KU Leuven

Biomedical Sciences Group

Faculty of Pharmaceutical Sciences

Department of Pharmaceutical & Pharmacological Sciences

Developing a patient decision aid to improve shared decision making in breast cancer

Niki VER DONCK

Supervisor	Prof. Isabelle Huys
Co-supervisor	dr. Sarah Verschueren
Chair	Prof. Pieter Annaert
Jury members	Prof. Trudy van der Weijden
	Prof. Jeroen Mebis
	Prof. Karin Slegers
	dr. Irina Cleemput

Dissertation presented in partial fulfilment of the requirements for the degree of Doctor in Pharmaceutical Sciences

December 2020

DANKWOORD

Een doctoraat maken voelt aan als het maken van een lange reis. En net als bij reizen, is het niet alleen waar je naartoe trekt, maar vooral met wie je je reis deelt, wat de ervaring memorabel zal maken. Daarom wil ik hier graag iedereen bedanken die bepaalde etappes of de volledige weg met mij hebben meegereisd.

Allereerst wil ik graag mijn gids tijdens deze lange tocht bedanken. Isabelle, bedankt om de voorbije vier jaar mijn promotor te zijn, je deed dat geweldig! Bedankt om mij vertrouwen en kansen te geven, vanaf het moment dat je mij als masterstudent voorstelde om een doctoraat te starten en tijdens alle momenten nadien. Je kan luisteren als geen ander en de manier waarop je steeds voor iedereen het beste tracht te doen, bewonder ik enorm. Jouw enthousiasme en aanmoediging zorgden ervoor dat ik elke uitdaging op mijn pad kon aangaan.

Daarnaast wil ik graag mijn co-promotor Sarah bedanken. Jouw constructieve feedback en *down-to-earth* aanpak apprecieerde ik ten zeerste. Graag bedank ik ook Ine, die in het begin van het project de rol van co-promotor op zich heeft genomen en altijd haar enthousiasme voor dit project met mij gedeeld heeft.

Vervolgens bedank ik ook graag alle juryleden wiens opmerkingen en feedback een belangrijke meerwaarde hebben gegeven aan dit doctoraat. Prof. Pieter Annaert, prof. Karin Slegers en dr. Irina Cleemput, hartelijk dank voor jullie interessante opmerkingen en wetenschappelijk advies gedurende de voorbije vier jaar. Bedankt om tijd te maken voor mij wanneer ik bepaalde aspecten meer in detail wilde bespreken. Prof. Trudy van der Weijden en prof. Jeroen Mebis, hartelijk dank voor jullie welwillendheid om mijn thesis na te lezen en het stellen van kritische vragen.

Dit doctoraat zou niet mogelijk geweest zijn zonder de hulp en waardevolle inzichten van heel wat experten. Graag bedank ik prof. Patrick Neven om te geloven in de meerwaarde van een beslishulp voor patiënten en zijn wetenschappelijke bijdrage aan de inhoud ervan. Verder bedank ik ook graag Melissa Reymen om mijn project mee te ondersteunen vanuit UZ Leuven. Jouw praktijkkennis was een geweldige bijdrage voor zowel de inhoud als de vorm van de beslishulp die we ontwikkelden. Mijn dank gaat ook uit naar dokter Josephine Van Cauwenberge, zonder wie de realisatie van hoofdstuk 5 niet mogelijk was geweest. Josephine, bedankt om zo sterk in het project te geloven! Jouw inzet en enthousiasme hebben het testen van de beslishulp in de praktijk mogelijk gemaakt. Verder bedank ik ook graag Lienke Vandezande voor de fijne samenwerking en coördinatie zodat mijn project gelijktijdig met andere projecten kon uitgevoerd worden in UZ Leuven.

Aangezien een beslishulp maar gebruikt kan worden in de praktijk als hij voldoet aan de noden en wensen van zowel patiënten als zorgverleners, bedank ik heel graag iedereen die ik heb mogen interviewen tijdens mijn doctoraat. Bedankt aan alle patiënten die tijd hebben vrijgemaakt en hun persoonlijke ervaringen wilden delen. Mijn dank gaat ook uit aan alle lotgenotengroepen die deelname aan mijn project stimuleerden. Bedankt tot slot aan alle artsen en verpleegkundigen, voor de tijd die jullie vrijmaakten en de waardevolle input die jullie bezorgden.

Gelukkig kon ik mijn reis delen met heel wat medereizigers, die erbij waren om alle successen mee te vieren maar die ook hulp of een luisterend oor boden wanneer het nodig was. Bedankt Alessandra, Ciska, Elfi, Eline, Evelien DS., Evelien M., Jane, Janne, Khadidja, Kim, Laurenz, Liese, Rosanne, Stefanie, Robbe, Sissel, Steven, Teodora, Teresa, Tim en Yannick. Speciale vermelding voor de collega's met wie ik het hele traject samen heb kunnen afleggen: Ciska, Eline, Evelien, Liese, Laurenz en Rosanne. Bedankt voor alle fijne momenten op en naast het werk (zeker de congressen samen waren fantastische ervaringen!) en de hulp bij het uitzoeken van zowel praktische als inhoudelijke aspecten die we op onze weg tegenkwamen.

Aangezien ik mijn doctoraat uitvoerde onder de vorm van een Baekeland mandaat, wil ik ook de bedrijven ISMS en Mindbytes bedanken voor de kans en ondersteuning die ze mij geboden hebben. Ook hier kon ik rekenen op hele fijne collega's; Aldo, Charlotte, Evi, Leni, Joke, Michelle, Minou, Sara, Sofie, Tine, Tinne en Wim; bedankt voor alles wat jullie mij geleerd hebben en bedankt voor alle fijne momenten tijdens en na het werk. Graag wil ik Evi extra bedanken voor de inhoudelijke ondersteuning, Leni voor het nalezen van manuscripten en het ontwerpen van de cover van dit boekje, Joke voor alles wat ik geleerd heb over het maken van e-learnings en Wim om een luisterend oor en wijze raad te bieden telkens ik die nodig had. Jullie waren allemaal fantastisch en ik had deze reis nooit kunnen afmaken zonder jullie!

Graag wil ik ook mijn vrienden bedanken om mij op tijd en stond af te leiden van het werk, maar ook om te luisteren wanneer ik even mijn hart wilde luchten en mij aan te moedigen wanneer nodig. Speciale dank aan Annelies, Femke, Laura, Leen, Lies, Liese, Marjan, Rani L., Rani F., Silke en Vizinha. Ook bedankt aan alle anderen die ik hier niet bij naam kan noemen, jullie zorgden voor heel wat geweldige momenten die de voorbije vier jaar zoveel aangenamer maakten.

Tot slot wil ik mijn familie bedanken, niet alleen voor de onvoorwaardelijke steun de voorbije vier jaar, maar simpelweg voor *alles*. Fabienne, bedankt om altijd je enthousiaste zelf te zijn en om vier jaar lang te luisteren naar alles wat goed en minder goed ging tijdens mijn doctoraat; ik kijk er naar uit om voor jou hetzelfde te blijven doen de komende jaren! Graag wil ik ook mijn ouders bedanken om mij te steunen in elke uitdaging die ik aanga en om me te doen geloven dat ik deze uitdagingen ook werkelijk tot een goed einde kan brengen. Papa, bedankt om de studie in hoofdstuk 5 te redden met jouw technische ondersteuning en mama, bedankt om mij aan te moedigen om vol te houden op die momenten dat ik bijna klaar was om aan het hele project de brui te geven. Zonder jullie aanmoediging had ik nooit apotheker of doctor kunnen worden. Verder bedank ik ook graag mijn schoonouders voor alle aanmoedigingen en goede raad de voorbije vier jaar.

Het is een reis geweest met veel ups en downs en er is één persoon die deze allemaal van wel heel dichtbij heeft meegemaakt. Arne, bedankt om mij eindeloos aan te moedigen, naar mijn frustraties en gezaag te luisteren en mij *nog wat meer* aan te moedigen wanneer nodig. Er is geen betere remedie om het werk even te vergeten dan plannen maken en uitvoeren met jou (en het waren er veel de voorbije vier jaar!). Ik had het gewoonweg niet zonder jou gekund, bedankt om er altijd te zijn.

- Niki –

You are braver than you believe,
stronger than you seem,
and smarter than you think.

- A. A. Milne -

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

AJCC	American Joint Committee on Cancer
BWS	Best-worst scaling
CA	Conjoint analysis
COVID-19	Coronavirus disease 2019
DCE	Discrete Choice Experiment
DCIS	Ductal carcinoma in situ
DCS	Decisional conflict scale
EMA	European Medicines Agency
EUPATI	European Patients' Academy
FDA	Food and Drug Administration
FDE	Feedback-driven Exploration
HTA	Health technology assessment
IPDAS	International Patient Decision Aid Standards
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
KCE	Belgian Health Care Knowledge Centre
LCIS	Lobular carcinoma in situ
MDIC	Medical Device Innovation Consortium
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHDI	National Institute for Health and Disability Insurance
PtDA	Patient Decision Aid
PREFER	Patient preferences in benefit-risk assessments during the drug life cycle
QALY	Quality-adjusted life year
SADR	Separated Adaptive Dual Response
SDM	Shared decision making
SDM-Q-9	9 Item Shared Decision Making Questionnaire
SDR	Separated dual response
TNM	Tumour-node-metastasis
US	United States
UZ	University hospital
VAS	Visual Analogue Scale
VCM	Value clarification method
VLAIO	Flanders Innovation and Entrepreneurship

LIST OF TABLES

LIST OF FIGURES

GENERAL INTRODUCTION

1 SHARED DECISION-MAKING

1.1 ORIGINS OF THE CONCEPT SHARED DECISION MAKING

Traditionally, the most adopted approach for treatment decision making is the paternalistic model, in which the treating physician assumes the dominant role [1, 2]. This model was built on certain assumptions, such as the fact that for most diseases, one single superior treatment option could be identified. Furthermore, in contrast to their patients, physicians possessed the required medical knowledge to make treatment decisions and they had the ethical obligation to act in their patient's best interest [1, 3, 4]. Gradually, these assumptions were questioned, as for many health care problems no single best treatment option could be identified. Moreover, as more treatment options became available, more complex benefit-risk tradeoffs had to be made to select the best possible treatment for every patient [1]. At the same time, a shift occurred from acute care to chronic care, causing patients to experience the impact of both their disease and treatment for a longer period of time [2]. The understanding grew that as patients have to deal with the effects of their medical condition and treatment every day, they are best placed to weigh different benefits and risks and make these tradeoffs [5, 6]. From an ethical perspective, the principle of patient autonomy has been advocated to be equally important as the principles of beneficence and doing no harm to a patient [7, 8]. As a counter reaction to the paternalistic model, a paradigm shift occurred creating both the models of informed decision making and **shared decision making** (SDM) [9, 10]. These models aim to decrease the power asymmetry between patients and physicians by adequately informing patients and empowering them to take control of treatment decisions that impact their quality of life [2]. Within the model of informed decision making, the physician shares medical information on the disease and treatment benefits and risks with the patient, allowing the patient to take control of the decision-making process and making a treatment decision. The physician's treatment preferences for the patient are not included in the decision making [2]. The patient then considers the options and is the sole decision maker. Within the model of SDM on the other hand, the patient and the physician share both medical information and personal preferences; they discuss the potential treatment options and personal preference for potential benefits, risks and uncertainty related to these aspects. They should also discuss the patient's desire for involvement in the decision-making, make or defer the decision and arrange follow-up if applicable [1, 7]. Figure 1 provides an overview of these three decision-making models.

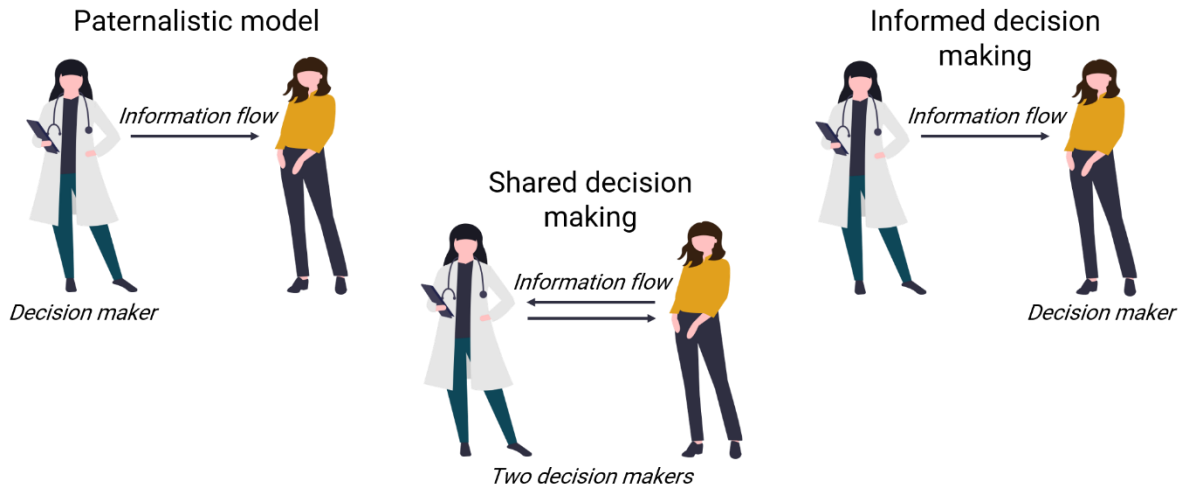

Figure 1: Medical decision models[1]

1.2 When to apply shared decision making

How to decide when each of the presented decision making models should be applied in practice? It is clear that differing circumstances ask for different approaches to make treatment decisions [9]. In emergency situations, when difficult decisions have to be made in a short time, the paternalistic model may still be the preferred one, or even the only one feasible given the situation [2]. On the other side of the spectrum, informed decision making occurs, for example in case of informed consent by patients before they can enrol in clinical studies [11]. In this case, it is indispensable that patients are adequately informed on all aspects related to the study and of the fact that they have the right to refuse participation or can withdraw consent at any time without reprisal [11]. The medical information flow should go from the physician, who may not share his/her personal preferences for the patient, towards the patient, who is the sole decision maker [1]. The more difficult medical decisions are situated somewhere in between; when there is no clear single best decision; when the evidence supporting certain options is considerably uncertain; or when the tradeoffs between potential benefits and risks depend on individual preferences and may vary greatly between patients and physicians [6, 7]. In these cases, that are referred to as '**preference-sensitive' decisions**', SDM would be the optimal model to make treatment decisions [6, 12]. Indeed, in many health care decisions, two or more options can be medically appropriate with none of them clearly being superior[6]. Moreover, since patients are directly confronted with the consequences of their individual treatment decisions, their assessment of treatment benefits and risks is particularly important[5]. This emphasizes the need for information sharing during decision making; patients need evidence-based information on benefits and risks and physicians need to know the patient's preferences related to these aspects[13]. In 2010, 58 people

from 18 different countries have participated in a Salzburg Global Seminar and issued a statement to call on *both* patients *and* clinicians to engage in SDM [14].

1.3 How to apply shared decision making

Stiggelbout *et al*. refined the process of SDM that was earlier presented by Elwyn *et al*., by distinguishing four sequential steps [7, 15]. First, the physician informs the patient that a decision has to be made and that the patient's opinion and preferences are important to include. Second, the physician explains the potential options and informs the patient on the benefits, risks and uncertainty related to every option. Third, the patient and the physician discuss the patient's preferences, at which the physician may support the patient in weighing different benefits and risks. Finally, the patient and physician discuss the patient's preferred role in the decision making, they make or defer the decision and they discuss the need for follow-up [7]. During this process it is crucial to provide patients with high quality information and to elicit whether what they already know is actually correct [15]. These are important conditions to guarantee that patients can consider what matters most to them and can construct informed preferences. In order to present all required information in a clear and unbiased manner and to support patients to form and articulate preferences in the best possible way, **patient decision aids** (PtDAs) can be used [12].

2 Patient decision aids

2.1 Aims and qualifying criteria for patient decision aids

PtDAs are tools designed to help patients participate in medical decision making, by (I) making the decision explicit and providing evidence-based information to patients on their condition, potential health care options and their features; (II) helping them to clarify their values and preferences; and (III) supporting them to communicate these preferences to their health care providers [16, 17]. PtDAs should supplement, rather than replace the interaction between a patient and health care provider during consultations [18]. They can be used either before, during or after a consultation to engage patients in their medical decision making. If the PtDA is provided some time before a consultation, patients will have more time to let the acquired information sink in and discuss the decision with whomever they like, however, this is not feasible in every decision context [12]. PtDAs can appear in various formats, ranging from leaflets to audio tapes, videos or even interactive digital applications [18]. They differ from general health education materials, because they can be tailored to a specific person's health situation and decision needs, explicitly preparing him/her for decision making. General health education materials aim to inform people on their diagnosis, treatment and health

management but they are not focused on specific decisions [12, 19]. As PtDAs may influence a patient's choice, the development of PtDA should be performed according to recognized scientific methods to avoid bias. With the goal of establishing a quality framework for PtDAs, the International Patient Decision Aids Standards (IPDAS) Collaboration was created in 2003 [18]. They conducted a two stage Delphi process involving researchers, practitioners, patients and policy makers, to determine the importance of potential quality criteria. This research resulted in a checklist with 74 quality criteria covering 12 different domains for the development and assessment of PtDAs. The quality domains can be attributed to three main categories: content, development process and effectiveness. 'Content-related' quality criteria are context-specific to the health decision that is covered by the PtDA, whereas the categories 'development process' and 'effectiveness' contain generic criteria that are relevant for all PtDAs [18]. Table 1 provides an overview of the different quality criteria within each category.

Table 1: 12 quality dimensions of the International Patient Decision Aids Standards Checklist

Content	Development process	Effectiveness
I. Providing information about options II. Presenting probabilities III. Including methods for clarifying and expressing values IV. Including guidance or coaching in deliberation and communication	I. Balancing the presentation of options II. Having a systematic development process III. Basing information on up to date scientific evidence IV. Disclosing conflicts of interest V. Using plain language VI. Using patient stories VII. Delivering patient decision aids on the internet	I. Establishing effectiveness - Decision process - Decision quality

To establish the effectiveness of PtDAs, evidence is required that both the **process of decision making** and the **quality of the choice made** are improved [20]. See figure 2 for constructs related to both aspects. A Cochrane analysis from 2017 found that PtDAs increase patients' knowledge and their accuracy of risk perception and improve the congruency between patient's informed values and the decision option chosen compared to standard care [12]. Furthermore, PtDAs decreased decisional conflict related to feeling uninformed and indecision about personal values, and reduced the proportion of people who did not actively engage in decision making. Finally, PtDAs reduced the number of patients that were undecided and positively impacted the patient-physician communication as patients who used a PtDA were equally or more satisfied with both their decision making process and final decision [12]. Potential instruments that can be used to assess key constructs related to the decision process and decision quality were examined by Sepucha *et al.* [20]. Examples include the decisional conflict scale (DCS) to assess the constructs 'feel informed' and 'feel clear about values' or

the perceived involvement in care scale (PICS) to assess 'recognize decision' and 'discuss goals with health care provider'. They concluded that although the evidence base for these instruments is strong and growing, there is no consensus on which instruments should be used when. Moreover, no single instrument is capable of assessing all constructs related to either decision process or decision quality [20].

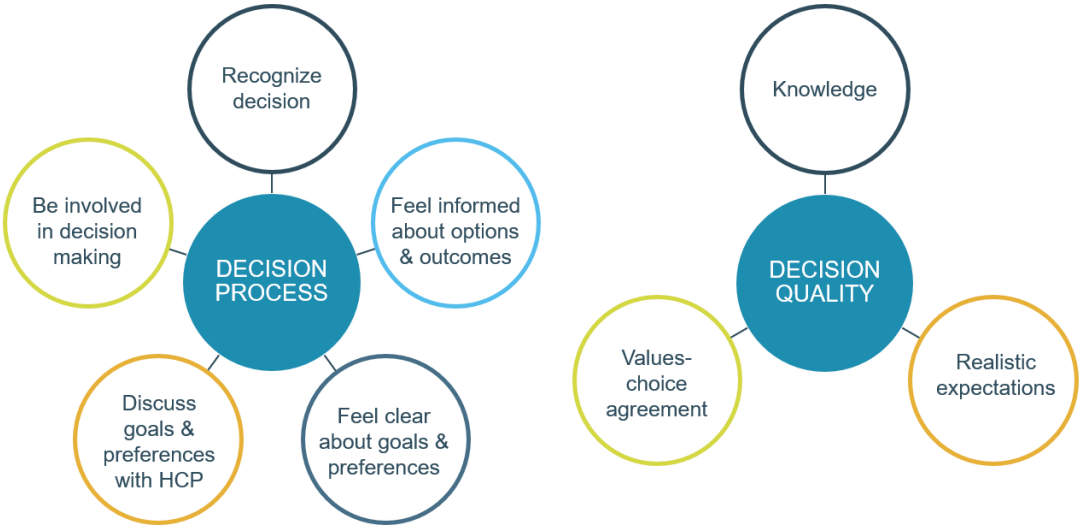

Figure 2: Key constructs used to assess the quality of a decision making process and of the decision itself[20].

HCP: Health care provider

2.2 AIM 1 OF PATIENT DECISION AIDS: PROVIDING INFORMATION

The primary purpose of PtDAs relates to **providing evidence-based information** on a specific health decision context [16, 17]. One of the IPDAS requirements related to this topic, is that the evidence provided should be critically appraised by the PtDA developers[17]. Systematic reviews that avoid selection bias, assess the quality of the included studies and summarize the main effects, preferably quantified in a meta-analysis, may provide the 'best available' information [21]. Next to providing evidence-based information, a PtDA should provide information on potential conflicts of interest, such as authors and their affiliations and source of funding [22]. Several descriptive theories of decision making suggest that patients need to derive relevant knowledge for their decision context to establish their preferences for either particular aspects of the decision options, or an option as a whole [23]. The difficulty lies within the fact that 'relevant' knowledge can only be determined based on individual patient needs. Although some information might be clearly relevant for all individuals, the need for other information aspects may vary between individuals [24]. This implies a challenge for the development of PtDAs, as these tools aim to satisfy the information needs of a wide variety of patients. Moreover, patients' knowledge is not only impacted by *what* type of information is presented, but also *how* it is presented [23]. IPDAS standards require that information and decision options are presented

in a neutral and balanced manner [17]. Otherwise, cognitive bias may occur and affect patients' understanding, perception of benefits and risks and even preferences [25]. Research showed that if different options are presented sequentially, this may shift preferences. A side-by-side presentation of different options on the other hand, helps patients to make direct comparisons [23, 25]. However, the most optimal way on how to provide information, also varies greatly between individuals[26–28]. According to Feldman-Stewart *et al*., further research is needed to determine how PtDAs can be tailored to optimally inform individual patients [23].

2.3 AIM 2 AND 3 OF PATIENT DECISION AIDS: PREFERENCE ELICITATION AND COMMUNICATION

The second and third purpose of PtDAs is related to **clarifying and communicating patient preferences** [16, 17]. The Cochrane review by Stacey *et al*. from 2017 stated that there are two approaches to accomplish supporting patients in clarifying their values and preferences, and communicating them to a health care provider [12]. PtDAs may either describe the options in sufficient detail, allowing patients to imagine what it is like to experience the physical, emotional, and social effects of every option; and/ or they may provide structured guidance to consider and tradeoff treatment characteristics [12]. Providing guidance may be incorporated in a PtDA in various ways; for example by providing a stepwise approach for decision making, by including a worksheet for patients to identify questions to ask their health care provider, by including value-clarification methods (VCMs), or by generating a summary of the patient's knowledge and preferences, which they can share with their health care provider during a consultation [29]. VCMs can be either implicit and non-interactive as explicit and interactive methods that can be used to help patients evaluate the desirability of different treatment characteristics (attributes) within a specific decision context and can identify their preferred option [30]. In other words, explicit VCMs are used to ***clarify*** and ***elicit patient preferences*** for health care decisions in an individual decision context [6]. A range of different preference elicitation methods can be applied; varying from simple rating scales and considering pros versus cons, to prioritization, tradeoffs and utility assessments such as conjoint analysis (CA) [30, 31]. Earlier research indicates that VCMs may help to better prepare patients for decision making and improve decisional outcomes, however, it is still unclear which aspects of VCMs exactly cause this improvement [30, 32, 33]. Potential methods that support patients to imagine and assess potential effects of different decision options are less thoroughly investigated. One approach that is suggested in the literature is to include personal stories in PtDAs. According to Bekker *et al*., personal stories are "*narratives, testimonials, or anecdotes that provide illustrative examples of others' experiences relevant to the decision*" [34]. Narrative communications are already being used to encourage people to change their health behaviour and are seen as a particularly useful communication strategy for people with limited literacy and numeracy, as

they are a comfortable and familiar way to receive information [26, 27, 34, 35]. However, in the context of using a PtDA to prepare for SDM, it is crucial that patients are supported to form their own personal preferences. It is still unclear whether personal stories may urge patients to make decisions based on the values and preferences shown in the narrative or that they are being supported to make informed decisions on their own [33, 34]. Narratives seem a promising way for patients to explore the consequences of different decision options and to help them translate the potential impact of these consequences on their everyday life.

2.3.1 WHY PATIENT PREFERENCES MATTER

During the last two decades, the general idea behind medical decision making has revolved around one central principle; that of patient-centred care, which is characterized by respect for individual patient preferences, needs, and values in guiding clinical decisions [36]. This resulted in a growing interest in including patients' perspectives and experiences in health care decision making [37]. Several factors have accelerated this evolution. First of all, as patients are the end-users of medical products, they are considered to be the most important stakeholder in the process of health care and therefore deserve to be involved in the decision making [38, 39]. Second, due to an increase in available health care options, patients have become 'consumers' in a more traditional sense [40]. Within the field of consumer research, the true value of a product has always been determined by the end-user of that product. By involving consumers in the development and evaluation process, new products entering the market are better aligned with consumer needs. Third, including patients' views in medical decision making will improve the transparency and acceptability of these decisions [41]. Finally, as patients and their caregivers live with their condition on a daily basis, they have become an expert on their disease and the potential benefits and risks of their treatment [42]. Aligning medical decisions with patients' unmet needs, preferences and experiences, will simply result in higher quality decisions [38].

The combination of these factors and the fact that many health care decisions simply failed to sufficiently incorporate the patient's view in the past, urged multiple stakeholders to better align their decision making with patients' unmet need. Globally, and across various health care domains, initiatives were taken to assess how best to represent patients' views in various health care decisions [39, 41, 43, 44]. Regulatory agencies such as the European Medicines Agency (EMA) and the United States Food and Drug Administration (FDA), as well as Health Technology Assessment (HTA) agencies and the pharmaceutical industry have all been investigating how to measure patient preferences and how to incorporate this data in a structured decision process [39, 42, 45, 46]. The FDA defines patient preference information as "*Qualitative or quantitative assessments of the relative desirability or acceptability to patients of specified alternatives or choices among outcomes or other attributes that*

differ among alternative health interventions" [42]. This type of information could be particularly relevant for decision makers in the following situations: when multiple treatment options are available, none of which is superior for all patients; when the evidence supporting a favoured option is considerably uncertain or variable; and when patients' opinions on the benefits and risks of treatment options vary considerably within a patient population or differ from the opinion of regulatory or HTA decision makers [37, 45]. These situations were earlier identified as 'preference-sensitive decisions'.

2.3.2 How to elicit patient preferences

Two types of methods exist to identify patient preferences; exploration methods and elicitation methods [47]. Preference exploration methods are qualitative by nature and adopt either an individual approach such as (semi-) structured or in-depth interviews and complaints procedures; or a group-based approach such as focus groups, the Delphi technique, or a dyadic interview [47]. Qualitative exploration methods may be particularly useful in earlier stages of the medicinal product life cycle, for example for attribute identification [42, 45]. Preference elicitation methods, on the other hand, are quantitative methods that collect quantifiable data that can be used for statistical analyses to obtain preference weights on a common scale to allow comparisons [42, 47]. This makes them suitable for weighing and comparing attributes from different health interventions or to identify subgroups of patients that value certain attributes differently [42]. Elicitation methods can be divided into four main categories: discrete-choice-based methods, ranking methods, indifference methods and rating methods [47]. These methods vary in their complexity and ability to generate data to answer a small or larger set of research questions. Rating methods like swing weighting or a visual analogue scale are simpler methods, whereas indifference methods such as a standard gamble or time tradeoff require respondents to make tradeoffs by choosing between alternatives. Next, ranking methods like the object case and profile case best-worst scaling (BWS) can capture the preferred order of attributes within a specified set. Finally, discrete-choice based methods such as a discrete choice experiment (DCE) or the multi-profile case BWS and adaptive conjoint analysis (ACA) can be used to determine the importance of tradeoffs between attributes through a series of choice sets that present potential alternatives. This type of method forces respondents to explicitly choose between multiple alternatives that have multiple attributes with differing attribute levels, to resemble complex real-life decisions [48].

2.3.3 The need for clear guidelines

The use of preference methods for various decisions within the medical product lifecycle has increased significantly over the last three decades [47]. The potential application area for patient preference studies varies from early drug discovery, over (pre-) clinical development and obtaining marketing

authorization to reimbursement and post-marketing follow-up [5]. However, many stakeholders such as regulators, HTA agencies, payers, and European and US industry have limited experience in performing and assessing patient preference studies as well as implementing its results [5]. Therefore, several national and international initiatives have been launched to guide the development and execution of patient preference studies and the use of patient preference information in decision-making. In Europe, the Patient Preferences in Benefit and Risk Assessments during the Treatment Life Cycle (PREFER) project, funded by the Innovative Medicines Initiative was launched in 2016 [46]. This project aims to strengthen patient-centric decision making throughout the medicinal product life cycle by providing recommendations on how patient preferences could be measured and incorporated in benefit-risk decision-making by industry, regulators and HTA bodies/payers. A total of 33 partners ranging from academic institutions to pharmaceutical companies, patient organizations and a HTA body are involved in this project[46], that will issue recommendations in 2021. In the Unites States (US), the Medical Device Innovation Consortium (MDIC) issued a guideline in 2015 on how to incorporate patient preference information in benefit-risk assessments and which methods could be used to collect this data. This public-private partnership focused on medical device approval processes [45]. Also in the US, the FDA has issued a guideline in 2016 on how patient preference information may be used by the FDA staff when performing benefit-risk assessments for decision making for premarket approval applications and *de novo* classification requests [42]. This guideline aimed to encourage the voluntary submission of patient preference information by sponsors, to provide recommendations for said submissions and to recommend certain qualities of patient preference studies. Important to note is that both the MDIC and FDA guidance documents provide only suggestions or recommendations for the industry, not required actions [42]. Another organization that has provided "good research practices" for patient preference studies is the International Society for Pharmacoeconomics and Outcomes Research (ISPOR). The ISPOR task force on CA provided a set of three research papers which included a checklist for performing CA in health care and two additional publications focusing on experimental design and statistical analysis [49–51]. The checklist discusses the following ten items related to the process of developing, conducting and presenting a CA experiment: 1) research question; 2) attributes and levels; 3) construction of tasks; 4) experimental design; 5) preference elicitation; 6) instrument design; 7) data-collection plan; 8) statistical analyses; 9) results and conclusions; and 10) study presentation[49]. Finally, both individual HTA agencies and the International Network of Agencies for Health Technology Assessment have taken initiatives to provide guidelines on how to collect and use patient preference data [39, 52]. Overall, many different guidelines and initiatives try to advance the collection and use of patient preference data. However, most guidelines focus on particular aspects related to patient preference studies. A complete overview covering all relevant aspects when conducting patient preference experiments is still missing. For

example, although information from the ISPOR series contains plentiful information on how to develop a preference experiment, guidance on how patients perceive a CA experiment or what kind of information or instructions they require to perform this task, is lacking. Information related to these topics can be sought in other guidelines, for example in the IPDAS 'Quality Dimensions' series, in which they dedicated multiple papers to the topic of providing information [23, 25, 28, 53]. Indeed, preference elicitation on the meta level (eliciting preferences from a group of patients for regulatory or HTA decision making) shares quite some similarities with individual preference elicitation (within the context of SDM). Guidelines from either level can undoubtedly improve some aspects for the other level as well. At this time, a variety of guidelines provides insights on different aspects related to patient preference elicitation. Some of them are restrictive for the type of product that is assessed (medical device or drug), for the time within the medicinal product life cycle it is applied and for the context (meta or individual level) in which it is applied. When developing or conducting a preference elicitation experiment with patients for the purpose of SDM using a PtDA, a combination of the available guidelines is required to cover all relevant aspects. How to optimally inform patients on the included attributes and attribute levels, for example, is an aspect that is important in both the individual and meta setting of preference elicitation. Another aspect could be the optimal duration and combination of different preference elicitation methods that should be used for an experiment to limit respondent burden while delivering sufficient data.

2.3.4 Building on consumer research

Preference elicitation methods such as DCE and CA were initially introduced in the context of marketing, with the aim to forecast consumer choices [54]. These methods have been, and are still being applied to elicit consumer preferences for new products that are in development and not yet available on the market. An important condition to obtain accurate results, is that participants require a basic understanding of the product they are evaluating [55]. This knowledge is necessary to assess the importance or impact of new product characteristics. For example, when measuring consumer preferences for a new type of smartphone, the respondents already need to know what a smartphone is. If respondents are not yet familiar with the product you are presenting, simply because that type of product is not yet available on the market (e.g. the first smartphone developed), they need to acquire a basic understanding of this product first [48]. Adequately informing participants on the product characteristics prior to a preference elicitation experiment is therefore extremely important in this case [55]. Otherwise, respondents might make tradeoffs between product characteristics that they do not yet fully understand, resulting in unstable preferences. This in turn, will result in inaccurate preference elicitation [48, 55]. During the 1990', these preference elicitation techniques have found their way into the health care setting and have been increasingly applied to elicit patient preferences

[56]. As preference elicitation is not yet systematically applied in health care, examples from the consumer research field may still provide valuable insights on how to optimize patient preference elicitation. Current health care guidelines, for example, do not provide clear instructions on how to adequately inform patients to avoid eliciting unstable preferences. This research area in particular may be further inspired by consumer case examples. In many health care application areas, patients' preferences for medicinal products of which they have no basic understanding, will be elicited. This could be the case for either experiments set up to inform regulatory decision making regarding a new market authorization or to gather information for reimbursement decisions, as well as individual treatment decisions in the context of SDM.

2.3.5 TERMINOLOGY

Different aspects and terms related to the patient's perspective have been introduced in the previous paragraphs. These terms are sometimes used or interpreted in different ways in the existing literature, with slightly different meanings. Therefore, an overview of key terms and how they are defined within this PhD thesis are provided next, in order to avoid confusion in the following chapters.

The **patient perspective**; an overarching term that captures many aspects, for which the definition provided by Zanini *et al*. is used: "*the self-perceived impact of the health condition on their [i.e. patients'] life, as their expectations of the consultation or the doctor, and as their priorities regarding the outcomes of the treatment.*" [57]

Patient values; a complex term that is defined by Bastemeijer *et al*. in which three different aspects can be identified: "*1) values are concerned with the life and philosophy of the patient; 2) values in relation to the characteristics and behaviour of the professional, and 3) values in relation to the relationship between the patient and the professional*." [58] The term "values" concerns not only 'what' aspects are important, but also 'how' some healthcare aspects (such as the decision making for example) should be addressed.

Patient preferences; the results from some form of deliberation, for which the definition by the FDA is used: "*Qualitative or quantitative assessments of the relative desirability or acceptability to patients of specified alternatives or choices among outcomes or other attributes that differ among alternative health interventions.*" [42]

Patient experience; a very broad definition is used, as provided by the Beryl Institute: "*the sum of all interactions, shaped by an organization's culture, that influence patient perceptions, across the continuum of care.*" [59]

3 STATUS OF SDM IN BELGIUM AND IDENTIFICATION OF DISEASE AREAS WITH HIGH UNMET NEED

3.1 LACK OF GUIDELINES AND INITIATIVES TO IMPLEMENT SDM IN BELGIAN PRACTICE

Guidelines on how to implement SDM in clinical practice are available in some countries. The National Health Service (NHS) in England, for example, has issued a best practice guideline in 2019 to improve local implementation of SDM [60]. It contains a checklist designed to communicate with key stakeholders to allow for a local assessment in terms of SDM practice and to support improvements by changing key elements. Furthermore, this guideline highlights the following societal advantages of applying SDM. First of all, when treatment decisions are based on patients' personal preferences, they are more likely to adhere to their chosen treatment, which will result in improved outcomes. Secondly, by identifying patients' informed preferences on a population level and using this information to determine necessary health services, resources can be allocated more efficiently. Finally, applying SDM approaches in clinical practice may significantly improve health outcomes for disadvantaged people and reduce health inequalities within society [60]. A comparable guideline for Belgium is currently not available. Furthermore, a bibliometric analysis from 2019 identified the top 10 countries that have participated in SDM studies between 2009 and 2018. Although the top 3 is reserved for the United States, England and Canada, multiple (Western) European countries are included in the top 10; Netherlands, Germany, Italy, Switzerland, France, and Spain [61]. Disregarding the Grand Duchy of Luxembourg, Belgium is the clear absentee in this list.

3.2 IDENTIFYING POTENTIAL AREAS OF APPLICATION FOR SDM

As explained earlier, PtDAs are the primary tools to support SDM in clinical practice [16, 17]. Currently, there are more than 500 PtDAs available, however, the majority has not been tested in a randomized controlled trial[18]. The Cochrane review from 2017 that compared PtDAs to usual care or alternative interventions, identified 50 different decisions that were targeted by PtDAs, the most common ones being surgery, screening, genetic testing and medicinal treatments [12]. The Ottawa Hospital Research Institute provides an inventory for publicly available decision aids on its website, including PtDAs that fulfil the following conditions: satisfy the definition of a PtDA, report the date for the last update (usually not more than 5 years old) and provide reference to the scientific evidence used for the development [62]. Furthermore, an assessment for every PtDA is included for 29 -or 33 in case of screening or testing decisions- quality criteria based on the IPDAs criteria from table 1. A total of 336 PtDAs was included in May 2020, covering 148 different decision topics. These topics ranged from various disease areas (Alzheimer's disease, breast cancer, diabetes, haemophilia, osteoporosis,

rheumatoid arthritis,…) to health topics covering child birth, weight control or assisted living during the COVID-19 pandemic. Most PtDAs were developed for breast cancer (24 PtDAs) and prostate cancer (15 PtDAs) [62]. These disease areas have earlier been identified as relevant contexts for SDM [63, 64]. Decision topics that include at least five different PtDAs are shown in table 2. Although there are PtDAs available for various disease areas, so far they are not routinely implemented in clinical practice [65].

