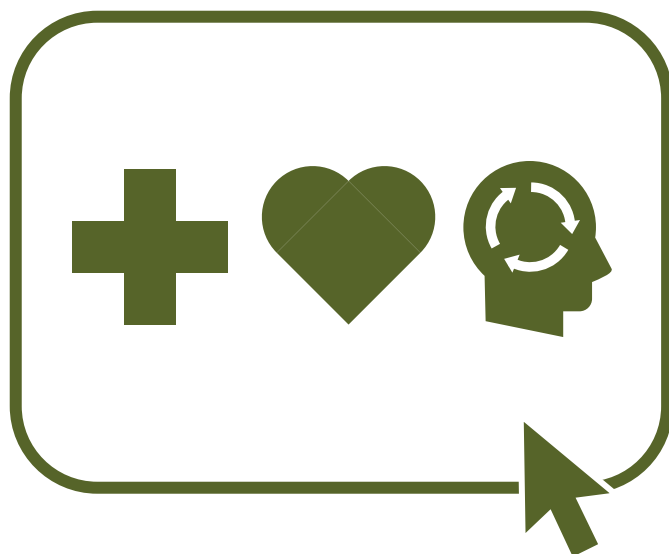


# Web-based support for young adults with reproductive concerns following cancer – development, process and outcome evaluation of a self-help psychoeducational intervention



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Institutet**

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HEALTH

Karolinska Institutet, Stockholm, Sweden

**WEB-BASED SUPPORT FOR YOUNG  
ADULTS WITH REPRODUCTIVE  
CONCERNS FOLLOWING CANCER –  
DEVELOPMENT, PROCESS AND  
OUTCOME EVALUATION OF A SELF-  
HELP PSYCHOEDUCATIONAL  
INTERVENTION**

Claire Micaux



**Karolinska  
Institutet**

Stockholm 2021

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Published by Karolinska Institutet.

Printed by Universitetsservice US-AB, 2021

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ISBN 978-91-8016-029-2

Web-based support for young adults with reproductive concerns following cancer – development, process and outcome evaluation of a self-help psychoeducational intervention  
THESIS FOR DOCTORAL DEGREE (Ph.D.)

By

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The thesis will be defended in public at Karolinska Institutet, Stockholm, February 26, 2021 at 1pm.

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*“These hearts that you would get, somehow they make you feel supported, that you’re not alone in this.”*

A participant in Fex-Can Fertility talking about her experience of the discussion forum



## POPULAR SCIENCE SUMMARY OF THE THESIS

An increasing number of people are living with a history of cancer. Cancer is unusual in younger people and survival rates are very good. But after going through a cancer treatment, it is common to suffer from long-term side effects. Some cancer treatments, such as chemotherapy, radiation and hormonal treatment, may affect a person's ability to have biological children. Only in some cases is it possible to protect fertility before the treatment starts, by for example freezing eggs or sperm. Research shows that being infertile increases the risk of anxiety, depression and having a lower quality of life. Many people also do not know to what extent their fertility has been impaired by the cancer treatment, and some feel they do not get enough support from healthcare professionals in managing their concerns about fertility.

In this thesis, I describe how mainly organizational factors may prevent physicians in cancer care from bringing up the topic of fertility with newly diagnosed patients. The thesis then centers on the development and evaluation of a web-based program that was devised to support young adults (women and men aged 19-40) one to two years after diagnosis, when active treatment in most cases has ended. The self-help program was designed to increase people's knowledge about the impact of cancer treatment on fertility so that they would be able to make informed choices about and come to terms with their situation. There were also videos with personal survivor stories and a discussion forum where participants could share experiences. We theorized that if participants felt competent and connected to others, they would also be able to act consciously in a way consistent with their long-term aspirations. This in turn would increase their wellbeing and reduce their concerns about having biological children. The 12-week *Fex-Can Fertility* program was developed together with a group of young adults with cancer histories and was then tested on another group to see if it would be feasible in the target group.

When the program was tested in a larger nationwide setting and compared with a control group, participants felt that it was useful and that they had fewer concerns. Despite the overall positive experiences, few participants were very active in the program and it was not possible to prove statistically that the program was effective in reducing concern about fertility and parenthood, except for concerns related to transmitting a genetic cancer risk to one's children. The program also increased knowledge about fertility after cancer, but other outcomes were not improved. To understand why we got these results, I discuss some of the possible reasons and present a few suggestions on how to design similar projects in the future, including which questions need to be further investigated.

Nurses and physicians need to be aware of the importance of fertility to people with a history of cancer. To complement regular healthcare, a web-based self-help program like *Fex-Can Fertility* may help in educating patients and connecting them with peers, and thereby help in self-management of one of the long-term consequences of cancer treatment.



## SVENSK SAMMANFATTNING

Antalet personer som lever med en cancerdiagnos ökar. Cancer är ovanligt hos yngre och överlevnaden är god. Men efter att ha genomgått en cancerbehandling är det vanligt med seneffekter och sena biverkningar. Vissa cancerbehandlingar såsom cytostatika, strålning och hormonbehandling kan påverka förmågan att få biologiska barn. Bara i vissa fall är det möjligt att innan behandlingen skydda fertiliteten genom att till exempel frysa in ägg eller spermier. Forskning visar att infertilitet ökar risken för oro/ångest, depression och lägre livskvalité. Många vet heller inte om eller i vilken utsträckning deras fertilitet har påverkats av cancerbehandlingen, och vissa upplever att vården inte ger tillräckligt stöd i att hantera dessa frågor.

I denna avhandling beskriver jag hur främst organisatoriska faktorer kan leda till att läkare i cancervården inte tar upp frågan om fertilitet med nydiagnostiserade patienter. Avhandlingen kretsar sedan kring hur vi utvecklat och utvärderat ett webbaserat program som utformats för att stödja unga vuxna (kvinnor och män mellan 19 och 40 år). Detta självhjälpsprogram syftade till att öka deltagarnas kunskap om cancerbehandlingens möjliga påverkan på fertiliteten, så att de skulle kunna fatta informerade beslut och bearbeta sin situation. Det fanns också personliga filmer och ett diskussionsforum där deltagare kunde dela med sig av sina erfarenheter. Baserat på självbestämmandeteorin antog vi att om deltagarna kände sig kompetenta och kände samhörighet med andra i liknande situationer, så skulle de också kunna handla på ett medvetet sätt som stämde överens med deras långsiktiga livsmål. Detta i sin tur skulle öka deras välbefinnande och minska oron kring att få biologiska barn. Det webbaserade 12-veckorsprogrammet *Fex-Can Fertilitet* utvecklades tillsammans med en grupp unga vuxna som själva genomgått cancerbehandling, och testades sedan på ytterligare en grupp för att undersöka om det var genomförbart i den tänkta målgruppen. När programmet i en rikstäckande studie jämfördes med en kontrollgrupp, fann vi att de som lottades till deltagande i programmet tyckte det var användbart och att deras besvär förbättrades. Trots att övervägande positiva upplevelser framkom var få deltagare aktiva i programmet på den nivå som vi hade hoppats. Det gick heller inte att visa på någon statistiskt säkerställd effekt när det gällde programmets förmåga att minska oro kring fertilitet och föräldraskap, utom när det gäller oro för att föra över en genetisk risk för cancer till sitt barn. Programmet stärkte i övrigt kunskapen kring fertilitet efter cancer men hade ingen effekt på andra utfall vi mätte. I avhandlingen diskuterar några av de möjliga orsakerna till dessa resultat och föreslår några frågor att undersöka närmare för att bättre kunna utforma liknande studier i framtiden.

Sjuksköterskor och läkare behöver vara medvetna om vilken viktig roll fertilitet spelar för personer som genomgått cancerbehandling. Som ett komplement till annat psykosocialt stöd kan det vara användbart att erbjuda ett web-baserat självhjälpsprogram som kan ge patienter ökad kunskap och kontakt med andra i liknande situationer. Därigenom kan man stärka egenvårdsförmågan att hantera en av de långsiktiga konsekvenserna av cancerbehandling.

## **ABSTRACT**

**AIM:** To describe the development process and explain the outcomes of Fex-Can Fertility, a self-help web-based psychoeducational intervention aiming to alleviate reproductive concerns in young adults with cancer.

**METHODS:** The thesis comprises five papers; one cross-sectional survey study of oncologists' and hematologists' fertility-related communication (I), one study describing the development of the Fex-Can intervention in a participatory process (II), one feasibility study testing the preliminary version of the web-based program (III), and one RCT testing the effect of the final intervention (IV). Study V was a qualitative interview study examining participants' experiences in relation to the theory behind the intervention.

**RESULTS:** The results of the five papers are presented according to the structure of a process evaluation. The context of the intervention was one where physicians in cancer care often but not always talk about fertility with their patients. Persons contributing to, requesting and participating in the Fex-Can intervention were predominantly female and well educated. The intervention was developed in a participatory process with people representative of the target group while keeping with theoretical underpinnings in psychology and eHealth technologies. Feasibility testing indicated that the intervention would be acceptable to users, but recruitment and retainment was below the anticipated figures. The RCT was underpowered and had modest outcomes, with significant effects only on concerns about genetic risks and on treatment-related fertility knowledge, where the effect sizes were moderate. Mechanisms of impact were investigated mainly in the interview study. Participants described how the intervention had supported their needs for competence, relatedness and autonomy, but also that some missed tailoring to their specific needs and that keeping up with the intervention was too time-consuming. Degree of activity did not seem to have a clear relationship with effect of the intervention.

**CONCLUSIONS:** Despite meticulous preparation and adherence to every step of the framework for intervention development, the present intervention did not meet our expectations for efficacy in reducing fertility-related distress. Challenges include refining recruitment strategies, finding appropriate main outcome measures and ways to further ensure active participation. Still, the Fex-Can Fertility intervention was appreciated by most users and no adverse events were recorded, suggesting it can be of value if offered as a supplement to standard psychosocial support in clinical cancer care.

**Key words:** cancer, complex intervention, eHealth, fertility distress, process evaluation, RCT, young adult

## LIST OF SCIENTIFIC PAPERS

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- IV. Micaux, C., Wiklander, M., Eriksson, L.E., Wettergren, L. & Lampic, C. Efficacy of Fex-Can Fertility, a self-help web-based psychoeducational intervention for young adults with fertility distress following cancer – randomized controlled trial. *Manuscript*
- V. Micaux Obol, C., Lampic, C., Wettergren, L., Ljungman, L. Eriksson LE (2020). Experiences of a web-based psycho-educational intervention targeting sexual dysfunction and fertility distress in young adults with cancer – A self-determination theory perspective. *PLOS ONE* 15(7):e0236180. doi.org/10.1371/journal.pone.0236180

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## SCIENTIFIC PAPERS NOT INCLUDED IN THE THESIS

- I. Lampic C, Ljungman L, Micaux Obol C, Eriksson LE, Wettergren L. (2020). A web-based psycho-educational intervention (Fex-Can) targeting sexual dysfunction and fertility-related distress in young adults with cancer: study protocol of a randomized controlled trial (2019). *BMC Cancer*. Apr 11;19(1):344. doi: 10.1186/s12885-019-5518-3.
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## LIST OF ABBREVIATIONS

ACT	Acceptance and commitment therapy
ART	Assisted reproductive technology
CG	Control group
Fex-Can	Fertility and Sexuality Following Cancer
EORTC QLQ-C30	The European Organisation for Research and Treatment of Cancer quality-of-life questionnaire
ES	Effect size
HADS	Hospital Anxiety and Depression Scale
HCP	Healthcare professional
HrQoL	Health-related quality of life
(I-)CBT	(Internet-delivered) Cognitive behavioral therapy
IG	Intervention group
IRL	In real life
IVF	In vitro fertilization
LMM	Linear mixed models
MRC	Medical Research Council
OR	Odds ratio
p	probability
PRP	Patient research partner
RCAC	Reproductive Concerns After Cancer scale
RCT	Randomized controlled trial
SDT	Self-Determination Theory
YA	Young adults (19-40)

# 1 INTRODUCTION

Going through a cancer diagnosis and treatment is a complex experience affecting the body, mind, and social relations. Support needs may vary over time and between individuals. People living with and beyond cancer, their close relatives, healthcare professionals, and policymaking agencies have requested web-based resources to complement conventional care. There is great faith in the potential of eHealth to provide support, but eHealth interventions are complex, and implementation is hampered by the lack of evidence. As a PhD student and a nurse encountering people with cancer, I have been lucky to be involved in the great learning experience of designing, developing and evaluating a web-based intervention in the intersection between psychology and nursing. In this thesis, I will attempt to describe the rationale, development, feasibility testing and evaluation of this complex intervention while integrating elements from a process evaluation. The objective is to explain and understand the outcomes of the Fex-Can intervention in order to facilitate the further development of clinically useful web-based resources.

## 1.1 NURSING RESEARCH IN CANCER CARE

### 1.1.1 A holistic view of the person experiencing illness

Nursing is both a professional activity and a basic science driving discipline-specific knowledge to generate questions about how to improve care Barrett (2017). Nursing science, like health psychology, physiotherapy and occupational therapy, is part of the healthcare sciences, bridging the natural and social sciences, but it is also a discipline in its own right. Various attempts have been made to define nursing and nursing science (Barrett, 2002). Most theorists agree that the constant feature of nursing is the holistic approach and the focus on each unique individual, stressing the diversity of perceptions, feelings, needs and preferences. Symptoms must be understood from a wider biopsychosocial perspective in which health, caring, person and environment (also known as nursing's core concepts) are considered. This model has been questioned over the years and the core concepts have been reformulated in various ways, often with a focus on *care and health processes* and *relational practices* (Fawcett, 2020). Some theorists argue that caring is the core of nursing and prefer the term caring science (Turkel, Watson, & Giovannoni, 2018).

The *nursing practice* perspective focuses on understanding signs and symptoms that are observed in ill people, and takes its departure in the individual who experiences ill health. According to the International Council of Nurses (2002), nursing “*encompasses autonomous and collaborative care of individuals of all ages, families, groups and communities, sick or well and in all settings. Nursing includes the promotion of health, prevention of illness, and the care of ill, disabled and dying people. Advocacy, promotion of a safe environment, research, participation in shaping health policy and in patient and health systems*



*management, and education are also key nursing roles.*” Thus, the term *nursing* embraces both what nurses do and how they theorize about what they do.

The nurse in cancer care must be able to acknowledge the whole spectrum of the cancer experience and meet the person seeking care where the person currently is. Cancer can be understood on the molecular level, as mutational changes to DNA leading to uncontrolled cell growth. It is also a concept with social and cultural associations, sometimes referred to as “the Big C” or “the disease you do not mention.” Cancer is surrounded by myths, prejudice and fear and often talked about using war metaphors (Vrinten et al., 2017). In the cancer care setting, it refers not to one single disease but to over 200 diagnoses. With approximately 60,000 new cases annually in Sweden (National Board of Health and Welfare, 2017), there are a myriad of possible combinations of biological and socioeconomic and cultural background factors, treatment circumstances and individual coping styles – making each care encounter a unique situation. Additionally, precision oncology has introduced the concept of “personalized cancer therapy” based on the genomic structure of each tumor (H. Z. Chen, Bonneville, & Roychowdhury, 2019). It is no longer possible, from either a medical or a nursing perspective, to treat cancer *only* by following a pre-specified protocol. At the same time, it is important to follow guidelines and ensure cancer care is equal and evidence-based. Great professional and ethical challenges persist in maintaining a person-centered nursing approach while attending not only to preferences and perceived needs, but also to individual variation in tumor expression and the presence or absence of risk factors. In a clinical situation with high technology but limited personnel resources, oncology nurses are constrained by organizational and societal factors beyond their control and therefore at risk for compassion fatigue and burnout (Xie et al., 2020). It is also a rising challenge to respond to increasing demands from patients to have updated and very specific knowledge about various sequelae of the cancer treatment. As the focus shifts from survival to survivorship, effective interventions that can redirect personnel resources where they are best needed are warranted.

### **1.1.2 Ontological and epistemological standpoints in nursing science**

For over a century, medical research has been a discipline imbued with post-positivism, with its core concepts of hypothesis testing and falsification, and the realist worldview according to which there is an independent reality that can be studied objectively.

Within nursing science, there is an ongoing debate as to whether nursing research belongs to the post-positivist tradition or not. There are often considered to be two main paradigms in nursing research – the totality and the simultaneity paradigms (Barrett, 2002; Cody, 1995) – while several authors also stress that nursing science relies on a variety of philosophical standpoints and methodologies. The totality paradigm is based on the human as a biopsychosocial being, where the goal of nursing is to restore health following an assessment of the individual and substantial focus is placed on norms, prediction, and control. This view

has been associated with a biomedical or psychological perspective, applied nursing science (practice) and a postpositivist or realist tradition, often articulated in RCTs. The simultaneity paradigm instead emphasizes the importance of understanding the human being, who is always more than the sum of its parts. Health is the result of a co-creative process that cannot be objectified. The simultaneity paradigm is associated with constructivism, post-modernism, qualitative methods and person-centeredness (Cody, 1995). Some scholars have argued that this divide is detrimental to nursing as a whole because it isolates the philosophical parts of nursing research from the more practice-oriented parts, and also from other healthcare professions (Corry, Porter, & McKenna, 2019). One could also argue that modern nursing science is able to accommodate both post-positivism and constructivism and that the divide is artificial. For instance, thematic analysis can be used in both realist and constructivist approaches, depending on which type of knowledge is sought after, but the perspective will determine research questions and how meaning is theorized (Braun & Clarke, 2014).

In the present thesis, I take my point of departure in the idea put forward by Corry et al. (2019) that contemporary nursing research methodology is characterized by a necessary pluralism. It should then be possible to study health behaviors and related phenomena from several perspectives, and not be limited to either the postpositivist/realist or the constructionist viewpoint. Just as a triangulation of methods enhances the validity of results, it might be necessary to try both to explain and to understand.

## **1.2 COMPLEX INTERVENTIONS IN HEALTHCARE**

### **1.2.1 What makes an intervention complex?**

Complex interventions in healthcare usually contain several components and engage multiple stakeholders (Craig et al., 2008). Complexity can also stem from the type of change that is required from participants or from multiple outcomes (O’Cathain et al., 2019). Internet interventions concerning sexual and reproductive health can be regarded as complex interventions insofar as they target a symptom cluster with various components, using different techniques/strategies, and also by the fact that they are delivered in highly flexible settings (Craig et al., 2008).

The Medical Research Council (MRC) guidance first published in 2000 and updated in 2008 is still the key framework for developing and evaluating complex interventions in healthcare. It has been supplemented recently by a consensus statement adding the importance of stakeholder involvement at all levels of intervention development (O’Cathain et al., 2019). Components of the MRC guidance are summarized in Figure 1. The bidirectional arrows emphasize that intervention development and evaluation is a dynamic, iterative process and that the relationship between the various stages is not a linear one (O’Cathain et al., 2019).

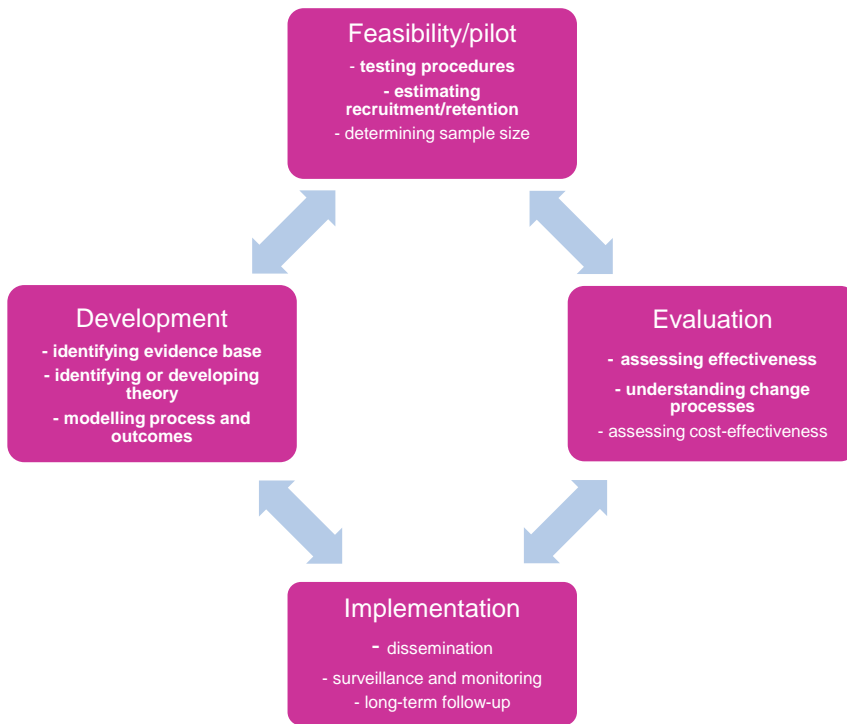


Figure 1. Development and evaluation of complex interventions in healthcare. Aspects investigated in this thesis in bold. Adapted from Craig et al. (2008).

### 1.2.2 The relationship between development, process evaluation and outcome evaluations

The MRC guidance encourages process evaluations but does not explicitly state how these should be conducted. Process evaluations are not only about establishing the effect or not, but also about understanding *why* or *why not*? This involves assessing *fidelity*, *dose and reach* (Steckler, 2002), all of which are particular challenges in the case of Internet interventions. Process evaluations require various types of data from different steps and time points in the process., i.e., feasibility testing, quantitative outcome measures and user experiences (G. F. Moore et al., 2015). Figure 2 describes the required parts of a process evaluation and Figure 3 how I understand the context as an umbrella overarching the development, feasibility and evaluation of the intervention, combining into a process that will be described in this thesis.

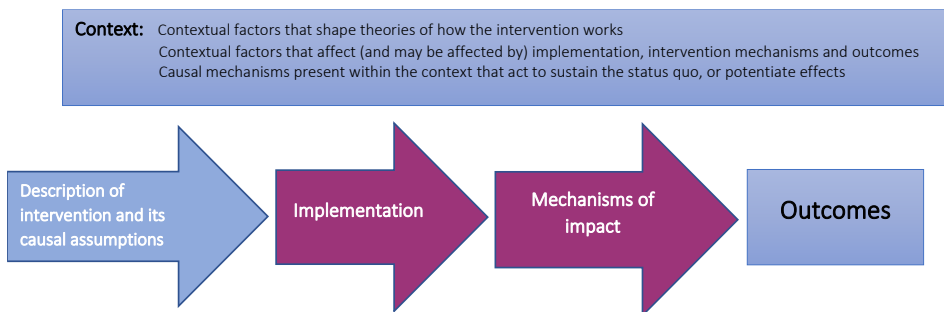


Figure 2. Components of a process evaluation. Adapted from Graham F. Moore et al. *BMJ* 2015;350:bmj.h1258.

In addition to description of the context and of the intervention itself, G. F. Moore et al. (2015) suggest the following elements should be considered when conducting a process evaluation:

**Mechanisms of impact** include: *Participants' responses to and interactions with the intervention*; how the intervention is received, used and experienced by the target group.

*Mediators* – known or unknown factors that might explain a certain effect on the outcome variables – an effect that would not occur without the presence of the mediator.

*Unexpected pathways and consequences* – any adverse events or unexpected outcomes of the intervention on any stakeholder level.

**Implementation** in this case does not refer to the establishment of an evidence-based intervention in clinical practice and in studying the behavior change of healthcare professionals, but instead to the way in which the intervention (in this case the feasibility study followed by the RCT) was conducted. This includes the *Implementation process* (how delivery is achieved – technical aspects and resources), as well as *What is delivered* (fidelity, dose, adaptations, reach) (G. F. Moore et al., 2015).

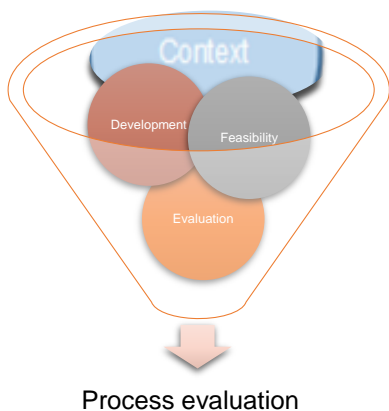


Figure 3. Synthesis of intervention development and process evaluation: my conceptualization of the Fex-Can program



## 2 LITERATURE REVIEW

### 2.1 BEING YOUNG WITH A CANCER EXPERIENCE

#### 2.1.1 Epidemiology and common side effects of treatments

Cancer is known as a disease of the ageing population. Of the approximately 65,000 people diagnosed with malignant disorders each year in Sweden, only about 2,300 (National Board of Health and Welfare, 2017) are between the ages of 18 and 39, the age span which is often referred to as young adulthood (Fidler et al., 2017). Becoming a cancer survivor of reproductive age therefore means being an exception. However, higher incidence alongside an overall five-year survival rate of about 85% makes living with and beyond cancer a relevant issue for an increasing number of young adults each year (van der Meer et al., 2020). The risk for most cancers will increase with age, even within the young adult bracket, except for leukemia, Hodgkin/non-Hodgkin lymphoma and sarcoma/bone tissue tumors, which are more common in adolescents. Two types of cancer affecting young people with rises in overall incidence rates are thyroid cancer and testicular cancer (Miller et al., 2020). Prevalence rates of various cancer types in young adults vary between countries, depending on the socioeconomic and public health situation. In Sweden, breast and testicular cancer are the most common diagnoses in young women and men, respectively (National Board of Health and National Board of Health and Welfare, 2017).

Cancer treatments include surgery, chemotherapy, radiotherapy, hormonal therapy, immunotherapy or targeted drugs (personalized cancer therapy, (H. Z. Chen et al., 2019), often given in combination. Side effects from cancer treatment can include acute, long-term or late effects. Psychosocial side effects, like the physiological ones, are generally dose-dependent but also moderated by individual factors. While hair loss, nausea and skin lesions occur during active treatment and generally are reversible (short-term side effects), fatigue and pain may persist long after the treatment has ended (long-term side effects). Other common long-term side effects or late effects (problems arising later but related to the cancer diagnosis and/or the treatment) include anxiety and depression, relationship difficulties and cognitive impairment. Late and long-term side effects sometimes lead to socioeconomic difficulties if the ability to work remains affected (Barnett et al., 2016; Patterson, McDonald, Zebrack, & Medlow, 2015; Stanton, Rowland, & Ganz, 2015).

Several cancer treatments may cause temporary or permanent subfertility or infertility in both women and men (Rodriguez-Wallberg, 2012; Vassilakopoulou et al., 2016). Negative effects on the reproductive system are especially common in connection with high-dose chemotherapy treatment with alkylating agents (Turan & Oktay, 2014) but may also occur after surgery, radiation and hormonal therapy (Rodriguez-Wallberg, 2012; Teh, Stern, Chander, & Hickey, 2014). In women, the extent to which these effects are reversible varies considerably depending on age, dose received, and pre-treatment ovarian reserve, but early menopause is not uncommon (Turan & Oktay, 2014). In men, the risk of permanent

subfertility is particularly related to receipt of high-dose chemotherapy for hematologic malignancies, or the disease itself in the case of testicular cancer (Vakalopoulos, Dimou, Anagnostou, & Zeginiadou, 2015). Obviously, in the case of surgical removal of reproductive organs the individual loses their ability to conceive. Lifetime fecundity and the probability of a first live birth are expected to be reduced following a cancer diagnosis during adolescence or young adulthood, especially for men (G. Armuand, Skoog-Svanberg, Bladh, & Sydsjo, 2017; Madanat et al., 2008; Tang et al., 2016). This means that although many former cancer patients can and do start families, they do not do so to the same extent as their peers.

The population studied in this thesis includes young adults aged 18-39 diagnosed with one or more of the tumors known to affect fertility and sexual function either by the anatomical location of the tumor or by the given treatment. Table 1 shows the number of new tumors and age-standardized incidence rates for those diagnoses in the years 2016 and 2017 (National Board of Health and Welfare, 2017). It is important to notice that for some diagnoses, e.g., breast cancer, it is common to report several tumors in the same individual and therefore the number of cases is superior to the number of persons affected.

Table 1. Incidence rates<sup>1</sup> of selected tumor types in the ages 20-39 in Sweden (National Board of Health and Welfare)

<b>Tumor type</b>	<b>2016</b>	<b>2017</b>
<b>Breast cancer</b>	30.08	43.03
<b>Cervical cancer</b>	16.36	16.27
<b>Ovarian cancer</b>	3.16	2.61
<b>Testicular cancer</b>	16.80	17.96
<b>Lymphoma</b>	2.12	3.13
<b>CNS tumors</b>	7.11	6.87
<b>Men (total)</b>	26.42	29.14
<b>Women (total)</b>	58.43	71.52

1. Per 100,000, age-standardized according to the population in 2000. Number of tumors may exceed number of persons.

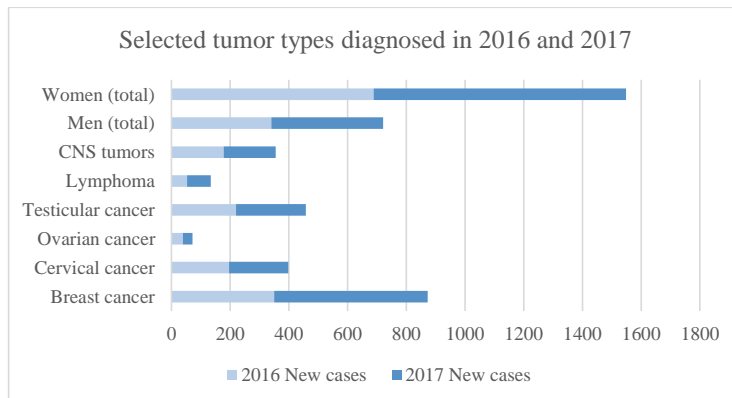


Figure 4. Reported incidence in Sweden in 2016 and 2017, ages 20-39, for tumor types included in Fex-Can Fertility (Socialstyrelsen, national statistics).

