IMPROVING PATIENT-CENTERED INFORMATION PROVISION IN FERTILITY CARE

Ellen Marie Sparidaens

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COLOFON

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For reasons of consistency within this thesis, some terms have been standardized throughout the text. As a consequence, the text may differ from the articles that have been published.

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General introduction, aim and outline of this thesis

This thesis focuses on research on information provision in fertility care. We hypothesized that the more complex an intervention is, the more extensive and specific information needs of patients are. Therefore, the focus of this thesis is on two groups of complex patients: couples undergoing ICSI with surgically retrieved sperm, and breast cancer survivors with reproductive concerns. In this chapter, an introduction is given to infertility, information provision in fertility care and the role of eHealth. Furthermore, the information needs of the two patient groups of this thesis are discussed. This chapter concludes with the aim and outline of this thesis.

INFERTILITY

Infertility is defined as the inability to conceive within 12 months of regular unprotected sexual intercourse [1]. One out of every seven couples is faced with infertility [1]. In the Netherlands, infertile couples are usually referred to a fertility clinic by their general practitioner. In the clinic a fertility work-up is performed. 25% of couples are diagnosed with a male factor, 45% with a female factor, 25% with unexplained infertility, while the remainder receive no diagnosis [2]. Possible treatment options include ovulation induction, intra-uterine insemination with or without mild ovarian hyperstimulation, in vitro fertilization and intracytoplasmic sperm injection (ICSI). Out of the men diagnosed with male factor infertility, 11% has azoospermia (i.e. the complete absence of spermatozoa in the ejaculate) [3]. Azoospermia can be caused by an obstruction along the seminal tract (obstructive azoospermia) or by an intrinsic testicular impairment of sperm production (non-obstructive azoospermia). For men with azoospermia, surgical sperm retrieval can be considered [3, 4]. If spermatozoa are found, they can be used for ICSI.

INFORMATION PROVISION

According to the Institute of Medicine, health care should be safe, effective, timely, efficient, equitable and patient-centered [5]. Patient-centeredness is described as ‘providing care respectful of and responsive to individual patient preferences, needs and values, and ensuring that patient values guide al clinical decisions’ [5]. Providing patient-centered fertility care improves quality of life and can reduce anxiety and depression [6]. Important dimensions of patient-centered fertility care are adequate information provision, continuity of care and active involvement of patients in their treatment [7-9].

Information provision in fertility care needs improvement [10, 11]. There is a need for more systematically provided information to all infertile couples, which should be ensured and monitored during treatment [11-13]. After consultation in a fertility clinic, a significant number of patients is not well informed on all the aspects that are relevant for treatment decision-making [10, 12]. Furthermore, up to half of the questions that are raised by patients in forums or during consultations cannot be answered by conventional information leaflets [14]. Most important topics that infertile couples lack information on are causes of infertility, diagnostic procedures, treatment options, success rates of treatment, physical risks of treatment and financial cost of treatment [11-13, 15].

eHEALTH

Over the last two decades, the internet has been an important source of information and support for infertile couples [16-19]. Although it is known that both partners search the internet for fertility related information, usually the female partners are the main internet users [16-19]. Other factors associated with internet use are high education, being a long-term patient and higher stress levels [17, 19, 20]. The most frequently researched topics are causes of infertility, treatment options, and scientific literature about infertility [19] Even nowadays, after 20 years of fertility related internet use, still one third of internet users states that their information needs are not met, which is related to greater levels of perceived stress and depressive symptomatology [19].

Patient-centered information provision can be improved by the use of eHealth tools, i.e. online applications in healthcare [21]. Infertile couples prefer personalized information online and appreciate the opportunity to communicate with professionals and peers [20, 22]. Online fertility related interventions only provide few interactive elements, but it is known that they can promote mental health [20, 23]. It is difficult to implement these interactive elements [24]. A facilitator for subscription to an online community is a marketing strategy that contains information tailored to different subgroups of the patient populations. Facilitators for a living online community are incorporation of interactive elements and frequent news and updates [24].

PATIENT POPULATIONS OF THIS THESIS

The focus of this thesis is on two groups of complex patients, a) couples undergoing ICSI with surgically retrieved sperm, and b) breast cancer survivors with reproductive concerns. These are both relatively small groups of patients within the context of general fertility care. Because of the complexity of the treatment trajectories, the specific information needs of these patients are high. Their treatment is multidisciplinary, which requires coordination between the various healthcare providers.

Within fertility care, ICSI with surgical sperm retrieval requires an invasive procedure from both the male and the female partner. The treatment trajectory involves a number of consecutive treatment phases and is therefore filled with insecurity for the couple. In case of obstructive azoospermia, there is a 96-100% chance spermatozoa can be obtained by either aspiration from epididymis or testis, or a testicular biopsy [25]. These spermatozoa can be used for ICSI, resulting in a life birth rate around 35% per ICSI cycle [25]. In case of non-obstructive azoospermia, there is a 50% chance that sperm cells can be retrieved surgically [4]. Only then, couples are able to continue with ICSI treatment. For them the chance of achieving an ongoing pregnancy is 22,3% per ICSI cycle [26]. Therefore, only a small proportion of couples with a diagnosis of non-obstructive azoospermia will experience the live birth of their own biological child. Because of the complexity of the treatment trajectory and the low success rate, the psychological impact is high. Therefore, it is particularly important that couples receive adequate information before and during their treatment trajectory.

Breast cancer is the most frequently diagnosed cancer among young women worldwide [27]. Treatments like chemotherapy and radiation therapy can be gonadotoxic, leading to temporary or permanent infertility, or premature ovarian insufficiency later in life [28]. Due to a social trend of women postponing motherhood to a later point in their lives combined with increasing breast cancer survival rates, half of premenopausal women who are diagnosed with breast cancer desire to conceive after they have finished cancer treatment [29, 30]. Young breast cancer survivors report a greater need for information and psychosocial guidance regarding topics like fertility and sexuality compared to older survivors [31, 32]. They report questions about their fertility status and are in need of preconceptional and periconceptional counseling. Some women had the opportunity of fertility preservation before gonadotoxic treatment by means of oocyte or embryo vitrification, or ovarian tissue cryopreservation [33]. They are in need of guidance on when and how to use the preserved materials. Other women did not have the possibility of fertility preservation before gonadotoxic treatment and seek counseling on secondary options. However, women indicate that the information they receive is insufficient or conflicting and that their information needs are not met [34, 35].

The majority of breast cancer survivors report concerns about their risk of infertility [29, 36]. These concerns are associated with depressive symptoms and a lower quality of life [37, 38], which can last years beyond the end of cancer treatment [39]. Loss of fertility can be experienced as painful as the cancer diagnosis itself [40]. Counseling about the risk of infertility prior to cancer treatment is known to improve quality of life after cancer treatment [41, 42]. International guidelines focus on informing breast cancer patients on the possibility of reduced fertility prior to treatment [33, 43, 44]. However, guidelines lack recommendations on information provision during cancer survivorship, although this is the phase in which the wish to conceive can become actual. As a result, current information provision during cancer survivorship depends on the practice of the individual healthcare provider. This calls for better understanding about the specific information needs regarding fertility and early menopause of young breast cancer survivors and for implementation of recommendations regarding these information needs in oncological guidelines.

THE AIM AND OUTLINE OF THIS THESIS

The aim of this thesis is to improve information provision in fertility care. In the first part we focus on the information needs of couples undergoing ICSI with surgically retrieved sperm and in the second part on the information needs of young breast cancer survivors. The aims of the separate studies are:

Part I

1. *To identify the information needs of couples undergoing ICSI with surgically retrieved sperm, including information content and the channels providing the information as a first step to improve patient-centered fertility care. (**Chapter 2: Information needs in fertility care**)*

2. *To design, develop, and qualitatively evaluate a multi-faceted online application for infertile couples undergoing ICSI with surgically retrieved sperm during their treatment trajectory. (**Chapter 3: Application development**)*

3. *To evaluate quantitatively the implementation of myFertiCare by using the HOT-fit framework and to study the effects of using myFertiCare on couples' knowledge about infertility , experienced burden of infertility and experienced patient-centered care. (**Chapter 4: Application implementation**)*

Part II

4. *To identify the fertility and early menopause related information needs of young breast cancer survivors and to design, develop and implement online information material with input of stakeholders. (**Chapter 5: Information needs during breast cancer survivorship**)*

Outline of the thesis

The information needs of couples undergoing ICSI with surgically retrieved sperm are studied in chapter 2 by using a qualitative study design consisting of semi-structured interviews with couples. We consider both the information content and the channels providing the information.

Based on the information needs that are identified in chapter 2, in chapter 3 we designed and developed an online application (myFertiCare) in collaboration with patients and professionals. The application is evaluated qualitatively for usability by using a think-aloud method.

The implementation of myFertiCare is evaluated quantitatively in chapter 4 by using validated questionnaires focusing on the Human, Organizational and Technology domains. Furthermore, the effect of using the application on couples' knowledge about infertility, experienced burden of infertility and experienced patient-centered care is studied.

In chapter 5, a qualitative study is conducted consisting of four phases: identification of information needs through semi-structured interviews from a professional perspective (1) and a patient perspective (2). Exploration of stakeholders perspective regarding development and implementation of online information material (3) and development and implementation of the information material (4).

This thesis concludes with a general discussion in chapter 6. This includes a reflection on the results from the previous chapters and a presentation of the main conclusions. Finally, the implications for future practice, policy making and research will be discussed.

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2

Information needs in fertility care

Sparidaens EM, Braat DDM, van den Berg M, D'Hauwers KWM,
Fleischer K, Nelen WLDM.

Informational needs of couples undergoing intracytoplasmic sperm injection with surgical sperm retrieval: A qualitative study. European Journal of Obstetrics, Gynecology, and Reproductive Biology. 2020 Dec;255:177-182.

ABSTRACT

Objective: Infertile couples consider patient information a very important dimension of patient-centered care. Although testicular sperm extraction (TESE) followed by intracytoplasmic sperm injection (ICSI) has long been offered to infertile couples, little is known about couples' informational needs. The aim of this study was to identify the informational needs of couples undergoing TESE and ICSI, including information content and the channels providing the information as a first step to improve patient-centered care.

Study Design: We conducted a qualitative study consisting of semi-structured interviews with 11 couples. The topic guide was based on a literature review and interviews with an expert panel. The number of interviews was determined with data saturation. The data were analysed using a constant comparative method.

Results: The couples needed information about many topics. They considered information about the success rates of the treatment, an explanation of the treatment procedure, and other patient experiences the most important. Regarding information channels, the couples preferred face-to-face information, but they also valued a leaflet, website, or an online application, especially when it is personalized or providing interactive functionalities.

Conclusion: We obtained in-depth insight into the information needs of couples undergoing TESE and ICSI. The results of this study give fertility clinics an opportunity to develop patient information that meets the needs of their patients and thus improve patient-centered fertility care.

INTRODUCTION

One of every seven couples is faced with infertility [1]. In 38–45% of the couples a male factor contributes to the infertility [2]. About 11% of these men have azoospermia. If azoospermia has a non-obstructive cause, testicular sperm extraction (TESE) can be considered. There is a 50% chance that sperm cells can be retrieved and used for intracytoplasmic sperm injection (ICSI) [2].

In general, the infertile population considers information provision a very important dimension of patient-centered fertility care [3,4]. Couples are often well-educated and frequently search the Internet for fertility-related information [5,6,7]. Although the female partners usually are the main Internet-users with regard to fertility-related issues [5, 6] it is also known that in general andrology the Internet is reportedly the patients' most popular source of information. Almost 40% of the men have already found online information before their first doctor's appointment [8]. The Internet especially is a very important source of information for well-educated men occupying a higher social position [9]. Given the established importance of information provision, it is disconcerting that only one-third of the Dutch fertility patients are completely informed about possible treatment complications [10]. Furthermore, conventional information leaflets do not answer up to 50% of the patient questions raised in forums or consultations [11].

We hypothesized that the complex intervention of testicular sperm extraction followed by intracytoplasmic sperm injection involves an extensive need for information for both the male and female partners. Although TESE followed by ICSI has been offered to infertile couples for years, we still do not know what information should be offered and how we can best provide it. Therefore, the aim of this study was to identify the informational needs of couples undergoing TESE and ICSI, considering both the information content and the information channels available for these needs as a first step to improve patient-centered fertility care.

MATERIAL AND METHODS

Study Design

We used a qualitative study design to gain insight into the patients' informational needs. We conducted semi-structured interviews with the participating couples. To supplement these qualitative data, participants composed a priority list with their most important items of patient information. The COREQ checklist guided the study conduct and reporting. Ethical approval was proposed but was not required according to the local research ethics committee (CMO Arnhem Nijmegen). All participants signed informed consent papers.

Setting

The study was established at one of the two Dutch clinics licensed to offer TESE in 2015. Dutch insurance companies cover three TESE and ICSI cycles, whether they are provided in the Netherlands or elsewhere. The TESE and ICSI treatment trajectory starts with intake appointments in the fertility clinic with a urologist (responsible for the TESE) whose complete andrologic evaluation includes clinical history, physical examination, and blood tests. At this time, there is also an intake appointment with the gynaecologist who is responsible for the subsequent ICSI procedure. In the existing clinical practice patients are informed about different aspects of the TESE- and ICSI-treatment at various moments via various information channels. Next to the intake appointments, they receive leaflets from the different departments. Furthermore, they could visit the pages of the hospital website of both departments.

Participants

All the couples with an outpatient appointment concerning possible TESE in the fertility clinic in May 2015 were invited for participation in an interview. We invited patients by post and telephoned them one week afterwards to ask if they were willing to participate. The aim was to recruit couples, but individuals could also participate. The interviews were performed face to face and lasted 0.5 to 1 hour. All couples were interviewed by the same female researcher (ES), who was not involved in their clinical care. There were no other persons present during the interview. The interviews took place in a small conference room adjacent to the fertility clinic. The number of interviews was determined by data saturation [12]. After reaching data saturation, two additional interviews were conducted to confirm saturation. After study completion participants received the main study findings through e-mail and were invited to comment on them. This yielded no additional information.

Data Collection

The topic guide for the couple interviews was developed by means of a literature review and interviews with an expert panel. The panel consisted of a gynaecologist, a urologist, an embryologist, an expert in patient-centered innovation, and a board member of Freya, the Dutch patient association for infertility problems. Table 1 shows the domains of the topic guide and their sources. The topic guide consisted of questions about the desired content of the patient information and the preferences for various information channels. The expert panel reached consensus about its completeness before the couple interviews. The interviews were digitally recorded. At the end of each interview the couple was asked to individually prioritize the five information items that were most important to them. They also completed a short questionnaire on demographic and medical characteristics.

Table 1. Topic guide

Domain	Derived from expert interview	Derived from literature	Reference
Online information- seeking behaviour	X	X	5, 6, 8
Choosing a fertility clinic	X	X	6
Male infertility	X	X	6, 21
TESE procedure	X	X	6, 15
Risks concerning TESE	X	X	10, 22
Treatment costs	X		
Success rates	X	X	6, 15, 22
Psychological impact	X	X	3, 6, 10, 19, 21, 22
After treatment	X	X	15, 22
Patient experiences	X	X	6, 19
Timing of information	X	X	3
Leaflet	X	X	15, 21
Website	X	X	6, 19
Online application	X	X	6, 18, 19

TESE: testicular sperm extraction

Analysis of the Interviews

Recorded interviews were transcribed verbatim. We analysed the data with Atlas.ti (version 7.1.5, Berlin) to code meaningful units using a constant comparative method [13]. A second researcher (MB) independently coded the units to obtain investigator triangulation [14]. An experienced qualitative researcher (WN) supervised the discussion of the emergent codes until consensus was reached. Data saturation was reached at the ninth interview and was confirmed in two additional interviews. Items were presented as results if participants raised them spontaneously or if at least 70% of the participants agreed on a subject that the researcher raised.

Analysis of the Patients' Priority Lists

We gave all items of patient information a score based on their ranking on the priority lists. Items ranked first received five points; second, four; third, three; fourth, two; and fifth, one. We ranked the items by their sum score. Differences in scores between men and women were reported.

RESULTS

Participants

Eighteen couples consecutively visiting the participating fertility clinic in May 2015 were invited for the interview. Eleven couples (61%) were willing to participate. From one of the couples only the male partner participated and from one couple only the female. Table 2 shows the demographic and medical characteristics. The main reason for not participating was intense emotions related to the subject.

Table 2. Demographic and medical characteristics of participants

Characteristic	**Men** *n* = 10	**Women** *n* = 10
Age in years		
Mean (SD)	33.6 (6.6)	29.9 (5.7)
Informational status**		
Low	3	2
Medium	4	5
High	3	3
	Couples n =11*	
Socio-economic status***		
Low	2	
Medium	6	
High	3	
Parental status		
No children	11	
Pregnant	-	
Children	-	
Duration of infertility		
Mean months (SD)	27.6 (15.3)	
Stage of progress within course of TESE–ICSI treatment		
Before TESE	5	
After TESE and before ICSI	2	
During ICSI	4	

ICSI, intracytoplasmic sperm injection; TESE, testicular sperm extraction

*From 9 couples both partners were present for the interview. From 1 couple only the male partner was present and from 1 couple only the female partner was present.

**Low educational status included no education and lower general secondary education

Medium educational status included higher general secondary education and intermediate vocational education

High educational status included higher vocational education and a university degree

***According to the Dutch Social and Cultural Planning Office:

Low socio-economic status included the status score ≤ -1;

Medium socio-economic status included the status score between -1 and 1;

High socio-economic status included the status score >1

Interviews

In general, patients appreciated both the complete information that the friendly, patient, and competent personnel provided, and the opportunity to ask questions (Table 3, Q1).

Table 3: Interview quotes

Quote	Interview	Gender	Quote
1	2	Male	*We received a lot of information from the gynaecologist and the urologist. We were able to ask all our questions. We also had questions about future subjects. They might not yet have been relevant, but they were all answered.*
2	7	Male	*In informing patients, you should make it clear why patients should come to your clinic. What distinguishes your clinic from other clinics in the Netherlands and abroad?*
3	2	Male	*A timeline would be a good thing. Actually, I thought this trajectory would take years, but today I found out that that's not the case.*
4	10	Male	*You can add a bar graph, but also something else.... For a larger group, there should be more narrative. The graphs are better suited for informational purposes when you don't have to deal with emotions.*
5	5	Male Female	*It is best to do that [providing information] verbally, face-to-face.* *Yes, so that if you have questions, you can ask them immediately.*
6	9	Female	*I think a paper version of the leaflet is easier for people to read than the Internet version. They have to take action themselves to find it on the Internet.*
7	11	Female	*I should keep it [the information given] the same, otherwise I would wonder if I have missed something.*
8	1	Female	*I like to have subheadings to click on. Otherwise you have to search through a lot of information.... Some people specifically look for something and they don't want to read everything.*
9	4	Female	*Yes, an online application!*
10	4	Male	*In these modern times, you can make it all personal.... You can do a lot with that.*
11	10	Male	*A platform where patients can tell their story. That's much more appealing than an explanation from a physician.... You can recognize yourself in a story.*

Content of the Patient Information

The participants needed information on several topics. Most said they wanted to choose their fertility clinic very consciously on the basis of patient reviews and the feeling that the chosen clinic had the most expertise in TESE. They felt that patient reviews should provide this information (Table 3, Q2). The couples also wanted information about how TESE can be put into practice, recovery after the TESE procedure, and the trajectory after a successful or unsuccessful procedure.

Furthermore, they appreciated a timeline for what to expect from the moment of intake (Table 3, Q3). Further, the participants wanted information about the cryopreservation procedures for TESE semen: how it works, how long it can be stored, the chance it will be successfully thawed, and the policy about contagious diseases. All the couples wanted a link to the Freya website. They valued the information about the psychological impact of the treatment and the availability of professional support. The participants wanted to learn about patient experiences, in written text. All of them wanted to read success stories, but there was some debate about the provision of unsuccessful stories. They needed illustrations that schematically explain male anatomy and TESE. They wanted to know the success rates of TESE and subsequent ICSI, preferably expressed per treatment phase, categorized by the women's age, and compared with the rates from other clinics. Most preferred data in a bar graph. They criticized pie charts as unclear. Although graphs were important, they wanted explanations of the data as well (Table 3, Q4).

Information Channels

The couples made it clear that no information channel can replace face-to-face information, but they also valued several channels (Table 3, Q5).

TESE leaflet

The participants preferred a paper version of a leaflet, ideally provided before intake (Table 3, Q6).

