0.31	0.899
12 weeks usage						
Non-active users		Ref			Ref	
Passive users	-2.05	-5.26 to 1.17	0.210	-4.57	-7.71 to -1.44	0.005*
Active users	-3.90	-7.46 to -0.34	0.032*	-5.81	-9.27 to -2.35	0.001*
Living with someone	3.10	-0.73 to 6.94	0.112	2.06	-1.67 to 5.79	0.276
Age	-0.14	-0.30 to 0.02	0.082	-0.24	-0.39 to -0.08	0.003*
Female	-0.69	-4.09 to 2.72	0.691	1.16	-2.04 to 4.36	0.472

[a]BDI-II: Beck Depression Inventory Scale-II
[b]DASS-21: Depression Anxiety Stress Scale-21; only the stress subscale of the DASS-21 was used
[c]SUS: System Usability Scale
[d]uMARS: the User version of the Mobile Application Rating Scale
[e]PEOU: Perceived Ease of Use
[f]PU: Perceived Usefulness
*significant at p<0.05.

When users were categorized into non-active, passive, or active groups, the gender difference in depressive symptoms becomes statistically insignificant (B=-0.69; 95% CI: -4.09 to 2.72, p=0.691). Older age was also found to be significantly associated with reduced stress symptoms (B=-0.24; 95% CI: -0.39 to - 0.08, p=0.003) (Table 6).

6.5 Satisfaction of the NEVERMIND system (Study IV)

The one-item satisfaction question, at four weeks, ,revealed that 68.24% (n=72/104) of participants deemed the system as good or excellent; in contrast, 30.76% (n=32/104) found it acceptable or poor. A similar trend was observed at 12 weeks, with 65.42% (n=70/107) rating the system as good or excellent, and 34.58% (n=39/107) rated it as acceptable or poor.

Through thematic analysis, three themes and nine categories were identified, illustrating the specific elements of the user experience that contribute to patient satisfaction or dissatisfaction with the NEVERMIND system, as shown in Table 7.

Table 7. Identified themes and categories from user experiences on the NEVERMIND system.

Themes	Categories
1. Fostering personal agency and motivation: Satisfaction rooted in holistic well-being and supportive connection	(A) Impact on emotional and physical well-being (B) System interaction and relatability (C) Lifestyle integration and practicality
2. Engagement and interaction experiences: Balancing user-friendly interfaces with technical and comfort challenges	(D) System functionality and user-friendliness (E) Personalization and interaction preferences (F) Procedure efficiency and timing
3. Content quality and relevance: Seeking greater content diversity and relevance to cancer diagnosis	(G) Clarity of system purpose and instructions (H) Quality and variety of content (I) System flexibility and customization

Theme 1: Fostering personal agency and motivation: Satisfaction rooted in holistic well-being and supportive connection

Users acknowledged the NEVERMIND system for its significant contribution to overall emotional and physical well-being (category A). They underscored the relevance of the physical activity module, nutritional guidelines, and methods for fostering holistic health. Users pointed out that sleep hygiene helped improve their sleeping habits and patterns, where they noticed a change in their nightly routines and the positive impact it had on their overall well-being. Representative quotes include the following:

- "A bit of everything but especially the advice on sleep and depression." (Breast cancer patient)
- "Mindfulness practices have helped me manage moments of anxiety through breathing. At work, when I am agitated, I stop for a moment and breath consciously" (Prostate cancer patient)

A sense of connectivity with oneself, others, and nature was enhanced (category B). However, challenges in recording personal feelings and integrating the system into daily routines have been identified (category B). Representative quotes include the following:

- "…it teaches us the need to appropriate some time, our time, to dedicate it to ourselves…" (Prostate cancer patient)
- "I had a hard time reconciling it with my daily life." (Breast cancer patient)

The first theme highlights that users had a positive experience, which was useful even when the system was used only for a few minutes. The practices made them more aware of their environment and gave moments for themselves to connect with their bodies and emotions fostering personal agency and motivation alongside providing holistic well-being and supportive connections.

Theme 2: Engagement and interaction experiences: Balancing user-friendly interfaces with technical and comfort challenges

Users found that the tailored modules and interactions were user-friendly, facilitated by the visual presentations and graphical view of gathered patterns of their use (category D). Nonetheless, some users faced navigation challenges and technical issues that impacted engagement levels. Users expressed that the mobile app had technical issues, particularly with the audio quality, weekly crashes, and freezes. Users mentioned that these negative experiences impacted their engagement, desire to continue, and decreased their overall satisfaction. Similarly, users also found the shirt to be uncomfortable and the procedure to set it up too long (category F). Users also voiced concerns about the system not being personalized or tailored to their individual needs and capacities (category E). Highlighted quotes are:

- "I find the presence of sleep, heart rate, and breathing graphs very useful..." (Prostate cancer patient)
- "The application is not very streamlined and intuitive." (Breast cancer patient)
- "Sensors too large Skin discomfort, it was not possible to sleep on your stomach." (Breast cancer patient)

This theme underscores the balance between creating user-friendly interfaces to enhance engagement and interaction experiences, while also addressing technical, interface, and comfort challenges that may hinder user satisfaction.

Theme 3: Content quality and relevance: Seeking greater content diversity and relevance to cancer diagnosis

Although users appreciated the recommendations on dietary habits, highlighting the recipes and the clarity of the nutritional recommendations, users expressed a desire for clearer explanations (category G). While some felt that certain contents, such as physical exercises and recipes, were too complicated to follow, others found the practices repetitive (category H). Feedback also highlighted the need for physical activities that resonated more with individual capabilities and a greater variety within each practice (category I). The selected quotes include the following:

- "The nutrition part and all the advice in this regard, furthermore, the practices were also very followed and appreciated." (Breast cancer patient)
- "I struggled to find a connection between the various functions of the application. I would have liked to have had an instruction manual supplied, explaining the various functions and their integration." (Breast cancer patient)
- "The physical activity was only on breathing, and it should be expanded." (Breast cancer patient)

The final theme encapsulates a focus on improving the quality and breadth of content provided to users diagnosed with breast and prostate cancer, ensuring that it is both diverse and relevant to their needs and experiences. Quality relates to the reliability and relatedness of the content. It highlights the value of an explanation or instruction of how the content and functionalities of the NEVERMIND system are related to one another.