### **2.1.2 Psychosocial aspects of living with and beyond cancer**

The concept of cancer survivorship means “living with a cancer diagnosis following primary treatment for cancer through the end of life” (Feuerstein, 2007; Kim, Kim, & Mayer, 2017). Being diagnosed with cancer as a young person is a multi-faceted and dynamic experience with many consequences on the individual level. In spite of many difficulties, young cancer survivors also describe positive consequences from cancer treatment (Husson et al., 2017a; Lehmann et al., 2014; Quinn, Goncalves, Sehovic, Bowman, & Reed, 2015). Finding benefit in the cancer experience, also known as post-traumatic growth, has been reported as one aspect of survivorship, alongside more problem-oriented ones (Howard-Anderson, Ganz, Bower, & Stanton, 2012; Stanton et al., 2015).

Although sequelae from cancer treatment are extremely variable depending on the person, diagnosis, treatment and other circumstances, late or long-term side effects may interfere with important life goals for a young adult person. Many young cancer survivors report cognitive impairment and prolonged fatigue (Barnett et al., 2016; John, Sender, & Bota, 2016), which may in turn impact several of the other important dimensions of life. Among the consequences are limitations in educational attainment and employment, often resulting in financial burden and postponed independence. Stages of development that may be complicated by the cancer diagnosis include building intimate relationships and, when desired, having children (Canada & Schover, 2012; Duffy & Allen, 2009). It is not surprising that such a pervasive disruption of taken-for-granted events in the life course may lead to a feeling of not living up to age-appropriate expectations about work, leisure and social relationships. Indeed, young adult cancer survivors have been found to report lower health-related quality-of-life (HrQoL) scores than the general population of the same age and sometimes perceive a lack of social support (Husson et al., 2017b; Quinn et al., 2015; Sinnott & Park, 2019). Interventions directed specifically at young cancer survivors are scarce and report mixed results (Barnett et al., 2016). Sexual and reproductive health is one of the areas where unmet care needs are frequently reported by young adults, warranting improved support (Olsson, Jarfelt, Pergert, & Enskär, 2015).

### **2.1.3 Reproductive concerns**

Most people wish to have children. A survey of Swedish university students showed 96% of women and 97% of men wanted to become parents (Lampic, Svanberg, Karlström, & Tydén, 2005). Becoming a parent is associated with becoming an adult and with managing one’s gender identity. After a cancer diagnosis, the fear of post-treatment infertility therefore further disrupts psychological wellbeing for many survivors (Ussher & Perz, 2018). Reproductive concerns, or fertility distress, are defined as concerns related to fertility and/or parenthood (J. R. Gorman, Malcarne, Roesch, Madlensky, & Pierce, 2010; Wenzel et al., 2005). The concept is broader than just the physical capability of having biological children. It also encompasses psychological resources in handling relationships, pregnancy, and parenthood, including worries about recurrence and about transmitting a



genetic cancer risk to one's offspring. Reproductive concerns also inversely reflect acceptance of possible infertility. The term *concerns* is usually used in the US while literature from the British Commonwealth tends to use *distress* for the same phenomenon. In this thesis, I use the terms interchangeably yet I wish to emphasize that neither reproductive concerns nor fertility distress is, in my view, a psychiatric disorder or an anomaly but rather a logical and sound reaction to the threatening biographical disruption caused in this case by the cancer experience. Fertility-related distress is reported by approximately 40-50% of cancer survivors diagnosed in young adulthood (Ljungman et al., 2018; Ljungman et al., 2019; Logan, Perz, Ussher, Peate, & Anazodo, 2019; Young et al., 2019), with women in the higher range. This figure seems to be relatively stable across populations and settings.

In the general population, the prevalence of infertility and subfertility is generally estimated at 10-15%, with roughly equal proportions of male and female infertility (Sun et al., 2019). There is a shortage of studies on reproductive concerns outside the cancer context. In a cross-sectional study of young adults in Sweden without cancer, the proportion of respondents reporting high levels of distress varied from 1% of men feeling distressed about achieving a pregnancy, to 13% of women reporting low levels of acceptance of potential infertility. Conversely, 53% of women and 31% of men reported at least one sexual dysfunction (Ljungman, Lampic, & Wettergren, 2020). These results indicate, first, that fertility-related distress is much more specific to the cancer diagnosis than is sexual dysfunction and, second, that the prevalence of fertility distress is much higher among young adult cancer survivors than in people of the same age who have not had cancer. Fertility distress may extend long after treatment completion (Ahmad, Fergus, & McCarthy, 2015; Canada & Schover, 2012; Meneses, McNeese, Azuero, & Jukkala, 2010). Fertility distress has been associated with comparatively poor quality of life (Ahmad et al., 2015; Benedict et al., 2018; Howard-Anderson et al., 2012), and depressive symptoms (Jessica R Gorman, Su, Roberts, Dominick, & Malcarne, 2015). In a population of pre-menopausal women with breast cancer, concerns about menopause and infertility were associated with distress. Younger women with fertility distress had worse quality of life and more depressive symptoms than both the general population *and* older women with breast cancer (Howard-Anderson et al., 2012). In a pioneer study, social support, gynecologic problems, and reproductive concerns accounted for about two-thirds of the variation in quality-of-life scores among young breast cancer patients (Wenzel et al., 2005). This suggests that infertility and problems related to premature menopause place a particular added burden on younger female cancer patients.

Being faced with an acute threat to one's own life and to fertility may change a young person's priorities regarding what is important in life. A systematic review found that cancer was likely to affect reproductive motivations (Schmidt, Richter, Sender, & Geue, 2016). This conclusion is confirmed by several qualitative studies. Geue et al. (2014) found that for cancer survivors wanting to become parents, intensity in child wish could increase

post-diagnosis. It has also been reported that desire for children may change in both directions following the cancer diagnosis (G. M. Armuand, Wettergren, Rodriguez-Wallberg, & Lampic, 2014).

It appears that fertility-related distress in several ways potentially limits the health-related quality of life in younger cancer survivors. This underscores the need for timely and appropriate communication about fertility at various levels of healthcare.

## **2.2 FERTILITY SUPPORT FROM HEALTHCARE**

The field of research and medical services related to the detrimental effect of cancer treatments on reproductive ability is referred to as oncofertility. Oncofertility is an umbrella term encompassing various HCP resources ranging from experimental fertility preservation treatments to investigation and evaluation of psychological support provided to cancer survivors (Anazodo, Ataman-Millhouse, Jayasinghe, & Woodruff, 2018).

### **2.2.1 Information provision**

There are international guidelines recommending that the issue of fertility be addressed as early as possible, preferably before the cancer treatment starts (Lee et al., 2006; Loren et al., 2013; Rodriguez-Wallberg & Oktay, 2014). Even if the young adult expresses no plans for trying for a child at the time of diagnosis, there is a need for offering individualized fertility counseling throughout the disease trajectory (G. Armuand, Wettergren, Nilsson, Rodriguez-Wallberg, & Lampic, 2017; Schmidt et al., 2016). Counseling may involve contraception during treatment as well as fertility preservation measures when possible. Fertility counseling can be given both pre- and post-treatment to counteract a shortened expected reproductive span or subfertility due to treatment (Rodriguez-Wallberg, 2012). In the event the patient becomes infertile, there is also the need to discuss alternative options to biological parenthood.

Several systematic reviews concerning patient support needs have established that information about fertility is considered important or highly important, especially among younger women with recently diagnosed breast cancer (S. Logan, J. Perz, J. M. Ussher, M. Peate, & A. Anazodo, 2018b) and women 18-45 with gynecological cancer (Deshpande, Braun, & Meyer, 2015). Discussion with an HCP about fertility and satisfaction with this discussion has been associated with lower levels of distress and with involvement in the decision-making process (Ussher & Perz, 2019). Conversely, unmet informational needs regarding oncofertility have been associated with lower quality of life (Benedict et al., 2018). The estimations of the extent to which cancer patients receive adequate information about fertility following cancer vary between studies. Previous findings from our research group (G. M. Armuand et al., 2012; G. M. Armuand, Wettergren, Rodriguez-Wallberg, & Lampic, 2015) have indicated that women may have more negative experiences of fertility-related communication, or its absence, than men. There are several factors potentially hindering fertility discussions. Organizational difficulties such as a high workload, resource constraints and working in a patient-funded healthcare system have been mentioned. It has also been

suggested that healthcare professionals in general avoid the issue of sexuality with their patients (Dyer & das Nair, 2013) and some physicians report feeling embarrassed talking to young male patients about the fertility preservation procedure since it includes masturbation (S. Logan, J. Perz, J. Ussher, M. Peate, & A. Anazodo, 2018a). There are also indications in the international literature that physicians and nurses refrain from addressing fertility based on patient factors like age, relationship status, sexual orientation and, importantly, prognosis of the disease. The most important barrier reportedly is poor prognosis for the patient (Leung, Goldfarb, & Dizon, 2016).

The fact that patients still report not recalling fertility-related discussions suggests a need for improved communication and diversified sources of information. Since people seeking healthcare have differing abilities as concerns understanding and processing information at different time points, it is important that the information given is individualized, repeated and followed up all along the disease trajectory.

### **2.2.2 Limitations of fertility preservation and alternative ways of becoming a parent after cancer**

Options for preserving threatened fertility range from routine procedures to experimental treatments and include cryopreservation (freezing) of sperm, embryos, oocytes, ovarian tissue, or testicular tissue. Another possibility for some diagnoses may be fertility-sparing surgery, which aims to conserve the natural ability to conceive and, in the case of women, carrying a pregnancy to term (Rodriguez-Wallberg et al., 2020). Assisted reproductive technologies (ART) following FP measures are also available free of charge in Sweden for singles or partnered persons who have no more than one child in the current relationship. In other cases, the procedures may be performed at the charge of the individual. Frozen tissue is kept for ten years (previously five). Strict age limits apply for subsequent IVF procedures; the woman must be <40 years on each occasion, the man <56 years old, and if the couple already has children, charges apply. In addition, the following rules apply for persons treated for cancer: a certificate from the responsible oncologist that the risk of recurrence is low using saved gametes. The parent(s) are subject to a psychosocial investigation to make sure there is no advice against parenthood (Region Stockholm, 2020).

Swedish legislation surrounding ART and fertility preservation has changed in recent years. At the time of planning the present research project, procedures involving donated sperm or egg cells were only allowed to be performed at university hospitals. Furthermore, one person in the couple, or the single woman should the case be, needed to have a genetic link with the offspring. In practice, this precluded all gay men, lesbian couples in which none of the women had functioning oocytes, as well as heterosexual couples in which both the man and woman lacked functional germ cells, from using ART at all. In 2019, embryo donation and ART using only donated germ cells became legal in Sweden (Swedish Parliament, 2018) and these operations were no longer restricted to university hospitals. However, surrogacy is still not allowed, implying that for gay men and for women without a uterus, adoption is still the only alternative. Previously, response to ART has shown to be poorer in female cancer

survivors than in women without a cancer history (Barton, Missmer, Berry, & Ginsburg, 2012), unless donated eggs are used (Luke et al., 2016). Despite medical advances, the general success rates for ART procedures also remain relatively low (about 25% live birth rates per ART cycle) and decline as the woman's age increases (Volgsten & Schmidt, 2017).

When ART is not possible or not successful, adoption may be a way to become a parent. In Sweden, national adoptions are very rare, except for close family members. The number of international adoptions has fallen in recent years, from 1108 in 2002 to 170 in 2019 (Authority for Family Law and Parenthood Support, 2020). Although age limits for adoptive parents have been softened, many sending countries have changed their approach and prioritize domestic solutions. Pre-adoption investigation time has increased and most children who are adopted have some disability or special needs. Additionally, strict health policies on presumptive adoptive parents apply in some countries and a cancer history may be grounds for rejection (Authority for Family Law and Parenthood Support, 2020).

### **2.2.3 Psychosocial support during cancer treatment**

The Swedish National guidelines for cancer rehabilitation in effect from 2019 (Regional Cancer Centers, RCC, 2019) complement previous Standardized Care Pathways (Standardiserade vårdförlopp) in asserting that every person treated for cancer is entitled to an Oncology Nurse Navigator (kontaktsjuksköterska). The guidelines list specified recommendations to be observed in cancer survivorship. Being younger, according to these guidelines, is considered a risk factor for psychological distress. The treating physician and the nurse navigator have joint responsibility for assessing the patient's psychosocial needs. Assessment should be done at the first visit to the clinic and then repeated continually, especially at the end of active treatment and when other significant changes in the person's situation occur.

The nurse navigator is meant to be the primary contact during treatment, but availability of psychosocial support from a counselor or social worker (kurator), who often have basic training as psychotherapists, is also mandatory. People with more severe psychological distress should be referred to appropriate psychiatric care services or to a psychologist (RCC, 2019).

One of the recommendations concerns fertility and sexuality, stating that every region should develop appropriate guidelines, but that generally any patient receiving potentially fertility-threatening treatment should be offered fertility counseling and, when possible, fertility preservation. The recommendation highlights that loss of fertility may negatively influence a person's identity and self-image even if there is no current child wish. It is stressed that information should be repeated and complemented with written and web-based material, and that discussions about fertility should be initiated even when chances to conceive are small (RCC, 2019).

After active treatment ends, it is somewhat unclear where the person should turn. There is psychosocial competence in primary care, but sometimes waiting times are long and some

patients are referred to private psychotherapists or initiatives financed by religious bodies. For shorter interactions, there are helplines such as Cancerrådgivningen (“Cancer Counseling”) where anyone affected by cancer can call anonymously and talk with an experienced oncology nurse. The national healthcare advice website, 1177.se, also contains updated and quality-controlled medical information about oncofertility. Considerable psychosocial support is also offered by civil society organizations such as Ung cancer (“Young Cancer,” for people up to age 30), and by various diagnosis-specific organizations. These organizations often have moderated discussion forums or live group sessions, access to expert consultants, and are represented in the Regional Cancer Centers, and thereby stakeholders in guideline development and influencing policy. Lastly, there are more informal support groups on social media that also offer peer support.

### **2.3 EHEALTH INTERVENTIONS IN SURVIVORSHIP – EVIDENCE AND KNOWLEDGE GAP**

The Internet has great potential in delivering geographically and socioeconomically equal, accessible and cost-effective psychosocial support, especially since the widespread use of smartphones. There are several overlapping concepts or umbrella terms in use to describe all types of healthcare delivered via the telecommunication technologies: eHealth, mHealth, telehealth, Internet, web-based support, etc. In this project, we have chosen to use the terms “Internet,” “web-based” and “eHealth” interchangeably when referring to the Fex-Can project.

#### **2.3.1 The role of eHealth in cancer care**

There are numerous eHealth (web-based or mobile applications) interventions aimed at supporting people during primary cancer treatment (Bouma et al., 2015; Zhu, Ebert, & Wai-Chi Chan, 2017), often focusing on the management of symptoms and immediate side effects. The growing field of survivorship care includes interventions for long-term sequelae and may be delivered outside of the healthcare context, making survivorship interventions increasingly complex. When active treatment or even the monitoring period has ended, the person may no longer have a regular healthcare contact person. This introduces difficulties in reaching those who still need support but also creates possibilities for alternative solutions, including eHealth. Cancer patients are often already used to turning to the Internet to inform themselves about their condition, and to find peer support (Leykin et al., 2012; Meneses et al., 2010). The widespread use of social media as a part of everyday life for many young people would logically enhance adherence to an intervention provided online.

#### **2.3.2 Effectiveness of general psychosocial web-based interventions**

A systematic search I performed in November 2017 for reviews of web-based psychosocial interventions for chronic conditions in young adults resulted in 13 reviews based on a total of 257 original studies. Most of the reviews, despite several of them being of high quality, were unable to draw any conclusions regarding the evidence base for Internet-based interventions

for psychosocial problems in cancer care, and several point to the difficulty in synthesizing information effectively. The lack of meta-analyses did not reflect a poor potential for efficacy of web-based interventions, but rather the heterogeneity in intervention design, study design and outcome measures. The reported effects were inconsistent, with a tendency toward more interventions reporting effects on HrQoL than on anxiety, depression and self-efficacy (Bouma et al., 2015; Kim et al., 2017). Substantial numbers of interventions evaluated with an RCT design also reported zero or ambiguous effects. One of the main challenges of evaluating the effects of web-based interventions through RCTs are low adherence rates, especially among adolescents (Antonson, Thorsen, Sundquist, & Sundquist, 2018; Lillevoll, Vangberg, Griffiths, Waterloo, & Eisemann, 2014). Regarding which intervention components are required, one review focusing on intervention features and moderating variables found that only five out of sixteen included studies had assessed the needs of the target population before developing the contents of the intervention (Ventura, Öhlén & Kindberg, 2013).

We are aware of only one previous intervention focusing specifically on fertility after cancer that has been tested. This project, targeting breast cancer survivors with an educational focus, had a pre-post non-controlled design, reported improved fertility knowledge, and concluded that this was a “promising” research and treatment area (Meneses et al., 2010). Additionally, one randomized controlled survivorship intervention following breast cancer has evaluated reproductive concerns, but only as a secondary outcome (Su et al., 2019). There are also a few interventions for people seeking infertility treatment outside of the cancer context. A scoping review of Internet-based support in general reproductive medicine indicated that in order to be effective, interventions needed to include more interactive components than what was currently the case (Aarts et al., 2012). To our knowledge, no later research synthesis has been published in the area.

### **2.3.3 Guided web-based interventions**

Guided web-based interventions include personal contact with an HCP. In the last two decades, psychological treatment over the Internet has been widely tested. In particular, Internet-delivered cognitive behavioral therapy (ICBT) for various psychological disorders has been used extensively and found to basically be as effective as one-to-one psychotherapy (Barak, Hen, Boniel-Nissim, & Shapira, 2008). A literature review on patients with breast cancer receiving various types of web-based interventions showed that ICBT led to significant improvements in psychosocial outcomes in four out of five studies (Post & Flanagan, 2016). It was concluded that web-based CBT seemed to have positive outcomes for cancer patients, but original studies were difficult to compare due to heterogeneity in design and varying outcome measures.

### **2.3.4 Self-help (self-management) web-based interventions**

Barak, Klein, and Proudfoot (2009) have defined a self-help Internet intervention as: “*a primarily self-guided intervention program that is executed by means of a prescriptive online*

*program operated through a website and used by consumers seeking health- and mental-health related assistance. The intervention program itself attempts to create positive change and or improve/enhance knowledge, awareness, and understanding via the provision of sound health-related material and use of interactive web-based components.*” (Barak et al., 2009, p. 5).

This approaches the definition of self-management intervention proposed by Cuthbert et al. (2019) in their more recent systematic review of self-management interventions (both Internet- and non-Internet-based): including *“an education component to improve patient knowledge of their disease and a component to promote positive coping and adaptation skills”* (Cuthbert et al., p. 2120).

What distinguishes a psychoeducational self-help web-based intervention from either a psychological treatment program or information sites is that the program has an educational goal, but also a proposition for behavior change and/or acceptance. However, it is not perceived as a structured therapy. Each participant is free to use the parts that apply to their respective situation and follow-up is not based on control or “homework.” The participant does not have regular and personalized contact with a therapist, but there is still a therapeutic goal. The expected effects of a self-help therapeutic intervention may occur on various levels, such as increased knowledge, symptom reduction and improved self-efficacy (Barak et al., 2009).

To summarize, previous research seems favorable to delivering educational and behavior-change interventions to cancer patients over the Internet. However, there are uncertainties considering their benefit. First, consistently structured and evaluated interventions in cancer care are scarce and the overall helpfulness of online interventions for cancer survivors remains unclear (Bouma et al., 2015; Leykin et al., 2012; McAlpine, Joubert, Martin-Sanchez, Merolli, & Drummond, 2015). In a state of unclear evidence, few interventions can and will be implemented in routine care. Second, there are concerns about the potential reach of Internet interventions, as recruitment, adherence and retention prove to be difficult issues. Third, few if any studies with an RCT design have focused on young adult people with cancer and reproductive concerns specifically, making conclusions difficult regarding this group.

## **2.4 THEORETICAL AND METHODOLOGICAL FRAMEWORKS USED IN THE FEX-CAN PROJECT**

### **2.4.1 The need for theory**

Research about complex interventions has consistently stressed the need for an articulation of theoretical assumptions and an operationalization of theoretical concepts. Theory is needed to formulate relevant research questions, choose appropriate outcome measures and, importantly, improve the uptake of interventions (Cuthbert et al., 2019; Kok et al., 2016; G. F. Moore et al., 2015). Designing efficacious interventions furthermore requires targeting the

relevant mediators (what is the link between cause and effect, i.e., for whom does this intervention work?) and moderators (the variable that predicts the strength of the relationship, i.e., what external factors explain the effect?). This requires not only articulating theory but linking it to specific intervention components and the chosen behavior change techniques (Gillison, Rouse, Standage, Sebire, & Ryan, 2019; Kok et al., 2016).

In sum, interventions need theory to be relevant, feasible and effective.

#### **2.4.2 Participation to enhance research and care outputs**

Patient and public involvement (PPI) has since the 1990s been increasingly incorporated into research and healthcare development strategies. There are two main factors explaining the political decisions supporting this development. One stems from a growing demand from the public for shared decision-making. The other factor grew out of the New Public Management movement, where participatory care is thought to enhance both satisfaction with care and cost-effectiveness of the care provided (Gibson, Britten, & Lynch, 2012). In Britain, PPI is now well rooted in legislation and present at all levels of the healthcare and research system. The INVOLVE initiative (Involve; Pandya-Wood, Barron, & Elliott, 2017) has been developed to support and enhance public involvement but there is no current equivalent in Sweden.

The idea behind community-based participatory research is to focus on practical problems of the end users, making research culturally relevant for the community in the real world (Jacquez, Vaughn, & Wagner, 2013). When patients become actively involved in the research process as equal collaborators, they may be referred to as “patient research partners.” This means they are equal to the researchers in terms of agenda-setting and initiative. In many cases, however, the actual degree of participation varies. A review of almost 400 articles classified as participatory research with young people showed that only 15% of studies actually had young people as active research partners (Jacquez et al., 2013). These results warrant some caution when assessing the impact of research projects allegedly using PPI as a design strategy. Public participation at the design stage is considered to enhance the quality of research (Involve; Pandya-Wood et al., 2017). However, factors hindering the collaborative process have been identified and may be related to trust, respect and excessive time commitment (Drahota et al., 2016).

PPI is thus not when researchers share their knowledge with the public, nor is it when patients are recruited to participate in a research study. According to INVOLVE, PPI can be defined as “research being carried out **‘with’** or **‘by’** members of the public rather than **‘to’**, **‘about’** or **‘for’** them.” The “public” here refers to patients, potential patients, families, and people who represent patients via organizations. Excluding the perspective of healthcare professionals, it is not synonymous with “stakeholder engagement.” There are various terms associated with involving the public in research. In this project, we have chosen to use “participatory research” and “patient research partners” to describe the process of collaborating with people representative of end users.



In addition to practice theories concerning intervention development and participatory research, the Fex-Can project incorporated several psychological theories, a few of which are outlined below.

### **2.4.3 Psychoeducation**

Psychoeducation is a central tenet of cognitive behavior therapy, first developed for use in schizophrenia to prevent relapse in psychotic episodes (C. M. Anderson, Hogarty, & Reiss, 1980). It is also a central part of the nursing practice formerly known as “patient education” (Syx, 2008), although the present person-centered discourse emphasizes partnership rather than an asymmetrical didactic relationship between nurse and patient (Loonen et al., 2018).

Psychoeducation is a systematic didactic activity aimed at promoting healthier outcomes by providing information and skills training as well as motivational and emotional support. It usually comprises the following four components or steps: 1) knowledge transfer concerning etiology, treatment and prognosis for the current illness; 2) problem-solving skills; 3) communication skills; and 4) self-assertiveness training (C. M. Anderson et al., 1980). This approach strengthens knowledge and competence and promotes insight. Psychoeducation has been shown to be effective in the treatment of various psychiatric disorders, including anxiety and depression (Donker, Griffiths, Cuijpers, & Christensen, 2009).

### **2.4.4 Handling uncertainty, moving towards acceptance**

It has been suggested that in modern society, loss of control is perceived as a great stressor. Fertility is an area that medicine strives to control, but in the end, outcomes remain unpredictable for most.

Illness uncertainty is a concept within cancer nursing which has mainly been described in conjunction with fear of recurrence (Mast, 1998b) and fatigue (Mast, 1998a). In other contexts, illness uncertainty has been associated with a sense of loss of control, and with maladaptive coping and general psychological distress (Johnson Wright, Afari, & Zautra, 2009). Just like long-term fatigue and fear of recurrence, reproductive concerns and possibly subjecting oneself to infertility treatment are survivorship issues that are in many ways characterized by uncertainty and low levels of control (Benyamini, Nouman, & Alkalay, 2016). Fundamentally, even if no one could know for sure that they would be able to have a baby before they have had one, and having children is no guarantee for being able to have more children in the future, it is common among young adults to lack “fertility awareness” and assume that they will be able to conceive whenever they wish (Pedro, Brandão, Schmidt, Costa, & Martins, 2018). Living with a cancer experience adds a few dimensions to potential fertility awareness:

- 1) It is difficult/impossible to know in the individual case the exact impact that the cancer treatment will have had (Rodriguez-Wallberg, 2012; Teh et al., 2014)
- 2) Fertility preservation measures are no guarantee for a live birth (Marklund et al., 2020)

For people who are certain they have lost their reproductive potential (e.g., through hysterectomy), the concept of *acceptance* becomes central. Borrowing inspiration from Eastern philosophy, acceptance and commitment therapy (ACT), including mindfulness-based stress reduction practices, have been put forward as a way of overcoming psychological distress (Towhig & Levin, 2017). Mindfulness is also used as a technique within *dialectical behavior therapy*, DBT, which stresses the necessary insight into, and balance between, accepting what cannot be changed and changing what needs to change (Lynch, Chapman, Rosenthal, Kuo, & Linehan, 2006). When used as a treatment for borderline personality disorder, DBT has been shown to enhance emotion regulation by teaching mindfulness skills and by promoting a therapeutic alliance (Rudge, Feigenbaum, & Fonagy, 2020).

The principles of balancing acceptance and change strategies could logically also be applied to uncertainty regarding fertility potential – i.e., people could train themselves to accept uncertainty as a fundamental condition, and to act when that is helpful. ACT and mindfulness practices have also shown to be teachable through self-help interventions (Cavanagh, Strauss, Forder, & Jones, 2014). Mindfulness has been used in a large number of eHealth designs for cancer survivors, and despite intervention heterogeneity, a systematic review of 24 trials found that web-based mindfulness programs could be as efficacious as face-to-face interventions in reducing stress, anxiety, depression and fatigue, and that they also facilitated posttraumatic growth (Matis, Svetlak, Slezackova, Svoboda, & Šumec, 2020). ACT-based interventions are fewer and although there are many projects underway (e.g., Mendes-Santos, Weiderpass, Santana, & Andersson, 2019), these have yet to prove their efficacy in reducing symptoms of psychological distress in cancer survivors (Graham, Gouick, Krahé, & Gillanders, 2016).

#### **2.4.5 Motivation and basic need satisfaction as predictors for behavior change**

Self-determination theory has been proposed as a way of understanding factors predicting motivation and human thriving (R. M. Ryan & Deci, 2000). It comprises several sub-theories, such as the theory of basic psychological needs that is used as a theoretical framework for the intervention described in this thesis. Satisfaction of the basic needs for competence, relatedness and autonomy seem to be universal (B. Chen et al., 2014) and applicable across sociocultural settings.

It is posited that when the surrounding environment acts in a way that supports the individual's feeling of competence (being able or capable to make well-informed decisions and acting effectively), relatedness (feeling socially and emotionally connected to others and the environment, i.e., the sense of coherence that follows from social support) and autonomy (steering one's own life in a desired direction through fully self-endorsed actions), adaptive psychological outcomes are promoted. Conversely, when basic needs are thwarted,

individuals, groups or societies experience ill-being and lack of motivation. As adults, people often react to strains and difficult events depending on whether their basic needs have been satisfied or not earlier in life.

Features of basic psychological needs and how they relate to SDT generally are illustrated in Figure 6.