Website

All couples already had fertility-related information from the Internet before intake. Mainly the women acquired this. They used search engines for causes and prevalence of azoospermia, treatment options, and patient experiences. They compared fertility clinics, both in the Netherlands and abroad, including the waiting times. The information was obtained mainly from hospital websites, the patient associations for fertility problems, and various forums. The participants felt that a hospital website should contain the same information as the hospital leaflets to prevent missing or contradictory information (Table 3, Q7). The participants preferred a website to be user friendly. For instance, they wanted clear headings on which they could click to get more extensive information (Table 3, Q8). A search function based on key words was also valued, just as video footage, in which a physician explains male infertility and TESE.

Online application

The idea of an online application was received enthusiastically. Various functionalities were suggested. The overall opinion was that the more functionalities an application provides, the better, so that people are motivated to use it. The participants specifically valued a personalized application, for example, one with options to see appointments, test results, or information about physicians, such as their specialization, work experience, and their photo (Table 3, Q9&10). Moreover, patients favoured being able to ask their physicians medical questions, provided that they received quick responses. They also suggested a forum for discussing experiences with peers, a checklist for the male lifestyle advice prior to TESE, and all the general information about TESE (Table 3, Q11). The interviewees also highlighted the safeguarding of confidential information, which they stated should be at the core of application development.

Patients' Priority Lists

The items of patient information that received the highest sum scores were success rates of the treatment (23%), an explanation of the treatment procedure (14%), and other patient experiences (14%; Table 4). Women were more pronounced in this ranking than men. Women allocated 57% of their points to these top three, men 44%. Men also valued information about the actual TESE. They gave the risks of TESE 11% of their points, almost three times as many as the women. Men gave 10% of their points to information about recovery after TESE; women did not mention it.

Table 4 Priority lists of information for patients undergoing TESE and ICSI

		Points allocated by		
Ranking	**Item**	**Women (%)** *n* **= 10**	**Men (%)** *n* **= 10**	**Sum score (%) N = 20**
1	Success rates	31 (27.2)	16 (17.0)	47 (22.6)
2	What is TESE?	14 (12.3)	16 (17.0)	30 (14.4)
3	Patient experiences	20 (17.5)	9 (9.6)	29 (13.9)
4	Treatment trajectory of TESE	9 (7.9)	9 (9.6)	18 (8.7)
5	Risks of TESE	5 (4.4)	10 (10.6)	15 (7.2)
6	Contact details	7 (6.1)	6 (6.4)	13 (6.3)
7	Continuing path after TESE	9 (7.9)	4 (4.3)	13 (6.3)
8	Recovery after TESE	-	9 (9.6)	9 (4.3)
9	Psychological and emotional support	4 (3.5)	4 (4.3)	8 (3.8)
10	Information about IVF and ICSI	5 (4.4)	-	5 (2.4)
11	Male endocrinology	5 (4.4)	-	5 (2.4)
12	Illustrations	-	4 (4.3)	4 (1.9)
13	Costs of treatment	1 (0.9)	2 (2.1)	3 (1.4)
14	Link for downloading application	-	3 (3.2)	3 (1.4)
15	Links to other websites and association for fertility problems	2 (1.8)	-	2 (1.0)
16	Waiting list	-	2 (2.1)	2 (1.0)
17	General introduction in leaflet	2 (1.8)	-	2 (1.0)
	Total score allocated	*114 (100)**	*94 (100)**	*208 (100)*

ICSI, intracytoplasmic sperm injection; TESE, testicular sperm extraction
Items received a score on the basis of their priority list ranking. Items ranked first received five points; second, four; third, three; fourth, two; and fifth, one. The items were ranked by their sum scores. Example: success rates received 31 points from women (31/114 = 27.2%) and 16 points from men (16/94 = 17.0%). Sum score 31+16=47 (47/208 = 22.6%).
* The total score allocated does not match the possible total score of 150 because some patients listed fewer than 5 items on their priority lists

DISCUSSION

Our study is the first to specifically explore the informational needs of couples undergoing TESE and ICSI. We have addressed both the content of the information and different information channels for information provision. Couples particularly valued information about the success rates of the treatment, an explanation of the treatment procedure, and other patients' experiences. Men also mentioned information on risks of TESE and recovery after the procedure to be important. This might suggest that women focus more on the treatment result and other patients' experiences, while men emphasize the actual TESE procedure and its physical consequences. Couples preferred face-to-face information, but also valued leaflets and websites or online applications, especially personalized ones and ones providing interactive functionalities. Apart from the need for complete information, our participants valued being able to ask questions and the friendly, competent and patient personnel. These factors are all covered by the 10 dimensions of patient-centered infertility care [3].

One previous study reports the perspective of men undergoing TESE about the quality of care [15]. Our participants agreed to the importance of some information items in that study, such as success rates and post-surgical recovery. We explored these items in more detail and also included a variety of other items. Furthermore, we did not focus exclusively on content; we also considered possible information channels. Our participants' preference for face-to-face information, complemented with leaflets and online information, correlates with previous research regarding men with fertility problems [7,8].

In our study, success rates were at the top of participants' priority lists for information items. They preferred to see the chances per treatment in a bar graph. Although this seems easy, one should be aware that different formats of presentation generate different perceptions among patients varying in numeracy [16]. Furthermore, independently of numeracy, patients given a risk in a positive frame, such as "90% do not get a rash", perceive this as less risky than those given a negative frame, such as "10% do get a rash" [16]. However, even though patients say they appreciate information about success rates, a Cochrane review reports that this neither changes consumer behaviour, nor improves care, nor has any impact on the behaviour of healthcare professionals or organizations [17].

In 2003, only 54% of the fertility patients in western countries used the Internet to search for fertility-related information [6]. Now, all patients use it for this purpose. We confirmed that women are the main Internet users, that couples specifically appreciate personalized information online, and that they value the interaction with professionals and peers [5,6,18]. It is known that interactive elements in online fertility-related interventions promote mental health [19], although implementation is a challenge [20]. We feel that professionals should be aware of their patients' omnipresent use of the Internet, and they should consider asking them about their online information-seeking behaviour in order to become familiar with their informational needs.

The qualitative method of this study was particularly suited to provide in-depth insight into the informational needs of couples undergoing TESE and ICSI. Findings from the qualitative interviews were triangulated by results from the literature review and expert panel interviews. Another methodological strength is that we included patients throughout all stages of TESE and ICSI, while none of our participants had children or was pregnant. This means that our results were not influenced by the TESE result nor the reproductive outcome. We made considerable effort to achieve a high response rate via flexibility in scheduling interviews directly before or after a regular outpatient appointment. In the analysis, investigator triangulation [14] and data saturation [12] contributed to the credibility and validity of our data. All interviews took place with the same researcher to improve the dependability.

Regarding limitations, only couples at one fertility clinic were included in this study. However, this center has the largest number of TESE procedures in the Netherlands per year. Moreover, since patients across Europe have similar views about patient-centered care [4], our results could also be relevant for other European countries. Further research should be performed to study generalizability of the study results. Second, we explored patients' informational needs through qualitative interviews until data saturation and made a start to provide some quantitative data using priority lists. However, the study population was relatively small for this type of research, so that statistic measurements were not possible. We decided not to include more participants specifically for this part of the research, since we considered the priority lists particularly valuable when they were obtained after an interview as participants were activated thinking of the subject.

CONCLUSION

The current study provides in-depth insight into the informational needs of couples undergoing TESE and ICSI. Information about the success rates of the treatment, an explanation of the treatment procedure, and other patients' experiences were valued as most important, just as face-to-face information provision. Since information provision is considered the most important dimension of patient-centered fertility care, study results can help to improve patient-centeredness of this care. Future research should focus on gathering more quantitative data about patients' informational needs and, in particular, about differences between men and women.

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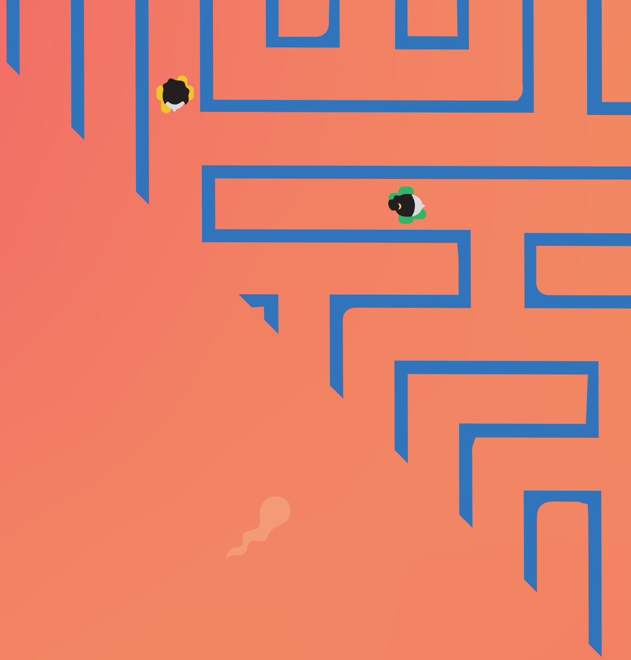


3

Application development

Sparidaens EM, Hermens RPM, Braat DDM, Nelen WLDM, Fleischer K.

Web-Based Guidance Through Assisted Reproductive Technology (myFertiCare): Patient-Centered App Development and Qualitative Evaluation. Journal of Medical Internet Research. 2021 Aug 3;23(8):e25389.

ABSTRACT

Background: Providing patient-centered fertility care is known to improve quality of life and can reduce anxiety and depression. In a previous study, we established the need for a web-based app providing personalized information and interactive functionalities among couples undergoing intracytoplasmic sperm injection with surgically retrieved sperm.

Objective: This study aimed to design, develop, and qualitatively evaluate a multifaceted web-based app for infertile couples undergoing intracytoplasmic sperm injection with surgically retrieved sperm during their treatment trajectory.

Methods: The web-based app was developed in three phases: (1) we established a patient-centered functional design, (2) developed the app in collaboration with medical and technical professionals, and (3) qualitatively evaluated the app among couples using a think-aloud method.

Results: The basis of the app is the couple's visualized treatment trajectory. The app provides personalized and interactive functionalities; for example, customized information and communication options. During qualitative evaluation, myFertiCare was highly appreciated and received a median score of 8 out of 10. The main improvements made upon conclusion of the think-aloud sessions were related to faster login and easier app navigation.

Conclusion: A patient-centered web-based app aimed at guiding couples through their fertility treatment course was systematically designed, developed, and positively evaluated by patients and medical and technical professionals.

INTRODUCTION

According to the Institute of Medicine, health care should be safe, effective, timely, efficient, equitable, and patient-centered [1]. Patient-centeredness is described as "providing care respectful of and responsive to individual patient preferences, needs and values, and ensuring that patient values guide all clinical decisions" [1]. Providing patient-centered fertility care can improve quality of life and can reduce anxiety and depression [2]. It has been reported that patient-centeredness in fertility care needs improvement [3,4]. Crucial aspects of patient-centeredness in fertility care are provision of adequate information, continuity of care, and active involvement of patients in their treatment course [5-8]. The internet is known to be an important source of information and support for infertile couples [9-11]. A possible instrument for improving patient-centeredness is the use of eHealth tools; that is, web-based apps in health care [12]. Previous eHealth initiatives in fertility care aimed mainly at information provision, support, and mental health promotion [13]. These initiatives only contained few interactive web-based components. Aarts et al [13] concluded that these initiatives could be improved by including more interactive and dynamic elements as their key components. Infertile couples are known to specifically prefer personalized information and appreciate being able to communicate with both their treatment team and fellow patients [3,10]. eHealth tools are a promising strategy to empower patients in managing their own treatment trajectory.

In a previous study [14], we established the need for a web-based app providing personalized information and interactive functionalities among couples undergoing intracytoplasmic sperm injection (ICSI) with surgically retrieved sperm. We hypothesized that a web-based app is specifically suitable for this group of patients because of the psychological and physical burden of the multidisciplinary treatment on both partners. Therefore, the aim of this study was to design, develop, and qualitatively evaluate a multifaceted web-based app for use by couples undergoing ICSI with surgically retrieved sperm during their treatment trajectory.

METHODS

Systematic Approach

MyFertiCare was developed in three phases: (1) we established a patient-centered, functional design for the app; (2) developed myFertiCare in collaboration with medical and technical professionals; and (3) had myFertiCare qualitatively evaluated for usability, with a think-aloud method.

Phase 1: Establishment of a Patient-Centered, Functional Design

The functional design of myFertiCare is based on (1) literature review; (2) interviews with an expert panel comprising a gynecologist, a urologist, an embryologist, an expert in patient-centered innovation, and a board member of Freya, the Dutch association for infertility problems; and (3) interviews with a patient panel. This was part of our previous study [14] on the informational needs of couples undergoing ICSI with surgical sperm retrieval. The patient panel consisted of 11 couples, a number that was determined through data saturation. We conducted semistructured interviews with each couple individually. The data were analyzed using a constant comparative method. The functional design that followed from this process was verified by the clinic's fertility treatment team and supplemented with their suggestions. Both the expert and the patient panels were enthusiastic about the idea of a web-based app to guide couples through their treatment trajectory. The overall opinion was that the more functionalities an app provides, the better the app, so that people are motivated to use it. The participants specifically valued personalized and interactive functionalities. Various functionalities were suggested, such as being able to view appointments, test results, and information about lifestyle advice; information about the clinic's fertility treatment team; and communication with physicians and peers. The interviewees also highlighted the safeguarding of confidential information, which they stated should be at the core of app development [14].

Phase 2: Development of myFertiCare

Based on the preferences of the expert and the patient panels, myFertiCare was developed in close collaboration with medical professionals from the department of Reproductive Medicine, Radboud University Medical Center (RUMC), and technical experts from a Dutch company specializing in eHealth. Together, they formed the project team. Development was an iterative process. The desired functionalities of myFertiCare were categorized by the medical professionals as must-have functionalities that had to be available before the app could be made available on the internet, or as nice-to-have functionalities that could be developed later. Subsequently, the must-have functionalities were developed by the technical experts and tested in a test environment by both the technical experts and the medical professionals. Technical adjustments were made as necessary, and the testing cycle was started over again. Once all the must-have functionalities were developed and tested by the technical and medical experts, myFertiCare was made available through the hospital website, the App Store, and Google Play Store to couples undergoing ICSI with surgical sperm retrieval. myFertiCare was also incorporated in the existing hospital information systems. After the app was live, all the nice-to-have functionalities were developed through the same development cycle. After each functionality was iteratively developed and tested, it was immediately made available to all myFertiCare users. The duration of the whole development trajectory was approximately 1.5 years.

Phase 3: Qualitative Evaluation of myFertiCare for Usability Through the Think-Aloud Method

After all the must-have and nice-to-have functionalities were implemented, we began the qualitative evaluation of myFertiCare. In total, 21 couples, who consecutively visited the fertility clinic, were invited by their physicians to participate in the think-aloud sessions. Six couples agreed to participate, which accounted for 9 participants (4 men and 5 women) (Tables 1 and 2). Reasons for nonparticipation were being too busy, already having too much going on, or simply not wanting to participate. Think-aloud is a research method in which participants verbalize their thought processes while interacting with a tool [15]. It provides a valid source of data about participants' thought processes and can be used effectively in qualitative studies [15]. Our aim was to identify usability flaws and to provide suggestions for design modification.

The participants were individually provided with 16 tasks to perform using myFertiCare while thinking out loud (Figure 1). Of these tasks, 11 were the same for every participant and 5 focused on the specific phase of treatment that an individual was in. By completing these tasks, the participants explored all the functionalities of myFertiCare. The researcher observed the participants and asked questions for clarification where needed. The researcher took notes, also focusing on nonverbal communication of participants. In addition, the sessions were audio-taped. After completing each task, the participants answered 3 task-linked questions ("I find this task easy," "I find this information useful," and "I find this information is in a logical spot") with a 5-point Likert scale to rate responses. They could also add free comments.

Immediately after each think-aloud session, the participants completed a self-developed questionnaire on their experiences using myFertiCare (Figure 2). The questions were about participants' attitudes toward usability, privacy, understandability of information, and the usefulness of various functionalities of myFertiCare. The questionnaire consisted of 20 questions: 17 with responses rated on a 5-point Likert scale, 2 yes/no questions, and 1 open question. Again, the participants could also write free comments.

The think-aloud sessions were conducted until saturation was reached. The duration of a session was approximately 15 to 20 minutes. The audio-taped sessions were transcribed verbatim. Data were analyzed anonymously. An open coding method was applied. We coded quotes that identified usability flaws or provided suggestions for modification of the app's design. A second researcher verified the coding process. Differences were discussed until consensus was reached. Ethical approval was proposed but was not required according to the local research ethics committee (CMO Arnhem Nijmegen, file# 2016-2485). All participants provided written informed consent.

Table 1. Demographic characteristics of the study participants (N=9).

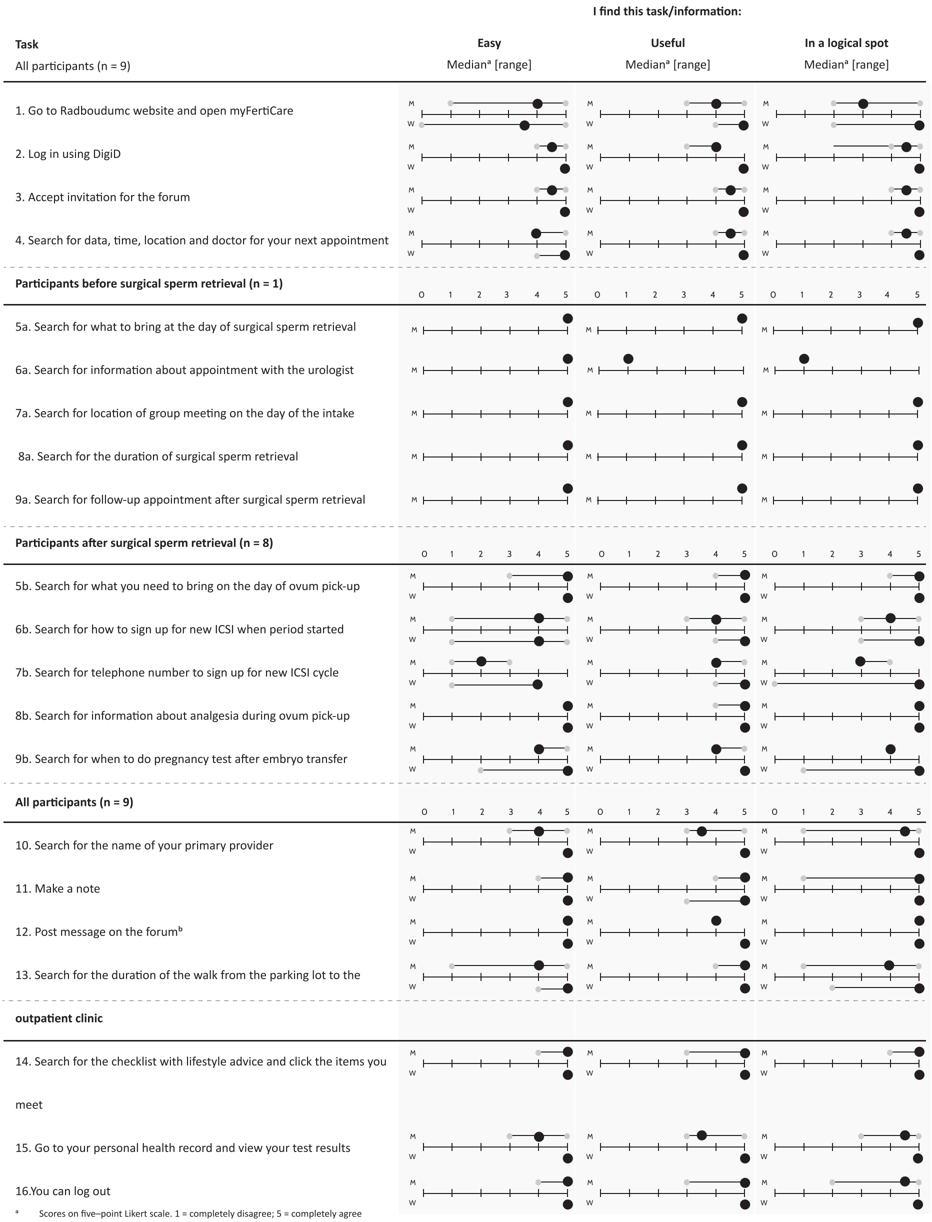
Characteristic	Men (n=4)	Women (n=5)
Age (years), median (range)	33 (27-47)	30 (28-36)
Daily internet usage in a private setting (minutes), median (range)	60 (45-60)	90 (60-180)
Treatment-related use of the internet, n	3	5
Use of myFertiCare prior to the think-aloud session, n	1	2
Educational status[a], n		
Low	0	0
Medium	1	2
High	3	3
Ethnic background, n		
Caucasian	3	4
Non-Caucasian[b]	1	1
Number who already have children, n		
Yes	0	0
No	4	5

[a] Low educational status includes no education and lower general secondary education. Medium educational status includes higher general secondary education and intermediate vocational education. High educational status includes higher vocational education and a university degree.
[b] One man from Indonesia and 1 woman from Suriname.