There was also a difference between what women (breast cancer patients) users focused on compared to men. Women highlighted that tailored modules and interactions made them feel cared for, supported, and less alone. The system's ability to resonate with their needs fostered a sense of connection and care, making them feel as if 'someone' was there for them. Men (prostate cancer patients) were satisfied with the NEVERMIND system as it helped increase their self-awareness and introspection. Selected quotes are shown below.

- "I liked the meditations with the male guide because they calmed me down. Like there was someone nearby to help me and I felt more protected." (Breast cancer patient)
- "the system is very helpful to people in a state of anxiety, especially cancer patients. it is a seed that is placed within us to be cultivated possibly every day. it teaches us the need to appropriate some time, our time, to dedicate it to ourselves, for a meditation break, to feel part of the natural world of which we are part." (Prostate cancer patient)

7 Discussion

7.1 Main findings

This thesis explored the usability, acceptability, and satisfaction of the NEVERMIND system among patients with breast and prostate cancer. The findings unfolded crucial insights regarding these dimensions and the factors that influence them.

This section provides a summary of the findings of each study, followed by a critical reflection on the findings, while also considering the theoretical and practical implications, methodological considerations and limitations, and possibilities for future research.

Study I examined the association between sociodemographic characteristics and the usability and use of the NEVERMIND system in 108 patients with breast and prostate cancer using measurements at four and 12 weeks. The system demonstrated good usability, but the mobile app was rated higher by females (breast cancer patients), while males (prostate cancer patients) had used the system more.

Study II investigated the relationship between different patients' characteristics, usability, and acceptability, through path analysis using Bayesian SEM in 100 patients

with breast and prostate cancer and found critical drivers for using the NEVERMIND system. Higher perceived usefulness and initial usage were associated with increased use at the 12-week mark. There was also a lack of explanation power that indicates a need for a more in-depth analysis of usage predictors.

Study III evaluated the relationship between the usability, acceptability, and clinical effectiveness of the NEVERMIND system in reducing depressive and stress symptoms in patients with breast and prostate cancer. Patients using the NEVERMIND system experienced a significant reduction in depressive symptoms, compared to the control group, at the 12-week follow-up. A key finding was that engaging with the system for over six weeks (active group) correlated with a significant decrease in both depressive and stress symptoms. Another finding was that females were predominately in the non-active group (using the system for less than two weeks).

Study IV focused on user satisfaction in 107 patients with breast and prostate cancer using a quantitative question and an abductive thematic analysis interpreted within the Information Systems (IS) success model. The results indicated that 65% of users were satisfied with the NEVERMIND system. Thematic analysis identified three themes for user satisfaction, highlighting the importance of fostering personal agency and motivation, ensuring interactive experiences, and maintaining high content quality and relevance. Gender-varied needs, particularly emotional support for female users, and self-awareness and introspection for male users, emphasize the importance of a user-centric approach for further user experience optimization.

7.2 Clinical effectiveness of the NEVERMIND system

For patients with breast and prostate cancer, the psychological burden is particularly salient. The emotional toll of a cancer diagnosis, coupled with the physical and psychological side effects of cancer treatment, can lead to a high prevalence of depressive symptoms in these patient populations (26, 27).

In a systematic review and meta-analysis conducted by Watts et al., the prevalence rates of depression in prostate cancer patients ranged between 14% and 23%, where the post-treatment depression prevalence was highest at 18.44% (154). This study by Watt et al. was based on 4,494 patients (154). Expanding on this, Brunckhorst et al., in a systematic review and meta-analysis, analysed data from 32,339 patients in 76 studies (155). Their findings indicated that 17.07% of these patients showed depressive symptoms (155). Additionally, 16.86% of 24,526 patients displayed significant anxiety symptoms (155). Two systematic reviews and meta-analyses, one covering 71 studies and the other 72, reported global depression rates among breast cancer patients. The 2019 study (156) found a rate of 32.2%, while the 2023 study reported 30.2% (28).

Within the context of the NEVERMIND study, out of 255 participants from both the intervention and control groups, 160 (62.74%) had a BDI-II below 13. Meanwhile, 48

(18.82%) exhibited mild depressive symptoms (with scores of ≥14 on the BDI-II), 32 (12.55%) had moderate symptoms (with scores ranging from 20-28 on the BDI-II), and 15 (5.88%) presented with severe depressive symptoms (with scores between 29-63 on the BDI-II) at baseline. Within the intervention group specifically, 44 patients (34.11%) had a BDI-II score of above 14, indicating at least mild depressive symptoms.

Thus, most patients did not show significant depressive symptoms at baseline. However, a significant portion did exhibit varying levels of depressive symptoms, from mild to severe. Direct comparison of the rates of depressive symptoms in the NEVERMIND study with the rates observed in the systematic reviews is challenging since the scales and the categorization used in the different studies are different from those in the NEVERMIND study.

In Study III, our findings indicated a statistically significant reduction in depressive symptoms among patients who used the NEVERMIND system for 12 weeks compared to the control group (B=-3.32; 95% CI -5.24 to -1.39, p=0·001). This finding aligns with previous studies evaluating the efficacy of similar DHTs (81, 82). However, comparing the NEVERMIND system with similar interventions presents a challenge owing to its multi-component nature, which contrasts with most alternatives that typically focus on a singular intervention aspect. This issue is further echoed in systematic reviews assessing the effectiveness of DHTs (80). In addition, looking at the clinical effectiveness within underlying phenomena such as the digital placebo (157) effect can offer additional insights. The digital placebo effect, introduced by Torous and Firth, is described as the "placebo-like outcomes observed in mobile health solutions like smartphone applications" (157).

This digital placebo effect mirrors the placebo response observed in antidepressant drugs. Central to both is the influence of the user's or patient's expectations and perceptions (157). While the placebo effect in antidepressant treatments is thoroughly researched and understood, the digital placebo effect remains relatively under researched with unclear mechanisms (157). Investigating the mechanisms of a digital placebo effect can help determine to what extent the observed efficacy of the DHT is attributed to its treatment components, usability, acceptability, and satisfaction. However, the methodology employed in this thesis does not provide definitive proof of a digital placebo effect. Establishing the existence of digital placebo effects requires a rigorous research design incorporating active (intervention) and placebo DHTs (158).