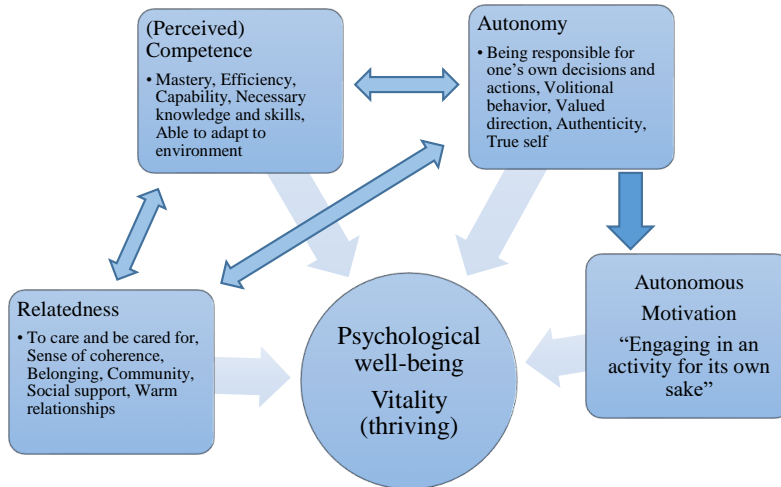


Figure 6. The basic psychological needs according to SDT and the associations between need satisfaction, autonomous motivation and psychological well-being.

The concept of autonomy is perhaps the one that has been the most criticized because it is colloquially conflated with independence. R. M. Ryan and Deci (2017) however, underscore that autonomy in their sense of the word is the opposite of external control, not the opposite of dependence. In fact, autonomy requires strong relatedness and mutual dependence with other human beings. It is also argued that perceived competence is a predictor of autonomous motivation (Brunet, Gunnell, Gaudreau, & Sabiston, 2015). Hence, none of the basic needs can operate without the two others and quantification of the needs is uninteresting as it is rather the *degree of need satisfaction* that will determine a person’s wellbeing. Therefore, it is not possible to compensate for deficits in relatedness by having “more” competence. Research on self-determination theory interventions has shown that the sustainability of behavior change depends on the presence and strength of autonomous motivation, i.e., engaging in an activity because it is fun and rewarding in itself, not because of external pressure or temporary rewards (Gillison et al., 2019). This has implications for how to evaluate and understand short-term and long-term intervention effects, respectively. One example of how self-determination theory can be applied in web-based intervention design, is to promote and examine intervention effects on self-efficacy, which is a proxy measure of perceived competence (R. M. Ryan & Deci, 2017) and has been shown to be a possible moderator for general intervention effects on HrQoL and other psychosocial measures (Leykin et al., 2012; Pingree et al., 2010).

The self-determination theory concepts, although stemming from psychology wishing to explain, predict and change behavior, have a strong focus on relationships and interdependence. In this way, SDT concepts also relate to nursing theory and practice. The basic need for relatedness may be articulated as humans striving to “care and feel cared for.” Caring, according to Watson, presupposes authentic presence and intentionality (Turkel et al., 2018), which are also described in SDT as features of autonomy (R. M. Ryan & Deci, 2000).

In the present project, the basic needs sub-theory of SDT was a guiding principle from the development phase onwards. Since no sustainable behavior change, or long-term psychological wellbeing, can be achieved without basic need satisfaction and promotion of autonomous motivation, SDT can even be said to be the overarching philosophical assumption behind the intervention.

## **2.5 RATIONALE**

Reproductive health is an important aspect of young adults’ lives. Experiencing fertility-related distress after being treated for cancer is a common clinical problem in the little but geographically dispersed group of young adult cancer survivors. The regular healthcare services often fall short of providing the requested psychosocial fertility support, especially when active treatment has ended. Although most people diagnosed with cancer are past their reproductive age, nurses in cancer care regularly meet young persons who are affected by fertility distress. Internet-delivered psychotherapy, psychoeducational and self-management web-based interventions have previously been used in the cancer population, albeit with inconclusive evidence. Further, interventions developed with, for, and tested by young adults with fertility distress are lacking. The flexibility, accessibility and affordability of web-based solutions should translate into personalized, equal and cost-efficient care, but intervention design and evaluation procedures need to be improved. If effective, a web-based psychoeducational self-help intervention for fertility distress could contribute to improving cancer care.



## 3 RESEARCH AIMS

### 3.1 OVERALL AIM OF THE THESIS

The overall aim of the thesis is **to describe the process and explain the outcomes of a self-help web-based psychoeducational intervention aiming to alleviate reproductive concerns following cancer**. The process evaluation includes the rationale for developing this intervention, a description of the development process in long-term collaboration with patient research partners, an assessment of the feasibility of the web-based program targeting fertility distress, and a theory-driven analysis of the experiences of program users. The outcome evaluation consists of an efficacy study with an RCT design.

### 3.2 SPECIFIC RESEARCH QUESTIONS

- How do Swedish physicians in cancer care communicate about fertility with their newly diagnosed patients? (Paper I)
- How can a web-based, theoretically underpinned intervention be designed using a participatory approach, in order to better help cancer survivors manage their concerns about sexuality and fertility? (Paper II)
- (To what extent) is the proposed intervention feasible for the intended target population? (Paper III)
- What are the effects of the intervention on levels of fertility distress, health-related quality of life, anxiety and depressive symptoms, fertility self-efficacy and fertility knowledge? (Paper IV)
- How does the theoretical orientation of the intervention, reflected in user experiences, help understand the effects? (Paper V)



## 4 MATERIALS AND METHODS

### 4.1 GENERAL STUDY DESIGN - SETTING

#### 4.1.1 The Fex-Can project

This thesis is embedded within a larger research project entitled *Fex-Can – Fertility and Sexuality following Cancer* conducted at Karolinska Institutet. The project follows a cohort of people aged 18-39 when diagnosed with cancer in 2016 or 2017, over the course of five years following diagnosis. Fex-Can investigates aspects of sexual and reproductive health alongside other psychosocial outcomes. Individuals rating sexual dysfunction or fertility distress approximately a year and a half after diagnosis were offered to participate in an RCT testing a 12-week web-based psychoeducational intervention. The RCT was planned according to the MRC framework for intervention development and evaluation (R. Anderson, 2008). This thesis describes the rationale, development, process and outcome evaluation of the entire intervention, with special focus on the fertility part.

Figure 7 situates the data collection for the doctoral project in relation to the larger research project.

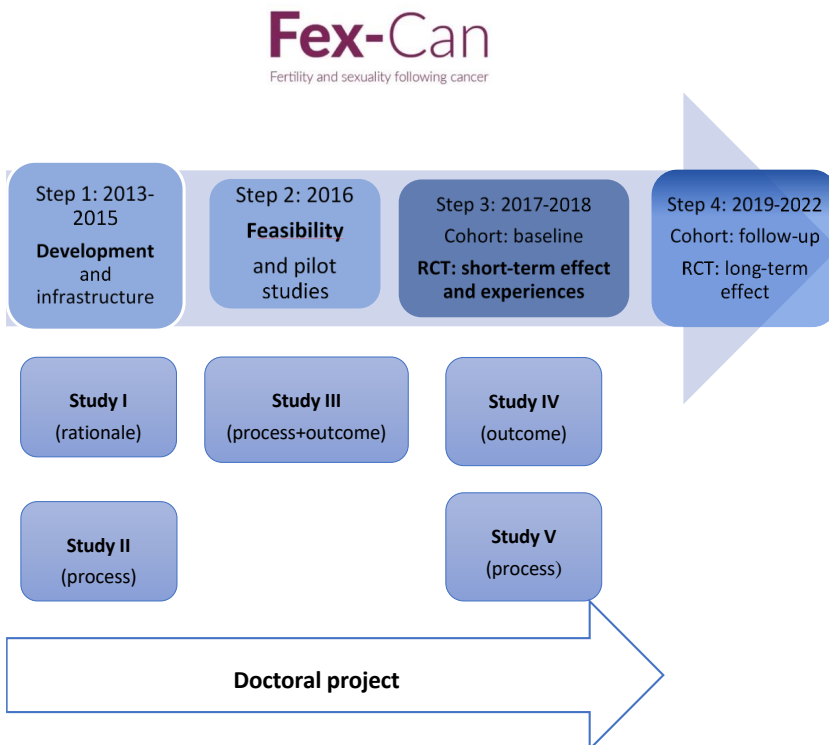


Figure 7. Overview of doctoral project in relation to larger research project.



### **4.1.2 The Fex-Can program**

The technical aspects of the intervention were developed successively in 2014-2017, in cooperation with a contracted software company. The contents and layout of the program were designed entirely by the research team, and modified throughout the development and feasibility testing phases (2015-2016). The website was located on the university server and accessible only by secure login. Responsive design ensured the program could be used on any device with an Internet connection.

The first prototype contained the basic components of a self-help therapeutic intervention according to Barak (Barak et al., 2009). During the development stage, the theoretical concepts were translated to various intervention components. Informative texts and quizzes were designed to increase competence by establishing and confirming participants' knowledge levels. Mindfulness and practical exercises focusing on problem areas were aimed at increasing autonomy by teaching problem-solving skills and acceptance strategies. Relatedness was addressed by using video vignettes, survivor stories and a discussion forum where participants could interact and share their experiences. The feasibility trial included an "ask the expert forum" but this feature was difficult to keep up to date and personalized since the involved expert could not give individual medical advice, and was therefore removed from the version that made it to the RCT. Interactivity was to be enabled by the moderated discussion forum and quizzes with automated feedback at the end of most chapters, as well as a timeline through which participants could follow their own progress in the program.

The final Fex-Can program was delivered in two versions: one focusing on improving sexual function (Fex-Can Sex) and one targeting reproductive concerns (Fex-Can Fertility, which is evaluated in this thesis and described in detail in Section 5.2.). We discussed combining the interventions for fertility and sexuality into one. This would have raised the number of participants in the forthcoming RCT. However, having only one program could also have led to lower adherence and retainment. We hypothesized that an individual would not necessarily be equally interested in improving sexual function and in managing fertility-related distress. We also wanted to take the opportunity to build an intervention specifically targeting reproductive concerns after cancer, since such interventions seemed to be lacking from the smorgasbord of survivorship care.

### **4.1.3 Design of doctoral project**

The PhD project focused on developing and testing the Fertility version of the Fex-Can program. In addition, the PhD project examined the extent to which physicians communicate about fertility, contrasting this with previous reports of patient experiences to form part of the rationale for offering a web-based self-help intervention. The present thesis aims to synthesize the process from idea to evaluation of the program and focuses on the process evaluation of a complex intervention, in the specific context of oncofertility support. The Methods section of the thesis is based on the MRC framework for development and

evaluation, and the Results are synthesized according to the components of a process evaluation.

The papers included in the thesis are summarized in Table 2.

Table 2. Included scientific papers: overview of aims and methods.

<i>Aim</i>	<i>Design</i>	<i>Data sources</i>	<i>Time of data collection</i>	<i>Participants</i>	<i>Analysis</i>	
<i>Study I</i>	To identify factors related to physicians discussing treatment impact on fertility with cancer patients	Quantitative, cross-sectional	Self-administered survey	2015	Physicians (n=329)	Multivariable logistic regression
<i>Study II</i>	To describe the development of a web-based intervention in long-term collaboration with patient research partners	Qualitative descriptive	Logbook/continuous documentation	2014-2016	PRPs, researchers (n≈20)	Descriptive synthesis of the development process, based on holistic framework for development of eHealth technologies
<i>Study III</i>	To evaluate the feasibility of a self-help web-based intervention to alleviate sexual problems and fertility distress in adolescents and young adults with cancer	Mixed-methods feasibility study	Questionnaire survey, website system data, telephone interviews	2017	Self-selected cancer survivors (n=23)	Descriptive statistics, Descriptive synthesis of text data based on demand, acceptability, functionality, and preliminary efficacy (deductive approach)
<i>Study IV</i>	To test whether the Fex-Can intervention was superior to standard care in reducing fertility-related distress and related psychosocial health outcomes in young adults with cancer.	Randomized controlled trial	Self-administered surveys	2017-19	Subsample of population-based cohort study of cancer survivors recruited through national registries (n=124)	Descriptive statistics, chi-square, independent t-tests, linear mixed models
<i>Study V</i>	To explore participant experiences of a web-based psychoeducational intervention targeting sexual dysfunction and fertility distress after cancer within the frame of the self-determination theory's concepts of basic psychological needs.	Qualitative interview study	Telephone interviews	2018	Purposive subsample from intervention groups in Study V (n=28)	Thematic (f)framework analysis

## 4.2 STUDY I: RATIONALE FOR THE INTERVENTION

### 4.2.1 Design

Study I was a population-based cross-sectional survey study aimed at describing physicians' self-reported practice behavior regarding fertility discussions, and identifying barriers to physicians discussing the cancer treatment's impact on fertility with their patients.

### 4.2.2 Sample

All clinically active oncologists and hematologists in Sweden were identified via professional registries.

### **4.2.3 Data collection**

A postal survey, which could be answered anonymously either on paper or online, was sent to eligible participants in 2015.

### **4.2.4 Instrument**

The survey contained a study-specific questionnaire based on two instruments previously used in the US (Duffy, Allen, Dube, & Dickersin, 2012; Quinn et al., 2009). The 54 items covered four dimensions: practice behavior, experienced barriers to fertility-related communication, attitudes toward fertility-related communication, and confidence in knowledge regarding cancer impact on fertility. Answers were given on a 5-point Likert scale ranging from “Never” to “Always.” In addition, sociodemographic and professional variables (experience in oncology and approximative number of patients of reproductive age seen per week) were recorded.

### **4.2.5 Analyses**

Primary outcome was the frequency of abstaining from fertility-related discussions with newly diagnosed cancer patients of reproductive age (women: 18-45; men 18-55). Responses on the two dependent variables “discussing treatment impact on fertility with male patients” and “discussing treatment impact on fertility with female patients” were dichotomized into “Often” (always/often) or “Seldom” (sometimes/seldom/never).

Univariable logistic regression was performed with the independent variables chosen based on the literature. Independent variables included demographic and professional variables, stated barriers and confidence in knowledge. Stepwise backwards logistic regression was then performed with those variables that were significantly predictive of practice behavior in univariate analyses. Independent variables were removed until the model fit did not improve. Lastly, logistic regression using the Enter method was performed with the independent variables that remained.

## **4.3 STUDY II: DEVELOPMENT PHASE**

### **4.3.1 Setting**

Study II was a qualitative descriptive account of the process of developing the Fex-Can intervention with its two web-based programs, Fex-Can Fertility and Fex-Can Sex.

Participants consisted of 12 patient research partners and seven to eight researchers (changes in staffing occurred over time). Several of the PRPs had previously participated in research studies on psychosocial outcomes and sexual and reproductive health following cancer during childhood or adolescence and were recruited directly by the research team. Oncology nurse navigators at a university hospital also engaged some of the PRPs. Ten of the research partners had personal experience from receiving cancer treatments for various diagnoses and at different ages, and two were mothers of persons diagnosed with cancer during childhood or adolescence. The PRPs were formally considered to be research partners and received

financial compensation for their working time and expenses relative to the project. The researchers had varying professional backgrounds (nursing, psychology, social work) and seniority.

### 4.3.2 Data collection

Data collection took place over a period of 18 months between 2014 and 2015. Sources consisted of minutes from meetings, written and oral feedback from patient research partners and researchers' individual notes from meetings.

### 4.3.3 Analyses

The development of the intervention was based on the “holistic framework” for eHealth technologies (van Gemert-Pijnen et al., 2011). The original model, entitled the “Centre for eHealth Research (CeHRes) Roadmap” (Figure 8) comprises five steps: contextual inquiry, value specification, design, operationalization and summative evaluation. Early identification of user requirements and value drivers ensures the creation of a viable business model for implementation and dissemination. Stakeholders' perspectives are to be incorporated at each step through formative evaluations.

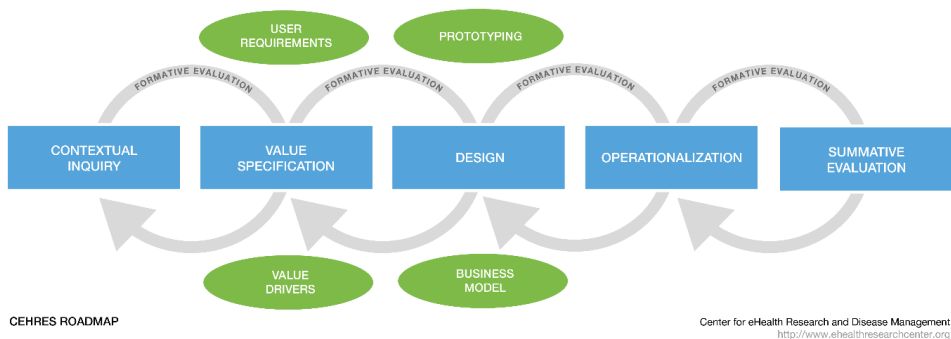


Figure 8. CEHRES Roadmap [Copyright](#) ©Julia EWC van Gemert-Pijnen, Nicol Nijland, Maarten van Limburg, Hans C Ossebaard, Saskia M Kelders, Gunther Eysenbach, Erwin R Seydel. Originally published in the Journal of Medical Internet Research (<http://www.jmir.org>), December 13, 2011.

In the present project, we operationalized the ideas behind the intervention by focusing on three main components of the CeHRES roadmap: *participatory development approach* (user requirements), *persuasive design* and *business modeling*. These were defined and incorporated into the development of the Fex-Can intervention, as demonstrated by Figure 9.

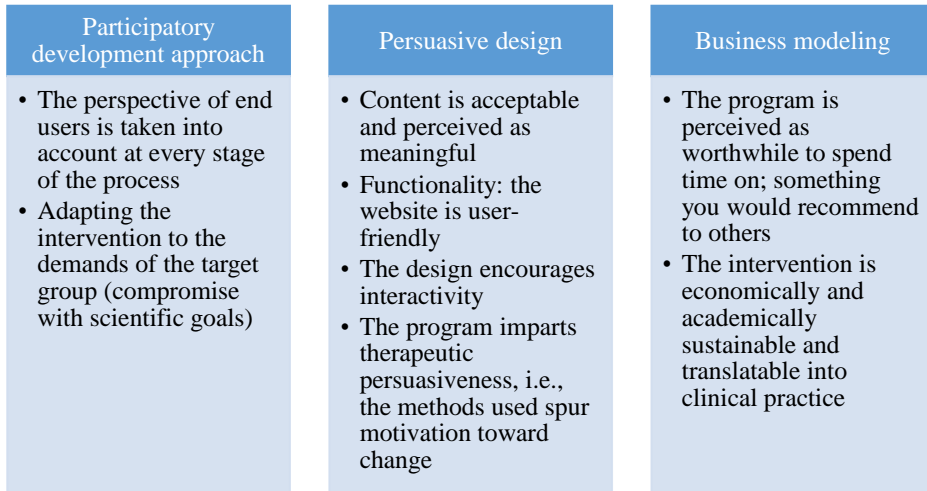


Figure 9. Operationalization of the CeHRES Roadmap for the Fex-Can project

To further define the outcomes of the participatory development process, we chose to focus on the following three types of intervention quality indicators derived from the holistic framework (Figure 10):

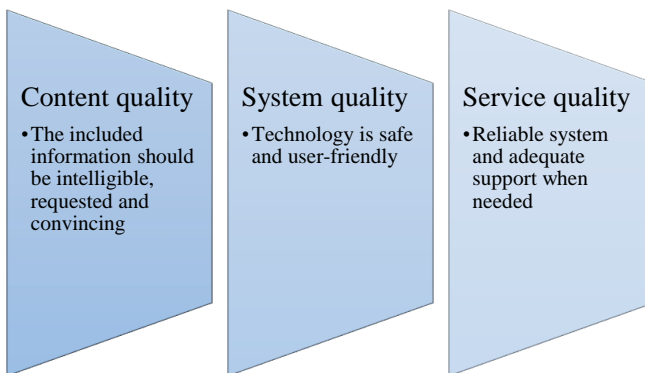


Figure 10. Quality indicators for the development process.

We used continuous feedback from the patient research partners to assess user requirements, start prototyping and, from there, gradually develop the entire program.

## 4.4 STUDY III: FEASIBILITY PHASE

### 4.4.1 Design

Study III was a mixed-methods feasibility study investigating the program’s capacity to respond to the four concepts of demand, acceptability, functionality and preliminary efficacy, adapted from previous research (Bowen et al., 2009; Eldridge et al., 2016). The concepts

were selected based on the perceived relevance for the current intervention. Figure 11 illustrates how the concepts were translated to the context of the Fex-Can program.

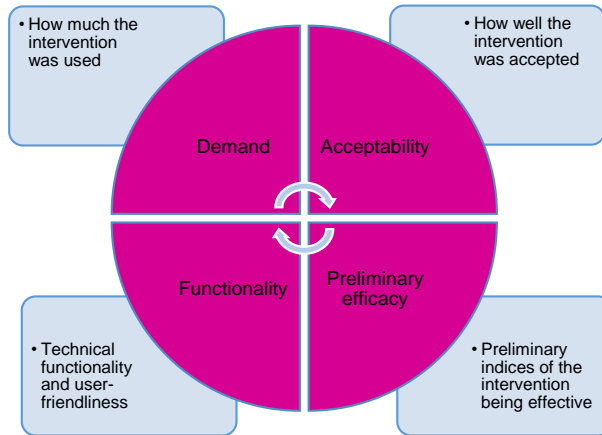


Figure 11. Aspects of feasibility.

#### 4.4.2 Sample

Recruitment aimed at finding individuals representative of the final target group for the intervention, i.e., young adults with a recent cancer experience and either sexual problems or fertility distress. Participants were recruited using newspapers, social media, patient organizations, notice boards at clinics and personal contacts with nurses and physicians. In addition, two reference persons were engaged from the patient organization Ung Cancer (“Young Cancer”) to comment on the intervention without actively participating. Interested participants got to test the preliminary version of either Fex-Can Fertility or Fex-Can Sex (participants’ discretion).

#### 4.4.3 Data collection

Data were collected over a period of two months in spring 2016; participants had access to the program website during this time. Due to seasonal time constraints, the intervention was tested for a period slightly shorter than the 12 weeks planned for the RCT. For a detailed description of the intervention components and the implementation process, please see the Results section.

**Website system data** were used to determine usage pattern in connection with demand and functionality. Two **semi-structured telephone interviews** were performed with each participant, one halfway through the intervention and one at the end of the two-month period. The first interview focused on use (demand) and functionality, and the exit interview was aimed at assessing the participant’s general experiences of the program’s content (acceptability, demand, preliminary efficacy) and mode of delivery (functionality). Both interviews were conducted by the same two members of the research team and documented either by taking notes (midway interview) or recorded and transcribed verbatim (exit

interview). There were also **online evaluation forms** at the end of each chapter, in which participants could rate on a 4-point Likert scale ranging from “disagree completely” to “agree completely” if the contents had been difficult to understand, distressing or, conversely, helpful. The phrasing of the items is presented in Figure 34, Section 5.5.2.

Preliminary efficacy was assessed according to the **main outcome measures** for the sexuality (Promis Sex-fS, selected domains) and fertility interventions<sup>1</sup> (Reproductive Concerns After Cancer, described in 4.5 Study IV), respectively, at baseline and on completion of the program. At baseline, the participants also answered **study-specific items** on socio-demographics.

#### **4.4.4 Analyses**

Quantitative data were analyzed with descriptive statistics and qualitative data with a descriptive synthesis of text and recorded audio files.

### **4.5 STUDIES IV AND V: EVALUATION PHASE**

#### **4.5.1 Design**

The final intervention was evaluated using an RCT design, where eligible individuals were randomized to either intervention group (IG) or control group (CG). The control group received standard care, which may or may not have included healthcare visits and/or psychosocial support during the intervention period. An embedded qualitative interview study investigated experiences of having access to the program, with a special focus on perceptions of basic need satisfaction. The aim of the evaluation phase was to understand and explain the observed effects in relation to the theoretical foundations of the intervention.

#### **4.5.2 Sample**

The sample for Study IV was drawn from the cohort study (Figure 12), where 1010 young adults answered a survey about fertility distress, sexual function, and related psychosocial health outcomes. Approach was organized via national quality registries for breast cancer, gynecological cancer, testicular cancer, lymphoma and CNS tumors (benign and malignant) so that people were contacted about a year and a half after diagnosis.

Those who scored above the cut-off point set at  $\geq 4$  on any of the six dimensions of the Reproductive Concerns After Cancer scale, and who did not simultaneously qualify for the sexuality intervention, were eligible for the fertility intervention and invited to the Fex-Cann Fertility RCT. Stratified block randomization taking into account sex and diagnosis was performed by an external statistician to create groups equal at baseline.

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<sup>1</sup> Described in detail in 4.5.4, Study IV: instruments.

For Study V, a purposive subsample of 28 individuals (24 women and four men) was drawn from the intervention group of Fex-Can Fertility and Fex-Can Sex in the months following completion of the program (Figure 12). The intent of the sampling process was to cover a range of possible experiences depending on age, gender, parenthood/relationship status, diagnosis, and level of usage of the program.

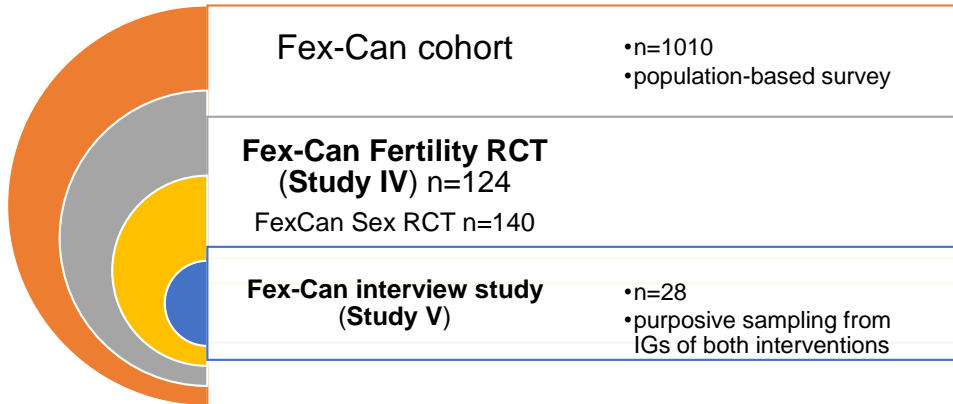


Figure 12. Sampling structure of the Fex-Can research project. Studies included in this thesis in bold.

#### 4.5.3 Data collection

The time period for data collection for the RCT extended from August 2017 to June 2019 (Figure 13). Eligible participants were approached at three different time points depending on diagnosis date and the RCT was then organized in three successive groups (A, n=41; B, n=31; and C, n=52). Participants were assessed at baseline (T0), directly post-intervention (T1) and three months after the intervention had ended (T2),

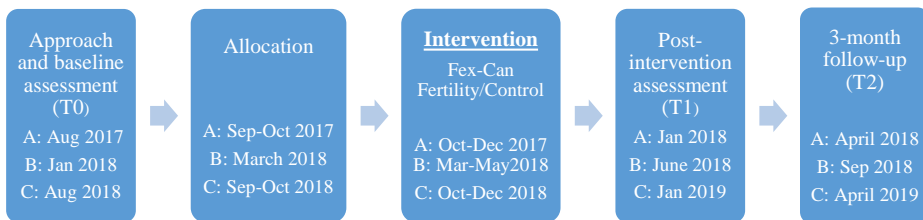


Figure 13. Timeline for the data collection, A, B and C RCT groups.

Data for Study V were collected between February and July 2018, in the first three months following participation in the Fex-Can program for groups A and B.



#### 4.5.4 Instruments

The main outcome measure for the RCT was the Reproductive Concerns After Cancer scale, RCAC (J. R. Gorman et al., 2014). The scale is composed of six dimensions, described in Table 3. Each dimension comprises three items, which are scored on a non-numbered Likert scale ranging from “Totally disagree” to “Totally agree.” According to instructions, the middle alternative (“Neither disagree nor agree”) should be chosen when the statement is perceived as not applicable.

One dimension of the RCAC, the one for *Acceptance*, is reversed when the Likert scale is transformed into a score from 1 to 5 and means are calculated, so that for every dimension, higher scores indicate higher levels of fertility-related distress.

Table 3. Dimensions of the main outcome measure: Reproductive Concerns After Cancer scale.

Dimension	Explanation	Example item
<b>Fertility potential</b>	Concerns about one’s ability to have biological children	I am afraid I won’t be able to have any (more) children.
<b>Partner Disclosure</b>	Concerns about telling a (potential) partner about (potential) infertility due to cancer treatment	The thought of telling my (potential) spouse/partner that I may be unable to have children makes me uncomfortable.
<b>Child’s health</b>	Concerns about the risk of one’s offspring contracting cancer through hereditary mechanisms	I am afraid my children would have a high chance of getting cancer.
<b>Personal health</b>	Concerns relating to fear of relapse, living long enough to raise a child and having the physical and mental capacity to parent a child	Having (more) children will make me more nervous about getting cancer again.
<b>Acceptance</b>	Degree of acceptance of (potential) infertility [reversed item]	I will be happy with life whether or not I have (more) children someday.
<b>Becoming pregnant</b>	Concerns relating to the difficulties involved in achieving a pregnancy after cancer treatment	It is stressful to think about trying to get pregnant (again).

In its prior uses, the total score or mean of the total score had been used as one measure (J. R. Gorman et al., 2014). However, during the course of the present research project, new publications have suggested that using the six dimensions separately may be more appropriate from a psychometric point of view (J. R. Gorman, Pan-Weisz, Drizin, Su, & Malcarne, 2019). It was therefore decided that the mean of the total score, *plus* the means of

each of the six dimensions of the RCAC scale, would count as primary outcome measures for Fex-Can Fertility.