Table 2: Decision topics with at least five publicly available patient decision aids (PtDAs) [62]

Decision topic	Number of PtDAs	Decision topic	Number of PtDAs
Breast cancer	24	Lung cancer	6
Prostate cancer	15	Alzheimer's disease	5
Osteoarthritis	10	Arthritis	5
End of life issues	9	Chronic kidney disease	5
Osteoporosis	8	Colorectal cancer	5
Atrial fibrillation	7	Depression	5
Childbirth	7	Heart failure	5
Cholesterol	7	Prenatal testing	5

Out of the 16 decision topics that are most often discussed in PtDAs, four are related to different types of cancer. This is not surprisingly, as treatment decisions in cancer are often characterized as difficult and preference-sensitive, with a high impact on quality of life [66–68]. Cancer patients generally have the highest preferences to implement a SDM approach [68–70]. Moreover, for chronic treatments, patient preferences may change over time and can influence treatment adherence and persistence [71–73]. In these cases it is particularly relevant to actively engage patients in SDM, both when the treatment decision is taken for the first time, as during follow-up.

3.3 Breast cancer

3.3.1 Incidence and prognosis

Breast cancer is the most frequently diagnosed cancer in European women, with 10627 diagnoses in 2017 in Belgium alone [74, 75]. Furthermore, it is also the most important cause of cancer deaths in both Belgian as European women [74]. The average age at diagnosis for Belgian women is 63.0 years, with the highest age-specific incidence rates for women between 65 and 70 years old (424.8 per 100 000 person-years) and between 70 and 75 years old (429.7 per 100 000 person years) in 2017 [75]. The prognosis of female breast cancer is relatively good, with an overall 5-year relative survival of 90.9% (2013-2017, Belgium). For patients between 50-69 years old, this number even increases to

93.5% (2013-2017, Belgium) [75]. These favourable rates can be explained by the combination of early detection and improved adjuvant treatment[74].

3.3.2 Diagnosis

The initial diagnosis of breast cancer is based on a triple assessment, which includes clinical examination, imaging (combination of mammography and ultrasound) and a biopsy of the lesion of interest [76, 77]. In Flanders, women between 50 and 69 years of age can receive a screening mammography every two years, which is free of costs for women that are affiliated with a Belgian health insurance fund [78]. When a suspected lesion has been identified on either imaging or clinical examination, a biopsy will be performed to assess tumor characteristics. Firstly, both estrogen and progesterone receptors are assessed using immunohistochemical testing for all primary invasive breast cancers. The hormone receptors' status is important for the initial prognosis of breast cancer and an important predictor for the benefit of (adjuvant) endocrine therapy later on. Patients with hormone receptor positive disease have a lower mortality risk compared to patients with estrogen and/ or progesterone negative disease [79]. However, they are known to have higher late recurrence rates, which is rather rare in triple negative tumors [80, 81]. Secondly, HER2 protein overexpression is assessed by gene amplification tests. The HER2 protein is part of the epidermal growth factor receptor (EGFR) family and is seen to be overexpressed in 20-30% of invasive breast cancers [82]. It is associated with a relatively poor prognosis. Several therapeutic strategies are focused on this overexpression specifically, for instance trastuzumab, lapatinib or anthracycline-based adjuvant therapy [82].

3.3.3 Types of breast cancer

According to Koh *et al*., breast cancer can be described as "*a group of diseases with different molecular characteristics that indicate different prognoses, patterns of recurrence, disseminations, and sensitivities to available therapies*" [83]. A distinction can be made between invasive and non-invasive breast cancer types [84]. As the basal membrane is intact, this type is by definition not associated with metastases. When assessing the growth pattern microscopically, two types can be defined; ductal or lobular carcinoma. Both of them can be either invasive or in situ. Lobular carcinoma in situ (LCIS) is known to occur later in life, possibly because of the slow progression rate. It is more bilateral and multifocal compared to ductal carcinoma in situ (DCIS). Both LCIS and DCIS are precursor lesions for invasive breast cancer. Invasive breast cancer is either early stage breast cancer, locally advanced breast cancer or metastatic breast cancer [84].

3.3.4 STAGING OF BREAST CANCER

In 2017, the American Joint Committee on Cancer (AJCC) published its 8th edition on tumor-node-metastasis (TNM) system for cancer staging [85]. The staging system significantly changed as biomarkers (such as hormone receptors, HER2 expression and tumor grade) were now incorporated into the traditional anatomic TNM stages, resulting in prognostic stages [83]. The tumor grade is based on the extent of tumor differentiation, with poor differentiated tumors resulting in worse prognosis. Rapidly dividing tumor cells show high expression of specific proliferation-related genes such as Ki-67. This tumor marker is used to measure tumor proliferation [86]. The original anatomic staging was based on the extent of the primary tumor (T), the status of the regional lymph nodes (N) and the metastasis status (M). First, the primary tumor size and the degree of loco-regional invasion determine the T stage, ranging from T1 to T4. Second, the N stage depends on the type and number of lymph nodes that are involved, ranging from N0 to N3. Finally, the M stage is based on the occurrence of distant metastases, translating in M0 when metastasis is not present and M1 for when metastasis is present. The combination of these different T, N and M stages resulted in nine potential breast cancer stages: 0, IA, IB, IIA, IIB, IIIA, IIIB, IIIC and IV[83]. In the 8th edition of the AJCC guideline, categories I to III received further subcategories to subdivide and clarify staging. Further, hormone receptor expression, HER2 expression and tumor grade were combined with the anatomic staging, as cohort studies had shown that these parameters could also affect survival[83, 85]. Four molecular subtypes can be identified: luminal A (hormone receptor-positive, HER2- negative, low Ki-67 values), luminal B (hormone receptor-positive, HER2-negative, high Ki-67 values), HER2 (HER2-positive, regardless of the hormone receptor status), and basal or triple-negative (hormone receptor-negative and HER2-negative) [83].

3.3.5 TREATMENT OF EARLY INVASIVE BREAST CANCER

For all patients with early invasive breast cancer, treatment is decided within a multidisciplinary team and may comprise the following therapies: neoadjuvant systemic therapy, breast and axilla surgery, locoregional radiotherapy, adjuvant chemotherapy and adjuvant endocrine therapy (in case of hormone-sensitive tumors); as determined in a guideline by the Belgian Health Care Knowledge Centre (KCE)[74]. Breast surgery is the main treatment for early invasive breast cancer. Depending on the size of the lesion, whether it is multicentric or not, the relation to the surrounding tissues, and the breast volume, either a breast conserving surgery or a mastectomy is performed. The KCE guideline emphasize that all patients eligible for breast-conserving treatment should be fully informed on their options and the final decision should be tailored to the individual patient [74]. Depending on the pre-operative results, axillary lymph nodes dissection or sentinel node procedure is performed. After

analysing the dissected tissue treatment, decisions regarding adjuvant therapy are made. These adjuvant therapies can be one (or a combination of) the following: radiotherapy, chemotherapy and endocrine therapy. In case both chemotherapy and radiotherapy are indicated, adjuvant therapy starts with chemotherapy. Either adjuvant therapy should start within eight weeks of breast surgery. Radiotherapy is recommended for all patients with breast-conserving surgery. High risk patients can further receive axillary or chest wall radiotherapy, which is determined for every individual patient during multidisciplinary team meetings. The choice for systemic adjuvant therapy is based on the hormone sensitivity and risk profile of the tumor and the age, menopausal status, and comorbidities of the individual patient. This decision is therefore always made on an individual basis. Adjuvant endocrine therapy can be given after chemotherapy and is indicated for all patients with hormone receptor positive breast cancer. Patients with luminal A show an excellent response to adjuvant endocrine therapy, whereas patients with luminal B are less responsive to adjuvant endocrine therapy and generally have worse prognoses than luminal A [83]. Premenopausal patients should receive tamoxifen, a selective estrogen receptor modulator, for at least five years, or an aromatase inhibitor (AI: anastrozole, letrozole or exemestane) with a luteinizing hormone releasing hormone (LHRH) agonist such as goserelin. Postmenopausal patients should receive at least five years of adjuvant endocrine therapy with either tamoxifen or an AI; or a combination by starting treatment with one of the two and switching after 2-3 years to continue with the other treatment up to a total of at least five years. The proposed endocrine therapy depends on the risk estimation of the tumor. Switching to an AI may be more effective for these patients to further reduce recurrence than continuing with tamoxifen [84]. Based on the results of several randomized clinical trials and meta-analyses, extended endocrine therapy (for a total of 7-10 years) can be offered to both pre- and postmenopausal patients with invasive breast cancer [84, 87]. The choice for the type of adjuvant endocrine therapy for extended use might be partially based on the patient's risk for side effects such as venous or arterial vascular disease or fractures [88, 89]. Further, patients with HER2-positive breast cancer are eligible to receive trastuzumab, a monoclonal antibody that targets the extracellular domain of HER2 proteins in the cell membrane. As this treatment may cause cardiovascular adverse events, cardiac function has to be monitored both during treatment and follow-up. HER2-positive patients without cardiovascular risk factors that are node-positive or high-risk node-negative who received chemotherapy, should receive trastuzumab for one year [74].

3.4 Unmet need for SDM for postmenopausal women with hormone-sensitive breast cancer

Patients with hormone-sensitive breast cancer may undergo a very long treatment pathway, with only the adjuvant endocrine therapy already lasting from five to ten years. During this time, patient survival is impacted by treatment adherence and persistence. Unfortunately, nonadherence is common in this patient group, resulting in an increased mortality risk [90]. Earlier research states that adherence to tamoxifen and AI varies between 65% to 79% and 72% to 80% respectively. However, about half of the patients discontinues treatment by the fourth or fifth year [90]. Next to the long treatment duration, treatment adherence is affected by the high burden on quality of life caused by these treatments [73, 90]. The overlapping adverse events for both tamoxifen and AI are mainly related to their estrogen-blocking effect on cancer cells and include hot flushes and mood disturbances, comparable with the effects of a natural menopause [91]. Other potential adverse events differ between both options, with gynaecological symptoms and an increased risk of thrombosis being typical for tamoxifen and musculoskeletal effects and cardiovascular diseases for AI [91]. Furthermore, the individual impact caused by these treatments varies considerably between patients. Therefore, it is a challenging task to tradeoff potential benefits and adverse events for individual patients. Even more so because the studies examining long-term effects of these treatments are usually ceased after approximately ten years [92]. The longest follow-up of a trial comparing tamoxifen to AI is currently the Breast International Group (BIG) 1-98 study, with a median follow-up of 12.6 years [92].

4 Research gaps

4.1 Very limited research regarding the use of patient decision aids to improve shared decision making in the Belgian context

SDM in health care has gained increasingly attention over the last two decades and is being implemented in many decision contexts [1, 7]. Research related to SDM is being performed in many countries, but Belgium seems to be running behind [61]. At the same time, PtDAs have been developed and applied to facilitate SDM in clinical settings [12, 16]. When the International Patient Decision Aid Standards (IPDAS) Collaboration established a set of 12 quality criteria for PtDAs, stakeholders from 17 different countries participated [18]. Potential participants were nominated through the IPDAS Collaboration, the Cochrane Collaboration Consumers Group, or by word of mouth among related networks. No Belgian Stakeholders participated, although neighbouring countries such as France, Germany and the Netherlands were included [18]. In 2017, a Cochrane review yielded 105 randomized controlled trials comparing PtDAs to usual care and/or alternative interventions, performed in ten

different countries; Belgium, again, not being among them [12]. Despite international attention for the application of PtDAs to improve SDM, these tools are not routinely being developed or applied in the Belgian health care setting. Very limited examples are available, most of them are situated in the areas of end of life decisions and prostate cancer [93–96]. Moreover, Engelen *et al*. stated in 2016 that PtDAs are still considered 'novelties' in Belgium, as most health care providers and patients are unfamiliar with them [97].

4.2 Lacking information on the need for a PtDA in breast cancer

There are currently no PtDAs available for Belgian patients with hormone-sensitive breast cancer, although their treatment pathway includes multiple preference-sensitive decisions, requiring an explicit assessment by the patient [67, 68]. As research indicates that both chronic patients and cancer patients may require more involvement in their medical decision making and both these factors are applicable to patients with hormone-sensitive breast cancer, this population may be especially interesting for the application of a PtDA to improve SDM [68–70]. By assessing the past experiences with SDM of patients and physicians in this treatment context and analysing their need for interventions that may improve SDM, a clear decision point can be identified for the development of a PtDA.

4.3 Limited research on optimal PtDA features to improve value clarification and preference elicitation

Research indicates that interactive features in computer-based decision aids may improve decision making by improving knowledge and reducing decisional conflict, however, it is still unclear what specific features can improve the decision making process or how these aspects can be refined [30, 32, 33]. Since preference elicitation experiments have been conducted in the field of consumer research for many more years, learnings from this field might equally inspire health care applications [54, 56]. As this research field is rapidly evolving in the health care setting, mainly with the objective to elicit patient preferences for inclusion in regulatory or reimbursement decision making, it should be assessed whether (part of) these methods can equally improve SDM at the individual level between patients and physicians.

4.4 Establishing a development process for a PtDA aligned with scientific international guidelines that meets stakeholder needs

Although guidelines on PtDA development are available from the IPDAS collaboration, various methodologies can be applied to achieve this aim [98]. Furthermore, the advantages and disadvantages of several potential PtDA features are still unclear. Evidence suggests that computer-based PtDAs may improve decision making compared to traditional (paper-based) approaches [33]. However, further research is needed to identify which interactive features are valued by patients and physicians and how they should be designed.

4.5 Testing a patient decision aid in the Belgian clinical context

Currently, only the minority of the PtDAs that are developed, are also adequately tested as prescribed by Coulter *et al*.; including field tests with patients and reviews or tests with clinicians not involved in the development process [12, 98]. Furthermore, the experience with PtDAs in the Belgian clinical context is limited. Testing a newly developed PtDA in Belgium will generate valuable information on how such an intervention is perceived by patients and health care providers and will help us to assess whether these interventions could be easily implemented within our healthcare system.

PROJECT OBJECTIVES

1 RESEARCH QUESTION

How can we elicit treatment preferences from patients with hormone-sensitive breast cancer and use this information to involve patients in their treatment decision making?

2 PROJECT AIMS AND OVERVIEW

The aim of this PhD project is to improve SDM in Belgium in the context of hormone-sensitive breast cancer. More specifically, this project aims to develop a PtDA that informs patients on different decision options, elicits their preferences for the available options and supports them to communicate their preferences to their treating physician. Therefore, the following four objectives were identified:

Objective 1: To identify novel elements in preference elicitation methods from consumer research that are not yet systematically used in patient preference research and to assess their applicability in health care.

Objective 2: To identify the needs of patients and physicians in hormone-sensitive breast cancer regarding the use of a PtDA to improve SDM.

Objective 3: To develop a prototype PtDA using an evidence-based methodology, taking both the patient and physician perspective and international guidelines into account.

Objective 4: To test the developed PtDA in a research (*alpha testing*) and clinical (*beta testing*) setting, including people both involved and not involved in the development process.

In order to reach the defined objectives, the project is divided into four work packages. Figure 3 provides an overview of the different work packages.

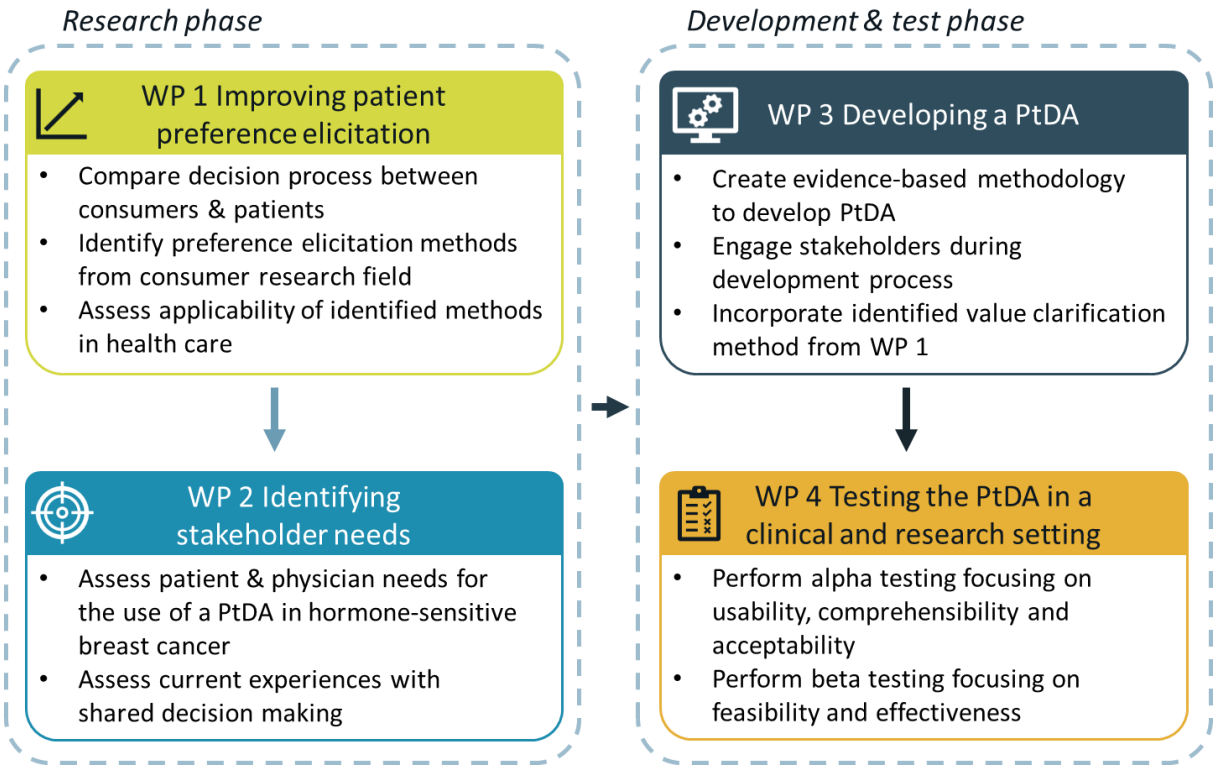

Figure 3: Project overview

WP: work package PtDA: patient decision aid

In order to meet the first objective, we compared the process of decision making between patients and consumers to identify similarities within **work package 1**. The different market evolution stages for consumers as described by Louviere [48] were translated into analogue examples for patients. Next, a literature review was performed to identify novel elements in methods from the consumer research field that could be applied to improve preference elicitation in health care. The results of this work package were used to optimize the preference elicitation component of the VCM during the development of the PtDA.

For **work package 2**, qualitative empirical research was performed to evaluate in-depth patient and physician needs regarding the implementation of a PtDA to improve SDM in breast cancer. Furthermore, experiences with the current practice for treatment decision making during consultations were assessed.

Next, within **work package 3**, an online PtDA that meets the needs of patients and physicians on the one hand and leading clinical practice guidelines such as KCE and NICE on the other hand, was developed according to international standards. The combination of an in-depth literature review and stakeholder interviews was used to determine the relevant attributes to be included and to create a user-friendly design. Furthermore, the developed PtDA aims to improve value clarification and preference elicitation by implementing results from work package 1.

To meet this project's final objective, the prototype PtDA was tested in a two-stage process during **work package 4**. First, the PtDA was alpha tested in a research setting focusing on usability and comprehensibility for patients and on usability and acceptability for health care providers. A mixed methods approach consisting of cognitive interviewing and semi-quantitative questionnaires was applied. Second, the finalized PtDA was beta tested in a clinical setting. A pilot trial was performed to assess the effectiveness of the PtDA by measuring its effect on the quality of the decision process and quality of the decision itself and to assess the feasibility of implementing a PtDA in breast cancer follow-up.

3 ADDED VALUE OF THIS PHD THESIS

Only a very limited number of PtDAs currently exist in Belgium and no single example could be identified in the disease area of breast cancer. Earlier research indicates that cancer patients generally require to be more involved in their medical decision making [68–70]. Within this PhD project, we assessed the needs of Flemish patients and physicians for a PtDA to improve SDM in hormone-sensitive breast cancer. Based on this needs assessment, a web-based PtDA was developed and tested in close collaboration with both stakeholders in order to close the research gap with currently existing international PtDAs. Special focus was put on improving the value clarification and preference elicitation methods included in the PtDA on the one hand, and on integrating interactive elements to improve understanding and engagement on the other hand. This PhD project was conducted under the form of a Baekeland mandate financed by Flanders Innovation and Entrepreneurship (VLAIO). Within a Baekeland mandate, doctoral research is carried out in close collaboration with one or more Flemish companies and a Flemish university. In this project, the companies ISMS and Mindbytes, and the University of Leuven were involved. The project aimed to build up scientific and technological knowledge on patient preference elicitation and the development of PtDAs, that can serve as a basis for economic applications for ISMS and Mindbytes.

PART I

DEVELOPING AN INTERACTIVE ONLINE PATIENT DECISION AID

CHAPTER 1

IMPROVING PATIENT PREFERENCE ELICITATION BY APPLYING CONCEPTS FROM THE CONSUMER RESEARCH FIELD

This chapter is based on:

Ver Donck N, Vander Stichele G, Huys I
Improving patient preference elicitation by applying concepts from the consumer research field: Narrative literature review
Interact J Med Res 2020;9(1):e13684

1 ABSTRACT

Background: Although preference research finds its origins in consumer research, preference elicitation methods have increasingly attracted attention in different decision-making contexts in health care. Simulating real-life decision making is believed to be important during consumer preference elicitation.

Objective: The aims of this study were to compare the process of decision making between patients and consumers and to identify methods from the consumer research field that could be applied in patient preference elicitation.

Methods: A narrative literature review was performed to identify preference elicitation concepts from a consumer context that could offer improvements in health care.

Results: The process of decision making between patients and consumers was highly comparable. The following five concepts from the consumer research field that could effectively simulate a real-life decision-making process for applications in health care were identified: simulating alternatives, self-reflection, feedback-driven exploration, separated (adaptive) dual response, and arranging profiles in blocks.

Conclusions: Owing to similarities in the decision-making process, patients could be considered as a subgroup of consumers, suggesting that preference elicitation concepts from the consumer field may be relevant in health care. Five concepts that help to simulate real-life decision making have the potential to improve patient preference elicitation. However, the extent to which real decision-making contexts can be mimicked in health care remains unknown.

2 INTRODUCTION

2.1 BACKGROUND

During the last decade, there has been growing interest in patient perspectives and experiences in health care decision making [37, 41]. The idea of patient involvement has become increasingly accepted, as patients are in a unique position to share their day-to-day experiences in dealing with an illness and its treatment. Information about patients' perceptions and tradeoffs has the potential to inform decision making on different levels. As patients are the end users of medical products, they are the utmost important stakeholder in the context of patient-centred health care and deserve to be involved in medical decision making [38, 39]. At the individual level, patients can find themselves in a situation where multiple treatment options exist, without having one option that is clearly superior compared to the others [42]. In some cases, clinical evidence is scarce, resulting in high levels of uncertainty about treatment benefits. In other cases, there is abundant information on the benefits and risks of available options, but patients' views on the desirability of these outcomes vary greatly, resulting in different opinions of "the best" option [6]. Patients should receive decision support when making these decisions, which are usually referred to as "preference-sensitive decisions" [6, 42]. The treating physician can provide decision support to make an informed preference-based choice in the context of shared decision making (SDM) [15]. In this particular context, the process of forming preferences is often referred to as a "value clarification," which is followed by preference elicitation [6, 30]; the combination of these two aspects is called a "value clarification exercise" (VCE) [30]. At the meta level, patient preference data can provide additional information for decisions on drug development, regulatory assessment, or reimbursement [44, 52, 99–101]. Patient preference information is defined by the Food and Drug Administration (FDA) as "Qualitative or quantitative assessments of the relative desirability or acceptability to patients of specified alternatives or choices among outcomes or other attributes that differ among alternative health interventions" [42]. From a societal perspective, the inclusion of the patient opinion could improve the transparency and acceptability of regulatory or reimbursement decisions [41, 102]. Finally, the quality of decisions at both the individual and societal levels might increase when decision making is aligned with the patients' unmet needs [38].

Patient involvement can be realized in a variety of ways: by asking for input from patients via unstructured methods (eg, testimonials, comments in correspondence) or via structured methods (eg, conducting surveys, collecting patient-reported outcomes, or revealing patient preferences) [42, 52]. As part of a structured process to reveal preferences, both qualitative and quantitative preference measurement methods can be used.

2.2 EXPERIENCE OF PREFERENCE ELICITATION IN CONSUMER RESEARCH

Quantitative methods for patient preference elicitation include discrete choice experiments (DCEs)/conjoint analysis (CA) or best-worst scaling [45, 99]. The DCE technique was introduced by Louviere and Woodworth in the context of marketing to forecast consumer choices [54]. In 1990, CA and DCEs entered the health care setting and have since been increasingly used for patient preference elicitation [56]. Respondents are asked to choose between two or more alternatives, which are usually profiles consisting of different attributes (including product characteristics such as efficacy, adverse events, and mode of administration) and corresponding attribute levels (eg, oral, injection, and inhalation). By analysing these results, researchers can derive the underlying utility of particular attributes or profiles [49, 56, 103]. Despite the application of DCEs in health care for several decades, the resulting data have not yet been systematically applied to societal decision making, and some uncertainties remain about the utility or validity of DCE results in particular decision-making contexts [104, 105]. At present, consensus is lacking on how patient preferences can be optimally measured and incorporated into different health care community decision-making processes [41, 68].

Since preference research has been conducted for decades in the context of consumers, experiences from this field might further inspire patient preference research [43, 106]. Moreover, several innovative approaches to optimize preference elicitation (CA or other techniques) have been explored in the field of consumer research. Indeed, multiple industries offering innovative durable goods rely on preference elicitation methods to guide the development of new products [107]. However, the main difficulty in measuring consumer preferences for new products is the lack of knowledge and experience of respondents with the new product [48]. As these products typically do not yet exist, consumers have no basic understanding about how to assess the importance of new favourable and unfavourable characteristics or how to assess the tradeoffs between these characteristics [48, 55]. Examples of such products are personal computers, smartphones, and electric cars [55, 108].

Lack of understanding of the basic characteristics of new products resembles a major issue in patient preference elicitation. Considering that almost one in two Europeans have limited health literacy [109], weighing potential risks and benefits could therefore be a very difficult task for laypeople. This poses a challenge, especially in patient preference research, given the association of worse health states with lower levels of health literacy [109]. Furthermore, patients' medical states might influence their ability to understand the information and engage in a preference elicitation experiment.

2.3 Applying consumer research experience to inform health care preference studies

According to Louviere, the external validity of DCEs depends on the extent to which all key aspects of a real decision are simulated [48]. Preference elicitation experiments that most closely resemble real choice situations (including framing of situations, relevant contexts, and consequences) should be able to provide real-life results. For this reason, simulations for informational purposes were introduced in consumer research many years ago so that all aspects, ranging from consumer reports, advertising, or even the whole store environment, can be simulated to resemble real-life decision processes as closely as possible [107, 108].

Furthermore, when consumers need to construct their preferences while acquiring information, the tradeoffs they consider might be unstable and depend on context effects. Therefore, the results may not reflect true preferences [48, 55]. Urban and colleagues offered a method to deal with forecasting problems with new products that they termed "information acceleration" [107, 110]. Louviere clearly described the use of information acceleration methodology as follows [48]: "*Acceleration of Information Methods rely on multimedia and other technologies to simulate the processes by which individuals become aware of new technologies/products, search for and acquire information about benefits and/or problem solutions, decide whether to consider them and whether they can take advantage of what they offer, decide if they want to buy a product now available, or wait to see how the product market develops and evolves over time*."

In other words, when designing an experiment to elicit patient preferences, patients need to experience the same process as they would in real life. Their lack of knowledge or experience can be overcome by providing the necessary information in a natural way and showing them the results of various options. Simple pictures or videos can be used; however, more interactive simulations allow for more user involvement while better stimulating learning and knowledge retention [111]. Further, Hoeffler stated that consumers who are forced to construct their preferences during an experiment may be unable to provide enduring preferences [55]. The need for deeper consideration of the decision problem is a natural process, which may cause preferences to change over time [6].

The decision process of consumers in the context of a tradeoff situation consists of the following stages: becoming aware of a specific need or a new product, deciding what information to acquire and how to acquire it, deciding which alternatives are available to attain the objectives, forming a utility function or decision rule, and ultimately deciding whether or not to purchase the product (depending on budget or other constraints). Finally, if they decide to purchase, consumers sometimes need to choose which option(s) to purchase [48, 112]. Acquiring the right information and learning the

different advantages and disadvantages of every option in order to make tradeoffs represents an important step of this process. The situation of naïve consumers might be comparable to that of patients being faced with certain treatment options or a specific disease for the first time. As with consumers, patients need to acquire and process information at a fast pace when confronted with a new product or treatment. CA techniques are well suited to analyse decision making in both cases, as they can either simulate already available alternatives (eg, to compare different therapies available to patients) or elicit preferences for goods that do not yet exist (eg, comparing therapies in the drug pipeline or before market authorization has been obtained). In both cases, using methods that simulate real-life choice situations, such as information acceleration, could potentially be useful in health care. However, a clear comparison between the decision-making process of consumers and patients is lacking, impacting the potential to transfer learnings from consumer to health research situations.

To fill this gap, the aim of this study was to compare the process of decision making between consumers and patients. Furthermore, the goal was to identify consumer research methods or concepts that may improve patient preference elicitation by simulating real-life decisions. Based on this analysis, the applicability of the identified methods or concepts in health care are assessed.

3 METHODS

3.1 COMPARATIVE DESCRIPTION OF THE DECISION-MAKING PROCESS FOR PATIENTS AND CONSUMERS

The decision-making process of consumers was compared to that of patients. First, the market evolution stages described by Louviere [48] were translated into analogue examples for patients engaging in decision making in one of two possible contexts. On the one hand, the context of individual patients engaging in SDM was considered; on the other hand, gathering preference data from a group of patients to inform development, regulatory, or reimbursement decisions was evaluated [15, 30, 113].

3.2 LITERATURE REVIEW OF INNOVATIVE PREFERENCE ELICITATION CONCEPTS IN THE CONSUMER RESEARCH FIELD

A literature search was conducted in the Scopus database to identify innovative concepts from the consumer research field that improve preference elicitation by simulating real-life decisions. Three key terms (Table 3) describing preference elicitation methods that resemble real-life decisions such as DCEs/CA were combined with several terms describing innovation, information methods, and the field

of consumer research. Every combination was searched for independently and duplicates were removed during the first step of the process. Papers with a publication date >5 years old (ie, published before 2012) were excluded, as older ideas may have already been applied in the health care context. Finally, only articles in English were included. All identified papers were screened for exclusion based on the title. The exclusion criteria were the following: studies performed in a health care setting (as these papers describe techniques that have already been implemented in health care) and studies without sufficient description of the performed method or describing an actual stated preference experiment. In cases of doubt, papers were retained for a second selection stage. In this second stage, abstracts were reviewed for exclusion based on the above-described and two additional exclusion criteria: describing standard DCEs without any new elements (as described by the current standards for patient preference elicitation) and focusing solely on willingness to pay. The remaining articles were retrieved in full-text form and reviewed in a two-step process by the authors. In the first step, each concept was critically evaluated with respect to its capacity to simulate real-life decisions by one author (NVD). In the second step, another author (GVS) independently reviewed this analysis. Differences were resolved by discussion and, when no consensus could be reached, ties were settled by the third author (IH).

Table 3: Search strategy

Key search term[a]	**Combined with (AND)**
Preference elicitation	Consumer – Innovative – Scenario based – Simulation – Virtual Reality – Simulation game – Market research – DCE OR conjoint analysis
DCE[b] or CA[c]	Innovative – Scenario based – Virtual Reality – Simulation game – Market research
measuring preferences OR measure preferences OR preference measurement	Consumer – Innovative – Scenario based – Simulation – Virtual Reality – Simulation game – Market research

[a]The key terms were combined using "AND" with each of the individual terms of column 2 in the same row.
[b]DCE: discrete choice experiment.
[c]CA: conjoint analysis.

3.3 Assessing the applicability of innovative elicitation concepts for patient preference elicitation

The current standards to conduct CA or DCEs in health care were reviewed based on leading guidelines in the field issued by the International Society for Pharmacoeconomics and Outcomes Research

(ISPOR), the US FDA, and the Medical Device Innovation Consortium (MDIC) [42, 45, 49]. These guidelines served as a baseline to assess the applicability of the identified methods and concepts from the consumer research field in a health care setting. For the applicability assessment, one author (NVD) evaluated each preference elicitation concept against every topic of the three guidelines by defining each concept as relevant or not relevant. The resulting findings were then reviewed by a second author (GVS). In case no consensus could be reached, ties were settled by the third author (IH). For every concept identified, the complementarity to current standards and the rationale for implementation were considered.

4 Results

4.1 Comparing the decision-making process for patients and consumers

Table 4 presents the health care analogy in both individual and group decision-making contexts, alongside the steps defined in the consumer context [48].

4.2 Concepts from consumer research methods

4.2.1 Article selection and retrieval

A total of 135 papers were identified using the described search strategy. After selection of titles, 40 papers remained and were screened further by abstract review using the aforementioned criteria. The full text of the resulting 12 papers was analysed. Five concepts were judged to be potentially interesting for health care and are discussed below. Reasons for excluding the other seven papers were as follows. One paper was excluded as there was no description of a preference experiment, and another paper was judged not to present any innovative ideas, as these turned out to be already included in standard software [114, 115]. Further, one paper focused on forecasting decision behaviour instead of quantitative preference measurement, and another discussed a compositional approach to evaluate the attributes one by one, which is not complementary with the concept of real-life decision making [116, 117]. The concepts of three papers were not applicable to health care: one method could only be applied on very similar products (in the example, different movies were used, whereas the attributes of health care options usually differ greatly); one method presented a framework consisting of 39 engineering parameters that could not be easily translated to health care equivalents; and the last method was particularly useful for products with 70-100 attributes, whereas in health care typically 3-7 attributes are used [118–120]. The five concepts that are potentially interesting in health care are discussed below in turn.

Table 4: Different steps of a decision process: health care analogy for the different market evolution stages

Market evolution stage	**Health care analogy**	
Consumer context [48]	**Individual context**	**Group context**
Becoming aware of a need Becoming aware of a product	Receiving a diagnosis and becoming aware of (possible) therapies	The experiment is described: patients become aware of different alternatives (therapies)
Deciding what information to acquire and how to acquire it	Deciding what information (on possible treatments) to acquire and how to acquire it, deciding who (eg, family members, caretakers) needs to be involved in the decision-making process	Deciding what information to use that has been made available
Forming decision rules: deciding whether and which options to consider	Forming decision rules: deciding whether and which treatment options to consider	Forming decision rules: deciding whether and which treatment options to consider
Deciding whether to choose now, delay, or never choose	Deciding whether to choose a possible treatment, choose no treatment (eg, watchful waiting), choose to delay treatment, or choose not to be involved in the decision process	Deciding whether to choose a possible treatment or choose no treatment (eg, watchful waiting)
If choosing now, deciding which option to choose	If choosing now, deciding which treatment option (including the option of watchful waiting) to choose	If choosing now, deciding which treatment option (including the option of watchful waiting) to choose

4.2.2 CONCEPT 1: SIMULATING ALTERNATIVES

By visualizing alternative land use scenarios, Vignola et al. [121] provided a useful method to clarify different options and explore collaboration among stakeholders. The method promotes discussions between stakeholders by presenting the pros and cons of different alternatives and accounting for uncertainties. The scenarios describe possible consequences of different courses of action to improve users' understanding of causal processes associated with every decision. Synthesized images of land use patterns and their consequences on a given landscape are accompanied by a stylized narrative, explaining the key changes depending on the context. Using land development scenarios to represent possibilities in the future has been suggested as a mental exercise to improve planning [122]. Scenario use helps respondents to understand different alternatives and their consequences by improving the cognitive processes in which people collect and combine information and draw inferences [122].

Furthermore, it is recommended to involve all stakeholders as much as possible during the scenario creation phase through interviews, focus groups, and follow-up discussions to refine every aspect [121].

4.2.3 Concept 2: Self-reflection

Hauser et al. stated that consumers only learn their preferences as they make realistic decisions [123]. To simulate a realistic decision-making process, people need time to self-reflect upon their options. Without self-reflection, preference elicitation methods might not measure enduring (true) preferences, which is in line with Hoeffler's findings on preferences for new products [55]. In the study, respondents completed three tasks. First, they formed consideration sets of 30 realistic profiles chosen randomly from all available profiles, which means they had to decide whether they would consider buying the product or not for each profile. Next, they performed a structured preference-articulation procedure (Casemap) by selecting the best and worst level per attribute set. The final task was to state their consideration rules in an unstructured email to a friend. One week later, the respondents again formed consideration sets from a random set of 30 profiles. The predictive ability of the articulated preferences was measured with the relative Kullback-Leibler divergence and the predictions were compared with the consideration-set decisions 1 week later. The authors found that self-reflection was facilitated either by completing the 30-profile consideration set or a highly structured Casemap task (as a best-worst exercise). Self-reflection improved a respondent's capability to articulate preferences that predict consideration sets 1 week later [123]. Finally, the authors suggested that if consumers are asked to articulate their preferences before self-reflection, this articulation would interfere with their abilities to articulate preferences even after they have had a chance to self-reflect [123].

4.2.4 Concept 3: Separated (adaptive) dual response

Some preference elicitation methods such as DCEs might encounter problems when "opt-out" options are provided, with respect to both context effects (ie, when a respondent chooses the opt-out option for a reason other than the lack of useful alternative products) and extreme response behaviour (ie, respondents will always or never choose the opt-out option under some conditions). Schlereth et al. introduced the concepts of separated dual response (SDR) and separated adaptive dual response (SADR) to counter these problems [124]. SDR implies separating forced- and free-choice questions, resulting in the respondents first choosing between two alternatives (forced choice) and then choosing whether or not they actually want the chosen option or would like to opt-out as a second step (free choice). This will overcome the context effects created by dominant alternatives (which decreases the likelihood of selecting the opt-out option) or the existence of very similar alternatives (not choosing is an "easy way out" in this case). SDR also eliminates extreme response behaviour since the respondents

do not have the opportunity to always or never go for the opt-out option. However, the authors noted that this method might introduce a new context effect of choice deferral, resulting in the respondents more frequently choosing the no-purchase option. They suggested solving this problem by separating the questions in time; that is, asking all forced-choice questions first and all free-choice questions later. SADR contains an extra adaptive mechanism that selects fewer, but more informative, free-choice questions.