Given the above challenges, it is crucial to contextualize the clinical effectiveness of the NEVERMIND system by considering:

(1) the specific characteristics of the participants included in the study

(2) the comprehensive content encompassed within the NEVERMIND system

(3) the dynamics of user engagement.

Characteristics of the participants included in the study

Variables such as the stage of cancer (159), time since diagnosis (160), and survivorship prediction (161, 162) are pivotal when tailoring DHTs, given their profound impact on patient experience and specific needs. Disparities exist, not only in the prevalence of depressive and stress disorders across different sub-groups (24, 25, 163), but also in the varied needs within these groups. In a systematic review and meta-analysis, Nead et al. explored the relationship between adjuvant androgen deprivation therapy (ADT) and depression in prostate cancer treatment (164). Analysing 18 studies with 168,756 participants, they found that individuals on ADT had a 41% increased risk of depression (164), a result also corroborated in other studies (165, 166). In this Ph.D. project, we included individuals diagnosed with advanced stage IV prostate cancer who had completed all treatments, except for ADT, and those with advanced stage III or IV breast cancer who had completed all treatments, except for hormonal or trastuzumab therapy. Furthermore, the received treatments for the included individuals had to have been completed at least one month prior to the start of the trial.

Thus, our study population encapsulates individuals in an advanced disease stage who have undergone recommended treatments, such as radiation and surgery, and are currently on hormonal therapy and targeted monoclonal antibody. It is, therefore, imperative to interpret the efficacy of the NEVERMIND system within this specific patient demographic context. For example, Oncokompas, a web-based eHealth app that supports cancer survivors in self-management by enabling them to self-monitor their quality of life and specific symptoms, has shown effectiveness in increasing health-related quality of life among survivors of breast and other cancers (167). However, no significant difference was identified among patients with the same cancer type at the incurable stage (161).

The comprehensive content of the NEVERMIND system

The various components and functionalities included in the NEVERMIND system should be commended as to why the NEVERMIND system was effective in reducing depressive symptoms. A scoping review of digital health interventions by Lee et al. (168) revealed that a substantial portion of interventions in cancer patients (47/231, 20.3%), similar to the diverse content within the NEVERMIND system, included multiple functional components. However, the NEVERMIND system not only leveraged various functions, including educational content about cancer diagnosis but offered different levels of self-management strategies. The tangible benefit of the NEVERMIND system was further substantiated by patients' descriptions of concrete practices and functionalities deemed most beneficial in Study IV.

Behavioural lifestyle changes play a pivotal role in enhancing the mental health of cancer patients. Among these changes, physical activity, mindfulness, sleep, and diet stand out as particularly effective methods to improve mental well-being in patients with cancer.

High rates of sleep disturbances, especially insomnia, have been observed in cancer patients, with breast cancer patients showing a high prevalence (169). While such disturbances are often most prominent at diagnosis (169, 170), they can persist for years after cancer treatment concludes (171). A meta-analysis reported disturbances in 59.7% of breast cancer cases and 44.8% of prostate cancer patients (172). Given the evident association between sleep quality and mental health (173) and its role in potentially reducing depression in breast cancer patients (174), incorporating sleep hygiene, as seen in the NEVERMIND system, becomes imperative.

Physical activity can significantly alleviate depressive symptoms in different population (175), including those with cancer (176). Research has demonstrated that moderate exercise lasting up to 12 weeks can lead to substantial reductions in depressive symptoms among cancer patients and survivors (177), especially in supervised exercises and in those aged 47-62 (176). Tailored physical activity modules, similar to those in the NEVERMIND system, can provide essential support for depression management (178).

Mindfulness practices, emphasizing focused attention on the present moment and acceptance without judgment, also offer profound benefits. These practices, ranging from breathing techniques to yoga, can significantly help manage depressive or stress symptoms in cancer patients (179-181). A systematic review and meta-analysis by Oberoi et al. (182) indicated that mindfulness interventions, when compared to non-active control groups, effectively reduced depression in adult cancer patients for up to six months following the intervention. Similarly, in our study, patients not only utilized mindfulness practices but also extended these practices beyond the confines of the NEVERMIND system, articulating the alleviation of stress through physical exercise.

Finally, dietary habits play a vital role in cancer patients' mental health. A balanced diet has been linked with reduced depression risks in these patients (183). Coupling a healthy diet with good mental health can further reduce mortality rates among cancer survivors (184).

Empowering patients by providing tools to navigate their environment stands out as a pivotal route to achieving mental health well-being, as highlighted by Elkefi et al. (185). Although our study did not evaluate secondary outcomes, such as self-efficacy or perceived stigma, insights from Study IV offer valuable perspectives on which strategies are advantageous and how patients derive benefits from them. Responses to open-ended questions in Study IV illustrated that the NEVERMIND system fostered acceptance and motivation and potentially reshaping their perceptions of their cancer diagnosis while diminishing self-stigma. Moreover, one of the themes that emerged in Study IV was that the NEVERMIND system empowered them with personal agency, enhancing their competency and autonomy in managing depressive symptoms. Study IV offers valuable insights that challenge the notion of a digital placebo effect (157) in the context of the NEVERMIND system. The feedback from users, detailing specific and

tangible benefits, moves beyond user's expectations and beliefs often associated with placebo effects (157). For instance, users noted that the mindfulness practices helped them gain self-awareness, allowing them to connect with their bodies and emotions. Similarly, the positive outcomes from the breathing exercises in managing stress were actual results that users' experienced. Such direct feedback and tangible outcomes, in addition to the observed reduced depressive symptoms in users who used the NEVERMIND system, emphasize that the benefits derived from the NEVERMIND system are rooted in its components and functionalities rather than the results of users' expectations.

In essence, the NEVERMIND system combined physical activity, sleep, mindfulness, and diet modules into one cohesive approach to reducing depressive symptoms in patients with breast and prostate cancer. However, the lack of significant treatment effect on stress symptoms (B=-1.38; 95% CI:-3.04 to 0.28, p= 0.103) could be attributed to the theory that stress symptoms are more trait-dependent than depressive symptoms (186). It can be stipulated that more intensive and distinct interventions than those provided in the NEVERMIND system are needed to reduce stress symptoms.