Table 2. Demographic characteristics of the couples who participated in the study (N=6).

Characteristic	Couples
Socioeconomic status[c], n	
Low	3
Medium	3
High	0
Stage of treatment, n	
Before surgical sperm retrieval	1
After surgical sperm retrieval and before ICSI[d]	2
During first ICSI cycle	2
After at least one full ICSI cycle	1
Duration of infertility (months), median (range)	28 (16-47)

[c] According to the Dutch Social and Cultural Planning Office: Low socioeconomic status included a status score of ≤–1; medium socioeconomic status included a status score between –1 and +1; high socio-economic status included a status score of >1
[d] ICSI: intracytoplasmic sperm injection.



[a] Scores on five–point Likert scale. 1 = completely disagree; 5 = completely agree

[b] This functionality appeared to be unavailable during the first think-aloud sessions due to a technical error. The error was solved after four sessions, so for this task men, n = 1; women, n = 4

ICSI intracytoplasmic sperm injection

Figure 1. Results from think-aloud sessions

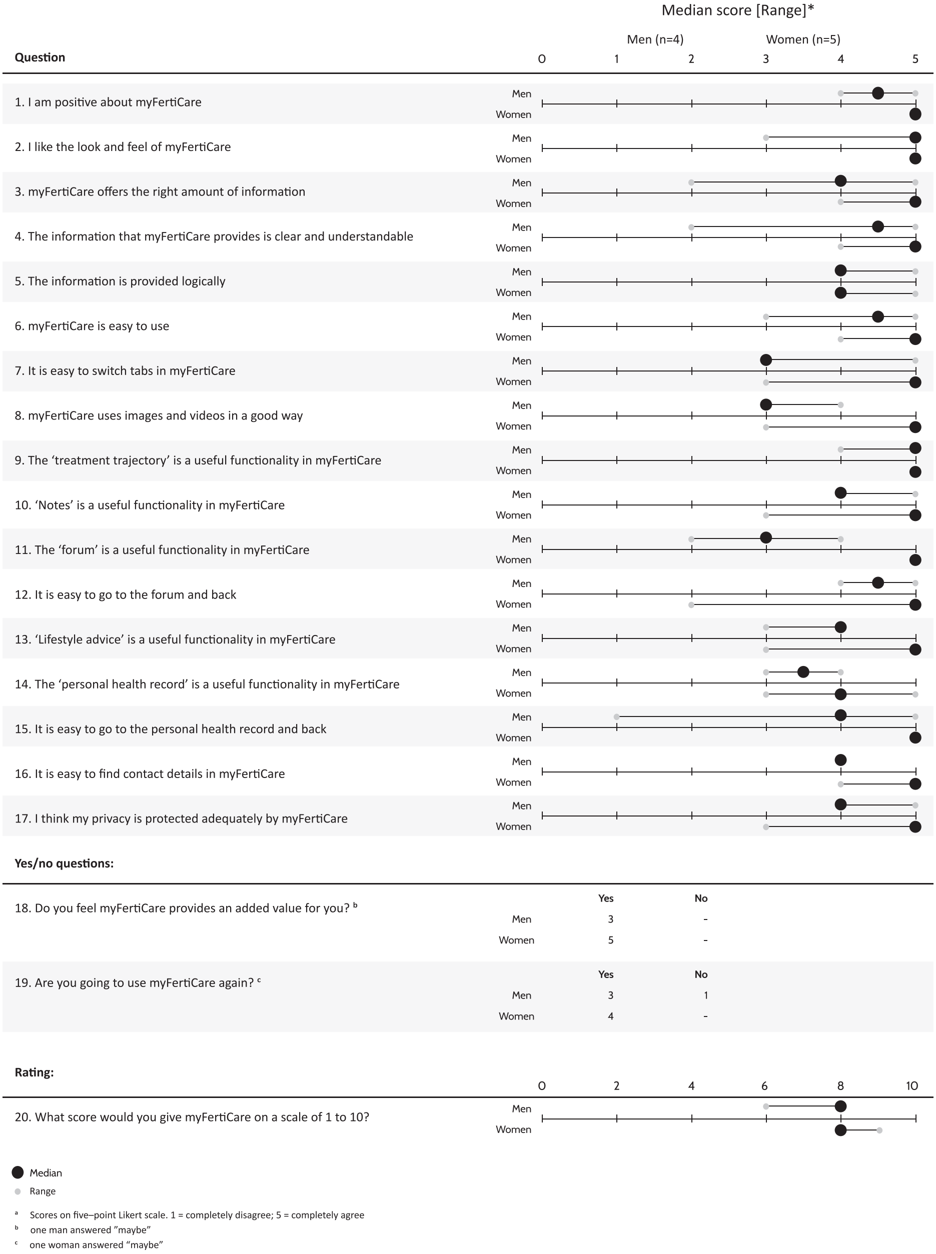


Figure 2. Results from questionnaire on experience using myFertiCare

RESULTS

Phases 1 and 2: Design and Development of myFertiCare

Based on the results of phase 1 [14], myFertiCare was developed as a web-based app available on the RUMC website, Google Play Store, and Apple App Store for couples undergoing ICSI with surgical sperm retrieval at the RUMC. Patients log in using their digital identity (DigiD), which is provided by the government of the Netherlands to assure safe access to all governmental institutions. This guarantees the safety of couples' medical data. The apps of both partners are synchronized, so that individuals can also see their spouse's information. myFertiCare is free for use and is offered in addition to usual care. A screenshot of the app is provided in Figure 3.

vrijdag 7 juli 2017
09:00 - 09:30

Verloskunde & Gynaecologie
Route 782
Bekijk de routebeschrijving

Mw. Dr. Bea Lintsen
Bekijk uw zorgverlener(s)

Vandaag staat de eicelpunctie gepland. Tijdens de punctie worden de rijpe eicellen uit uw lichaam gehaald. Hiervoor krijgt u pijnstilling via een infuus in uw arm. Uw partner mag tijdens de punctie bij u blijven. Het ontdooien van de ingevroren zaadcellen gebeurt ook op de dag van de punctie. De gehele afspraak neemt ongeveer twee uur in beslag, de daadwerkelijke eicelpunctie duurt meestal slechts 10-15 minuten.

Tip: als u dit wilt, kunt u op de polikliniek voorafgaand aan de eicelpunctie een rustgevende tablet krijgen.

☐ Actueel medicatieoverzicht. Deze kunt u opvragen bij uw apotheek.
☐ Identiteitsbewijs
☐ Verzekeringsbewijs

Figure 3. myFertiCare screenshot

myFertiCare contains personalized and interactive functionalities that are divided over 5 tabs:

1. Treatment trajectory: this is the basis of the application. The treatment trajectory is visualized as a subway map in which every stop stands for one of the appointments a couple must have in order to move forward. Couples can see their past appointments and future scheduled appointments with the corresponding data, time, physician, and location, but they can also see future appointments that are not scheduled yet. Thus, couples are better prepared for the upcoming trajectory and know what to expect. Each stop on the subway map provides information about the specific phase of the treatment trajectory and provides advice on how to prepare for the appointment, and, if applicable, informs them of anything they should bring with them for the appointment. Furthermore, users receive support messages before or after certain appointments to comfort them

or provide some advice. These support messages are sent via the app or via text message.

2. Notes: users can write notes that are synchronized with their spouse's notes. For example, couples can compose a topic list with questions they want to ask during their upcoming physician's appointment.

3. Care providers: an overview of the whole treatment team is provided through photographs, with an individual's primary care provider on top. Users can ask medical questions to the treatment team, and they are answered within 24 hours.

4. Forum: patients can communicate with peers on the forum. The forum is supervised by a clinician.

5. Lifestyle advice: this is provided as separate checklists for men and women. The aim is to improve treatment outcomes; that is, to improve the chance of retrieving semen through percutaneous epididymal sperm extraction or testicular sperm extraction and concomitantly the probability of conception. Users can click the boxes of the checklist, which are also synchronized with those of their partner.

In addition to the five tabs, myFertiCare provides a main menu with general information (eg, contact details and app settings) and a link to the user's personal health record. In the personal health record, users can see their own test results and read the correspondence between their primary care provider and their family physician.

Finally, for couples who are not yet being treated at RUMC and thus do not have login details, a preview version of myFertiCare is available. In this version, they can view the general treatment trajectory and consult the checklist with lifestyle advice. Thus, they can prepare themselves for their intake appointment.

Phase 3: Qualitative Evaluation of myFertiCare for Usability With the Think-Aloud Method

The think-aloud sessions yielded both positive and negative feedback. Given the aim of the study, we focused on opportunities to improve the app. As described earlier, every participant completed 16 tasks (11 generic and 5 personalized). This resulted in 21 different tasks. After each task, the participants answered 3 task-linked questions ("I find this task easy," "I find this information useful," "I find this information is in a logical spot") on a 5-point Likert scale (1="totally disagree," 5="totally agree"). Figure 1 shows a summary of the results. In general, participants considered the tasks (ie, the functionalities that myFertiCare provides) easy and useful. They also considered that the information was provided logically.

Although the scores for all tasks were high, the participants named some discomforts and suggestions for improving the app design. They commented that logging in with their DigiD was too cumbersome, since it consists of a username, password, and verification via text message. It was also noted that moving along the visualized treatment trajectory was difficult. The participants attempted to slide through the treatment trajectory, which was not possible. Instead, they had to click on stops to move to this specific stop. Furthermore, they noticed that the app did not open with the most recent appointment, which was the mode they preferred. When using the forum, participants regretted that they could not delete an erroneous message they had posted. Finally, participants expressed the need for a home button to lead them to the home screen of the application.

At the end of each think-aloud session, the participants completed a questionnaire about their experience using myFertiCare. Figure 2 shows a summary of the results. The participants allocated high scores to all surveyed items that related to usability, understandability of information, the usefulness of various functionalities, and privacy. The men were consistently slightly more critical than the women. The space for writing free comments revealed no additional information. All participants felt that myFertiCare provides an added value to them. All but 1 participant intended to use myFertiCare in the future. In conclusion, myFertiCare was rated 8 out of 10 (Figure 2).

Guided by the think-aloud sessions, we made various improvements in app design. We made it possible for myFertiCare users to create a 4-digit entry code after the first login with DigiD, so that fast but equally safe access was enabled for future use. Furthermore, opening myFertiCare with the most recent appointment was made possible, while proceeding through the treatment trajectory. We added an option to remove a message from the forum after it has been posted as well. A home button was incorporated, which leads users to the app's home screen.

DISCUSSION

Principal Findings

We designed, developed, and qualitatively evaluated an eHealth app for fertility care in accordance with a methodological framework, based on couples' information needs and input provided by health care providers. The basis of the app is the visualized treatment trajectory. The app provides both personalized and interactive functionalities, including customized information and communication options. On thorough qualitative evaluation, myFertiCare received high usability ratings. The participants felt that myFertiCare provides an added value during their treatment. The app was rated with a median score of 8 out of 10. The most important improvements after the think-aloud sessions were related to faster login and easier navigation through the app.

A large part of research in fertility care is aimed at the female partner. We chose to include both partners when developing the app, since it is recognized that men should have a well-defined role as an equal partner during fertility treatment, particularly in cases of male infertility [16]. A previous study by Sylvest et al [11] reported that men registered a marked time lag between diagnosis and treatment initiation. They felt “they were in a maze without a map” and expressed the need for detailed information about the treatment plan, including a timetable, so that they could control and manage their lives [11]. With a visualized treatment trajectory as the basis of myFertiCare, we aimed to meet this need and guide couples through their entire treatment trajectory. In our opinion, patient satisfaction with information provided by the clinic is an important indicator of the quality of fertility care, although in fertility care, the focus is often on live birth rates. Alper et al [17] further endorsed this idea.

There is literature available on eHealth initiatives in fertility care [13], primarily on online support groups. In general, there is a lack of initiatives that provide interactive and dynamic elements, and there is a lack of methodological standards for these complex interventions [13]. There has been 1 web-based initiative that provides both information and peer support, which showed high patient appreciation [18]. Furthermore, a web-based community has been reported in which couples could communicate and share information with professionals and peers [19].

Compared to previous initiatives, a strength of myFertiCare is that it provides a large variety of personalized and interactive functionalities centered around the visualized treatment trajectory of the couple. Another methodological strength of our study is the systematic approach in 3 phases: first, a functional design for the app was developed through a qualitative assessment of the informational needs of patients; second, myFertiCare was actually developed; and third, myFertiCare was qualitatively evaluated for usability through the think-aloud method. All 3 phases were carried out in collaboration with patients and medical and technical professionals, which is important for successful eHealth development and implementation [20]. Our qualitative evaluation of myFertiCare for usability is crucial since usability evaluations are critical to the success of adopting an interactive eHealth app [20,21]. The think-aloud method is preferred for uncovering usability problems, and it provides understanding of how users interact with myFertiCare [22]. Furthermore, the think-aloud method is especially suitable since we used both a concurrent method (ie, while performing the task) and a retrospective method (ie, immediately after performing the task) to report participants’ thinking, a method that has been suggested for producing optimal data quality [23].

Limitations

Our study also has some limitations. It could be argued that the study population for the think-aloud sessions was relatively small. However, studies have shown that for a think-aloud test, 5 participants are enough for success in identifying usability problems in a user interface [24]. Since we included 9 participants and achieved data saturation, we are confident that we have identified all the possible usability problems. Furthermore, it is known to be a challenge for a researcher to remain consistent when it is necessary to intervene in a think-aloud session; for example, when a participant is unable to complete a task, clarification on a participant's comment is required, or a participant sidesteps the functionality of interest [25]. In these situations, it is important to explain to a participant that it is the aim of the study to identify problems and to invite them to approach the problem otherwise. It has been reported that researchers often unintentionally intervene in theoretically inconsistent ways [25]. We made a conscious effort to achieve a reliable data set by being aware of these limitations and through triangulation of research methods (namely the think-aloud, task-linked questions, and researcher's observations) and the recording, transcribing, and coding of the interviews.

Practical Implications

This study provides a framework for patient-centered design, development, and evaluation of an eHealth app. Our systematic approach, in which patients and professionals participated in every phase of the process, is particularly suitable in the current era where patient-centeredness is highly valued. Furthermore, we obtained insight into the various functionalities that patients appreciate in a web-based app. The framework we developed for myFertiCare supports professionals in fertility care for guiding patients through their treatment trajectory and delivering patient-centered care. In the near future, myFertiCare will also be evaluated quantitatively. Expansion of eHealth tools to cover the whole fertility care journey and expansion to other medical disciplines is considered of high value. Development of eHealth tools from a patient's viewpoint is an opportunity to empower patients in managing their own treatment trajectories in the current era of patient-centered care.

Conclusions

We designed, developed, and qualitatively evaluated a multifaceted web-based app, myFertiCare, through a systematic approach in which patients and medical and technical professionals participated in every phase. This app aims to guide couples undergoing ICSI with surgically retrieved sperm through their treatment trajectory. myFertiCare provides personalized and interactive functionalities, facilitating the provision of patient-centered care and empowering patients to manage their own treatment trajectory. The app had a high usability rating and was highly appreciated by both male and female partners.

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4

Application implementation

Sparidaens EM, Logger JGM, Nelen WLDM, Braat DDM, Fleischer K, Hermens, RPM.

Web-based guidance through assisted reproductive technology (myFertiCare): a quantitative evaluation of an online application by using the HOT-fit framework. Journal of Medical Internet Research, in press.

ABSTRACT

Background: Assisted reproductive technologies (ART) are considered to be physically and mentally stressful. During their treatment trajectory couples express high information and communication needs. They appreciate using the Internet to obtain fertility-related information. In a previous study we developed myFertiCare, an eHealth tool providing personalized information and interactive functionalities for infertile couples in order to improve patient-centered care. The application has already been successfully evaluated qualitatively for usability.

Objective: The aim of the current study is to evaluate quantitatively the implementation of myFertiCare by using the HOT-fit framework and to study the effects of using myFertiCare on couples' knowledge about infertility, experienced burden of infertility and experienced patient-centered care. With these results, implementation can be further improved and patient-centered care can be enhanced.

Methods: A quantitative study was performed based on the HOT-fit framework, using validated questionnaires focusing on the Human, Organizational en Technology domains. Questions were added on the effect of using myFertiCare on couples' knowledge about infertility and treatment. Questions regarding burden of infertility, burden of infertility treatment, and experienced patient-centeredness were based on the main items of the validated fertiQol, and PCQ-Infertility questionnaires respectively. Also, non-users of the application were included to explore motivations for not using the application and identifying opportunities for improvement. Finally, user data were analyzed to provide insight into multiple variables concerning application usage.

Results: On the human and technology domain, myFertiCare showed good system usability, high user satisfaction and high information and interface quality. On the organizational domain, implementation was considered to be sufficient by both patients and staff. Usage of the application increased knowledge about the treatment, improved coping with treatment and enhanced experienced patient-centeredness. User data showed that women were the main application users and that usage of the application gradually declined during the treatment trajectory.

Conclusion: A multi-faceted online application, called myFertiCare, has been successfully evaluated quantitatively for implementation by using the HOT-fit framework. Usage of the application increased knowledge about the treatment, improved coping with treatment and enhanced experienced patient centeredness. Application use could be improved by creating more publicity. By providing myFertiCare, professionals in fertility care are supported to guide patients through their treatment trajectory and to deliver patient-centered care.

INTRODUCTION

Subfertility is defined as the failure to obtain a pregnancy after more than 12 months of unprotected intercourse [1]. It occurs in one out of every six or seven couples [2]. Depending on the results of diagnostic tests, assisted reproductive technologies (ART), such as in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI) are available for these couples. ART are considered mentally and physically stressful [3]. Couples undergoing ART are often young and well educated and want to be actively involved during their treatment [4]. As a result, these couples express high information and communication needs [4].

Subfertile couples appreciate using the Internet to obtain fertility-related information [5]. Usually, the female partner is the main Internet user. Most patients state that the Internet improves their knowledge about infertility [5]. In practice, at least half of subfertile couples uses the Internet for fertility-related purposes [5-8]. An online survey even characterized the Internet as the most heavily relied-upon source of information about infertility [9]. However, the quality of information provided on the Internet is variable; it is often incomplete, misleading, or inaccurate [10, 11]. Besides informational needs, other reasons for subfertile couples to use the Internet are availability of emotional and social support and help with decision making [11, 12]. Patients prefer personal medical information online, for example access to their medical records or interactive functionalities, such as the possibility to communicate with doctors and fellow patients [5]. They feel that online support from peers is helpful in dealing with emotional stress and social isolation [5, 13].

As described in our previous study, we were the first to design and develop an online application (myFertiCare) for infertile patients, providing personalized information and interactive functionalities regarding their fertility treatment in order to improve patient-centered care [14]. We established the need for such an online application specifically among couples undergoing ICSI with surgically retrieved sperm, because of the psychological and physical burden of the multidisciplinairy treatment. MyFertiCare provides personalized information and interactive functionalities as options for communication with doctors and fellow patients. The application has been successfully evaluated qualitatively for usability [14]. The aim of the current study is to evaluate quantitatively the implementation of the application by using the HOT-fit framework and to study the effects of using myFertiCare on couples' knowledge about fertility treatment, experienced treatment burden and experienced patient-centered care.

METHODS

Study design

We used a quantitative study design to evaluate the implementation of myFertiCare according to the HOT-fit framework. This framework states that a fit between Human, Organization and Technology factors is needed to successfully implement an eHealth intervention [15]. The HOT-fit was studied by using validated questionnaires focusing on these three domains. Furthermore, we studied the effect of using myFertiCare on: 1. Couples' knowledge about fertility treatment, 2. Experienced treatment burden and 3. Experienced patient-centered care. We also included non-users of myFertiCare to explore motivations for not using the application and identifying opportunities for improvement. Finally, we analyzed user data to provide insight into various app-related variables such as the number of users, visits and page views, and the frequency and duration of use. Ethical approval was proposed but was not required according to the local research ethics committee (CMO Arnhem Nijmegen).