4.2.5 Concept 4: Feedback-driven exploration

Boesch et al. proposed the implementation of feedback-driven exploration techniques to improve the validity and reliability when developing a stated-preference experiment [125]. This involves implementing continuous feedback between researchers, respondents, and all other stakeholders throughout the process. The authors formulated the following steps to be included in the research design [125]:

(i) Shape guiding research questions, concepts, theories, hypotheses.
(ii) Collect and process data.
(iii) Interpret and reflect on data (researcher, possibly with data providers).
(iv) Report tentative research findings to data providers (e.g. survey respondents, interview participants) and broadly review, discuss and explore results with research stakeholders to arrive at overall conclusions,
(v) Intermediate or preliminary results may indicate a need of getting back to earlier phases of the research process, or even of adjusting and starting the process anew.

The authors suggested that an iterative process (going through the different steps multiple times) might be necessary depending on the research question. Three aspects of a stated-preference experiment are specifically mentioned that may benefit from this approach. First, the validity and reliability of the results can be improved, which is particularly important when dealing with research questions for which no real-life data are available to validate the results. Second, the systematic approach of an overall framework will harmonize all of the different steps required to conduct a preference elicitation experiment. Third, all relevant stakeholders can be involved in the process, whereas experts from outside academia are often overlooked during the research and development phase [125].

4.2.6 Concept 5: Arranging profiles in blocks to improve performance

Adaptive CA consists of two consequential approaches: a composition and a decomposition method. First, respondents evaluate independent attributes (composition method), and then the most preferred attributes are combined in profiles and presented in blocks of two randomly arranged profiles (decomposition method) [126]. This approach is particularly useful when tradeoffs need to be

made between a high number of attributes in a user-tailored process. Huertas-Garcia et al. suggested a design strategy to improve the performance of the decomposition methodology in adaptive CA by arranging profiles, manually or automated by a computer algorithm, into subsets of two profiles [126]. With this strategy, the respondents are asked to evaluate only a subset of profiles rather than the whole choice set. Dividing the profiles in different blocks has advantages both from behaviour and statistical perspectives. Small choice sets are easier to handle and can be assessed faster by respondents. The statistical benefit is that both the variance and covariance of estimations are improved. The aim of this statistical design is to estimate the main factors and two-factor interactions in a quadratic equation with the lowest number of profiles. A limitation of their proposed design is that a maximum of four attributes can be analysed at the individual level. They argue, however, that this is the average number of preferred attributes obtained after the first step in an adaptive CA.

4.3 Assessing the applicability of innovative elicitation concepts for patient preference elicitation

4.3.1 Current standards for patient preference studies in health care

The ISPOR guideline (as published by Bridges et al. [49]) consists of a checklist of 10 topics to be addressed when performing a CA in health care that aims at eliciting preferences at the meta level: Research question, Attributes and levels, Construction of tasks, Experimental design, Preference elicitation, Instrument design, Data-collection plan, Statistical analyses, Results and conclusions, and Study presentation. The MDIC framework focuses on patient preferences regarding benefit-risk assessments of medical device technologies in regulatory decision making [45]. They further provide several topics to consider when developing a preference study, which can be summarized as: defining the research question, the fit of a particular method to the research question, and resources available to undertake a patient preference study. The MDIC guideline discusses both qualitative and quantitative methods and when to use which [45]. The FDA guideline specifically refers to the ISPOR checklist and two other ISPOR guidelines related to good research practices when performing preference elicitation experiments [42, 49, 50, 127]. The major complementarity of the FDA guideline to the other guidelines is its focus on how to inform or educate patients. This is equally important for preference elicitation at the individual or group level.

4.3.2 Applicability of innovative elicitation concepts

The five identified concepts provide ideas on how to improve patient preference elicitation. Table 5 displays the assessment of which guideline items could potentially be improved by applying the five identified concepts [42, 45, 49]. Some concepts are process-oriented and could therefore potentially

impact the entire development process. For example, the concept of feedback-driven exploration could have an impact on 9 out of the 10 steps described by the ISPOR guideline [49]. Other concepts focus on specific development steps, or even on more general challenges such as providing information to patients.

Table 5: Topics of health care guidelines that might benefit from implementing the identified concepts from the consumer research field

X: Guideline topic might benefit from concept implementation

—: Guideline topic not impacted by concept implementation

[a]ISPOR: International Society for Pharmacoeconomics and Outcomes Research

[b]FDA: Food and Drug Administration

[c]MDIC: Medical Device Innovation Consortium

Guideline and items	Simulating alternatives	Self-reflection	Separated adaptive dual response	Feedback-driven exploration	Arranging profiles in blocks
ISPOR[a] guideline					
Research question	—	—	—	x	—
Attributes and levels	—	—	—	x	—
Construction of tasks	—	x	x	x	x
Experimental design	—	x	x	x	—
Preference elicitation	—	x	—	x	—
Instrument design	x	—	—	x	—
Data collection	x	—	—	x	—
Statistical analysis	—	—	—	x	x
Results and conclusions	—	—	—	x	—
Study presentation	—	—	—	—	—
Total ISPOR guideline items that could be improved	2	3	2	9	2
FDA guideline[b]					
Patient centeredness	—	—	—	—	—
Representativeness of the sample and generalizability of results	—	—	—	—	—
Capturing heterogeneity of patients' preferences	—	—	—	—	—
Established good research practices by recognized professional organizations	—	—	—	—	—
Effective communication of benefit, harm, risk, and uncertainty	x	—	—	—	—

Table 5 (continued)

Guideline and items	Simulating alternatives	Self-reflection	Separated adaptive dual response	Feedback-driven exploration	Arranging profiles in blocks
Minimal cognitive bias	—	—	x	—	—
Logical soundness	—	—	—	x	—
Relevance	—	—	—	x	—
Robustness of analysis of results	—	—	—	—	—
Study conduct	—	—	—	—	—
Comprehension by study participants	x	—	—	—	—
Total FDA guideline items that could be improved	2	0	1	2	0
MDIC[c] guideline: conjoint analysis and dual response experiments review					
Methodology criteria	x	x	x	x	x
Sample criteria	x	—	—	—	—
Analysis criteria	—	—	—		x
Output criteria	—	—	—	x	—
Total MDIC guideline items that could be improved	2	1	1	2	2

5 Discussion

5.1 Comparing the decision-making process for patients and consumers

The decision-making process of consumers and patients is highly comparable. The main difference lies in the first step of the process, in which patients become aware of the decision context. More cognitive effort might be required to consider all relevant aspects of a health care context relative to that required for a consumer context. The remaining steps of the decision process are the same. For individual patients in the context of SDM, the process is equally comparable, with again only a few small differences. For example, upon receiving a diagnosis of breast cancer, a woman becomes aware of her need for therapy. The treating physician will provide information on the available options such as the possibility of breast-conserving surgery or mastectomy. The patient will then be advised to think about this for a few days and discuss her preferences with friends, family, or fellow sufferers. During a second consultation, the patient's preferences will be discussed, and a joint decision can be made. In case the patient is not ready to choose or does not want to participate in the decision-making process after all, the physician will propose their preferred option, which is likely to be carried out. The main difference here lies within the step of information gathering. High-quality information on diseases and

potential therapy options is usually more difficult to obtain than information on consumption goods. Ideally, the patient receives all of the relevant information, or information sources, from the treating physician. As a second difference, the need for discussing the potential impact of available options with others might be higher in a health care setting than in a consumer setting. The other steps of the decision process are the same for both consumers and patients engaging in SDM. It should be noted, however, that these steps only apply when patients are offered the chance to actively engage in the decision-making process. According to the National Health Service in England, "SDM is relevant in any non-life threatening situation when a health or care decision needs to be made and a range of options (including doing nothing) is available" [60]. Although the process of SDM was introduced in health care decades ago, implementation is still lacking [15, 128].

5.2 Applicability of identified concepts within current standards for patient preference elicitation

The identified concepts can be useful for one or more aspects of preference elicitation experiments as described by the guidelines. Some concepts can facilitate one or two specific items, whereas others can improve the entire development process. The latter is the case for process-oriented concepts such as feedback-driven exploration. By integrating all of the stakeholders' opinions in the development process, many aspects of preference experiments could be improved. For example, the attributes and levels could better reflect reality, as there is a smaller chance that relevant items will be left out. The construction of tasks, design, and data collection could be better adapted to patients' needs, resulting in clearer answers or higher performance rates. The same applies for developing a VCE as part of a decision aid for individual patients. Systematic development guidelines for decision aids already advise to work with a multidisciplinary team including patients and clinicians [98]. All relevant stakeholders should review multiple times and redesign as necessary. Owing to numerous initiatives, patients are now recognized as an important stakeholder in various aspects of health care [37, 41, 43, 45, 68, 129]. As the European Patients Forum describes, there has been a transition from "doing things *to* the patient" to "doing things *with* the patient" [130]. Current standards for patient preference elicitation already suggest the use of interviews, and focus groups, among others, to guide the further development in (quantitative aspects of) preference instruments [42, 45, 49].

The concept of simulating alternatives will mainly improve informational aspects, as it will help people to fully understand the available choice alternatives. This can benefit patients by facilitating the entire process from becoming aware that a decision needs to be made to making that decision. The concept is equally applicable for designing VCEs in an individual context and for developing experiments with a group of patients. Defining the context and effectively communicating the benefits, harms, risks, and

uncertainties is one of the first steps in both processes. The importance of this step has been highlighted by the FDA guideline [42]. Properly informing patients has been a longstanding challenge in health care; however, there are no satisfactory guidelines on *how* to do this. The PROTECT Benefit-Risk group compared visual representations to optimally provide information for a benefit-risk assessment [131]. They concluded that multiple formats (ranging from different graphs or plots to pictograms or risk scales) can be considered, and found no single visual type that was superior to others; however, the importance of considering the target audience when choosing a visual format was stressed. The authors further acknowledged the value of interactive/dynamic visuals, which enable active participation and improve understanding [131]. The use of simulating alternatives with photos or video materials seems to be a legitimate and feasible course of action to improve understanding and help create the necessary context to provide information [121]. For instance, researchers could show patients videos of how to use a medication with different modes of administration. This could help them to comprehend precisely what "an injection" entails, or how self-administration compares to administration by a nurse. This could be used by patients who recently underwent surgery and require anticoagulant therapy to prevent thrombosis, as these patients typically can choose between self-administering the injections or having a nurse administer the medication. If patients are shown a video of the complete procedure, including washing one's hands, disinfecting the skin area, using the right technique to pinch a fold of skin, injecting the syringe at the correct angle, and disposing the needle, they will be better equipped to make the decision of the administration method of the injections. When patients need to make an informed decision, it is important to adequately inform them on the different benefits and risks, but not influence their behaviour [132]. That is, we want them to truly understand the benefits and risks, enabling them to make a fact-based decision depending on their values [132].

When all of the relevant information has been provided, respondents need time for self-reflection to let the acquired information sink in and decide which alternative(s) would be the most beneficial in their individual situation [123]. Current standards for patient preference elicitation do not explicitly state requirements concerning time needs to acquire and process information. However, both the FDA and the ISPOR task force warn against information overload or yea-saying, and suggest quizzing the respondents to verify comprehension [42, 49]. The MDIC report also expressed the need to gain experience with preference studies and to learn how preferences that change over time can best be evaluated [45]. Implementing this concept by conducting preference elicitation experiments over the course of a few days or weeks might be a good starting point. Researchers could alternatively provide respondents with the necessary information and a preparatory task to think about their preferences on the first day of the experiment. After a few days, the researchers would provide the same

information and elicit their preferences during a final preference elicitation task. Of course, the downside to this approach is that the required time per respondent will almost double. Furthermore, the preferences of individuals with chronic diseases might change over time, along will their tradeoffs [45]. In the context of SDM, it is already considered to be good practice to provide patients with a decision aid in preparation for the consultation, as this will allow them to process the information, clarify their preferences, and prepare for a discussion [133].

After exploring the possible alternatives and taking the time to self-reflect, the next step in a decision process is deciding when to choose: now, later, or not at all (see Table 2) [48]. Including an opt-out option (opting not to make a choice or decision) in preference elicitation experiments can simulate the alternative of "choosing not to choose" [124]. In an individual context, this option may translate to watchful waiting or active surveillance. Another possibility is choosing to retain one's current course of action; for example, when a patient prefers their current treatment over all other options presented. As this situation is realistic, opt-out options should be included in patient preference elicitation experiments whenever relevant. This approach is already supported by the ISPOR health care guideline checklist [49]. An SADR can be used to overcome context effects or extreme response behaviour in these cases [124]. However, in cases for which it would not be medically responsible to abstain treatment, this option should not be included in experiments that elicit group preferences [134].

Finally, arranging profiles in blocks of two has the advantage of imposing a low burden on respondents, as it requires less cognitive effort to consider two profiles multiple times rather than multiple profiles a few times [126]. In this way, respondents can repeat the process several times. There is also a statistical advantage, given that with a low number of tasks, doubling the tasks per respondent is equally effective in increasing precision as doubling the number of respondents [135]. The decompositional part of adaptive CA can also be completed with partial profiles, but the main benefit of evaluating two full profiles is that the respondents have the chance to evaluate complete products; this is more similar to the real-life situation by capturing all relevant aspects to consider [48]. Tailoring the choice tasks for the user also fits within a natural decision-making process, as choosing must-have attributes can be a way of forming decision rules. For example, if a preference experiment comprises 10 different attributes, the respondents' answers could be used to gradually eliminate attributes that are considered less relevant by the respondent, resulting in fewer attributes that are used to form product profiles. This process can only be performed by a computer algorithm, implying the need for a computerized application. As this concept mainly provides statistical benefits, it is less relevant in a context of SDM where only the preferences of an individual patient have to be elicited.

5.3 Differences between consumers and patients: remaining challenges

The extent to which we can apply consumer preference elicitation methods to simulate real-life decisions in a health care context is still unclear, both at the individual and meta level. In some respects such as when providing information, these methods could clearly offer improvements to enhance understanding. However, applying consumer preference elicitation concepts in health care will encounter limitations owing to some fundamental differences between health care products and consumables. First, health care is often a very complex matter relative to other consumer needs, making it difficult to fully understand the decision context such as a certain disease or the characteristics of the available options. Trying out different alternatives (eg, different smartphones, cars) is a useful approach in consumer research to obtain information on product characteristics or to determine the option that is most in line with personal needs. However, this solution is simply not possible in health care, as patients cannot test therapy options in the same way that consumers can test a new car. Simulations may be a very helpful alternative, although this will always require a high level of cognitive effort from respondents. Second, the impact of decisions in health care is relatively high, as the decisions are often irreversible. Third, health is an intrinsic part of a person, whereas consumable goods are interchangeable and can be used temporarily. This implies that preference elicitation methods in health care need to provide patients with more complex and more personal information to prepare them for decision making. Fourth, it is important to consider that consumer and health care products are often introduced differently in people's lives depending on the preference elicitation context. Buying consumables is usually a deliberate decision such as the decision to engage in a preference elicitation experiment for gathering data on market approval or reimbursement. This is different in the individual context, in which the need for health care products can be sudden and unexpected, as is the case upon receiving a diagnosis that is followed by the need to decide on therapy together with the treating physician. Additionally, buying consumables is usually more of an individual decision, whereas the decision-making environment in health care is very complex, often involving multiple stakeholders such as different health care providers, payers, regulatory agencies, and patient advocacy groups. When multiple stakeholder opinions must be taken into account, this impacts the choice of methodology. Finally, another challenge in health care is that preference data can be useful for multiple purposes, ranging from individual to societal decisions. In addition to regulatory authorities, health technology assessment agencies or payers may also take patient preferences into account when making decisions regarding drug approval or reimbursement, respectively. Pharmaceutical companies might be equally interested in using this information to improve drug development. As each stakeholder evaluates preference data from its own perspective, it will be challenging to develop methods that fulfil all needs simultaneously. This versatile use of data

is absent in consumer research, where the main goal is to align product development with consumer needs.

5.4 LIMITATIONS

The limitations of the study are the following. Only one search engine was used to perform the literature review, and although the list of search terms was quite extensive, it is possible that not all relevant papers were included. The publication date was limited to a maximum of 5 years ago, although older publications might also have concepts that have not yet been introduced in health care. Further, the identified papers were screened for exclusion by only one author, which could have resulted in selection bias. Another limitation is that this study focused only on methods applied in the field of consumer research, although many other fields such as behavioural sciences, human-computer interaction and psychology have equally interesting publications regarding methods for preference elicitation. While this decision was made from a practical perspective, it should be acknowledged that some interesting elements of preference elicitation methods from these respective fields might have been overlooked.

6 CONCLUSIONS

The process of decision making is highly comparable between patients and consumers, although some small differences remain depending on the decision-making context. As a result, patients can be categorized as a subgroup of consumers. Therefore, learnings from the consumer research field might be valuable in health care. Five concepts from consumer preference elicitation that could help to simulate real-life decision making were identified in this study. Applying these concepts can result in structural improvements in the development process or improved execution of specific guideline items when eliciting patient preferences. However, the extent to which we can mimic real decision-making contexts in patient preference elicitation requires further research.

CHAPTER 2
ASSESSING PATIENTS' AND PHYSICIANS' UNMET NEED AND PREFERENCES FOR THE DEVELOPMENT OF A PTDA

This chapter is based on:

Ver Donck N, Reymen M, Neven P, Buffel C*, Huys I*
Assessing patients' and physicians' unmet need and preferences for the development of a breast cancer decision aid
Manuscript in preparation

** Joint last authors*

1 ABSTRACT

Purpose: Patient decision aids (PtDAs) are known to improve patients' knowledge and facilitate more actively the role of patients in medical decision making. As the concordance between informed preferences and medical decisions improves, it may even lead to better therapy adherence. Currently, there are few decision aids available in Belgium. The aim of this study was to evaluate patient and breast cancer clinician needs regarding a PtDA for postmenopausal women with hormone-sensitive breast cancer switching adjuvant endocrine therapy.

Methods: Four focus groups with a total of 21 patients who have been prescribed, or are currently taking adjuvant endocrine therapy, and five individual interviews with breast cancer clinicians all living in Belgium were conducted. This qualitative approach was used to assess their opinion regarding shared decision making (SDM), i.e. patient involvement in decision making, information needs and the added value of a PtDA in this context. All interviews were audio recorded, transcribed and afterwards analysed using the Framework Method Analysis.

Results: Decisions regarding adjuvant endocrine therapy were deemed ideal for a PtDA intervention by both patients and clinicians as these therapies can potentially have a high impact on quality of life and deliver limited benefits. Most patients indicated they experience little involvement in decision making about breast cancer therapy. About a third argued they prefer physicians making treatment decisions at the time of diagnosis, while others prefer to be more involved in all therapy-related decisions. Almost all patients were comfortable discussing treatment options during follow-up. Patients' information needs are high, with information lacking on the disease, risk of recurrence, treatment options and impact on quality of life. Clinicians acknowledged that informing patients correctly is an important requirement to participate in decision making but believe that for many patients this might be too troublesome. Clinicians further agree that SDM has become more important during the last decade, however, it remains unclear how to implement this in clinical practice. Patients and clinicians alike considered providing information and preparing patients for their next consultation as the most important goals of a PtDA. Both stakeholder groups further indicated that besides clear and evidence-based information, a PtDA should offer the possibility to write down questions and rate the impact of adverse events on daily life.

Conclusion: There seems to be a discordance as to how patients and physicians currently experience patient involvement in breast cancer decision making. A PtDA could close this experience gap by informing patients on their therapy options and preparing them to discuss their preferences with their clinician.

2 INTRODUCTION

Around 10500 women are annually diagnosed with breast cancer in Belgium [75]. As the most common form of cancer in women, three quarters of all breast cancers occur after the age of 50 and almost one in every nine women will develop breast cancer before they are 75 years old [136]. The 5-year relative survival is estimated to be 90.9% overall and 93.5% for patients ranging from 50-69 years at diagnosis [75]. Furthermore, patients with oestrogen or progesterone receptor positive early diagnosed breast cancer, who represent the majority of the patients, have lower mortality risks compared to patients with hormone-receptor negative disease, unless they have a HER2 positive breast cancer [74]. They are eligible for taking adjuvant endocrine therapy, either in the form of selective oestrogen receptor modulators (e.g., tamoxifen) or aromatase inhibitors (e.g., anastrozole, exemestane, letrozole) [137]. Research has shown that both treatments, that are usually prescribed for five to ten years, may cause a high burden on patients, often impacting treatment adherence and persistence [71–73]. A potential solution targeting this issue could be established by aligning therapy choices by efficacy and toxicity with patient preferences by implementing shared decision making (SDM) [7].

SDM was defined by Elwyn *et al.* in 2010 as "an approach where clinicians and patients make decisions together using the best available evidence" [138]. Easy access to evidence-based and understandable information was identified as the first of three conditions to implement SDM in clinical practice [138]. The second condition requires both physicians and patients to actively engage in the process, in which the physician supports the patient based on the best available clinical evidence, personal preferences and their individual quality appraisals of the decision options [139]. This is done by weighing the benefits, risks, uncertainties and possible consequences of every option to determine personal values and preferences [138]. The third important condition for SDM is a supportive clinical culture that allows patients to engage in decision making [138]. Openly discussing realistic treatment expectations and building a consensus on preferred treatment can facilitate this process [2]. Earlier research has shown that failing to inform patients properly or failing to reach consensus on the best therapy option may lead to non-adherence, what in turn can result in health deterioration and both economic and personal costs [140]. A guideline from the National Institute for Health and Care Excellence (NICE) states that therapy adherence presumes an agreement on certain recommendations between the prescriber and the patient [140]. The level of adherence is determined by the extent to which the patient's actions match these recommendations. For patients to fully agree on treatment recommendations, they need to be able to assess the impact that these treatments will have on their personal lives [7]. Increased patient participation in decision making may increase patient satisfaction and adherence [63, 141]. One approach to improve patient engagement in medical decision making is by using a patient decision aid (PtDA). PtDAs are tools that inform patients on their options and helps them to form, clarify and

communicate their preferences to their health care providers [16]. During the last decade, they have been increasingly applied to facilitate communication between patients and health care providers and to improve patients' knowledge and reduce their decisional conflict [12]. PtDAs have already been extensively researched to improve decision making in breast cancer, with decisions related to type of surgical treatment, fertility and type of aftercare [142–147].

This study aims to assess the needs of both Belgian patients and physicians regarding the use of a PtDA to make a joint decision when deciding on switching adjuvant endocrine therapy. A qualitative approach was adopted to assess these stakeholder's opinions regarding shared decision making, how to optimally meet patients' information needs and to identify specific barriers and facilitators for the use of PtDA in this context.

3 METHODS

Qualitative research was performed to inform the development of a PtDA by interviewing breast cancer clinicians (BCCs) from the University Hospital of Leuven and patients during individual interviews and focus groups, respectively.

3.1 PARTICIPANTS

Patients were recruited via support groups for women with breast cancer that are active in Flanders, Belgium. Every support group was informed of this study via email and was asked to disseminate the information letter amongst its members. In case no response was received, the support group was contacted via telephone if the number was publicly available. Patients who were interested in participating contacted the researchers via email, indicated on an information letter. Patients were eligible to participate if they were between 18 and 80 years of age, had received therapy for hormone-sensitive breast cancer in Belgium and were fluent in Dutch. Potential participants that fulfilled the inclusion criteria were asked to indicate the dates they were available and locations that were possible to attend a focus group. Whenever four or more people were able to participate on a given date, the focus group was scheduled.

BCC from the University hospital of Leuven that are involved in the aftercare of patients with hormone-sensitive breast cancer were invited to participate in individual interviews via email.

3.2 PROCEDURE

One week before participating in a focus group, patients received a sensitization exercise via e-mail[148]. This exercise consisted of four questions that prompted the participants to reflect upon

their experience with breast cancer and their treatment pathway. Sensitization is a process that prepares participants for a focus group, which will enhance both the quality and quantity of the contributions[148]. Patients from six different support groups responded to our information letter. A total of 21 patients participated in four focus groups held at different locations in Flanders. The focus groups were conducted outside hospitals to create a neutral and open environment for the participants. The duration of the focus groups varied between 2 hours and 20 minutes and 3 hours and 15 minutes and the number of participants varied between four and seven per focus group. Before starting the discussion, participants signed informed consent forms and filled out a demographic questionnaire. Afterwards, the participants received a €25 gift voucher. The discussions were audio recorded and the same researcher (NVD) served as moderator in all four focus groups.

Ten breast cancer specialists from the same hospital were approached via email, of which five agreed to participate. One-on-one interviews were conducted at a convenient location for the participants. The interviews lasted between 57 and 81 minutes and were all conducted by the same researcher (NVD). At the start of the interviews, participants signed informed consent forms after which the audio recording was started. Data collection for both stakeholder groups was completed when data saturation was reached. This study was approved by The Ethics Committee Research UZ / KU Leuven.

3.3 Data collection

A semi-structured interview guide was used for both the patient focus groups and individual specialist interviews. The following concepts were discussed with patients: 1) concept of SDM; 2) information need; 3) decision aid content validation and 4) decision aid design validation; and clinicians: 1) patient information need; 2) patient need for SDM and 3) decision aid prototype validation. Concepts 1 and 2 of both interview guides were used to assess the need for a patient decision aid in the context of breast cancer and are discussed in this paper. Concepts 3 and 4 were used to gather feedback on a prototype decision aid design and are discussed elsewhere. Both the focus groups and individual interviews started with an introductory question, related to decision aids for patients and related to SDM for clinicians. The demographic questionnaire for patients contained questions on age, year of diagnosis, level of education, previous breast cancer treatments and type of adjuvant endocrine therapy. Breast cancer specialists were asked to state their year of birth and clinical area of expertise.

3.4 Data analysis

The audio recordings from both the focus groups and individual interviews were transcribed ad verbatim and analysed by a researcher using NVivo 12. The framework method analysis was used to

analyse the main and subthemes, as described by Gale *et al*[149]. This is considered to be a systematic and flexible approach, increasingly applied in the field of health research[149]. This process starts with the transcription of the audio recordings and the researcher(s) getting familiar with the interviews. Next, the interviews are read line by line and important passages receive a 'code' (theme)[149]. The initial coding list was predetermined by two researchers (NVD, IH) based on the themes addressed in the interview guide. The coding list was then further refined by one researcher (NVD) through 'open coding' of the first two focus group and the first individual interview, to ensure that all relevant themes were covered. Codes handling the same subject were catalogued under the same category to create an analytical framework. This analytical framework (table 6 and 7) was then applied to all transcripts. Next, the software NVivo was used to create a framework matrix to allow easy data interpretation.

Table 6: Analytical framework for individual interviews

Information need
Extent of information
Information regarding breast cancer
Information regarding treatment
Patients searching independently for information
How to provide information
Decision aid use
Potential disadvantages of a decision aid
Potential role of a decision aid
Report created for physicians
When to use a decision aid
Shared decision making
Patient involvement in decisions
Methods that allow patient involvement
Patient preferences
Patients preparing to make a decision
Decision aid characteristics
Essential features
Additional features
Possibility for personalization

Table 7: Analytical framework for focus groups

Information need
Information regarding breast cancer
Information regarding treatment pathway
Information regarding treatment
Information on how to deal with adverse events
Information on treatment impact on daily life
Information on potential drug interactions
Information on risk recurrence
Information on location of follow-up
Where to find information
Decision aid use
Potential role of a decision aid
Decision aid characteristics
Essential features
Additional features
Possibility for personalization
Shared decision making
Involvement in decisions
Method of involvement
Physician communication
Preparing to make a decision
Asking questions
Searching independently for information
Personal preferences

4 RESULTS

4.1 PARTICIPANTS

A total of 21 women with hormone-sensitive breast cancer participated in four focus groups: seven patients participated in the first focus group, six patients in the second focus group and four patients in the third and fourth focus group. Data saturation was reached after four focus groups. The average age was 59 years old (range: 50-68) and the average age at diagnosis was 51 years old (range: 36-66). Five patients had already used both tamoxifen and an aromatase inhibitor, seven patients had only used tamoxifen and eight patients had only used an aromatase inhibitor. One patient was offered tamoxifen but had decided not to use adjuvant endocrine therapy. Previous treatments differed between patients: ten patients had surgery, radiotherapy and chemotherapy; seven patients had surgery and radiotherapy; one patient had surgery and chemotherapy and three patients only had surgery. The patients had education levels varying between primary education (1), secondary

education (6), college (9) and university (4). The education level of one patient is unknown. See table 8 for an overview of patient characteristics.

Table 8: Patient demographics

**The education level of one participant is unknown.*

Patient	Year of birth	Year of diagnosis	Age at diagnosis	Education level	Earlier treatment	Prescribed endocrine therapy (chronological)
1	1965	2006	41	Secondary education	Surgery - radiotherapy - chemotherapy	Tamoxifen - anastrozol - exemestan
2	1951	2007	56	College	Surgery - radiotherapy - chemotherapy	Letrozol
3	1965	2001	36	University	Surgery - radiotherapy - chemotherapy	Tamoxifen - letrozol
4	1965	2011	46	Secondary education	Surgery - radiotherapy	Tamoxifen
5	1951	1992	41	Primary education	Surgery - radiotherapy - chemotherapy	Letrozol
6	1952	2001	49	Secondary education	Surgery - radiotherapy	Tamoxifen - exemestan
7	1956	2013	57	Secondary education	Surgery - radiotherapy - chemotherapy	Letrozol
8	1960	2018	58	College	Surgery - radiotherapy	Letrozol - exemestan - tamoxifen
9	1955	2018	63	College	Surgery - radiotherapy	Tamoxifen
10	1962	2015	53	College	Surgery - radiotherapy - chemotherapy	Anastrazol
11	1961	2019	58	University	Surgery	Tamoxifen
12	1952	2018	66	College	Surgery - radiotherapy - chemotherapy	Letrozol
13	1955	2015	60	Secondary education	Surgery - radiotherapy - chemotherapy	Anastrazol (patient chose to quit after 1 year)
14	1969	2016	47	College	Surgery - radiotherapy	Tamoxifen (patient chose to quit after 1,5 years)
15	1968	2018	50	College	Chemotherapy - surgery	Letrozol
16	1969	2010	41	College	Surgery - radiotherapy - chemotherapy	Anastrozol
17	1964	2018	54	University	Surgery - radiotherapy	Tamoxifen: patient chose not to take this therapy
18	1967	2011	44	Unknown*	Surgery	Tamoxifen
19	1953	2007	54	University	Surgery - radiotherapy - chemotherapy	Tamoxifen - anastrozol
20	1956	2014	58	Secondary education	Surgery - radiotherapy	Tamoxifen
21	1968	2018	50	College	Surgery	Tamoxifen

Five face-to-face individual interviews were scheduled with breast cancer specialists, two of which were women and three of which were men. The clinicians had the following specializations: one gynaecologist-oncologist, one oncologist, two clinical fellows gynaecological oncology and one senior resident radiotherapy-oncology. The average age was 33 years old (range 32-36).

4.2 CURRENT EXPERIENCES WITH SHARED DECISION MAKING

4.2.1 PATIENT PERSPECTIVE

Patients indicated they currently experience very little opportunities for SDM. Patients that were involved in some of their treatment-related decisions, emphasized they had to insist multiple times before their opinion was taken into account. Although the participants acknowledged that not everyone is interested in participating in their medical decision-making, they stressed the importance of providing the opportunity to every single patient to be involved. They considered it the task of treating physician to ask patients to what extent they wish to engage in SDM. Furthermore, patients expressed the need for thorough discussions on both the intended benefits and potential adverse events related to therapies. Patients felt that physicians do not always appreciate them asking questions. They further believed that the communication approach of physicians might be age-dependent. Multiple patients were of the opinion that older physicians seem to share less information and sometimes even avoid conversations related to adverse events. Younger physicians, on the other hand, seem more often interested to discuss adverse events and potential remedies.

> **Patient from focus group 1:** "*I was involved in that decision [on adjuvant endocrine therapy], but only after insisting repeatedly.*"
>
> **Patient from focus group 2:** "*I believe [physicians] should definitely ask you whether you want to be involved in the decision making. You still have the opportunity to follow their advice, or to ask more questions, but at least they asked.*"

The extent to which patients want to be involved in their medical decisions, may evolve along their treatment pathway. Many patients indicated that they were not ready to participate in decision making at the time of diagnosis. However, by the time patients were eligible to receive adjuvant endocrine therapy, most of them wanted to be involved. Some patients also indicated that they would rather be involved in decision making related to switching adjuvant endocrine therapy, than decisions on whether to start the therapy at all. They pointed out they would like to base this decision, at least partially, on the adverse events they experience while taking this medication. Patients also acknowledged that their preferences might change over time, stressing the need for a continuous process of SDM. Finally, they also stated that in case patients experience a local relapse, they usually

want to be much more involved in the decision making process, as they better understand that there are often multiple options.

An important consideration for SDM was the provision of adequate and comprehensible information. Some patients indicated that once they acquired information on the intended efficacy and potential adverse events of adjuvant endocrine therapy, they found it much easier to make a decision.

> **Patient from focus group 3:** "*They always told me that if I wouldn't take [the adjuvant endocrine therapy], I would have a 50% chance to relapse. However, at an info evening I learnt that it reduces your chance of relapse with 50%. So then I asked, what is my chance to relapse? Because I received an early diagnosis and had clear lymph nodes at the time my chance to relapse without therapy was 10%, which could be reduced by 50%. In other words, the five years of my life that I am throwing away [because of decreased quality of life], only make a difference of 1 out of 20. I then quit therapy and felt so much better.*"

4.2.2 PHYSICIAN PERSPECTIVE

All five physicians indicated to perform SDM in practice. For one physician, this meant to come to an agreement with a patient on a certain treatment, which may or may not be the treatment the physician initially had in mind. For another, this meant to incorporate both patient experiences and a physician's medical knowledge in a given decision. This physician further emphasized that a patient cannot make clear decisions in these matters, as they are not fully aware of the potential consequences, therefore, a physician should take on a guiding role in SDM. The definition of a third physician seemed to be most in line with what patients expect: adequately informing patients to ensure that they can make decisions based on the correct medical data. This physician also underlined the idea that not every patient feels the need to engage in SDM and that physicians should assess this need.

> **Physician 1:** "*In theory, [shared decision making] should be what we do in practice.*"
>
> **Physician 2:** "*I don't know what impact certain adverse events have on a patient's life, only the patient herself knows. Therefore, it is very important that she shares this information so that we can act upon it, together.*"

BCC further declared that SDM is performed a lot more nowadays compared to the past, simply because more patients require to be involved in their medical decisions. However, they also emphasized that different physicians might approach this differently. Some physicians will probably push harder than others to convince a patient of taking certain therapies. They related this to the fact that a physician's intention is to cure a patient whenever possible and that they are probably willing to accept more adverse events along the way.

> **Physician 3:** "*I believe we try to perform SDM as much as possible, but it is not always feasible. In the past it was more often the case that when patients came to your consultation, they had no idea what was going on with them. You had to provide them with all the information and at the end [of the consultation] they agreed with you. Whereas nowadays, it is a lot more complex; people consult information online beforehand and they already have their own opinion about it*"
>
> **Physician 2:** "*If you as a patient, are willing to accept certain risks, I am completely fine with that, but I know that some colleagues will not accept the fact that patients don't want treatment. It is your body, I might have done things differently, but I am not you, so do your thing.*"

Most physicians agreed that the stronger a patient's indication is to receive treatment, the more important a physician's medial perspective is in decision making, compared to the patient's perspective. One physician pointed out that there is still a big cultural difference between for example Flanders and the Netherlands. In her opinion, many Flemish patients still do what they are told by their physician, whereas Dutch patients usually ask more questions and require more involvement in medical decisions.

One physician emphasized that SDM is not achieved in one single consult, but rather is a continuous process. This was contested by another physician, who declared that patients eligible to switch adjuvant endocrine therapy do not really have a choice. In case it is determined at the start of a patient's adjuvant treatment that she should receive an aromatase inhibitor for 2.5 years and afterwards tamoxifen for the remaining years, a PtDA would not be useful to help make that transition.

> **Physician 4:** "*That's why I find the term 'shared decision making' so difficult, as the decision in this context [of switching adjuvant endocrine therapy] has already been made in the past. So actually, [a decision aid] is meant to refresh a patient's memory, as the initial consult took place in a critical moment after they received surgery, in which patients are more vulnerable and tend to forget some things.*"

4.3 Information need

4.3.1 Patient perspective

Overall, patients indicated they want to receive more information as they consider current information channels inadequate. They require factual information that is easy to understand on both their disease and potential treatments. Especially information related to adverse events was mentioned by the majority of the patients. Some patients even stated that their physician does not acknowledge the adverse events they experienced or that not every physician is open to discuss them. Furthermore, patients argued that some adverse events are very difficult to discuss with their physician, such as

decreased vaginal dryness or decreased libido, but that these adverse events may have a big impact on their quality of life.

> **Patient from focus group 4:** "*This is why I wanted to participate in this study, I hope this will be used and [future patients] will be better informed.*"

More specifically for the setting of adjuvant endocrine therapy, patients wanted to be able to compare different options. For every option, they wanted to know the potential benefits, potential risks and the amount of people experiencing these effects. Especially numbers related to efficacy were mentioned by the majority of the patients. Ideally, a table could be provided comparing potential options in every aspect. Furthermore, patients would like to receive more information on various aspects of potential therapies: how to handle adverse events, potential interactions with other medicines or food supplements and co-morbidities that might be a contra-indication. Patients indicated they experience great difficulty with finding this information themselves.

> **Patient from focus group 4:** "*They always tell you [the medication] is meant to prevent relapse, that it is a preventive treatment. I have heard that a thousand times, but what are my chances if I don't take it?*"

Many patients admitted to search for information online, although they often find it difficult to identify reliable sources. Multiple patients said they looked for information on their hospital's website or the official website of national cancer organizations. Some patients tried to find studies reporting on randomized controlled trials, but rarely succeeded in finding this information.

> **Patient from focus group 4:** "*They never show you the studies that present the effects of potential therapies after ten years, nor can you find them anywhere online by yourself.*"

4.3.2 PHYSICIAN PERSPECTIVE

Physicians acknowledged that adequate information is essential for patients to become involved in decision making. However, multiple physicians argued that patients often use unreliable sources to inform themselves, resulting in unfounded contraindications and long discussions during consultations. One physician advocated for more quality information, made available by physicians or hospitals. On the other hand, some physicians raised the question whether patients are capable to understand the necessary information and interpret potential consequences correctly.