Dynamics of user engagement

Finally, usage patterns and their potential impact on depressive and stress symptoms showed interesting findings. Only 13% of participants engaged on the first day, and the lowest usage was observed in the initial three days, hinting at potential barriers during early engagement with the NEVERMIND system. At the third week, 80% of users were using the system, particularly the mindfulness module, but usage dropped around the 9th week. Similar trends were observed in the study by Enrique et al. where the engagement of participants in an internet cognitive behavioural therapy (iCBT) intervention for depressive symptoms began to decrease at week five (187). In addition, adherence was a crucial factor in the NEVERMIND study. When users showed consecutive days of inactivity, they were contacted on the third and again on the seventh day of inactivity. Should inactivity stem from depression or other mental health issues, users were redirected to a mental health care team.

Eysenbach sheds light on the importance of adherence, especially within eHealth interventions of DHTs (188). Eysenbach defines *adherence* as "the extent to which participants use and engage with the eHealth application as intended," asserting its importance for several reasons (188). Optimal health benefits from a DHT can only be realized when participants adhere to the intervention, ensuring they receive its full intended outcome. In the case of the NEVERMIND system, the non-predictive nature of a continuous 12-week usage variable on depressive or stress symptoms provided vital insights into the non-linear relationship between the system's use and its clinical effectiveness. Our findings in Study III showed that those who adhered to or used the NEVERMIND system for six weeks or more had significantly lower depressive (B=-3.90;

95% CI -7.46 to -0.34, p=0.032) and stress (B=-5.81; 95% CI -9.27 to -2.35, p=0.001) symptoms compared to those who only used in for two weeks or less. Edney et al. looked at user engagement in an app-based physical activity in 301 users, where users were randomized to receive a gamified, or basic, version of the app to improve physical health for 100 days (189). They found that users who engaged more with the app, whether the gamified or basic version, saw a statistically significant increase in their objective measure of physical activity compared to those who engaged less, where their physical activity decreased from baseline (189). The measure of user engagement in the study by Edney et al. (189), similar to how user engagement was measured in the studies of this Ph.D., did not account for personal variation. A review article by Torous et al. (190) captures the challenges of user engagement and dynamics in DHTs within mental health by reviewing a study by Chien et al. (191) and relating it to other user engagement issues cited in the literature.

In the study by Chien et al., data on 54,604 patients who were part of a clinician-supported iCBT program, targeting depression and anxiety, were used to create different patient groups using a probabilistic latent variable modelling using machine learning (191). Based on log data, patients were classified into five clusters based on their engagement level, captured through minute log data. All patients had a reduced score on depression and anxiety scales, but those in the highest engagement class had the highest decrease in depression and anxiety (191). Though the result from this study is in line with what was observed for users of the NEVERMIND system, Torous et al. (190) articulate limitations on how user engagement was defined and measured in the study by Chien et al. (191) and in the NEVERMIND study.

Torous et al. highlight that measuring engagement as static instead of variation does not capture the full depth and breadth of engagement (190). In the NEVERMIND study, users were classified into active, passive, and non-active groups based on the number of days users used the system, not accounting for fluctuations of use or patterns of use throughout the study period. This type of classification leads to categorizing users who log in briefly over many days with users who engage intensively but on fewer days. Lally et al. found different results when looking at the total duration users spent on the CaringGuidance program, a web-based psychoeducational distress self-management program after breast cancer diagnosis (192). After analysing the usage data of 54 users, Lally et al. found that neither the total duration nor the number of logins correlated with reduced distress levels (192). Instead, the authors found that the number of unique exercise views, representing the depth and content of the intervention, was significantly associated with reduced psychosocial outcomes (192).

7.3 Usability, acceptability, and satisfaction of the NEVERMIND system

While the following section presents various comparative analyses with existing systems, it is crucial to acknowledge that drawing a direct comparison is complex due to the multifaceted nature of the NEVERMIND system. Unlike most DHTs that typically focus on singular components, such as physical exercise or mindfulness, the NEVERMIND system intricately weaves together multiple elements, thereby making it challenging to establish a parallel with DHT studies that have a singular focus.

The NEVERMIND system demonstrated overall high usability, acceptability, and satisfaction. In Study I, the system usability scale (SUS) score was 73.4, a score above the scale average (68), and the user version of the mobile application rating scale (uMARS) score was 3.8, also above the average (3.5). In a meta-analysis by Hyzy et al. (139), the authors collected SUS scores of digital health apps published between 2011 and 2021, 10 years of representative samples of digital health apps. The mean SUS score for physical activity apps was 83.28 (±12.39), while other apps scored 68.05 (±14.05). Though this study by Hyzy et al. included all digital apps, irrespective of target group, physical activity apps have been shown to have high SUS scores in cancer patients (193, 194). Though the SUS score the NEVERMIND system received is above average, there is still room for improvement. The findings of Study IV also shed some insight into some of the statements in the SUS. For example, users found the application lacking intuitiveness and streamlined functionality, denoting a complex system or that the system's content quality was repetitive and lacked variety.

Similarly, the uMARS score, though above average, could be improved compared to other apps used for patient-reported mental health outcomes (194, 195). Wright utilized the MARS to evaluate two breast cancer mobile apps: Becca and OWise (195). While the Becca app "provides specialist support to help live with, through and beyond breast cancer", Owise "gives personalised, safe and reliable and credible information as well as practical support and guidance, in an easy-to-view place" (195). As an expert, Wright applied the MARS to determine the various MARS scores (engagement, functionality, aesthetics, and information score) and the mean score (195). Both the Becca and OWise achieved a high mean score of 4.38 and 4.55, respectively (195), surpassing the mean score of the NEVERMIND system, which was 3.8. However, the NEVERMIND system and the Becca apps scored the lowest in the engagement domain. In a systematic review, Amor-Garcia et al. reviewed 46 apps designed for cancer patients (196). Their findings indicated that the majority (14) out of the 46 apps targeted patients with prostate cancer (196). The average MARS score for all the apps was 2.98, with engagement being the domain that scored the least (196). The engagement sub-domain of the MARS evaluates an app's entertainment, interest, customization, and interactivity (140, 197). In Study IV, users cited the lack of personalization and dynamic interactivity, which aligned

with the low engagement score (3.5) observed in the uMRAS evaluation of the NEVERMIND system in Study I.