Secondary outcome measures were chosen based on their presumed association with fertility distress. Health-related quality of life was measured with the summary score of the EORTC QLQ-C30 questionnaire (Giesinger et al., 2016) and emotional distress with the Hospital Anxiety and Depression Scale (Annunziata et al., 2020), both of which have been shown to have adequate psychometric properties in the target population for this study. In addition, two study-specific questionnaires based on the theory behind the intervention (fertility-related knowledge and fertility self-efficacy) were used to assess some of the parameters or intermediate outcomes that would be amenable to change through the intervention. An overview of secondary outcome measures is presented in Table 4.

Table 4. Secondary outcome measures for Fex-Can Fertility.

Secondary outcome	Validated measure	Study-specific questionnaire	Scale and interpretation	Example item
<b>Health-related quality of life</b>	EORTC-QLQ-C30:  28 items (13 domains). 4-point Likert scale		Summary score 0-100, higher scores=better quality of life	During the past week, were you limited in doing either your work or other daily activities?
<b>Anxiety and depressive symptoms</b>	HADS:  7 items Anxiety subscale, 7 items Depression subscale  4-point Likert scale		0-21, higher scores=more anxiety/depression	I get a sort of frightened feeling as if something awful is about to happen.
<b>Fertility self-efficacy</b>		6 items, 4-point Likert scale plus “not applicable” alternative	1-4, higher scores=stronger self-efficacy	I feel confident that I can handle negative thoughts about my ability to have children
<b>Fertility-related knowledge – general</b>		4 items, 4-point Likert scale	1-4, higher scores=better perceived knowledge	I have good knowledge about the menstrual cycle and when a pregnancy may occur
<b>Fertility-related knowledge – cancer</b>		6 items, 4-point Likert scale	1-4, higher scores=better perceived knowledge	I have good knowledge about how the cancer treatment may impact the ability to have children

The baseline assessment survey also contained questions on socio-demographics, self-rated fertility potential and child wish, among other questions. At the end of the baseline questionnaire, respondents were encouraged to describe their thoughts about fertility and sexuality, or about the study, in their own words. The same open-ended question was asked at the post-intervention assessment point. Those who had been randomized to receive the intervention were also asked in additional items to provide feedback on the web-based program and to rate how their concerns had evolved over the past three months (on a 7-point Likert scale ranging from “Improved a lot” to “Worsened a lot”).

#### **4.5.5 Quantitative analyses**

The RCT was evaluated using descriptive statistics (means and standard deviations, percentages) and inferential analyses (chi-square test for categorical variables and Student’s t-test for continuous variables) to study participant characteristics and differences between the IG and CG. Effect sizes estimating Cohen’s *d* were calculated for analyses where no more than two groups were compared (Cohen, 1988). Linear mixed models (Pinheiro, 2005) were used to study changes and group difference over time on the main outcome measure, i.e., the six dimensions of the RCAC scale. To study whether baseline levels of fertility distress would affect intervention outcomes, participants were assigned to either subgroup “high RCAC” ( $\geq 4$ ) or “low RCAC” ( $< 4$  on the subscale mean at baseline). Another subgroup was created based on the level of activity, where “high” meant having spent at least 20 minutes on the program website, having opened at least half of the modules, and either one of the following: writing one post or spending at least three minutes in the discussion forum, or answering  $> 50\%$  of quizzes.

#### **4.5.6 Qualitative interviews**

For Study V, interviews were performed over the telephone (interviewees’ choice) by various members of the research team, using a semi-structured interview guide with questions adapted to level of use of the program. Questions had an open-ended, inductive approach such as: “How did you go about using the program?”, “How come you didn’t use the program so much?” or “What was it like reading other people’s stories in the discussion forum?”. Interviews varied in depth and lasted between 21 and 70 minutes.

#### **4.5.7 Qualitative analysis**

Data were analyzed using the Framework approach to thematic analysis (Ritchie, 2013), enabling the processing of large amounts of text by organizing into a thematic matrix. This approach also supports alternating between inductive and deductive perspectives, which was important in our case because we wanted to test the SDT sub-theory of basic needs against intervention experiences while staying open to inductive interpretation. Framework is also a suitable method for analyzing qualitative data in cross-disciplinary research teams involving both psychologists and nurses (Gale, Heath, Cameron, Rashid, & Redwood, 2013).

### **4.6 ETHICAL CONSIDERATIONS**

All studies within this thesis project were performed according to the ethical standards laid down in the Declaration of Helsinki and its later amendments (World Medical Association,

2013). They were subject to scrutiny and approved by the Regional Ethics Board in Stockholm (permit numbers 2013/1746-31/4; 2014/2201-31/4; 2014/2244-32; 2015/2042-32/4; 2017/916-32; 2017/1416-32). Principles of voluntarism, informed consent, confidentiality and respecting integrity were applied to all participants across the research project.

Planning an intervention study requires special ethical considerations since the effect of a new treatment is being tested. Eligible participants were identified via national registries and thus not approached via a healthcare contact. This procedure may have been both beneficial and problematic from an ethical point of view. On the one hand, a benefit of using registries is that we reached all potentially eligible persons within the cohort and there was no *a priori* selective sampling such as may occur in a clinic. Further, if a person is approached as a patient, they are potentially in a vulnerable situation and dependent on the HCPs who are asking for their consent to participate. On the other hand, the registry approach may lead to persons being contacted who do not wish to be helped or to be reminded of their disease. The survey also contained questions about fertility and sexual life, topics that may be perceived as sensitive or too intimate. To counteract these potential ethical problems and to ensure the validity of results, the instruments and study-specific items were tested with cognitive interviews, in the feasibility study and in two pilot studies (Ljungman et al., 2018; Ljungman et al., 2019) before rolling out the RCT, with very few negative reactions being recorded. All participants in the RCT received two tickets to the movies for answering the survey. Offering incentives for survey completion is uncommon in Sweden, and it is unsure whether such compensation enhances research results. However, we chose to do this due to the risk of having a low response rate in our surveys and thereby risking research waste. Another reason for compensating participants in the cohort study is that it took some time to fill out the questionnaires.

We hypothesized that the intervention would have mainly positive effects and that adverse effects would not pose a problem. However, there is always a risk that a psychoeducational intervention increases concerns or problems in some individuals due to increased attention to the problem. A plan was therefore made for referring persons who might need extra support, though it was not totally clear how we would become aware of these persons unless they actively contacted the research team.

To enhance the overall research quality of this research project, we involved end users as stakeholders from the beginning. The PRPs collaborating on Study II were not considered research participants but were remunerated as consultants, and a few of them co-authored a publication on the collaboration process (Hovén et al., 2020). It has been pointed out that there may be ethical issues or unintended effects arising from this kind of setup since public involvement is not subject to the same ethical requirements as empirical research (Pandya-Wood et al., 2017). Furthermore, because the PRPs are really not researchers and cannot decide about the research project, they might end up feeling “hijacked” by the more powerful researchers (Gibson et al., 2012). However, in the present project, we emphasized the

voluntary nature of their contribution in order to help prevent the PRPs from feeling pressured into working for the project. We also made an effort to create a warm and permissive atmosphere to signal that all attitudes and ideas about the research project were welcome. Overall, the collaboration with PRPs strengthened the project ethically, enabling us to offer an intervention that was relevant, attractive, and respectful from the perspective of the target group.

## 5 RESULTS

In Sweden, oncology and hematology specialists at university or regional hospitals are responsible for the provision of most treatments given to young adults with cancer, and for assessing patients' information needs. An important part of the context for fertility-related information therefore relies on the quality of medical encounters. Paper I was a cross-sectional survey study investigating aspects of fertility-related communication in cancer care from the perspective of clinicians, and forms part of the rationale for the Fex-Can intervention. Papers II and III describe the process from idea to completion of the intervention that was subsequently tested and evaluated in Papers IV and V. The results of this thesis are presented according to the structure of a process evaluation (Figure 14).

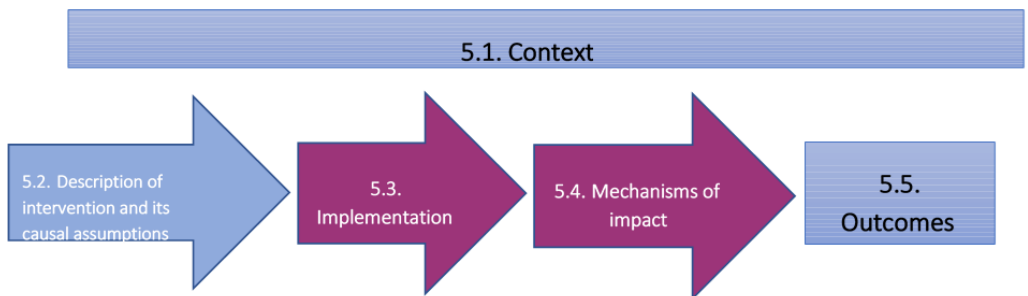


Figure 14. Structure of the results section. Adapted from Moore et al., (2015).

### 5.1 CONTEXT

#### 5.1.1 Factors related to physicians not bringing up fertility issues (Study I)

Study I was a nationwide population-based study where all registered oncologists and hematologists (n=821) were contacted. 329 clinically active physicians (58% women, 41% men) answered the survey (response rate 55%). Fifteen percent of participants had a specialist training other than oncology/hematology and seven percent were residents in training. Physicians with a self-stated lack of current clinical experience were excluded from the sample.

The results showed, on average, 70% of participants regularly addressed the topic of fertility with newly diagnosed patients (74% with women and 70% with men). A majority also often discussed fertility preservation options. More than 90% of physicians also agreed it was their responsibility to address fertility issues. The most common reasons to avoid fertility discussions were poor prognosis (stated by 78%) and the woman's age (63%).

In the logistic regression models, the organizational factors identified were high workload, (OR 3.30/4.81), having access to a reproduction clinic (OR 5.18/4.19), and seeing very few patients of reproductive age (OR 3.25/3.41). The patient already having children was also correlated with not initiating fertility discussions with female/male patients, respectively (OR

2.97/6.93). If the patient was female, physicians' limited experience (OR 3.30) and the requirement for immediate antitumoral treatment (OR 2.08) were also significantly associated with refraining from discussing fertility.

### 5.1.2 Context of the intervention (Studies II-V)

The development of the intervention took place in the context of the PRP–researcher interaction, and in separate interactions between the researchers and the software developers as well as the researchers and other people providing content and layout: a graphic illustrator, a photographer and an administrator. In addition, several cancer survivors recruited via clinics or patient organizations consented to have their stories about fertility and sexuality after cancer videotaped. Some also provided written stories to be published on the program website. Developing the program was an iterative process dependent on several factors: the time schedules of all the involved persons, ethical considerations, and legal as well as administrative procedures within the university as a state agency.

In the feasibility study (Study III), a total of 23 young people (19 women, 4 men; ages 18-43, median 30) with a previous cancer diagnosis and self-reported sexuality and/or fertility concerns, were recruited via notice boards, newspapers social media, patient organizations and personal contacts, and consented to test either the fertility or sexuality program (at their discretion). Time since diagnosis was approximately two years. About two-thirds of the recruited participants, i.e., 15 persons, completed the program, and were assessed at the end of the study. Seventy percent of the participants had a college or university educational level, and all lived in the Greater Stockholm area. All of the women (n=8) and the one man who chose to take part in the fertility program rated high levels of concerns on at least one of the dimensions of the RCAC scale prior to the study. Dimensions in which several participants rated high distress were *Fertility potential* (n=7), *Partner disclosure* (n=6) and *Child's health* (n=7).

In the subsequent RCT, women accounted for more than four-fifths of participants. The most common diagnosis was breast cancer (n=52) and the median age was 33 in the intervention group and 34 in the control group. About half of the participants already had biological children before they got cancer. Those who chose to participate after having reported >4 (high level of concerns) on at least one dimension of the RCAC were more likely to be female (p=0.041) and to have a current child wish (p<0.001), than those who declined or did not reply. Participants in the RCT also had significantly higher baseline scores for the *Fertility potential* and *Becoming pregnant* dimensions of the RCAC, as well as higher baseline acceptance (i.e., lower RCAC scores on the *Acceptance* dimension) than non-participants. Those who consented to take part in the RCT also had slightly higher baseline levels of anxiety (9.23 vs. 8.21, p=0.050). There was no statistically significant difference in educational level between participants and non-participants, but approximately 60% of responders to the baseline survey had a university-level education, compared to 56% of women and 41% of men in the general population aged 25-44 (National Board of Health and Welfare, 2019). For the interview study (Study V), a purposive maximum diversity sampling

strategy was applied to recruit people from the intervention group with varying experiences and points of view concerning the web-based program. The final sample consisted of twenty-four women and four men, with ages ranging from 19 to 40. All the diagnoses included in the Fex-Can RCT were represented.

In sum, the Fex-Can fertility intervention was developed, delivered and evaluated in an academic setting. The majority of study participants throughout the project, and all of the researchers involved, were well-educated women with a high level of Internet literacy.

## **5.2 DESCRIPTION OF INTERVENTION AND ITS CAUSAL ASSUMPTIONS**

### **5.2.1 Developing the intervention (Study II)**

The intervention was developed in a participatory process with PRPs representative of the intended end users commenting on each step of the development process. The technical aspects of the web-based program were developed in collaboration with a contracted software company, but the program was delivered through the Karolinska Institutet university server and is the property of the university. Hence, no commercial interests were driving development or delivery of the program.

The collaboration with patient research partners evolved over several years. The main form was through half-day meetings based on group discussion on a topic defined by the research group but with the possibility for PRPs to influence the course of discussion. Between meetings, PRPs were also involved in reading and commenting on material or the technical and visual layout of the different intervention components.





*Figure 15. Going through suggested material for the website at one of the meetings with patient research partners. Photograph by Tove Freijj.*

### **5.2.2 Content, system and service quality to inform the development of the intervention (Studies II and III)**

The PRPs contributed to continuous feedback on various aspects of the intervention, from the idea stage via prototyping through to the final version of the program.

Similarly, participants in the feasibility study (Study III) had the possibility to comment on each chapter directly online, and thereby provided continuous evaluation that led to adjustments of the program.

Table 5 summarizes findings from Study II regarding PRPs' contributions to quality parameters for intervention development. Each of the points was attended to through discussions, adjustments and further technical development.

Table 5. Results of Study II. Quality parameters for intervention development.

Content quality	System quality	Service quality
<p>Reporting:</p> <ul style="list-style-type: none"> <li>➔ Differing views on what type of information could be distressing</li> <li>➔ Initial skepticism about mindfulness exercises</li> </ul> <p>Request for:</p> <ul style="list-style-type: none"> <li>➔ Inclusive language, style and contents (appropriate also for non-heterosexuals and single people and concise enough for people with cognitive difficulties)</li> <li>➔ Detailed information concerning side effects</li> <li>➔ Tailorable information with more extensive material available in expanding content</li> <li>➔ Inclusion of personal stories and age-based groups in discussion forum and representative photographs, to convey relatedness and demonstrate awareness of the meaning of the cancer experience to individual participants</li> <li>➔ Continuous but non-controlling feedback on progress, as well weekly reminders to remain active</li> </ul>	<p>Reporting:</p> <ul style="list-style-type: none"> <li>➔ Technical malfunctioning</li> <li>➔ Website messy and difficult to navigate</li> </ul> <p>Request for:</p> <ul style="list-style-type: none"> <li>➔ Responsive design</li> <li>➔ Professional design, neat layout and uniform style</li> <li>➔ Reliable host server with a respected and well-known name (medical university)</li> </ul>	<p>Request for:</p> <ul style="list-style-type: none"> <li>➔ A plan for immediate support in case of technical problems</li> <li>➔ Allowing immediate postings in the discussion forum to avoid delay and retain user interest and engagement (at the expense of the researcher not checking content beforehand)</li> <li>➔ Responses within three working days from experts in the “Ask the expert forum”</li> <li>➔ Web-based and telephone support for technical and other questions staffed by members of the research team to ensure competent answers to most questions</li> </ul>

### 5.2.3 Causal assumptions

The final version of the Fex-Can Fertility program contained six modules spanning (but not exactly corresponding to) the six dimensions of the RCAC Scale<sup>2</sup> and aimed at enhancing the

---

<sup>2</sup> described in detail in Section 4.5.4.

satisfaction of basic psychological needs according to SDT<sup>3</sup>. The main causal assumptions were that:

- 1) If the content reflected all the dimensions of fertility-related distress, all participants would get at least some benefit.
- 2) If the intervention managed to increase perceived competence in a relatedness-fostering environment, the probability of participants acting in an autonomously motivated way concerning their fertility situation would increase. Reproductive concerns would thereby be reduced and other psychosocial outcomes would improve.

Additionally, the general principles of psychoeducation, as conceived in (I)CBT interventions, and promotion of the sound balance between action and acceptance, as in ACT or DBT interventions, were deemed to be inoffensive and to generally enhance the wellbeing of participants. In an autonomy-promoting and non-controlling attitude, no pressure was put on participants to complete or follow the program in a certain way. However, we also incorporated the idea from web-based self-help interventions that some behavior change was the ultimate goal. It was emphasized in the program that behavior change was not necessarily the result of an *action* of change, but rather a change in the mindset of the person. Beginning to accept what cannot be changed is also a change.

#### **5.2.4 Final contents and layout of the program**

Fex-Can Fertility included six consecutive modules released every two weeks, and one module including video vignettes with survivor stories that was available throughout the intervention period. Figures 16-23 show screenshots of the final layout of the program, excluding potentially identifying material such as stills from videos and potentially identifying quotes of contributing survivors or discussion forum posts from the RCT. The people appearing on photographs in the screenshots are models uninvolved in the research project.

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<sup>3</sup> described in Section 2.4.5.

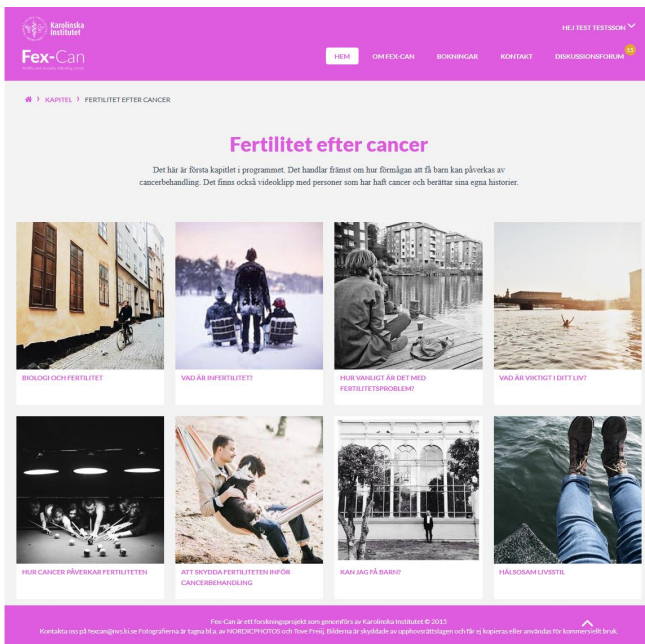


Figure 16. Main page and example of an article including interactive comment box, from Chapter 1, Fertility after cancer.

Karolinska Institutet

Fex-Can  
FLEXIBLE AND ADAPTIVE CANCER CARE

HEJ TEST TESTSSON


HEM OM FEX-CAN BOKNINGAR KONTAKT DISKUSSIONSFORUM 13

KAPITEL 2 ATT HANTERA ORO


## Att hantera oro

Att känna oro är normalt, det är kroppens sätt att signalera till dig att något behöver uppmärksammas. Ibland kan man dock känna så mycket oro att den blir ett hinder i livet. På kommande sidor kommer du att kunna läsa om vad som händer när man blir orolig och vad man kan göra för att kunna hantera sin oro. Kapitlet innehåller artiklar, filmer och övningar.


Funderingar och oro efter en cancersjukdom är helt begripliga, eftersom det är naturligt att oroa sig över sådant som är viktigt. Det här programmet inriktar sig på oro som gäller fertilitet och familjebildning. Vi vill förmedla att det både är helt naturligt att känna oro och att man kan göra något åt det.




VAD HÄNDER I KROPPEN VID ORO?




ÄR DET ORO JAG KÄNNER?




OLIKA SÄTT ATT HANTERA ORO




HANTERA DIN ORO GENOM ATT SKILJA PÅ FAKTA OCH OLIKA REAKTIONER



MÄNSKA SJÄLBÄRHÄT FÖR ORO GENOM ATT TA HAND OM DIG



MEDVETEN NÄRVÄRD



OROSTID OCH OROSFRJA ZONER – TVÅ BRA TEKNIKER FÖR ATT HANTERA ORO

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Figure 17. Main page of chapter 2, Handling anxiety.

## Minska sårbarhet för oro genom att ta hand om dig

Du kan minska din sårbarhet för oro genom att du tar hand om din kropps grundläggande behov av näring, sömn och aktivitet. Försök hitta dagliga rutiner som just du mår bra av.

Här är några grundläggande punkter att utgå från (klicka på punkterna för att komma till fördjupad text):

» **Ät regelbundet och näringsrikt**

» **Ha regelbundna sovtider**

» **Hiitta en balans mellan aktivitet och vila**

*Följ dagliga rutiner*

Många människor känner att de mår psykiskt bättre när de stiger upp på morgonen, tvättar sig, klär på sig, där ifrån gardinerna och släpper in ljus. På så sätt kan man känna sig mer kompetent. Det handlar inte om att vara "shuktig" utan att signalera till sig själv att man är igång. Om du har besvär med fatigue (vilket man kan ha flera år efter cancerbehandling) kanske du sedan måste gå och vila en stund, men det gör inget. Huvudsaken är att komma igång med dagen över huvud taget. De här rutinerna motverkar att man uppfattar sig själv som "deppig" och "sjuk".

Anpassa aktiviteten och aktivitetsnivån till vad du orkar och tycker om. Lite aktivitet är mycket bättre för kroppen än ingen aktivitet alls. Om du har problem med fatigue finns särskilda råd på t.ex. <https://www.cancerfonden.se/om-cancer/trotthet-vid-cancer>.

*Att ta ledigt från sina rutiner*

*Bilans* kan det också vara skönt att göra tvärtom mot punkterna ovan; nämligen att ta ledigt. Det kan innebära att man under några timmar eller en hel dag minimerar kraven på sig själv: Man kan ta sovmoden, låta tvätten och disken vara, köpa färdigmat, bara göra det nödvändigaste. Kom ihåg att det här bara brukar vara hälsosamt att göra under en avgränsad tid, lever man så under en längre tid brukar det istället skapa problem eftersom negativa konsekvenser hopar sig. Det här kan vara till hjälp om man haft det stressig flera dagar i rad och kroppen och huvudet behöver återhämta sig.

» **Gör något trevligt och känn dig kompetent**

» **Sköt om din hälsa och dina vårdkontakter**

» **Ta det försiktigt med alkohol och avstå från droger**

*Att hitta rutiner du mår bra av*

Till den här artikeln finns ett arbetsblad för registrering av dagsrutiner. Du kan använda arbetsbladet för att först registrera dina dagsrutiner under en vecka, sedan planera nästa vecka utifrån vad som fungerade bäst den första veckan. Om du vill kan du även prova att lägga till en ny rutin och utvärdera (t.ex. mellanmål, promenad) eller prova att ta bort någon ovana (t.ex. att kolla mail precis innan du ska sova). Experimentera och utvärdera vad som passar dig!

- Vecka 1: Registrera vad du gör vid olika tidpunkter.
- Vecka 2: Planera veckan. Utgå från vad du vet om dig själv. Är du trött eller pigga på morgnarna? Behöver du vara vaken en stund innan du åter frukost? Planera vilka rutiner som kan fungera bäst för dig utifrån vad du redan brukar göra.
- Vecka 3: Testa gärna någonting nytt! Det kan finnas bra rutiner som du inte hittat ännu. Testa den nya rutinen under minst en vecka och utvärdera sedan.
- Vecka 4: Testa att sluta med saker som du misstänker att du mår sämre av. Prova att hoppa över den vanan en vecka och utvärdera sedan.

Människor har olika stort behov av ordning och kontroll. Det finns inget som är rätt eller fel i det avseendet, men fundera på vad du mår bra av. Känns livet ofta kaotiskt kanske du skulle må bra av lite mer struktur, dvs. mer ordning och reda. Känns livet för inrutat kanske det vore befriande att ta dagarna lite mer som de kommer. Ha detta med lagom grad av kontroll i bakhuvudet när du arbetar med att planera dina dagsrutiner.

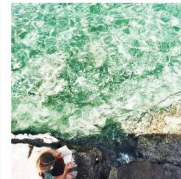
Lycka till!

TILLBAKA VIDARE

### ARBETSBLAD: DAGSRUTINER

Nedan finns ett arbetsblad Dagsrutiner i olika filformat, för att kunna registrera dagsrutiner och testa olika förändringar. Klicka på önskat format för utskrift eller för att kunna skriva i dokumentet och spara på din egen dator (word/open doc för att kunna skriva i på datorn)

Dagsrutiner som pdf  
Dagsrutiner som wordfil  
Dagsrutiner som open doc



*Jag tror det har hjälpt mig väldigt mycket att det på tillvar med hur jag mår, och inte slitta upp omöjliga mål.*

*Kristoffer*

*Jag har inte samma energi eller kapacitet som tidigare. Det tar längre tid att återhämta mig. Detta jobbar jag också med fortfarande och här gäller det att hitta balans i livet!... Jag hade gärna vetat mer om hur kroppen reagerar (på cytostatika) för hur man ska lägga upp träning och kost för att komma tillbaka till livet. Mår man bra i kropp och själ så kanske man också kan bena ut känslor kring familj.*

*Maria*

Figure 18. Article showing expanding content, external links and downloadable exercises, within chapter 2, Handling anxiety.

Karolinska Institutet

Fex-Can

HEJ TEST TESTSSON

HEM OM FEX-CAN BOKNINGAR KONTAKT DISKUSSIONSFORUM

KAPITEL > ATT FÖRSÖKA FÅ BARN EFTER CANCERBEHANDLING

## Att försöka få barn efter cancerbehandling

NÄR ÄR DET MÖJLIGT ATT FÖRSÖKA FÅ BARN?

FERTILITETSUTREDNING

FERTILITETSBEHANDLING - SÅ GÅR DET TILL

ATT GÅ IGENOM FERTILITETSBEHANDLING

ATT ANVÄNDA DONERADE ÄGG ELLER SPERMIER

REGLER OCH LAGSTIFTNING KRING FERTILITETSBEHANDLING

AVSLAPPNING SOM HJÄLP VID ORO

ÖVNING - REFLEKTION KRING DET DU LÄST HITTILLS I PROGRAMMET

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Figure 19. Main page of chapter 3, Trying to have children after a cancer treatment.

Fex-Can  
REPRODUKTIVSÄKERHET

HJ TEST TESTSTON ▾

HEM
OM FEX-CAN
BOKNINGAR
KONTAKT
DEKUSIONSFORUM

» KAPITEL » ATT FÖRSÖKA FÅ BARN EFTER CANCERBEHANDLING » FERTILITETSUTREDNING (2/8)

## Fertilitetsutredning

Fertilitetsutredningar kan göras i öppenården (värdcentral eller gynekologmottagning), eller ibland på reproduktionsmedicinsk eller andrologisk klinik på ett sjukhus. Nedan beskrivs hur en fertilitetsutredning går till för män respektive kvinnor med olika undersökningar och provtagning. I en fertilitetsutredning brukar det också ingå en genomgång och behandling av andra saker som kan påverka förmågan att få barn, som eventuella övriga sjukdomar eller medicinering, och livsstilsfaktorer. Det gäller till exempel rökning eller kraftig övervikt.

**Män**

Män får lämna ett spermprov. Det man då tittar på är hur många spermerna är och hur de rör sig. Om det första spermprovet visar att det finns få spermier eller att de rör sig dåligt brukar mannen få lämna ett andra spermprov för att få ett säkrare resultat. Det bästa är om mannen kan lämna sitt spermprov på kliniken där det ska analyseras. Män kan också få göra provet hemma om man transporterar det till kliniken inom max en timme och håller det kooltvarmt under transporten. Mer detaljerad information om hur man lämnar spermprov kan man få vid sitt sjukhus eller här.

**Kvinnor**

När man utreder en kvinnas förmåga att få barn ingår det som rutin att kontrollera sköldkörtelns funktion med hjälp av ett blodprov som mäter hormonet TSH (dyyreoidstimulerande hormon). Lätt underfunktion i sköldkörteln (hypothyreos) är en behandlingsbar åkomma som är mycket vanlig. Obehandlad hypothyreos kan leda till rubbningar i menstruationscykeln, svårare att bli gravid och även påverka fostret under graviditeten. Därför undersöker man med ultraljud om äggstockarna fungerar som de ska och hur aggressiven ser ut. Man undersöker även med blodprov hormonet FSH, som stimulerar äggstockarna. När en kvinna närmast sig klimakteriet stiger halten av FSH, eftersom feedback kommer till hypofysen om att äggstockarna producerar allt mindre östrogen. Det finns också ett annat hormon, AMH (anti-Müllerian hormone) som tillsammans med kvinnans ålder, mängden FSH och ultraljudsundersökning av äggstockarna ger en fingervisning om hur stor aggressiven är. För att uppnå graviditet måste ägget inte bara mogna och lossas utan även kunna passera från äggstocken genom äggledaren. Hur passagen genom äggledaren är kontrolleras vid en ultraljudsundersökning. Om det är viktigt kan man ibland lägga detta med ett kirurgiskt ingrepp. Man behöver också kontrollera att livmodern är normalstor och kan klara att växa i takt med ett foster.