Setting

The study was established at a Dutch university medical centre specialised in ART and surgical sperm retrieval for men with azoospermia. ICSI with surgical sperm retrieval is a multidisciplinary treatment involving a urologist, responsible for the andrological evaluation and surgical sperm retrieval, a gynaecologist, responsible for the subsequent ICSI procedure, a psychologist for easily accessible mental support and, if necessary, a clinical geneticist. In January 2016, the online application myFertiCare was launched and available via the clinic's website, the Apple App Store and Google Play Store.

Participants

All couples visiting the outpatient clinic for possible ICSI with surgical sperm retrieval between January 1, 2016 and July 1, 2017 were invited to use myFerticare and to participate in the questionnaire study. Men undergoing surgical sperm retrieval for fertility preservation purposes and couples of which both partners did not understand Dutch language were excluded. All participating couples signed for informed consent.

Data collection

The study comprised two separate questionnaires. One questionnaire was targeted at users of myFertiCare and one was targeted at non-users of the application. The questionnaires were available both on paper and digital (using Castor EDC). They were sent out in June 2017. Both questionnaires contained questions on demographic and medical characteristics of the participants (Table 1).

The user questionnaire was based on the principles of the HOT-fit framework [15]. The *Human* domain consisted of system use and user satisfaction. Both were evaluated through validated questionnaires, the System Usability Scale (SUS) [16] and the End-User Computing Satisfaction (EUCS) [17], respectively. The *Organization* domain consisted of the structural and environmental context of fertility care and was evaluated through self-developed questions in the user questionnaire (no validated questionnaire because questions are unique to the context of the organization) and through short face-to-face structured interviews with staff members of the department of reproductive medicine. The interview questions focused on staff's experiences with the organization and implementation of myFertiCare. These interviews were performed face to face because this allowed more elaborate motivations. Relevant items regarding the implementation of myFertiCare were identified and reported as results. The *Technological* domain included the quality of the system, information, and service (interface). This was studied through the information and interface quality domains of the validated Computer System Usability Questionnaire (CSUQ) [18]. All validated questionnaires were translated into Dutch language by the researcher. Translation was checked by letting it translate back into English by another member of the research team. Both researchers were proficient in English and Dutch. Discrepancies were discussed until consensus was reached. Supplementing the HOT-fit framework, questions were added concerning knowledge about infertility, the burden of infertility and fertility treatment, and the extent to which couples experienced patient-centered care. Couples were asked if using myFertiCare increased their knowledge about the cause and treatment of infertility. Questions concerning the burden of infertility and infertility treatment were based on the main items as described in the validated fertiQol questionnaire [19]. Questions about patient-centeredness were based on the eight subheadings of the validated PCQ-Infertility questionnaire [20]. The complete user questionnaire consisted of 72 questions with answer options being open, on a 5- or 7-point Likert scale, or on a unipolar verbal scale.

The questionnaire for non-users of myFertiCare consisted of four questions regarding familiarity with the availability of myFertiCare, motivations for not using the application, suggestions to increase its usage and the use of other online sources of information. The questions were self-developed by the research team due to the specific context of the organization.

Both questionnaires were pilot-tested with three couples attending the outpatient clinic. Couples considered the questions clear and understandable, so no major changes were necessary. The questionnaires were sent out via post mail by a member of the treatment team. One questionnaire per couple was sent, addressed to the couple, because a close connection and interaction between partners during the treatment was assumed. Each couple received both the user and non-user questionnaire and had to decide which of the two questionnaires was applicable. Use was defined as the minimum of one login in the application; non-use was defined as never logged in. Patients had to write down who completed the questionnaire, i.e. the male partner, female partner, or both. Couples could return the questionnaire via post mail or e-mail. Non-responders were sent a reminder two weeks after the initial invitation. Questionnaires were collected from July 1, 2017 until August 18, 2017 and provided with a code which was only available for the researcher. All data were analyzed confidentially.

User data were automatically transferred to an anonymized Microsoft Excel file. In this way, all application visits and pageviews could be logged by date and time and analyzed later. Included were all patients who used myFertiCare between January 1, 2016 and July 1, 2017, whether they participated in the questionnaire study or not.

Data analysis

Statistical analysis was performed using Microsoft Excel and SPSS (version 22). Baseline characteristics of the study population, user data and results of the questionnaires were analyzed using descriptive statistics (median (range), means (sd), frequencies, etc.). Regarding user data, we focused on possible differences between men and women as well. P-values were calculated using independent sample-T tests, Mann-Whitney U tests and Chi-square tests to find possible significant differences ($P < 0.05$) between users/non-users and men/women.

RESULTS

Study population

In total, 314 ICSI couples were invited for participation (Figure 1); 151 couples (48%) completed and returned the questionnaire. There were 21 ‘user-versions’ and 111 ‘non-user versions’ returned. Additionally, 19 couples returned both versions of the questionnaire. If both versions were returned, user data were consulted to classify these couples as users or non-users and the appropriate questionnaire was included in the analysis. Nine non-user questionnaires were excluded because no questions were filled in, or because the couples actually were users, which was defined as three or more logins. Finally, the user-group consisted of 35 couples and the non-user group of 107 couples (Figure 1). Demographic and medical characteristics of the participating couples (users and non-users) are provided in Table 1.

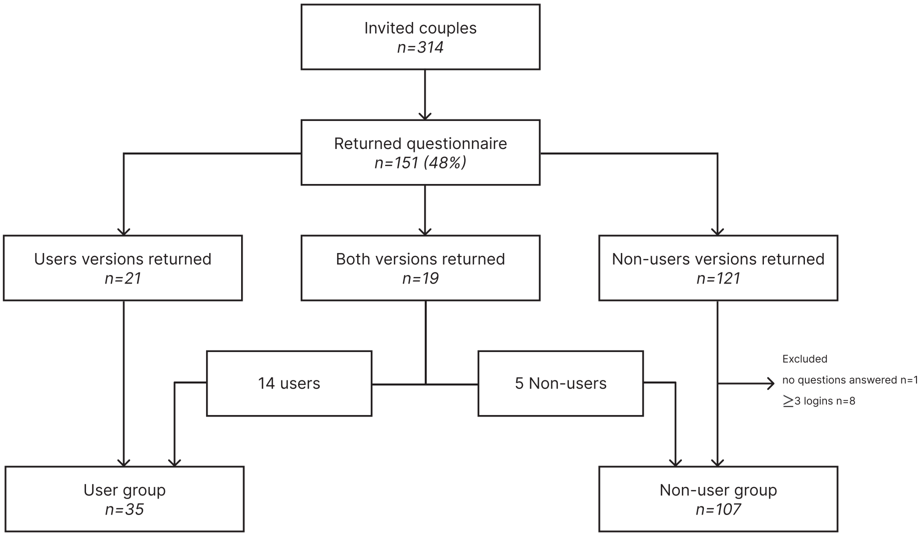

Figure 1. Overview of the participating couples

Table 1. Demographic and clinical characteristics of study participants, both users and non-users

	Users *35 couples*		Non-users *107 couples*		P-value
	Male	*Female*	*Male*	*Female*	
Age (mean ± SD), *years*	37 ± 7.7	32 ± 4.3	37 ± 7.6	32 ± 4.0	NS$^{¥}$
Dutch background	35 (100%)	32 (91%)	103 (96%)	103 (96%)	NS§
Educational status [1]					
Low	6 (18%)	2 (6%)	10 (10%)	5 (5%)	NS$^{\emptyset}$
Medium	12 (36%)	13 (37%)	40 (40%)	48 (47%)	
High	15 (46%)	20 (57%)	51 (50%)	50 (48%)	
Parental status					
Children	12 (34%)	12 (34%)	44 (41%)	35 (33%)	NS$^{\Omega}$
No children	23 (66%)	23 (66%)	63 (59%)	72 (67%)	NS$^{\Omega}$
Currently pregnant	-	7 (20%)	-	31 (29%)	NS$^{\Omega}$
	Couple		*Couple*		
Social-economic status [2]					
Low	11 (31%)		19 (18%)		NS$^{\emptyset}$
Medium	21 (60%)		78 (73%)		
High	3 (9%)		10 (9%)		
Duration of infertility (median; range), *months*	24; 8-120		30; 2-120		NS$^{£}$
Current stage of infertility treatment					
Out of treatment [3]	17 (49%)		80 (75%)		0.033$^{\emptyset}$
Before surgical sperm retrieval [4]	1 (3%)		3 (3%)		
After surgical sperm retrieval, before ICSI [5]	2 (6%)		3 (3%)		
During first ICSI-cycle [6]	6 (17%)		7 (7%)		
During a following ICSI-cycle or cryo-cycle	9 (26%)		14 (13%)		

[1] Educational status: low=VMBO, MAVO; medium= HAVO, VWO, MBO; high=HBO, WO.

[2] Social-economic status: status scores based on postal code according to the Dutch Social and Cultural Planning office.
Low < -1; medium -1 < 1; high > 1.

[3] Couples either pregnant or having exhausted all treatment options.

[4] Diagnostic process until surgical sperm retrieval

[5] Evaluation of surgical sperm retrieval, preparation for ICSI.
[6] Start of ICSI-cycle until pregnancy test.
NS: Not significant. ¥ Independent sample T-test. § Fishers Exact Test. ∅ Fisher-Freeman-Halton Test. Ω Chi-Square Test. £ Mann Whitney Test.
¤ Contain small subgroups that are not mergeable, numbers are shown for informational purposes only.

myFertiCare users

35 couples' questionnaires from myFertiCare users were analysed according to the HOT-fit framework.

Human and technology domain

In 42% of the couples the female partner was the only user of myFertiCare. In 19% only the male partner used the application. In 39% of the couples both partners used the application. All of these 39% of couples had at some point used the application together, and in 92% of them the female partner was the main user.

The results of the three validated questionnaires for the human and technology domain, the SUS, EUCS (both human domain) and CSUQ (technology domain), are shown in Table 2. Mean SUS-score was 73, which implies good system usability (scale 0-100 with 100 being the best possible score) [21]. All sub items of the EUCS showed high user satisfaction (total score 47 on scale 12-60 with 60 being the best possible score) [17]. The CSUQ showed high information quality (score 18 on scale 7-49 with 7 being the best possible score) and interface quality (score 9 on scale 3-21 with 3 being the best possible score) [18].

Table 2. Scores of the System Usability Scale (SUS), End-User Computing Satisfaction (EUCS) and Computer System Usability Questionnaire (CSUQ) questionnaires of users of myFertiCare.

Questionnaire	Response (n)[1]	Median score (range)	Theoretical range of scores (bolded numbers are the best possible scores)
SUS	25	73 (43-93)	0-**100***
EUCS			
content	24	15 (4-19)	4-**20**
accuracy	23	8 (2-10)	2-**10**
format	23	8 (2-10)	2-**10**
ease of use	24	8 (2-10)	2-**10**
timelines	22	8 (2-10)	2-**10**
total	21	47 (12-59)	12-**60**
CSUQ			
information quality	22	18 (6-36)	**7**-49
interface quality	22	9 (3-20)	**3**-21

[1]Response was defined because not every couple (n=35) answered every question.

Users stated that they would recommend myFertiCare to a friend (96%), because they considered the application to be informational and easy to handle. They would use a similar application whenever visiting another medical department (96%). The most appreciated functionality was the visualized treatment trajectory, which shows their scheduled and future yet unscheduled appointments on a visual timeline. Some couples mentioned suggestions for future application functionalities, such as a medication schedule and a mood tracker. Couples were confident that the application safeguarded their personal information (96%). Suggestions to achieve more frequent application usage were increased publicity, more activity on the forum, and usage of the application during outpatient appointments.

Organization domain

Couples were asked how they found out about the availability of myFertiCare. Most of them remembered to be informed verbally or in writing by a member of the treatment team (78%). A minority did not remember to be informed but found the application on the hospital website (9%). Information about the application was considered complete and well-timed. Couples who could not remember to be informed about the availability of myFertiCare would have appreciated this. The majority of couples felt that myFertiCare was well used in fertility care (82%) and that the treatment team was sufficiently familiar with the application (76%). One third of couples was not aware of who to ask questions about the application (36%). All couples that did ask a question about the application to a member of the treatment team, received a satisfying answer.

The organization domain was also studied through interviews with members of the treatment team (n=17). Interviewed were three fertility doctors, three nurses, three medical assistants, three secretaries, two gynecologists, a laboratory employee, an embryologist and an operational manager. All team members were aware of the availability of myFertiCare, they were informed about myFertiCare by a presentation from the researchers or via e-mail. They described the application with the terms: digital support, information about treatment trajectory and appointments, timeline, finding advices and test results, chat function with peers, asking questions to the treatment team. Ten of them did not know if patients were sufficiently aware of the functionalities of myFertiCare and five of them wanted to know more about the functionalities themselves. All team members were aware of who to contact in case of questions about or problems with myFertiCare. Furthermore, all team members recommended using myFertiCare to patients. Usage of the application could be improved by creating more awareness, expanding use to other ART-treatments, maintenance of up-to-date information and evaluation of use during outpatient appointments.

Effects of application use

Supplementing the evaluation according to the HOT-fit framework among application users, the effect of usage of myFertiCare on 1) knowledge about infertility and treatment, 2) burden of infertility and treatment and 3) patient centeredness was studied.

Knowledge about infertility and treatment. Half of the couples reported that usage of myFertiCare not at all or only slightly increased knowledge about the cause of infertility. However, 79% did feel like myFertiCare increased knowledge about the fertility treatment (Figure 2).

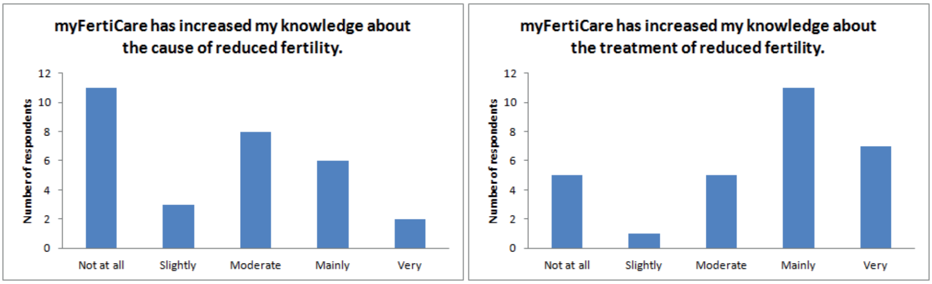

Figure 2. Effect of myFertiCare on knowledge.

Burden of infertility and treatment. Half of the couples indicated that myFertiCare contributed positively to coping with treatment (Figure 3). A neutral to denying response tendency was seen for the possible effect of myFertiCare on handling of daily activities, physical health, relationship with partner, social support, sexuality and mood (Figure 3). The general opinion was that myFertiCare is mainly a source of information instead of a tool that significantly influences burden of infertility and treatment.

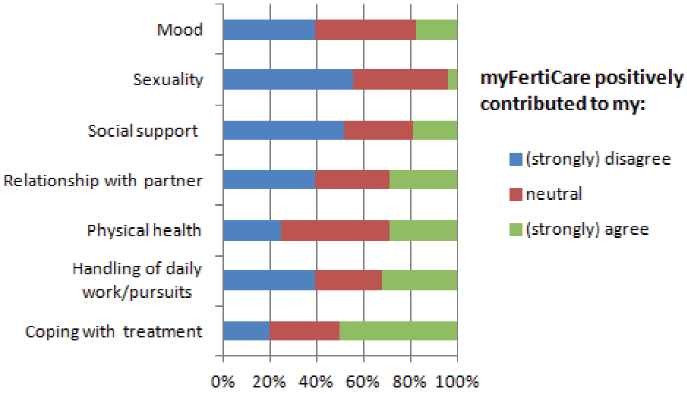

Figure 3. Effect of myFertiCare on burden of infertility and treatment.

Patient-centeredness. Couples were positive about the effect of myFertiCare on the experience of patient centered fertility care. All eight surveyed items (i.e., accessibility, information, communication, involvement, attention for wishes and needs, agreement and collaboration, professionality, organization of healthcare) were improved by the use of myFertiCare (Figure 4).

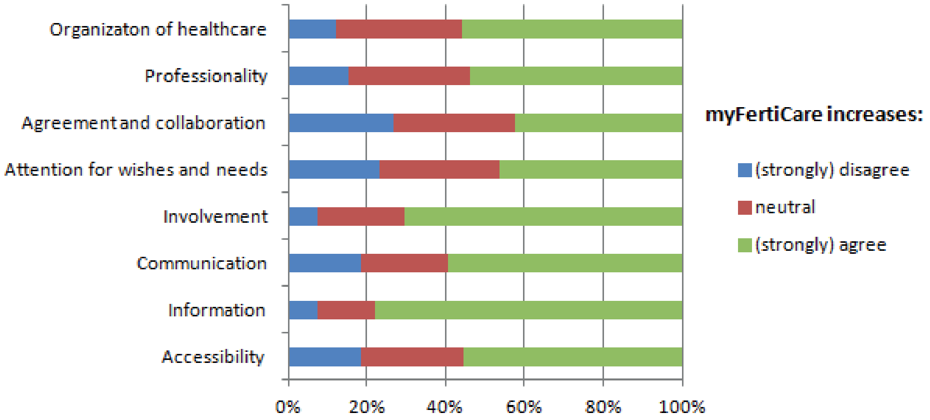

Figure 4. Effect of myFertiCare on (the experience of) patient centeredness.

myFertiCare non-users

107 couples' questionnaires of non-users of myFertiCare were analyzed. Although providing information about myFertiCare was part of routine care, only 25% of non-users remembered to be informed about the availability of myFertiCare. The main reason of non-usage was a lack of need or interest. Out of the couples that did not remember to be informed about myFertiCare, half of them said that they would have liked to use the application. The other half felt like they did not need the application due to sufficient information via other sources. The majority of non-users of myFertiCare used other sources of online information about infertility or treatment (66%).

User data

Supplementing the questionnaire study, user data were analysed. In total, 163 individual patients used myFertiCare, composed of 139 couples. At couple level, 21% consisted of a male user only, 47% of a female user only, and in 32% both partners were users. If both partners were users, the female partners were the most frequent application users with a median number of 9 visits, versus a median of 3 visits per male partner. All user data are shown in Table 3. Finally, it appeared that use of myFertiCare gradually declines during the treatment trajectory, which is illustrated in Figure 5.

Table 3. User data of myFertiCare from December 8, 2015 until August 4, 2017.

	Total	Men	Women	P
Users	163	61	102	**-**
Visits	951	192	759	-
Page views	17097	3734	13363	-
One-visit-users, %	51 (31%)	25 (41%)	26 (26%)	**0.039** $^{¥}$
Visits per user $^{\Omega}$	3 (1-85)	2 (1-23)	3 (1-85)	**0.001** §
Frequency of visits, *a visit per .. days* $^{\Omega}$	5.4	12	3.6	**0.006** §
Duration per visit*, *min* $^{\Omega}$	1.03 (0-107)	1.55 (0-107)	0.93 (0-51)	0.116 §
Time between first and last visit, *days* $^{\Omega}$	30 (1-499)	63 (1-499)	20 (1-347)	**0.010** §
Total duration of use, *min* $^{\Omega}$	9.6 (0-268)	5.9 (0-119)	13 (0-268)	**0.010** §
Page views per user** $^{\Omega}$	59 (0-1254)	47 (0-375)	76 (1-1254)	**0.002** §
Page views per visit** $^{\Omega}$	11 (0-139)	10 (0-88)	11 (0-139)	0.964 §

$^{\Omega}$ median (range). $^{¥}$ Chi-square test. § Mann-Whitney test.
* user was logged out automatically after 20 minutes of inactivity.
**excl. navigation pages (login, logouts etc.).

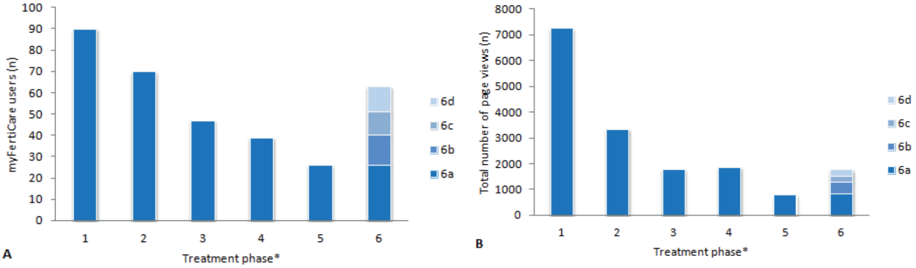

Figure 5. Use of myFertiCare per treatment phase.
A, Users per treatment phase. **B,** Total number of page views per treatment phase. *1: before surgical sperm retrieval. 2: after surgical sperm retrieval, preparation for ICSI. 3: during ICSI treatment, but before visits to the outpatient clinic. 4: during ICSI treatment, between first and last visit to the outpatient clinic. 5: during ICSI treatment, period between embryo transfer and pregnancy test. 6: after ICSI. 6a: period between negative pregnancy test or cancel of treatment until start of new treatment. 6b: period between positive pregnancy test and first ultrasound. 6c: during pregnancy, period after first ultrasound. 6d: having exhausted all treatment options (no pregnancy).