> **Physician 1:** "*It may be an incentive for doctors to make more quality information materials available. After all, patients wish to be better prepared for a consultation. I believe that is an invitation for us [doctors] to make more information available for patients using online channels.*"

One physician admitted that informing patients correctly is often a challenge and physicians are not always adopting the appropriate communication techniques to communicate numbers. Furthermore,

physicians stated that they always try to adjust the information they deliver to individual patient needs. They fear that this would not be possible when patients use a decision aid. The physicians further agreed that a decision aid should contain sufficient information to adequately inform patients on the one hand, but that it should be concise enough to make sure that patients do not get scared on the other hand.

> **Physician 1:** "*I belief that there is too little attention in our education for this matter. I am sure that many physicians use relative risks in their communication, but this tells you nothing. We should use absolute numbers or rather proportions to discuss numbers. Use phrases as 'one in X patients' or explain terms as number needed to treat. There is definitely room for improvement on this matter for physicians*."

The most important aspects patients should be informed about, according to physicians, were: type of breast cancer, risk of recurrence, adverse events and impact on quality of life. The objective of a treatment or intended effects were considered to be the most important. Next in line is information on adverse events, although physicians pointed out to focus on the most important ones, not to scare patients. Another physician believed that communication related to adverse events could be improved.

> **Physician 2:** "*I believe we should communicate openly on adverse events, because patients do experience them in reality. I think this is often downplayed by physicians.*"
>
> **Physician 2:** "*I want patients to have realistic expectations about the efficacy [of treatments] and no unrealistic fear of adverse events*."

4.4 Potential role and useful features of a patient decision aid

4.4.1 Patient perspective

The most important role of a PtDA would be to provide clear, fact-based information. Ideally, it should contain a table providing a comparison that is easy to understand. Having all the relevant information in one place is a major advantage, as patients do not have to look for information themselves. Patients would primarily want to use the decision aid to prepare for an upcoming consultation, as the lack of time during a consultation often makes them feel they have no time or no opportunity to engage in SDM.

> **Patient from focus group 3:** "*It's only at the time of your consultation that you are informed on what you need to do [treatment that is prescribed] (…) Adverse events are not discussed because you only have 5-10 minutes available. All your questions come to mind afterwards, and you have no time available anymore to make a decision, or you don't feel like you can still engage in the decision making."*

Next to using the decision aid before switching adjuvant endocrine therapy, patients also expressed the need for evaluating their current therapy. They argued that patients can only assess treatment impact on quality of life properly after using that treatment. Furthermore, they stated that this assessment or their preferences might change over time.

> **Patient from focus group 4:** "*I believe that the burden you experience because of treatment, may change over time. Hopefully this decreases, but I feel that some adverse events may cause such a heavy burden after a few years, that you want to reconsider [your treatment].*"

Features of a PtDA that were considered to be useful were: the possibility to write down notes or questions, patient stories or testimonials, links to interesting websites, a method to rate the impact of adverse events related to current therapy and a glossary with medial terms. Patients emphasized that they would like to use the decision aid to prepare for a consultation and would want to use the notes section to prevent them from forgetting anything.

4.4.2 PHYSICIAN PERSPECTIVE

Informing patients on the intended benefits and potential adverse events are considered to be the most important goal of a PtDA by physicians. Some physicians added that a PtDA can help them to assess whether the patient has an adequate view of the potential therapies. Another advantage would be to assess to what extent patient preferences are in line with physician preferences for that patient's therapy. This could open up the conversation and ensure that all relevant aspects for the patient are discussed.

> **Physician 3:** "*It is important to discover any discordances between patients' beliefs on the intended effect of therapies and reality. Some people think that there is no use in taking [adjuvant endocrine therapy] whereas other people are entirely convinced that they would relapse immediately in case they don't take it.*"

Four our of five physicians agreed that ideally the PtDA is provided one week in advance of a consultation, as this could help making consultations more efficient. However, one physician stated that it would be best if patients could use the PtDA together with their treating physician, but that this would not be feasible in practice due to time constraints. They estimated that the majority of patients would be willing to use the PtDA individually, but that some patients would require help from a nurse or would not want to use the PtDA. Furthermore, one physician acknowledged the added value of using the PtDA to evaluate treatments.

> **Physician 3:** "*Either you and your patient want to make the same decision, which will result in less time needed during the conversation to inform the patient as you can move faster to making that decision; or there is a disagreement between you and the patient, in which case you need to assess why there is a disagreement. Perhaps the patient places more value on certain aspects you thought were less relevant?*"

Regarding the necessary features of a PtDA, physicians agreed that the possibility to make notes or write down questions would be positive. Furthermore, physicians would value questions that assess the importance patients place on certain aspects or the opportunity for patients to quiz themselves on the obtained information.

5 Discussion

5.1 How to design a PtDA so as to optimally improve SDM

Although patients stated that they have experienced very little SDM in their breast cancer treatments, the physicians were of the opinion that they routinely incorporate patient preferences in their treatment decisions. The definition of SDM adopted by the different physicians, however, varied to some extent. Earlier research already showed that clinicians can take up different roles during consultations (expert; authority figure; persuader; and advisor) which will impact their approach towards SDM [150]. As there currently seems to be a misalignment between patient and physician expectations regarding communication, a PtDA could potentially resolve this issue. Research by Tiedje *et al*. showed that PtDAs supported health care providers to adequately present information and inform patients. Patients on their turn felt that they received more information on certain topics that might otherwise not have been addressed, such as costs or weight gain [150]. Most physicians in our study agreed that they primarily need to inform patients on their disease and potential treatment but at the same time believed they should take a leading role in the decision making process. The main reason being fear that the majority of the patients would have difficulties understanding the treatment benefits and risks. This urges the need for clear and understandable information for patients. Especially since almost all patients indicated they wanted to receive more information on their disease and potential treatments. Earlier research has also shown that physicians might discuss treatment benefits more than treatments risks or adverse events [151], which was echoed by patients in this study. PtDAs could meet the current information need, as many developed PtDAs have already shown to improve understanding and knowledge retention in patients [12]. More detailed information may improve patients' knowledge even more compared to simple information [23]. Many patients in this study wanted to receive more detailed information, although BCC expressed their concerns that this information might be too difficult for patients to understand. This highlights the need for the involvement of both parties in the development of a PtDA [23]. Another advantage of PtDAs is that they seem to improve patients' ability to accurately interpret risk compared to usual care without a PtDA [12].

5.2 FACTORS RELATED TO PTDA IMPLEMENTATION

To ensure the quality of a PtDA, all information should be evidence based and must be presented in a clear and unbiased manner [21]. The Food and Drug Administration (FDA) has issued a guideline for communicating risks and benefits in 2011 that provides clear instructions for both qualitative and quantitative information dissemination [132]. Furthermore, Abhyankar *et al.* performed a review on how to balance information in PtDAs, as this is a standard requirement for the development of PtDA according to the International Patient Decision Aid Standard (IPDAS) Collaboration [17, 25]. They concluded that a side-by-side presentation of information is believed to be a good format for balanced information. Multiple patients in this study specifically asked for a side-by-side presentation of intended benefits and potential risks, as this would allow them to easily compare different options. Furthermore, the importance of adjusting a PtDA's content to the target population's health literacy and numeracy, cannot be underestimated [28, 53]. In another study from IPDAS, key principles for risk communication were highlighted [53]. Clear presentations of the chance that benefits or adverse events can occur is an example that was requested by most patients in this study.

Earlier research has shown that PtDAs can improve patient-clinician communication by increasing patient involvement in the decision making [12]. The main barriers to engage in SDM as perceived by patients in this study were lack of information, lack of time to consider or discuss their options during consultations and the feeling that there were no other options (for example switching or quitting therapy) were available to them. Each of these aspects could be improved by providing patients with a PtDA in preparation of their next consultation. A potential PtDA feature that was highly valued by many patients was the opportunity to write down questions or to evaluate the benefits and risks of potential or current therapies. Patients furthermore requested that their notes could be printed after using the PtDA, and they believed this would remind them to discuss their concerns during the consultation. The inclusion of a worksheet or question list that allows patients to discuss certain aspects with others is already included in the IPDAS quality criteria for PtDAs [17].

Finally, the adjuvant endocrine setting was found appropriate by both stakeholder groups to introduce a PtDA. Research by Chewning *et al*. has already shown in 2012 that cancer patients more often want to participate in their medical decision making compared to the general population [68]. It further showed that patients with cancer or other chronic conditions increasingly preferred to engage in SDM in 2012 compared to the period before 2000. Patients in this study stated they feel more comfortable to engage in decision making as their treatment progresses. Physicians on the other hand, had varying opinions. Some believed that no therapies should be imposed on patients in the adjuvant setting, especially as these therapies may have a big impact on patient's quality of life. Involving the patient in decision making would thus be beneficial. One physician, however, argued that the prescription of

adjuvant endocrine therapy is determined after the patient received surgery and should therefore not be discussed again during treatment. Patients should always have the opportunity to weigh in on their treatment decisions, especially as patients' preferences may evolve over time.

5.3 Strengths and limitations

The patient sample used in this study seems appropriate to represent the target population of postmenopausal women with hormone sensitive breast cancer. Patients ranging 50-68 years of age were included from different demographic areas and all of them were prescribed adjuvant endocrine therapy in the past. All but one patient took this therapy for at least one year. Another strength of this study is that both patients' and BCCs' views were assessed. Both stakeholder groups are required, not only to engage in the process of SDM but also to provide input for the development of a PtDA [18]. A potential limitation of this study is the average age of BCCs that participated. As all these clinicians are from the same (relatively young) age group, their beliefs on SDM might differ from older generation clinicians. Especially as the evolution from a more paternalistic model in health care to a model of patient centered care including SDM took multiple years [1]. Furthermore, the interviewed clinicians were not the treating physicians of the interviewed patients. A direct comparison between patient and physician perspectives on the same experience is therefore not possible. All interviews and focus groups were conducted, transcribed, and analyzed by the same researcher, which is a potential strength and limitation at the same time. On the one hand, by applying the same approach for conducting and analyzing the qualitative research, methodological rigor may have been improved. On the other hand, as the research was only interpreted by one researcher, this may have caused bias.

6 Conclusions

Both stakeholder groups confirmed that treatment decisions on adjuvant endocrine would be a good target for the use of a PtDA. Although BCCs stated that they are increasingly applying SDM, patients still believe they have very little opportunity to engage in their medical decision making. The most important barrier for patients to engage in SDM, is lack of understandable information. In order to meet this need, a PtDA should provide evidence-based information on both intended benefits and potential adverse events. Furthermore, a PtDA should facilitate patients' preparation for their next consultation, by allowing them to evaluate their current therapy and write down questions for their BCC. As the perspectives of patients and BCCs vary to some degree and both stakeholders may value potential PtDA features differently, the involvement of both parties in the development process will be crucial.

CHAPTER 3
DEVELOPMENT OF AN INTERACTIVE ONLINE PTDA

This chapter is based on:

Ver Donck N, Verschueren S, Buffel C, Vander Stichele G*, Huys I*
Development of a web-based patient decision aid for patients with hormone-sensitive breast cancer eligible for switching adjuvant endocrine treatment
Manuscript in preparation

** Joint last authors*

1 ABSTRACT

Background: Patient decision aids (PtDAs) are increasingly used to implement shared decision making in clinical practice. The aim of this study was to develop a PtDA to optimally inform and prepare patients for decisions regarding switching adjuvant endocrine breast cancer therapy.

Methods: The development process was based on a combination of the Ottawa decision support framework and the 'SERES Methodological Framework for development of evidence-based digital health tools'. Patients' and physicians' unmet need was evaluated by performing an in-depth literature review and explorative stakeholder interviews and focus groups. The content and design of the PtDA were determined based on clinical trial endpoints and information from patient leaflets, followed by stakeholder discussions. An interview-based, iterative process was applied to determine the optimal communication approach and user-friendly design.

Results: Based on the clinical pathway for breast cancer developed by the Belgian Health Care Knowledge Centre, stakeholders indicated that there is a need for a PtDA when deciding to switch adjuvant endocrine therapy. The International Patient Decision Aids Standards (IPDAS) informed the design of the following modules: (I) an educational module that provides fact-based information on the health condition and treatment characteristics, (II) a scenario-based module that helps patients to imagine the impact of treatment outcomes and (III) a value clarification exercise that elicits patient's preferences. Five attribute categories (containing a different number of attributes) were identified based on the literature review and stakeholder input: efficacy (2), adverse events (13), use (3), impact on quality of life (1) and mechanism of action (1). The final attributes per module, selected based on rankings by stakeholders, include breast cancer mortality, treatment duration, osteoporosis, and increased thrombosis risk. During the development, stakeholder feedback was gathered from 21 breast cancer patients in four focus groups and five physicians in individual interviews. The feedback was implemented and discussed during the following stakeholder meeting in an iterative process. Finally, a prototype PtDA was created, ready for alpha testing in a research setting.

Conclusion: The co-development process lead to a prototype PtDA that incorporates not only an educational component but also a preference elicitation exercise to clarify patient values. The developed PtDA addresses the needs identified in the target population and has therefore an optimal chance of achieving the intended outcomes, which will be verified in a research setting in a next step.

2 INTRODUCTION

2.1 THE NEW MODEL FOR CLINICAL PRACTICE: SHARED DECISION MAKING (SDM)

Patient empowerment and patient involvement in decision-making have become more important during the last decades, resulting in a new model for clinical practice: shared decision making (SDM) [15, 68, 130]. SDM was defined by Elwyn *et al.* as "*an approach where clinicians and patients share the best available evidence when faced with the task of making decisions, and where patients are supported to consider options, to achieve informed preferences*" [15, 138]. Patient preferences are defined by the Food and Drug Administration (FDA) as "*qualitative or quantitative statements on the relative desirability or acceptability to patients of specified alternatives or choice among outcomes or other attributes that differ among alternative health interventions*" [42]. These attributes can include all characteristics that influence the benefit-risk trade-off, for example adverse events, risks, efficacy, duration of effect, duration and frequency of use, route of administration and dosing regimens. Preferences for these attributes differ not only between patients and health care providers [152], but also among patients. Informed preferences are crucial, as they lead to patients better understanding the decision, including accurate expectations about both positive and negative consequences, and result in a decision consistent with personal preferences [15].

2.2 THE ROLE OF PATIENT DECISION AIDS IN SDM

A patient decision aid (PtDA) followed by a consultation between the patient and the physician can help to implement SDM in clinical practice [138]. According to the International Patient Decision Aids Standards (IPDAS) Collaboration, "*Patient decision aids are tools designed to help people participate in decision making about healthcare options. They provide information on the options and help patients clarify and communicate the personal value they associate with different features of the options"* [17]. According to the IPDAS Collaboration, the aim of decision aids is threefold: (1) to provide evidence-based information about a health condition, the possible decision options and the associated features such as benefits, harms and uncertainties; (2) to help patients recognize the value-sensitive nature of a decision and help them to clarify their personal values they place on the features such as benefits, harms and uncertainties that matter most to them; (3) to provide structured guidance in the steps of decision-making and communication with involved parties, helping people to share their preferences with their health care practitioner and others [12].

PtDAs can occur in different formats: ranging from paper-based brochures over online tools using simple text and images to full multimedia applications. A Cochrane review from 2017 yielded 50 different healthcare decision areas in which PtDAs were developed and tested in a randomized clinical

trial. The most common disease areas included prostate cancer, colon cancer, diabetes, atrial fibrillation and breast cancer [12].

2.3 THE NEED FOR INTERACTIVE ONLINE PATIENT DECISION AIDS

The Ottawa Hospital has an inventory of publicly available decision aids on its website [62]. To be included in the inventory, decision aids need to meet the definition of a PtDA; report the date when it was last updated (maximum 5 years ago) and provide references to the scientific evidence used. Further, every single DA is rated on 29 criteria based on the IPDAS criteria. DAs about screening or testing include 4 additional criteria. When comparing these ratings for the 24 DAs available for patients with breast cancer, only 5 DAs have evidence available that they improve the match between the features that matter most to the patient and the option that is chosen. For 15 DAs there is evidence that they help people know about the available options and their features [62]. Overall, the vast majority of DAs in breast cancer already provide clear and unbiased information on both the positive and negative features of options, but the way in which they allow patients to explore the different options and what this could mean for their personal life could be improved. The best way for patients to develop informed preferences is through exploration, as this enables them to compare the different options in an intuitive manner [6, 30].

Implementing a SDM process in practice is challenging as there are multiple barriers to overcome. Although physicians often make many efforts to inform their patients adequately, they are faced with certain limitations like insufficient consultation time or lack of clinical training [60]. A study by Légaré *et al.* showed that health professionals perceive time constraints, lack of applicability due to patient characteristics and lack of applicability due to the clinical situation as the most important barriers to SDM [128]. Further, it is challenging for clinicians to adapt their communication to an individual patient's health literacy, language and culture. Earlier research has shown that patients do not always receive their preferred amount of information or that they feel their preferences are not sufficiently incorporated in the decision-making process [146]. As patients' needs differ tremendously, physicians need to be flexible in adapting the SDM process in various ways to help patients understand the impact of different options and weigh benefits and risks. To overcome all these barriers and improve the process of SDM, high quality interventions that focus on both patient and physician needs are necessary. Electronic educational tools and serious games have previously been identified as promising ways to address health education and decision support [153–156].

2.4 Research questions to be addressed in this study

In Belgium, 10627 women were diagnosed with breast cancer in 2017 [75]. Thanks to a wide range of potential treatments, the prognosis for female breast cancer is relatively good, with a 5-year relative survival of 90.9% (Belgium, 2013-2017) [75]. Although there are 24 decision aids internationally in use in breast cancer, there are none available to facilitate SDM for breast cancer treatments in Belgium [62]. Earlier research indicated that patients with breast cancer require clear and understandable information and wish to engage in treatment decision making [24, 146, 157]. Moreover, international research already highlighted the need of cancer patients in general to engage in SDM [68]. The aim of this study is:

- To identify the treatment decision point with the highest unmet need regarding SDM in breast cancer.
- To determine the needs of the target group regarding content and design of the PtDA.
- To develop a prototype PtDA that addressed the identified needs in collaboration with both patients and breast cancer specialists.

3 Methods

3.1 Development process

The development process of the decision aid is based on the systematic development process for DAs, described in a meta-analysis from Coulter *et al.,* and the SERES Methodological Framework for development of evidence-based digital health tools from Mindbytes [98, 155]. This process comprises an analytical and development phase, as shown in figure 4.

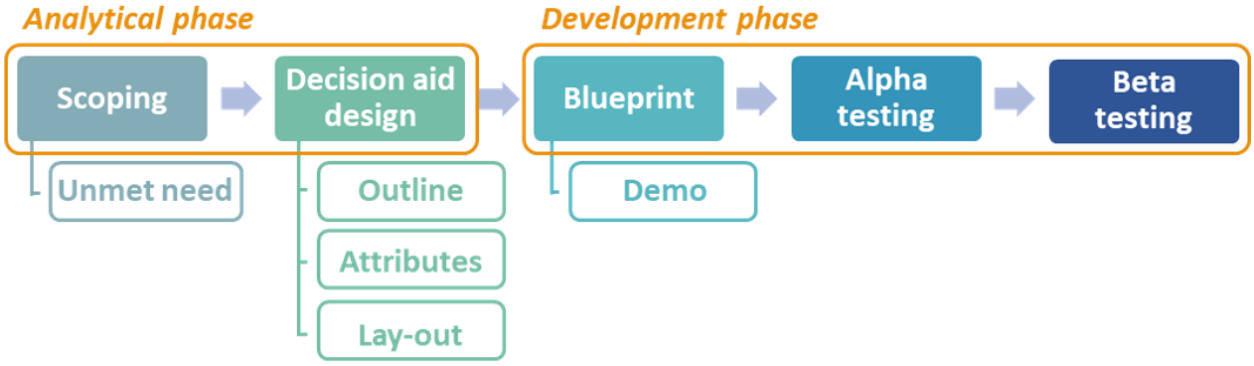

Figure 4: Development process of decision aid.

3.1.1 ANALYTICAL PHASE

Scoping: determining the decision point for a DA intervention based on unmet need

To identify relevant decision points for a PtDA intervention, the breast cancer treatment pathway as published by the Belgian Health Care Knowledge Centre, was analysed using two criteria[74]. Firstly, the decision needed to qualify as "preference-sensitive", as these decisions have no '*single best choice*' and decision aids could be used to inform patient on the available evidence, according to Stacey *et al*.[12]. According to FDA, therapeutic decisions are preference-sensitive *when multiple therapy options exist and no option is clearly superior for everyone; when the supporting evidence for one of the potential options is uncertain or variable; or when patient's preferences regarding benefits and risks of potential options vary considerably within a patient population, or between patients and healthcare providers*[42]. Secondly, a relevant number of patients should face this decision annually in Belgium to justify resource allocation from a business perspective. Based on these criteria, a selection of possible decision points was presented to two Belgian health care providers active in the field of breast cancer. In addition, the need for and possible added value of a DA was discussed during exploratory meetings with the same health care providers and five patients to determine the scope of the study. This explorative qualitative research was approved by the ethics committee of UZ / KU Leuven. The added value of a PtDA covering this decision point was confirmed during focus groups with patients and individual interviews with breast cancer specialists.

Design: determining DA outline

The PtDA is divided into three different modules to meet the IPDAS aims discussed above as well as the specific stakeholder unmet needs identified in the scoping step.

1. Module 1: An educational module in which patients can inform themselves on the different decision options (to meet aim 1 of IPDAS). The necessary information for this module is determined based on the qualitative research performed in the next steps of the development process.

2. Module 2: A scenario-based module in which patients construct their preferences while exploring the consequences of the different options on their life (to meet aim 2 of IPDAS)[155]. This module helps patients to understand the potential impact of the different choice options explained in module 1 on their personal lives. The module further collects patients' assessment of the importance of certain attributes for decision making, as this is relevant information for the treating physician to make a shared decision.

3. Module 3: A value clarification exercise (VCE) in which patients' preferences concerning specific attributes are elicited (to meet aim 3 of IPDAS). The exercise is an adaptive conjoint analysis (ACA)[30]. This preference elicitation method was initially determined by a literature review and then presented to both patients and HCPs to determine whether the method was clear and easy to use for patients

and yielded the necessary information for HCPs. Earlier research showed that preference methods should resemble real-world decisions as much as possible [48, 158]. Therefore, a choice-based approach was preferred over simpler methods as rating scales or ranking exercises. A systematic review by Weernink et al. showed that adaptive conjoint analysis (ACA) is the choice-based method that is most often used to elicit individual preferences for clinical decision making [159]. It further reported that patients valued the need to actively think about the relevant trade-offs and generally found the ACA exercises useful and informative. The ACA uses several attributes and levels, which represent the features of the potential treatments, organized in different categories: benefits, harms/risks, impact on quality of life and use; to construct potential product profiles. Patients are first asked to indicate the relevance per attribute. Second, patients are asked multiple times to choose the best of two given profiles.

Design: attribute determination and selection

Earlier research has stated that there is currently no consensus on how to determine the required content for PtDAs [98]. A systematic review by Weernink *et al*. showed that attributes and levels for individual value clarification methods are identified by performing a literature review, consulting clinicians or performing in-depth qualitative research [159]. Only one study was identified in which patients had to rank the attributes to select the top attributes [146, 159]. A combined two-step approach was used to identify and select attributes in this study. First, clinical evidence on benefits and risks of the two potential therapeutic options (tamoxifen or aromatase inhibitors) was gathered during a narrative literature review. Published randomised controlled phase 3 and 4 trials comparing tamoxifen with aromatase inhibitors (anastrozole, letrozole and exemestane) and a meta-analysis from the Early Breast Cancer Trialists' Collaborative Group were retrieved via Pubmed for analysis, see appendix A [92, 137, 160–162]. Information related to efficacy, adverse events, use and impact on quality of life was retained. The information related to adverse events was further supplemented with information from online patient leaflets[163]. As there were much more potential attributes for the category of adverse events than for the other categories, a selection was made.

To select the most important adverse events, only those that were categorized as very common (more than 1 in 10) or common (up to 1 in 10) were included. Based on this research, a preliminary list of attributes was created for every attribute category. Attributes from the category 'Adverse events' were divided in two groups using the Common terminology criteria for adverse events (CTCAE), version 5.0, as published by the National Cancer Institute[164]. Adverse events that were considered severe/ medically relevant and potentially life-threatening (categories 3-5) were allocated to the group 'Adverse events that contain a certain risk'. Adverse events that fell into categories 1-2 were allocated to the group 'Adverse events that mainly impact quality of life'. This categorization made the long list

of adverse event attributes slightly more structured for stakeholders to evaluate. Second, the resulting attribute list was presented to patients and health care providers to obtain individual rankings within the product categories and an overall ranking of the different categories (bottom-up approach). Respondents were asked to individually rank the attributes from most to least important for the categories 'efficacy' and 'use' and to indicate and rank the six most important 'adverse events', taking both adverse event groups into account. Respondents were asked to rank a limited number of adverse events, to limit the cognitive burden of the exercise. The adverse events were divided in sub-categories using the following rules:

Subcategory A: Attributes that were considered the number 1 most important by two patients or physicians OR number 2 most important by three patients or two physicians

Subcategory B: Attributes that were chosen four times or more across the positions 1-6 by either patients or physicians

Subcategory C: Attributes that were chosen 1-3 times across the positions 1-6 by patients or 1-2 times by physicians

Furthermore, respondents had the opportunity to add adverse events that were missing for their ranking, as only common or very common adverse events were selected. This qualitative research was approved by the ethics committee of UZ / KU Leuven.

After completion of the qualitative research, an overall ranking per stakeholder group was created based on the obtained individual rankings. Patient and health care provider rankings were compared and the relevant attributes per module were determined for the blueprint of the PtDA, based on the following rules:

- If some attributes are considered more important by patients versus health care providers, patient rankings will be retained. However, all attributes will be presented to breast cancer specialists for final refinement and approval.
- The most important attributes should be included in module 3, the value clarification exercise. To limit the burden and time necessary to complete this module, a maximum of 8 attributes will be selected based on stakeholder rankings from at least two different attribute categories.
- Every attribute included in module 3 should be first explained in module 1
- As some people require more information than others, module 1 should contain information on attributes that is required to read (=the ones that are also used in module 3) and information that is optional (=other attributes that are not included in the VCE but are considered important enough to mention based on stakeholder rankings and clinical expertise)
- For module 2, attributes that are difficult to understand for patients (e.g. due to inherent uncertainty of the available evidence or limited numeracy) should be explained further, with special focus on how these attributes can affect everyday life. Attributes that differ between

treatment options should be explained, attributes that are applicable to both therapies can be skipped to prevent the DA from becoming too lengthy.

Design: visualisation

Next, the design requirements (including lay-out, graphic design, and infographic representations) of the PtDA were determined, based on the needs of postmenopausal woman with hormone-sensitive breast cancer. These requirements were identified in a three-step process. First of all, the initial design was based on earlier research performed by Vanderweyen *et al.* for the same target population[165, 166]. Second, by analysing characteristics of the target population, such as gender, age, familiarity with online tools, and general knowledge of and experience with breast cancer and potential treatments, basic design features were determined. EDU-GRID, a tool developed by Mindbytes was used to perform this analysis (personal communication). Finally, an FDA guideline on how to communicate benefit-risk information to patients and a publication by Fagerlin *et al*. on how to improve patients' understanding of benefits and risks to prepare them for decision making were consulted and implemented where possible[132, 167].

3.1.2 Development phase

Creating the blueprint

At the start of the development phase, a blueprint (pre-prototype) PtDA was created based on the PtDA outline and design requirements. The identified design requirements were applied to the three PtDA modules and presented to and discussed with patients and health care providers during qualitative research. Feedback from both stakeholder groups on the PtDA blueprint was implemented and evaluated in an iterative process. Four focus groups with patients and five individual interviews with health care providers were planned over the course of a few months to allow for multiple iterations and revisions. Specific questions were asked to evaluate the concept and content of the three different modules, the clarity, understandability and relevance of the blueprint, special features (for example the possibility to write down questions), the colour scheme, avatar design, scientific and infographic representations, neutrality of the design and navigation options. Every topic was discussed individually or until consensus was reached between the focus group respondents. At the conclusion of the qualitative research, the IPDAS checklist was compared to the blueprint to identify aspects that needed refinement. See appendix B on how the blueprint scored on the IPDAS criteria.

Creating a demo version

Based on all the feedback gathered during previous stages of the development process, an offline demo version of the DA was created. This demo version is ready for alpha-testing using semi-structured

interviews, focussing on the usability and comprehensibility for patients and on the usability and acceptability for healthcare providers.

4 RESULTS

4.1 ANALYTICAL PHASE

Scoping: Determining unmet need

Seven decision points were identified in the treatment pathway of breast cancer patients in Belgium and only two of them fulfilled the two criteria stated above: decisions on type of surgery and decisions related the choice of adjuvant therapy in case of hormone-sensitive breast cancer. Both decision points were discussed with two health care providers and five patients. Based on patient numbers and unmet information need, the treatment decision to switch between adjuvant endocrine therapy after 2-3 years of initial therapy was deemed an ideal decision point for an intervention with a PtDA. This decision includes the following options for patients [74]:

- switch from tamoxifen to aromatase inhibitors (AI): anastrozole, letrozole or exemestane
- switch from AI to tamoxifen: anastrozole, letrozole or exemestane to tamoxifen
- no switch

The target audience was defined as postmenopausal women with hormone-sensitive breast cancer, who have completed at least 2-3 years of adjuvant endocrine therapy and are eligible for a switch.

Design: determining DA outline

The following 3 sequential modules were designed to meet the 3 aims of the IPDAS guidelines as described above.

1. Module 1: Based on stakeholder input during the qualitative research, information on breast cancer, hormone-sensitivity of breast cancer and the process of shared decision making was included. The attribute rankings from the 'attribute determination' step were used to determine the necessary information on the different treatment options (see table 1).

2. Module 2: To optimally help patients translate the factual information into the potential impact on their personal lives, narrative scenarios with simplified visual representations were applied. The content of every scenario was determined based on the attribute rankings from the 'attribute determination' step and stakeholder discussions during the qualitative research (see table 2). To limit the cognitive burden of this module, the most important efficacy attribute and the two most important adverse event attributes that differed between the two potential therapeutic options were selected.

3. Module 3: A value clarification exercise (VCE) in which patients' preferences concerning specific attributes are elicited. The ACA exercise consisted of two different parts: importance questions and paired questions. The importance questions were posed at the beginning, to determine how important it is for respondents to receive the best level instead of the worst level for every attribute. These initial values were used to determine the order in which attributes are investigated in the next part[168]. This next part with paired questions consisted of a total of 16 questions showing two potential product profiles to choose from. The first eight questions contained profiles built up using two different attributes, by the next eight questions contained profiles consisting of three different attributes. Sawtooth software uses the respondents' previous answers to compose product profiles for the next question, resulting in individualized content for every user. After 16 questions, utility weights of every selected attribute are calculated within the ACA software used and shown to the patient. See figure 5 for an example.

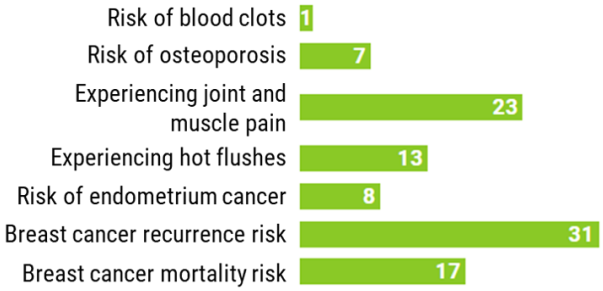

Figure 5: Module 3 output showing importance weights per attribute

Design: attribute selection

The top-down approach resulted in a preliminary list of 46 attributes, divided into four different categories: efficacy, use, adverse events and quality of life (see appendix A). This preliminary list was discussed with health care providers to form a final list of 39 attributes that was clear and relevant to be discussed with patients and health care providers. In three cases, 2 attributes were considered to represent the same adverse events, which were grouped together. For six attributes, the wording was altered and four attributes were removed as the experts considered them less clinically relevant (carpal tunnel syndrome, loss of appetite, and bone pain) or difficult to understand for patients (time to relapse)(see appendix A).

During the bottom-up approach, the 39-item attribute list was presented to 21 patients in four focus groups and 5 breast cancer specialists during individual interviews. Patients' age varied from 50 to 68 years old, their mean age at diagnosis was 52 years and their education level varied from elementary school to university. All patients were prescribed adjuvant endocrine therapy in the past. The physicians' age varied between 32 and 33 years old and they were all working at the same university hospital at the time of the interview. Attributes that were added by patients were: weight gain (added

by four patients), concentration disorders (added by one patient) and aging of the body (added by one patient); the health care providers included no new attributes in the lists. All attributes were selected at least once, except for the attributes 'vaginal blood loss' and 'vaginal itching'. The individual rankings per attribute category for both patients and health care providers were combined to form a ranking per stakeholder group (see table 9) to allow for a comparison.

Finally, respondents ranked the four types of attributes in an overall ranking: efficacy, adverse events, use and impact on quality of life (see table 9).

Design: concept and lay-out

Characteristics of the target population (postmenopausal women with hormone-sensitive breast cancer) that were analysed to determine basic lay-out requirements using EDU-GRID included: age, health literacy, comfort with and knowledge of the diagnosis and therapeutic options, and comfort with online applications. Examples of design features that were determined based on this analysis include avatar design, the narrative level and interactivity level. Design ideas adopted from Vanderweyen *et al.* included avoiding the colour pink in the colour scheme, creating avatars with realistic proportions and using the 'home' and 'bedroom' scenario settings [165]. The remaining scenario settings that are used to illustrate potential adverse events were determined based on stakeholder interviews and focus groups. See table 11 for an overview of the scenario settings used in module 2. The feedback on both the initial design (visuals that complement the scientific information of the first module and visual representations of breast cancer patients for the second module) and lay-out focussed mainly on avatar styles. Developed avatars were adapted two times during the iterative process of qualitative feedback. During the last discussions with either stakeholder group, the avatars, the colour scheme and scientific visuals were approved.

Table 9: Combined attribute rankings by patients and physicians.

Attributes with an asterisk (*) were added by participants during the interviews or focus groups. The category 'Impact on quality of life' contains only one attribute and is therefore only used in the overall ranking.

Attribute category	Patient's ranking	Physician's ranking
Efficacy	I. Disease-free survival II. Breast cancer mortality III. Progression-free survival IV. Overall survival V. Contralateral breast cancer VI. Death without recurrence VII. Death after recurrence	I. Disease-free survival II. Progression-free survival III. Overall survival IV. Breast cancer mortality V. Contralateral breast cancer Death without recurrence VI. Death after recurrence
Use	I. Treatment duration II. Dose frequency III. Mode of administration IV. Dose	I. Treatment duration II. Dose frequency III. Dose IV. Mode of administration
Adverse events **Subcategory A** (in alphabetic order)	Fatigue Hot flushes Increased risk of blood clots Modified liver function Osteoporosis Painful, sore joints Weight gain*	Hot flushes Osteoporosis Painful, sore joints
Subcategory B (in alphabetic order)	Anaemia Concentration disorders* Eye defects Hypersensitivity reactions Hypertriglyceridemia Insomnia Light-headedness Loss of libido Musculoskeletal pains Uterine changes (benign) Vaginal dryness (may cause pain during intercourse) Vomiting, diarrhoea, constipation	Increased risk of blood clots Vaginal dryness (may cause pain during intercourse)
Subcategory C (in alphabetic order)	Aging of the body* Decreased strength Enlarged uterus Fluid retention (ankles) Headache Leg cramps Nausea Sensory changes Skin rash Thinning hair, hair loss Vaginal discharge	Fatigue Hypertriglyceridemia Thinning hair, hair loss Uterine changes (benign)
Overall ranking categories	I. Efficacy II. Impact on quality of life III. Adverse events (all subcategories) IV. Use	I. Efficacy II. Impact on quality of life III. Adverse events (all subcategories) IV. Use

4.2 DEVELOPMENT PHASE

Creating the blueprint

Based on discussion with breast cancer specialists, the following refinements were made to the attribute list (see appendix A). Adverse event attributes that were not distinctive for adjuvant endocrine treatment or not considered to affect the majority of the patients as evaluated by the clinicians were removed (light-headedness; vomiting, diarrhoea, constipation; hypersensitivity reactions, anaemia and modified liver function); attributes were grouped together where possible (vaginal dryness and vaginal discharge were combined into vaginal changes; painful, sore joints and musculoskeletal pains were combined into joint and muscle pain); one attribute was renamed to lay language (hypertriglyceridemia was changed to heart and vascular diseases) and one attribute was renamed based on clinical evidence (the information between brackets was deleted for uterine changes, as this can potentially be malign) and moved to subcategory A. Furthermore, within the attribute category 'efficacy', the attribute 'disease-free survival' (defined as the time from randomization to tumour recurrence or death) was replaced with 'recurrence risk' as this would be easier to understand for patients. Finally, the attribute category 'mechanism of action' was added based on information leaflets used by the physicians in daily practice. These changes were made to ensure the PtDA includes a clear overview of the relevant attributes that are easy to comprehend by both patients and physicians. As the PtDA will be used to inform patients before their consultation, treatment discussions will be facilitated if both stakeholders have the same understanding of the different attributes. By applying the selection procedure (as described under attribute determination and selection), the necessary attributes per module were determined, see table 10. For the category 'adverse events', subcategory A was catalogued as 'must read' for all patients, subcategory B was catalogued as 'might read'.

The blueprint consisted of PowerPoint slides with examples of visual representations and textual content of the DA that was assessed on clarity, understandability and relevance; for example: the process of SDM, hormone-sensitive breast cancer, potential benefits and potential risks of available therapeutic options. Patients' and clinicians' feedback was gathered during an iterative qualitative process, resulting in an updated blueprint for every next interview or focus group. The respondents' feedback varied from altered wording, to adapted visual representations or the inclusion of features such as the possibility to make notes, contact a healthcare provider or support group or read testimonies of other patients.

Furthermore, five examples of scenarios for module 2 were discussed in an iterative process by the same stakeholders to select relevant and clear examples, that provide an added value to module 1 (see

table 11). One scenario was approved as presented; a patient having fear of falling due to an increased risk of osteoporosis. One scenario received minor adaptations: a patient experiencing a blood clot (the setting was altered from driving home from the airport to being at home). One scenario received major adaptations: a patient experiencing joint and muscle pain during a yoga class was adapted to a patient having trouble to get out of bed or perform fine motor skills due to joint and muscle pain. As the setting of doing yoga with fellow-sufferers was considered appropriate by stakeholders, it was used to explain the efficacy and adverse events and the uncertainty related to these attributes. Finally, one completely new scenario was chosen during the stakeholder discussions, which included a patient being confronted with a yearly gynaecologist appointment to monitor uterine changes. One proposed scenario setting was not approved by stakeholders: a patient going out for a run and having to quit early; and another scenario was approved but not implemented to avoid making the module too lengthy: a patient experiencing hot flushes after alcohol consumption.