A potential alternative strategy to enhance engagement is the incorporation of gamification within the app. There have been successful implementations of gamified mental health interventions for adolescents and young adults, such as the 'SPARX 3-D' interactive game designed to treat depressive symptoms (198). A systematic review and meta-analysis of 12 RCTs indicated that while gamified interventions might be effective for depressive symptoms, they might not be as effective for anxiety, in youth mental health (199). In parallel, there has been growing interest in incorporating gaming elements to increase engagement across various age groups, physical illnesses, and demographics. Cheng and Ebrahimi conducted a meta-analysis review of 42 studies involving 5,792 participants aged between 8-74 to determine the efficacy of gamified interventions in mental health (200). They found a medium effect size in reducing anxiety and depressive symptoms, particularly among males, in non-clinical samples, in interventions lasting no longer than two months, and when focusing on specific measures of anxiety (200).

The insights gained from these studies can inform modifications to the NEVERMIND system, particularly in enhancing user engagement. By understanding the elements that can contribute to higher SUS and uMARS scores and the benefits of gamification, there is potential to improve the NEVERMIND system's user experience.

7.4 Gender-based disparities

While there was a reduction of depressive symptoms over time across participants, females had higher levels of depressive symptoms than males- though this is concurrently correlated with the cancer type. In Study III, the statistical significance of the "Female" fixed effect was evident ($p<0.001$), suggesting that, when other factors are held constant, being a female was linked with higher BDI-II and DASS-21 scores with a moderate to large effect size at 12 weeks. This is reflected in the data showing that female users scored 6.54 points more on the BDI-II (B=6.54, 95% CI 4.50 to 8.58, $p<0.001$) and 6.77 points more on the DASS-21 stress (B=6.77, 95% CI 4.56 to 8.98, $p<0.001$) compared to their male counterparts.

This gender difference in the rates of depression has been reported in different studies and different populations (201-204). The underlying reasons for these differences have been ascribed to the higher risk of first onset (202), the interplay of biological (205, 206), hormonal (201), psychosocial (201), and interpersonal factors (206). In the NEVERMIND system, females had higher depressive symptoms than males (B=6.54, 95% CI 4.50 to 8.58, $p<0.001$) after using the system for 12 weeks. One theory is that studies have consistently, over time, shown that women in high-income countries are more likely than men to use DHTs (207) and have a higher health help-seeking behaviour than men, including mental health services (208, 209). It might be the case that the

NEVERMIND system added more benefits to men than to women since mental and psychological support was lacking. In contrast, women might have already sought help online and educated themselves.

Contrary to existing research, which indicates that women are more likely than men to engage with practices and exercises aimed to reduce mental health symptoms, such as stress and depression, and are also more likely to engage and interact with self-help interactive programs (210), our findings from Study III present a different narrative. In Study III, when users are categorized into non-active, passive, or active groups, the gender difference in depressive symptoms becomes statistically insignificant (B=-0.69; 95% CI: -4.09 to 2.72, p=0.691). The insignificant result can be attributed to 45% of women users (n=30/68) falling into the non-active group, in contrast to only 20% of male users (8/40). This categorization mirrors the results from Study I, where men showed a small, yet significant, higher usage index compared to women. This engagement discrepancy underscores the importance of adherence and usage in measuring usability, acceptability, and satisfaction (188). It also prompts the question of why there exists a usage difference, even when women have rated the NEVERMIND mobile app higher, on the user version of the mobile application rating scale (uMARS) score, than men have.

Besides self-management systems being particularly helpful for males since they exhibit lower help-seeking behaviour (208, 209), several theories can be laid out to explain these contrasts. First, other unmeasured factors, such as expected usefulness, motivation, digital literacy, and prior exposure to DHTs, can interact with gender. The person-based approach, introduced by Yardley et al. (211) and drawing similarities to self-determination theory (212), emphasizes the importance of understanding the end-users' perspectives by focusing on the user experience related to behaviour change techniques. Yardley et al. argue for the implementation of a person-based approach alongside the evaluation of usability, acceptability, and satisfaction in DHTs (211). They highlight the integration of different factors, including psychosocial factors and motivation, which correlate with behavioural change processes (211). Such integration is essential to identify design features of digital tools that are particularly important within specific contexts (211). In Study IV, a difference emerged in how female and male users valued the NEVERMIND system. Women users predominately valued the strong sense of emotional support they felt from the app, while men emphasized the NEVERMIND system's role in facilitating greater self-awareness and introspection. This divergence might suggest the primary motivation and driving force behind using the NEVERMIND system. It also suggests that the NEVERMIND system might be more equipped with features promoting self-awareness and introspection (like the mindfulness module) rather than continuously providing a sense of emotional support.

Another influencing factor in why female had low engagement might be the time and commitment required. Feedback from Study IV consistently highlighted the challenges

users faced in integrating the system into their daily routines. While this aspect wasn't explicitly measured in our studies, it is possible that females, due to familial or caregiving duties, might face some limitations in their engagement with the NEVERMIND system, leading a majority to be categorized as non-active.

7.5 Influence of perceived usefulness and early engagement on long-term use

In the context of the NEVERMIND intervention study, a focus on perceived usefulness (PU) and early engagement (usage at two weeks) in predicting system use at 12 weeks has demonstrated results that warrant consideration. In the data analysis for the NEVERMIND system, it is evident that early engagement with the system and perceptions of its usefulness play a pivotal role in predicting the sustainability of its use at 12 weeks.