**✓ Checklista inför läkarbesök**

För att få lista som pdf för utskrift, klicka [här](#)

**Vad du kan göra för att förbereda dig inför läkarbesöket:**

- Skriv ner eventuella symtom du har som du tror kan ha samband med förmågan att få barn (till exempel: problem med att få utlösning, oregelbunden mens).
- Skriv ner viktig personlig information, familjeförhållanden, arbete, livsstil och annat som kan påverka.
- Skriv ner din familjehistoria. När och hur fick dina föräldrar, mor- och farföräldrar barn? Eventuella sjukdomskomplikationer?
- Gör en lista över alla mediciner, vitaminer eller kosttillskott som du tar.
- Håll reda på all dokumentation kring din cancerdiagnos och behandling, samt eventuella fertilitetsbevarande åtgärder. Be att få journalkopior att ta med om du träffar olika vårdgivare.
- Överväg att ta med en familjemedlem eller vän. Ibland kan det vara svårt att ta till sig all information under ett möte. Fyra öron hör mer än två och därför kan det vara bra att ha med sin partner, annan anhörig eller vän.
- Skriv ner frågor att ställa din läkare.

**Frågor att ställa vid läkarbesöket.**

Att förbereda en lista med frågor (de viktigaste först) kan vara bra för att utnyttja tiden. Exempel på frågor:

- Exakt hur påverkas fertiliteten av den sjukdom och behandling jag har haft?
- Behöver jag göra några fler tester?
- Vilka behandlingsalternativ finns tillgängliga för mig?
- Vilka är fördelarna med varje behandling du rekommenderar?
- Vilka är biverkningarna av de olika behandlingsalternativen?
- Hur kommer varje behandling påverka mitt dagliga liv? Kan jag fortsätta arbeta?
- Finns det någon behandling du rekommenderar framför de andra?
- Hur vet du att dessa behandlingar kommer att gynna mig?
- Vad skulle du rekommendera till en vän eller familjemedlem i min situation?
- Hur snabbt behöver jag ta ett beslut om fertilitetsbehandling?
- Vad händer om jag inte vill ha fertilitetsbehandling?
- Kommer det att kosta mig något?
- Ska jag söka en "second opinion"?
- Finns det broschyrer eller annat tryckt material som jag kan ta med mig? Vilka webbplatser eller böcker rekommenderar du?

---

**Quiz - fertilitetsutredning**

Var görs fertilitetsutredning?

På värdcentralen

Hos gynekologen

På onkologikliniken eller där man fått sin cancerbehandling

På sjukhusets reproduktionsmedicinska enhet

I företagshälsövården eller studenthälsan

Fråga 1 av 4

◀
▶

TILLBAKA
VIDARE

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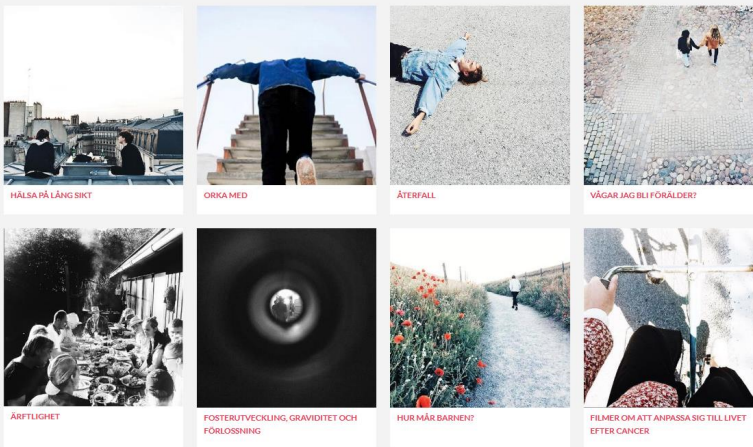
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Figure 20. Article including expanding content and a quiz, Chapter 3, Trying to have children after a cancer treatment.



## Min egen och barnets hälsa

I det här kapitlet kan du läsa om hur hälsan kan påverkas av cancer på längre sikt. Det gäller både ork att vara förälder och konsekvenser för den fysiska hälsan. Kapitlet handlar också om hur barn till personer som genomgått cancerbehandling mår.



## Fosterutveckling, graviditet och förlossning

### Ingen ökad risk för missbildningar

Det är i regel behandlingen man får mot cancer, och inte själva sjukdomen, som kan påverka ett framtida barn. Ett undantag är män med testikelcancer, där man tror att det är själva sjukdomen som påverkar spermiekvaliteten och därmed ger en något ökad förekomst av missbildningar (även lindriga) hos barn som blivit till under sjukdomstiden och upp till två år efter behandling. Men det kan även vara cytostatika och strålning mot bäcken som har den effekten. Det ska poängteras att risken för fosterskador är *liten*, och att den helt försvinner om man väntar två år efter behandlingens slut. Män som tar cytostatika eller andra cancerläkemedel rekommenderas att använda kondom om partnern är gravid, för att helt undvika att cytostatika kommer i kontakt med ett foster under utveckling.

Problem i samband med födseln, som fortidsbörd (för tidig förlossning), påverkas inte av om *pappan* har haft cancer.

För samtliga cancer typer och båda könen har man i stora, befolkningsbaserade studier kunnat se något samband alls mellan eventuella skador på barnet och föräldrarnas tidigare sjukdom. Risken för missbildningar och medfödda sjukdomar är lika stora, eller *liten*, hos barn vars föräldrar inte har haft cancer.

### Graviditetskomplikationer

Kvinnor som har behandlats för cancer och blir gravida löper en något ökad risk att barnet föds för tidigt och väger lite. Detta gäller särskilt om man har gjort operationer i underlivet. Det är därför bra om man kan gå på extra kontroller under graviditeten och eventuellt remitteras till specialismödravården. Barmorskan i mödravården frågar alltid om tidigare sjukdomar så detta kommer inte att missas.

### Att föda efter cancer

Om man bedömer att det finns ärbrändning eller liknande som gör att det blir svårt med en vaginal förlossning kan ett planerat kejsarsnitt övervägas.


### KAN FOSTRET TA SKADA AV FÖRÄLDRAVNAS CANCERSJUKDOM?

Om man väntar den rekommenderade tiden efter avslutad cytostatika- och/eller strålbehandling påverkas *inte* fostret. Graviditet och förlossning kan dock i vissa fall bli *lite mer* komplicerade om det är *mamma* som har haft cancer.



*Att vara gravid har inte känts som någon härlig upplevelse [...] för all det här det satt i mig hela tiden, sjukdomsbilden och allting: man mår illa, som man gör av cellgifter, man får andra smakiökar som man får av cellgifter. Jag försökte inställa mig hela tiden att "jag är inte sjuk -*

Figure 21. Main page and example article from Chapter 4, My own health and my child's health.



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KONTAKT


DISKUSSIONSFORUM 15

» KAPITEL » ATT INTE KUNNA FÅ BARN PÅ BIOLOGISK VÄG


## Att inte kunna få barn på biologisk väg




SORG ÖVER ATT INTE FÅ BARN



ATT BYGGA ETT BRA LIV UTAN BARN



LÄSTIPS



ATT ENGAGERAS I FÖR BARN

### Vad kan man göra när man känner sorg?

*Umgås med andra*

Att få stöd från omgivningen betyder mycket när man känner sorg. Det kan handla om att bara vara tillsammans, att göra saker eller att få tala om hur man känner sig. Att tala med människor som står en nära är till stor hjälp när man känner sorg och beskrivs av många som lättare än att söka professionell hjälp. Ibland kan det dock vara skönt att tala med någon som inte står en så nära och du som deltar i programmet har möjlighet att delta i vårt diskussionsforum.

*Självtröst*

Det är till stor hjälp att få tröst av andra, men man kan också trösta sig själv. Självtröst kan vara att man säger vänliga ord till sig själv, att man tar hand om sig själv genom att göra något man tycker om (ta en promenad, ta ett bad, dricka sitt favoritkaffe, se en film, ringa en god vän), att man pysslar om kroppen (till exempel smörjer in huden med en skön lotion), att man klappar eller kramar sig själv (kan låta konstigt, men det fungerar faktiskt!) eller sätter på sig bekväma favoritkläder.

*Medveten närvaro*

Längst ner på sidan finns en länk till en övning i medveten närvaro. Övningen kan fylla olika funktioner, bland annat hjälpa en att känna sig mer närvarande i livet. När det gäller att hantera sorg är övningen bra just för att man tränar på att byta fokus, genom att lägga märke till sina sännesintryck. När man känner överväldigande sorg och behöver minska känslan lite eller ta en paus, kan man lägga märke till sännesintryck för att minska känslans intensitet, för att känna mer kontroll, för att få lite distans (uppleva känslan utan att bli ett med den) och för att trösta sig själv.

*Acceptans*

Man har upptäckt att övning i acceptans kan göra många svåra situationer lättare. Det är ofta provocerande att läsa om acceptans, det uppfattas lätt som att man ska finna sig i en dålig situation. Det har dock visat sig att man kan minska sitt lidande om man tolererar att det finns.

Psykologen Anna Käver, som skrivit en bok om acceptans, förklarar acceptans så här:

”Ett accepterande förhållningssätt innebär inte att avstå från att söka förändring i en svår situation, utan att sluta föra krig mot tillvaron och sig själv. Acceptans innebär att välja att se både sin inre och yttre verklighet, utan att fly eller döma den”

(Att leva ett liv, inte vinna ett krig: om acceptans, 2007)

Acceptans i samband med svårigheter att få barn, kan exempelvis vara att tillåta sina känslor. Här nedanför finns en länk till en övning i acceptans av dig själv och din situation just nu.

» [Övning i acceptans](#)

» [Övning i medveten närvaro](#)

**Sant och falskt om sorg**

När man sörjer finns det olika stadier man måste gå igenom.

Sant

Falskt

⏪
Fråga 1 av 3
⏩

TILLBAKA
GÅ VIDARE

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Figure 22. Example of main page and an article including exercises and a quiz, within Chapter 5: Not being able to have biological children.

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KAPITEL RELATIONER

## Relationer

Välkommen till avsnittet om relationer! Avsnittet vänder sig både till dig som är i en relation och till dig som är singel.

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KAPITEL RELATIONER ÖVNINGAR FÖR ATT UTFORSKA SINA TANKAR (8/9)

## Övningar för att utforska sina tankar

Här är förslag på några korta övningar för att kartlägga dina tankar, upptäcka tankefallor och hitta möjliga alternativa tankar. Du kan göra en eller flera av övningarna. De här exemplen gäller att utforska sina tankar om relationer, men man kan använda samma metod för att utforska andra situationer där tankarna får en att dra förhastade slutsatser om verkligheten.

- Tänk på en social situation som hänt nyligen.**  
Försök att komma på hur du tänkte om dig själv i den situationen. Vad tänkte du om den andra personen och er relation? Hammade du i några tankefallor?

*Exempel 1: Skrev på Facebook om min nya cykel, fick fem likes, tänkte att folk tycker jag är barnslig eftersom så få gillade. Tankefalla: bland annat tankeläsning, att dra slutsatser om vad folk tänker istället för att ta reda på hur det faktiskt är.*

*Exempel 2: Man kanske kört sig generad för att man visat sina känslor i en situation och tänkt att andra tyckte man var pinsam. Tankefalla: bland annat känslotänkande, man kände skam och trodde andra tyckte man var pinsam eller "skämig".*- Läs igenom punkterna om tankefallor i förra artikeln.**  
Fundera på om du brukar hamna i några av tankefallorna, om du känner igen dig. Minns du något särskilt tillfälle när du tänkt på något av sätten?
- Fundera på alternativa tankar och förklaringar till de exempel du kommit på.**  
*Alternativ tanke till exempel 1 ovan: Vänerna kanske inte såg ens inlägg, vänerna kanske inte bryr sig om ens cykel men gillar en som person.*  
*Alternativ tanke till exempel 2 ovan: En alternativ tanke kan vara att andra kanske tyckte man var modig, ärlig eller mänsklig som visade sina känslor*
- Brukar du ha några negativa automatiska tankar som gäller relationer?**  
Det kan vara tankar om att man inte duger på olika sätt. I så fall kan du prova att identifiera sådana tankar i olika situationer, testa deras sannolikhet och komma på alternativa tankar. Beskriv situationen, skriv ner dina automatiska tankar i en kolumn och skriv ner alternativa tankar i kolumnen bredvid. Om du vill kan du uppskatta hur sannolikt det är att din automatiska tanke är sann (från 0 till 100 procent). Kan du koppla tankarna till några av de tankefallor som beskrivs i förra artikeln? Här nedanför finns förslag på saker du kan ha med i tabellen samt ett exempel.

Situation (beskriv kort)	Automatisk tanke	Sannolikhet att tanken är sann (0-100)	Alternativ tanke
Träffar gamla skolkompisar	De tycker jag är töntig  Tankefalla: tankeläsning för gissar bara vad de tycker	25%	De kanske också känner sig lite osäkra och kanske tycker det är trevligt att träffa mig och tycker det är skönt att jag inte är så väldigt cool

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Figure 23. Example of a CBT-inspired exercise – “Explore your thoughts about relationships.” within Chapter 6, Relationships.

**Articles** would typically contain an introductory main body text with psychoeducational and supportive content on a given topic. **Expanding content** was available for those wanting to probe into the subject in more detail. At the bottom or in the right-hand margin of the page, links to **exercises** and **video snippets**, as well as **authentic quotes** from young adult cancer survivors were provided to add life to the more academic information on the subject at hand. The number of quoted and filmed people was limited to enhance the personal feeling of connection, but great care was taken to include various situations and approaches to the topics, so that participants would feel included regardless of relationship status, gender or sexual orientation. Videos would open in a separate window for easy return to the main page. **Exercises** included the “raisin experience,” in which participants were instructed to examine the nature of a raisin in a mindful way in order to increase awareness of bodily sensations and practice mindful reflection. Instructions for the mindfulness exercises were available in text and as audio files. Other examples of exercises were CBT-inspired forms, where participants could list automatic negative thoughts and ways to counteract them, or fill in a checklist for daily routines. The exercises and most of the texts were downloadable and printable (Figure 23).

**Psychoeducational graphics** were used to explain biological facts and processes as well as psychological concepts (Figures 24-28).

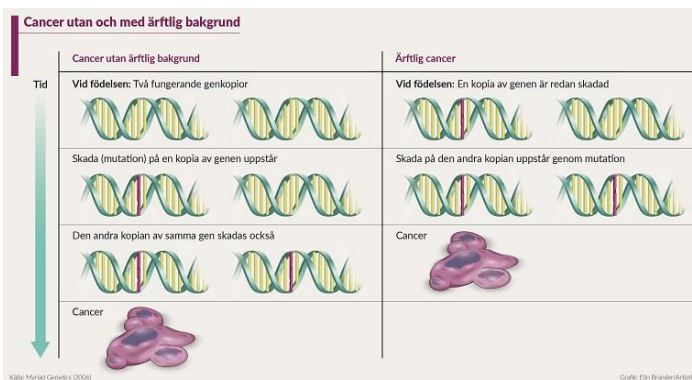


Figure 24. Explanation of the mechanism behind hereditary cancer. Graphics by Elin Brander.

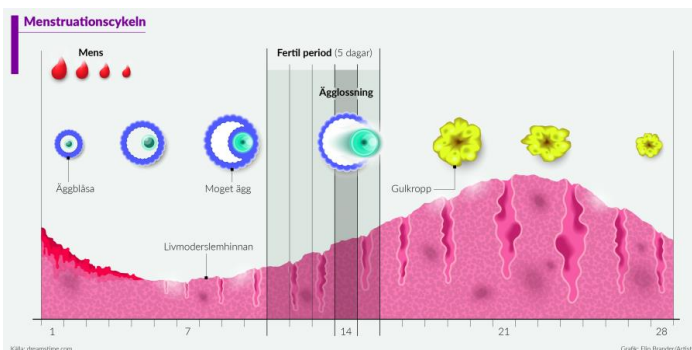


Figure 25. Explanation of the fertile window in the menstrual cycle. Graphics by Elin Brander.

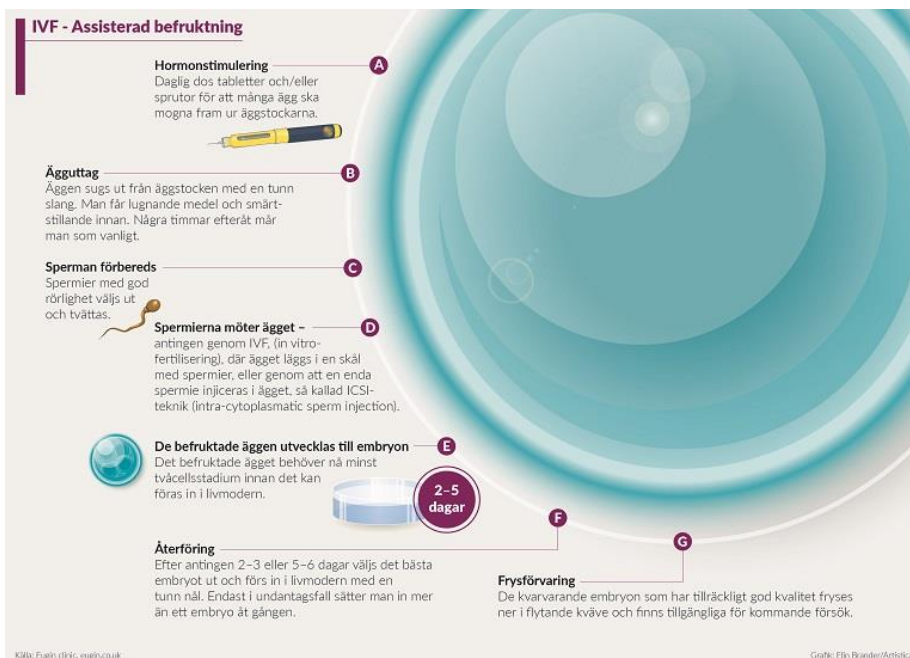


Figure 26. Explanation of the IVF procedure. Graphics by Elin Brander.

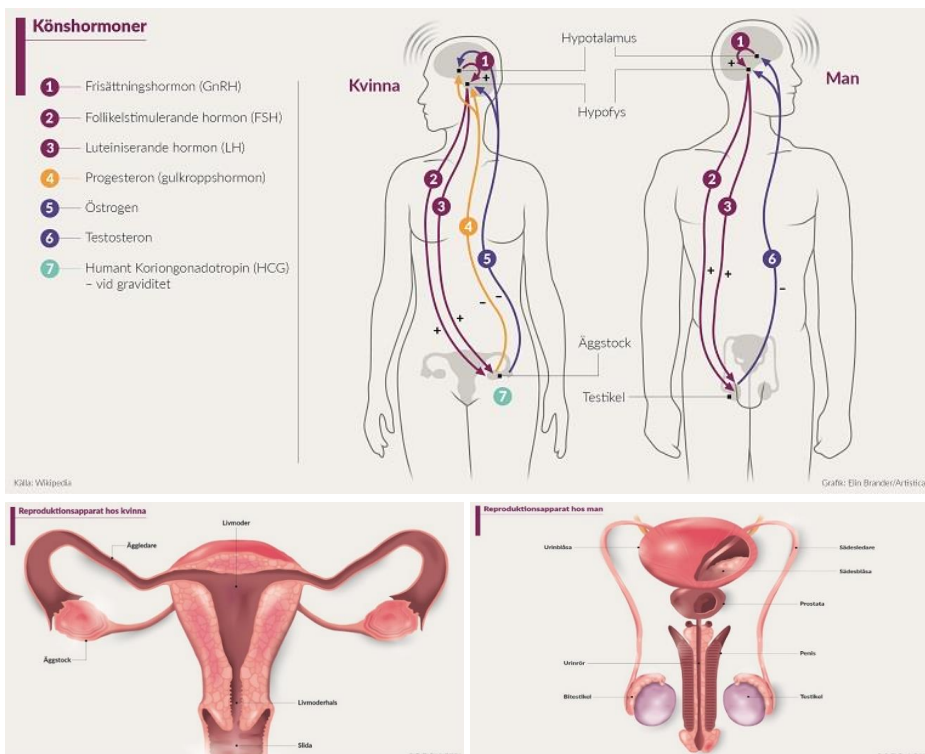


Figure 27. Illustration of the hormonal system (gonadal-pituitary axis); female and male reproductive organs. Graphics by Elin Brander.

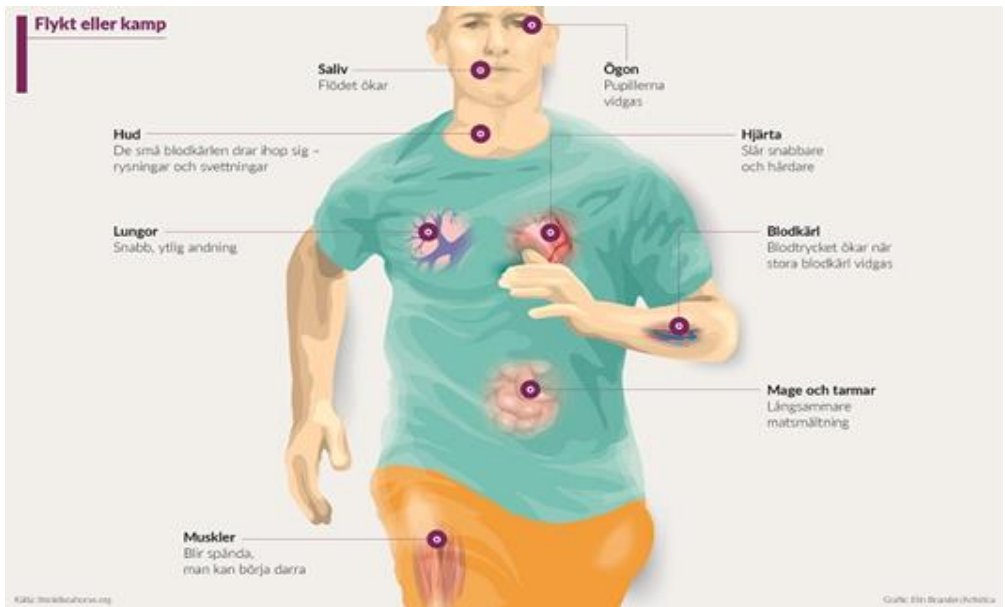


Figure 28. "Body-emotions-thoughts-behavior in relation to the environment". "Fight or flight". Psychoeducational illustration of the concepts of automatic thoughts and anxiety reactions from the Fex-Can Fertility program. Graphics by Elin Brander.

The program also contained many **photographs of young adult people** in various situations. To the extent possible, we tried to be inclusive and reflect everyday life in the pictures.



*Photographs by Tove Freijj/Nordic Photos.*

Contents of the six modules are summarized in Table 6.

Table 6. Structure and contents of the Fex-Can Fertility program.

Headline and contents of main article	Expanding content (or links)	Exercises	Quizzes/Interactivity	Survivor stories
<b>Presentation of survivors contributing with videos and texts/quotes (available the whole 12+2-week period)</b>				
<b>Chapter 1: Fertility after cancer (week 1-3)</b>				
<b>Biology and fertility</b> – The hormonal system, the fertile window for women and men; “Teaser” on what is to come later in the program	Puberty, Menopause, Sex hormones, When will fertilization occur? Start of a pregnancy, Contraceptives		True and false about puberty and menopause (Multiple choice questions, immediate feedback)	
<b>What is infertility?</b>  Definition and examples of different types of sub-/infertility  Statement that the Fex-Can program is about wishing for children, regardless of fertile ability			What does infertility mean to you?: What are your expectations on the program? (free text answers, interactive boxes)	
<b>How common are fertility problems?</b>  Methods to enhance fertility: lifestyle, hormonal stimulation, ART; Teaser on upcoming article about ART in chapter 3	Common causes of subfertility in men/women; When is fertile age?: The ovarian reserve		What do you remember from the first articles? (Multiple choice questions with immediate feedback)	Quotes
<b>What’s important in your life?</b>  Introducing the concept of valued direction	Self-compassion		Link to discussion forum	Quotes; Video on changed priorities concerning parenthood
<b>How the cancer treatment affects your fertility</b>  General information about treatment and disease effects on the reproductive system, and the importance of contraceptives during treatment.	Chemotherapy, Radiation, hormonal treatment, targeted drugs; Brain tumors, Lymphoma, Testicular cancer, Breast cancer, Ovarian cancer, Cervical cancer			Videos on 1) hormonal treatment to avoid relapse of breast cancer; 2) Asking your physician for help with erectile dysfunction



Headline and contents of main article	Expanding content (or links)	Exercises	Quizzes/Interactivity	Survivor stories
<b>Protecting fertility before a cancer treatment</b> General principles of fertility preservation	More information on different fertility preservation (fp) measures; Which are the fp measures that might be available for me?			Quotes; Video on the sperm banking experience
<b>Will I be able to have children?</b> Information on how to “check” fertility status after treatment	Link to association for single parents		Different short articles to read depending on current child wish	Video on deciding to find out whether fertility had been compromised by treatment
<b>Healthy lifestyle</b> (weight, physical activity and avoiding drugs)	Check your alcohol consumption; Links to sites on tobacco, alcohol and other drugs		Calculate your BMI; What do you remember from articles 6-8 (multiple choice questions with immediate feedback)	Quotes on bodily changes and accepting a new body image
<b>Chapter 2: Handling anxiety<sup>4</sup> (week 3-)</b>				
<b>What happens in your body when you feel worried?</b> Fight and flight, anxiety reactions (play dead)				
<b>Is it anxiety that I’m feeling?</b> How to differentiate between anxiety/depression and fatigue	Fatigue and chemo brain			
<b>Different ways of handling worry</b> Action or acceptance	Self-soothing, a way of handling worries my doing something	Accepting yourself right now		Quotes and Videos on: 1) Acceptance that fluctuates; 2) How to tackle adversities; 3) Avoiding certain information; 4) Strategies to handle distress

<sup>4</sup> The Swedish word that was used is “oro”, which is also used in the phrase “fertilitetsoro” (fertility distress or reproductive concerns). It denotes a feeling of unease, in this context stronger than worries but milder than anxiety.