Table 10: Selected attributes per module

Attribute	***Included in:***		
	Module 1	**Module 2**	**Module 3**
Mechanism of action	x		
Efficacy			
Recurrence risk	x	x	x
Breast cancer mortality	x		x
Use			
Treatment duration	x		
Mode of administration	x		
Treatment dose	x		
Adverse events			
Concentration disorders	x		
Eye defects	x		
Fatigue	x		
Heart and vascular diseases	x		
Hot flushes	x		x
Increased risk of blood clots	x	x	x
Insomnia	x		
Joint and muscle pain	x	x	x
Loss of libido	x		
Osteoporosis	x	x	x
Uterine changes	x	x	x
Vaginal changes	x		
Weight gain	x		
Impact on quality of life		x	

Table 11: Overview scenario settings used for module 2

Target decision	Scenario setting	Scenario aim
Switching from tamoxifen to aromatase inhibitors	Home (living room) receiving a telephone invitation from a friend for a bike tour.	Explaining the potential impact of osteoporosis as an adverse event.
	Home (bedroom and kitchen): performing a morning routine while experiencing joint- and muscle pain	Explaining the potential impact of joint and muscle pain as and adverse event
	Yoga class with fellow sufferers	Explaining the efficacy and adverse events and the uncertainty related to these attributes.
Switching from aromatase inhibitors to tamoxifen	Home (living room): experiencing a deep venous thrombosis	Explaining the potential impact of a blood cloth causing a deep venous thrombosis and what to do when it happens
	Home (kitchen): noticing an appointment at the gynaecologist to follow up on vaginal blood loss	Explaining the potential impact of malign uterine changes
	Yoga class with fellow sufferers	Explaining the uncertainty related to experiencing adverse events or efficacy attributes

Creating a demo version for pilot testing in a clinical setting

Based on the final attribute selection and the feedback from stakeholders on the DA blueprint, a demo version of the PtDA was created. This demo version is a web-based digital tool that can be used both online and offline. The software Articulate 360 was used to develop modules 1 and 2 and Sawtooth software was used to create module 3. Ideally, patients receive an e-mail invitation to use the PtDA in preparation of a consultation from their treating physician, during their follow-up period after using adjuvant endocrine treatment for two to three years. In this e-mail it should be explained for which treatment decision the patient is eligible and personal login information for the website should be provided. At the start of the PtDA, patients have to indicate the therapy class they are eligible to switch to (from tamoxifen to aromatase inhibitors or vice versa). This way, patients will only view information that is relevant to their situation. The patient can consult the different modules consecutively. At the end of module 1 and 2, patients have the possibility to print out the questions they have written down and at the end of module 3, patients can print the results from their individual ACA exercise. Patients can bring these various printouts to their consultations to discuss with their treating physician. When

using the DA online, patients have the opportunity to pause between modules. Modules created with both software packages can be put on online servers connected to an SQL database for data storage. See appendix C for screenshots of the DA demo.

5 DISCUSSION

This research resulted in the development of a PtDA for postmenopausal women with hormone-sensitive breast cancer, eligible to switch their adjuvant endocrine therapy. By including the relevant stakeholders throughout the systematic development process, this PtDA should meet the needs of both patients and physicians. The input and feedback received from both stakeholder groups was similar to a great extent, although their opinion was different regarding some aspects. The adverse event 'weight gain' was added to the attribute list by multiple patients, but not once mentioned by physicians. Although the attribute 'vaginal dryness (may cause pain during intercourse)' was considered important by both stakeholder groups, patients mentioned that physicians rarely discuss the sexual aspect during consultations. As some of the adverse events might be difficult to discuss, patients welcomed this information in a PtDA. Co-creation with stakeholders, including multiple interaction rounds, is therefore essential for the development of a decision aid, as earlier stated by Coulter *et al*. and the SERES Methodological Framework [98, 155]. To the authors' knowledge, this is the first patient DA developed in Flanders for this target population.

A main advantage of the developed decision aid, is the fact that it is an web-based digital tool. This allows for the incorporation of interactive elements, personalization and real-time presentation of the VCE results. The PtDA can be incorporated in a hospital's online environment, allowing easy access for patients and notifying them of an upcoming consultation for which they can prepare themselves by using the PtDA. This PtDA aims to be time efficient as the patient can use the PtDA in preparation for a planned consultation, hereby addressing the needs of physicians that consider time-constraints as a major barrier to implement SDM [128]. The results provided by the ACA exercise in module 3 can be discussed at the start of the consultation. This way, physicians know immediately which topics to discuss and which concerns to address. Furthermore, patients may be better prepared for the decision after having the opportunity to consider the different options and to write down any questions.

The possibility to personalize the content based on patients' needs, is another advantage of electronic, online tools. The developed PtDA provides multiple layers of information to meet the information needs of individual patients [146]. Module 1 provides an overview of the minimal required information to be prepared for SDM, but at the same time, allows patients to access additional information, for example information about less common adverse events or how to use the medication.

Earlier research has shown that many breast cancer patients are non-adherent to their adjuvant endocrine therapy due to insufficient consultation with their treating physician and a lack of understanding the risks and benefits of different therapy options, resulting in therapy choices that are not aligned with personal preferences [73, 169]. In the developed PtDA, patients have the opportunity to compare the potential options for every attribute category in module 1. Next, during module 2, patients are encouraged to think about their preferences by indicating the importance of certain attributes or choosing one attribute from a list that they find most important to consider when making a decision. Earlier research has shown that these preparatory questions can prompt patients to self-reflect and form preferences [123]. This type of preparation is particularly relevant when followed by a quantitative preference elicitation method such as ACA, as it will ensure the measurement of accurate and enduring preferences.

5.1 Strengths and limitations

One of the limitations of this study, is the lack of heterogeneity between the involved breast cancer specialists. All five involved specialists worked in the same university hospital and were all from the same age group. However, the research team also included an experienced breast cancer specialist and specialist nurse as clinical experts that provided their expertise. The 21 patients that participated in the focus groups were from four different demographic areas and had varying educational levels, resulting in a sufficiently heterogeneous sample for this research. In order to meet the needs of patients with different educational levels, basic textual and visual explanations were assessed and refined during the focus groups to improve understandability. Furthermore, when developing the informational module of the PtDA, hospital patient brochures were consulted to select appropriate wording. The information used to provide the content of the PtDA was identified using a narrative literature review in combination with stakeholder assessments. Although a systematic literature review would have been a more robust approach, by using a meta-analysis and clinical trial reports in combination with in-depth qualitative research, the researchers are confident that relevant information was identified and selected. Another potential limitation is that patients were not involved in the selection of the VCE type. Although this decision was based on a systematic review and earlier research of the authors, alpha testing will show whether ACA is considered an appropriate VCE for this target population. Finally, the current version of the PtDA is still a prototype version. The development process will only be completed after incorporating patient and physician feedback gathered during alpha and beta testing.

6 CONCLUSIONS

This study led to the development of a prototype PtDA that contains three consecutive modules to meet the IPDAS aims for PtDAs. The first module allows patients to gradually acquire information on potential therapeutic options, the second module uses scenarios to help patients imagine the potential impact on their quality of life and the third module consists of a VCE to elicit patient's preferences. The main advantage of the prototype PtDA is the inclusion of interactive elements, personalization and real-time presentation of the VCE results. This can prepare patients for decision making and facilitate discussions with the treating physician. Furthermore, stakeholder involvement of both patients and physicians is an essential aspect for the development of an interactive PtDA. A total of 20 attributes, grouped into 5 attribute categories, was selected to determine the content of the PtDA. This way, patients will receive the information they require, what might result in therapy decisions that are aligned with personal preferences. To the authors' knowledge, this is the first electronic PtDA addressing the decision to switch adjuvant endocrine breast cancer therapy for Flemish patients. The effectiveness of achieving the intended outcomes will be tested in a research and clinical setting in the next step of this research.

PART II

TESTING THE DEVELOPED PATIENT DECISION AID IN A TWO-STEP PROCESS

CHAPTER 4
ALPHA TESTING THE PTDA: A MIXED METHODS APPROACH

This chapter is based on:

Ver Donck N, Huys I
Alpha testing of a patient decision aid for patients deciding on adjuvant endocrine treatment during breast cancer aftercare: a mixed methods approach
Manuscript in preparation

1 ABSTRACT

Background: Patient decision aids (PtDAs) are increasingly being applied to facilitate shared decision making in clinical practice, however, very few examples are available within the Belgian health care. Earlier research indicated that less than 50% of the developed PtDAs are field tested with patients and physicians not involved in the development process.

Objective: The aim of this study is to alpha test a PtDA for patients with hormone-sensitive breast cancer, eligible to switch adjuvant endocrine therapy.

Methods: Eleven patients and five health care providers (HCP) tested the PtDA in a research setting. Cognitive interviewing was applied while respondents were using the PtDA and a short semi-structured interview was conducted afterwards. Respondents were asked to rate the content, lay-out, user-friendliness, quality and completeness of the PtDA and filled out the system usability scale (SUS).

Results: The average SUS score varied from 77.27/100 for patients, to 82.00/100 for HCP, indicating adequate usability. Patients rated the content, lay-out and user-friendliness on a scale from 1 to 10, resulting in scores of 8.9, 8.5, and 8.2 respectively. HCPs were asked to rate similar aspects, resulting in 8.4 for quality, 8.4 for completeness, 8.2 for lay-out and 8.0 for user-friendliness of the PtDA. All aspects were rated either good or very good, meaning that no major alterations on the PtDA were required. The average time spent while using the PtDA was 65.2 minutes for patients compared to 59.3 minutes for HCPs. The majority of participants considered the length of the PtDA appropriate, although reducing the length of module 3 specifically could be beneficial. Patients indicated that the PtDA would allow them to inform themselves and prepare them to discuss their therapy with their treating physician. The combination of textual information with graphic design and infographic representations was considered to be an advantage. HCPs stated that the PtDA could be helpful for patients to clarify their values, which can open up the conversation and facilitate SDM.

Conclusions: Patients and HCPs believed that the PtDA provides sufficient information in a clear and understandable way and facilitates value clarification. The relatively high scores from both stakeholders regarding usability, content, quality, completeness, lay-out and user-friendliness indicate that only minor alterations are required to prepare the prototype for the next testing phase.

2 INTRODUCTION

Shared decision making (SDM) has increasingly gained attention over the last decades [1, 7, 13]. However, it often remains difficult for both patients and physicians to adopt this approach in practice [15, 128, 170]. Many interventions, such as patient decision aids (PtDAs), have been developed to overcome this hurdle and improve SDM. According to the International Patient Decision Aid Standards (IPDAS), the aim of PtDAs is threefold: (1) providing fact-based information on the medical condition suffered by the patient, potential treatment options and treatment features; (2) helping people to clarify what matters most to them; and (3) helping them to share these values with a health care provider (HCP) [17]. The 2017 review of the Cochrane Collaboration reported that PtDAs improve patients' knowledge and help them to clarify their values, resulting in a more accurate understanding of potential benefits and risks[12]. Furthermore, the study showed evidence for patients participating more in decision-making after using a PtDA [12]. Despite the available evidence on the positive effects of PtDAs on the quality of the decision-making process and the quality of the decision itself, implementation in routine practice is still lacking [20, 171]. One of the reasons for this slow uptake could potentially be due to a misalignment between stakeholder needs and the developed PtDA interventions. Coulter *et al*. published a framework for the systematic development of PtDAs in 2013 in which they stated that the needs, including barriers and facilitators, of various stakeholders should be taken into account when developing a PtDA [98]. It was further stated that only about half of the published development processes for PtDAs included field tests with patients, and even fewer included reviews by clinicians not involved in the development process[98]. As the SDM process requires two partners, a patient and a physician, to be successful, both stakeholder needs should be incorporated in the design of PtDAs aiming to be implemented in routine practice.

Currently, the use of PtDAs to improve SDM is not routinely implemented in Belgium. Moreover, there is no PtDA available for women with hormone-sensitive breast cancer deciding on adjuvant endocrine therapy, although this therapy may cause a high burden on patients' quality of life, what in turn may influence their therapy adherence [72].

This paper describes the alpha testing of a recently developed PtDA for postmenopausal women with hormone-sensitive breast cancer. More specifically, the PtDA informs patients that are currently taking adjuvant endocrine therapy on the possibility to switch treatment from aromatase inhibitors (anastrozole, letrozole or exemestane) to selective estrogen receptor modulators (tamoxifen) or vice versa. The decision point for the intervention and the actual development of the PtDA were determined based on patient focus groups and physician interviews reported elsewhere [chapters 2 and 3]. The main objective of this study was to gather qualitative feedback from stakeholders on the usability and comprehensibility of the PtDA for patients and on the usability and acceptability for HCPs.

Furthermore, the added value of the PtDA as perceived by the participants was assessed. The gathered feedback will be used to improve and finalize the PtDA before starting beta testing in a clinical setting.

3 METHODS

A mixed methods approach was applied to alpha-test a developed PtDA for postmenopausal women with breast cancer, deciding on switching their adjuvant endocrine therapy. According to Coulter *et al.*, alpha tests aim to assess the usability, comprehensibility, acceptability, and perceived added value of a PtDA [98]. Cognitive interviewing (using the 'think aloud method') was combined with semi-quantitative questionnaires for both Belgian patients and HCPs. This approach is increasingly used for the evaluation of healthcare tools [172–174]. The prototype PtDA consists of three consecutive modules: an information module that contains information on SDM, hormone-sensitive breast cancer and the benefits, risks and related uncertainty associated with the available treatment options; a scenario-based module that explains the potential impact of different options; and a value clarification method (VCM). The VCM consists of an adaptive conjoint analysis (ACA) exercise in which patients state their preference for potential attributes or make tradeoffs between different profiles. The first part of the ACA exercise comprises importance questions for every single attribute and in the second part users are asked to make tradeoffs between two potential profiles. The first eight questions compare profiles consisting of two different attributes, the last eight questions compare profiles consisting of three different attributes. Screenshots from the prototype can be found in appendix C.

3.1 PARTICIPANTS AND RECRUITMENT

Belgian patients that had previously provided feedback during the development of the PtDA and had indicated that they could be contacted again, were approached via email. Belgian HCPs, both breast cancer specialists and breast cancer nurses, active in the aftercare of breast cancer from three different hospitals were contacted via telephone. Both HCP involved and not involved in the earlier development process were contacted. Interested participants received the information letter of the study via email. In case participants confirmed their participation, an interview was scheduled. Patients were eligible to participate if they were between 18 and 80 years of age, Dutch-speaking, diagnosed with hormone-sensitive breast cancer and were currently taking or had taken adjuvant endocrine therapy. HCPs had to be fluent in Dutch and familiar with the treatment context of patients receiving adjuvant endocrine therapy.

3.2 STUDY PROCEDURE

A total of 13 patients and 7 HCPs were invited to participate in this study. They were asked to use the prototype PtDA during an individual interview and evaluate it afterwards. Both patients and HCPs were asked to think aloud while testing the PtDA and to freely express their opinion on content functionalities, format and layout. The interviewer used scripted prompts (such as 'What do you think of this visual representation?', 'Is it clear where you can click next?' or 'What do you think of this explanation?') to elicit participants' thoughts when they stopped thinking aloud [174]. The patients and HCPs were observed while using the PtDA and the interviewer made extensive notes about the usability and time spent per module. Immediately after testing the PtDA, participants were asked to fill out a demographic and usability questionnaire (see appendix D). Furthermore, patients were asked to rate the content, lay-out and user-friendliness on a scale from 1 (worst) to 10 (best). HCPs were asked to rate the quality, completeness, lay-out and user-friendliness using the same scale. Afterwards, a semi-structured interview was conducted with both patients and HCPs to discuss the following themes more in-depth: usability, clarity, efficiency, acceptability, and content (see appendix D). Interviews were held at a neutral location for patients and at convenient workplaces for HCPs. All appointments were scheduled to take up 2 hours maximally (90 minutes for testing and 30 minutes for the interview) to limit the burden of the respondents and for organization purposes. At the start of every interview, participants had to sign informed consent forms. All interviews were audio recorded and conducted by the same researcher (NVD). After completion of the interview, participants received a gift voucher of €25. Data collection for both stakeholder groups was completed when data saturation was reached. This study was approved by the Ethics Committee Research UZ/ KU Leuven (Belgium).

3.3 DATA ANALYSIS: QUANTITATIVE DATA

3.3.1 PARTICIPANT CHARACTERIZATION

The demographic questionnaire for patients contained questions on age, year of diagnosis, level of education, previous breast cancer treatments and type of adjuvant endocrine therapy prescribed. HCPs were asked to state their year of birth and clinical area of expertise. Data collected via the demographic questionnaire was analysed using descriptive statistics.

3.3.2 TIME SPENT USING THE PTDA

The time spent per module while using the PtDA was measured in minutes. However, the clock was not stopped when the participant provided feedback or asked questions. As a result, the time measured will be an overestimate of the actual time spent on testing the PtDA.

3.3.3 USABILITY

A Dutch version of the System Usability Scale (SUS, see appendix D) was used to assess the usability of the prototype PtDA [175]. This tool, created originally by John Brooke, contains 10 statements for which respondents have to indicate their level of agreement varying from 1 (strongly disagree) to 5 (strongly agree) [176]. To calculate the total score per respondent, the user's response score minus one is used for odd items, whereas for even-numbered items, the user's response is subtracted from five. This procedure scales all values from zero to four, with four being the most positive response. The sum of the converted responses is then multiplied by 2.5 to become the overall usability score [176]. Final usability scores then range between zero and 100 and can be used to assess overall usability. SUS scores lower than 50 are considered to be unacceptable whereas SUS scores above 70 are considered to be good or even excellent for scores of 85 or higher [177].

3.3.4 RATING QUESTIONS ON CONTENT, QUALITY, COMPLETENESS, LAY-OUT AND USER-FRIENDLINESS

Furthermore, the content (patients only), quality (HCPs only), completeness (HCPs only), lay-out and user-friendliness of the PtDA were rated on a scale from one to ten, with higher numbers indicating better scores (see appendix D). An average score above 7 or 8.5 was considered good or very good respectively, based on discussions with clinicians. Scores below 7 were considered unsatisfactory and required further adjustments. The scores obtained by the rating questions were analysed using descriptive statistics.

3.4 DATA ANALYSIS: QUALITATIVE DATA

The audio recordings from every single interview were transcribed *ad verbatim* by the same researcher that conducted the interviews. The framework method analysis was applied to analyse the data[149]. This process starts with the researcher becoming familiar with the interviews by re-listening to the audio recordings and making notes on emerging themes. Next, the transcripts are carefully read, and important passages are labelled. The initial coding list was based on the topics of the semi-structured interview guide (appendix D). Themes that became apparent during the process of coding were added to the list, creating an analytical framework. This framework (see table 12) was used to code every interview using the software NVivo 12. Finally, all the labelled passages were put together in a framework matrix to facilitate data interpretation and analysis [149]. Requested adjustments were gathered per module to allow for a comparison between the patient and HCP perspectives. Requests were automatically implemented if they were made by multiple respondents and if they were not contradicted by anyone. Requests made by only one respondent, or in case of conflicting requests, alterations were discussed by the researchers of this study before implementation.

Table 12: Analytical framework for qualitative research

Clarity of the patient decision aid
Instructions
Textual information
Visualizations
Perceived added value
Patient decision aid quality
Effect on shared decision making
Patient decision aid structure
Length of the patient decision aid
Pace of the patient decision aid
Specific feedback on module 3
Use and sequence of different modules
Splitting up the different modules
Usability

4 RESULTS

4.1 PARTICIPANT CHARACTERIZATION

From the 13 patients that were contacted, 11 agreed to participate in this study. Patients' mean age was 62 years old (range 55-69) and their average age at diagnosis was 52 years old (range 36-66). Six patients had received prior treatment under the form of surgery, radiotherapy, and chemotherapy. Four patients had received surgery and radiotherapy and only one patient had only received surgery as a prior treatment. All patients were eligible to receive adjuvant endocrine therapy; four patients received an aromatase inhibitor, three patients received tamoxifen and four patients received both. Patients' education levels varied from primary education (1) or secondary education (3) to college (5) or university degree (2).

A total of five (four women and one man) out of the seven contacted HCPs agreed to participate in this study. Only one of them was involved in earlier stages of the PDA development process. Their specializations varied between radiotherapy-oncology (1), gynaecology-senology (2) and specialized breast cancer nursing oncology (2). The average age of the HCPs was 38 years old (range 31-52 years old, the age from one breast cancer nurse is missing).

4.2 QUANTITATIVE DATA

4.2.1 TIME SPENT USING THE PTDA

Patients spent an average of 65.2 (range 36-102) minutes while alpha-testing the decision aid, whereas HCPs spent an average of 59.3 (range 53-69) minutes; both numbers are based on the sum of the averages per module. Two patients did not finish the PtDA within the foreseen timeframe of 90 minutes, which resulted in some questions of module 3 that were skipped to allow sufficient time for the interview afterwards. The time spent on module 3 for these two patients is therefore an underestimation of the required time. However, for all interviews, discussions took place during testing, resulting in overestimations of the required time per module. The average time per person therefore only provides an estimate of the required total time for proper use. See table 13 for additional figures.

Table 13: Average time participants spent using the patient decision aid

	Average time spent using the PtDA (in minutes) by:	
	Patients	**Health care providers**
Module 1	28.5 minutes	29.8 minutes
Module 2	12.3 minutes	10.5 minutes
Module 3	23 - 24.4 minutes*	19 minutes
Total	**65.2 minutes**	**59.3 minutes**

**23 minutes when excluding the two patients that were not able to complete this entire module and 24.4 minutes when including the time spent on the third module by these two patients*

4.2.2 USABILITY

Based on the SUS questionnaire, usability scores were calculated. The average usability score indicated by patients was 77.27/100 (range: 65-97.5/100), compared to an average score of 82.00/100 (range 72.5-90/100) based on HCPs' responses. The average usability score for all participants was 78.75. Only 2 out of 11 patients and none of the HCPs rated the usability below 70/100. See appendix E for full responses of all participants.

4.2.3 RATING QUESTIONS ON CONTENT, QUALITY, COMPLETENESS, LAY-OUT AND USER-FRIENDLINESS

Patients were asked to rate the content, lay-out and user-friendliness on a scale from 1 to 10, which resulted in the following average scores: 8.9 for content, 8.5 for lay-out and 8.2 for user-friendliness. HCPs were asked to rate similar aspects, resulting in the following scores: 8.4 for quality, 8.4 for

completeness, 8.2 for lay-out and 8.0 for the user-friendliness of the PtDA. All aspects were rated either good or very good, meaning that no major alterations on the PtDA were required.

4.3 QUALITATIVE DATA

4.3.1 CLARITY OF THE PTDA

Overall patient thought the PtDA provided very clear instructions. Three patients suggested to alter the wording of the questions in module 3 from 'what is most desirable' to 'what is most important'. One patient indicated that it was good that instructions were sometimes repeated during the use of the PtDA. Both patients and HCPs liked the use of red arrows that indicated specific instructions or red buttons that indicated where to click next.

All patients agreed that the information provided in module 1 and 2 was very clear and easy to understand. One patient noted that some of the terminology might be too difficult for people that are not familiar with breast cancer, but that this is not likely to be the case for people in breast cancer follow up. Another patient suggested to include a glossary with medical terms, or to use markers that explain certain terms more often. The majority of patients indicated that the PtDA contains sufficient information, however, three patients suggested to add some extra information regarding dealing with adverse events. This remark was shared by two HCPs. One HCP believed the PtDA contains too much information for some patients. The opinion of patients and HCPs regarding the attributes included to explain the treatment options differed in some aspects. The most prominent one was the adverse event ‘weight gain’, as patients considered this to be very important and very bothersome. Most patients argued that the 2-3 kilograms of weight gain that are mentioned in the prototype PtDA are an underestimation of reality. Some patients even stated that they dislike the fact that physicians do not acknowledge this adverse event properly. HCPs from their side thought the 2-3 kilograms were a realistic estimate and even wondered why this adverse event was included among the most important adverse events, as they did not consider this to be important.

Generally, patients believed that the infographic representations supported the written text well. HCPs also considered the combination of textual and visual information as an added value. One patient specifically stated that an infographic representation of 'X out of 100' was more informative than the corresponding percentages. Another patient and one HCPs believed that the scenarios used in module 2 were not necessary to further explain the factual information, but other patients

contested this. Some patients asked for less text or better spacing in module 3 to improve readability.

> **Patient:** "*The numbers [displayed in an infographic representations of 'X out of 100'] seemed so much more than the percentages shown. So it is very good that you provide both.*"

4.3.2 USABILITY AND PTDA STRUCTURE

All patients thought the PtDA was user-friendly and it could be used in practice if a few small adjustments are made. This idea was shared by the HCP as they considered the PtDA to be self-explanatory. Three HCPs specifically referred to the logical build-up that ensures that users cannot make mistakes while using the tool. The possibility to go back to previous parts of the PtDA was also considered an advantage.

Nine patients found the use and sequence of the different modules appropriate. Module 1 was considered to provide the necessary information, whereas module 2 provided a welcomed change from the textual information and scientific visualizations and helped the participating patients to assess potentially relevant effects on their lives. Finally, module 3 was considered quite lengthy and complex, although most patients believed this was worthwhile given the preference weights as output. Overall patients believed that module 1 and 2 prepared them for the adaptive conjoint analysis (ACA) exercise that serves as a VCM in module 3. From the HCP perspective, three of them thought the use and sequence of the different modules was very good. One HCP suggested to start with module 2, as this one is considered the most approachable of the three modules. Two HCPs suggested to alter the visual representations used in module 2, as they considered this to be quite childlike. However, the remaining HCPs and the majority of patients contested this and stated that they liked the look and feel of module 2. Overall, module 3 was considered the most complex and burdensome. Two HCPs suggested to make module 3 optional, as this might be too difficult for some patients. On the other hand, the relative preference weights generated by module 3 were considered very useful during consultations.

> **HCP:** "*The clear output from module 3 is very useful because you can see at one glance what is important [for a patient]. I don't think that there are doctors who would not like to use that.*"

Regarding the length of the PDA, most patients thought this was appropriate as it helps you with an important decision. Two patients, however, indicated the PtDA was too lengthy. Although the average use by patients was 63 minutes for the alpha testing, four HCPs also thought that the length of the PtDA was reasonable. Both patients and HCPs suggested to shorten module 3 if possible. Patients further stressed the importance of informing potential users on the average duration at the

start of the PtDA. This way patients can prepare themselves and select an appropriate time to do this. HCPs praised the fact that the interactive elements keep you focussed and you can determine the pace of the PtDA yourself. The possibility to revisit earlier information was equally appreciated by patients. Therefore, HCPs agreed that patients who are interested in informing themselves on their medical choices will be willingly to spend an hour to do this. Most patients shared this opinion. Furthermore, both patients and HCPs suggested to provide patients the opportunity to pause between different modules to avoid decreasing attention.

4.3.3 Perceived added value of PtDA intervention

Patients believe that they will mainly benefit from the information provided in the PtDA as it will allow them to inform themselves before a consultation and will prepare them to discuss their therapy and ask relevant questions. Using the PtDA can empower them to actively engage in treatment discussions and the decision-making process. At the same time, all HCPs agreed that the PtDA could be helpful to open up the patient-physician conversation and thus facilitate SDM. Four HCPs referred to the fact that the PtDA will assist patients to clarify their personal preferences, which in turn will help patients to discuss these topics during consultations. One HCP specifically referred to the potential effect on treatment adherence if medical decisions would be more in line with patients' preferences.

> **Patient:** "*I believe patients will be more confident [after using the PDA]. You will have better insights in the matter, whereas you usually don't know what you are talking about. When you receive a prescription, you have to find all the information yourself. This will be improved with the PDA.*"
>
> **HCP:** "*Even when I have to make a treatment decision for a patient, I want to know this patient's preferences because I want this patient to adequately adhere to her therapy. It would be useful if a PDA could help patients to communicate their preferences, indicate what they would like to discuss or even indicate which aspects are definitely a 'no-go'; because this could inform you on whether the patient intends to actually use the prescribed therapy. This might not be ideal SDM, but it would be much more SDM than it is currently the case.*"

Furthermore, both patients and HCPs appreciated the feature that allows users to make notes during module 1 and 2. At the end of both modules, users are offered the possibility to print these notes. The majority of patients stated that they would use this feature to write down questions they did not want to forget during the consultation. Another advantage of the PtDA according to HCPs, would be that patients are better informed on their potential therapy. As some patients require more information than what they receive in current practice and consultation time is limited, an

online PtDA would be an ideal preparation. Providing the PtDA in the week before a planned consultation, was considered an appropriate timing.

5 Discussion

5.1 Providing information

Earlier research has shown that patients rarely receive their preferred information to participate in SDM [146]. This was confirmed for this study population of postmenopausal breast cancer patients in an earlier study [Chapter 2]. Patients were generally pleased with the content and extent of information provided by the PtDA during alpha testing, corresponding with an average content score of 8.9/10. However, multiple patients and HCPs suggested to add extra information regarding dealing with adverse events. On the other hand, some participants were concerned that the current amount of information might be too much for some patients. The authors believe that this issue is already partially addressed in the PtDA, as it includes content control that allows patients to skip parts of the information module. Users are required to go through the required basic information for every attribute (mechanism of action, use, efficacy, and adverse events) in module 1, but are allowed to skip additional information providing more details or comparisons with their current therapy. Content control was already identified in earlier research as a potential feature to improve knowledge and decrease decisional conflicts in PtDAs[33]. This approach is particularly useful, considering that not all patients require the same amount of information [24]. One HCP stated that is was very good that 'essential information' was obligatory and that patients had to go through these basic slides, as this is required to obtain informed decision making. The potential consequences of letting patients select their required information in interactive PtDAs was already pointed out in earlier research [178]. A study from Molenaar *et al*. reported that information selection was influenced by patients' therapy preferences; patients that preferred a mastectomy selected fewer information topics from the module on breast conserving therapy and vice versa [178]. This might result in unbalanced or incomplete information, which in turn might affect patient preferences. Ensuring that all patients receive the minimal information to make an informed decision is therefore crucial. Moreover, a meta-analysis containing 21 studies from 2013 showed that PtDAs that provide more detailed information increases patients' knowledge and reduces feelings of being uninformed, compared with PtDAs that provide simpler information [23].

5.2 Role of VCM

After providing the necessary information regarding potential treatment options, discussing these treatment options is the next step in SDM [7]. Usually a VCM is integrated in PtDAs to support patients forming treatment preferences and to elicit those preferences [30]. The ACA included in the developed PtDA was found useful by both stakeholder groups (see appendix C for visual example). Tradeoff exercises provide a realistic approach for decision making, as patients are forced to tradeoff different risks and benefit as they would have to do in real life decisions [33]. Patients considered this exercise to be useful to clarify their preferences before the planned consultation and physicians believed it would provide insights in the patient's preferences in an efficient and timely manner. One physician explicitly stated that knowing patients' preferences will result in improved treatment decisions and improved adherence. This corresponds to earlier research that showed that treatment adherence may be influenced by treatment-related factors such as adverse events or decision-related factors such as non-optimal roles of patients during treatment decision making [1, 71, 141, 179]. By helping patient to communicate their treatment preferences and preferred decision making role, the process of SDM is facilitated [7]. Treatment adherence is indeed known to vary substantially among patients using adjuvant endocrine therapy [73, 169]. A Cochrane review from Stacey *et al*. has previously stated that future research should focus on the effects on treatment adherence when using a PtDA [12]. Furthermore, both stakeholders liked the opportunity to make notes and print them at the end of module 1 and 2, which is another interactive feature that has been identified to improve value clarification and decision making [33]. Participants from both groups asked for the possibility to print the calculated preference weights from module 3, as this was considered a very good starting point for the consultation. This feature was therefore added to the prototype. Earlier research with a decision aid for breast cancer patients reported that many patients print pieces of information from the decision aid to support them to discuss it with others [178].

5.3 Importance of co-creating PtDAs

Generally, patients and HCPs provided similar feedback on the content of the PtDA, however, their opinion regarding the attribute 'weight gain' was very different. Patients judged this attribute to be much more important than HCPs and some of them even argued that their weight gain caused by the medication was greater than 2-3 kg. Only one HCP agreed that an estimate of 5-6 kg weight gain would be more realistic, other HCPs that were interviewed in an earlier stage of the PtDA development contested this [Chapter 3]. Such differences in stakeholder opinions also occurred in other research [152], although the importance of open and trustful communication between patients and their HCPs

has been highlighted in the past [63, 141]. Another, more general difference between patients and HCP is their estimate of the understandability of the provided information. Only one patient indicated that the provided information might be too difficult for the target population, whereas all other patients believed this was sufficiently comprehensible. HCPs were of the opinion that the developed PDA was adequate for some patients but might be too difficult for the majority of the patients. This is why involvement of all stakeholders is inadmissible for the successful development and implementation of high quality decision aids [98]. Better understanding of the barriers and facilitators for SDM that both patients and physicians experience, can help developers to create PtDAs that meet both stakeholders needs [98]. During the development process of this PtDA, stakeholder input was sought at several stages: to determine the exact decision point for a PtDA intervention; to collect input on the initial draft and essential features and finally; to collect feedback on the developed PtDA prototype. The obtained scores on content, lay-out, quality and usability reflect that this prototype PtDA meets the needs of patients and HCP to a great extent. This is probably due to the co-creation with these stakeholder groups.

5.4 Limitations and strengths

A strength of this study is the inclusion of both patients and HCPs to represent both stakeholder's needs, however, other potential stakeholders such as policy makers or experienced PtDA developers could have provided additional insights. Potential limitations are the possibility for selection-bias to have occurred, as only patients who were already interviewed at the start of the development process were contacted and the limited number of respondents that participated in this study. However, the majority of the received feedback was very comparable and patient interviews were only stopped when data saturation was completed. It is possible that additional HCP interviews may have yielded additional feedback. Another potential limitation lies in the nature of the chosen methodology, as a participant's verbal abilities may be an impacting factor in cognitive interviewing. The researchers tried to limit this effect by using scripted probes while participants were testing the PtDA.

6 Conclusions

Patients and HCP alike thought that the PtDA provided clear and easy to understand information. Especially the infographic representations were considered useful, as they clarified the quantitative information. Both stakeholders believed the adaptive conjoint analysis exercise in module 3 improves value clarification, which in turn can facilitate discussions during the consultation. Furthermore, PtDA features that allowed to make and print notes while using module 1 and 2 and print the results of

module 3 were considered valuable to improve SDM. As the opinion of patients and health care providers differed on some subjects, the involvement of all stakeholders is crucial to reach consensus for the development of the PtDA. Finally, the prototype PtDA received relatively high scores from both patients and HCP regarding usability, content, quality, completeness, lay-out and user-friendliness. Only minor alterations are required to prepare this interactive, online PtDA for the next testing phase.

CHAPTER 5
BETA TESTING THE PTDA: A PILOT STUDY

This chapter is based on:

Ver Donck N, Van Cauwenberge J, Neven P, Huys I
Beta testing of a patient decision aid for patients deciding on switching adjuvant endocrine treatment during breast cancer follow up: a pilot study
Manuscript in preparation

1 ABSTRACT

Aim: This study aimed to assess the usability, effectiveness and feasibility of implementation of a patient decision aid (PtDA) in a pilot trial in Flanders, Belgium. The target group were women with hormone-sensitive breast cancer, eligible to switch adjuvant endocrine therapy from tamoxifen to an aromatase inhibitor or vice versa.

Methods: A total of nine patients tested the PtDA one week before a planned follow-up consultation at the university hospital of Leuven. The effectiveness of the PtDA was assessed by measuring the following constructs: knowledge, values-choice agreement, feeling informed, feeling clear about values, discussing goals with health care providers, and being involved. Patient preferences for different treatment characteristics were elicited using an adaptive conjoint analysis. Usability was assessed using the system usability scale. Wilcoxon matched pairs rank tests were used to compare knowledge scores before and after using the PtDA and decisional conflict right after consultation and one month after consultation.

Results: The pilot trial indicated a significant increase in patient knowledge and low levels of decisional conflict, both immediately after the consultation and one month after the consultation. Patient preferences regarding treatment characteristics varied considerably, with risk of recurrence being selected three times as most important attribute. Patients indicated that they were not really involved in the treatment decision making, with shared decision making scores being very low.

Conclusion: This pilot trial indicates that the developed PtDA increases patients' knowledge and decreases their decisional conflict. The extent to which a shared decision making approach was adopted during consultations could still be improved. The variability in elicited patient preferences indicates the need for personalized approach in treatment decision making. The results of this pilot study should be confirmed in a larger follow-up trial, that should also include interventions directed to improve health care providers' shared decision making skills.

2 INTRODUCTION

Breast cancer is the most frequently diagnosed cancer (24.2%, 2018) and the leading cause of cancer death (15.0%, 2018) in women worldwide [180]. In Belgium, 10627 women received a breast cancer diagnosis in 2017[75]. Overall, these patients have a relatively good prognosis with a 5-year survival rate of 90.9% (2013-2017, Belgium) [75]. Early invasive breast cancer often requires a long treatment pathway, comprising surgery in combination with various adjuvant therapies such as radiotherapy, chemotherapy and endocrine therapy [74]. The choice of adjuvant treatment is determined based on the patient's risk profile and biomarkers. For patients with hormone-sensitive breast cancer, the treatment pathway can be particularly long, as adjuvant endocrine therapy is usually prescribed for five to ten years [74]. This therapy, which may include either tamoxifen or an aromatase inhibitor or a combination of both, is further characterized by a range of adverse events that may impact patients' quality of life [91]. On the other hand, treatment benefits are not obvious to these patients as they are clinically cancer free [91]. These factors, taken together with the fact that treatment impact can vary considerably between individual patients, urge the need for shared decision making (SDM) in which patient preferences are taken into account. Moreover, this concept is strengthened by the fact that patient and physician perceptions regarding acceptable levels of benefit from adjuvant endocrine therapy differ significantly [152].