DISCUSSION

Principal results

In this quantitative study, the implementation of myFertiCare was evaluated by using the HOT-fit framework. On the human and technology domain, myFertiCare showed good system usability, high user satisfaction and high information and interface quality. On the organizational domain, based on high scores in the user questionnaire and positive feedback in the staff interviews, implementation was considered to be sufficient. Application use could be improved by creating more awareness among patients and staff. Usage of the application increased knowledge about the treatment, improved coping with treatment and enhanced experienced patient centeredness.

The current study shows that women are the main application users. Either the female partners were the only users, or both partners used the application, but then the female partner was the main user. This observation is in correspondence with previous research [5, 7, 8, 22]. This is attributed to gender differences in health-related internet use, the experience of infertility and fertility treatment, and strategies to cope with fertility related issues [23]. However, we found that although men are less frequent myFertiCare users, the duration and number of page views per visit is equal for both sexes.

User data showed that usage of the application was highest before surgical sperm retrieval and gradually declined thereafter. The observed gradual decline in application usage is in contradiction to previous research, where highest user activity was seen in later treatment phases, namely between oocyte retrieval, embryo transfer and the pregnancy test [26], which was attributed to high stress levels during this particular treatment phase [3, 27]. This could be explained by the law of attrition, which is the phenomenon of participants discontinuing to use an eHealth intervention that is neither mandatory nor critical to their direct well-being [24]. However, a part of this decline is also caused by the expected treatment dropout that occurs with a negative result from the surgical sperm retrieval. It is known that in half of the men with non-obstructive azoospermia no sperm cells can be retrieved [25]. Therefore, these couples were not able to continue their fertility treatment with an ICSI procedure. The treatment stopped as did the use of myFertiCare. Furthermore, as a result of a higher rate of fertilization failure in our study, related to the use of surgically retrieved sperm instead of the use of ejaculated sperm [28], a larger proportion of our participants probably did not proceed to embryo transfer, and therefore were not using the application in this treatment stage. On the other hand, couples that continued with an ICSI treatment were possibly satisfied with the information they received and the need of application use declined.

It is remarkable that the majority of non-users of the application did not remember to be informed about the availability of myFertiCare. All couples received this information as part of standard care during an informative group consultation by a specialized nurse at the beginning of the treatment trajectory. It is known that patients' memory for medical information is often poor and inaccurate, especially when the patient is anxious [29]. This underlines the necessity of repeating important information on several occasions and to provide written information.

By studying the effects of application usage, we found that users considered myFertiCare being mainly a source of information, instead of a tool that significantly decreases burden of infertility and treatment. However, couples were outspoken that usage of myFertiCare improved experience of patient-centered care, which meets the goal we set at the start of the study. Therefore, myFertiCare forms an innovative tool to help professionals in providing patient-centered care. We hypothesize that myFertiCare could score higher on influencing the burden of infertility and treatment, if the application would be supplemented with functionalities targeted at this effect. In the current study we developed an online application for a pilot population and were not equipped with resources to add extra functionalities. Another factor that might improve application usage could be an application that also provided a benefit for the treatment team, i.e. by making it easier, better or more efficient to provide care for their patients. Therefore, we call for other medical professionals to continue developing online interventions in collaboration with their patients and staff, so that patient-centered care can be improved from the perspective of the patient and the professional.

Numerous eHealth interventions with different functionalities targeted at a variety of patient categories have been reported. It is remarkable that in most interventions evaluation is only performed at the end of the intervention, although the importance of conducting evaluation throughout the intervention is regularly discussed [30]. When eHealth evaluations are studied, it is striking that only 64% of studies evaluate clinical aspects, 48% evaluate human and social aspects, 20% evaluate technological aspects and 16% evaluate organizational aspects [30]. A recent example of an eHealth intervention that did include human, organization and technology factors in the evaluation, used a qualitative study design with semi-structured interviews to explore patients' experiences and described these on the basis of the three domains [31]. Therefore, we feel that the major strength of the current study is the study design. By using validated questionnaires on the human, organizational and technological domain we quantitatively studied implementation of the application. Furthermore, we studied the effects of application usage and analyzed user data. Finally, we also included non-users of the application in the study, to explore motivations for not using the application and identifying opportunities for improvement. This way, we provided a complete framework for application design, development, implementation, evaluation and improvement. We call for better evaluation of eHealth interventions, so that successful long-term implementation will be facilitated.

Our study has also some limitations. There was a relative low response rate of 25% (35 out of 139 couples) for the user questionnaires. For the non-user questionnaires the response rate was 61% (107 out of 175 couples). A possible explanation could be that we sent out the questionnaires in June 2017 to all couples who were treated between January 2016 and July 2017. It could be that a significant proportion of these couples already dropped out or finished treatment. Another hypothesis is that the response rates could be caused by the length of the questionnaires. Because of the multiple validated questionnaires on different domains, the user questionnaire was quite extensive, whereas the non-users questionnaire contained only four questions. However, there was a good consistency in the data from the user questionnaires, which supports reliability of the study data. Another limitation is that we studied the effects of application usage (i.e. knowledge about infertility and treatment, burden of infertility and treatment, and patient centeredness) based on a self-reported difference before and after application usage, instead of measurements before and after application usage. Motivations for this approach were that we did not want patients to feel like they had to perform an exam instead of a questionnaire, and that we did not want to make the questionnaire more extensive to study patients' knowledge.

Conclusion

A multi-faceted online application, called myFertiCare, has been successfully evaluated quantitatively for implementation by using the HOT-fit framework. Usage of the application increased knowledge about the treatment, improved coping with treatment and enhanced experienced patient centeredness.

Practice implications

In our previous study, myFertiCare was successfully designed, developed and qualitatively evaluated for usability. In the current study, implementation of the application was positively evaluated quantitatively based on the HOT-fit framework and the effects of application usage were studied. Through these consecutive studies, a framework has become available for the complete trajectory of application development, implementation, evaluation and improvement, in which both patients and professionals are involved in every study phase.

By providing myFertiCare, professionals in fertility care are encouraged to guide patients through their treatment trajectory and to deliver patient centered care. Furthermore, myFertiCare offers an opportunity to empower patients and help them manage their own treatment trajectories. It would be valuable for future research to improve the application based on couples' and professionals' suggestions so that more support is perceived, and to expand application usage to other patient categories and medical departments. We appeal to professionals both in fertility care and other medical departments, to provide eHealth initiatives to their patients, in which both patients and professionals are involved in every phase of design, development, implementation and evaluation.

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5

Information needs during breast cancer survivorship

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Exploration of fertility and early menopause related information needs and development of online information for young breast cancer survivors. BMC Womens' Health. 2022 Aug 3;22(1):329.

ABSTRACT

Background: Approximately half of premenopausal women diagnosed with breast cancer desire to conceive after they finish treatment. Counseling about the risk of infertility prior to cancer treatment has been proven to improve quality of life after cancer treatment. As a result of this, guidelines focus on informing women on this topic prior to treatment. However, it is equally important to provide fertility related information after primary treatment has been completed, when the wish to conceive might become actual. Therefore, the aim of this study was to identify the fertility and early menopause related information needs of young breast cancer survivors and to design, develop and implement online information material with input of stakeholders.

Methods: A phenomenological qualitative study consisting of four phases was performed: identification of information needs through semi-structured interviews from a professional perspective (1) and a patient perspective (2). Exploration of stakeholders perspective regarding development and implementation of online information material (3) and development and implementation of the information material (4).

Results: Professionals indicated that there are no guidelines regarding the provision of fertility related information during cancer survivorship. Survivors reported unmet information needs. Women identified the following as most important information needs a) fertility preservation options, b) the risk of menopause or infertility, and c) long term consequences of early menopause. A wide range of stakeholders involved in breast cancer care were interviewed. Based on their proposed design the information material was implemented on a nationwide website aiming at informing and supporting breast cancer patients.

Conclusions: Fertility and early menopause related information needs of young breast cancer survivors and their professionals were identified. Information material has been designed, developed and nationally implemented. This way, professionals in breast cancer care are provided with an information tool that helps them meet the information needs and preferences of their patients.

INTRODUCTION

Breast cancer is the most common cancer in women aged 15-39 years worldwide [1]. Treatment can be gonadotoxic, leading to temporary or permanent infertility, or premature ovarian insufficiency (POI) later in life [2-4]. Furthermore, young women with a hormone-positive tumor are often treated with adjuvant antihormonal treatment for years after their primary treatment has finished; a period in which they are not able and not recommended to conceive. Whether fertility is regained after the completion of primary and adjuvant treatment depends on factors such as age, type of treatment and cumulative dose of chemotherapy received [2-4].

Due to the social trend of women having children later in life, a growing proportion of women diagnosed with breast cancer does not have completed their family yet [5]. Significant advances in oncology practice over the years have improved breast cancer survival rates. This contributes to the fact that approximately half of premenopausal women diagnosed with breast cancer desire to conceive after they finish treatment [6]. The majority of women experience concerns about the risk of infertility after cancer treatment [7]. These concerns often present as depressive symptoms and a diminished quality of life among young cancer survivors [8-11]. This occurs not only shortly after diagnosis and treatment but has been found to last years beyond the completion of treatment [12]. For women and their partners, the grief associated with the loss of fertility can be as painful an experience as the cancer diagnosis [13].

Younger premenopausal breast cancer survivors report a greater need for information and psychosocial guidance compared to older postmenopausal women regarding topics like fertility and sexuality [14, 15]. Premenopausal women often feel that the information they have received is insufficient or conflicting [16-18]. Professionals do not always feel the necessity of discussing fertility, and women often do not feel encouraged to ask questions about it [16, 19]. This particularly appears to be the case for women who are single at the time of their diagnosis and women who have a poor prognosis [20]. However, receiving information on fertility is important to all premenopausal breast cancer patients [18]. Counseling about the risk of infertility prior to cancer treatment has been proven to significantly improve quality of life after cancer treatment [10, 21].

Current international breast cancer guidelines focus on informing breast cancer patients on the possibility of reduced fertility prior to treatment [22-24]. This is important, because this is the moment a woman needs to be aware of the risks of various treatments for her fertility and the different available fertility preservation options, in order to make well-informed treatment decisions [4, 5, 22-25]. However, concerns about fertility may also arise after cure for cancer in both women who were and were not previously concerned about their fertility [20, 26]. Therefore, it is equally important to provide fertility related information after primary treatment has been completed, when the wish to conceive might change. Since current guidelines lack any recommendations on which information should be provided to breast cancer survivors and how this should be offered [22-24], the present study was designed. Our research question was: what are the fertility and early menopause related information needs of young breast cancer survivors from both professionals' and patients' perspectives and how should this information be provided?

METHODS

Setting

Breast cancer care in the Netherlands is provided in university hospitals, large non-university teaching hospitals and small non-teaching hospitals. Women are primarily diagnosed and treated by a medical oncologist and/or a surgical oncologist. Treatment is multidisciplinary and can also involve a radiation oncologist, radiologist, pathologist, breast cancer nurse, clinical geneticist, plastic surgeon, gynecologist, and a psychologist. The breast cancer nurse coordinates the treatment, is easily accessible for the women, discusses many practical and emotional issues with them and delivers a part of the follow up care. Current Dutch guidelines clarify that all women should be informed about the risk of infertility prior to their treatment and that they should be referred to a specialist in fertility preservation if desired [22], although implementation of this guideline is still inadequate. The specialist in fertility preservation provides information about the risk of infertility or POI and provides counseling about fertility preservation options. A potential delay in breast cancer treatment is considered and discussed with the oncologist. The oncologist is supposed to revisit the subject at the start of follow-up and refer women to a gynecologist again if they have questions [27]. Fertility preservation is centralized in In Vitro Fertilization-centers in the Netherlands.

Study design

The design of this phenomenological qualitative study, performed in the Netherlands, consisted of four phases: 1) identification of relevant topics concerning fertility and early menopause related information from a professional perspective, 2) identification of fertility and early menopause related information needs from a patient perspective, 3) exploration of needs and preferences of stakeholders involved in breast cancer care regarding development and implementation of online information material , 4) development and implementation of the information. Ethical approval of this study was proposed but was not required according to the local research ethics committee (METC Oost-Nederland file number 2015-1779). All participants signed for informed consent. The COREQ checklist guided the study conduct and reporting.

Phase 1: identification of relevant topics from a professional perspective

Participants

In this phase, the information needs from a professional perspective were identified. Thirteen semi-structured interviews were conducted with a panel of professionals in providing breast cancer care, consisting of five medical oncologists, two surgical oncologists, two gynecologists specialized in fertility preservation, three breast cancer nurses and one specialist in adolescent and young adult cancer care (AYA). Data saturation was reached after the eleventh interview, i.e. no new information items could be added to the topic guide. The experts originated from two university hospitals and three large teaching hospitals throughout the Netherlands via purposeful sampling [28].

Data collection and analysis

All interviews were conducted by the first author (EMS) between January and June 2016. The interviews were preferably conducted face to face (n=11), otherwise by phone (n=2). The duration of the interviews ranged from 23 to 44 minutes. Interviews were audio recorded and transcribed verbatim. The topic guide for the interviews was based on a PubMed search on the terms ‘information’, ‘fertility’, ‘menopause’ and ‘breast cancer’. Items regarding fertility and menopause related information for women diagnosed with breast cancer were included in the topic guide. Experts were asked about their experiences concerning fertility and early menopause with women before, during and after breast cancer treatment. For example: which information do they offer women concerning these topics? What questions do women ask? Is there information material available in writing or online? The topic guide for the interviews with professionals is included in Appendix A. Relevant items concerning fertility or early menopause were identified by EMS, which was supervised by WN. No discrepancies arose during analysis. All items that were identified, were included in the topic guide for the interviews with breast cancer survivors (phase 2).

Phase 2: identification of information needs from a patient perspective

Participants

In this phase the information needs from a patient perspective were identified, using semi-structured interviews. Eligible for inclusion were young female breast cancer survivors, aged 20-45 years old, who had completed their initial treatment, i.e. surgery, chemotherapy and/or radiation therapy, and were currently in their follow up period in one of two participating clinics, i.e. a university hospital and a large teaching hospital. Some women still received antihormonal treatment. Women were consecutively invited to participate during follow up appointments with their oncologist or breast cancer nurse and received written information about the study. Women who agreed to be informed, were contacted by the researcher a few days later, to see if they had further questions and if they wanted to participate. A total of eighteen women participated in an interview, which was determined by data saturation [29]. Data saturation was reached at the sixteenth interview. Two additional interviews yielded no new information. Duration of the interviews ranged from 20 to 60 minutes. Mean age at breast cancer diagnosis was 35,5 years old, ranging from 21 to 44 years old. Time since diagnosis varied from nine months to twelve years. Most women had been treated with surgery and chemotherapy. Eight out of eighteen participants still had a future childbearing wish at the time of their diagnosis, five of them had chosen fertility preservation. Sociodemographic characteristics are presented in table 1.

Data collection and analysis

The interviews were conducted by the female first author (EMS, MD) between April and December 2017. The interviewer was working as a PhD student and had previously received training in qualitative research techniques and had experience with interviewing techniques. She was not involved in the participants treatment. Interviews were preferably conducted face-to-face (n=13) in the clinic, but if this was not possible, they were conducted by phone (n=5). Interviews were audio recorded and transcribed verbatim. Field notes were made by the first author. Each interview started with an explanation of the research goals. The topic guide of the interviews was based on the results of phase 1, i.e., the interviews with the expert panel. It contained open questions, for example on the information women received on fertility and early menopause, current information needs, and online information seeking behavior. Women were encouraged to elaborate on their answers. The topic guide was flexible to allow for new topics that were brought up by participants. The topic guide is included in Appendix B. At the end of each interview women completed a short sociodemographic questionnaire (Table 1). They were also asked to compose a priority list with a top 5 of most important items concerning fertility and early menopause related information.

Thematic analysis was performed. All transcripts were coded individually by the first author and a research assistant (female medical student) to obtain investigator triangulation [30]. Coded were all items regarding fertility or menopause related information (using Atlas.ti version 8.1.28). Emerging codes were discussed until consensus was reached. If consensus would not be achieved the fourth author (WN) would be consulted, although this was not necessary. Cross-case analysis was conducted, where data from all participants were combined rather than analyzed as individual cases. Individual codes were divided in sub-themes. A constant comparative method was used to interpret the data, continuously reviewing the transcripts [29]. Themes were identified by dominant concepts in the raw data [31].

Analysis of the priority lists included all items that were noted concerning fertility or early menopause. These items received a score based on their ranking on the specific priority list (first ranked 5 points, second one 4 points, third one 3 points, etc.).

Table 1 Sociodemographic characteristics of 18 breast cancer survivors (phase 2)

Characteristic	Number of participants (%)
Time since diagnosis	
< 12 months	1 (6)
12 – 48 months	6 (33)
> 2 years	11 (61)
Socio-Economic Status (SES)*	
Low	9 (50)
Medium	5 (28)
High	4 (22)
Level of education**	
Low	2 (11)
Medium	6 (33)
High	10 (56)
Treatment received	
Surgery	18 (100)
Radiotherapy	13 (72)
Chemotherapy	17 (94)
Hormone therapy	12 (67)
Currently	8 (44)
Immune therapy	5 (28)
Currently	1 (6)
Relationship status at time of diagnosis	
Married or committed relationship	15 (83)
Single or widowed	3 (17)
Already having children	14 (78)

* According to zipcode area status scores were assigned by the Social Cultural Planbureau of the Netherlands, using the average income, percentage of low income households, percentage of lower vocations and unemployment rates.
Low <-1; Medium > -1 and < 1; High > 1
** Low (ISCED 0-2): No education, Basic education, Secondary education
Medium (ISCED 3-4): Lower vocational education
High (ISCED 5-8): Medium vocational education, university

Phase 3: exploration of needs and preferences of stakeholders regarding development and implementation of online information material

Participants

The goal of this phase was to identify the needs and preferences of major stakeholders involved in breast cancer care, concerning the design, development and national implementation of information material about fertility and early menopause for young breast cancer survivors. Eighteen stakeholders were interviewed, representing eight patient organizations, seven professional associations in the field of breast cancer care and three medical insurance companies.

Data collection and analysis

Stakeholders were asked about their view on nine aspects of design, development and implementation of the information material which were compiled by the research team:

- When should the information be offered?
- Who should offer the information?
- Should every premenopausal breast cancer patient receive the information?
- How detailed should the information be?
- In what format should the information be available?
- Should the information be personalized or interactive?
- What attributes to trustworthiness of information for patients?
- Should the information be integrated in existing platforms?
- How should understandability of the information be ensured?

The interviews were conducted by a research assistant (female medical student). They were audio recorded and transcribed verbatim. The research assistant analyzed the interviews, which was supervised by the first author (EMS). For each of the nine aspects described earlier, different scenarios for implementation were extracted. The scenarios were weighted by both researchers based on six criteria:

- Patient preferences
- Expert preferences
- Financial investment
- Time investment
- Existing literature
- The proportion of patients that is being reached in a scenario

This eventually led to the conclusion of a widely supported recommendation concerning the design, development and national implementation of the information material.

Phase 4: development and implementation of online information material

In phase 1 and 2 the information needs from both a professional and a patient perspective were identified. Phase 3 led to the conclusion of a widely supported recommendation concerning the design, development and national implementation of the information material. Finally, in phase 4 the information material was developed and implemented based on the results of the previous phases. The information material was developed by the researchers in collaboration with stakeholders interviewed in phase 3. There were several rounds of feedback from both, professionals and patients, before the information material was implemented.

RESULTS

Phase 1: identification of relevant topics from a professional perspective

All relevant information items concerning fertility or early menopause that were identified, were included in the topic guide for the interviews with breast cancer survivors, which were performed in phase 2. The topic guide is presented in Appendix B.