Headline and contents of main article	Expanding content (or links)	Exercises	Quizzes/Interactivity	Survivor stories
<p><b>Handle your anxiety by separating facts from your reactions</b></p> <p>Introducing the concept of mindfulness</p>		Practice identifying and writing down your reactions (printable sheets)		
<p><b>Reduce your vulnerability by taking care of yourself</b></p> <p>Finding routines that make you feel well</p>	Eat regularly and healthy; Sleep on regular hours; Find a balance between activity and rest; Do something enjoyable and feel competent; Take care of your health and healthcare contacts; Be careful with alcohol and say no to drugs	Daily routines (Printable worksheets)		Quotes on lifestyle changes after treatment
<b>Mindfulness</b>		The raisin experience; Noticing sensations (body scan)		Quotes on different ways of practicing mindfulness
<b>Time to worry and worry-free zones – two good ways of handling anxiety</b>				
<b>Chapter 3: Trying to have children after a cancer treatment (week 5-)</b>				
<p><b>When is it possible to try to get pregnant?</b> (separate information for men/women)</p> <p>During treatment, If you are on hormones, After treatment, If you already know you are infertile</p>				Quotes and videos about starting to attempt pregnancy at different time points following treatment, and about feeling stressed trying to achieve a pregnancy
<p><b>Fertility investigation</b> Men/Women</p> <p>Contact information: fertility clinics in university hospitals</p>	Checklist before your visit to the physician		Quiz on fertility investigation procedures (multiple choice questions with immediate feedback)	
<p><b>Fertility treatment</b></p> <p>Different types of ART procedures</p>	Link to a film on ART		Quiz: Different types of ART procedures (multiple choice questions with immediate feedback)	Quotes: experiences from ART

Headline and contents of main article	Expanding content (or links)	Exercises	Quizzes/Interactivity	Survivor stories
<b>Going through fertility treatment</b> (success rates, physical strain, possible relationship strain, costs involved)				Video: contacting the fertility clinic once again after the cancer treatment
<b>Using donated sperm or eggs</b>	Link to article on donation from reproductive medicine clinic			
<b>Legislation about ART</b>	Links to: the Parliament's webpage, national guidelines for ART			Video about not accessing your frozen sperm because you are gay
<b>Relaxation to reduce anxiety</b>  Does stress limit the chances of getting pregnant?		Relaxation exercises (body awareness)		
<b>Exercise – reflection on what you have read so far in the program</b>  (free text answers)			Describe your current status after going through half the program; Did anything you read make you want to take further actions?; Is there something you have read about that you're not able to influence and that worries you? (interactive text boxes)	
<b>Chapter 4: My own health and my child's health (week 7-)</b>				
<b>Health in the long run</b>  What you can do with self-care to prevent or minimize harmful late effects; follow-up controls in healthcare	Maintaining a healthy diet and weight; Physical activity; Balancing living healthy with living well			Quotes on bodily changes. Video on starting to exercise again after the cancer treatment
<b>Coping with life</b>  Memory and concentration difficulties, lack of energy; How to find support in everyday life	Fatigue			Quotes about managing daily life challenges
<b>Relapse</b>  What are my chances to remain healthy? Can a pregnancy cause a			True and false about relapse (quiz with immediate feedback)	Quotes and video on fear of relapse

Headline and contents of main article	Expanding content (or links)	Exercises	Quizzes/Interactivity	Survivor stories
relapse? When are you cured from cancer?				
<b>Do I dare become a parent?</b>  The responsibility of being a parent makes you think about perhaps not being there			Link to discussion forum	Quotes and video about different dilemmas about parenthood after cancer
<b>Heredity</b>  Is my cancer hereditary?; Explanation of the (limited) role of heredity in tumor development	Link to information on pre-implantation genetic diagnostics		True and false about heredity (quiz with immediate feedback)	Quote on experiences of carrying BRCA mutation and on genetic counseling  Video on thoughts about heredity when trying to get pregnant with IVF
<b>Fetal development, pregnancy and delivery</b>  No elevated risk for genetic malformations; Pregnancy complications  Delivering after cancer				Quotes on concerns about pregnancy  Video on experiencing fear about pregnancy and delivering following cancer, and how the person got support from healthcare
<b>How do the children fare?</b> Biological children; Adoptive children; Children born through IVF with or without donation	External links to material on having a parent with cancer, from Swedish Cancer Foundation and Nära cancer		Share your thoughts about disclosing or not to a child that the parent had cancer before the child was born. (Link to discussion forum).	Quotes and video about talking to your child about your cancer history.
<b>Films about adapting to life after cancer</b>				Three videos on 1) accepting your new situation 2) finding yourself again 3) menopause before the age of 30
<b>Chapter 5: Not being able to have biological children (week 9-)</b>				
<b>Grief over not having children</b>  Grief is a natural reaction to loss; The grieving process; Different emotions, thoughts and bodily reactions are normal;	Acceptance exercise; Mindfulness exercise		True and false about grief (quiz with immediate feedback)	Videos about 1) wishing for children and considering the alternatives; 2) not being able to have more children after

Headline and contents of main article	Expanding content (or links)	Exercises	Quizzes/Interactivity	Survivor stories
Finding support from others when in grief; Practical tips on how to take a break from difficult emotions				the cancer treatment  Quote on coming to terms with difficult emotions when seeing other people with children
<b>Building oneself a good life without children</b>			Communicate with others in a similar situation (Link to discussion forum)	Quotes about reorienting toward a good life without biological children
<b>Suggested readings</b>  Novels and non-fiction books about infertility	Links to patient organizations for in- or subfertile people			
<b>To engage with children in need</b>	Becoming a contact family or person; Voluntary work			Quote about having children in your life without being a biological parent
<b>Foster home</b>	Link to organization for foster homes; Internal link to article on “coping with life”			
<b>Adoption</b>	Contact information of adoption organizations; Different steps in the adoption process		Quiz: rules concerning adoption (multiple choice questions with immediate feedback)	Quotes and video about adoption
<b>Films about infertility and alternative parenthood</b>				Videos on 1) alternative ways to parenthood after hysterectomy 2) knowing oneself and the importance or not of a genetic link to one’s child 3) adopting after cancer
<b>Chapter 6: Relationships (week 11-)</b>				
<b>Knowing oneself</b>  Awareness of how the cancer experience may have affected you as a person				Quotes and video about self-image after the cancer treatment

Headline and contents of main article	Expanding content (or links)	Exercises	Quizzes/Interactivity	Survivor stories
<p><b>Being single</b></p> <p>Reflect on whether you want to start dating, or if you feel comfortable with being single right now</p>				Quotes about managing being single after cancer
<p><b>Dating</b></p> <p>It is normal to feel insecure when dating</p>				Quotes and video about dating
<p><b>Telling people about potential difficulties having children</b></p> <p>It may help to practice telling before you do it IRL</p>				Videos: 3 different ways of telling
<p><b>Talk to your partner</b></p> <p>Practical advice on couple communication</p>				Videos: 3 different examples of communication in a relationship
<p><b>Take care of your relationship</b></p> <p>Practical tips on how to show empathy, accepting and validating your partner, and on handling problems early</p>				
<p><b>Thoughts and mindtraps</b></p> <p>Examples of automatic thoughts and their consequences</p>				Quotes with personal examples on automatic thoughts and how they can be challenged
<p><b>Exercises to explore your thoughts</b></p>		Formulate your automatic thoughts, analyze and challenge them (Printable worksheets)		
<p><b>Congratulations, you have now completed the Fex-Can program!</b></p>			What are your reflections about fertility and family life now? (Interactive text boxes)	

## 5.3 IMPLEMENTATION

### 5.3.1 Implementation process (Studies III and IV)

Study III evaluated the implementation process of the web-based program – according to demand, acceptability, functionality and preliminary efficacy. Following a few corrections, the program was found to be feasible for the target group. The findings of Study III are summarized in Figure 29.

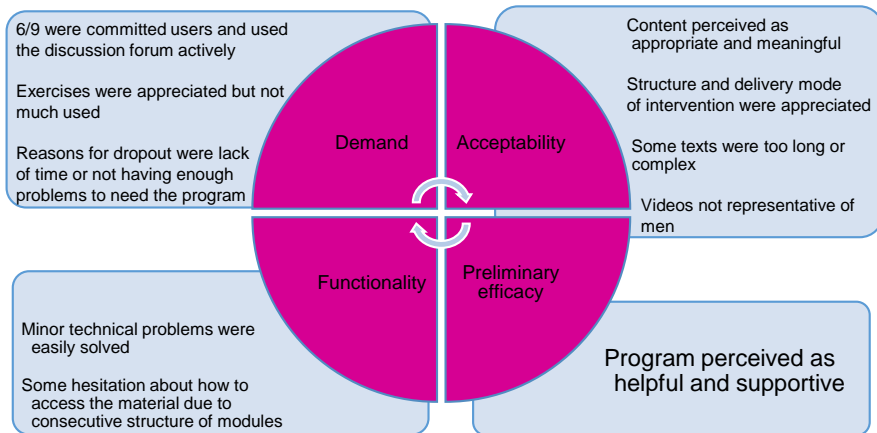


Figure 29. Summary of feasibility assessment (Study III).

As a next step, the process of eligibility assessment including registry-based distribution of the baseline survey was tested in a pilot trial not included in this thesis (Ljungman et al., 2018; Ljungman et al., 2019).

The full RCT was then conducted in three consecutive cohorts named A-C, depending on diagnosis date (Figure 13, Section 4.5.3.). Baseline and follow-up assessments were coordinated within the research team, which included an external data manager responsible for linking national quality registries to the population registry in order to obtain correct postal addresses. An external statistician was responsible for determining eligibility based on calculations of mean scores on the main outcome measure, and when individuals scoring above the cutoff had accepted the invitation to the RCT, the statistician also performed randomization on blinded data. A hired administrator assisted the research team in mailing, receiving and securely filing the questionnaires, and in administering the database. During the 12-week period in which participants had access to the program, members of the research team and one of the PRPs took turns moderating the discussion forum, attending to possible login difficulties, and answering questions or solving other technical problems, sometimes after consulting the software developers. Overall, the process ran smoothly although it required considerable administration.

### 5.3.2 Fidelity, dose, adaptations, reach (Studies III and IV).

The automated structure of the program ensured *fidelity*, since it was not possible to change the contents, chronology or time frame for the delivery. Fex-Can Fertility included six consecutive modules released every two weeks, and one module including video vignettes with survivor stories that was available throughout the intervention period. An email and a text message were sent to participants the evening before the start of the program and then again at 9am on the days when a new module opened. To enhance use of the program, reminders were sent by text message to those who one week through each module had not opened the current chapter. The message would include a link to the website so that participants could log on directly from their smartphones. As the intervention had a progressive design, participants had to go through all preceding modules in the given order before being able to open the next one. At the end of the intervention, participants had access to all the material for another two weeks.

*Dose*, or adherence was determined by using website system data. In the feasibility study, the term ‘committed users’ was used to refer to those (n=15/23) who had opened at least half of the modules and who responded to the post-intervention assessment. In the RCT, the concept of dose was further operationalized as one of the subgroup analyses involving stratification based on three levels of adherence to the program (high, low, control). The threshold between high and low was refined to include a minimum time spent on the website (to ensure participants had not just clicked through chapters), and one measure of interactivity<sup>5</sup>. Fourteen individuals met these conditions and were categorized as “high activity”. All participants who did not reach these criteria (n=50) were categorized as “low activity”, which could also include not having logged on to the program at all.

The successive *adaptations* of the program during the development and feasibility phases have been described in Section 4.1.2.

The *Reach* of the intervention is described in Section 5.5.1. Briefly, the entire target population was reached with the exception of individuals with severe cognitive impairment or not able to read and write Swedish. A few persons answered the survey over the telephone and a few others with the help of a lay translator; however, a certain level of reading capability and mastery of the Swedish language was required to actively take part in the intervention.

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<sup>5</sup> described in detail in section 4.5.5.



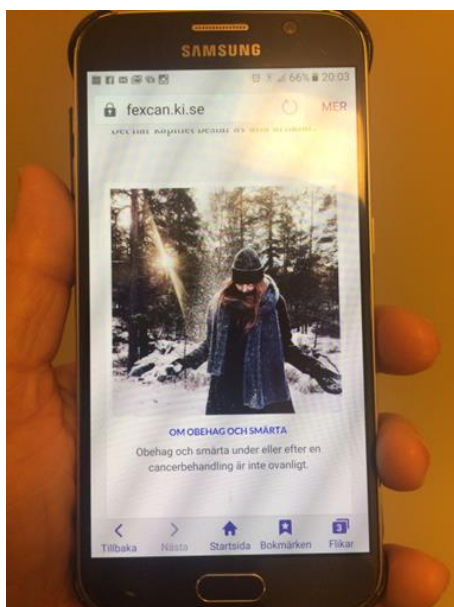


Figure 30. User interface of the program as represented on a smartphone.

## 5.4 MECHANISMS OF IMPACT

### 5.4.1 Participant responses to and interactions with the intervention (Studies III, IV and V)

In general, the Fex-Can intervention was well received.

The feasibility study (Study III) recorded mostly positive views concerning the acceptability of the intervention (Figure 34 in Section 5.5.2., results of exit survey). Similarly, in the post-intervention assessment for Study IV, 60% of participants stated that their concerns had improved over the course of the past three months. In addition, many expressed that they were happy with the contents, layout and the inclusive atmosphere in the program. However, despite our efforts to include diverse perspectives and situations, a few of the intervention participants felt excluded by the content, which they perceived as focusing too much on biological parenthood.

The discussion forum had variable activity over the course of the intervention. Some participants in Study V explained that they liked reading others' discussions but had no need to write their own posts. The overall activity in the forum was low and dependent on a few committed individuals.

Experiences of taking part in the program as part of the IG of the RCT were analyzed in Study V. Study V was designed as part of the process evaluation of the intervention and describes in more depth participant responses to and interactions with the intervention. Interviewees described how they had interacted with the intervention in various ways depending on their approach to the program – not using it as much as intended, seeing it as a “task” or “homework” or “going all in” – which didn't necessarily mean spending a lot of

time on the program website or completing all the modules. Rather, “going all in” was the attitude that the program was helpful and had added some value to their lives. The same individual might also fluctuate between the approaches over the course of the intervention period – depending on personal circumstances and their varying interest in the topics.

The abductive approach used in Study V led to categorization of participant experiences of the RCT into nine subcategories under the major headings Competence, Relatedness and Autonomy (Figure 31).

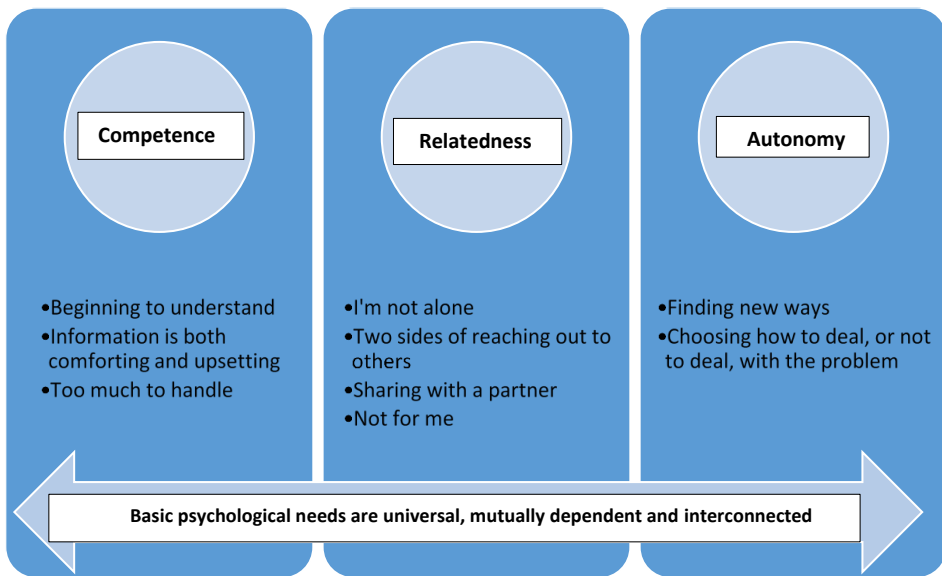


Figure 31. Themes and subcategories derived from the Framework analysis in Study V.

The theme *Competence* was illustrated by the perception that information could be reassuring but also lead to new concerns through increased awareness.

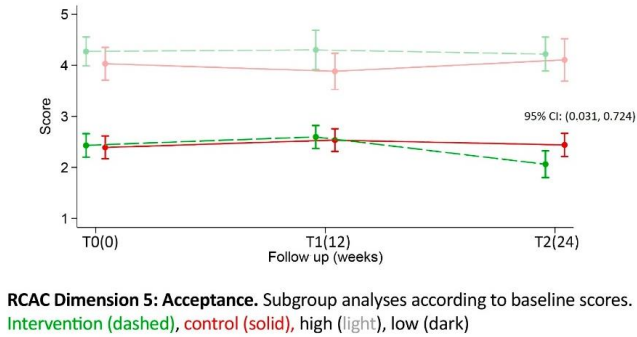
*Relatedness*: Participants described how the program had made them feel related, confirmed and “normalized” in their role as cancer survivors, sometimes contrasting this with the behavior encountered in close or more distant relationships with people who did not share their cancer experience.

Descriptions of *autonomy* in relation to the program were ambiguous and multifaceted. Some had experienced that the program made them see new solutions or alternative ways to deal with their situations, whereas others had made the decision not to act in a given direction at the moment.

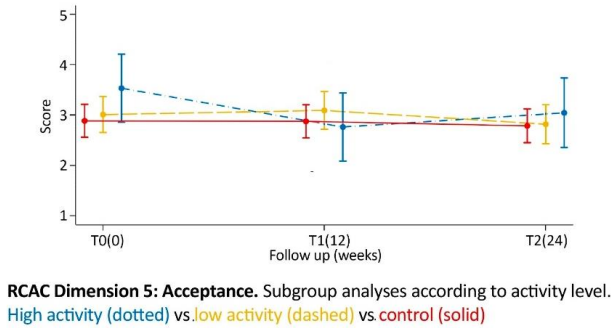
#### 5.4.2 Mediators (Study IV)

The current project did not perform any proper mediation models, but we hypothesized that individuals with more concerns at baseline would benefit more from the intervention. These

analyses only yielded significant results for one of the dimensions of the RCAC, Acceptance. Results indicated that individuals with high baseline acceptance (i.e., low RCAC scores on that variable), improved more than other participants (Figure 32).



**RCAC Dimension 5: Acceptance.** Subgroup analyses according to baseline scores. Intervention (dashed), control (solid), high (light), low (dark)



**RCAC Dimension 5: Acceptance.** Subgroup analyses according to activity level. High activity (dotted) vs. low activity (dashed) vs. control (solid)

Figure 32. Significant group differences for RCAC Dimension 5, Acceptance.

Another hypothesis concerned the intensity of use of the intervention. Study V revealed that the individual’s perception of their own activity had little objective connection to their website activity, and to their experience of the intervention as helpful. Subgroup analyses of the effect of program activity on intervention outcomes also showed inconsistent tendencies toward larger effects in users who were less active, compared to high-level users and the control group.

### 5.4.3 Unexpected pathways and consequences (Studies IV and V)

Several participants in Study IV commented in the post-intervention survey or in qualitative interviews that answering the questionnaires alone had helped them process thoughts and concerns surrounding fertility and parenthood. Some of the participants in the CG even thought they were in the IG or were unsure, because the survey was perceived as an intervention in itself.

Few participants who had received the intervention reported adverse events. In the post-intervention assessment, 2% in the IG (one individual, adding the comment that it was not due to the program) reported a worsening of symptoms and 36% stated their level of problems had not changed. Some of the interviewees in Study V also described how they had stopped using the program because it was too painful to think about their situation. Still, they were generally positive about the program in that it could be useful for other people or for themselves at a different points in time or in different circumstances.

One of the criticisms that came up was the chronological order of the chapters, where participants had to go through information about normal fertility and biological parenthood before reaching material on adoption and other alternative forms of living with children. This was perceived as demotivating and somewhat offensive to people with confirmed infertility.

## **5.5 OUTCOMES**

### **5.5.1 Recruitment and retention (Studies III and IV)**

In Study III, 15 of the recruited 23 participants (6 out of 9 who tested the Fertility program) were assessed post-intervention (65% retention rate).

The flow of participants in Study IV is described in Figure 33. At the three-month follow-up, the response rate was 81%. Participants were considered lost to follow-up if after two reminders they had not returned the questionnaire.

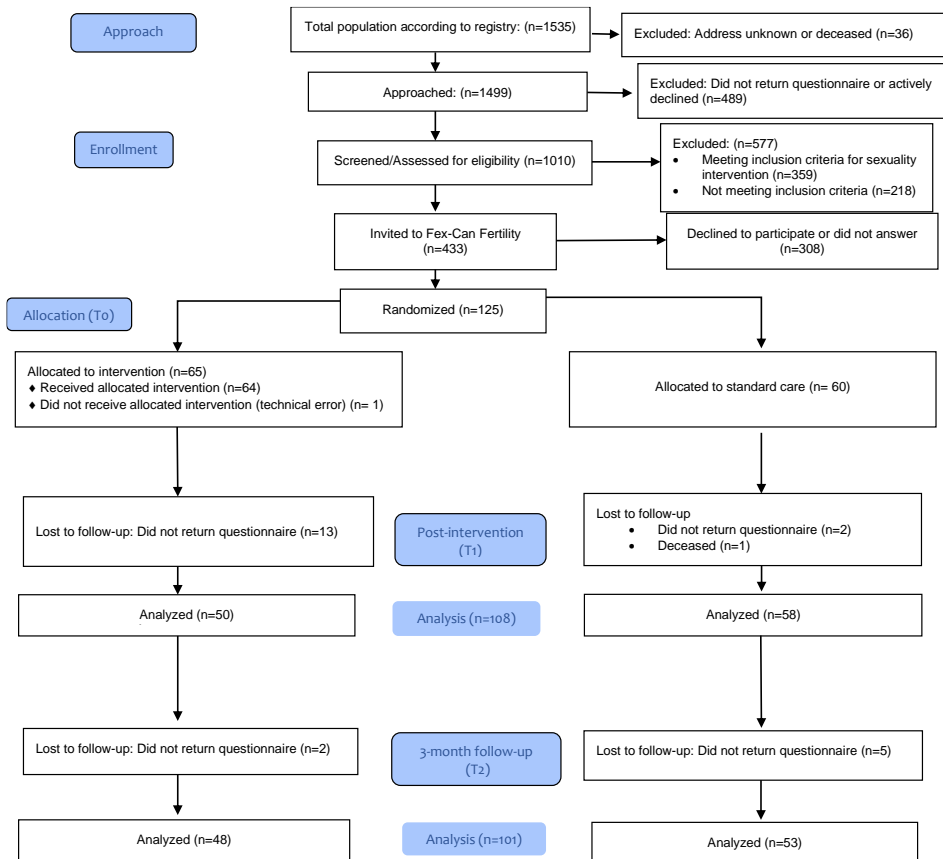


Figure 33. Flow of participants (CONSORT SPI-2018 Flow diagram).

## 5.5.2 Outcomes of the feasibility (Study III) and RCT (Study IV)

In Study III, descriptive statistics of quantitative process and outcome data from the 15 completers was coupled with qualitative data from the exit interviews and post-intervention survey to form a mixed-methods outcome evaluation. Completers of the fertility program were too few for their responses to be evaluated separately, including on the intended outcome measure RCAC.

The results of Study III indicated that most participants perceived the intervention as helpful. While a few reported temporary increases in worry or negative feelings, some also perceived personal growth and increased capacity for dealing with their situation. Responses to the exit survey (Figure 34) showed all responding participants found the content was easy to understand and agreed that it seemed correct from a medical point of view, and only a small minority felt overwhelmed by too much information. Further, a majority agreed that the

information contained in the program had helped them see new solutions to their emotional or sexual/fertility-related problems.

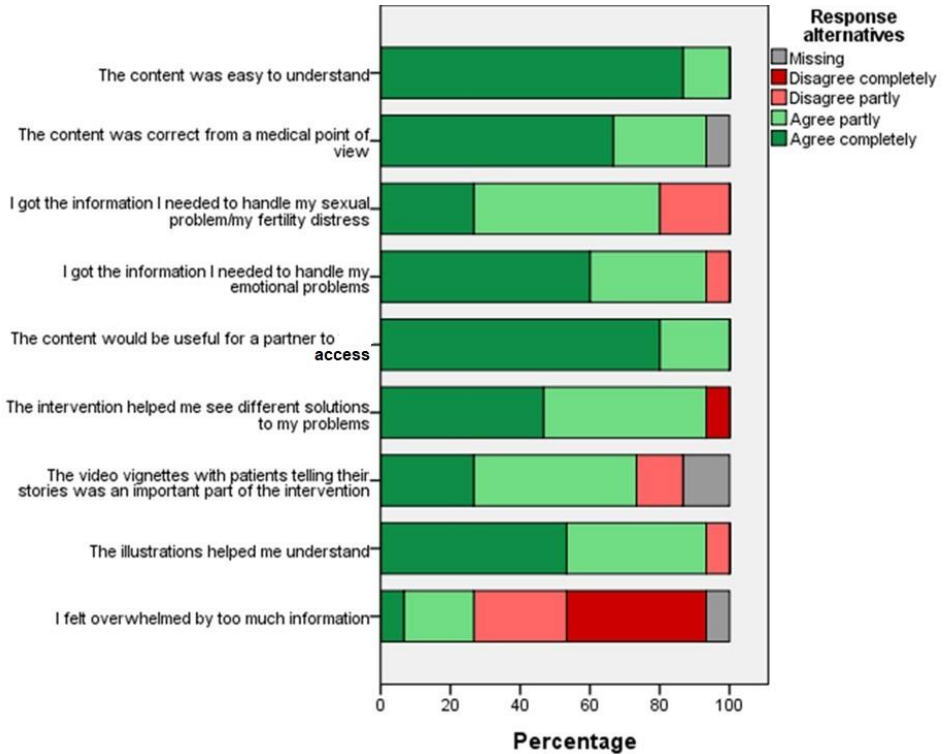
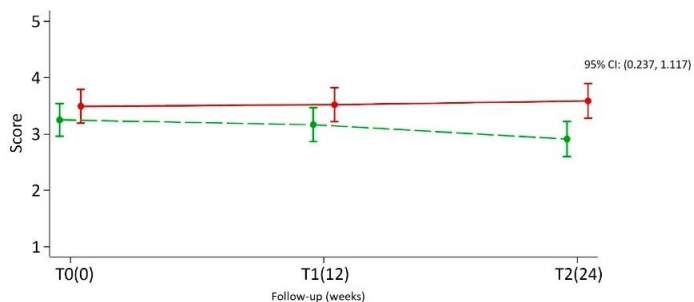


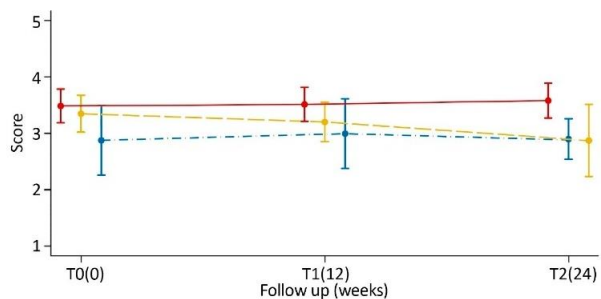
Figure 34. Results from the exit questionnaire in the feasibility study (n=15).

In the RCT (Study IV), 108 and 101 participants, respectively, were assessed on the two follow-up measurements (Figure 33). There were no significant group differences on the main outcome measure immediately post-intervention. At the three-month follow-up (T2), the intervention group had significantly lower mean scores on the *Child's health* dimension of the main outcome measure, RCAC (p=0.002, ES=0.64). Participants in the intervention group were significantly more confident than the control group in their knowledge concerning the cancer treatment's impact on fertility, on both follow-up occasions (p=0.05/0.013, ES=0.35/0.48). On the other secondary outcome measures (HRQoL, anxiety/depression and fertility self-efficacy), there were no detectable group differences.

Linear mixed models applied to the main outcome measure (RCAC mean score plus the means of each of the dimensions) confirmed that concerns relating to *Child's health* improved in the group that had access to the program, but only three months after the end of the intervention (p=0.003, ES=0.58). Additionally, those with low activity improved more than those with high activity and both these groups more than the control group (p=0.021) (Figure 35).



**RCAC dimension Child's health** . Intention to treat.  
 Intervention (dashed), control (solid)



**RCAC dimension Child's health** . Subgroup analyses according to activity level.  
 High activity (dotted) vs. low activity (dashed) vs. control (solid)

Figure 35. Significant group differences for RCAC Dimension Child's health.

On all dimensions except *Child's health*, there was a tendency toward a higher activity in those who had higher baseline levels of fertility-related distress, i.e., the IG participants with high activity consistently scored higher at baseline than IG participants with low activity and the CG, however the difference was not significant.

Results of the totality of quantitative analyses in Study IV are summarized in Table 8. In total, eight analyses showed significant group differences.

Table 8. Results of Study IV. Significant results in bold italic, white background. Data Source: RCT: N=108 (T1, 12 weeks) N=101 (T2, 24 weeks)

Outcome	Outcome measure	Analysis	Results	Effect size
<b>Fertility distress</b>	RCAC mean total score	T-test	No significant difference between IG and CG	
		LMM – ITT and baseline RCAC	No significant difference between IG and CG	
		LMM Activity in the program high/low/control	<b><i>Participants with low activity consistently improved. Participants with high activity improved between T0 and T1 and deteriorated between T1 and T2. CG was stable. (T1: <math>p=0.026</math>; T2: <math>p&lt;0.001</math>)</i></b>	<i>Not calculated</i>
<b>Fertility potential</b>	RCAC Dim 1	T-test	No significant difference between IG and CG	
		LMM Activity in the program high/low/control	<b><i>Participants with low activity consistently improved. Participants with high activity improved between T0 and T1 and deteriorated between T1 and T2. CG also improved but less than IG. (T1: <math>p=0.009</math>; T2: <math>p&lt;0.001</math>)</i></b>	<i>Not calculated</i>
<b>Partner disclosure</b>	RCAC Dim 2	T-test	No significant difference between IG and CG	
		LMM		
<b>Child's health</b>	RCAC Dim 3	T-test	<b><i>IG improved in comparison with CG at T2. (<math>p=0.002</math>)</i></b>	<b>0.64</b>
		LMM, Intention to treat	<b><i>IG improved in comparison with CG at T2 (<math>p=0.003</math>)</i></b>	<b>0.58</b>
		Activity in the program high/low/control	<b><i>Less active IG participants had better scores compared to the more active IG participants, and to the CG at T2 (<math>p=0.021</math>)</i></b>	<i>Not calculated</i>
<b>Personal health</b>	RCAC Dim 4	T-test	No significant difference between IG and CG	
		LMM		
<b>Acceptance</b>	RCAC Dim 5	T-test	No significant difference between IG and CG	
		LMM - ITT	No significant difference between IG and CG	



Outcome	Outcome measure	Analysis	Results	Effect size
		LMM – baseline RCAC	<i>Participants with higher baseline acceptance improved from baseline to T2, in comparison with participants in the control group with lower baseline acceptance (T2: p=0.033)</i>	0.53
		LMM - Activity in the program high/low/control	<i>Participants with higher activity improved from baseline to T2, in comparison with less active participants and to the CG (T2: p= 0.003).</i>	Not calculated
<b>Becoming pregnant</b>	RCAC Dim 6	T-test	No significant difference between IG and CG	
		LMM		
<b>Health-related quality of life</b>	EORTC-QLQ-C30	T-test	No significant difference between IG and CG	
<b>Anxiety and depressive symptoms</b>	HADS	T-test	No significant difference between IG and CG	
<b>Fertility knowledge – general</b>	Study-specific	T-test	No significant difference between IG and CG	
<b>Fertility knowledge – cancer</b>	Study-specific	T-test	<i>The IG had significantly higher mean scores at T1 (p=0.050) and T2 (p=0.013)</i>	0.35/0.48
<b>Fertility self-efficacy</b>	Study-specific	T-test	No significant difference between IG and CG	

In sum, the RCT had clear effects on treatment-related fertility knowledge immediately post-intervention and three months later, and on concerns relating to genetic risks for children of cancer survivors (*Child's health*) at the three-month follow-up. Effect sizes were small to moderate.