The Bayesian SEM identified two primary paths as predictors for the usage of the NEVERMIND system at 12 weeks. Firstly, the path moving from perceived ease of use (PEOU) at four weeks through PU at 12 weeks and ultimately impacting system usage at 12 weeks. Specifically, this path illustrates a progression where early PEOU directly influences PU, which in turn significantly influences the use of the system at 12 weeks. The standardized regression coefficients are $\beta = .589$ for PEOU at 12 weeks, predicted by PEOU at four weeks; $\beta = .581$ for PU at 12 weeks, predicted by PEOU at 12 weeks; and $\beta = .384$ for use at 12 weeks, predicted by PU at 12 weeks. The second path underlined the correlation between system usage at two weeks and usage at 12 weeks, quantified with a β of .239. This latter pathway underscores that early engagement with the NEVERMIND system substantially influences the probability of its sustained use.

The link between PU and use has been extensively studied within the technology acceptance model (TAM) (77, 213). This relationship has held up consistently across various domains (213, 214), reaffirming the results of our study but also the centrality of PU in influencing user's decision to use DHTs. This critical link between PU and subsequent use highlights the importance of orienting efforts toward a user-centric design in DHTs. However, other factors have also been found to be associated with PU. In a survey of 362 health professionals (nurses, physicians, physiotherapists, and psychologists), Nissinen et al. analysed the relationships between demographic variables and the usefulness and ease of use of telehealth services (215). Their findings showed that the type of profession, work experience related to telehealth services, and information and communication technology (ICT) skills were associated with how useful participants found telehealth services. In contrast, only ICT skills were associated with ease of use (215). In Study II, digital skills, or literacy, as well as the type of occupation of user groups, should have been accounted for, hinting at the simplicity of the model that was used.

Ensuring that users immediately recognize the tools' usefulness can establish a positive trajectory for its adoption. Research on the efficacy of DHTs often yield mixed results, with several assessments indicating minimal desired outcomes, potentially due to participants not using DHTs as intended (216–218). The challenges with engagement with DHTs need improvement (216).

In addition, predictors of engagement are context dependent. While some studies find that females and those with higher education level have higher engagement (219), other studies show that low education level (220), older age (221), and higher baseline mental health symptoms (222) have greater engagement. Despite the inconsistent findings, there is consensus that engagement is crucial for the success of DHTs. Enrique et al. observed that those who experienced a reduced depression had the highest engagement with an iCBT intervention for depression in the first four weeks, with the difference in reduced depression coming from the usage during the first week (187). This suggests that the initial engagement period offers an opportunity to increase DHTs' efficacy (187). For example, strategic emphasis in the early intervention phases, particularly in the initial two weeks, may involve education about the system's benefits, practical tutorials, and responsive support mechanisms. Strategies like gamification (200), personalized introduction sessions, detailed user guides, or interactive tutorials could boost initial engagement and positive perception (223). These might be reinforced by sharing data about the system's benefits, thereby also actively shaping the perceived usefulness of the tool.

7.6 Methodological considerations and limitations

A comprehensive approach was employed in the NEVERMIND trial's data collection and assessments, leveraging diverse metrics and scales to explore various dimensions of the participants' mental health, usability, acceptability, satisfaction, and engagement with the NEVERMIND system. The following considerations pertain to methodological reflections and limitations based on the described methods.

7.6.1 Sample size

The sample size for the studies in this Ph.D. thesis was predefined based on the number of available patient data in the NEVERMIND RCT. There was a high completion rate (83.7%, 108/129) among participants initially allocated to the NEVERMIND system, and the lack of significant baseline differences between dropouts and completers strengthens the validity of our findings. Determining sample size for usability tests has been investigated thoroughly (224, 225), and studies have identified that sample size ranging from five users to 100 users was adequate to find usability problems, depending on the number of usability problems one wants to identify, cost-benefit analyses, type of usability testing used among other factors essential for the research aim (224–226).

We conducted a post-hoc analysis in Study III to determine if the sample size was adequate to find a significant effect size for the linear mixed model we used (LMM). The results showed that given the sample and effect size, the power was 96.3%. In Study II, the sample size for the Bayesian SEM was adequate following the rule for 10 observations per estimated parameter (147).

7.6.2 Mental health and sociodemographic assessment

Employing well-established and widely recognized tools like the BDI-II and DASS-21 to measure depression and stress ensures methodological robustness due to their substantial validation and reliability in diverse populations (227-230). However, the stress scale of the DASS-21 was reported to be unsatisfactory regarding internal consistency in one study (227). However, it is pivotal to acknowledge that self-reports bear inherent limitations, primarily related to subjective bias and potential discrepancies between reported and actual symptoms. Therefore, the correlations drawn between mental health statuses and other variables might lack insight.

When assessing mental health symptoms in cancer patients, perceived stigma should have been considered in conjunction. *Perceived stigma* refers to the subjective experience of being stigmatized or discriminated against because of one's illness. Studies have shown that patients with advanced cancer exhibit a higher prevalence of perceived stigma and self-blame, which are associated with lower well-being and increased stress and depressive symptoms (231, 232). These insights suggest that perceived stigma is an important factor to consider when evaluating the effectiveness, usability, acceptability, and satisfaction of DHTs.

While the methodological approach for recoding sociodemographic variables like education and employment status ensures cleaner analyses by consolidating categories, the potential for nuanced disparities within these consolidated groups to influence results should be acknowledged. For instance, the diverse experiences and mental health impacts amongst the unemployed, retired, or those not working due to unspecified health problems could be distinct, which may impose limitations on the insights drawn about these populations in a consolidated manner. Similarly, combining various levels of educational attainment into broad categories might obscure more subtle, education-related, disparities in interactions with digital health tools. However, due to the small sample size in each original category, categorization was deemed appropriate.

Despite the lack of significant results between mental health symptoms and usage of the NEVERMIND system at two weeks, incorporating mental health variables and sociodemographic characteristics into the TAM as individual factors could potentially address some of the criticism directed against the model regarding its 'simplicity' (126). This integration might facilitate a more holistic understanding of technology acceptability and adoption by accounting for how different demographic groups

interact with and perceive DHTs, thereby bridging the gap between generalized technology acceptance theories and the specific, often complex, realities of diverse user experiences and needs. Furthermore, recognizing mental health, not merely as an outcome, but as an influencing factor within the TAM may explain how mental well-being intersects with technology use and acceptance. Fuhr et al. found that older age and higher depressive symptoms were associated with higher user engagement (222) and further our stance in incorporating other variables into the TAM. Taking a leaf out of the person-based approach introduced by Yardley et al. (211), the TAM needs to incorporate, in addition, psychosocial factors (e.g., level of support a user has, and intrinsic motivation) and potentially be specifically developed for each target population after gaining a deep understanding of the target population's attitudes and behaviours.