Patient decision aids (PtDAs) can be applied to implement SDM in clinical practice [7, 16]. PtDAs are tools designed to involve patients in their medical decisions and supplement the patient-physician interaction [18]. The aim of PtDAs is threefold: (I) providing evidence-based information on a patient's illness in general and potential treatments, (II) helping patients to clarify their values and preferences towards the options that are available to them and, (III) supporting them to communicate their preferences to their health care provider [16, 17]. They are known to improve patients' knowledge and risk perception, promote active engagement in decision making and decrease decisional conflict [12]. The online inventory from the Ottawa Hospital Research Institute provides an overview of more than 300 publicly available PtDAs, covering almost 150 different decision topics in the context of disease treatments in general [62]. A total of 24 PtDAs covers decisions related to breast cancer.

There are currently no PtDAs available for Belgian patients with breast cancer although earlier research indicated that these patients prefer to be more involved in their treatment decision making [67–70]. Therefore, a PtDA was developed to support postmenopausal patients with breast cancer when deciding about switching adjuvant endocrine treatment [chapter 3]. The prototype PtDAs was alpha tested with 11 patients and five health care providers focusing on usability, comprehensibility and acceptability [chapter 4]. The prototype was then updated based on the received feedback to finalize

the PtDA for beta testing in a pilot trial. The aim of this study was to assess usability, effectiveness and feasibility of implementation of the developed PtDA.

3 METHODS

The PtDA consists of three consecutive modules: an information module, a scenario-based module that helps patients to imagine the potential impact of different treatment options and a value clarification method (VCM). The VCM consists of an adaptive conjoint analysis (ACA) exercise in which patients have to state their preference for potential attributes or make tradeoffs between profiles existing of two or three different attributes. Screenshots from the prototype can be found in appendix C. Minor text revisions were made to the developed PtDA, based on feedback from physicians who's patients could participate in this study. All revisions were in function of adjusting the PtDA content to the medical procedures of the university hospital where the beta testing took place.

3.1 PARTICIPANTS AND RECRUITMENT

Thirteen patients were recruited to receive the developed PtDA between May 2020 and July 2020. Patients with hormone sensitive breast cancer who were taking antihormonal adjuvant therapy and were eligible for to switch treatment from tamoxifen to aromatase inhibitors or vice versa could participate in this study. Other inclusion criteria were an age between 18 and 80 years old and mastering the Dutch language. Exclusion criteria included cognitive impairment that rendered patient incapable to provide informed consent or to understand the study materials and the lack of a computer device with internet connection at home. Patients were recruited via telephone by a physician of the university hospital of Leuven. Patients that agreed to participate provided their email address which was used by a researcher of this study to provide the link to the online questionnaires and the PtDA. Participants were asked to fill out a questionnaire at three different points in time, see figure 6 for a schematic overview. Up to two reminders were sent by the authors per questionnaire. Both the online questionnaires and the PtDA were administered through a website specifically set up for this study. Patients logged on to the website using their personal username and password, which they received via email. The first time participants logged on to the website, they had to provide informed consent to confirm agreement to participate in the study and the processing of their data. Patients that completed all questionnaires, received a financial compensation of 25 euro for their time investment under the form of a gift certificate. As this study took place during the Belgian lockdown to prevent the spreading of COVID-19, many of the planned face to face consultations at the hospital were either changed to telephone consultations or delayed to a further date. This study was approved by the Ethics committee of UZ / KU Leuven under number S63328.

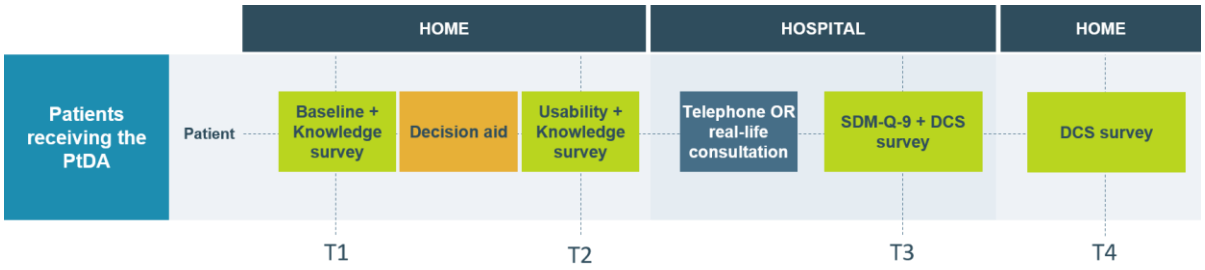

Figure 6: Study design

DCS: Decisional conflict scale SDM-Q-9: Shared decision making questionnaire

T1 = In the week before a planned patient consultation, before using the PtDA

T2 = In the week before a planned patient consultation, after using the PtDA

T3 = During the week after a planned patient consultation

T4 = One month after a planned patient consultation

3.2 Study procedure

At the start of the study, patient characteristics were gathered using a demographic questionnaire. After consulting the PtDA, patient assessed the general *usability* of the PtDA. According to the IPDAS guidelines, the *effectiveness* of a patient DA can be established if both the decision process and decision quality can be improved [17]. Sepucha *et al.* provided an overview of instruments that can be used to measure constructs related to quality of decision and quality of decision process [20]. Quality of decision can be measured via the following constructs: knowledge, realistic expectations and values-choice agreement; whereas the quality of the decision process can be assessed using the constructs: recognizing decision, feeling informed, feeling clear about values, discussing goals with health care professional and being involved [20]. Based on the research of Reumkens *et al.* [181] and Klaassen *et al.* [147], the following constructs will be used to evaluate the effectiveness of the developed PtDA: knowledge, values-choice agreement, feeling informed, feeling clear about values, discussing goals with healthcare providers and being involved. Since a combination of multiple instruments is required to assess these constructs, only six out the possible eight constructs are assessed in order to limit the burden for respondents. Table 14 provides an overview of the instruments used. Finally, the feasibility to implement the PtDA in the hospital setting will be assessed.

Table 14: Applied instruments and corresponding questionnaires to assess effectiveness

SDM: shared decision making

HCP: health care professional

Construct	Quality parameter	Instrument	Evaluation
Knowledge	Decision quality	Knowledge questionnaire with 10 true or false questions	≥ 7 is good < 7 is poor*
Values-choice agreement	Decision quality	Percentage of patients who received treatment that matched their stated treatment preference	75% or higher match is considered good*
Feeling informed and feeling clear about values	Quality of decision process	Decisional Conflict Scale (DCS) [181]	Scores > 37.5: uncomfortable with the decision Scores < 25: absence of decisional conflict [182, 183]
Discussing goals with HCP and being involved	Quality of decision process	SDM 9-item questionnaire (SDM-Q-9) [147]	Total score between 0 and 45, with higher scores indicating higher perceived level of SDM

* The evaluation standard was based on discussions with clinicians and input from a Cochrane analysis[12]

3.3 Study instruments and data analysis

3.3.1 Patient characteristics

The demographic questionnaire (see appendix F) contained questions regarding age, year of diagnosis, level of education, previous breast cancer treatments and current type of adjuvant endocrine therapy. The time spent while using the PtDA was also recorded. These data were analysed by means of descriptive statistics.

3.3.2 System usability scale

The Dutch version of the System Usability Scale (SUS) was used to assess the PtDA's usability at T2 [175, 176]. The scale consists of ten statements that can be answered with a score ranging from 1 to 5, where 1 means 'strongly disagree' and 5 means 'strongly agree'. Total scores can be calculated by subtracting one from the user responses for odd items and by subtracting the user responses from 5 for even-numbered items. This procedure scales all values from 0 to 4, with 4 being the most positive response. The aggregated converted scores are then added up and multiplied by 2.5. The resulting data ranges from 0 to 100 and can be used to interpret the data [184]. The average usability score for internet-based applications is 68.05 [177]. All scores lower than 50 are considered unacceptable,

whereas scores above 70 are considered acceptable, with better products scoring in the high 70s to upper 80s [177]. See appendix F for the SUS.

3.3.3 KNOWLEDGE QUESTIONNAIRE

The knowledge questionnaire consisted (see appendix F) of 10 closed-ended questions (true, false or unsure) and was based on guidelines provided by the Ottawa Hospital Research Institute [185]. Items were given a score value of 1 (if the respondent correctly selected 'true' or 'false') and 0 (if incorrect or respondent answered 'unsure'). All items were added up to calculate a total score. To investigate the effect of the PtDA on the patients' knowledge, their results before (T1) and after (T2) using the PtDA were compared. A Wilcoxon matched-pairs ranks test was applied, which is a non-parametric test that can be applied in limited sample sizes.

3.3.4 VALUES-CHOICE AGREEMENT

Patients' relative preference weights were elicited in module 3 of the PtDA using an ACA exercise for the following attributes: recurrence risk, breast cancer mortality, hot flushes, risk of blood clots, joint and muscle pain, osteoporosis, and risk of endometrium carcinoma. These attributes were determined using patient and physician input during the development of the PtDA [chapter 3]. The average relative importance of every attribute was calculated using Ordinary Least Squares regression. Patients' single most important attribute was compared with their decision to keep or change adjuvant endocrine therapy to assess values-choice agreement. The final decision was consulted in the clinical records of the patient, by a physician of the Multidisciplinary Breast Centre of UZ Leuven.

3.3.5 DECISIONAL CONFLICT SCALE

The Decisional Conflict Scale (DCS) (see appendix F) measures a patient's perception of: "*1) uncertainty in choosing options; 2) modifiable factors contributing to uncertainty such as feeling uninformed, unclear about personal values and unsupported in decision making; and 3) effective decision making such as feeling the choice is informed, values-based, likely to be implemented and expressing satisfaction with the choice*"; as stated by O'Connor [183]. The questionnaire consists of 16 items with 5 response categories varying from strongly agree to strongly disagree, resulting in a score from 0-4 respectively. The sum of the scores ranges from 0 to 100, corresponding with no decisional conflict or extremely high decisional conflict respectively. Patient DCS scores were compared between T3 (after consultation) and T4 (one month later). A Wilcoxon matched-pairs ranks test was used as this non-parametric test can be applied in limited sample sizes.

3.3.6 Shared Decision Making Questionnaire (SDM-Q-9)

The Shared Decision Making Questionnaire (SDM-Q-9**)** (see appendix F) measures patient perception of the extent of SDM during a physician-patient consultation, according to Rodenburg-Vandenbussche *et al*. [186]. It consists of 9 statements which are scored on six-point Likert scales ranging from 0 to 5, corresponding with completely disagree to completely agree [186]. The aggregated scores lead to a total raw score between 0 and 45, with 0 indicating the lowest and 45 indicating the highest level of perceived SDM.

3.3.7 Feasibility

To inform a larger follow-up trial, feasibility of implementation is assessed using the following parameters: recruitment rate (the number of patients contacted to participate compared to the number of patients that enrolled in the study), data collection method (based on completeness of data) and dropout rate.

4 Results

4.1 Patient characteristics

In total, 14 patients were contacted to participate, 13 of them enrolled in the study and 9 of them completed all questionnaires. The four patients that dropped out either never visited the study website (3) or visited the website but did not provide informed consent (1). Participants were 60 years old on average (SD: 8,67) and none of them had a low education level. All patients were diagnosed with breast cancer between 2016 and 2018 and had previously received either radiotherapy and chemotherapy (4 patients) or radiotherapy alone (5 patients). Four patients were using tamoxifen at the start of the study and five patients were using an aromatase inhibitor. Table 15 shows an overview of patient characteristics. Three patients received a telephone consultation instead of a consultation in person at the hospital, the remaining six patients had a consultation at the hospital as usual. The average time patients spent using the PtDA was 42 minutes, with an average of 19 minutes (SD:9,82), 7 minutes (SD: 2,71) and 16 minutes (SD: 5,51) for module 1-3 respectively. Seven patients completed the entire PtDA, whereas two patients only completed module 1 and 2.

4.2 System usability scale

The overall average usability score was 71,25 (SD: 8,56) based on 8 complete SUS questionnaires. One patient did not answer item number 9 on the questionnaire, therefore the usability score could not be calculated for this patient. When using the average value received for item number 9 for this patient,

the overall average usability score would be 71,39 (SD: 8,01). Appendix G provides all responses received on the SUS.

Table 15: Patient characteristics at baseline (T1)

Characteristic	N	%
Age (years), mean (SD)	60 (8,22)	
Year of diagnosis		
2016	1	11
2017	6	67
2018	2	22
Education level		
Secondary education	3	33
College education	2	22
University education	4	44
Primary treatment		
Radiotherapy	5	56
Radiotherapy and chemotherapy	4	44
Current medication		
Tamoxifen	4	44
Aromatase inhibitor (letrozole or exemestane)	5	56

4.3 KNOWLEDGE QUESTIONNAIRE

The mean knowledge score at T1 was 5,33/10 (SD: 2,87), compared to 7,78/10 (SD: 0,83) at T2. Eight out of nine patients achieved a score of seven or higher at T2, which was considered to be a good score. The score of six patients improved by 1-8 points and the scores of three patients remained status-quo. Based on the six patients that improved, a Wilcoxon matched-pairs rank test showed significant improvement in knowledge (table 16).

Table 16: Knowledge questionnaire scores

Knowledge questionnaire (N=9)	**Mean (SD)**		**Wilcoxon matched-pairs rank test**	
Score range 0-10	**T1**	**T2**	**Z**	**p-value**
Knowledge	5,33 (2,87)	7,78 (0,83)	2,20	0,03

4.4 VALUES-CHOICE AGREEMENT

Only seven out of nine patients completed the third module of the PtDA. The elicited average importance for all attributes is shown in table 17. The single most important attribute varied considerably between patients, with risk of recurrence being selected by three patients and risk of blood clots, osteoporosis, joint and muscle pain, and risk of endometrium carcinoma each being selected by one patient. The most important attribute per patient was compared with the treatment choice that was made during the consultation, to assess values choice-agreement. These comparisons

can be found in table 18. For six patients, a treatment decision was made during the consultation that was consistent with their most important attribute. Two patients that valued risk of recurrence as the most important attribute, decided during the consultation not to switch from an AI to tamoxifen. For the patient that valued risk of endometrium carcinoma as most important, it was decided to switch from tamoxifen to an AI. For the patients that considered joint and muscle pain and osteoporosis to be the most important attribute, it was decided not to switch from tamoxifen to an AI. One patient had indicated her wish to cease treatment, which was also decided during the consultation. In this case, the patients' decision was based on an adverse event that was not included in our ACA experiment (i.e. mood disorders). For one patient, the therapy choice seemed less consistent with her preferences, as she had indicated to find the risk of recurrence the most important attribute and during the consultation, it was decided to switch from an AI to tamoxifen. The preference weights for every single attribute per patient can be found in table 19.

Table 17: Average importance weights elicited in the adaptive conjoint analysis of module 3.

Attribute	**Average Importance (SD)**
Risk of blood clots	12,91 (9,57)
Osteoporosis	12,75 (9,80)
Joint and muscle pain	13,91 (9,26)
Hot flushes	5,21 (2,58)
Risk of endometrium carcinoma	17,35 (8,86)
Recurrence risk	23,64 (7,36)
Breast cancer mortality	14,22 (7,85)

Table 18: Comparison between most important attribute per patient and therapy choice made.
Patient 6 and 9 did not complete the adaptive conjoint analysis in module 3 of the patient decision aid.
P: Patient

	Most important attribute	**Current treatment**	**Therapy choice made**
P1	Risk of recurrence	Aromatase inhibitor	Switch to tamoxifen
P2	Risk of recurrence	Aromatase inhibitor	Continue aromatase inhibitor
P3	Osteoporosis	Tamoxifen	Continue tamoxifen
P4	Joint and muscle pain	Tamoxifen	Continue tamoxifen
P5	Risk of blood clots	Tamoxifen	Cease therapy
P7	Risk of endometrium carcinoma	Tamoxifen	Switch to aromatase inhibitor
P8	Risk of recurrence	Aromatase inhibitor	Continue aromatase inhibitor

Table 19: Individual attribute importance weights per patient.

All attributes sum up to 100% per respondent. The most important attribute per patient is highlighted. Patient 6 and 9 did not complete the adaptive conjoint analysis in module 3 of the patient decision aid.

P: Patient

	Individual attribute importance (%)						
Attribute	**P1**	**P2**	**P3**	**P4**	**P5**	**P7**	**P8**
Risk of blood clots	13,21	6,32	17,85	0,37	30,70	10,89	11,06
Osteoporosis	7,38	2,22	31,79	6,81	14,58	9,07	17,42
Joint and muscle pain	12,19	19,46	3,84	29,02	20,06	6,57	6,22
Hot flushes	5,40	3,63	4,17	9,87	7,02	1,92	4,49
Risk of endometrium carcinoma	21,01	6,89	25,92	19,05	3,55	26,28	18,74
Risk of recurrence	27,36	35,19	13,66	22,17	15,83	23,72	27,56
Breast cancer mortality	13,45	26,29	2,77	12,70	8,25	21,56	14,51

4.5 DECISIONAL CONFLICT SCALE

The average DCS score was 18,06 (SD: 15,65) at T3 and 47,05 (SD: 11,31) at T4. All individual scores were higher one month after consultation. Six out of nine patients had none to low (<25) decisional conflict at T3, two patients had some decisional conflict (between 25 and 37.5) and one patient had high decisional conflict (>37,5). Furthermore at T3, the average subscore for values clarity was the lowest with 11,11 (13,82) and the subscore for uncertainty was the highest with 22,22 (25,69). At T4, values clarity was still the lowest subscore, however, it increased significantly to 41,67 (SD 11,02); and support had the highest subscore with 50,00 (SD: 16,67). Only one patient had low decisional conflict at T4, all other patients had high decisional conflict. Detailed information can be found in table 20.

Table 20: Patients' decisional conflict after consultation (T3) and one month after consultation (T4)

Decisional conflict scale (N=9)	**Mean (SD)**		**Wilcoxon matched-pairs rank test**	
Score range 0-100	**T3**	**T4**	**Z**	**p-value**
Total score	18,06 (15,65)	47,05 (11,31)	2,67	0,008
Informed	19,44 (21,65)	47,22 (22,44)	2,67	0,008
Values clarity	11,11 (13,82)	41,67 (11,02)	2,67	0,008
Support	21,30 (18,69)	50,00 (16,67)	2,55	0,011
Uncertainty	22,22 (25,69)	48,15 (20,32)	2,52	0,012
Effective decision	16,67 (16,54)	47,92 (13,26)	2,67	0,008

4.6 SHARED DECISION MAKING QUESTIONNAIRE (SDM-Q-9)

The average SDM-Q-9 score at T3 was 20 (SD: 5,53) out of a possible 45. The median score was 18; only three patients scored 22,5 or more out of a possible 45.

4.7 FEASIBILITY

The recruitment rate for this study was 92,86% and the dropout rate was 30,77%. Data collection was complete for questionnaires at T3 and T4, data on one or two questions were missing for one patient for questionnaires at T2 and T1 respectively.

5 DISCUSSION

This study presents the beta testing of a developed PtDA in a pilot trial in Flanders (Belgium). This PtDA aims to support patients with hormone-sensitive breast cancer that are eligible to switch adjuvant endocrine therapy to engage in SDM. Therefore, the PtDA informs patients on their disease and the treatment options that are available to them and supports patients to clarify their values and to communicate their preferences to their health care provider. Earlier research indicated that patients with breast cancer often do not receive the information they require to be engaged in SDM [146, 187]. This was also confirmed for Flemish patients in general, based on a patient-reported experience measure (PREM) questionnaire that was used to assess patient experiences in 56 Flemish hospitals in 2018 [188]. The PREM questionnaire showed that Flemish patients wish to receive more information on their disease and treatment options and wish to be more involved in medical decision making regarding medical tests or treatments [188]. The developed PtDA aims to fulfil both patients' information and SDM needs.

5.1 KNOWLEDGE AND DECISIONAL CONFLICT

The results of the knowledge questionnaire applied in this study, seem to indicate that the PtDA succeeds in increasing patients' knowledge. It should be noted, however, that the average education level of the participants may have been skewed towards higher education. Furthermore, the low decisional conflict at T3 for the informed subscale of the DCS, confirms that patients feel informed. These results may indicate that the PtDA meets the information needs of the target population, enabling them to engage in SDM. As patients achieved an average score of 7,78 out of 10 after using the PtDA, they already accomplished a basic understanding of the decision context. Treatment discussions with health care providers could therefore take place more easily, as suggested by breast cancer clinicians in earlier research [chapter 4]. Furthermore, the other average scores on the DCS indicate that decision conflict was very low, only one patient at T3 indicated high decisional conflict. Furthermore, the values clarity subscale seems to suggest that patients were very clear about their personal treatment preferences at the time of their consultation. This might be due to the use of modules 2 and 3 of the PtDA, in which the potential consequences of treatment benefits and risks are

explained, and patient preferences are elicited using an ACA exercise. However, the average DCS scores increased significantly one month after the consultation compared to right after the consultation. At T4, all but one patient indicated high decisional conflict. It should be noted that patients only had access to the PtDA in the week before their consultation. It might be beneficial for patients to still have access to the PtDA after their consultation, in case they want to reconsult the information, retake the VCE or reconsider their options. A broader framework might be needed to guide patients in their treatment decisions and support them to engage in SDM. These results might indicate that patients could benefit from a follow-up consultation to discuss their remaining concerns, especially if there was no true SDM during the initial consultation. A continuing care process could help to implement SDM and support patients to discuss their preferences or concerns at all times, which would result in true patient centered care. A larger follow-up trial with a longer follow-up period would be needed to confirm these hypotheses.

5.2 Effect of value clarification on decisional conflict

The low scores gathered for the decisional conflict subscale 'values clarity' indicate that patients were very clear about their values after the consultation. This may be due to the combination of the second and third module of the PtDA, that aim to help patients clarify their values. The stories included in the scenarios of the second module may have helped patients prepare for the ACA in module 3. The use of narrative stories in PtDAs has earlier been advocated, although others warned to be careful for patients making a decision based on preferences shown in the scenarios instead of their own values [34, 181]. Patients that participated during alpha testing have encouraged the use of scenarios and provided feedback on the design [chapter 4]. The ACA that has been used as a VCM in module 3 of the PtDA, has been used in other PtDAs as well [159]. A systematic review by Weernink *et al*. stated that future research should focus on more flexibility in the included set of attributes and levels, which feedback patients want to receive, and how the results fit within the patient-physician dialogue [159]. As it is not possible to let patients add new attributes in an ACA design, the attributes included in this PtDA were determined based on attribute rankings by patients and physicians [chapter 3]. Next, patients helped determine the visual format of the ACA and the results shown at the end. During alpha testing, patients requested the opportunity to print their results to discuss them with their treating physician. This feature was therefore added to the PtDA, however, there are no data available as to how many patients made use of this feature during the pilot trial.

5.3 VALUES-CHOICE AGREEMENT AND SHARED DECISION MAKING

The results from the ACA further confirmed that treatment preferences vary considerably between patients, highlighting the need for individual discussions and treatment decision making. Seven out of nine patients (77,78%) completed the ACA experiment, which may indicate that this value clarification exercise is feasible for the majority of the patients. For six out of seven patients, values-choice agreement was established. One patient that indicated the risk of recurrence to be the most important, decided to switch to tamoxifen. Although aromatase inhibitors are known to be a little more effective in avoiding recurrence, tamoxifen might be equally appropriate for low-risk patients. The authors could not assess what was discussed during consultations, therefore values-choice agreement can only be estimated. In this case, the patient could have had a low risk of recurrence, resulting in a treatment course of 2-3 years of aromatase inhibitor and tamoxifen up till five years of treatment to be sufficient. In each of the cases, it is difficult to assess whether patient preferences were explicitly discussed and taken into account when making treatment decisions. The SDM-Q9 scores; however, seem to indicate that no real SDM took place. The average score of 20 out of 45 is rather low compared to other studies that used the SDM-Q-9 [189]. The developed PtDA seems to fulfil the needs of patients to engage in SDM by providing clear and understandable information and helping them to clarify their values using the ACA exercise. However, the health care providers that performed consultations in this study may, not yet possess optimal SDM skills. This highlights the need for interventions directed at health care providers to improve SDM in clinical practice [69]. Specific trainings for health care professionals have already shown to improve their SDM skills, although physicians may remain reluctant to explicitly discuss patients' decision making preferences [69, 93, 190].

The need for SDM training for health care professionals, fits within the general need for more SDM initiatives in Belgium. In its neighbouring countries, SDM is already a more widely adopted approach [190, 191]. At this time, there are no clinical guidelines available that promote SDM and research towards potential interventions is very limited. Only very few PtDAs are available, in only a handful of clinical settings. The authors hope that this study can contribute to create awareness regarding the use of PtDAs to improve SDM.

5.4 LIMITATIONS

The main limitation of this study is the small sample size that was used for the analysis, although this sample size was taken into account when choosing the appropriate statistical test. A non-parametric test was chosen, as the normal distribution of the sample could not be assessed. The main reason for this small sample size is the fact that this study was planned to be executed between March and June

2020 but due to SARS-CoV-2, Belgium was in lockdown as of March 18. Planned consultations at hospitals were either delayed or replaced by a telephone consultation. The delayed consultations caused fewer patients of our target population to be available to participate. This also resulted in three patients of our sample receiving a telephone consultation instead of a consultation in person at the hospital. The telephone consultations may have impacted the extent to which SDM was carried out. Furthermore, a selection bias towards higher educated patients may have occurred, although the sample showed a good variability regarding patients' primary and current treatment. Another limitation is that the extent of SDM was only assessed from the patients' perspective. Although a questionnaire for health care professionals is available, this was considered too much of a burden for the health care professionals involved in the study. Another possibility was to observe the consultations to assess SDM. This information could have been useful to determine whether patient preferences were actually taken into account and to assess values-choice agreement. Due to practical reasons, this was considered not to be feasible. Finally, it was not assessed whether and how soon the treatment decisions discussed at the consultation were implemented. Patients that would change their current therapy, might have started with their new treatment right away, or they still might have used their previous medication for a few weeks. This could have impacted the results on the DCS questionnaire one month after the consultation.

6 CONCLUSIONS

The results of this pilot trial suggest that the developed PtDA meets the needs of breast cancer patients eligible to switch adjuvant endocrine treatment. Patients' knowledge increased by using the PtDA and their decisional conflict was low both right after their consultation as one month later. Patients indicated that no real SDM took place during the consultations, although the variability in treatment preferences elicited highlights the need to discuss individual treatment preferences and take them into account during decision making. Combining the PtDA with specific interventions for health care professionals may be a more effective approach to obtain SDM. The results of this pilot trial beta testing should be confirmed in a larger follow-up trial in Flanders.

GENERAL DISCUSSION

Within this PhD project, an interactive PtDA was developed and tested in a two-phase process. First, preference elicitation methods from the consumer research field were examined for potential application in health care in chapter 1. Next, Belgian stakeholder needs regarding a PtDA were assessed in chapter 2, using qualitative research and an extensive literature review. The development process of the PtDA was subsequently executed in chapter 3 with input from both patients and physicians, aligned with international guidelines. Finally, the PtDA was tested during an alpha and beta testing phase in chapters 4 and 5.

The following sections will first discuss how the developed PtDA can meet the need of Belgian stakeholders and support the implementation of SDM, by providing access to clear and understandable information and offering value clarification support. Next, learnings regarding the implementation of a PtDA in a clinical setting, economic considerations regarding the costs and benefits of a decision aid intervention, and the current use of SDM in Belgium will be discussed.

1 THE NEED FOR A PTDA TO IMPROVE SDM IN BREAST CANCER

Patients' information and decision making needs were assessed in chapter 2. The majority of the patients that participated in this study wanted to be more involved in (at least some of) their medical decision making. Although about one third of the patients indicated that they were not comfortable to participate in treatment decision making at the time of diagnosis, most patients prefer to be more involved when discussing adjuvant endocrine treatment. Earlier research already reported that patient preferences for involvement change over time [70]. A study investigating the pre- and post-consultation preferences for decision making of 683 patients with breast cancer from five different countries (Australia, New Zealand, Switzerland, Germany and Austria) reported similar results. Almost half of the patients preferred a shared decision and 24% preferred a patient-directed decision (i.e. informed decision making) before consultation took place [157]. Two weeks after the consultation, 40.8% and 22.4% preferred a shared and patient-directed decision respectively. At both times, the majority of the patients wanted to be involved in the decision making process [157]. Another study involving 238 French patients with breast cancer found that 72% of patients preferred at least some involvement in their treatment decision making. Only 3% of these patients preferred patient-directed decisions, 42% preferred an approach in which there is some sharing and 27% preferred a SDM approach [192]. Other international studies also indicate that the majority of cancer patients usually wants to be more involved [68, 70], which was echoed by the patients that participated in the qualitative study of chapter 2. There are currently no numbers available to assess quantitatively which proportion of Belgian patients with breast cancer want to be more involved in their medical decision making. However, available national and international research indicates that a significant proportion

wishes to engage in SDM. The extent to which patients want to participate in SDM should therefore be discussed during a consultation [68, 140]. Moreover, physicians should assess *why* patients prefer a certain level of involvement in the decision making or which barriers they fear to experience [193]. If patients prefer to assume a more passive role in the decision making process because this better suits their personality and preferred communication style, their wish should be respected. If, however, patients assume a more passive role in the decision-making process because they lack information or fear to be perceived as 'being difficult', the treating physician should still try to implement a SDM process [193, 194]. When patients understand the potential consequences of a medical decision on their daily life, they might be better motivated to engage in SDM. In any case, SDM is not an '*all or nothing*' situation but rather a continuum which will result in different levels of involvement for different patients [193, 195].

Furthermore, the vast majority of the patients expressed a need for more understandable, quantified information on treatment benefits and risks. One study from 2018 investigated the need for health information and the preferred model for decision making of people living in Flanders [196]. The results showed that about a quarter of the respondents found it difficult to find relevant health information and almost half of them thought it was difficult to assess the reliability of the retrieved information. Furthermore, around 90% of respondents indicated the importance of SDM and the possibility to question decisions made by physicians [196]. The authors suggested the use of a patient portal; an electronic application that is linked to the health records of their treating physician. Such an application could offer an up-to-date medication list, medical test results, personalized information and more [196]. Another study that assessed patient experiences in Flemish hospitals between 2016 and 2018 reported that about half of the patients wish to receive more information on their disease, potential treatments and the cost related to hospitalization [188]. Furthermore, only about 40% of the patients reported to always be encouraged to participate in decision making [188]. These results align with the findings from chapter 2. The patients in this study welcomed the idea of a PtDA that could fulfil their information need and hereby empowered them to engage in SDM.

Moreover, patients acknowledged that both their therapy and decision making preferences might change over time, stressing the need for SDM to be implemented as a continuous process [197]. The UK National Health Service (NHS) has stated earlier that SDM is "*a process in which clinicians and individuals work together to select tests, treatments, management or support packages, based on evidence and the individual's informed preferences*" [60]. This highlights the need to truly anchor SDM within our health care, rather than only implementing it at specified decision points. This will require a paradigm shift in how both patients and health care providers approach medical decisions during consultations. Ideally, the developed PtDA should be extended so it can be used throughout the breast

cancer treatment pathway. Many PtDAs have already been developed in other countries for decisions regarding breast cancer screening or regarding the type of breast surgery as primary treatment [144, 146, 198]. By harmonizing and combining the decision support available within one treatment pathway, patients will become familiar with this method to acquire information and prepare for decision making before a consultation. A patient portal could be used to make the appropriate part of the PtDA available, depending on the medical decision the patient is facing at that time.

The need for SDM or PtDAs might be perceived somewhat differently by health care professionals, who often describe multiple barriers regarding the application of SDM. A systematic review from 2008 identified several facilitators and barriers for the implementation of SDM from the perspective of health professionals [128]. The most important barriers were time pressure in clinical practice and lack of applicability for SDM due to specific patient characteristics or the clinical decision context. Patients' preferences and their preferred role in decision making were also considered important barriers [128]. These findings were confirmed within chapter 2, as physicians believed that SDM would be too troublesome for many patients and they seemed to accept more adverse events that impact quality of life than patients do. Moreover, earlier research found that physicians and patients have different views regarding acceptable levels of benefit from adjuvant breast cancer treatment [152, 187]. These differences are important to acknowledge and highlight the need for SDM. Another finding from the research within chapter 2 and chapter 4, is that physicians in Flanders may have diverging views on SDM and how it should be applied in practice. Although only a very limited number of health care professionals were interviewed in these chapters, their views varied substantially: ranging from the opinion that treatments could never be imposed on patients in the adjuvant setting to the opinion that if patients initially agreed with the suggestion of the multidisciplinary oncology consultation (MOC) to take adjuvant endocrine therapy for 5 years (including a switch after 2-3 years) they should not reverse this decision during treatment. International research has earlier identified different roles that physicians can take up during decision making (for example, authority figures, persuaders or advisors) and confirmed that many health care professionals have different views on SDM [150, 199]. Even physicians who claim or believe that they practice SDM, might still contradict themselves while trying to persuade a patient to take certain treatments [150]. The 'Empowering patients in the management of chronic diseases' (EMPATHiE) study funded by the Health Programme of the European Union, reported 19 topics that could act as either facilitator or barrier to enable patient empowerment in general in 2014. Based on focus groups and an online survey performed in 26 different countries, the attitudes of health care professionals were identified as an important barrier for patient engagement [130]. More specifically, health care professionals should work together, take the necessary time to communicate with patients and use new technologies [200]. Health care professional perspectives and

perceived barriers for SDM have only been investigated in limited disease settings in Belgium [93, 97]. These barriers should be investigated in future research, as it is crucial to overcome them in order to implement SDM. The pilot study in chapter 5 showed that an intervention with a PtDA directed only at patients, is not sufficient to enable SDM. Interventions directed at health care providers are equally required. Légaré *et al*. already concluded in 2008 that a wide range of measures is needed to address all the different barriers perceived by health professionals [128]. For example, communication trainings have been suggested to teach physicians SDM and preference elicitation skills [69, 191, 201, 202]. Furthermore, physicians should receive training on how they can adapt their consultation style depending on individual patient's needs [69]. Only when health care professionals understand and acknowledge the value of SDM, they will support its implementation in clinical practice.

Table 21: Lessons learned for the development of a patient decision aid

- ✓ **Co-creation with stakeholders leads to optimal information providing**
  - Patients and physicians preferred the use of side-be-side displays to balance information
  - Patients required quantitative information regarding treatment benefits and risks
  - The option 'to do nothing' should be thoroughly discussed with all stakeholders: patients wanted to include this option but physicians did not consider this as an option
  - Information needs of both lower and higher educated patients seems to be fulfilled
- ✓ **Allowing patients to gather information as they require, simulates real life decision making**
  - Content control may improve quality and usability of the patient decision aid
  - The majority of the patients regarded the use of narratives useful to process information
- ✓ **Explicit preference elicitation can prepare patients for shared decision making**
  - Self-reflection exercises may facilitate patients' value clarification
  - Stakeholders consider elicited preference weights a good starting point for the consultation
  - The results of an adaptive conjoint analysis underline preference heterogeneity

2 Evaluating the developed patient decision aid: lessons learned

2.1 Providing information

2.1.1 Co-creation with stakeholders leads to optimal information providing

One study suggests that patients more often wish to receive more information rather than to actually participate in SDM [187]. This seems to indicate that patients' information needs are even greater than their need for decision making, which corresponds with findings from chapter 2. All patients indicated the need for more information, whereas the proportion of patients that wanted to engage in SDM varied depending on the decision context. The primary aim of a PtDA is therefore to provide

understandable, evidence-based information. Other research showed that patients and physicians may have conflicting views on how to present information or which side effects to include [144]. This was confirmed in chapters 2-4, underlining the importance of involving all stakeholders and integrating different perspectives during the development process. Using a PtDA increases patients' knowledge and reduces feelings of being uninformed [12, 23]. Moreover, a meta-analysis of 21 studies showed that PtDAs that provide more detailed information achieve slightly higher scores on both parameters compared with PtDAs that provide simpler information [23]. The PtDA developed within this PhD project included quite detailed information and resulted in a mean knowledge score of 7,78 out of 10, based on a knowledge questionnaire containing ten closed-ended questions during beta testing in chapter 5. The average knowledge score improved significantly after using the PtDA. Furthermore, patients rated the content of the PtDA 8.9/10 during alpha testing from chapter 4. An important, if not the most important, need for patients is hereby met.

Furthermore, women with breast cancer often do not receive quantitative estimates of potential benefits and risks, although this is important to enable patients making tradeoffs between different options [187]. Based on patient input in chapter 3, quantitative information regarding the attributes that were identified as most important, was included in the PtDA. The IPDAS guidelines for PtDAs stipulate that decision options and related information should be presented in a complete and balanced manner, allowing patients to process the necessary information without bias [25]. If these requirements are not met, patients will lack understanding of treatment benefits and risks to optimally assess available options and make tradeoffs, what in turn might affect patients' preferences. The order in which different options are presented was earlier identified as a factor that may influence patients' preferences [23]. Research indicated that PtDAs containing a side-by-side display are more likely to be perceived as balanced and it helps patients to make direct comparisons [23]. Therefore, side-by-side formats were applied to communicate numbers regarding treatment benefits or risks for the development of the PtDA in chapter 3. This side-by-side format was requested by health care professionals included in the study and was also the preferred display by the majority of the patients. When qualitative rather than quantitative information was displayed, the PtDA could not make use of side-by-side displays because of space limitations when showing visuals. Information regarding the treatments mode of administration or use was therefore displayed sequentially. To counter this shortcoming, a summary table was shown at the end that did provide side-by-side display without visuals.

According to international guidelines, the option to 'do nothing' should be included in a PtDA for some health decisions, to present the information in a balanced matter. One patient decided to cease therapy during beta testing of chapter 5. However, based on discussions with health care professionals

in chapters 2 and 4, this option is not routinely discussed, nor preferred by physicians. They generally prefer patients taking adjuvant endocrine therapy, as this improves (although in some cases only a few percentages) patients' overall survival [203]. Quality of life-related aspects may sometimes be undervalued, which may prevent physicians from really considering the option of *not administering* adjuvant endocrine therapy. Some physicians involved in the different studies stated that the option of doing nothing should not be included in the PtDA as they do not routinely include this option in their consultations either. Physicians seem to fear that many patients would consider not taking adjuvant endocrine therapy if this option were provided. Based on IPDAS guidelines, this option should still be added to the developed PtDA, to truly inform patients of every available option. However, this option should then also be acknowledged and discussed by health care providers. This highlights the need for thorough discussions with all stakeholders to reach consensus during the development of the PtDA.