## 5.6 SUMMARY OF RESULTS

### 5.6.1 Results of included papers (paper by paper)

In **Study I**, 70% of physicians claim to often discuss fertility impact with their newly diagnosed patients, and >90% agree that the topic is important. Factors associated with not bringing up fertility were high workload, having near access to a reproductive clinic and seeing very few patients of reproductive age. Physicians were also less likely to have fertility discussions with patients who already had children.

**Study II** found that with the cooperation of patient research partners on the content, system and service quality of a web-based program, it was possible to design a complex, theory-based intervention with an RCT design that would be relevant for the end users.

**Study III** assessed feasibility according to the concepts of demand, acceptability, functionality and preliminary efficacy, and reached the conclusion that the intervention, following slight changes, was feasible for the intended target group.

**Study IV** evaluated the short-term efficacy of the intervention in reducing fertility distress and related psychosocial outcomes. On a group level, differences between intervention and control were small, and significant results were found mainly for concerns relating to heredity that could impact a future child's health, and confidence in knowledge about fertility after cancer. Linear mixed models also indicated significant differences between intervention and control for the total scores for *Fertility potential* and *Acceptance of infertility*.

**Study V** described the experiences of a subsample of the intervention group in the RCT, from the perspective of the web-based program's capacity to satisfy the basic psychological needs for competence, relatedness and autonomy. The findings demonstrate the nuances, flexibility and complexity of basic needs and emphasize the difficulty in designing an intervention that caters to all.

## 5.6.2 Process evaluation of the intervention

A summary of the main findings from the process evaluation is presented in Table 9.

Table 9. Summary of process evaluation

**Context: Participants throughout Studies II-V had high levels of education and were predominantly female with a median age of 30-33. All the eligible diagnoses were represented. About one-third chose to participate, signaling limited interest for the intervention in the target group, even for those scoring high levels of fertility-related distress at baseline.**

Description of intervention and its causal assumptions	Implementation	Mechanisms of impact	Outcomes  (fertility intervention only)
<p><b>Intervention development and content:</b></p> <p>Participatory design according to holistic framework; content, system and service quality were assessed during the development phase.</p> <p>Theory for understanding eHealth interventions – based on SDT, satisfaction of basic needs competence, relatedness and autonomy as intermediate outcomes for fertility-related distress, HRQoL, anxiety and depression.</p> <p>→ <b>Program was designed with successive modules with psychoeducational and behavior change content, including exercises and interactive components</b></p>	<p><b>Dose:</b> Usage was lower than expected: Feasibility: Two-thirds were “committed users.” RCT: Use of the intervention was categorized as either “high” (n=14) or “low” (n=50). “High usage”= &gt;20 mins on website</p> <p><b>Reach:</b> Feasibility – recruitment via clinics/contacts in Stockholm. RCT: nationwide recruitment via registries/baseline assessment. Low recruitment but high retention rates. Intervention was accessible for everyone with an Internet connection and a computer/tablet/smartphone.</p>	<p><b>Reactions:</b> Participants appreciated reliable information and contact with others.</p> <p><b>Mediators:</b> Adherence and baseline fertility distress only partly predicted intervention effects.</p> <p><b>Unexpected pathways and consequences:</b> No apparent connection between dose and effect.</p>	<p>High retention through post-intervention assessments.</p> <p>Inconsistent effect on two out of six dimensions of fertility distress (<i>Child’s health and Acceptance</i>).</p> <p>Moderate effect on treatment-related (specific) fertility knowledge.</p> <p>No effect on other secondary outcome measures.</p>

## **6 DISCUSSION**

This thesis has demonstrated the complexities and challenges involved in fertility-related communication with cancer survivors. The perceived need for psychosocial interventions targeting fertility-related distress following cancer does not necessarily translate into broad uptake of such an intervention in a web-based format. Despite a theory-based design, careful planning according to established frameworks for intervention development, and a long and close cooperation with end users, few of the outcomes were statistically significantly better for the intervention group than for controls receiving standard care. The initiative was generally appreciated by the target group, but adherence did not meet our expectations. Below, I discuss some of the possible reasons behind these findings, including the wider context of the intervention.

### **6.1 CONTEXT: FERTILITY DISTRESS FOLLOWING CANCER**

#### **6.1.1 The need for information, knowledge and competence about fertility following cancer**

Studies from the patient perspective point out that there is a wish for HCPs to initiate talks about delicate issues such as sexual and reproductive health (Ahmad et al., 2015). In addition, dissatisfaction with care and the reporting of unmet information needs occur when the HCP does not actively respond to signals that fertility is an important question (Logan et al., 2018b). Most young adults with cancer types prone to cause infertility are treated at either oncological or hematological units. We therefore wanted to investigate the perspective of Swedish oncologists and hematologists, who are responsible for the medical care, decisions regarding treatment and possible referrals to other specialists.

In Study I, 70% of oncologists and hematologists stated they often discuss the cancer treatment's impact on fertility with their newly diagnosed patients. This figure is in line with the results of a systematic review of clinician provision of support (Logan et al., 2018a), and indicates that guidelines are known and applied by most physicians in cancer care. Study I investigated reported reasons for not engaging in fertility discussions, and the logistic regression models indicated that physicians experiencing a high workload, seeing very few patients of reproductive age or working in a hospital with access to a reproduction clinic, talk about fertility with their patients to a lesser extent than other physicians. These findings about structural or organizational barriers have been corroborated by a systemic review (Lampic & Wettergren, 2019) and highlight the general need for education on oncofertility. HCPs may need specific training in initiating discussions about fertility when a patient is in for cancer treatment. Whether conversations about fertility should be mainly a task for the physician, for the nurse, for other HCP categories, or a joint responsibility for all, can be debated. There is a strong case, however, for including and addressing nurses in cancer care to step forward and tackle concerns and fear associated with the cancer treatment in general, and fertility should be no exception. Nurses are often the ones with the most frequent contacts with patients and, in addition, people receiving a cancer diagnosis in Sweden are entitled to a personal nurse navigator, who should be a suitable contact person for managing various physical and

psychosocial side effects of cancer treatment (Regionala Cancercentrum i Confederation of Regional Cancer Centers, 2019). Conversation techniques and specific knowledge on oncofertility are increasingly incorporated into specialist nursing curriculums (Quinn et al., 2016; Winterling, Lampic, & Wettergren, 2020). In Sweden, the Fex-Talk initiative was tested in the educational curriculum for oncology nurses and was evaluated as helpful in managing organizational barriers and overcoming difficulties in addressing the topic (Winterling, 2020). Permanently adding similar training to the curriculum for oncology nurse navigators would be a suitable extension since, especially in the Swedish context, nurse navigators play an important role in coordinating care and providing general support for people affected by cancer. It would therefore have been interesting to extend the study on HCPs to also study nurses' practice behavior, attitudes and confidence in knowledge about oncofertility. Another potential target group could be other specialist physicians such as surgeons or GPs, who are also often involved in the care of young adults with cancer.

Other previously known barriers to addressing fertility that depend on individual patient characteristics include prognosis, the woman's age and, more rarely, cognitive impairment or complicated circumstances such as concurrent HIV infection. Additional factors that have been associated internationally with not discussing fertility are relationship status and sexual orientation. In our sample, these factors were not significant, despite frequent patient reports of discrimination and invisibility in the healthcare setting (Russell, Galvin, Harper, & Clayman, 2016). These previous findings, and the results of Study I, must be seen in the light of recent developments in information provision. Despite previous research indicating insufficient information provision (Goossens, 2014; Logan et al., 2018b), in the cohort from which the sample for the RCT was drawn 81% of men and 78% of women reported having had fertility discussions with an HCP (Wide A., 2020, submitted). In this cohort, pre-treatment child wish was associated with recalling information, as was being born in Sweden. Identifying as heterosexual and, for women, being younger than 35, increased the likelihood of being informed about fertility preservation options (Wide A., 2020). This largely confirms the perspective of oncologists and hematologists in Study I, with the addition of vulnerable groups such as foreign-born and sexual minorities, where unmet care needs persist. It seems apparent that awareness-raising activities from academia and patient organizations have contributed both to informing policy and to changing practice behavior in the past couple of years, although some barriers remain to including vulnerable groups in fertility discussions. Addressing the topic of fertility is now mentioned in the implemented national guidelines "Standardiserade vårdförlopp" (Standardized Care Pathways) for several cancer diagnoses and in the national guidelines for cancer rehabilitation (RCC, 2019). Another important reason for encouraging timely discussion of fertility, and if possible, fertility preservation, is the higher likelihood of a successful outcome. A recent Swedish cohort study comparing women with breast cancer with or without fertility preservation (mean age 32 and 33 years, respectively) found that women who received fertility preservation were significantly more likely to bear children after cancer and also utilized ART to a greater extent (Marklund et al., 2020). It could therefore be argued that at least to women with breast cancer and in a context with fully subsidized healthcare, it is worthwhile to consistently offer fertility preservation. In cases where pre-treatment fertility preservation is not possible, an honest discussion about potential post-treatment FP measures, or alternative pathways, would be beneficial for patients expressing a child wish.

Importantly, HCPs need to be reminded that child wish might change over time (G. M. Armuand et al., 2014; Schmidt et al., 2016) and that fertility discussions might have to be repeated or re-initiated at various points in the disease trajectory.

Study IV showed that the Fex-Can program had a beneficial effect on fertility knowledge relating to cancer, such as treatment impact on reproductive function and the availability of fertility preservation and ART. This is an important finding considering that there is sometimes the attitude in healthcare that you should not give too much information. HCPs fear that general information might not be applicable in the current case, and that too much information might cause additional worry and concern. Indeed, the findings of Study V point out that information may be both comforting and upsetting, but the overarching results of Studies II-V solidly point in the direction that young people with a cancer diagnosis request and are able to handle updated and authoritative information regarding their health. If the information is delivered in an individualized format taking into account educational level, age and current parenthood wishes (without precluding the possibility of latter changes of mind), many people are better off knowing more, even if that includes negative or distressing information. This also is in line with a person-centered approach in which the care is built through communication and partnership (Loonen et al., 2018).

Another conclusion from the RCT is that the Fex-Can program was efficacious in educating participants about genetic cancer risks. After completing the program, the intervention group were significantly less concerned about their biological children having an elevated risk of getting cancer. As a possible concern that the cancer risk might be genetically transmissible is rather easily dismissed by providing accurate information about the low proportion of hereditary mutations, this can be interpreted as an extension of fertility-related knowledge. Reading and processing information about the low to nonexistent risk that their children would get cancer because of their parent's health history, it is likely that the specific concerns measured in the *Child's health* dimension of the RCAC would also be dissipated. This is unlike several of the other dimensions, which instead entail uncertainty (e.g., *Fertility potential*, where information could potentially *increase* concerns), or require an active behavior change (e.g., *Acceptance*, *Partner disclosure*), aspects which might be more difficult to address in a psychoeducational self-help intervention (Kok et al., 2016; Teixeira, 2020).

Previous research has demonstrated that in women, pre-treatment fertility counseling may be associated with *higher* levels of reproductive concerns post-treatment, even when adjusting for receipt of fertility-threatening cancer treatment (Young et al., 2019). Drizin, Whitcomb, Hsieh, and Gorman (2020) found that this also holds true for young adult men. Receipt of fertility counseling was likewise associated with higher scores on all dimensions of the RCAC except *Personal health* and *Acceptance*. Does this mean that people who are distressed to a greater extent seek counseling, or that counseling makes people more anxious? Drizin et al. (2020) conclude that the men's concerns may have been inadequately addressed by the fertility counseling provided. There is also the possibility that people who have a low risk for infertility (and know it) do not seek out fertility counseling. If we transfer this reasoning to the Fex-Can project, it is likely that people who were uninterested

in the topic would not respond to the survey, and that those with confirmed low infertility risk probably either had low RCAC scores or declined participation in the RCT. An alternative explanation for the observed correlation in Drizin's study could be that the men got more anxious from the information they received. This possibility might also be reflected in the inconclusive results of our RCT. Some individuals, when learning more about fertility risks, may have become more aware of the problem and increased concerns on some aspects may have thus outweighed the positive effects of the program. The intervention provided reliable and requested information concerning fertility, but some participants may have become more anxious.

### **6.1.2 The need for community**

This thesis has established that, apart from the communication with HCPs, young people diagnosed with cancer long for interaction with their peers and to regain a feeling of belonging that was lost due to the cancer experience. Without necessarily adopting an identity as a "cancer survivor," people are propelled towards telling their story, voicing their opinion and alleviating their loneliness by sharing with others in similar situations.

Participants (Studies III, IV and V) and research partners (Study II) expressed the need for *relatedness*, described as not being alone, and as putting one's own situation into perspective (Hovén et al., 2020). Relatedness is one of the basic psychological needs, the universality of which has been demonstrated in previous research (B. Chen et al., 2014). Every human being needs to feel connected socially to their surroundings. Although overall activity in the discussion forum was low both in the feasibility study (Paper III) and in the RCT (Paper IV), many participants read the posts, reflected on other people's experiences and described relatedness aspects as the most beneficial part of the intervention. Indeed, research on young adults with cancer-related fertility distress highlight loneliness as a central feeling (Goossens, Delbaere, Beeckman, Verhaeghe, & Van Hecke, 2015). It seems that the Fex-Can intervention at least to some extent contributed to alleviating this loneliness, and the web-based format did not seem to constitute an obstacle. On the one hand, participants in Study V pointed out that patient organizations, informal groups on social media, friends and close relatives might also contribute to filling this gap. On the other hand, use of social media when feeling lonely has been associated with worse psychosocial outcomes and may not have the intended supportive effect (Tolby et al., 2020). Most of the participants of Studies IV-V had partners; the intervention was perceived as inclusive even for those who were single, although relationship status might affect the actual availability of fertility preservation options and of achieving parenthood. Great care was taken when designing the intervention to try to ensure that people would feel included regardless of relationship status. However, the social norm of living in a heterosexual couple relationship cannot be disregarded and probably to some extent influenced participants' perceptions.

One reflection concerns the role of partners or next of kin. In Study II, two mothers of former patients participated as research partners. In Studies III, IV and V, the topic of involving a partner or other family members came up. It appeared that the support of a partner could not

be taken for granted and several participants expressed the wish for interventions directed at partners or at the couple as a dyad. In previous research, interventions aimed at partners have mainly addressed wives or female partners of men with prostate cancer or male partners of women with breast cancer (Hedden et al., 2017; Jones et al., 2013), but some programs also extend to target the dyad directly (Lewis et al., 2019). This focus might be due to those diagnoses being the most common ones, but is also reflective of gender stereotypes, especially considering sexual and reproductive health. In some cultural contexts, it is assumed that to achieve behavior change in men, it is necessary to influence their wives (Bergner, Cornish, Horne, & Griffith, 2018). The RCT did not include the perspective of partners. Participants in Study V described the complexity of their relationships with (often male) partners. Partners of both genders often wished to be involved, but some participants had experienced a distancing and described feeling isolated from their partner. These participants anticipated that if partners had been invited to the study and educated about side effects of cancer treatment, it would have been easier for them to offer support by showing empathy and understanding. Furthermore, in some cases, factors such as the (female or male) *partner's* depression or infertility affected the participant more than their own cancer diagnosis and treatment. This shows the need for considering the individual in their full context and not reducing fertility distress to an individual problem. Considering the importance that many people and cultures place on intimate relationships, an alternative design for the Fex-Can intervention could have been to incorporate the perspective of the partner and to allow partners to participate. This might have further strengthened participants' relatedness needs. However, we prioritized remaining open and inclusive towards those living alone, since child wish and becoming a parent do not necessarily need to include having a partner.



Photograph by Tove Freij



Another implication of the need for community is that web-based interventions may not always be sufficient to satisfy the need for relatedness. Some people may benefit more from personal, IRL contacts with HCPs or peers. Study V indicated that some of those who enrolled in the RCT did not initially believe that psychosocial support in the web-based format would be effective. Such ideas may have limited the general uptake of the intervention.

### **6.1.3 Fertility distress – whose problem?**

It seems that the prevalence of fertility distress in the population that we turned to is similar to what has been previously reported. Out of the 1010 responding to the baseline assessment, 433 turned out to be eligible for the intervention, i.e., 42.9% (46% of women and 36% of men) reported elevated levels on at least one subscale of the RCAC.

In the general population, fertility distress is very rare (Ljungman et al., 2020). This could be an argument to keep developing tailored interventions for cancer survivors, since they have particular concerns. But the observed difference in prevalence of fertility distress could also be reflective of the fact that cancer survivors have received fertility counseling, and thus made aware of the potential threat to fertility. This contrasts with young adults in the general population, who might take their fertility for granted (as you will likely not know before trying for a child if you are fertile or not, unlike sexual problems, which are more frequently manifest). It should be noted, however, that it is not solely the cancer diagnosis that will explain individual risk of infertility and fertility distress following cancer. It is known that for women, lower pre-diagnosis ovarian reserve is a strong predictor for the risk of post-treatment amenorrhea and premature menopause (Levine, Kelvin, Quinn, & Gracia, 2015). Moreover, the relationship between actual or potential infertility and experiencing fertility distress is not a linear one. There are psychological and psychosocial circumstances affecting the way an individual handles the threat of infertility, whether this involves uncertainty regarding fertility potential or overcoming the certain loss of fertility that will result from hysterectomy. Fertility has been found to be one of the main sources of illness uncertainty for young adults (Panjwani et al., 2019) and interventions targeting uncertainty may be efficacious in improving psychological outcomes (Germino et al., 2013). Through its mindfulness and CBT-inspired exercises, the Fex-Can intervention aspired to help participants manage uncertainty and enhance acceptance. Still, some of the PRPs and participants in Studies III, IV and V requested detailed and personalized information that the program could not provide, and had difficulty managing the uncertainty aspect that is embedded in fertility and childbearing.

As has also been noted in previous research, child wish, regardless of having children before the onset of cancer, is associated with higher levels of reproductive concerns (G. M. Armuand et al., 2014; Logan et al., 2019; Patterson, Perz, Tindle, McDonald, & Ussher, 2020; Wenzel et al., 2005). Still, Study I found that physicians were less likely to discuss fertility if the patient already had children. This may be related to either the non-acknowledgement of the emotional importance of child wish even for those who already are parents, or be reflective of

the Swedish regulation concerning government-funded access to fertility preservation and ART (in some regions only given to couples or single women who do not already have biological children).

The results of subgroup analyses in Study IV add to this that for most dimensions of the RCAC, baseline levels of fertility distress were not related to intervention uptake or to the measured outcomes. Study IV suggests that acceptance of fertility distress might be a possible moderator of intervention outcomes. But the overall conclusion is that fertility-related distress is a very complex phenomenon. In the literature, reproductive concerns have been shown to correlate with depressive symptoms (Jessica R Gorman et al., 2015) in women, and psychological distress in both genders (Ussher & Perz, 2019). Among both women and men, negative associations have been found with health-related quality of life (Benedict et al., 2018; Canada & Schover, 2012), relationship satisfaction, and acceptance (Patterson et al., 2020; Ussher & Perz, 2019). For men with testicular cancer, a negative body image appears to be a predictor for reproductive concerns (Ljungman et al., 2019). Both HCPs and patient representatives underline the importance of fertility. But still, in Study III, only 6 out of 9 participants were “committed” (opened at least 50% of the chapters), and in the RCT, less than 30% of eligible participants chose to enroll, suggesting that fertility distress, although an important issue, might be overshadowed by other aspects of life. Indeed, Study V revealed that it was difficult to prioritize the program over other activities such as work, exercise and family life.

Another possible explanation for the hesitant results of the intervention could be varying coping styles. Coping styles are usually divided into task-oriented, emotion-oriented or avoidant (Endler & Parker, 1990). An avoidant coping style has been associated with worse psychosocial outcomes in long-term testicular cancer survivors (Rutskij et al., 2010). In Study V, some participants described that processing information about fertility could become “too much to handle.” If the negative thoughts became too intrusive, they would shut down the webpage or perhaps even stop using the program. At the same time, participants described oscillating between wanting to act and not being able to process difficult feelings. Although coping style is often framed as a personality trait, it would have been interesting to study the possible correlation between satisfaction of basic psychological needs and coping style.

To understand the complexity of our results, it is also important to consider the sociocultural context in which this intervention was delivered. In virtually every society, there is a strong reproduction norm, and having children is associated with many social advantages. In Western societies, it is assumed that childlessness is a free and informed choice, which may make disclosure about infertility more difficult (Patterson et al., 2020). Infertility, on the other hand, is stigmatizing in any cultural context. Research shows that a lack of social support in a traditional society increases the stress perceived by infertile women, while perceived support reduces feelings of loss of control (Nouman & Zanbar, 2020). The individualistic approach (also underlying the studies included in the present thesis) ignores the strong social pressure imposed on the individual, and the degree to which such pressure might be internalized and

manifested as “reproductive concerns.” Study IV of the present thesis indicated that people with higher levels of acceptance of (potential) infertility were more likely to participate in the intervention, and showed greater increases in level of acceptance than those with lower baseline acceptance. Patterson et al. (2020) suggest that the relationship between acceptance of illness, quality of life and reproductive concerns could be mediated by sociocultural factors rather than individual-level variables. Their conclusion is that psychosocial interventions for young adults need to provide strategies for handling potentially distressing social situations. The Fex-Can program tried to fulfill this need by incorporating texts and exercises on relationships and “mind traps” related to sensitive situations, and by including the study-specific outcome measure entitled “Fertility self-efficacy.” It should be noted that the intervention had no statistical effect on fertility self-efficacy and that participants had strong fertility-related self-efficacy already at baseline (average 3.2 out of 4 points, although no clinical threshold had been determined).

In conclusion, it would perhaps be vain to expect a large effect on complex psychological and psychosocial outcomes such as fertility-related distress through a short-term and relatively flexible intervention like Fex-Can fertility. It might be more difficult than hypothesized to affect the underlying factors, which may be both individual and social.

## **6.2 DESIGNING AND DELIVERING A COMPLEX INTERVENTION REQUIRES MORE THAN...**

### **6.2.1 Participation, adherence and commitment**

The Fex-Can intervention was developed in collaboration with a group of former cancer patients referred to as “patient research partners” (PRPs), as described in Study II. A few had participated previously in a research study and the majority had some education at the college or university level, suggesting they had some familiarity with the topic and with research methodology in general. The patient research partners’ level of involvement varied from attending a few meetings to co-authoring publications (Hovén et al., 2020). The commitment to communicating the cancer experience may have several motivators, both for patient research partners and for subsequent participants in the intervention studies. One reason for engaging could be negative experiences of care encounters, which might trigger a quest for more knowledge among HCPs or improved treatment options. Enrolling in research might also be a way of processing one’s own experiences, showing solidarity with those who are patients now or in the future, or “giving back” to a healthcare system for which one is profoundly grateful (Lawton et al., 2019). Throughout Studies II-V, participants and collaborators demonstrated considerable commitment to producing the most relevant research, and to communicating research results to inform healthcare practice. This is not a feature specific to fertility issues or fertility-related distress but rather a common rationale for engaging in medical or healthcare research (Lawton et al., 2019).

For Study III, we recruited by actively seeking out people with self-reported fertility distress, via newspapers, social media, notice boards, personal contacts in clinics and by snowballing. In Study IV on the other hand, a screening procedure was applied to every single person in the cohort having received a cancer diagnosis during a given time period. It could be discussed whether the different recruitment strategies would affect adherence to the program?

Study IV showed some tendency towards a higher activity in those who had higher baseline levels of fertility-related distress. The difference was not statistically significant, but it is a reasonable assumption that people with more problems would feel more motivated to take part. Unfortunately, neither high activity nor high baseline levels were consistently associated with better outcomes than the control group. An alternative way would have been to investigate percentage of change and/or proportion of participants who moved from high to moderate levels of fertility distress. This approach has been used in another RCT studying a general survivorship program for breast cancer, and showed that the intervention reduced concerns related to fertility potential (Su et al., 2019).

Adherence to web-based interventions is often difficult to assess, and even more so the relationship between adherence and intervention outcomes. In eHealth, adherence is often defined as “the more the better” without specifying a threshold. In web-based mental health interventions in particular, measures of adherence tend to be lacking (Sieverink, Kelders, & van Gemert-Pijnen, 2017). According to Sieverink et al. (Sieverink et al., 2017), determining adherence to eHealth interventions presupposes that it is *possible to measure the usage*, that *intended use has been operationalized*, and that *the definition of intended use is being justified* (using theoretical or methodological arguments). To some extent, these three criteria were all met in the Fex-Can Fertility trial. However, one limitation of the present project is that we did not specify adherence and intended use beforehand, including to participants, meaning they had no “target” for activity. Instead, we created a post-hoc adherence measure based on our idea of minimal involvement in the various components of the program to allow us to divide participants into “high users” (n=14) and “low users.” (n=50). The low level of adherence recorded using this measure surprised us, although similar or lower figures have been reported from other trials (Baumel & Yom-Tov, 2018). It should be noted that non-usage dropout may also have occurred because participants had reached their goals and need not necessarily be due to lack of interest (Eysenbach, 2005). It would have been wise to define adherence through a tailor-made measure, i.e., to define for each participant when the goal had been achieved. Another intervention for early cancer survivors used referral systems according to baseline status to enable each individual to know which parts of the intervention would be of interest (Kanera et al., 2016). This way sets an individualized threshold for adherence and a goal for the participants.

### **6.2.2 Finding the right target**

One of the aims of the process evaluation was to determine in what circumstances and for which group of patients the Fex-Can intervention would be useful. This question cannot be fully answered with the data available for this thesis.

Study V aimed to evaluate qualitatively whether the timing of the intervention was right. It seems the perception of the timing varied considerably depending on the total context including diagnosis and treatment schedule for each participant; some would have preferred to have it earlier, some later and some thought it was just right.

Men were underrepresented throughout the studies in this thesis. We could also note that the patient research partners as well as participants in the feasibility trial and the RCT had a higher-than-average level of education and that the vast majority were born in Sweden. These facts raise concerns about the generalizability of findings.

In the feasibility study (Study III), we used social media and clinics for recruitment. Recruitment was an issue, despite previous research suggesting that studies using social media to recruit get more motivated participants (Benedict, Hahn, Diefenbach, & Ford, 2019). Ure et al. (2020) have suggested that for women with breast cancer, using social media to seek out adequate, timely and personalized support is a way of regaining control after the loss of control inflicted by the cancer treatment, but seeking alleviation for emotional distress in social media may also be counterproductive (Tolby et al., 2020). In another study, social media attracted more participants than clinic enrollment and participants recruited via social media also had higher levels of reproductive concerns but suffered from more psychological ill-being (Benedict et al., 2019). For the Fex-Can RCT, we instead recruited via national registries. This approach should have enabled enrollment of a more representative sample, since participants did not have to actively seek contact. However, despite varying recruitment strategies between studies, we still ended up with rather similar demographic characteristics in all our samples. It remains unclear whether we managed to enroll those who would have benefitted the most from the intervention.

### **6.2.3 Strengthening satisfaction of basic needs**

The theory behind the intervention assumed that by strengthening competence and relatedness, the program would in the end enhance autonomous motivation to either change a health behavior or accept that behavior change would not improve the situation. There was a pedagogical challenge in explaining that “acceptance” does not equal “doing nothing” but rather actively adopting a stoical attitude when faced with irreversible infertility. The point was that if the person had gone from non-acceptance to some degree of acceptance, that in itself would be an active and autonomously motivated change. Teaching acceptance included mindfulness exercises. During the development stage, there had been discussions of whether to include mindfulness exercises or not in the intervention and there was some skepticism and disagreement both in the research group and among participant research partners. Several of the participants in both Study III and Study V also explained that they were already familiar with mindfulness techniques and had used them in other settings. There were also exercises in the program aimed at finding one’s own valued direction (a CBT concept introduced in the program, referring to long-term life goals according to one’s values, rather than short-term

accomplishments). It seems the intervention mainly affected people who had already reached some level of acceptance. In the RCT, those who already had a higher level of infertility acceptance seemed to show an even greater increase in acceptance. What does this tell us? Probably that the intervention did not reach those who had not already to some extent processed the threat to fertility. It could also suggest that people with more avoidant coping strategies were more ambivalent towards the intervention.

When discussing whether the intervention strengthened autonomy or not, or whether the theoretical framework managed to improve effects, there is the risk of ending up in a dead end with still no answer to the question of how to best promote satisfaction of basic psychological needs through a web-based intervention. According to Ryan & Deci (2017), self-efficacy may be a proxy for perceived competence, and perceived competence predicts and mediates the autonomous motivation required for effective behavior change. Healthcare interventions focusing on strengthening autonomous motivation seem to have better effects regardless of the participants' baseline levels of motivation. That is, autonomy and the degree of autonomous motivation should be possible to influence and not only due to personality orientation.

How is an autonomy-strengthening intervention achieved then? General need satisfaction through behavior change techniques has been scrutinized by Gillison et al. (2019). Some links between autonomous motivation and health outcomes have been established in behavior change interventions (Ng et al., 2012). Teixeira (2020) proposed a structured classification of 21 different intervention techniques consistent with basic need satisfaction. These include, for example, "use of non-controlling informational language," "provision of choice" and "exploration of [participants'] life aspirations and values" (autonomy), "acknowledge and respect perspectives and feelings," "show unconditional regard," "provide opportunities for ongoing support" (relatedness), "address obstacles for change," "clarify expectations" and "explore ways of dealing with pressure" (competence).