7.6.3 Usability, acceptability, satisfaction, and use assessment

The application of both the system usability scale (SUS) and the user version of the mobile application rating scale (uMARS) offers a layered assessment of system usability, providing insights into both the technical and user-experience facets of interacting with the NEVERMIND system. While the SUS is the most widely used usability scale (106), making it easy to compare one DHT to another, it poses some limitations. Within the ISO definition, usability encompasses three constructs- effectiveness, efficiency, and satisfaction (69). However, the SUS provides a single score, making it hard to evaluate specific usability constructs as calculating scores for individual questions is not part of the standard process. Broekhuis et al. acknowledge that the SUS might be too broad to be used in eHealth or DHT context without first defining which usability aspect we are measuring (233). Unlike the SUS, other questionnaires like the Poststudy System Usability Questionnaire (PSSUQ) (107) clearly define the facts they measure, such as information quality and interface quality (233). However, as user experiences with DHTs are multifaceted and influenced by factors like tech proficiency and digital literacy, achieving a fully representative usability assessment can be complex. In the NEVERMIND study, digital literacy and tech proficiency were measured by asking if users were able to send and receive emails on their mobile phones, a question not covering the complexities and proficiency needed to navigate through the NEVERMIND system. The potential of other unaccounted variables affecting usability warrants consideration, ensuring that findings are contextualized adequately.

Acceptability and satisfaction assessments via perceived usefulness (PU), perceived ease of use (PEOU), and quantitative and qualitative questions provide insights into the lived experiences and perceptual contexts of participants. However, considering the experiential subjectivity inherent to DHT use, it is pivotal to acknowledge that results may not uniformly translate across varied populations or DHTs. For example, Valokivi et al. examined the role and utilization of digital health services among the general population in Italy, Finland, and Sweden (234). The trends in usage among the general population varied across these countries (234). In Finland, 49% of older adults utilized

eHealth services, compared to 33% in Sweden and 24% in Italy (234). The disparity becomes even more pronounced when considering the percentage of older individuals seeking health advice online, with 76.3% in Finland, 62.2% in Sweden, and 34.9% in Italy (234). Given that users in our study were from Italy, generalizability might be constrained, and application to other interventions or populations should be cautiously considered.

The IS success model used in Study IV to interpret satisfaction served as a guiding theory to position our findings within a theoretical framework. However, the emergence of themes centred on usability and acceptability highlight the potential benefit of integrating the IS success model with other models such as the technology acceptance model (TAM) (77) or the Unified Theory of Acceptance and Use of Technology (UTAUT) (235) to capture and understand user experience, given that satisfaction is a construct found in both usability (70) and acceptability (75).

While calculating the use of the system based on days of interaction provides a quantitative metric of engagement, it falls short of capturing the depth and pattern of engagement, as described in section 7.2. The simplistic approach, not accounting for duration and frequency of use, or looking at module completion, may overlook usage patterns, thus providing a somewhat superficial depiction of system interaction (190). A systematic review on adherence to e-therapies or technology-driven interventions in digital health technologies (DHTs) sheds light on this issue (236). After reviewing 74 articles from 69 individual studies, the authors found that usage metrics such as logins, self-reported activity completions, and time spent online were not significantly associated with reducing depression and anxiety (236). Instead, it was module completions and the number of program views that correlated with the outcome, a result also mirrored in the CaringGuidance web-based program used to decrease distress in newly diagnosed breast cancer patients (192). The challenge extends to comparing findings across different studies due to variations in how they define and quantify use, whether continuously or categorically, and in how the interventions in the DHTs are designed to achieve an outcome (236). Therefore, the best method to measure engagement is to first define what constitutes optimal use, followed by identifying the aspects of use that are essential for the specific intervention and study, and finally, acknowledging the aspects of user experience that are not captured by the chosen method (190, 236). In this Ph.D. thesis, we adopted a methodology, in which using the system multiple times per day, and using it just once, were both recorded as a single instance. The approach was primarily driven by the limitations of the server-provided data for both the shirt and the mobile app. However, our focus was on capturing general usage patterns over time, rather than exploring detailed daily usage.

The categorization of usage into non-active, passive, and active users is reflective of the findings by Donkin et al (237). The authors analysed 214 participants in an online CBT program, with 94 participants (43.9%) reporting a significant reduction in depressive

symptoms after using an iCBT program, as assessed by the Patient Health Questionnaire-9 (PHQ-9) (237). They found that high uses benefited the most compared to low users, whereas medium users derived minimal or no additional benefits relative to low users (237). Following, Donkin et al. introduced the concept of a dose-response plateau, suggesting that users might reach a threshold of engagement beyond which no further benefits are obtained (237).

Within the NEVERMIND system, we observed a trend where active users experienced a significant reduction in depressive symptoms compared to non-active users, yet no significant difference was noted between passive and non-active users. In the context of the NEVERMIND system, the 'plateau' appears to be reached by active users. However, when evaluating stress, a different trend was observed: passive users compared to non-active users had a statistically significant reduction in stress (B=-5.81; 95% CI -9.27 to -2.35, p=0.001), and active users also had a significant reduction compared to non-active users (B=-4.57; 95% CI -7.71 to -1.44, p=0.001). The data on stress indicates a marginal difference between active and passive users, thereby suggesting that medium usage can yield benefits comparable to high usage.

Triangulating this quantitative finding with the qualitative finding in Study IV, patients indicated that practices within the NEVERMIND system were repetitive and lacked diversity. This feedback suggests that users might have reaped the benefits after a certain level of engagement, aligning with the idea of a dose-response plateau as theorized by Donkin et al (237). It would be beneficial to delve deeper into the characteristics of passive and active users to understand what motivates consistent use.