Another factor that affects patients' understanding of the presented options is their health literacy and numeracy. Research by McCaffery *et al*. reported that lower health literacy was associated with less desire for involvement in decision making, less questions asked by patients during decision making and higher decisional uncertainty and regret [28]. Only a very small minority of developed PtDAs addresses the need of patients with lower health literacy and only 10% of PtDA trials report user's health literacy or readability of the PtDA. Health literacy was not directly measured when pilot testing the PtDA, however, patient education levels were collected as a proxy measure. These education levels varied between primary education and university degree for the alpha testing from chapter 4 and between secondary and university education for the beta testing from chapter 5. In both cases, patients with higher education participated in our study, resulting in limited information regarding the usability of the developed PtDA in lower education patients. Furthermore, a study comparing an interactive multimedia PtDA with an audiobooklet-control aid containing the same learner content, showed that patients with low health literacy benefitted from using the interactive PtDA [27]. Patients were more engaged in decision making, felt clearer about their values and preferences and felt more empowered to find and master information. There was no difference between the interactive PtDA and the audiobooklet-control aid for high-literacy patients [27]. As the PtDA developed within this PhD thesis already makes use of interactive features, it may be easier accessible for patients with lower health literacy. Four patients with primary and secondary education levels confirmed usability and clarity of the PtDA during alpha testing. This might indicate that the developed PtDA could also fulfill the needs of lower education patients. However, additional research could confirm this, or provide advise on how the PtDA could be further adapted for patients with lower health literacy.

2.1.2 Allowing patients to gather information as they require, simulates real life decision making

Earlier studies from the field of psychology have confirmed that people construct their preferences while engaging in a preference experiment, rather than having well-defined preferences in advance [204]. This highlights the importance of how the required information is presented to the respondents, as well as how the preference elicitation tasks are designed. There are several possibilities on how to present information in a way that feels natural for the respondents. A review from Syrowatka *et al*. assessed whether interactive features of computer-based decision aids are associated with higher-quality decision making [33]. Content control was hereby identified as a potential feature to improve the decision making process, which means that the patient using the PtDA has control over when and how much information to access. This approach is particularly useful, considering that not all patients require the same amount of information. The results of one study by Matsuyama *et al*. indicated that patients with lower education levels had higher information needs [205]. Another study by Feldman-Stewart *et al*. confirmed the variability in aspects considered to be important for patients with hormone-sensitive breast cancer deciding on adjuvant endocrine therapy [24]. Content control can be integrated in a PtDA by using navigation functions such as a menu bar, by clarifying the information using a glossary or summary, by providing optional information that provides more detail or by providing access to external sources such as clinical practice guidelines [33]. However, Syrowatka *et al.* further reported that navigation reduced the quality of decision making in contrast to the other features that allow content control. As navigation is considered to be a basic feature of computer-based tools, the authors acknowledged that this feature may have been underreported in the literature which may have created a bias in their results [33]. Navigation features simply allow the user to move back and forth within the provided information, thereby also allowing users to revisit information when needed. The developed PtDA makes use of a menu when explaining the attributes of different options, allowing patients to control which information to access when. However, slides containing basic information (e.g. use, mechanism of action, benefits, risks and a summary) that was considered essential, based on IPDAS guidelines and stakeholder meetings, could not be bypassed using the menu. Furthermore, patients could determine the pace at which they consulted the PtDA, allowing them to revisit earlier sections if needed. This navigation option was considered especially useful during alpha testing from chapter 4. Allowing patients to gather and process information as they require, was found to simulate a real-life decision process in chapter 1.

Other features such as tailoring information or patient narratives, were earlier identified as features that could both reduce or improve decision making quality [26, 33, 34]. Narratives might be particular relevant for some patient populations, but further research is required to ensure that patient

preferences are not influenced by certain narratives [26, 34, 35]. Patients participating in the development process of chapter 3 have asked to include narratives in the PtDA. Narratives were therefore incorporated in the second module of the PtDA, that helps patients to understand the impact of potential benefits and risks and helps them to understand the uncertainty related to these attributes. In order to avoid that patients would base their preferences on the values shown in the narratives, the scenarios used a rather simplistic avatar, which was co-designed with patients. A balance should be sought to ensure that patients can familiarize themselves with the avatar, but can still make reflections to what the presented impact could mean for their personal life. Some patients still provided feedback after participating in the beta testing from chapter 5, stating that they would like to know more stories from other patients that have already made the decision they are facing now. These stories could for example be added as additional information in written form. Tailoring information entails adjusting the content for individual patients based on their demographics, clinical condition, medical preferences, and beliefs and knowledge deficits. Hoffman *et al*. suggested to use tailoring to adjust the level of detail on clinical information needed by patients, based on pre-existing knowledge on the decision context [206].The developed PtDA makes no use of automated tailoring, although patients are provided with the opportunity to decide on the level of detail they require or to revisit specific information parts after taking a quiz. A study by Molenaar *et al*. from 2007 investigated which information patients select when using an interactive decision aid for patients with breast cancer having to choose between breast conserving therapy and mastectomy [178]. They reported that patients who preferred breast conserving therapy consulted less information from the module on mastectomy compared with the module on breast conserving therapy [178]. When patients only gather information on the treatment they prefer in advance, this might result in biased preferences. Therefore, ensuring that all patients receive a basic level of information on all potential options seems the best practice.

2.2 Eliciting preferences

2.2.1 Explicit preference elicitation can prepare patients for shared decision making

In chapter 1, concepts from consumer preference elicitation that simulate real-life decision making were identified. Some of these concepts were applied in chapter 3, for the development of the PtDA. First, the concept of self-reflection was used to prepare patients for decision making. Patients were asked simple rating questions in module 2, that stimulated them to think about their preferences in preparation of module 3. Furthermore, the PtDA was used in the week before a consultation, allowing patients to consider their options and to prepare them to discuss potential options during the consultation. Module 3 consisted of an ACA exercise that served as value clarification method. Some

patients that participated in alpha and beta testing stated that they wanted to repeat the ACA after discussing options with friends or family. Repeating module 3 was not possible within the context of the pilot trial, although this could be advantageous for patients in clinical practice as it would allow patients to retake the VCE after self-reflection. Most patients during alpha testing indicated that this was not an easy exercise to complete, and that patients might benefit from guidance by a nurse. It should also be acknowledged that patients had less opportunity to change the design of module 3 than they had with the other two modules. Patients provided very clear feedback on module 3 during alpha testing and many changes were made to implement their requests such as omitting a type of exercise that was perceived as too difficult and changing the general lay-out of the instructions at the start of the module. However, some adaptations were challenging to implement due to the inherent possibilities of the software used. These restrictions made it difficult to fully involve users in a participatory design process. Although this would have likely resulted in an even more patient-centred design of this specific module, this was not feasible from a practical perspective [204]. However, the resulting preference weights seemed to correctly represent the patient's therapy preferences during alpha testing. Based on discussions with patients and physicians from chapter 2, patients had the opportunity to print the results of their ACA exercise. Both stakeholders acknowledged during alpha testing that this printout, together with the questions the patient wrote down, could be a good starting point for the consultation.

Although only seven complete results were obtained during beta testing in chapter 5, some preliminary conclusions can be made. Overall, the chance of relapse was considered the most important attribute by patients with an average importance score of 23.64/100. However, only three out of seven patients, indicated this as the most important attribute. Physicians, practicing evidence-based medicine, usually also consider this the most important attribute. Four patients indicated an adverse event related attribute as the most important one. For these patients, their preference to avoid certain adverse events should be incorporated in the decision for the type of adjuvant endocrine therapy. This is especially true for adverse events that occur more often in one of the two types of endocrine therapy, such as osteoporosis and joint and muscle pain for aromatase inhibitors and the risk of thrombosis and endometrium carcinoma for tamoxifen. It was earlier acknowledged that preferences vary significantly between patients, or between patients and health care providers [42, 45, 152, 207]. Eliciting patient preferences for potential attributes using ACA may help patients to clarify their values and discuss the attributes they find most important [6, 159]. Clear, quantified results that visualize the patient's preferences can furthermore facilitate communication between patients and physicians, as acknowledged by participants during alpha testing. When looking at the 24 publicly available decision aids in breast cancer on the Ottawa Hospital Research Institute website, only five of them provide

sufficient evidence that they improve the match between a patient's preferences and the chosen decision option [62]. The extent to which the chosen decision option matches with the attributes that matter most to an informed patient is also referred to as the level of value-choice agreement [20]. The results obtained during beta testing seem to indicate that values-choice agreement improved, however, this could not be assessed properly because the decision-making process during consultation was not observed. It should be noted that if patient preferences are elicited and quantified, it will be easier to communicate these preferences to the treating physician, which can in turn facilitate making the final decision accordingly. A larger trial could confirm whether values-choice agreement increases when using the PtDA.

2.3 Implementing a patient decision aid in clinical practice

Coulter *et al*. reported in 2013 that only about 50% of the developed PtDAs have been field tested with patients and even fewer have been reviewed or tested by clinicians who were not involved in the development process [98]. However, conducting alpha and beta testing provides indispensable information regarding the implementation of a PtDA in clinical practice. It may provide information on how patients can be made aware of the possibility to consult a PtDA, whether the PtDA can be easily accessed by patients, or whether the PtDA is explicitly discussed during consultation. During beta testing (chapter 5), it became clear that barriers for the implementation of the PtDA should be assessed early in the development process. Within the development process (chapter 3), focus was put on meeting patient and physician needs. However, additional focus is required on how to integrate the PtDA within the patient's care path at the hospital. Expert nurses that support patients using adjuvant endocrine therapy, could also advise the patients on when and how to use the PtDA. Furthermore, integrating the PtDA in the hospital's online environment could be beneficial for both patients and health care professionals. Another option is to provide the PtDA via a patient portal, as researched by Van den Bulck *et al*. [196].

3 Economic considerations: costs and benefits of a PtDA intervention

Implementing PtDAs in clinical practice may generate increased costs, which in turn requires the generation of benefits that can offset these costs and hereby result in a cost-effective intervention [208]. Making an economic evaluation of PtDAs using a standard cost-utility analysis is a challenging task, because the benefits of a PtDA intervention are usually not measured in quality adjusted life years (QALYs) [209]. In comparison with other health interventions, a PtDA intervention is therefore rarely economically evaluated. The first challenge when assessing the cost-effectiveness of a PtDA intervention is listing the generated costs and benefits. Time and resources required for training health

care professionals are an important cost, next to time and resources required for the development of a PtDA. Furthermore, an increase in physician time has been suggested as an additional cost [208]. However, this was contradicted by Légaré *et al*., as there is currently no clear proof that PtDA interventions systematically result in increased consultation time [12, 210]. Some studies even report shorter consultation times, meaning a PtDA can make the consultations more efficient [210]. The variation in scientific evidence regarding PtDA outcomes is currently still a complicating factor when assessing the cost-effectiveness. Some studies indicate a positive impact on health outcomes and resource use, while other studies indicate variable effects on consultation times [12, 210, 211]. Some authors state that there is still a lack of evidence to assess the effect on costs or resource use [12, 212]. When developing an online, interactive PtDA that requires alpha and beta testing with stakeholders, the costs associated with the development and implementation process may be significant, although they can vary considerably, depending on the steps taken and choices made during the development process. Examples of factors influencing the total costs include the following; the extent of qualitative research and literature reviews, the choice of software to design and build the tool, the type of webhosting with or without database functionalities, and the amount of man-hours to develop and update the PtDA. Another method to estimate the costs saved by implementing a PtDA was suggested by Thomas Butt. He stated that since a PtDA informs patients and prepares them for medical decisions, it could be seen as a substitute for (a part of) physician consultation time. He therefore suggested to use hypothetical physician consultation time that is saved by providing patients with a PtDA as a measure for economic evaluations [209]. The consultation time can be reported in minutes or converted to monetary units based on the cost of physician consultation time [209]. After listing the costs associated with a PtDA intervention, the generated benefits should be identified. A potential benefit from using a PtDA to implement SDM is improved adherence, which in turn may lead to improved health outcomes [63]. These indirect health outcomes, however, are not the main beneficial outcomes regarding PtDA use. The direct outcomes are considered to be broader than 'health gain', for example by increasing knowledge or reducing decisional conflict [209, 212]. Such procedural-related outcomes could be measured using patient-reported outcome measures (PROMs) or patient-reported experience measures (PREMs). When performing a cost-utility analysis, it is likely that the benefits of a PtDA would be underestimated if only (indirect) health outcomes would be taken into account, resulting in an undervaluation [209]. Instead of using a standard cost-utility analysis; procedural, quality-related outcomes could be included in a cost-consequence analysis or a general health technology assessment. A cost-consequence analysis is a form of health-economic evaluation that lists all direct and indirect costs and a wide range of outcomes for every alternative [213]. As different outcome measures can be combined, the result is not a clear cost-outcome ratio. The decision maker has to weigh both costs and outcomes to determine their relative importance [213]. Public

Health England, an agency of the UK government, proposes to use cost-consequence analyses for the evaluation of complex digital products that have multiple effects, particularly patient-oriented outcomes, that cannot be easily combined in one single measure [214]. Another benefit of this type of analysis is the fact that decision makers can choose the combination of costs and effects that are most relevant within their decision context. As a consequence, important drawbacks include the fact that results are less generalizable because the choice of relevant aspects is so context-specific and the potential risk for cherry-picking positive outcomes, resulting in a more subjective evaluation [214]. Another preliminary framework for economic evaluations that extends beyond health gain has been suggested by Ara *et al.*, but further research is required before it can be put into practice [212]. They have identified four components that may impact the cost-effectiveness of a PtDA intervention: impact on treatment and uptake, resources, benefits, and preferences over health and non-health outcomes [212]. Non-health benefits such as impact on decision quality and quality of the decision making process could be estimated by performing tradeoffs with health outcomes using societal preferences as suggested by the Canadian Agency for Drugs and Technologies in Health [212, 215]. Methods such as time-trade-off or standard gamble could be used for this purpose [215].

4 Assessing the current status of shared decision making in Belgium

The practice of SDM has received considerable interest during the last 30 years [216]. In many countries, guidelines have been issued, and patient or physician-centred interventions have been developed to improve the implementation of SDM in clinical practice [170, 187, 190, 191, 197, 202, 216, 217]. In 2007, the first special issue on 'shared decision making in diverse health care systems' was published in the German 'Journal for evidence and quality in health care' [218]. Eight countries (Australia, Canada, France, Germany, Italy, the Netherlands, the United Kingdom, and the USA) participated in this issue by reporting on the status of SDM within their respective countries. By the time the next special issue on this topic was published, in 2011, five additional countries (Brazil, Chile, Israel, Spain, and Switzerland) contributed by describing how SDM was implemented within their health care system [216]. Finally, the most recent update on this special issue occurred in 2017, when a total of 22 countries explained how patient-centred care and SDM are implemented in clinical practice [197]. For this issue, new contributions were made by West Africa, Argentina, China, Denmark, Iran, Malaysia, Norway, Peru and Taiwan. The need for more decision support tools, such as PtDAs, and better implementation has been highlighted in these publications [197, 202]. This can occur either via *de novo* development or by translating existing PtDAs [191]. It was earlier acknowledged that simply translating PtDAs will not be possible for every decision context due to cultural differences [197]. Adjusting the content and design of a PtDA based on the available therapeutic options and the specific

knowledge and cultural believes of the target population can be required. As opposed to its neighbouring countries who already reported on SDM research in 2007, Belgium, however, seems to be running behind regarding the implementation of SDM. There is currently no official guideline that supports SDM or provides practical tips for the implementation in clinical practice. Moreover, SDM does not seem to be high on the research or political agenda, resulting in limited funding and research projects. Furthermore, the research from chapters 2 and 4 demonstrated that health care professionals have differing views on when or how to perform SDM. In 2018, the federal public health service organized a symposium on SDM [219]. Although this symposium was part of the continuing professional development curriculum for physicians and pharmacists, its aim was rather informational than to provide concrete tips for clinical implementation. In Belgium, general practitioners who wish to acquire accreditation need at least 20 credits (corresponding with 1 credit per hour for trainings) per reference period of 12 months. Promoting and educating physicians on SDM could, for example, occur within the local quality groups, who aim to discuss, and peer review the medical practice of its members to improve the quality of care. Furthermore, both nursing and medical students should receive training in how to implement SDM in clinical practice. In the past, this was covered during communication trainings in both bachelor's and master's degrees for medical students. However, SDM will have a more prominent role in the new revised medical training at Flemish universities (personal communication). For nursing students, the practice of SDM is covered within communication and coaching seminars. However, there may be wide variations between different college institutions and a more comprehensive training may be required, as patients that participated in chapters 2 and 4 have also suggested that coaching from nurses regarding SDM might be beneficial.

In 2012, the Belgian Health Care Knowledge Centre (KCE) issued a report on chronic care: "Organization of care for chronic patients in Belgium: development of a position paper" [220]. This position paper proposed 20 recommendations to improve chronic disease management. SDM and patient decision aids are only mentioned within the chapter "Highlights from the international perspective" (4 times and 1 time respectively), and are not yet represented in the specific recommendations [220]. However, patients have indicated in chapter 2 that their decisional needs and preferences may vary over time and should therefore be considered everywhere along their treatment pathway. Next, in 2018, the KCE published another scientific report, "Towards an integrated evidence-based practice plan in Belgium: part 1", that provides the scientific background for the development of an evidence based practice plan for Belgium [221]. Evidence based medicine (EBM) or evidence based practice (EBP) aims to integrate the clinical expertise of an individual with the best available external clinical evidence from systematic research to make health care decisions for individual patients. The report acknowledges that applying EBM, without taking individual contexts or patient's preferences into

account, will not result in high quality care. Next to the scientific evidence, it foresees a prominent role for the patient in clinical decision making. Especially in case of preference-sensitive decisions, SDM is promoted. It is further specified that health care professionals need to develop specific attitudes, competencies and skills to perform SDM in clinical practice. Specific tools or interventions, such as the PtDA developed within this PhD project, can aid clinicians in applying SDM during a clinical encounter. When defining physicians' needs, the report states that "*it is often difficult to negotiate with patients about a certain treatment (shared decision making) because tools are not available, patient are misled by wrong information (Dr Google) or patients lack insight in EBP*". Indeed, the fear for misinformation by patients consulting Google was already expressed in 2014, when the Flemish government wanted to warn the public not to google their symptoms [65, 222]. An online video explained the risks of googling health information and referred to an independent website of the Belgian Center of Evidence-Based Medicine (CEBAM), that provides reliable and easy-to-access health information. The fact that people go online to find the health information they require, illustrates their need for information. It could be argued that patients would not be so easily misled by wrong information, if they had simply better access to understandable and correct information. The developed PtDA aims to fulfil this information need. Patients should always know where to find information. Physicians, both in primary and secondary care, nurses, pharmacists, and hospitals should help to achieve this. A centralized platform that provides correct and understandable information for patients on various health conditions seems the best choice. This is currently available for the public on the CEBAM website 'Gezondheidenwetenschap.be', but could still be supplemented with additional information regarding health conditions, information regarding SDM and PtDAs for specific health decisions [223]. The overview of publicly available PtDAs on the website of the Ottawa Hospital Research Institute could be a good example, although patients in Belgium will mainly require PtDAs in Dutch and French [62].

There are currently only very few PtDAs available in Flanders. On the website 'gezondheidenwetenschap.be' there are two PtDAs freely available; one on hormone replacement therapy during menopause and one on vaccines [223]. Furthermore, a PtDA for patients with localized prostate cancer was developed in 2007 and SDM in clinical practice was researched in the settings of dementia care and advanced lung cancer[93–96]. More funding is needed to develop PtDAs and to investigate how they can optimally be implemented in clinical practice. Additionally, awareness for SDM and patients' informational needs should be increased. Some organizations representing the patient perspective already promote SDM or the use of decision aids in Flanders. Kom op tegen Kanker for example, is a non-governmental organization that aims to improve cancer care. They focus on measures to avoid cancer (e.g. no smoking policies), early screening possibilities, quality cancer treatments and optimal psychosocial care. In their five-year plan (2017-2021) they stated the need for

the development of quality decision aids in both the context of secondary cancer prevention as in the context of informed choice as a patient's right [224]. Kom op tegen Kanker provides funding for various research projects; the development of PtDAs or the implementation of SDM could qualify as psychosocial research that improves patients' quality of life. Another organization that could support the implementation of SDM in clinical practice is the Flemish Patient Platform (VPP). This non-profit organization unites patient organizations and represents the patient perspective in stakeholder meetings on different policy levels. In 2015, they supported the Patient Empowerment (E5) campaign of the European Patients Forum (EPF) that promoted five dimensions of patient empowerment: education, expertise, equality, experience and engagement [225]. The individual dimensions of empowerment (education, expertise, and equality) are all crucial elements to apply SDM for individual patients. The organizational (experience) and policy related (engagement) dimensions can support the implementation of SDM in care pathways or national guidelines [130, 225].

5 METHODOLOGICAL CONSIDERATIONS

Study-specific considerations are described within each chapter. This section will discuss the overall strengths and limitations of the PhD thesis.

A PtDA was developed, based on literature reviews and qualitative research to assess stakeholder needs. Next, the developed prototype was tested in both a research and clinical environment. Although guidelines for the development and testing of PtDAs are available, there is no standardized protocol or one-size-fits-all approach that can be applied.

A literature review was conducted in chapter 1 and part of chapter 3. Within chapter 1, a narrative literature review was performed to identify novel elements in preference elicitation methods from consumer research that could be applied in health care. The scope of the review was limited to recent (<5 years) publications and only one search engine was used. Useful methods or elements within methods that were older or not widely published may have been missed. However, the literature yielded some interesting methods, some of which have been applied further on in the project. The literature from chapter 3 combined information from randomized trials and grey literature to identify relevant attributes, however, no systematic review was undertaken. These attributes were afterwards assessed by stakeholders to maximize the validity of the results.

Qualitative research was applied in chapters 2-4. These methodologies allow to examine different aspects in-depth, which was necessary for the development and evaluation of the PtDA. However, the results of qualitative research cannot be easily generalized outside of the study sample, as they largely depend on the experiences of individual participants. Furthermore, a selection bias for participation

may have occurred. Different interviewing techniques such as focus groups, individual interviews and cognitive interviewing were applied to obtain the most optimal results. Health care providers were each interviewed individually for chapters 2-4, whereas patients participated in focus groups for chapters 2-3 and individual interviews in chapter 4. The sampling for the focus groups was limited by the response of breast cancer support groups in Flanders, however, four focus groups took place in different locations in Flanders. Afterwards, patients from two different locations participated again in the alpha testing of chapter 4. Although this can be considered a limitation of the study since these patients participated twice instead of collecting input from new stakeholders, the advantage was that they were already familiar with the project goals and they could assess whether the previous input was correctly implemented.

Quantitative research methods were applied as descriptive statistics in chapter 4-5 and statistical analysis in chapter 5. For the statistical analysis in chapter 5, non-parametrical tests were applied in accordance with the limited sample size. Due to this limited sample size, the results cannot be generalized for the larger patient population. They can, however, provide some indication of the effects the PtDA may produce in a larger sample.

6 VALORISATION OF THE BAEKELAND MANDATE

As stated in the introduction, this project was carried out as a Baekeland mandate, meaning that it should generate scientific and technological knowledge for the companies involved. The evidence generated in chapter 1, can facilitate, and improve the development of preference elicitation experiments. As these experiments are being increasingly applied in health care, the opportunities to valorise this research will even increase in the future. The creation of a development framework for PtDAs in chapter 3 complements the existing MindBytes SERES framework for digital tools. The performed alpha and beta testing in chapters 4 and 5 generated expertise that will result in a competitive advantage in comparison with similar companies. Especially since only a handful of PtDAs have been developed in Flanders so far. Furthermore, the dissemination of the results obtained during this project can help to create brand awareness. Finally, the results obtained by the ACA exercise in module 3 of the PtDA may be the subject of further patient preference research by ISMS or others.

GENERAL CONCLUSION

This project aims to create awareness for SDM in Flanders within the disease area of breast cancer and provides information on how this concept could be applied in clinical practice. Moreover, the experience generated during this PhD can inform potential next steps to help researchers and health care providers in Belgium to close the gap with international standards regarding the development and application of PtDAs.

First of all, important informational and decision making needs were identified in Flemish women with hormone-sensitive breast cancer. SDM may be better applied when making decisions regarding adjuvant endocrine therapies that can potentially have a high impact on quality of life. Secondly, although patient preference elicitation is increasingly applied in health care, there is still room for improvement. As most patients are not yet familiar with preference elicitation techniques, they require additional information on how to participate and how the results can be used for their personal decision making. Methods that simulate real-life decisions as closely as possible, are known to generate more accurate results. However, these methods usually include complex tradeoffs which may be difficult for some patients. Guidance by specialized nurses that can support patients to use PtDAs could potentially resolve this issue. Finally, the developed PtDA seems to improve patients' knowledge and was considered user-friendly by patients. However, interventions aiming to improve SDM should focus on both patients and health care providers. Ideally, the developed prototype should be supplemented with physician trainings, to help physicians interpret the relative preference weights provided by the PtDA and to provide feedback on how they can implement SDM during consultations.

1 RECOMMENDATIONS FOR THE DEVELOPMENT OF PATIENT DECISION AIDS

The use of PtDAs is currently very limited in Belgium, with applications being tested in only a few disease areas. More research is needed to develop PtDAs in other disease areas, to deliver patient centred care that meets patients' informational and decision making needs. As a first step, the need for SDM should be assessed for different patient populations that are confronted with preference-sensitive decisions. Next, stakeholder input should be incorporated throughout the development process, especially since different stakeholders may have different views on which aspects should be included or how they should be displayed. Asking all stakeholders to rank potential attributes might facilitate the determination of essential and preferable attributes to include in the PtDA. In case of differing views on how to display the information, alpha-testing multiple formats or displays with the target audience is good practice. Online applications have the advantage to be readily available for most patients. The **use of narratives or interactive design features that enable content control** may improve decision making. Furthermore, **preference elicitation methods that stimulate self-reflection** and help patients to clarify their values by **simulating real-life decisions** generate promising results.

Incorporating these methods in PtDAs can reduce decisional conflict with the patient. Moreover, the results of this exercise, **individual preference weights** for all the attributes, are considered to be a good **starting point for treatment discussions** with the treating physician. Apart from focus on the content and design of the PtDA, **attention for more practical aspects of implementation** is also required. A centralized platform that collects the available PtDAs in all disease areas would be ideal. This can either be integrated in a government-funded patient portal that also offers personalized information or can be used to monitor one's health, or it can be integrated into an informative website such as 'gezondheidenwetenschap.be'. The use of a Belgian or Flemish centralized platform would make it easy to use for patients, however, this will presumably require a vast investment. Another option could be that a commercial company provides access to PtDAs. In the Netherlands, the website 'keuzehulp.info' provides more than 70 PtDAs developed by PATIENT+ that can be accessed both publicly as through a referral by a health care provider. By adapting the PtDAs to the specific setting of customers (for example hospitals), licensing the PtDAs, providing training for health care professionals and assisting with implementation, a sustainable business model is created. However, it is unsure whether this would currently be a sustainable business model in Belgium or Flanders, as the general awareness regarding SDM and the use of PtDAs is still low. The use of digital media is preferred over paper-based PtDAs in several situations, as it allows to include more advanced information techniques such as video and audio. It can also provide easy access to contact information of support groups or other relevant information. Furthermore, interactive features can be applied to enhance user experience and fully engage them while using the tool. Finally, digital PtDAs provide the opportunity to collect relevant information that can automatically be stored in the patient's file, or shared with the treating physician. A potential pitfall is that not everyone is equally familiar with online (or computerized) communication or not everyone simply has easy internet access. Paper-based alternatives can still be very useful in this case. However, the success of paper-based PtDAs would depend on the extent to which patients receive and use them. Therefore, investing in the implementation of SDM will probably achieve a higher impact in clinical practice. PtDAs can help patients and physicians to apply SDM, but the ultimate goal remains to provide patient-centred care, in which patient preferences are taken into account whenever possible.

2 Recommendations to improve shared decision making in Belgium

First of all**, a strong signal from policy makers** is required to create awareness for SDM and to support the implementation in clinical settings in Belgium. The combination of **guidelines** describing how to perform SDM in the clinical encounter and **practical measures** that allow easy implementation are necessary. These practical measures may include logistic support, such as the development of a

centralized platform that provides access to the available decision support tools, combined with financial support allowing for educational campaigns that can inform the public on SDM and available support tools. The barriers experiences by health care professionals when performing SDM should be identified and addressed accordingly. Financial support, for example, can be used to reimburse physicians for the time spent conducting SDM. This reimbursement can be compared with the compensation a pharmacist receives for performing counselling on the proper use of medicines, in Dutch "*begeleidingsgesprek voor goed gebruik van geneesmiddelen*" (GGG). This can be applied for patients with diabetes type 2, for chronic patients with asthma that receive a corticosteroid inhaler for the first time or patients with asthma whose disease is insufficiently under control. In these cases, the pharmacist provides care that is free of cost for the patient, as it is fully reimbursed by the National Institute for Health and Disability Insurance (NIHDI). This practice can be compared to the implementation of SDM in clinical practice, as both consultations aim to provide patient-centred care, based on a thorough discussion that meets the needs of an individual patient. Furthermore, both practices primarily aim to improve the quality of care. Reimbursing the implementation of SDM in clinical practice is already being applied in the Netherlands. Finally, financial support will be required to fund research focusing on SDM and potential decision support tools and to identify the needs of the Belgian public and (potential) patients. Both non-governmental organizations and government-related institutes such as VLAIO or the Research Foundation Flanders (FWO) may play a role in providing financial support.

Second, **initiatives from various stakeholders should be integrated in one collective approach** to avoid regional differences in implementation. Patient organizations, medical organizations and research institutions should collaborate to support health care professionals to accomplish SDM. Since there already has been extensive research on the international scene, the relevance of the obtained insights should be estimated for the Belgian setting and applied whenever possible. Best practices from countries with comparable healthcare systems, for example the Netherlands, are likely to be applicable in the Belgian context too. Care pathways in primary and secondary care should be revised and redesigned where necessary, allowing patients and physicians the required time and resources to prepare for and perform SDM. Whenever patients are eligible to receive new therapeutic or diagnostic options, they need time to acquire information on potential options and to clarify their preferences before they can engage in SDM. In order to avoid extra consultations; one in which the decision context and information is explained, and another one in which preferences are discussed and the decision is made; PtDAs may be used to cover the topics of the first consultation. The fact that patients can consult decision support from the comfort of their own home, can be considered an additional benefit. Furthermore, quality instruments should be used to monitor how SDM is applied and how it could still

be improved. Assessing whether a consultation fulfilled a patient's wishes regarding SDM could be done using standardized questionnaires. Moreover, comparing how a patient and a health care professionals experienced a consultation may provide valuable lessons.

Third, **health care professionals should be trained on both the theoretical aspects of SDM, as well as practical implications** for clinical practice. Focusing on patient directed interventions alone, will not be sufficient for the implementation of SDM. These trainings should not only be included in the university curriculum of medical and nursing students but should also be represented in the continuing professional development trainings for physicians and nurses. As the practice of SDM might require a change of culture and mindset, training methods that support reflection and provide real-time feedback for physicians should be encouraged. Physicians might also need additional training on how to inform patients on the benefits, risks and uncertainty related to these aspects regarding potential decision options.

Finally, but perhaps most importantly, **the public should be made aware of patients' rights to engage in SDM**. Patients should have the possibility to inform themselves on their disease and potential decision options at all times and should be empowered to assume the decision making role they prefer. The abovementioned centralized platform can further educate patients on what exactly SDM is and when it can be applied. More decision support tools, such as PtDAs, should be made available to patients. Next to supporting Belgian institutions or organizations to develop these tools, translations in Flemish, French and German could be made of existing international PtDAs, that are adapted to the Belgian clinical setting.

If these recommendations were implemented, we could start our journey towards true patient-centred care, of which providing information and discussing personal preferences should be the corner stones.

REFERENCES

1. Charles C, Gafni A, Whelan T. Decision-making in the physician-patient encounter: Revisiting the shared treatment decision-making model. Soc Sci Med. 1999;49(5):651–61.
2. Charles C, Gafni A, Whelan T. Shared decision-making in the medical encounter: What does it mean? (Or it takes, at least two to tango). Soc Sci Med. 1997;44(5):681–92.
3. World Medical Association. The WMA international code of medical ethics. 57th WMA General Assembly, Pilanesberg, South Africa; 2006.
4. Sandman L, Munthe C. Shared decision making, paternalism and patient choice. Heal Care Anal. 2010;18(1):60–84.
5. van Overbeeke E, Whichello C, Janssens R, Veldwijk J, Cleemput I, Simoens S, et al. Factors and situations influencing the value of patient preference studies along the medical product lifecycle: a literature review. Drug Discov Today [Internet]. 2019;24(1):57–68. Available from: https://doi.org/10.1016/j.drudis.2018.09.015
6. Llewellyn-Thomas HA, Crump RT. Decision Support for Patients: Values Clarification and Preference Elicitation. Med Care Res Rev. 2013;70(1_suppl):50S-79S.
7. Stiggelbout AM, Pieterse AH, De Haes JCJM. Shared decision making: Concepts, evidence, and practice. Patient Educ Couns [Internet]. 2015;98(10):1172–9. Available from: http://dx.doi.org/10.1016/j.pec.2015.06.022
8. Veatch RM. Models for Ethical Medicine in a Revolutionary Age. Hastings Cent Rep. 1972;2(3):5.
9. Braddock CH, Edwards KA, Hasenberg NM, Laidley TL, Levinson W, Page P. in Outpatient Practice Time to Get Back to Basics. Jama. 1999;282(24):2313–20.
10. Moumjid N, Gafni A, Brémond A, Carrère MO. Shared decision making in the medical encounter: Are we all talking about the same thing? Med Decis Mak. 2007;27(5):539–46.
11. World Medical Association. Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects.
12. Stacey D, Légaré F, Lewis K, et al. Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev. 2017;2017(4):1298–304.
13. Makoul G, Clayman ML. An integrative model of shared decision making in medical encounters. Patient Educ Couns. 2006;60(3):301–12.
14. Salzburg Global Seminar. Salzburg statement on shared decision making. BMJ. 2011;342(March).
15. Elwyn G, Frosch D, Thomson R, Joseph-Williams N, Lloyd A, Kinnersley P, et al. Shared decision making: A model for clinical practice. J Gen Intern Med. 2012;27(10):1361–7.
16. Volk RJ, Llewellyn-Thomas H, Stacey D, Elwyn G. Ten years of the International Patient Decision Aid Standards Collaboration: Evolution of the core dimensions for assessing the quality of patient decision aids. BMC Med Inform Decis Mak. 2013;13(SUPPL. 2):1–7.
17. IPDAS. Criteria for Judging the Quality of Patient Decision Aids. 2005.
18. Elwyn G, O'Connor A, Stacey D, Volk R, Edwards A, Coulter A, et al. Developing a quality criteria framework for patient decision aids: online international Delphi consensus process. BMJ [Internet]. 2006;333(7565):417–0. Available from: http://www.bmj.com/cgi/doi/10.1136/bmj.38926.629329.AE

19. National Institute for Health and Care Excellence (NICE). Medicines optimisation: The safe and effective use of medicines to enable the best possible outcomes. Mancehster;

20. Sepucha KR, Borkhoff CM, Lally J, Levin CA, Matlock DD, Ng CJ, et al. Establishing the effectiveness of patient decision aids: Key constructs and measurement instruments. BMC Med Inform Decis Mak. 2013;13(SUPPL. 2).

21. Montori VM, LeBlanc A, Buchholz A, Stilwell DL, Tsapas A. Basing information on comprehensive, critically appraised, and up-to-date syntheses of the scientific evidence: a quality dimension of the International Patient Decision Aid Standards. BMC Med Inform Decis Mak. 2013;13(S5).

22. Barry MJ, Chan E, Moulton B, Sah S, Simmons MB, Braddock C. Disclosing conflicts of interest in patient decision aids. BMC Med Inform Decis Mak. 2013;13(SUPPL. 2).

23. Feldman-Stewart D, O'Brien MA, Clayman ML, Davison BJ, Jimbo M, Labrecque M, et al. Providing information about options in patient decision aids. BMC Med Inform Decis Mak. 2013;13(SUPPL. 2).

24. Feldman-Stewart D, Madarnas Y, Mates M, Tong C, Grunfeld E, Verma S, et al. Information for decision making by post-menopausal women with hormone receptor positive early-stage breast cancer considering adjuvant endocrine therapy. Breast [Internet]. 2013;22(5):919–25. Available from: http://dx.doi.org/10.1016/j.breast.2013.04.020

25. Abhyankar P, Volk RJ, Blumenthal-Barby J, Bravo P, Buchholz A, Ozanne E, et al. Balancing the presentation of information and options in patient decision aids: An updated review. BMC Med Inform Decis Mak. 2013;13(SUPPL. 2).

26. Wise M, Han JY, Shaw B, McTavish F, Gustafson DH. Effects of using online narrative and didactic information on healthcare participation for breast cancer patients. Patient Educ Couns. 2008;70(3):348–56.

27. Volk RJ, Jibaja-Weiss ML, Hawley ST, Kneuper S, Spann SJ, Miles BJ, et al. Entertainment education for prostate cancer screening: A randomized trial among primary care patients with low health literacy. Patient Educ Couns. 2008;73(3):482–9.

28. McCaffery KJ, Holmes-Rovner M, Smith SK, Rovner D, Nutbeam D, Clayman ML, et al. Addressing health literacy in patient decision aids. BMC Med Inform Decis Mak. 2013;13(SUPPL. 2).

29. Stacey D, Kryworuchko J, Belkora J, Davison BJ, Durand MA, Eden KB, et al. Coaching and guidance with patient decision aids: A review of theoretical and empirical evidence. BMC Med Inform Decis Mak. 2013;13(SUPPL. 2):1–11.

30. Fagerlin A, Pignone M, Abhyankar P, Col N, Feldman-Stewart D, Gavaruzzi T, et al. Clarifying values: An updated review. BMC Med Inform Decis Mak. 2013;13(SUPPL. 2).

31. Witteman HO, Scherer LD, Gavaruzzi T, Pieterse AH, Fuhrel-Forbis A, Chipenda Dansokho S, et al. Design Features of Explicit Values Clarification Methods: A Systematic Review. In: Med Decis Making. Phoenix, Arizona; 2016. p. 452–71.

32. Feldman-Stewart D, Tong C, Siemens R, Alibhai S, Pickles T, Robinson J, et al. The impact of explicit values clarification exercises in a patient decision aid emerges after the decision is actually made: Evidence from a randomized controlled trial. Med Decis Mak. 2012;32(4):616–26.