It is important to consider that although a health behavior is involved, the Fex-Can intervention did not target a behavior that would immediately affect a health outcome. Although it was posited that rumination, negative thoughts and avoidance strategies would affect the general level of psychological distress, quitting these behaviors could not in any case lead to improved fertility or better reproductive outcomes in the way that smoking cessation would immediately improve an individual's cardiovascular health and reduce the risk of lung cancer. However, many of the stated possible need-strengthening techniques were used in the Fex-Can intervention.

In sum, there are indications that the Fex-Can intervention succeeded in reaching people who already had a certain level of motivation for change. Whether it is a problem in this particular context that we did not reach those who lacked initial motivation, is a different question.

#### 6.2.4 Finding the active ingredient

Despite having a theory-based intervention that was carefully developed according to guidelines, we failed to see significant results to the extent expected. There is now widespread agreement that interventions need to be theory-based (Cuthbert et al., 2019; Fernandez, Ruiters, Markham, & Kok, 2019) and tailorable to the needs of the individual (Barnett et al., 2016; Kanera et al., 2016; Willems et al., 2017). It remains difficult to discern exactly what differentiates those interventions that are effective in randomized controlled trials and in the real-world setting, respectively. This is partly due to the heterogeneity in designs and choice of outcomes measures, but also reflects the fact that nobody really knows what the “active ingredient” is in any web-based intervention. It seems, from our results, that the active ingredient may be different for different people. In Study V, some participants really appreciated the informative texts and anatomical illustrations, whereas others were only interested in the interactive parts and in communicating with peers. We also had a number of participants from the cohort study through to the qualitative interviews who were convinced of the efficacy of responding to a survey. A few persons, even in the control group, confounded the baseline assessment and follow-up surveys with the actual intervention, and were really happy with the help they had received to start processing thoughts about fertility.

The review on self-management interventions in cancer care by Cuthbert et al. (2019) found that knowledge was among the few outcomes that consistently improved, whereas outcomes such as quality of life and self-efficacy developed heterogeneously across interventions. Other reviews have found positive effects on fatigue and quality of life, although there are few meta-analyses due to the multitude of outcome measures (Boland, Bennett, & Connolly, 2018; Kim et al., 2017; Seiler, Klaas, Tröster, & Fagundes, 2017). Boland, Bennet & Connolly (2018) stress that effects of self-management interventions for cancer patients are too diverse for the effects to be easily summarized. In addition, few of the RCTs targeting fatigue and other psychosocial issues were sustainable beyond the short-term evaluations. These results suggest there is often a discrepancy between daily life in real-world survivorship and intervention design. Another interpretation of the general lack of sustainability in self-management interventions could be that interventions fail to promote autonomous motivation, which is considered required for effective maintenance of behavior change (Gillison et al., 2019; R. M. Ryan & Deci, 2017). With regard to Fex-Can Fertility, two comments can be made. First, several participants signaled it was difficult to make space for the program in their lives and perceived the program as too demanding and time-consuming. Second, the effects were small throughout but a little more pronounced at the second post-intervention assessment, i.e., three months after the end of the program. This could be due to the Fex-Can RCT being a flexible and non-controlling intervention, where results are more likely to last over time.

Does this mean that we should target only educational goals? Or rather that we need to improve the way we work toward self-efficacy and satisfaction of basic needs?

### **6.2.5 Navigating the complexity of eHealth interventions – specific implementation challenges of the web-based format**

EHealth interventions place different demands on all stakeholders in comparison with pharmacological, medical or “IRL” psychosocial interventions. The main challenges stem from the flexibility of Internet use and the abundance of possible data via website systems, which are also two of the main advantages of delivering an intervention online.

While guided ICBT treatments and some survivorship interventions in cancer care seem to have similar success rates as face-to-face support (Mehta, Peynburg, & Hadjistavropoulos, 2019; Seiler et al., 2017), the state of evidence for self-help eHealth interventions remains unclear.

EHealth is subject to a particular difficulty in controlling the environment for both intervention and control groups when conducting RCTs. In our post-intervention measure, there was no significant difference between intervention and control groups in the tendency to seek healthcare support for emotional distress or fertility counseling. Apart from these figures, we have little information on what type of support the control group may have received during the intervention period.

The present intervention had recruitment rates comparable or better to those of similar programs (Baumel & Yom-Tov, 2018; Lillevoll et al., 2014). The efficacy on trial retention of using email and text message prompts, including participants’ reactions to these prompts, is understudied (Frampton, Shepherd, Pickett, Griffiths, & Wyatt, 2020) and we have not analyzed whether this approach enhanced the usage, engagement or retention of the Fex-Can intervention. Sporadic participant reactions from Study V said reminders were useful if kept at the top of the inbox or marked as unread, but for some it also triggered guilt and stressful feelings. It can also be noted that our study retainment, as defined by responding to the post-intervention measures, was relatively high at >80%. However, quantitative usage of the intervention was lower than anticipated, with less than half of participants reaching more than a total of 20 minutes over a 12-week period.

It can be argued that the observed usage pattern in combination with our very inclusive eligibility criteria enhances generalizability and increases the likelihood of our findings approaching the much needed “real world evidence” (Khozin, Blumenthal, & Pazdur, 2017) applicable outside of the RCT setting. According to a review of real-world engagement with self-guided web-based interventions, the monthly usage time averaged nine minutes. The review also showed therapeutic persuasiveness (including goal-setting and tailored feedback) and therapeutic alliance predicted usage, but visual design, user engagement and content did not (Baumel & Yom-Tov, 2018).

Perhaps the artificial setting of an RCT is not the best-suited design for evaluating effectiveness of this type of intervention. It becomes a catch-22 because although the overreliance on post-positivist-oriented RCTs has been criticized (Corry et al., 2019), they are still considered the preferred way to achieve evidence, and healthcare policy favors evidence-



based interventions. On the one hand, it is necessary to know an intervention is efficacious before implementing; on the other hand, this might be difficult to prove and many “good” interventions therefore never get implemented.

During the Fex-Can project period, there has been considerable development in the field of eHealth, and the pre-existing guidelines for eHealth interventions (Eysenbach, 2011) have been supplemented with an increasing number of primary publications, reviews and reporting guidelines for complex interventions in healthcare (O’Cathain et al., 2019). These guidelines highlight the need for a clear theoretical framework and for involving stakeholders, particularly end users, at all stages, which is something that we carefully attended to in the Fex-Can project. Compared to when we started, the evidence for eHealth self-help interventions is now much more extensive and synthesized to a greater extent. It is notable that even recent reviews come to the same conclusions as earlier ones; interventions still need to be theoretically improved and reported more transparently. Although there is a lagging behind in research syntheses and many promising projects are ahead of publishing, the state of the evidence underlines the complexity of eHealth interventions and the difficulty of translating feasibility, pilot and randomized controlled trials into real-world evidence. The process of developing a new intervention is lengthy and may be resource-intensive at best, research waste and an exercise in “reinventing the wheel” at worst. Therefore, initiatives to speed up the process could include a collective effort to produce more stringent reports and to synthesize data not only from RCTs, but also from feasibility and pilot studies. A too-conservative focus on statistical significance, paired with a lack of cost-efficiency analyses, may impede the implementation of treatments that would benefit some people and have few or no negative side effects. This highlights the importance of including pragmatic trials as well as qualitative evidence in the assessment of eHealth interventions.

### **6.3 GENERAL METHODOLOGICAL CONSIDERATIONS**

This thesis was written from the perspective of personal long-term involvement in all stages of intervention planning, intervention development and implementation of a full-scale RCT, attempting process evaluation as a way of understanding the subsequent outcomes. According to guidelines (G. F. Moore et al., 2015), a process evaluation should be done by a person or persons external to the research team, presumed to be neutral concerning the design and implementation of the trial. A proper process evaluation uses mixed methods, combining various data collection techniques, such as participant observation and interviews with all stakeholders, and mixing qualitative and quantitative data within the same analysis (Richards et al., 2019). While Paper II attempts to describe the process using continuous documentation, and stakeholders have been interviewed about their experiences in another publication from this research group (Hovén et al., 2020), the included studies in the thesis are not able to respond to all the requirements of a process evaluation. Notably, we lack sufficient information on the mechanisms of impact and not all the available data concerning the context have been processed. In addition, data collection including semi-structured and in-depth interviews was conducted by members of the research team who had been involved in

the development of the intervention. This may constitute a risk of bias, although from a constructivist perspective, the researcher's personal involvement is not only unproblematic but a prerequisite for doing relevant research. Nevertheless, the risk of social desirability affecting responses to research team activity (whether in collaboration with PRPs or in interviewing or surveying participants) must not be disregarded, and could be a reason for the discrepancy between reported satisfaction with the intervention and the lack of firm effects.

Despite these limitations, the design of the project had several benefits. Thanks to the access to national registries, we managed to reach a sufficiently large sample for generalization (Study I) and for conducting an RCT (Study IV). The only exclusion criteria applied at the enrollment stage for the RCT were inability to read Swedish or cognitive inability to answer the survey. This differentiates the Fex-Can study from many other psychosocial interventions, where recruitment bias may be a serious issue, and recruitment or financial difficulties often make initiatives tumble before even reaching the efficacy stage (McCann, 2019). One of the ethical concerns voiced against registry-based recruitment is the risk of unsolicited attention to sensitive and potentially distressing issues. The research team got some negative feedback concerning the registry-based recruitment, as some people who did not acknowledge having been treated for cancer were contacted because they were in the registry. A few potential participants also got upset about the nature of the questions in the survey. Luckily, these negative reactions were very few, which strengthens the conclusion that sensitive issues should not be avoided for fear of triggering negative feelings. Another study on Swedish young adult cancer survivors confirms that if approached with care and respect, people are appreciative and willing to respond (Olsson, Steineck, Enskär, Wilderäng, & Jarfelt, 2019). The intervention itself further recorded very few adverse events. Only one participant reported subjectively worse fertility distress post-intervention, adding the comment that the deterioration had nothing to do with the program but with other personal circumstances.

For reasons of transparency and replicability, we took great care to report and register all parts of the intervention in appropriate databases and to follow recognized reporting guidelines. To the greatest possible extent, validated outcome measures were chosen. The study-specific measures were partly based on existing instruments and were tested for face validity before use. Statistical analyses were chosen and performed in collaboration with external statisticians to ensure scientific correctness and reduce the risk of bias. For example, in Study I, we chose to perform logistic regression, which is a suitable method when the dependent variable is dichotomous and you wish to control for one or more independent variables. The choice of independent variables was based on the literature and on which variables were significant in univariable analyses. To avoid problems associated with collinearity (Ranganathan, Pramesh, & Aggarwal, 2017), we performed a combination of backwards stepwise and enter models. Even if the dichotomization of the dependent variable may be questioned and the response rate was moderate, our findings must be considered robust and generalizable to the population of physicians treating people of reproductive age in Sweden. In Study IV, linear mixed models were chosen for the benefit of allowing use of all available data, regardless of possible missing values. In a longitudinal design, the method

compensates for sporadic dropout, and also takes into account the dependency introduced by measuring the same individual several times (Molenberghs & Verbeke, 2001). These methodological choices enhance replicability and comparisons with other studies, increasing the possibility that the Fex-Can project may be included in forthcoming reviews. In this respect, the findings from the present thesis may contribute to increasing the evidence base about oncofertility in the Swedish context.

Another strength is the participatory design. It has been pointed out that many previous interventions for cancer survivors lack active involvement of end users and therefore may have limited relevance for the intended target group (Boland et al., 2018; G. Moore, Wilding, Gray, & Castle, 2019; Post & Flanagan, 2016). In the Fex-Can project, great care was taken to obtain regular feedback on the content, style and user-friendliness of the program.

Finally, the strong theoretical connection with relevant frameworks for each stage of the project contributes to stringency and generalizability. The theoretical orientation of the present thesis also steers away from too strong a focus on the software application and other technical aspects. It is my conviction that a psychosocial intervention affects people with its content and that the delivery mode is accessory. As devices and communication modes may change swiftly, such an approach enhances the long-term viability of results and findings. Tying intervention components to more general and universal psychological mechanisms also increases the clinical importance and the transposability of the intervention into different modes of delivery, settings or populations.

The Fex-Can intervention was very broad in terms of the diagnoses that were included and the age span of participants, although the topic for the intervention was narrowed down to fertility distress. Several participants mentioned that they would have liked more detailed information about the specific treatment that they had received. Some also brought up that they felt the program was addressing someone younger or older than themselves. Still, the number of participants in each diagnosis was so small it precluded subgroup analyses based on diagnosis and/or age brackets. These circumstances reflect the demographic situation of Sweden as a small country with only 10 million inhabitants and approximately 1700 people aged 18-39 diagnosed yearly with any of the included diseases. The trade-off between wide inclusion criteria and the risk of “washing out” possible effects was frequently discussed throughout the project. Following methodological compromise, the Fex-Can intervention was divided into two separate programs focusing on either sexuality or fertility. In the follow-up surveys and interviews, several participants stated that they would have liked information about the “other” topic, leading us to the conclusion that it would have been wise, for several reasons, to mix the programs or at least to assess all participants on all the outcome measures. Such a design would have helped in formulating hypotheses about the relationship between sexual function and fertility distress in this population. It would also have increased the statistical power of the analyses. All in all, there were too few participants in the RCT to produce statistically significant results. Prolonging data collection by a few months, i.e., by

adding a “group D,” would have given the necessary numbers for achieving a fully powered trial, but was not feasible due to lack of project resources.

Another limitation concerns the choice of outcome measures in relation to the predicted determinants for behavior change. We stipulated the intervention would be autonomy-supportive via increased fertility-related competence and satisfaction of the need for relatedness. According to the literature, satisfaction of basic needs would then be the proximal outcome on the way to more distal outcomes such as reduced fertility distress and improved quality of life. However, although the qualitative interviews explored participants’ perceptions of their autonomy, we did not include any of the existing and validated measures of basic need satisfaction (Johnston & Finney, 2010). It could be argued that fertility self-efficacy, although a non-validated measure, could be a proxy for perceived fertility-related competence, but we did not see any significant results of the intervention on that scale. On the other hand, the fertility knowledge scale measured confidence in knowledge rather than knowledge of distinct facts and may thus be interpreted as a proxy measure of perceived competence.

When examining the outcomes of Study IV, we chose to perform subgroup analyses based on baseline levels of fertility-related distress and on activity in the program (dose/adherence). These decisions were made without regard to any possible correlation between these two variables, and, more importantly, without having pre-specified a measure for adherence and a given threshold level for intended usage (Sieverink et al., 2017). One problem with performing a large number of linear mixed models is the risk of significance due to multiple comparisons rather than to there being a true difference in the population (Molenberghs & Verbeke, 2001). The way the RCAC scale is constructed, with six subscales and one total mean score, we ended up with seven primary outcome measures that were then subject to subgroup analyses, which was not ideal. For this reason, our results concerning the outcomes of the RCT are uncertain. Another possibility that would perhaps have yielded further information about the potential efficacy of the intervention despite a heterogeneous and rather small sample, would have been to control for age or parenthood status, factors known from previous studies to be possible moderators or mediators of fertility-related distress (G. Armuand, Wettergren, et al., 2017; Benedict et al., 2018; Logan et al., 2019).

A final limitation is that neither the present thesis nor any of the studies included in the research project have attempted to assess cost-effectiveness as part of the evaluation, as recommended by the MRC framework (Craig et al., 2008). For the intervention to be implemented in healthcare, the evidence for efficacy as well as a health economic assessment would have needed to be clearly established.



## 7 CONCLUSIONS

This thesis has described the rationale and co-creative process of developing, delivering and evaluating a web-based psychoeducational self-help intervention targeting fertility-related distress following cancer. From the study on physicians' practice behavior (Study I) and from developing and testing the Fex-Can Fertility intervention on various groups representative of the target population (Studies II-V), I draw the following conclusions:

- Physicians in cancer care are aware of how important fertility is to patients and most of them allow for fertility discussions at the time of diagnosis. Some organizational barriers persist for the one in three physicians who do not regularly discuss fertility.
- Fertility continues to be one of several important survivorship issues. There is a demand for interventions catering to unmet care needs at various points of time in the cancer trajectory. What is requested is accurate, up-to-date and detailed information tailored to individual needs.
- Developing a web-based intervention is a time- and resource-consuming endeavor, but also very rewarding scientifically and socially if done in a participatory manner.
- Despite careful planning and attending to most of the pitfalls previously identified in the literature on complex interventions in eHealth, the efficacy of the present intervention on fertility-related distress and related psychosocial outcomes could not be proven statistically. This was at least partly due to the trial being underpowered.
- The flexible web-based format and the possibility to communicate with others in similar situations appealed to users, although some would have appreciated more individualized medical information.
- Perceived competence regarding cancer-related fertility increased and concerns about genetic risks diminished.
- For some participants, the intervention seems to have leveraged acceptance of infertility and autonomously motivated actions when faced with different alternatives.
- Reported adverse events were mild and very few, and participants generally appreciated the program.

## **8 POINTS OF PERSPECTIVE**

### **8.1 CLINICAL IMPLICATIONS**

This thesis has described the complexity of developing and delivering a web-based intervention for reproductive concerns following cancer. The findings emphasize the need for honest communication and knowledgeable information following a cancer diagnosis. Nurses and physicians in cancer care should be aware of the importance of fertility-related distress and be prepared to discuss this with patients in the clinical encounter. They need also acknowledge the preference of people diagnosed with cancer to search for information online and the importance of relatedness with others in similar situations. To ensure the safety and wellbeing of patients and to comply with national guidelines for cancer rehabilitation, it is important that nurses are familiar with and can make recommendations for reliable sources of information and online communities that will support people with cancer and help manage late and long-term effects of treatment.

### **8.2 SUGGESTIONS FOR FURTHER RESEARCH**

The present attempt at conducting a process evaluation leaves unanswered questions about which are the mechanisms of impact of web-based interventions and what factors within the context act to sustain the status quo, i.e., hinder change.

To get closer to understanding these processes, the following questions require further investigation:

- How to better understand fertility distress and the psychological impact of sexual dysfunction as well as possible interrelatedness of these phenomena and their correlation with other psychosocial variables, i.e., the importance of fertility-related distress in comparison with other stressors in the life of a cancer survivor.
- Investigation of basic need satisfaction as a mediator for fertility-related distress and other psychosocial outcomes. More specifically, investigation into the possible mediating role of perceived competence for autonomous motivation in behavior change associated with acceptance of infertility.
- Testing outcome measures to adequately assess reproductive concerns in an intervention setting.
- How to find individuals with high risk of fertility distress and/or sexual dysfunction and who are motivated for change, and conversely, how to reach those who are not motivated.
- How to determine the correct timing for various diagnoses or situations: self-referral or recruitment via social media?
- How to find the right level of relatedness support and/or human involvement and feedback for web-based interventions.
- How to technically develop web-based interventions with a greater level of tailoring to individual needs in terms of information and communication.

- How to design decision aids for cancer care based on these individual needs, so that efficient interventions are offered at the right time to the right individual.
- How to ensure economic viability and technical updates of web-based resources and secure cost-effectiveness if the intervention were to be implemented in the clinic.





## 9 ACKNOWLEDGEMENTS IN SWEDISH

Det finns ett stort antal personer utan vilka det här arbetet aldrig hade blivit gjort.

Först och främst vill jag tacka alla studiedeltagare, forskarmedverkare och andra som bidragit till programmet med personliga berättelser. Varmt tack för att ni gett av er tid och engagerat er för att öka kunskapen kring fertilitet efter cancer bland forskare och i vården.

Därefter vill jag tacka mina handledare som haft idén till, planerat och drivit forskningsprojektet:

Docent Claudia Lampic, min huvudhandledare under inte mindre än sex och ett halvt år. Du har varit en utmärkt (och uthållig!) guide in i forskarvärlden och delat med dig av ditt kunnande på många plan. Jag uppskattar särskilt de alltid noggranna, genomtänkta och konstruktiva kommentarer jag fått på mitt vetenskapliga skrivande, och din stora förståelse för att saker inte alltid blir som man tänkt sig. Tack!

Docent Lena Wettergren, bihandledare som med en aldrig sinande energi tar sig an nya projekt. Tack för din nyfikenhet på världen och ditt genuina engagemang i våra forskningsfrågor, som alltid får mig att tänka ett varv extra.

Docent Lars E Eriksson, bihandledare som alltid funnits där som en referenspunkt när det behövs eftertanke och kloka kommentarer. Jag uppskattar särskilt vårt samarbete i delarbete 5, som vi till sist rodde i land. Stort tack!

Tack också till tre duktiga forskare jag haft turen att få arbeta med under åren och som är goda förebilder för mig och många andra:

Doktorerna:

Maria Wiklander, en klippa i utvecklingen av programmet och i flera delarbeten i avhandlingen. Inser nu när jag har satt samman alltihop hur mycket du bidrog till innehållet! Du har med en blandning av humor och allvar lärt mig det mesta jag kan om de fyra p:na: psykologi, psykoterapi, psykometri. Och så lite Pokémon, även om det var motvilligt från min sida.

Lisa Ljungman, saknad room-mate och klok storasyster fast du är yngre än jag. Din skarpa hjärna var ofta omsluten av stora hörlurar, men du lyssnade alltid ändå, satte dig snabbt in i situationen och kom med kloka råd. Nu flyger du vidare i forskarvärlden på starka vingar. Så glad att jag fick förmånen att jobba med dig en tid!

Marie Nilsson, vilket lyckokast att jag fick börja arbeta med dig på Akademiskt Primärvårdscentrum (APC)! Otroligt effektiv, kunnig och generös med din kunskap, men framförallt genuint omtänksam och har alltid nära till skratt. Jag ser fram emot vårt fortsatta samarbete!

Sedan vill jag tacka några andra forskare som gett mig knuffar i rätt riktning: med dr Gabriela Armuand som tipsade mig om Forskarskolan och det här projektet och med dr Jeanette Winterling som var en viktig person i utvecklingsfasen av projektet och för delarbetena 2 och 3. Professor Kerstin Nilsson vid Göteborgs Universitet som uppmuntrade mig att söka till forskarutbildningen och professor Lena Törnkvist vid Sektionen för Allmänmedicin och APC, som gav mig en chans att kliva fram och som haft överseende med mitt utdragna doktorerande. Tack också till med dr Lena Lundh som öppnade dörren till APC (dåvarande Cefam) och till min mentor professor Jeanette Westman. Ni har alla visat att ni tror på mig och jag är väldigt tacksam för det.

Tack till doktorandkollegorna Marie-Thérèse Crafoord, Siri Lilliesköld, Kristina Fagerkvist och Charlotta Bergström och till bitr lektor Ewa Andersson för att ni läste och kom med konstruktiva synpunkter på kappan i slutfasen av avhandlingsarbetet. Särskilt tack till Charlotta som även ställer upp på pannlampelopp i lervälling. 😊

Övriga nuvarande och tidigare doktorander som varit mina trevliga och omtänksamma rums- och korridorskamrater på Avdelningen för Reproduktiv hälsa: Andreas Widbom, Gunilla Lönnberg, Katarina Kornaros och Susanne Åhlund, och på Sektionen för omvårdnad: Maria Fjell och Tina Gustavell. Tack för spännande utbyten på seminarier och kurser, och för att ni stöttat och hjälpt mig på olika sätt. Samt inte minst att vi har haft roligt och kunnat prata om allt möjligt. Ska bli spännande att följa er alla och jag hoppas våra vägar korsas snart igen!

Tack också till alla som varit involverade på olika sätt i Fex-Can-projektet och i mitt avhandlingsarbete:

Tidigare projektmedlemmar; Johanna Strandquist som är delad förstaförfattare till delarbete 2 i avhandlingen. Britta P. Pelters och Helena Hellström som bidrog med nya perspektiv i utvecklingsskedet av programmet. Annele Claeson som var en effektiv administratör men framförallt en oförglömlig och uppskattad glädjespridare i samband med datainsamlingen. Poorna Anandavadivelan, postdoc som skrev metodartikeln om RCAC och var en uppskattad rumskamrat på W8.

Karl Wahlin, Sara Runesdotter och Matteo Bottai, för värdefull hjälp med statistiken. Särskilt tack till Gunilla Rudander för att du lärt mig grunderna i syntax och för dina trevliga och pedagogiska SPSS-veckobrev som fortsätter att dimpa ner.

Elin Brander för de stilrena illustrationerna från Fex-Can-portalen och Tove Freij för vackra fotografier, varav jag återanvänt några i avhandlingen. Nina Sandberg för proffsiga grafer till manus nr 4. Daniel Andersson för hjälp med omslagsbilden i alldeles sista minuten. Tack också till Adrian Levitsky och Kimberly Kane för goda råd kring engelska ordval.

Forskarskolan i Vårdvetenskap som möjliggjorde en strukturerad forskarutbildning med ett brett kursutbud, samt administratören för forskarutbildning på KBH, Caroline Rådestad, och Ruket Negasi på disputationskommittén, som höll flera vakande ögon på min disputationansökan. Annica Karlsson, Ulla Cronfalk-Hernlund och Maria Ankarcrona på NVS samt Emily Montgomerie, Charlotte Ovesen och Sandra Brogårde på KBH, för professionell och vänlig vägledning med det administrativa. Helena Lindgren för tydligt ledarskap i en svår pandemitid. Nataliia Tschmestruk för sällskap på kontoret.

Alla tålmodiga personer som supportat mig med olika typer av IT-problem, särskilt Jobel Teklebrhan på FixIT och Jonas Pettersson på KIB som ägnade timmar åt EndNote-eländet.

Docent Gonçalo Castelo-Branco för att du gav mig handledarens perspektiv på en forskarutbildning vid KI, för att du är en vetenskaplig förebild och för att du alltid kommer när det är dags för kusinträff. 😊

Utanför KI och forskarvärlden vill jag tacka följande personer som haft stor betydelse för mig under den här tiden:

Före detta kollegorna på Fem Husläkare, den arbetsplats jag stannat längst tid på. Saknar er och den speciella stämningen på Fem Hus! Särskilt tack till Berit Isaksson som alltid peppade mig med goda råd, vänligt stöd och några gapskratt då och då när det blev för snurrigt.

Kollegorna på ASIH Grimstagatan. Tack för att ni har tålamod med en ringrostig syrra och för att jag får gästspela i verkligheten ibland.

Alla kollegorna på APC i kunskapsteam Cancer i Primärvården och teamet kring Aktiva överlämningar. Särskilt tack till Emma Granlund Hjelm för att vi samarbetar så bra i projektet med våra olika perspektiv!

Alla härliga medarbetare, funktionärer och medlemmar på Friskis&Svettis i Sollentuna och Hagastan. Vilket vattenhål det har varit att komma till den här gemenskapen när kroppen behövde tänka och hjärnan vila!

Jag hade förstås inte heller klarat av den här utmaningen utan mina vänner. Först två doktorandkollegor som med tiden blev fantastiska vänner:

Anja Gebhardt, tack för din genuina omtanke, din takt (både musikaliskt och socialt) och för mysiga utflykter där jag även fått lära känna din familj. Hoppas det blir många fler tillfällen i framtiden!

Anna Jervaeus, du var den första jag mötte när jag klev in på KI 2014, och du har guidat mig genom den här världen. Din uppriktiga vänskap och lille Viktors charm har berikat mitt liv de senaste åren och kommer definitivt få mig att gå många fler steg på Sörmlandsleden. Kanske plockar vi en dag upp fiolerna? 😊

Alla gamla och nya vänner som inspirerat mig på olika sätt i livet och gjort mig till den jag är idag. Tack för att ni finns (kvar), har hejat på mig och stått ut med mig även när jag varit odrägligt självupptagen och bara tjatat om forskning. In order of appearance 😊:

Anna Stenqvist Castelo-Branco, Helena de Beau, Ulrika Berg Roos, Mirjam Bengtsson, Fatima-Zahra Slaoui, Daniel Andersson, Mia Blohm, Sofia Ljungberg Igbe, Nina Lamm Rejkjaer, Maryam Zeitoni Dicker, Fidan Hansen – ni är underbara personer och jag hoppas kunna umgås mycket mer med er framöver när den här förfärliga pandemin snart är över.

Sist men störst, min familj:

Manfred och Nina. Jag har under de här åren blivit världens lyckligaste faster till Jonathan och Cornelia som har de klokaste, mest varmhjärtade föräldrarna. Tack för att ni trots eget livspussel alltid har tid och plats (i hjärtat i alla fall) för mig och mina barn. Ser fram emot att kunna ställa upp som barnvakt i det nya stora huset!

Collin, du är den bästa och mest kärleksfulla pappa mina barn kunde få. Tack för att du ansträngt dig lite extra för att hjälpa mig när jag verkligen behövde det.

Mina föräldrar Marie och Wandrille. Tack för att ni finns. Tack för att jag finns. Tack för att ni alltid visat er kärlek genom att låta mig göra det jag vill och gå min egen väg, oavsett vilka tokigheter det inneburit. Hade inte vågat eller klarat detta utan all er hjälp.

Mina älskade barn Edgar, Vera och Louise. Ni är som solens strålar. Saknar er så fort jag inte ser er, men när ni är här är det ibland lite... intensivt. Nu när ni växer upp så fort hoppas jag att jag lyckas övertyga er om att en annan värld är möjlig och att era drömmar, vilka de än är, är värda att kämpa för. Ni är meningen med allt.



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