7.6.4 Use of quantitative and qualitative methods

In Studies I through III, quantitative methods were used. While Studies I and II used multiple regression analyses to examine the 'simpler' associations between different variables and the usability, acceptability, and clinical effectiveness of the NEVERMIND system, Study II employed Bayesian SEM in a path analysis to underscore the complexity of relationships between variables, such as user engagement patterns and demographic characteristics. Ensuring that the model accurately reflects the multifaceted nature of engagement with the NEVERMIND system while also thoughtfully incorporating relevant prior knowledge is crucial for affirming the accuracy and relevance of the model outputs.

The path analysis of the Bayesian SEM also had some limitations. The model constructed was based on available user data, where other confounding and unaccounted variables could have skewed the estimates found in Study II. In addition, the model was not as adept as explaining variance at two and four weeks. Thus, it is worth to explore other variables that need to be added, such as digital literacy or examine relationships that could be nonlinear, such as usage.

Study IV emphasizes user satisfaction, involving quantitative and qualitative methodologies to give a balanced perspective to the assessment. Employing a mixed-methods approach in Study IV not only aligns with a comprehensive evaluation of satisfaction but also integrates the TAM and IS success model by offering a mechanism through which user feedback (qualitative) can be contrasted and compared with system use and mental health outcome data (quantitative). The qualitative feedback could inform refinements in understanding system quality and information quality of the IS success model (79). An additional qualitative study to further examine usage could have also helped to understand whether the decline in use was only due to factors such as system-related factors or other external factors like changes in personal circumstances or health conditions.

By comparing qualitative user feedback, such as interface design and personalization, with quantitative mental health outcomes, the IS success model's components, such as 'use' and 'user satisfaction,' can be evaluated in relation to 'net benefits' to understand if and how usage translates into net benefits in mental health well-being. Concurrently, qualitative insights can lend texture to understanding user perceptions around perceived ease of use (PEOU) and perceived usefulness (PU) from TAM, ensuring that user experience is incorporated in understanding DHTs.

7.7 Conclusions

Digital health tools (DHTs) can enhance patient-provider communication, fostering a collaborative approach to care. While some studies demonstrate the potential benefits of such tools, others highlight the challenges and limitations that need to be addressed before fully deploying them.

This Ph.D. project assessed the usability, acceptability, and satisfaction of the NEVERMIND system in patients with breast and prostate cancer. The findings indicate overall good usability, acceptability, and satisfaction while underpinning some areas of improvement.

This Ph.D. thesis underscores the importance of assessing usability, acceptability, satisfaction, and overall use while designing DHTs in addressing mental health challenges for patients with breast and prostate cancer, and possibly other somatic diseases. These aspects are essential as they extend beyond merely evaluating the effectiveness in an experimental setting. Even an effective tool could lose a lot of its potential if patients do not find it usable or acceptable.

The implication for research and clinical practice is also essential. Integrating DHTs into survivorship care plans offers tailored interventions, real-time monitoring, and timely support, making them an essential tool in improving the quality of life for cancer patients and survivors. There is a need to design, develop, test, and implement DHTs that specifically meet the needs of this population. Collaborative efforts between

oncologists, mental health professionals, digital health professionals, user experience designers, and system developers will be crucial in shaping the future of engaging, useful, easy-to-use DHTs.

7.8 Future Directions

Given the ageing population, it is estimated that there will be 28 million new cancer cases worldwide by 2040 (238). As early screening increases along with improved treatments, the survivorship of individuals with cancer will also increase. In the US, 74% (19.2 million) of cancer survivors in 2040 will be aged 65 or older (239), and the most common cancer will be breast cancer (240). In Europe, the number of new cases of cancer is expected to reach 3.4 million by 2040 (241) where the current 20 million cancer survivors (242) is expected to increase. As the number of survivors grows, addressing the holistic well-being, including mental health, of these individuals becomes a priority (26, 27), and DHTs are emerging as promising solutions to address these concerns.

The results from the NEVERMIND system, both in terms of usability, acceptability, and satisfaction and its impact on mental health, have set the stage for a paradigm shift in how we can approach mental health support for cancer survivors using DHTs. Given the anticipated increase in cancer survivors in the coming years, there should be a focus on how to fine-tune DHTs, such as the NEVERMIND system.

The studies presented in this Ph.D. thesis have highlighted several areas for improvement and potential modifications to enhance the NEVERMIND system in future research:

1. ***User-centric design and customization***: Feedback from users emphasizes the need for greater personalization and dynamic interactivity. The system's future iterations could benefit from an adaptive algorithm that not only curates content based on user preferences and capabilities but also their engagement patterns. The integration of additional machine learning models could make this adaptation more effective.

2. ***Enhancing engagement through gamification***: Gamification, as discussed, has proven to be an effective strategy in increasing engagement in DHTs, especially in those targeting depressive symptoms. Incorporating game elements, challenges, and rewards can make the user experience more engaging, increasing adherence and continuous use.

3. **Developing and validating a comprehensive engagement measurement framework**: A comprehensive engagement measurement framework can help understand user interactions within the NEVERMIND system and similar DHTs. This framework could go beyond counting days of interaction to analysing the depth and quality of engagement on a module-specific level. By blending quantitative methods with user feedback, this approach could provide more insights into user engagement and help compare different studies.

4. ***Addressing gender disparities***: The observed gender differences in engagement and outcomes warrant a more in-depth exploration. The NEVERMIND system could benefit from gender-specific modules, developed through focus groups, to incorporate diverse experiences and needs from both male and female users.

5. **Transitioning from a shirt to a smartwatch**: Feedback from users highlights the need for improvement in the wearable component of the NEVERMIND system. Users have mentioned the challenges associated with the shirt (e.g., difficulty sleeping with the shirt and lengthy procedures in setting it up). In future iterations, the NEVERMIND system should consider transitioning to a smartwatch, allowing for constant physiological monitoring with potentially minimal inconvenience for users.

6. **Scalability and expanding accessibility**: While the usability, acceptability, satisfaction, and clinical effectiveness of the NEVERMIND system were evaluated in two centres in Italy, efforts should be directed towards assessing the usability, acceptability, and satisfaction in diverse populations, including individuals with varying levels of digital literacy.

Digital health technologies, like the NEVERMIND system, offer a promising solution. However, their design and deployment should be grounded in research with appropriate methodologies, user feedback, and a deep understanding of user experience.

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