Findings originating from the interviews with professionals were that they stated that the consequences of breast cancer treatment on fertility and possible early menopause were mainly discussed before the start of treatment and only occasionally during and after treatment. Professionals felt like it is their task to initiate the conversation on these topics, since they feel that women struggle to address these topics themselves. Professionals indicated that there are no guidelines on when to discuss these topics, but they do so based on their own intuition. During breast cancer treatment and during the follow up period, both medical and surgical oncologists said that they receive very little questions on fertility and possible early menopause. On the other hand, breast cancer nurses did say that they are asked about these topics by patients, although they feel that they don't possess the knowledge to properly answer these questions. Both breast cancer nurses and surgical oncologist indicated that they feel the medical oncologist is the designated professional to elaborate on these topics with patients and survivors.

Phase 2: identification of information needs from a patient perspective

Patient interview results

Several information themes were identified from the interview data and are consecutively described below in italic headings. Quotes from the interviews are presented in table 2.

Table 2 Interview quotes

Quote number	Participant number	Quote
1	**8**	'I brought it up myself with my oncologist, when discussing hormone therapy. I had prepared my questions in advance, because I felt like: This is about my fertility and this is very important to me.'
2	**12**	'Very little can be found online. Of course, I know that there are women who had breast cancer and became pregnant after that, often years later. But how that came to be? Did they have IVF or something like that before their treatment? (...) No one tells you how.'
3	**14**	'I think it is very important that people can decide for themselves how deep they want to go into the subjects. Because you can fill a website with success stories of people who started a family after breast cancer. But for a lot of people that would be too painful.'
4	**10**	'When you are ill, the first priority of your body and your head is: the cancer needs to go. You are not concerned about your fertility, because it does not fit into the picture (..) And I think, during that struggle for survival someone needs to remind you and occasionally tell you 'this (fertility) matters too''
5	**2**	'What if I quit hormone therapy after three years (instead of five)? What are the consequences? Because it is a preventive treatment. So how much does my risk of breast cancer recurrence increase if I do this? And would it increase my chance of restored fertility?'
6	**13**	'What are the consequences? You read about menopausal women that their bones are in worse shape, their hair thins out, skin quality declines. Does that mean that, compared to my mother, when I turn 70 years old I will look a lot older? Or my bones are much more fragile? I do not know and I cannot find that anywhere.'
7	**11**	'It (menopause) is not something that is visible, and not something you like to share with everyone. Who is proud of going through menopause? (...) So, I think if your relatives or the people close to you know, that would make things easier. Because now they think 'It is all over, we will celebrate and move on'. But it is not.'
8	**7**	'I feel rather lonely. I am around 35 years old. My friends all have children. No one really understands me. (...) I wish I could share my feelings and emotions with someone who is in a similar situation, or to receive information from someone I have not found myself. '
9	**12**	'That feeling remains. The breast cancer took that (having a second child) away from me. I understand that I had no choice, we needed to start chemotherapy quickly.'
10	**17**	'I contacted the hospital myself because it was not endurable. I got mad over nothing. I was cold all the time but suddenly hot. I had no appetite but was gaining serious weight. And I was so unhappy. I had become a completely different person. They really should have informed and guided me on how to deal with that.'

Counseling on possible infertility and early menopause

The risk of infertility and early menopause was discussed with most participants at the time of their diagnosis by their medical oncologist, surgical oncologist or breast cancer nurse. Women in this study identified that the most important topics were the risk of diminished fertility, fertility preservation, chemotherapy-induced menopause, contraception, and hereditariness of breast cancer. However, almost half of the women (8 out of 18; 44%) were not satisfied with the amount of information they received and four of them (22,2%) reported not having received any information on the subject.

After completion of their initial treatment, most of the women in this study reported having brought up the topic themselves because they did not feel like they received enough information. They preferred discussing the topic with their breast cancer nurse, medical oncologist or surgical oncologist (Table 2, quote 1). They identified that the most important topics at this point in time were the current fertility status, menopause related symptoms and their treatment, whether to start hormone therapy and contraceptive advice. Only one woman who participated in an interview was referred to a gynecologist.

Availability and design of information material

Many participants reported to have consulted other healthcare professionals for support and specialized knowledge, for example their general practitioner, a physical therapist, gynecologist, psychologist or an orthomolecular physician. Furthermore, most women searched for infertility and early menopause-related information online. Search terms that were often used were self-care advices, fertility after breast cancer, menopausal symptoms, side-effects of cancer treatment, sexuality and psychological matters. Women in this study mainly relied on the website of their hospital and the website of the Dutch Breast cancer Association (BVN) to assess reliability of online information. They often described struggling to find reliable information specific to their situation as a young premenopausal woman with breast cancer, or young breast cancer survivor, since most information deemed generic or unreliable to them. (Table 2, quote 2)

Women in this study reported to need written information on fertility and early menopause. They wanted to prepare themselves for hospital visits and read the information again afterwards. This gave them a feeling of being in control and being able to acquire information in their own pace. The preferred medium was a website. The use of a short folder or business card with some information highlights and the link to the website was recommended. Women suggested that a website should use a filter, for example by age or stage of treatment, or use chapters or hyperlinks in the text to avoid women from feeling overwhelmed by the amount of information.

They identified that the information should be both concise and detailed, factual and easily accessible. (Table 2, quote 3)

Most participants stated that the information should be developed in collaboration with patient organizations and various hospitals, so that the information is tailored to patient's needs, perceived as reliable and easy to find. Many participants wanted to be able to ask questions online, preferably to health care professionals. Some women preferred a forum to share experiences with peers. Other women were concerned about a forum, worrying that it would be easily contaminated with overly dramatic stories and unconfirmed claims.

Participants believed that every premenopausal woman who is diagnosed with breast cancer should receive information about fertility and the risk of early menopause, regardless of their age and marital status. Furthermore, they indicated that these topics should be revisited throughout follow up appointments, as they feel their information needs change throughout time. (Table 2, quote 4)

Information topics: fertility

Women in this study were in need of personalized information that is specific to their situation as a young woman with a diagnosis of breast cancer. They had questions such as: When should I give up hope of my menstruation cycle returning? When would my body be ready for pregnancy? And when are the risks minimal? Does a pregnancy increase the chance of breast cancer recurrence? Is it safe to stop hormone therapy to try and conceive? (Table 2, quote 5)

Furthermore, women had questions like: Should I be using contraception? If I want to conceive, should we try ourselves? For how long? When can I approach a fertility specialist? When can I use cryopreserved eggs or embryos? Can my child be healthy? Is my chance of a miscarriage increased? Will I be able to breastfeed? What are the alternatives to biological parenthood?

Information topics: early menopause

Women in this study indicated that they wanted to understand more about the physiology of menopause. They wanted to learn about hormonal changes and the impact on their body. Most of the participants had experienced or were still experiencing menopause related symptoms. They were in need of information on possible treatment and self-care advices, such as nutrition and exercise. Furthermore, they wanted information on the long term consequences of early menopause. (Table 2, quote 6)

Participants wished for information that also targets their relatives. They felt like their relatives are also in need of support in dealing with the disease. Furthermore, relatives would be able to better support them if they had received more information on their situation. (Table 2, quote 7)

Psychosocial impact of unmet fertility and menopause-related information needs
When looking back, some of the women in this study recognized they did not obtain sufficient fertility-related information. For some of them, this would have changed the choices they had made and they were still struggling with that. Not being able to complete their family brought grief. (Table 2, quote 8 and 9)

Furthermore, women reported feeling abandoned after treatment was finished. They needed guidance, also concerning their menopause-related symptoms. (Table 2, quote 10)

Priority lists

At the end of each interview participants composed a priority list of the 5 most important information items concerning fertility or early menopause. Some women wrote down less than five items on their priority list, others noted multiple topics per rank. All priority lists were included in the analysis. The sum scores are shown in Table 3. Highest scores were allocated to a) fertility preservation options, b) the risk of menopause or infertility, and c) long term consequences of early menopause.

Table 3 Priority lists for information items (n=18)

Topic	Sum score
Fertility preservation options	54
Risk of menopause/infertility	49
Long term consequences of early menopause	37
Menopausal symptoms	25
Psychological impact of infertility/menopause	10
Self-care advices to improve overall health	9
Referral options	7
Treatment options of menopausal symptoms	7
Options for non-biological parenthood	6
Experiences of peers	5
Dealing with stress	4

All information items received a score based on their ranking on the specific priority list: first ranked 5 points, second one 4 points, third one 3 points, etc.

Phase 3: exploration of needs and preferences of stakeholders regarding development and implementation of online information material

We identified the needs and preferences of eighteen major stakeholders involved in breast cancer care, concerning information material about fertility and early menopause for young survivors. This led to a widely supported recommendation on nine aspects of design, development and implementation of information material:

When should the information be offered?

It was recommended that the information is provided at the moment of diagnosis when also fertility preservation options are being discussed. The information should be revisited when the primary treatment has been completed.

Who should offer the information?

The information should be offered to women by the medical oncologist, who has the most expertise on the topic, or by the breast cancer nurse, who is easily accessible to women, has time and attention for psychological issues, and is already frequently involved in follow up care.

Should every premenopausal breast cancer patient receive the information?

It was recommended that every women is asked if she is interested in the information material. The actual information material is only provided to women who express their interest.

How detailed should the information be?

In general, patients expressed the wish for very detailed information. A proportion of professionals was concerned regarding the feasibility of providing very detailed information, without a professional present to put things into perspective and to provide clarification about what applies to a particular patient. A balance should be found between these visions.

In what format should the information be available?

The information should be offered on a website, preferably supplemented with a small paper leaflet to hand over during a consultation, so that a woman can find the information online once she is at home. The information should also be available for women with a language-barrier.

Should the information be personalized or interactive?

It was recommended that women have the possibility to personalize the information by using a flowchart. This should help women with lower health literacy to understand the information that is applicable to them. Women who do not prefer personalization should be able to read all the available information. It was not recommended that the information material contains interactive options, since this requires a large investment in both time and finances. Instead, there could be referred to existing online communities.

What attributes to trustworthiness of information for patients?
To increase the sense of trustworthiness, the information material should mention the organizations that support the information, for example by placing their logo. Furthermore, these organizations should link to the information material on their website.

Should the information be integrated in existing platforms?
To maximize the number of women who are reached with the information material, it was considered helpful if many organizations refer to the information on their website. Hosting the information on an existing platform would be time and cost effective. Moreover, it is an advantage that the information can then be updated by a professional organization, instead of the research group.

How should understandability of the information be ensured?
It was recommended that the information material has a simple, professional design. Understandability can be enhanced by providing personal patient experiences, providing video explanations and by designing the information like a funnel, with the options to click for more detail if a woman wishes so.

Phase 4: development and implementation of online information material

Based on the results of phase 1-3 online information material was developed in collaboration with the nationwide website (www.kanker.nl) aimed at informing and supporting cancer patients. This website is supported by all major stakeholders who are involved in Dutch cancer care, namely the KWF Dutch Cancer Society, the Dutch Federation of Cancer Patient Organizations and the Netherlands Cancer Registry. By choosing for this collaboration, it became possible to benefit from the combination of the knowledge concerning information needs gained through this study, and the professional experience in information provision and wide reach of the cancer organization. This way, we were able to implement the information material concerning fertility and early menopause for breast cancer patients on the cancer organization website and ensured easy and wide access and regular updating of the information (information link: Kanker en vruchtbaarheid bij vrouwen).

DISCUSSION

In our study we investigated the fertility and early menopause related information needs of young breast cancer survivors and their professionals through a phenomenological qualitative study consisting of four study phases. Professionals in providing breast cancer care indicated that there are no guidelines concerning the provision of fertility and early menopause related information, but they address the topic based on their own experience. From a patient perspective it appeared that almost half of the women were not satisfied with the amount of information they received. Furthermore, they struggled to find reliable online information specific to their situation. They needed information on a large variety of topics. Women in this study identified the most important topics as 1) fertility preservation options, 2) the risk of menopause or infertility, and 3) long term consequences of early menopause. Finally, after interviewing a wide range of stakeholders involved in breast cancer care, we executed their proposed design and implementation of information material, being on a nationwide website aiming at informing and supporting cancer patients.

Breast cancer is the most frequently diagnosed cancer among women aged 15-39 years worldwide [1]. Counselling about fertility preservation takes place before the start of oncological treatment [22-24]. This is a phase in which women receive a lot of information in a short time frame. Together with the emotional stress that is caused by the cancer diagnosis, this impairs their ability to remember all information they receive. It is therefore important to provide high quality and easily accessible information to women about the risk of infertility at various points. This includes at the time of diagnosis, throughout the treatment and after treatment has ceased. This way, women can revisit the information at home at the moment fertility related questions arise. Serving these information needs has a positive effect on women's wellbeing [8-11].

The setting of breast cancer care in the Netherlands differs from most other countries. In the Netherlands, women are primarily diagnosed and treated by a medical oncologist and/or a surgical oncologist, instead of a gynecologist. Women only consult a gynecologist if they are referred for fertility preservation counseling or because of an active wish to conceive. This could possibly impact the experience of unmet fertility and early menopause related information needs among the participants in the current study. However, the current findings largely correspond with previous research. In the current study breast cancer survivors expressed unmet information needs and often reported that they had to bring up the topic themselves during consultations, which is in accordance with previous studies [17, 32]. Literature highlights that young breast cancer patients appreciate information on fertility preservation options, contraception, impact of pregnancy on recurrence of breast cancer, impact of chemotherapy on the health of future children, menopausal symptoms and hormonal therapy [16, 18, 26, 33, 34]. In the current study participants agreed to this and further added information needs on self-care, long term consequences of early menopause, sexuality and information targeted at their relatives. Furthermore, they confirmed the need for information to take home, preferably a pamphlet referring to an online source [18, 35].

The major strength of this study is its multi-phase design. We identified information needs from both, a professional and patient perspective. Furthermore, we consulted various stakeholders in providing breast cancer care concerning the design and implementation of the information material. In this way, we implemented a widely supported information tool that is nationally available for all professionals and patients.

Our study has some limitations. It took a reasonable period to complete all study phases. However, this enabled us to approach the subject from all relevant perspectives and also to implement our recommendations on the nationwide website aimed at informing and supporting cancer patients, which is supported by all major stakeholders involved in Dutch cancer care. Since the start of this study, no comparable initiatives have been carried out, which ensures the relevance of our data to date. Furthermore, it is possible that there has been a selection bias concerning the professionals and patients who chose to participate in the study. This phenomenon is to be expected and underlines the value of providing quantitative data in a larger population through future research.

CONCLUSION

Fertility and early menopause related information needs during breast cancer survivorship have been identified and information material has been designed, developed and implemented. The material offers extensive information on these subjects, aimed at young breast cancer survivors. This research has accommodated professionals who provide breast cancer care with an important education tool that helps them provide evidence-based information to the women they are caring for. Future research is needed to evaluate the effect of the new information material and could also explore the added value of such an information tool for other cancer survivors.

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APPENDIX A. TOPIC LIST INTERVIEWS EXPERT PANEL

Introduction: explanation of study goals and methods.

Background: in which phase of treatment and/or follow up do you see women with breast cancer?

Do women ask you questions about their fertility or possible early menopause?

If yes:
- When?
- What kind of questions do they ask?
- What do women want to know?
- Do you feel like you are able to answer all questions? What would you need in order to be able to provide better answers?
- Do you address fertility and early menopause related topics?

If no:
- Why do you think these questions are not asked?
- Should these questions be asked?
- Which topics should be addressed? When? Which informations should be provided?
- Do you feel like you are able to answer all questions? What would you need in order to be able to provide better answers?
- Do you address fertility and early menopause related topics?

Do you have access to written information (on paper or digital) about fertility and early menopause aimed at breast cancer survivors, or cancer survivors in general?

If yes:
- Which information?
- Do you refer patients to this information?
- What is the quality of the information?
- Is the information complete? What could or should be added?
- How could this information best be offered to survivors?

If no:
- Is there a need for this information? From yourself of from your patients?
- Which information topics should be included in the information?
- When should this information be offered to survivors?
- How can this information best be offered to survivors?

How do you experience the cooperation between different breast cancer care providers (medical or surgical oncologist, radiation therapist, gynecologist etc)

How do you think we can improve healthcare for breast cancer survivors?

APPENDIX B. TOPIC LIST INTERVIEWS BREAST CANCER SURVIVORS

Introduction: explanation of study and interview

Background: which treatments did you have? In which phase of follow up are you currently?

Did you receive information about possible risks for your fertility, before you started treatment?

- If yes: How did you experience this? Which information did you receive? Who provided the information? Was the information sufficient? Were there questions left unanswered? Did you chose for fertility preservation? Why or why not?
- If no: How did you experience this? Did you miss information? If yes: which information? Who should have provided this information to you?

Has your fertility been discussed with you on a later moment?

- If yes: When? How often? What was discussed? By who? Was this sufficient? Why of why not? Were there questions left unanswered? Which ones?
- If no: Did you miss this? What should have been discussed? By who? When?

Have you discussed your fertility or related topics with your general practitioner of other healthcare providers outside the hospital? How did this go?

Do you currently have questions about your fertility or related topics? What questions? Who would you want to discuss this with? What do you want to know? Do you feel like you can address this topics? Why or why not?

Have you ever tried to find information about breast cancer, fertility or related topics? Where did you search this information?

Were there information materials, like websites or pamphlets, that you thought were of good quality?

- If yes: Which? Why do you feel like they are of good quality? Was the information clear? Were all your questions answered?

Would you appreciate receiving information material about fertility and possible early menopause that is aimed at young breast cancer survivors?

- If yes: which information topics should be included? When do you want to receive this information? By who? How would you like to receive it? How should the information look? Should the information be personalized or interactive? Should there be a collaboration with professional organizations or patient organizations? Should there be a collaboration with existing (online) platforms? Which?

- If no: why not?

How do you think we can improve healthcare for breast cancer survivors?

6

General discussion

This thesis focuses on improving information provision in fertility care. In this general discussion, we present the main findings of the different studies and discuss clinical and methodological considerations. Finally, we conclude with implications for clinical practice, policy making and future research.

MAIN FINDINGS

In the first part of this thesis, we studied the information needs of couples undergoing ICSI with surgically retrieved sperm (chapter 2) and developed, implemented (chapter 3) and evaluated (chapter 4) an online application, called myFertiCare, to meet these needs. In the second part of this thesis, we studied the information needs of young breast cancer survivors on fertility and developed online information material to meet their needs (chapter 5).

Part I

- In-depth insight into the information needs of couples undergoing ICSI with surgically retrieved sperm gives fertility clinics an opportunity to develop patient information that meets the needs of their patients and thus improve patient-centered fertility care.
- Couples undergoing ICSI with surgically retrieved sperm need information about many topics. They consider information about the success rates of the treatment, an explanation of the treatment procedure, and experiences from other patients the most important.
- Couples undergoing ICSI with surgically retrieved sperm prefer face-to-face information, but also value a leaflet, website, or an online application, especially when it is personalized or provides interactive functionalities.
- A patient-centered online application, called myFertiCare, aimed at guiding couples through their fertility treatment could be systematically designed and developed by patients, medical professionals and technical professionals. MyFertiCare provides personalized and interactive functionalities. The basis of myFertiCare is the couple's visualized treatment trajectory.
- myFertiCare was evaluated qualitatively using a think aloud method. Couples appreciate myFertiCare with a median score of 8 out of 10.
- In the quantitative evaluation of myFertiCare using the HOT-fit framework, on the human and technology domain myFertiCare shows good system usability, high user satisfaction and high information and interface quality. On the organizational domain, implementation is sufficient according to patients and staff.
- Usage of myFertiCare increases knowledge about the treatment, improves coping with treatment and enhances experienced patient-centeredness.
- Women are the main users of myFertiCare. Either the female partners were the only users, or both partners used the application. Although men are less frequent

application users, the duration and number of page views per visit is equal for both sexes.
- Usage of myFertiCare gradually declines during the treatment trajectory.
- Providing myFertiCare supports professionals in fertility care to guide patients through their treatment trajectory and to deliver patient-centered care.

Part II

- Professionals in providing breast cancer care indicate that there are no guidelines regarding the provision of fertility related information during cancer survivorship. They address the topic to their patients based on their own experience.
- Young breast cancer survivors report unmet information needs regarding fertility and the risk of early menopause.
- Young breast cancer survivors struggle to find reliable online information regarding fertility and early menopause specified on their situation.
- Young breast cancer survivors need information on a large variety of topics concerning fertility and early menopause. They identify the following topics as most important information needs a) fertility preservation options, b) the risk of menopause or infertility, and c) long term consequences of early menopause.
- Interviews with a wide range of stakeholders involved in breast cancer care led to a widely supported recommendation on nine aspects of design, development and implementation of information material regarding fertility and early menopause aimed at young breast cancer survivors.
- Information material regarding fertility and early menopause is developed and implemented on a nationwide website [www.kanker.nl] aiming at informing and supporting cancer patients. This way, young breast cancer survivors are provided with easily accessible information and professionals in breast cancer care are provided with an information tool that helps them meet the information needs and preferences of their patients.

DISCUSSION OF MAIN FINDINGS

Part I

The position of the male partner in fertility care

In this thesis both the male and female partners were included in all study phases. This is important because infertile men expect healthcare professionals to approach them equally with their partner [1]. However, men undergoing fertility treatment report that professionals communicate primarily with their female partner. Psychosocial consequences of severe male-factor infertility are not sufficiently addressed, illustrating the need for professionals to develop more inclusive communication skills [1, 2]. Men undergoing surgical sperm retrieval report not only to focus on clinical effectiveness of their treatment, but patient-centeredness of care is equally important to them [3].

Furthermore, there is a lack of high-quality online sources of information on male infertility [4]. Many websites target their information to women only [4]. Also in general media, little if any attention is paid to male infertility, and men with the problem appear to be reluctant to discuss it here compared with their female counterparts [5]. Even in social scientific research on infertility, research studies are far more likely to be focused on the understandings and experiences of women than those of men [6]. By developing patient-centered information that equally includes male and female partners and that addresses psychosocial consequences of male-factor infertility, in chapters 2-4 we contributed to the improvement of information provision for couples undergoing ICSI with surgical sperm retrieval and last but not least to the improvement of patient-centered fertility care.

Implementation of eHealth

In chapters 2, 3 and 4 myFertiCare was designed, developed, implemented, and evaluated in several phases:

1. Identification of the information needs of couples undergoing ICSI with surgical sperm retrieval (chapter 2)
2. Establishment of a patient-centered functional design (chapter 3)
3. Development of the application in collaboration with medical and technical professional (chapter 3)
4. Implementation for all couples undergoing ICSI with surgical sperm retrieval (chapter 3)
5. Qualitative evaluation, by using a think aloud method (chapter 3)
6. Quantitative evaluation based on the HOT-fit framework and evaluation of the effect of application usage (chapter 4)

Based on the experience gained during these study phases, it is possible to point out several factors that are crucial to successful eHealth development and implementation:

- *Involvement of patients*
  Patient-centeredness is described as providing care respectful of and responsive to individual patient preferences, needs and values, and ensuring that patient values guide all clinical decisions [7]. Adequate information provision and active involvement of patients in their treatment are important aspects of patient-centeredness in fertility care [8]. Therefore, it is crucial for the development of a successful eHealth tool to include patients from the beginning. In the development of myFertiCare both patients as well as medical and technical professionals were involved in all study phases.

- *Do not focus on one theme*
  In chapter 2, the overall opinion of the patient panel was that the more functionalities an application provides, the better, so that people keep being motivated to use it. What we observe in daily practice is that there are a lot of parties, such as medical departments, professional organizations, hospitals and pharmaceutical companies, who engage in eHealth development. Most of the initiatives that are developed, focus on one main theme, such as personal health records, medical information, lifestyle or mental health. This can result in situations where a patient visiting a single medical department is offered various eHealth tools for a variety of purposes. Therefore, we advocate the development of multi-faceted eHealth tools that incorporate all these themes and provide the functionalities suited for a specific patient population. By doing this, patients are more invited to use a tool and they keep being triggered to use it. Also, this will minimize the effect of the law of attrition, which is the phenomenon of participants discontinuing to use an eHealth intervention that is neither mandatory nor critical to their direct well-being [9].

- *Personalized and interactive functionalities*
  Participants stated in chapter 2 that they specifically value a personalized application. For example, one with options to view appointments, test results and personal information about their healthcare providers, such as their specialization, work experience, and their photo. Participants favored being able to ask their physicians medical questions and suggested a forum for discussing experiences with peers. These functionalities are all incorporated in myFertiCare. This preference for personalized and interactive functionalities is in line with previous research of our group [10-12]. It is also known that interactive elements in eHealth promote mental health [13]. Therefore, we recommend that personalized and interactive functionalities are incorporated in all eHealth initiatives.

- *The role of the healthcare provider*
  Once an eHealth tool is implemented for a patient population it always requires a certain effort from the healthcare providers. Patients have to be informed about the tool and questions need to be answered. Whenever it is decided to collect either personalized or anonymous data about the use of the application, somebody has to interpret these data and act upon the results. The enthusiasm and motivation of healthcare professionals to execute these tasks is crucial for successful long-term implementation of an eHealth tool. To ensure this motivation it is beneficial to involve professionals in the design, development and maintenance of the tool. Also, if the eHealth tool provides an added value for the healthcare professional, for example with functionalities that make it easier, better or more efficient to provide care the chance of long-term success will be significantly increased. The aim of myFertiCare was to lower the pressure mainly

on telephone consultation hours by providing information that is specific for the couple's treatment phase and upcoming appointment type and by providing the opportunity to ask questions to the treatment team. Furthermore, members of the treatment team were involved in the establishment of the functional design of the application in order to ensure their long-term motivation.

- *Challenges in creating and moderating an active forum*
  As stated before, it is recommended to provide interactive functionalities in an eHealth application because of their potential to promote mental health. This is particularly valuable in male infertility: after all in an analysis of posts in a male infertility community, it is observed that posts by men had higher authenticity score, suggesting more honest or personal texts, but lower clout scores, suggesting a more tentative or anxious style of writing, compared with posts by women [14]. There are four types of social support men are offered and receive, namely appraisal, emotional, informational, and instrumental, with appraisal support being the most used to support other men [15]. These results suggest a role for physicians to engage with patients on these platforms and connect them to accurate resources, in addition to opportunities to improve in-office patient education [14]. However, it is also known that it is a challenge to implement such a platform [16]. MyFertiCare offers a forum where couples can communicate with peers, which is supervised by a clinician. It turned out to be a challenge to create and maintain a lively forum. A phenomenon which we encountered was that patients met each other on the forum, but then decided to leave the forum with their peers and continue their conversation on popular social media such as facebook or whatsapp communities. When we asked patients about their motivations they stated that the existing social media platforms are so embedded in their daily lives, that it was more convenient to continue the conversation on that platform. Although they appreciated the presence of a clinician on the myFertiCare forum, this was not enough motivation to continue the conversation there. This left us wondering: is it still feasible or even desired by patients in the current social media landscape to provide and moderate such a forum? To answer this question, more research should be done to study motivations of the parties involved and the effects on experienced support.

- *Performing structured evaluation*
  The use of technology in health care is driven mostly by the assumptions about the benefits of eHealth rather than its evidence [17]. It is important to conduct evaluation throughout the intervention. Reliable evidence generated through comprehensive evaluation of eHealth interventions can assure long-term successful implementation [17]. In the development of myFertiCare, evaluation was performed in different study phases. First, a qualitative usability evaluation was performed (chapter 3), which is critical to the success of adopting

an interactive eHealth application [18]. The think aloud method is preferred for uncovering usability flaws and to provide suggestions for modification of the design [19]. Second, a quantitative evaluation was performed to study successful implementation of the application on the human, organizational and technology domains (chapter 4). Furthermore, the effects of application usage were studied and user statistics were analyzed (chapter 4). We call for other parties who engage in eHealth development to perform structured evaluation of their initiatives so that transferability of their results among similar studies can be improved.

Part II

Don't forget about cancer survivors' specific information needs

Due to an increase in the incidence of malignant diseases and improved survival rates there is a growing group of young female cancer survivors [20]. These women carry on their cancer history for the rest of their lives. They can experience long-term side effects of their treatment and often deal with fear of cancer recurrence [21]. As a result they will always have more or less different information needs compared to their peers without an oncological history. Infertility can be one of the long-term side effects of oncological treatment [22]. Counseling about this risk and the possibility of fertility preservation before starting oncological treatment is known to increase quality of life after surviving cancer [23-25] and there is increasing awareness regarding the implementation of this counseling [22, 26-28]. However, there is little awareness regarding information needs on fertility and other topics during cancer survivorship. Therefore, we call for professionals not to forget about cancer survivors' specific information needs in their consultation room, in research and in policy making.

Development of online information for cancer survivors

Breast cancer is the most common cancer in women aged 15-39 years worldwide [29]. In the second part of this thesis the information needs of young breast cancer survivors regarding fertility and the risk of early menopause were studied and online information material was developed to meet these needs. This process was divided over several study phases (chapter 5):

1. Identification of relevant topics from a professional perspective
2. Identification of relevant topics from a patient perspective
3. Exploration of needs and preferences of stakeholders involved in breast cancer care regarding development and implementation of online information material
4. Development and implementation of the information

Based on the experience gained during these study phases the following recommendations regarding information provision for cancer survivors can be provided:

- *Include recommendations on information provision in oncological guidelines*
  Currently, the consequences of breast cancer treatment on fertility and the risk of early menopause are mainly discussed before the start of treatment and only occasionally during and after treatment, although women are clear about the need for this information (chapter 5). Professionals indicate that there are no guidelines on when to discuss these topics, or which information to provide (chapter 5). Therefore, we advocate the inclusion of recommendations on information provision about fertility and the risk of early menopause during cancer survivorship in oncological guidelines. These recommendations should state which information should be provided, by whom, when and to whom. This way, structured counseling during cancer survivorship will be facilitated.

- *Think about how to reach the intended population*
  When developing information material for cancer survivors, it is important to realize that the target population may not (regularly) have follow up appointments with their oncological healthcare providers anymore. Cancer survivors should be able to easily find the information themselves, without a healthcare provider to inform or guide them. In chapter 5 we aimed to overcome this hurdle by implementing the information on a nationwide website [www.kanker.nl] aiming at informing and supporting breast cancer patients that is supported by all major stakeholders who are involved in Dutch cancer care.

- *Provide complete and uniform information and ensure regular updating*
  In chapter 5, breast cancer survivors indicated that they searched for infertility and early menopause related information online, but they struggled to find reliable information specific to their situation as a young breast cancer survivor. In daily practice, patient information is often fragmented on different websites and aimed at a specific moment before or during treatment. The need to improve availability and quality of the information has been previously reported [29]. In order to provide complete and uniform information to the intended population and to make it easy to revisit the information on different moments during and after completing treatment, websites of nationwide platforms are very suitable. These national organizations have a lot of experience with large scale information provision and can initiate regular updating of the information. It is also important to involve healthcare insurers in these trajectories, since long-term financing of eHealth is challenging and requires a structural approach. The importance of information provision is also illustrated by the eleven key recommendations for high quality female oncofertility care that are selected by a multidisciplinary expert panel, in which information provision is an important aspect of all four domains [26]. However, the unavailability of written information, the lack of guidance after completing treatment and disagreement on who is

responsible for discussing the information are known barriers for the improvement of female oncofertility care [27, 29].

- *Be inclusive to patients with limited health literacy*
  Health literacy is defined as people's knowledge, motivation and competences to access, understand, appraise and apply health information in order to make judgments and take decisions in everyday life concerning health care to maintain or improve quality of life during the life course [30]. It is obvious to state that patient information should also be suited for people with limited health literacy. However, an analysis of the quality of information regarding female oncofertility on websites of (inter)national oncology, fertility and oncofertility organizations showed that no websites evaluated were at the recommended 7th-8th grade reading level [29]. Furthermore, research on shared decision making shows that in Dutch implementation projects, higher-educated persons are overrepresented, while patients with limited health literacy are underrepresented [31]. This is a major pitfall as 25% of the Dutch adult population have limited health literacy [32]. This percentage is comparable to the situation in the United States [33] and even relatively low compared to eight European countries, which report a prevalence of limited health literacy between 29% and 62% [34]. Furthermore, patients with limited health literacy are more likely to regret their chosen treatment compared to patients with higher health literacy [35]. It is therefore crucial that inclusion of patients with limited health literacy is at the forefront of information development.

METHODOLOGICAL CONSIDERATIONS

The most important strength of the research in this thesis is that we included patients, professionals and stakeholders in every study phase. Therefore it was possible to develop widely supported information materials. Development of the information materials was structured in various phases starting with identification of information needs, followed by design and development of the information material and concluding with implementation and evaluation.

Most of the research in this thesis (chapter 2, 3, 5) has a qualitative study design. Qualitative research methods are specifically suited to study unexplored complicated topics and to provide in-depth insight in the needs and preferences of participants. To assure data quality, the COREQ criteria guided study conduct and reporting [36]. Most important limitation of these qualitative methods is that selection bias can occur in terms of patients, professionals and stakeholders who choose to participate in the studies. As a result of this phenomenon, it is possible that individuals with strong opinions or emotions, or a high sense of urgency regarding the subject are more likely to participate in a study compared to individuals who have more neutral feelings or experience less urgency regarding the topic, who are more likely to decline to participate. However, this was considered not to influence the study results, since the aim of the studies was to explore all relevant aspects of information needs and preferences and not to quantify these aspects, which would require a quantitative study design.

In chapter 4 we also conducted a quantitative study evaluating the implementation of myFertiCare by using the HOT-fit framework. With validated questionnaires focusing on the human, organizational and technology domains successful implementation of the application could be studied. Furthermore, the effects of using myFertiCare on couples' knowledge about infertility, experienced burden of infertility and experienced patient-centered care were studied and user statistics were analysed. This type of quantitative eHealth evaluation is not common, but in our opinion crucial to assure successful long-term implementation of an application [17]. It would have been desirable to achieve a higher response rate for this study. However, there was good data consistency, which supports the reliability of the study data.

IMPLICATIONS FOR CLINICAL PRACTICE

In chapters 3 and 4, myFertiCare was designed, developed, implemented and evaluated. The framework that forms the basis of the application is currently being used in a variety of medical departments in 12 clinics throughout the Netherlands under the name of MediMapp (soulve.webflow.io). This has several advantages. Firstly, not every clinic has to develop their own eHealth application, but knowledge, experience and resources are centralized in one organization. It also assures that the framework can be continuously updated and improved. As a result, a growing number of patients has access to a qualitative sound eHealth application to guide them through their treatment trajectories. In the future, the use of MediMapp will be extended to a variety of medical departments in clinics throughout the Netherlands.

In chapter 5, information material regarding fertility and early menopause was developed and implemented on a nationwide website [www.kanker.nl] aiming at informing and supporting cancer patients. As a result, information tailored to young breast cancer survivors has become easily accessible for women throughout the Netherlands. Not only does this make an important contribution to patient-centered and uniform information provision for female breast cancer survivors, it also supports professionals in breast cancer care to meet the information needs and preferences of their patients. It would be beneficial for future clinical practice to add information specific for survivors of other oncological diagnoses, to provide options for easy updating of the information by professionals, and to extend the use of the information material to other countries.

IMPLICATIONS FOR POLICY MAKING AND FUTURE RESEARCH

We call for professionals in fertility care to equally involve male and female partners in their fertility treatment by developing more inclusive communication skills and by developing high-quality online sources of information. It would be interesting for future research to study the generalizability of our study results and the implementation of eHealth for the general subfertile population in the Netherlands as well as abroad.

In general, we advocate the involvement of patients during and after their treatment in both oncological research and oncological guideline development. In guideline development there should also be more focus on information provision in general and specifically about the topics of fertility and the risk of early menopause. We suggest future research to study the effect of our developed information material on the experienced information needs of breast cancer survivors. Furthermore, research should be done to explore the specific information needs regarding fertility and the risk of early menopause of patients during and after treatment for other oncological diagnoses.

FINAL CONCLUSION

This thesis focused on improving information provision in fertility care for two groups of patients with extensive information needs, namely couples undergoing ICSI with surgically retrieved sperm, and breast cancer survivors with reproductive concerns. Improving patient-centered information provision in the current era is inextricably linked with the development of eHealth tools. This need exists both from patients and healthcare providers.

In the development of eHealth tools it is crucial for researchers, medical and technical professionals, patients and healthcare insurers to collaborate in order to ensure complete, uniform, patient-centered and up-to-date information provision, and the protection of personal data. It would be beneficial for future practice if companies providing digital patient records take the lead in the development of eHealth tools that meet the needs of patients and healthcare providers, so that the tools incorporate patients' personal data and are also incorporated in professionals' daily practice.

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Summary - Samenvatting

SUMMARY

This thesis focused on research to improve information provision in fertility care for two groups of complex patients, namely couples undergoing intracytoplasmic sperm injection (ICSI) with surgically retrieved sperm, and breast cancer survivors with reproductive concerns. Because of the complexity of their treatment trajectories, the specific information needs of these patients are high. Meeting these information needs is an important aspect of patient-centered fertility care.

As we described in **Chapter 1**, assisted reproductive technologies (ART) are both physically and mentally stressful. Providing patient-centered fertility care is known to improve quality of life and can reduce anxiety and depression. Infertile couples consider patient information a very important dimension of patient-centered care. Patient-centered information provision can be improved by the use of eHealth tools. Within fertility care, ICSI with surgical sperm retrieval requires an invasive procedure from both the male and the female partner. The treatment trajectory involves a number of consecutive treatment phases and is therefore filled with insecurity for the couple. Because of the complexity of the treatment trajectory and the low success rate, the psychological impact is high. Therefore it is particularly important that couples receive adequate information before and during their treatment trajectory.

Cancer treatments like chemotherapy and radiation therapy can be gonadotoxic, leading to temporary or permanent infertility, or premature ovarian insufficiency later in life. Breast cancer is the most frequently diagnosed cancer among young women worldwide. Approximately half of premenopausal women diagnosed with breast cancer desire to conceive after they finish treatment. Counseling about the risk of infertility prior to cancer treatment has been proven to improve quality of life after cancer treatment. As a result of this, guidelines focus on informing women on this topic prior to treatment. However, it is equally important to provide fertility related information after primary treatment has been completed, when the wish to conceive might become actual.

In **Chapter 2**, we identified the information needs of couples undergoing surgical sperm retrieval and ICSI, including information content and the channels providing the information, as a first step to improve patient-centered care. A qualitative study was conducted, consisting of semi-structured interviews with 11 couples. The topic guide for these interviews was based on a literature review and interviews with an expert panel. The data were analyzed using a constant comparative method. The couples needed information about many topics. They considered information about the success rates of the treatment, an explanation of the treatment procedure, and other patient experiences the most important. Regarding information channels, the couples preferred face-to-face information, but they also valued a leaflet, website,

or an online application, especially when it is personalized or providing interactive functionalities.

As a second step to improve patient-centered care for couples undergoing surgical sperm retrieval and ICSI, in **Chapter 3** we developed a multifaceted application, called myFertiCare, that guides couples through their treatment. myFertiCare was developed in three phases: (1) we established a patient-centered functional design, (2) developed the application in collaboration with medical and technical professionals, and (3) qualitatively evaluated the application for usability among couples using a think-aloud method. The basis of myFertiCare is the couple's visualized treatment trajectory. The application provides personalized and interactive functionalities; for example, customized information and communication options. During qualitative evaluation, myFertiCare was highly appreciated and received a median score of 8 out of 10. The main improvements made upon conclusion of the think-aloud sessions were related to faster login and easier app navigation.

In **Chapter 4,** we quantitatively evaluated the implementation of myFertiCare and studied the effects of using myFertiCare on couples' knowledge about infertility, experienced burden of infertility and experienced patient-centered care. A quantitative study was performed based on the HOT-fit framework, using validated questionnaires focusing on the Human, Organizational and Technology domains. Questions were added on the effect of using myFertiCare on couples' knowledge about infertility and treatment. Questions regarding burden of infertility, burden of infertility treatment, and experienced patient-centeredness were based on the main items of the validated fertiQol, and PCQ-infertility questionnaires respectively. Also, non-users of the application were included to explore motivations for not using the application and identifying opportunities for improvement. Finally, user statistics were analyzed to provide insight into multiple variables concerning application usage. On the human and technology domain, myFertiCare showed good system usability, high user satisfaction and high information and interface quality. On the organizational domain, implementation was considered to be sufficient by both patients and staff. Usage of the application increased knowledge about the treatment, improved coping with treatment and enhanced experienced patient-centeredness. User statistics showed that women were the main application users and that usage of the application gradually declined during the treatment trajectory. We concluded that myFertiCare has been successfully implemented. By providing myFertiCare, professionals in fertility care are supported to guide patients through their treatment trajectory and to deliver patient-centered care.

In **Chapter 5**, our focus switched to the population of breast cancer survivors with reproductive concerns. The aim of this study was to identify the fertility and early menopause related information needs of young breast cancer survivors and to design, develop and implement online information material with input of stakeholders. A phenomenological qualitative study was conducted, consisting of four phases: identification of information needs through semi structured interviews from a professional perspective (1) and a patient perspective (2); exploration of stakeholders perspective regarding development and implementation of online information material (3) and development and implementation of the information material (4). Professionals indicated that there are no specific guidelines regarding the provision of fertility related information during breast cancer survivorship. Survivors reported unmet information needs. Women identified the following as most important information needs a) fertility preservation options, b) the risk of menopause or infertility, and c) long term consequences of early menopause. A wide range of stakeholders involved in breast cancer care were interviewed. Based on their proposed design the information material was implemented on a nationwide website aiming at informing and supporting breast cancer patients. We concluded that with the results of this study, young breast cancer survivors are provided with easily accessible information and professionals in breast cancer care are provided with an information tool that helps them meet the information needs and preferences of their patients.

Finally, in **Chapter 6** the main findings of this thesis and their clinical implications are discussed. In the development of eHealth tools it is crucial for researchers, medical and technical professionals, patients and healthcare insurers to collaborate in order to ensure complete, uniform, patient-centered and up-to-date information provision, and the protection of personal data. It would be beneficial for future practice if companies providing digital patient records take the lead in the development of eHealth tools that meet the needs of patients and healthcare providers, so that the tools incorporate patients' personal data and are also incorporated in professionals' daily practice.

SAMENVATTING

Dit proefschrift richt zich op het verbeteren van informatievoorziening voor twee complexe patiëntengroepen binnen de voortplantingsgeneeskunde, namelijk paren die een ICSI-behandeling ondergaan met chirurgisch verkregen zaadcellen, en jonge vrouwen die zich na een borstkankerbehandeling zorgen maken over hun vruchtbaarheid. De informatiebehoefte van deze patiënten is groot vanwege de complexe behandeltrajecten die zij doorlopen. Het voldoen aan deze informatiebehoefte is een belangrijk aspect van patiëntgerichte fertiliteitszorg.

Zoals beschreven in **Hoofdstuk 1**, zijn vruchtbaarheidsbehandelingen zowel fysiek als mentaal belastend. Het is bekend dat het verlenen van patiëntgerichte fertiliteitszorg de kwaliteit van leven van patiënten kan verbeteren en het optreden van angst en depressie kan verminderen. Paren met vruchtbaarheidsproblemen beschouwen patiënteninformatie als een zeer belangrijk onderdeel van patiëntgerichte zorg. Patiëntgerichte informatievoorziening kan verbeterd worden door het gebruik van eHealth. Een ICSI-behandeling waarbij gebruik wordt gemaakt van chirurgisch verkregen zaadcellen vereist een invasieve procedure bij zowel de man als de vrouw. Het behandeltraject bestaat uit een aantal opeenvolgende fasen en zorgt daardoor voor langdurige onzekerheid voor het paar. De psychologische impact van de behandeling is groot als gevolg van de complexiteit van het behandeltraject en de lage succeskansen. Dit maakt het in het bijzonder belangrijk dat paren adequate informatie ontvangen zowel voorafgaand aan als tijdens hun behandeltraject.

Oncologische behandelingen zoals chemotherapie en radiotherapie kunnen schadelijk zijn voor de vruchtbaarheid, leidend tot tijdelijke of permanente onvruchtbaarheid, of premature ovariële insufficiëntie later in het leven. Wereldwijd is borstkanker de meest gediagnosticeerde vorm van kanker onder jonge vrouwen. Ongeveer de helft van de premenopauzale vrouwen die gediagnosticeerd worden met borstkanker heeft een kinderwens na het afronden van de oncologische behandeling. Counseling met betrekking tot het risico op onvruchtbaarheid voorafgaand aan de behandeling heeft een positief effect op de kwaliteit van leven na de behandeling. Als gevolg hiervan focussen richtlijnen op het informeren van vrouwen met betrekking tot dit onderwerp ten tijde van de diagnose. Echter, het is net zo belangrijk om in informatie over vruchtbaarheid te voorzien nadat de behandeling is afgerond, aangezien dit het moment is waarop een kinderwens actueel kan worden.

Als eerste stap in het verbeteren van patiëntgerichte fertiliteitszorg hebben we in **Hoofdstuk 2** de informatiebehoeften geïdentificeerd van paren die een ICSI-behandeling met chirurgisch verkregen zaadcellen ondergaan, zowel wat betreft de inhoud van de informatie als de manier waarop deze informatie aangeboden moet worden. We hebben een kwalitatieve studie uitgevoerd, die bestond uit semigestructureerde interviews met 11 paren. De te bespreken onderwerpen voor deze interviews waren gebaseerd op een literatuurstudie en op voorafgaande interviews met een panel van professionals binnen de voortplantingsgeneeskunde. De data werden geanalyseerd met een kwalitatief analyseprogramma. De paren hadden behoefte aan informatie over veel verschillende onderwerpen. Het meest belangrijk vonden zij informatie over de succeskansen van de behandeling, een uitleg over de procedure van de behandeling, en de ervaringen van andere patiënten. De paren hadden een voorkeur voor face-to-face informatie, maar zij waarderen ook een papieren folder, een website, of een app, met name wanneer deze gepersonaliseerd zijn of interactieve functionaliteiten bevatten.

Als tweede stap in het verbeteren van patiëntgerichte zorg voor paren die een ICSI-behandeling met chirurgisch verkregen zaadcellen ondergaan, hebben we in **Hoofdstuk 3** myFertiCare ontwikkeld. MyFertiCare is een veelzijdige app die paren begeleid door hun behandeltraject. De ontwikkeling van myFertiCare verliep in drie fasen: (1) we ontwikkelden een patiëntgericht functioneel design, (2) we ontwikkelden de app in samenwerking met medische- en technische professionals, en (3) we evalueerden de gebruiksvriendelijkheid van de applicatie middels een kwalitatieve think-aloud methode. De basis van myFertiCare wordt gevormd door het gevisualiseerde behandeltraject van het paar. De applicatie biedt gepersonaliseerde en interactieve functionaliteiten, zoals gepersonaliseerde informatie en mogelijkheden tot communicatie met professionals en lotgenoten. Uit de kwalitatieve evaluatie bleek dat myFertiCare zeer gewaardeerd werd door paren. De applicatie kreeg een score 8 op een schaal van 1 tot 10. De belangrijkste verbeteringen die werden doorgevoerd naar aanleiding van de kwalitatieve evaluatie betroffen de mogelijkheid tot sneller inloggen in de applicatie en vereenvoudigde navigatie door de applicatie.

In **Hoofdstuk 4** hebben we de implementatie van myFertiCare kwantitatief geëvalueerd en hebben we de effecten onderzocht van het gebruiken van myFertiCare op de kennis die paren hebben over onvruchtbaarheid, op de belasting die zij ervaren als gevolg van hun onvruchtbaarheid en de behandeling, en op de mate waarin zij patiëntgerichte zorg ervaren. De kwantitatieve onderzoeksopzet was gebaseerd op het HOT-fit model, waarbij gevalideerde vragenlijsten werden gebruikt gericht op het menselijke (Human), organisatorische (Organizational) en technologische (Technology) domein. Tevens werden vragen toegevoegd over het effect van het gebruiken van myFertiCare op de kennis die paren hebben over onvruchtbaarheid en vruchtbaarheidsbehandelingen. Vragen met betrekking tot de belasting die paren ervaren als gevolg van hun onvruchtbaarheid en de vruchtbaarheidsbehandeling, en de mate waarin zij patiëntgerichte zorg hebben ervaren, waren gebaseerd op de belangrijkste onderdelen van respectievelijk de gevalideerde fertiQol en PCQ-infertility vragenlijsten. Ook werden niet-gebruikers van de applicatie geïncludeerd in de studie om inzicht te krijgen in hun motivatie en in mogelijkheden tot verbetering.

Tenslotte werden gebruikersstatistieken geanalyseerd om inzicht te verkrijgen in verschillende variabelen met betrekking tot het gebruik van myFertiCare. Op het menselijke en technologische domein bleek myFertiCare gebruiksvriendelijk te zijn, bleken patiënten tevreden met de app, en bleek de kwaliteit van de informatie en de interface hoog. Op het organisatorische domein bleek myFertiCare volgens zowel patiënten als medewerkers voldoende geïmplementeerd in de praktijk. Het gebruik van myFertiCare vergrootte de kennis van paren over de behandeling, verbeterde de coping met de behandeling en vergrootte de mate waarin paren patiëntgerichte zorg ervaren. Gebruikersstatistieken lieten zien dat vrouwen de meest frequente gebruikers van myFertiCare waren en dat het gebruik van de applicatie langzaam afnam gedurende het behandeltraject. We concludeerden dat myFertiCare succesvol is geïmplementeerd. Door het aanbieden van myFertiCare worden professionals in de voortplantingsgeneeskunde geholpen om hun patiënten door het behandeltraject te begeleiden en om patiëntgerichte zorg te leveren.

In **Hoofdstuk 5** hebben we onze focus verlegd naar jonge vrouwen die na een borstkankerbehandeling vragen hebben over hun vruchtbaarheid. Het doel van deze studie was het identificeren van de informatiebehoeften met betrekking tot vruchtbaarheid en vervroegde menopauze van jonge vrouwen na een borstkankerbehandeling en om online informatiemateriaal te ontwikkelen en te implementeren in samenwerking met direct betrokkenen in de zorg voor deze vrouwen. Een fenomenologische kwalitatieve studie werd opgezet, bestaande uit 4 fasen: identificatie van informatiebehoeften middels semigestructureerde interviews vanuit het perspectief van de professional (1) en het perspectief van de patiënte (2); exploratie van het perspectief van direct betrokkenen in de zorg voor deze vrouwen met betrekking tot de ontwikkeling en implementatie van online informatiemateriaal (3) en de ontwikkeling en implementatie van dit informatiemateriaal (4). Professionals gaven aan dat er geen specifieke richtlijnen zijn met betrekking tot het geven van informatie over vruchtbaarheid na een borstkankerbehandeling. Patiëntes gaven aan dat huidige informatievoorziening onvoldoende in hun behoeften voorziet. De belangrijkste onderwerpen waarover vrouwen informatie wilden waren a) mogelijkheden tot behoud van de vruchtbaarheid, b) het risico op onvruchtbaarheid of vervroegde menopauze, en c) de lange termijn consequenties van een vervroegde menopauze. Verschillende betrokkenen in de zorg voor jonge vrouwen met borstkanker werden geïnterviewd over hun visie op het ontwerp van online informatiemateriaal. Gebaseerd op de resultaten van deze interviews werd online informatiemateriaal ontwikkeld en geïmplementeerd op kanker.nl, een landelijke website gericht op het informeren en ondersteunen van mensen met kanker. We concludeerden dat met de resultaten van dit onderzoek jonge vrouwen na een borstkankerbehandeling zijn voorzien van makkelijk toegankelijke online informatie over vruchtbaarheid en dat professionals in de zorg voor vrouwen met borstkanker worden ondersteund om in de informatiebehoeften van hun patiënten te voorzien.

Tenslotte worden in **Hoofdstuk 6** de belangrijkste bevindingen uit dit proefschrift en de klinische implicaties daarvan bediscussieerd. In de ontwikkeling van eHealth is het cruciaal dat onderzoekers, medische- en technische professionals, patiënten en verzekeraars samenwerken om te zorgen voor volledige, uniforme, patiëntgerichte en up-to-date informatievoorziening, en om te zorgen voor bescherming van patiëntgegevens. Wij pleiten ervoor dat bedrijven die elektronische patiëntendossiers aanbieden de leiding nemen in de ontwikkeling van eHealth tools die voorzien in de behoeften van zowel patiënten als zorgprofessionals, zodat deze eHealth tools medische gegevens van patiënten kunnen incorporeren en ook ingebed zijn in de dagelijkse praktijk van zorgprofessionals.

&

Appendix

Abbreviations
Research data management
PhD portfolio
Bibliography
Curriculum Vitae
Dankwoord

ABBREVIATIONS

ART	Assisted Reproductive Technology
CSUQ	Computer System Usability Questionnaire
DigiD	Digital Identity
Et al.	Et Alii, And Others
EUCS	End-User Computing Satisfaction
HOT-fit	Human Organization Technology-fit
ICSI	Intracytoplasmic Sperm Injection
IVF	In Vitro Fertilisation
POI	Premature Ovarian Insufficiency
RUMC	Radboud University Medical Center
SUS	System Usability Scale
TESE	Testicular Sperm Extraction

RESEARCH DATA MANAGEMENT

This thesis is based on the results of human studies which were conducted in accordance with the principles of the Declaration of Helsinki, the Medical Research Involving Human Subjects Act (WMO), the Guideline for Good Clinical Practice, and all other applicable regulatory requirements.

For all studies in this thesis (chapters 2-5) ethical approval was proposed but was not required according to the Medical Research Ethics Committee of Arnhem-Nijmegen as they were non-WMO-obligatory (chapter 2 reference number 2015-1591; chapter 3 reference number 2016-2485; chapter 4 reference number 2017-3538; chapter 5 reference number 2015-1779). In addition, three local ethical committees for patient-related research confirmed this (Rijnstate Hospital, Jeroen Bosch Hospital, University Medical Center Groningen) for the study conducted in chapter 5.

This research project is stored in the digital research environment of the Radboudumc. All study participants provided written informed consent to participate in all of our studies. The hard copies of the informed consent files and of the surveys were stored in the department archive of the Radboudumc.

The privacy of the study participants is warranted by use of unique individual subject codes for data analysis. Members of the research team have access to the key of the code. This key of the code was stored separately from the study data, also in the digital research environment.

The data will be saved for 15 years after termination of the studies. Using these patient data in future research is only possible after renewed permission by the patient as recorded in the informed consent. These data analysed during these studies are available from the corresponding author on reasonable request.

PHD PORTFOLIO of Ellen Marie Sparidaens

Institute for Health Sciences
Radboudumc

Department: **Obstetrics and Gynaecology**
Graduate School: **Radboud Institute for Health Sciences**
PhD period: **17-11-2014 – 26-07-2022**
Promotor(s): **Prof. dr. D.D.M. Braat, Prof. dr. R.P.M. Hermens**
Copromotor(s): **Dr K. Fleischer, Dr. C.C.M. Beerendonk**

Training activities	Hours
Courses	
PubMed workshop (2015)	2.00
RIHS - Introduction course for PhD candidates (2015)	15.00
Radboudumc - eBROK course (for Radboudumc researchers working with human subjects) (2015)	26.00
Endnote workshop (2015)	2.00
RU - Kinderen enthousiasmeren voor Wetenschap (2015)	42.00
ESHRE precongress course (2015)	8.00
RU - The Art of Presenting Science (2015)	36.00
RU - Qualitative Research Methods and Analysis (2016)	84.00
RU - Scientific Writing for PhD candidates (2016)	84.00
Radboudumc - Scientific integrity (2017)	20.00
Seminars	
Research Round theme Women's Cancers (2014-2017)	28.00
Conferences	
Space4AYA, Amsterdam (2015)	8.00
Annual conference of the Dutch-Belgian Reproductive Research Society, Antwerpen (2015)	8.00
ESHRE annual meeting, Lisbon, poster presentation (2015)	35.00
Symposium on Cryopreservation, Elsendorp (2017)	8.00
ESHRE annual meeting, Barcelona, poster presentation and poster discussion (2018)	35.00
Annual conference of the Dutch-Belgian Reproductive Research Society, Tilburg, oral presentation (2018)	8.00
Symposium Dutch Menopause Society, Houten (2018)	8.00
National fertility specialists division day (VVF symposium) (2015-2021)	56.00
Other	
Journal club/scientific meetings reproductive medicine (2014-2017)	56.00
Lecture for gynaecologists, gynaecology residents and medical students (2015-2017)	4.00
Peer-reviewing medical paper related to eHealth development (2021)	14.00

Teaching activities	Hours
Supervision of internships / other	
Mentoring Bachelor student for excellent student programme (2nd year of Medicine) (2015)	28.00
Supervision of 2 student-assistants (2015)	28.00
Supervision of 3 Master students for research internship (6th year of medicine) (2016-2018)	336.00
Supervision of 2 Master students for consultancy internship (Faculty of Arts) (2016, 2019)	224.00
Total	**1,203.00**

Radboud University

Radboudumc
university medical center

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CURRICULUM VITAE

Ellen Marie Sparidaens werd op 30 december 1989 geboren in Goirle als dochter van Ronald en Marie-José Sparidaens en groeide op in Tilburg. Na het cum laude behalen van haar vwo-diploma aan het Theresialyceum te Tilburg, startte zij met de studie Geneeskunde aan de Radboud Universiteit te Nijmegen.

Haar aanvankelijke plan om huisarts te worden, stelde zij bij toen ze tijdens haar coschap Gynaecologie en Verloskunde haar interesse voor dit vak, en in het bijzonder voor de voortplantingsgeneeskunde, ontdekte. Vanaf dat moment startte zij als student met wetenschappelijk onderzoek binnen de gynaecologie onder begeleiding van dr. Bekkers in het Radboudumc te Nijmegen. Haar interesse voor de gynaecologie werd bevestigd tijdens haar senior coschap in het Elisabeth-TweeSteden ziekenhuis te Tilburg. Tijdens haar wetenschappelijke stage in het Radboudumc deed zij voor het eerst onderzoek naar informatiebehoeften in de voortplantingsgeneeskunde onder begeleiding van dr. Nelen. Hier groeide ook haar interesse in de wetenschap.

Na het behalen van haar artsenbul in november 2014 mocht Ellen Marie het onderzoek uit haar wetenschappelijke stage voortzetten in de vorm van een promotieonderzoek, wat heeft geresulteerd in dit proefschrift. Het promotietraject werd begeleid door prof. dr. Braat, dr. Nelen, dr. Beerendonk en dr. Fleischer. Tijdens het traject nam prof. dr. Hermens de begeleiding van dr. Nelen over.

Kort na de start van haar promotieonderzoek startte zij ook als fertiliteitsarts in het Radboudumc. Na nog ervaring te hebben opgedaan in het Amphia ziekenhuis te Breda, werkt zij inmiddels sinds 2019 als fertiliteitsarts in het Centrum Voortplanting Brabant, onderdeel van het Elisabeth-TweeSteden ziekenhuis te Tilburg. Het is haar passie om mensen voor wie een zwangerschap niet vanzelfsprekend is, zo goed mogelijk te begeleiden.

Ellen Marie is getrouwd met Martin en samen met hun zoon Ferre (2016) en dochter Madée (2020) wonen zij in Tilburg.

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Dit proefschrift was er niet geweest zonder de hulp en steun van velen. Graag wil ik iedereen bedanken die heeft bijgedragen aan mijn promotietraject. Een aantal personen wil ik hierbij in het bijzonder bedanken.

In de eerste plaats wil ik alle patiënten bedanken die hebben deelgenomen aan de onderzoeken uit dit proefschrift. Jullie hebben de moeite genomen om je in een stressvolle fase in jullie leven in te zetten voor het verbeteren van zorg. Onderzoek doen naar patiëntgerichte informatievoorziening was uiteraard nooit mogelijk geweest zonder jullie inbreng. Ik hoop dat we met de resultaten van dit proefschrift een bijdrage zullen leveren aan de zorg voor de patiënten die na jullie komen.

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Professor R.P.M.G. Hermens, beste Rosella, jij werd pas halverwege het traject aan mijn promotieteam toegevoegd, maar nam je rol direct serieus. Ondanks dat de meeste onderzoeken al waren opgestart zonder jouw inbreng, wist jij in no-time precies waar ik mee bezig was en wist je waardevolle adviezen te geven. Jouw bijdrage is onmisbaar geweest. Zonder jouw kennis en ervaring met kwalitatieve onderzoeksmethoden was dit proefschrift er niet in deze vorm geweest. Bedankt voor de uitgebreide feedback die je altijd op mijn artikelen hebt gegeven, hiervan werden de stukken per definitie beter. Niet in de laatste plaats bedankt voor je interesse in mij als persoon.

Dr. K. Fleischer, beste Kathrin, met jouw kritische blik weet je feilloos knelpunten in een studie aan te wijzen. Je hebt niet alleen oog voor de inhoud van een artikel, maar de ‘schwung’ vind je net zo belangrijk. Dank voor jouw bijdrage aan dit traject. Ook wil ik je bedanken voor de kans die ik heb gekregen om ervaring als fertiliteitsarts op te doen. Ik hoefde geen drempel te voelen om je te bellen wanneer ik met een lastige punctie bezig was. Jij nam de tijd en in plaats van het over te nemen, leerde je me hoe ik het alsnog zelf kon doen. Van deze vaardigheden heb ik nog steeds profijt.

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