33. Syrowatka A, Krömker D, Meguerditchian AN, Tamblyn R. Features of Computer-Based Decision Aids: Systematic Review, Thematic Synthesis, and Meta-Analyses. J Med Internet Res. 2016;18(1):e20.

34. Bekker HL, Winterbottom AE, Butow P, Dillard AJ, Feldman-Stewart D, Fowler FJ, et al. Do personal stories make patient decision aids more effective? A critical review of theory and evidence. BMC Med Inform Decis Mak. 2013;13(SUPPL. 2):1–9.

35. Hinyard LJ, Kreuter MW. Using narrative communication as a tool for health behavior change: A conceptual, theoretical, and empirical overview. Heal Educ Behav. 2007;34(5):777–92.

36. Barry MJ, Edgman-Levitan S. Shared decision making - The pinnacle of patient-centered care. N Engl J Med. 2012;366(9):780–1.

37. Ho M, Saha A, McCleary KK, Levitan B, Christopher S, Zandlo K, et al. A Framework for Incorporating Patient Preferences Regarding Benefits and Risks into Regulatory Assessment of Medical Technologies. Value Heal [Internet]. 2016 Sep;19(6):746–50. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1098301516000681

38. Van Til JA, IJzerman MJ. Why should regulators consider using patient preferences in benefit-risk assessment? Pharmacoeconomics. 2014;32(1):1–4.

39. Facey KM, Hansen HP, Single AN V. Patient Involvement in Health Technology Assessment [Internet]. 1st ed. Facey KM, Ploug Hansen H, Single ANV, editors. Vol. 32. Singapore: Springer Singapore; 2017. 434 p. Available from: http://link.springer.com/10.1007/978-981-10-4068-9

40. Lowe MM, Blaser DA, Cone L, Arcona S, Ko J, Sasane R, et al. Increasing Patient Involvement in Drug Development. Value Heal [Internet]. 2016;19(6):869–78. Available from: http://dx.doi.org/10.1016/j.jval.2016.04.009

41. Mühlbacher AC, Juhnke C, Beyer AR, Garner S. Patient-Focused Benefit-Risk Analysis to Inform Regulatory Decisions: The European Union Perspective. Value Heal. 2016;19(6):734–40.

42. FDA. Patient Preference Information – Voluntary Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and De Novo Requests, and Inclusion in Decision Summaries and Device Labeling [Internet]. 2016. p. 26. Available from: https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm446680.pdf(Archived by WebCite® at http://www.webcitation.org/75K37o6uo)

43. Johnson FR, Zhou M. Patient Preferences in Regulatory Benefit-Risk Assessments: A US Perspective. Value Heal. 2016;19:741–5.

44. Klein A V., Hardy S, Lim R, Marshall DA. Regulatory Decision Making in Canada—Exploring New Frontiers in Patient Involvement. Value Heal. 2016;19(6):730–3.

45. MDIC. Medical Device Innovation Consortium Patient Centered Benefit-Risk Project Report: A Framework for Incorporating Information on Patient Preferences Regarding Benefit and Risk into Regulatory Assessments of New Medical Technology [Internet]. Medical Device Innovation Consortium (MDIC). 2015. Available from: https://mdic.org/wp-content/uploads/2018/05/MDIC_PCBR_Framework_Web.pdf(Archived by WebCite® at http://www.webcitation.org/75K3smD1m)

46. de Bekker-Grob EW, Berlin C, Levitan B, Raza K, Christoforidi K, Cleemput I, et al. Giving Patients' Preferences a Voice in Medical Treatment Life Cycle: The PREFER Public–Private Project. Patient. 2017;10(3):263–6.

47. Soekhai V, Whichello C, Levitan B, Veldwijk J, Pinto CA, Donkers B, et al. Methods for exploring and eliciting patient preferences in the medical product lifecycle: a literature review. Drug Discov Today [Internet]. 2019;24(7):1324–31. Available from: https://doi.org/10.1016/j.drudis.2019.05.001

48. Louviere JJ. What you don't know might hurt you: Some unresolved issues in the design and analysis of discrete choice experiments. Environ Resour Econ. 2006;34(1):173–88.

49. P Bridges JF, Brett Hauber best imitate A, Marshall D, Lloyd A, Prosser LA, Regier DA, et al. Conjoint Analysis Applications in Health—a Checklist: A Report of the ISPOR Good Research Practices for Conjoint Analysis Task Force Background to the task force report. JVAL. 2011;14:403–13.

50. Johnson FR, Lancsar E, Marshall D, Kilambi V, Mühlbacher A, Regier DA, et al. Constructing experimental designs for discrete-choice experiments: Report of the ISPOR conjoint analysis experimental design good research practices task force. Value Heal. 2013;16(1):3–13.

51. Brett Hauber A, Marcos Gonzalez J, Groothuis-Oudshoorn KG, Professor A, Prior T, Marshall DA, et al. Conjoint Analysis Statistical Analysis: An ISPOR Conjoint Analysis Good Research Practices Task Force Report Methods for the Statistical Analysis of Discrete-Choice Experiments: A Report of the ISPOR Conjoint Analysis Good Research Practices Task Force. Sr Res Econ Heal Prefer Assess RTI Heal Solut.

52. Danner M, Hummel JM, Volz F, van Manen JG, Wiegard B, Dintsios C-M, et al. Integrating patients' views into health technology assessment: Analytic hierarchy process (AHP) as a method to elicit patient preferences. Int J Technol Assess Health Care. 2011;27(4):369–75.

53. Trevena LJ, Zikmund-Fisher BJ, Edwards A, Gaissmaier W, Galesic M, Han PKJ, et al. Presenting quantitative information about decision outcomes: A risk communication primer for patient decision aid developers. BMC Med Inform Decis Mak. 2013;13(SUPPL. 2):1–15.

54. Louviere JJ, Woodworth G. Design and Analysis of Simulated Consumer Choice or Allocation Experiments: An Approach Based on Aggregate Data. J Mark Res. 1983;20(4):350–67.

55. Hoeffler S. Measuring Preferences for Really New Products. J Mark Res. 2003;XL:406–20.

56. Lancsar E, Louviere J. Conducting Discrete Choice Experiments to Inform Health Care Decision Making : A User's Guide. Pharmacoeconomics. 2008;26(8):661–77.

57. Zanini C, Sarzi-Puttini P, Atzeni F, Di Franco M, Rubinelli S. Doctors' insights into the patient perspective: A qualitative study in the field of chronic pain. Biomed Res Int. 2014;2014.

58. Bastemeijer CM, Voogt L, van Ewijk JP, Hazelzet JA. What do patient values and preferences mean? A taxonomy based on a systematic review of qualitative papers. Patient Educ Couns [Internet]. 2017;100(5):871–81. Available from: http://dx.doi.org/10.1016/j.pec.2016.12.019

59. The Beryl Institute Website, Defining patient experience. [Internet]. [cited 2020 Oct 18]. Available from: https://www.theberylinstitute.org/default.aspx?page=DefiningPati

60. NHS. Shared Decision Making: Summary guide [Internet]. 2019. Available from: https://www.england.nhs.uk/wp-content/uploads/2019/01/shared-decision-making-summary-guide-v1.pdf

61. Lu C, Li X, Yang K. Trends in Shared Decision-Making Studies From 2009 to 2018: A Bibliometric Analysis. Front Public Heal. 2019;7(December):1–9.

62. The Ottawa Hospital Research Institute. Alphabetical List of Decision Aids by Health Topic [Internet]. [cited 2020 May 28]. Available from: https://decisionaid.ohri.ca/AZlist.html

63. Fraenkel L, McGraw S. What are the essential elements to enable patient participation in medical decision making? J Gen Intern Med. 2007;22(5):614–9.

64. Charles C, Gafni A, Freeman E. Implementing shared treatment decision making and treatment decision aids: A cautionary tale. Psicooncologia. 2010;7(2–3):243–55.

65. Elwyn G, Quinlan C, Mulley A, Agoritsas T, Vandvik PO, Guyatt G. Trustworthy guidelines - excellent; customized care tools - even better. BMC Med. 2015;13(1):1–5.

66. O'Brien MA, Whelan TJ, Vilhsis-Keever M, Gafni A, Charles C, Roberts R, et al. Are cancer-related

decision aids effective? a Systematic review and meta-analysis. J Clin Oncol. 2009;27(6):974–85.

67. Stiggelbout AM, De Haes JCJM. Patient preference for cancer therapy: An overview of measurement approaches. J Clin Oncol. 2001;19(1):220–30.

68. Chewning B, Bylund CL, Shah B, Arora NK, Gueguen JA, Makoul G. Patient preferences for shared decisions: A systematic review. Patient Educ Couns [Internet]. 2012;86(1):9–18. Available from: http://dx.doi.org/10.1016/j.pec.2011.02.004

69. Bieber C, Nicolai J, Gschwendtner K, Müller N, Reuter K, Buchholz A, et al. How Does a Shared Decision-Making (SDM) Intervention for Oncologists Affect Participation Style and Preference Matching in Patients with Breast and Colon Cancer? J Cancer Educ. 2018;33(3):708–15.

70. Gattellari M, Butow PN, Tattersall MHN. Sharing decisions in cancer care. Soc Sci Med. 2001;52(12):1865–78.

71. Huiart L, Ferdynus C, Giorgi R. A meta-regression analysis of the available data on adherence to adjuvant hormonal therapy in breast cancer: Summarizing the data for clinicians. Breast Cancer Res Treat. 2013;138(1):325–8.

72. Murphy CC, Bartholomew LK, Carpentier MY, Bluethmann SM, Vernon SW. Adherence to adjuvant hormonal therapy among breast cancer survivors in clinical practice: A systematic review. Breast Cancer Res Treat. 2012;134(2):459–78.

73. Wigertz A, Ahlgren J, Holmqvist M, Fornander T, Adolfsson J, Lindman H, et al. Adherence and discontinuation of adjuvant hormonal therapy in breast cancer patients: A population-based study. Breast Cancer Res Treat. 2012;133(1):367–73.

74. Wildiers H, Stordeur S, Vlayen J, Scholten R, van de Wetering F, Bourgain C, Carly B, Christiaens M-R C, V, Lifrange E, Schobbens J-C, Van Goethem M, Villeirs G, Van Limbergen E NP. Breast cancer in women: diagnosis, treatment and follow-up. Good Clinical Practice (GCP). Brussels; 2013.

75. Belgian Cancer Registry. Cancer Fact Sheet Breast Cancer, incidence year 2017 [Internet]. Brussels; 2019. Available from: https://kankerregister.org/media/docs/CancerFactSheets/2017/Cancer_Fact_Sheet_FemaleBreastCancer_2017.pdf

76. Kreienberg R, Kopp I, Lorenz W, Budach W, Dunst J, Lebeau A. Interdisciplinary S3 Guidelines for the Diagnosis and Treatment of Breast Cancer in Women. Frankfurt; 2003.

77. Scottish Intercollegiate Guidelines Network (SIGN). Management of breast cancer in women. A national clinical guideline. Edinburgh; 2003.

78. Bevolkingsonderzoek borstkanker. De screeningsmammografie: Wij doen het. En wat doe jij? [Internet]. 2017. Available from: www.bevolkingsonderzoek.be

79. Anders CK, Carey LA. Biology, Metastatic Patterns, and Treatment of Patients with Triple-Negative Breast Cancer. Clin Breast Cancer. 2009;9(1):1–7.

80. Wangchinda P, Ithimakin S. Factors that predict recurrence later than 5 years after initial treatment in operable breast cancer. World J Surg Oncol [Internet]. 2016;14(1):1–8. Available from: http://dx.doi.org/10.1186/s12957-016-0988-0

81. Ribelles N, Perez-Villa L, Jerez J, Pajares B, Vicioso L, Jimenez B, et al. Pattern of recurrence of early breast cancer is different according to intrinsic subtype and proliferation index. Breast Cancer Res [Internet]. 2013;15(5). Available from: http://breast-cancer-research.com/content/15/5/R98%5Cnhttp://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed11&NEWS=N&AN=2014029055

82. Dhesy-Thind B, Pritchard K, Messersmith H, O'Malley F, Elavathil L, Trudeau M. The role of HER2/neu in systemic and radiation therapy for women with breast cancer. A clinical practice guideline. Toronto; 2006.

83. Koh J, Kim MJ. Introduction of a new staging system of breast cancer for radiologists: An emphasis on the prognostic stage. Korean J Radiol. 2019;20(1):69–82.

84. National Institute for Health and Care Excellence. Early and locally advanced breast cancer: diagnosis and management, NICE guideline. 2018;(July 2018):62. Available from: https://www.nice.org.uk/guidance/ng101/resources/early-and-locally-advanced-breast-cancer-diagnosis-and-management-pdf-66141532913605

85. Gress DM, Edge SB, Greene FL, Washington MK, Asare EA, Brierley JD, et al. AJCC Cancer Staging Manual. AJCC Cancer Staging Man. 2017;

86. Wishart GC, Rakha E, Green A, Ellis I, Ali RR, Provenzano E, et al. Inclusion of KI67 significantly improves performance of the PREDICT prognostication and prediction model for early breast cancer. BMC Cancer. 2014;14(1):1–6.

87. Petrelli F, Coinu A, Cabiddu M, Ghilardi M, Lonati V, Barni S. Five or more years of adjuvant endocrine therapy in breast cancer: A meta-analysis of published randomised trials. Breast Cancer Res Treat. 2013;140(2):233–40.

88. Jinih M, Relihan N, Corrigan MA, O'Reilly S, Redmond HP. Extended Adjuvant Endocrine Therapy in Breast Cancer: Evidence and Update — A Review. Breast J. 2017;23(6):694–705.

89. Matthews A, Stanway S, Farmer RE, Strongman H, Thomas S, Lyon AR, et al. Long term adjuvant endocrine therapy and risk of cardiovascular disease in female breast cancer survivors: Systematic review. BMJ. 2018;363:10–3.

90. Moon Z, Moss-Morris R, Hunter MS, Carlisle S, Hughes LD. Barriers and facilitators of adjuvant hormone therapy adherence and persistence in women with breast cancer: a systematic review. Patient Prefer Adherence [Internet]. 2017;11:305–22. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5328144/pdf/ppa-11-305.pdf

91. Monnier A. Clinical management of adverse events in adjuvant therapy for hormone-responsive early breast cancer. Ann Oncol [Internet]. 2007;18(SUPPL. 8):viii36–44. Available from: http://dx.doi.org/10.1093/annonc/mdm264

92. Ruhstaller T, Giobbie-Hurder A, Colleoni M, Jensen MB, Ejlertsen B, De Azambuja E, et al. Adjuvant letrozole and tamoxifen alone or sequentially for postmenopausal women with hormone receptor-positive breast cancer: Long-term follow-up of the BiG 1-98 trial. J Clin Oncol. 2019;37(2):105–14.

93. Goossens B, Sevenants A, Declercq A, Van Audenhove C. Improving shared decision-making in advance care planning: Implementation of a cluster randomized staff intervention in dementia care. Patient Educ Couns [Internet]. 2020;103(4):839–47. Available from: https://doi.org/10.1016/j.pec.2019.11.024

94. Goossens B, Sevenants A, Declercq A, Van Audenhove C. "We DECide optimized" - Training nursing home staff in shared decision-making skills for advance care planning conversations in dementia care: Protocol of a pretest-posttest cluster randomized trial. BMC Geriatr. 2019;19(1).

95. Isebaert S, Van Audenhove C, Haustermans K, Junius S, Joniau S, De Ridder K, et al. Evaluating a decision aid for patients with localized prostate cancer in clinical practice. Urol Int. 2008;81(4):383–8.

96. Pardon K, Deschepper R, Vander Stichele R, Bernheim JL, Mortier F, Schallier D, et al. Preferred and actual involvement of advanced lung cancer patients and their families in end-of-life

decision making: A multicenter study in 13 hospitals in Flanders, Belgium. J Pain Symptom Manage. 2012;43(3):515–6.

97. Engelen A, Vanderhaegen J, Van Poppel H, Van Audenhove C. The use of decision aids on early detection of prostate cancer: views of men and general practitioners. Heal Expect. 2016;20(2):221–31.

98. Coulter A, Stilwell D, Kryworuchko J, Mullen P, Ng C, van der Weijden T. A systematic development process for patient decision aids. BMC Med Inform Decis Mak [Internet]. 2013;13(Suppl 2):S2. Available from: http://bmcmedinformdecismak.biomedcentral.com/articles/10.1186/1472-6947-13-S2-S2

99. Bewtra M, Johnson FR. Assessing patient preferences for treatment options and process of care in inflammatory bowel disease: A critical review of quantitative data. Patient. 2013;6(4):241–55.

100. Mühlbacher AC, Zweifel P, Kaczynski A, Johnson FR. Experimental measurement of preferences in health care using best-worst scaling (BWS): theoretical and statistical issues. Health Econ Rev. 2015;6(1):1–12.

101. European Patients' Academy on Therapeutic Innovation. Guidance for patient involvement in industry-led medicines R&D [Internet]. European Patients' Academy. Brussels; 2016. Available from: https://www.eupati.eu/patient-involvement/guidance-for-patient-involvement-in-industry-led-medicines-rd/(http://www.webcitation.org/75JzygMyz)

102. Bernabe RDLC, Van Thiel GJMW, Van Delden J. Patient representatives' contributions to the benefit'risk assessment tasks of the European Medicines Agency scientific committees. Br J Clin Pharmacol. 2014;78(6):1248–56.

103. De Bekker-Grob EW, Ryan M, Gerard K. Discrete choice experiments in health economics: A review of the literature. Health Econ. 2012;21:145–72.

104. LaVela S, Gallan A. Evaluation and Measurement of Patient Experience. Patient Exp J. 2014;1(1):28–36.

105. Dirksen CD, Utens CMA, Joore MA, van Barneveld TA, Boer B, Dreesens DHH, et al. Integrating evidence on patient preferences in healthcare policy decisions: Protocol of the patient-VIP study. Implement Sci. 2013;8(1):1.

106. Cohen SH, Neira L. Maximum Difference Scaling: Improved Measures of Importance and Preference for Segmentation. Sawtooth Softw Res Pap Ser. 2003;

107. Urban GL, Hauser JR, Qualls WJ, Weinberg BD, Bohlmann JD, Chicos RA. Information acceleration: Validation and Lessons From the Field. J Mark Res. 1997;XXXIV:143–53.

108. Urban GL, Weinberg BD, Hauser JR. Premarket Forecasting of Really-New Products. J Mark. 1996;60(1):47.

109. Sørensen K, Pelikan JM, Röthlin F, Ganahl K, Slonska Z, Doyle G, et al. Health literacy in Europe: Comparative results of the European health literacy survey (HLS-EU). Eur J Public Health. 2015;25(6):1053–8.

110. Urban GL, Hauser JR, Roberts JH. Prelaunch Forecasting of New Automobiles. Manage Sci. 1990;36(4):401–21.

111. Kolb AY, Kolb DA. Experiential learning theory: A dynamic, holistic approach to management learning, education and development. In: The SAGE Handbook of Management Learning, Education and Development. 2009. p. 42–68.

112. Louviere, Jordan J.; Henser, David A. and Swait JD. Stated Choice Methods Analysis and

Application. Seventh. 2000. 402 p.

113. Ali S, Ronaldson S. Ordinal preference elicitation methods in health economics and health services research : using discrete choice experiments and ranking methods. Br Med Bull. 2012;103:21–44.

114. Domigall Y, Albani A, Winter R. Identification of customer preferences for new service development in the electricity domain. Proc - 16th IEEE Conf Bus Informatics, CBI 2014. 2014;1:207–14.

115. Lancsar E, Swait J. Reconceptualising the External Validity of Discrete Choice Experiments. Pharmacoeconomics. 2014;32(10):951–65.

116. Holm S, Lemm R, Thees O, Hilty LM. Enhancing Agent-Based Models with Discrete Choice Experiments. J Artif Soc Soc Simul. 2016;19(3).

117. Eimecke J, Baier D. Preference Measurement in Complex Product Development: A Comparison of Two-Staged SEM Approaches. Data Sci Learn by Latent Struct Knowl Discov. 2015;239–50.

118. Rossi S, Barile F, Di Martino S, Improta D. A comparison of two preference elicitation approaches for museum recommendations. Concurr Comput . 2017;29(11):1–11.

119. Wang CH. Using the theory of inventive problem solving to brainstorm innovative ideas for assessing varieties of phone-cameras. Comput Ind Eng [Internet]. 2015;85:227–34. Available from: http://dx.doi.org/10.1016/j.cie.2015.04.003

120. Huang D, Luo L. Consumer Preference Elicitation of Complex Products Using Fuzzy Support Vector Machine Active Learning. Mark Sci. 2016;35(3):445–64.

121. Vignola R, Gonzalez-Rodrigo B, Lane O, Marchamalo M, McDaniels T. A scenario approach to assess stakeholder preferences for ecosystem services in agricultural landscapes of Costa Rica. Reg Environ Chang. 2017;17(2):605–18.

122. Xiang WN, Clarke KC. The use of scenarios in land-use planning. Environ Plan B Plan Des. 2003;30(6):885–909.

123. Hauser JR, Dong S, Ding M. Self-reflection and articulated consumer preferences. J Prod Innov Manag. 2014;31(1):17–32.

124. Schlereth C, Skiera B. Two New Features in Discrete Choice Experiments to Improve Willingness-to-Pay Estimation That Result in SDR and SADR: Separated (Adaptive) Dual Response. Manage Sci. 2017;63(3):829–42.

125. Boesch I, Schwaninger M, Weber M, Scholz RW. Enhancing Validity and Reliability Through Feedback-Driven Exploration: A Study in the Context of Conjoint Analysis. Syst Pract Action Res. 2013;26(3):217–38.

126. Huertas-Garcia R, Gázquez-Abad JC, Forgas-Coll S. A design strategy for improving adaptive conjoint analysis. J Bus Ind Mark. 2016;31(3):328–38.

127. Hauber AB, González JM, Groothuis-Oudshoorn CG, Prior T, Marshall DA, Cunningham C, et al. Statistical Methods for the Analysis of Discrete Choice Experiments: A Report of the ISPOR Conjoint Analysis Good Research Practices Task Force. Value Heal. 2016;19(4):300–15.

128. Légaré F, Ratté S, Gravel K, Graham ID. Barriers and facilitators to implementing shared decision-making in clinical practice: Update of a systematic review of health professionals' perceptions. Patient Educ Couns. 2008;73(3):526–35.

129. European Patients' Academy on Therapeutic Innovation. Eupati Project : Executive Summary [Internet]. Brussels; 2017. p. 5. Available from: https://3qksc436bu713cqimwcfglyj-wpengine.netdna-ssl.com/wp-content/uploads/2017/06/EUPATI-Final-Project-Executive-

Summary-1.1.pdf.(Archived by WebCite® at http://www.webcitation.org/75K9yzhtQ)

130. European Patient Forum. EPF Background Brief: Patient Empowerment [Internet]. A Strong Patient´s Voice to Drive Better Health in Europe. Brussels; 2015. Available from: http://www.eu-patient.eu/globalassets/campaign-patient-empowerment/briefing_paperpatient-empowerment_final_external.pdf.(Archived by WebCite® at http://www.webcitation.org/75KA8IU25)

131. Hallgreen CE, Mt-Isa S, Lieftucht A, Phillips LD, Hughes D, Talbot S, et al. Literature review of visual representation of the results of benefit–risk assessments of medicinal products. Vol. 25, pharmacoepidemiology and drug safety. 2016.

132. Fischhoff B, Brewer NT, Downs JS. Communicating Risks and Benefits: An Evidence-Based User's Guide [Internet]. Food and Drug Administration, Silver Spring; 2011. Available from: https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/REports/UCM268069.pdf .(Archived by WebCite® at http://www.webcitation.org/75K5KabXh)

133. Stacey D, Légaré F, Nf C, Cl B, Mj B, Kb E, et al. Decision aids for people facing health treatment or screening decisions (Review) Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev. 2014;(1):Art. No.: CD001431.

134. Mühlbacher A, Bethge S. First and Foremost Battle the Virus: Eliciting Patient Preferences in Antiviral Therapy for Hepatitis C Using a Discrete Choice Experiment. Value Heal. 2016;19(6):776–87.

135. Johnson RM, Orme BK. How Many Questions Should You Ask in Choice-Based Conjoint Studies ? [Internet]. Vol. 98382, Sawtooth Software Research paper series. 2002. p. 1–24. Available from: https://www.sawtoothsoftware.com/download/techpap/howmanyq.pdf.(Archived by WebCite® at http://www.webcitation.org/75KAJZ3ZG)

136. Klein M, Liessens O, Macq G, Maswaku LM, Mertens A, Rosskamp M, et al. Cancer Burden in Belgium: 2004-2017 [Internet]. 2019. Available from: https://kankerregister.org/media/docs/publications/CancerBurdenfeb2020reduced.pdf

137. Bradley R, Burrett J, Clarke M, Davies C, Duane F, Evans V, et al. Aromatase inhibitors versus tamoxifen in early breast cancer: Patient-level meta-analysis of the randomised trials. Lancet [Internet]. 2015;386(10001):1341–52. Available from: http://dx.doi.org/10.1016/S0140-6736(15)61074-1

138. Elwyn G, Laitner S, Coulter A, Walker E, Watson P, Thomson R. Implementing shared decision making in the NHS. Br Med J. 2010;341(Novemebr):971–3.

139. Alden DL, Friend J, Chun MBJ. Shared decision making and patient decision aids: knowledge, attitudes, and practices among Hawai'i physicians. Hawaii J Med Public Health. 2013;72(11):396–400.

140. NICE. Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence - NICE guideline | RCP London [Internet]. 2017. Available from: https://www.rcplondon.ac.uk/guidelines-policy/medicines-adherence-involving-patients-decisions-about-prescribed-medicines-and-supporting-adherence%0Ahttps://www.nice.org.uk/guidance/cg76

141. Martin LR, Williams SL, Haskard KB, DiMatteo MR. The challenge of patient adherence. Ther Clin Risk Manag. 2005;3(1):189–99.

142. Belkora JK, Miller MF, Dougherty K, Gayer C, Golant M, Buzaglo JS. The need for decision and communication aids: a survey of breast cancer survivors. J community Support Oncol [Internet]. 2015;13(3):104–12. Available from: www.jcso-online.com

143. Peate M, Meiser B, Cheah BC, Saunders C, Butow P, Thewes B, et al. Making hard choices easier: a prospective, multicentre study to assess the efficacy of a fertility-related decision aid in young women with early-stage breast cancer. Br J Cancer [Internet]. 2012;106(6):1053–61. Available from: http://www.nature.com/doifinder/10.1038/bjc.2012.61

144. Savelberg W, Van Der Weijden T, Boersma L, Smidt M, Willekens C, Moser A. Developing a patient decision aid for the treatment of women with early stage breast cancer: The struggle between simplicity and complexity. BMC Med Inform Decis Mak. 2017;17(1):1–14.

145. Volz S, Moore DH, Belkora JK. Do patients use decision and communication aids as prompted when meeting with breast cancer specialists? Heal Expect. 2015;18(3):379–91.

146. Hawley ST, Newman L, Griggs JJ, Kosir MA, Katz SJ. Evaluating a decision aid for improving decision making in patients with early stage breast cancer. Patient. 2016;9(2):161–9.

147. Klaassen LA, Dirksen CD, Boersma LJ, Hoving C, Portz MJG, Mertens PMG, et al. A novel patient decision aid for aftercare in breast cancer patients: A promising tool to reduce costs by individualizing aftercare. Breast. 2018;41:144–50.

148. Sleeswijk Visser F, Stappers PJ, van der Lugt R, Sanders EB-N. Contextmapping: experiences from practice. CoDesign. 2005;1(2):119–49.

149. Gale NK, Heath G, Cameron E, Rashid S, Redwood S. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. BMC Med Res Methodol [Internet]. 2013;13(1):1. Available from: BMC Medical Research Methodology

150. Tiedje K, Shippee ND, Johnson AM, Flynn PM, Finnie DM, Liesinger JT, et al. “They leave at least believing they had a part in the discussion”: Understanding decision aid use and patient-clinician decision-making through qualitative research. Patient Educ Couns [Internet]. 2013;93(1):86–94. Available from: http://dx.doi.org/10.1016/j.pec.2013.03.013

151. Shabason JE, Mao JJ, Frankel E, Vapiwala N. The Role of Shared Decision Making in Patient Experiences in Radiation Oncology. Int J Radiat Oncol [Internet]. 2013;87(2):S180–1. Available from: http://dx.doi.org/10.1016/j.ijrobp.2013.06.466

152. Thiel FC, Schrauder MG, Fasching PA, Löhberg CR, Bani MR, Häberle L, et al. Shared decision-making in breast cancer: Discrepancy between the treatment efficacy required by patients and by physicians. Breast Cancer Res Treat. 2012;135(3):811–20.

153. Reichlin L, Mani N, McArthur K, Harris AM, Rajan N, Dacso CC. Assessing the acceptability and usability of an interactive serious game in aiding treatment decisions for patients with localized prostate cancer. J Med Internet Res. 2011;13(1).

154. Franklin L, Plaisant C, Minhazur Rahman K, Shneiderman B. TreatmentExplorer: An interactive decision aid for medical risk communication and treatment exploration. Interact Comput. 2016;28(3):238–52.

155. Verschueren S, Buffel C, Vander Stichele G. Developing Theory-Driven, Evidence-Based Serious Games for Health: Framework Based on Research Community Insights. JMIR Serious Games. 2019;7(2):e11565.

156. Buffel C, van Aalst J, Bangels A-M, Toelen J, Allegaert K, Verschueren S, et al. CliniPup®, a web-based serious game for health to reduce perioperative anxiety and pain in children: a Pilot Study. JMIR Serious Games. 2018;7(2).

157. Brown R, Butow P, Wilson-Genderson M, Bernhard J, Ribi K, Juraskova I. Meeting the decision-making preferences of patients with breast cancer in oncology consultations: Impact on decision-related outcomes. J Clin Oncol. 2012;30(8):857–62.

158. Ver Donck N, Vander Stichele G, Huys I. Improving Patient Preference Elicitation by Applying

Concepts From the Consumer Research Field: Narrative Literature Review. Interact J Med Res. 2020;9(1).

159. Weernink MGM, van Til JA, Witteman HO, Fraenkel L, IJzerman MJ. Individual Value Clarification Methods Based on Conjoint Analysis: A Systematic Review of Common Practice in Task Design, Statistical Analysis, and Presentation of Results. Med Decis Mak [Internet]. 2018;38(6):746–55. Available from: https://doi.org/10.1177/0272989X18765185

160. Derks MGM, Blok EJ, Seynaeve C, Nortier JWR, Kranenbarg EMK, Liefers GJ, et al. Adjuvant tamoxifen and exemestane in women with postmenopausal early breast cancer (TEAM): 10-year follow-up of a multicentre, open-label, randomised, phase 3 trial. Lancet Oncol [Internet]. 2017;18(9):1211–20. Available from: http://dx.doi.org/10.1016/S1470-2045(17)30419-9

161. Cuzick J, Sestak I, Baum M, Buzdar A, Howell A, Dowsett M, et al. Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 10-year analysis of the ATAC trial. Lancet Oncol [Internet]. 2010;11(12):1135–41. Available from: http://dx.doi.org/10.1016/S1470-2045(10)70257-6

162. Regan MM, Price KN, Giobbie-Hurder A, Thürlimann B, Gelber RD. Interpreting breast international group (BIG) 1-98: A randomized, double-blind, phase III trial comparing letrozole and tamoxifen as adjuvant endocrine therapy for postmenopausal women with hormone receptor-positive, early breast cancer. Breast Cancer Res. 2011;13(3):1–16.

163. Het Belgisch Centrum voor Farmacotherapeutische Informatie [Internet]. [cited 2020 Mar 9]. Available from: https://www.bcfi.be/nl/start

164. U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES. Common terminology criteria for adverse events. Version 5.0 [Internet]. 2017. Available from: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf%0Ahttp://www.uptodate.com/contents/common-terminology-criteria-for-adverse-events

165. Vanderweyen E. Ontwikkeling van een interactief educatie programma , SERES TM Borstkanker , in coöperatie met patiënten en hulpverleners Development of an interactive educational tool ,. KULeuven; 2018.

166. Vanderweyen E, Vandekerckhove L, Vandezande L, Nevelsteen I, Swinnen J, Buffel C, et al. Development of an Interactive Educational Tool to support women with breast cancer taking adjuvant endocrine therapy. In: CHi Congress on Psychosocial Oncology. 2019.

167. Fagerlin A, Zikmund-Fisher BJ, Ubel PA. Helping patients decide: Ten steps to better risk communication. J Natl Cancer Inst. 2011;103(19):1436–43.

168. King WC, Hill A, Orme B. The “Importance” Question in ACA: Can It Be Omitted? Sawtooth Softw Conf Proc. 2004;98382(360).

169. Bosco-Lévy P, Jové J, Robinson P, Moore N, Fourrier-Réglat A, Bezin J. Persistence to 5-year hormonal breast cancer therapy: A French national population-based study. Br J Cancer. 2016;115(8):912–9.

170. National Institute for Health and Care Excellence. Guideline scope Shared decision making. 2019.

171. Elwyn G, Scholl I, Tietbohl C, Mann M, Edwards AG, Clay C, et al. “Many miles to go.”: A systematic review of the implementation of patient decision support interventions into routine clinical practice. BMC Med Inform Decis Mak. 2013;13(SUPPL. 2):1–10.

172. Ahmed N, Bestall JC, Payne SA, Noble B, Ahmedzai SH. The use of cognitive interviewing methodology in the design and testing of a screening tool for supportive and palliative care

needs. Support Care Cancer. 2009;17(6):665–73.

173. Eccles DW, Arsal G. The think aloud method: what is it and how do I use it? Qual Res Sport Exerc Heal [Internet]. 2017 Aug 8;9(4):514–31. Available from: https://doi.org/10.1080/2159676X.2017.1331501

174. Kelly-Blake K, Clark S, Dontje K, Olomu A, Henry RC, Rovner DR, et al. Refining a brief decision aid in stable CAD: Cognitive interviews. BMC Med Inform Decis Mak. 2014;14(1).

175. Wever D, Vollenbroek-Hutten MMR, Jansen-Kosterink SM, Hermens HJ, Huis in 't Veld HA. Differences in Use of a Exercise-based Tele-rehabilitation Service Delivered as Substitute of or Supplement to Conventional Care. Proc Sixth Int Symp e-Health Serv Technol Third Int Conf Green IT Solut. 2012;44–51.

176. Brooke J. SUS-A quick and dirty usability scale. In: Usability Evaluation in Industry (P W Jordan, B Thomas, B A Weerdmeester, & A L McClelland (Eds)). London: Taylor and Francis; 1996. p. 189–94.

177. Bangor A, Kortum PT, Miller JT. An empirical evaluation of the system usability scale. Int J Hum Comput Interact. 2008;24(6):574–94.

178. Molenaar S, Sprangers M, Oort F, Rutgers E, Luiten E, Mulder J, et al. Exploring the black box of a decision aid: What information do patients select from an interactive Cd-Rom on treatment options in breast cancer? Patient Educ Couns. 2007;65(1):122–30.

179. Joosten EAG, DeFuentes-Merillas L, De Weert GH, Sensky T, Van Der Staak CPF, De Jong CAJ. Systematic review of the effects of shared decision-making on patient satisfaction, treatment adherence and health status. Psychother Psychosom. 2008;77(4):219–26.

180. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424.

181. Reumkens K, Tummers MHE, Gietel-Habets JJG, van Kuijk SMJ, Aalfs CM, van Asperen CJ, et al. The development of an online decision aid to support persons having a genetic predisposition to cancer and their partners during reproductive decision-making: a usability and pilot study. Fam Cancer [Internet]. 2019;18(1):137–46. Available from: http://dx.doi.org/10.1007/s10689-018-0092-4

182. Metz MJ, Franx GC, Veerbeek MA, de Beurs E, van der Feltz-Cornelis CM, Beekman ATF. Shared decision making in mental health care using routine outcome monitoring as a source of information: A cluster randomised controlled trial. BMC Psychiatry [Internet]. 2015;15(1):1–10. Available from: http://dx.doi.org/10.1186/s12888-015-0696-2

183. O'connor AM. Validation of a Decisional Conflict Scale. Med Decis Mak. 1995;15(1):25–30.

184. Sauro J. MEASURING USABILITY WITH THE SYSTEM USABILITY SCALE (SUS) [Internet]. 2011 [cited 2020 Jul 31]. Available from: https://measuringu.com/sus/

185. O'Connor A. User Manual – Knowledge [Internet]. Ottawa: Ottawa Hospital Research Institute. 20000. p. 1–4. Available from: http://decisionaid.ohri.ca/docs/develop/User_Manuals/UM_Knowledge.pdf .

186. Rodenburg-Vandenbussche S, Pieterse AH, Kroonenberg PM, Scholl I, van der Weijden T, Luyten GPM, et al. Dutch Translation and Psychometric Testing of the 9-Item Shared Decision Making Questionnaire (SDM-Q-9) and Shared Decision Making Questionnaire-Physician Version (SDM-Q-Doc) in Primary and Secondary Care. PLoS One [Internet]. 2015;10(7):e0132158. Available from: http://dx.doi.org/10.1371/journal.pone.0132158

187. Pieterse AH, Baas-Thijssen MCM, Marijnen CAM, Stiggelbout AM. Clinician and cancer patient

views on patient participation in treatment decision-making: A quantitative and qualitative exploration. Br J Cancer. 2008;99(6):875–82.

188. Vlaams Indicatoren Project voor Patiënten en Professionals. Resultaten peiling patiëntervaring in Vlaamse ziekenhuizen informatieverstrekking over kosten en behandeling . Evolutie 2016-2018. 2019.

189. Doherr H, Christalle E, Kriston L, Haèrter M, Scholl I. Use of the 9-item Shared Decision Making Questionnaire (SDM-Q-9 and SDM-Q-Doc) in intervention studiesA systematic review. PLoS One. 2017;12(3):1–16.

190. van Veenendaal H, van der Weijden T, Ubbink DT, Stiggelbout AM, van Mierlo LA, Hilders CGJM. Accelerating implementation of shared decision-making in the Netherlands: An exploratory investigation. Patient Educ Couns [Internet]. 2018;101(12):2097–104. Available from: https://doi.org/10.1016/j.pec.2018.06.021

191. Härter M, Dirmaier J, Scholl I, Donner-Banzhoff N, Dierks ML, Eich W, et al. The long way of implementing patient-centered care and shared decision making in Germany. Z Evid Fortbild Qual Gesundhwes [Internet]. 2017;123–124:46–51. Available from: http://dx.doi.org/10.1016/j.zefq.2017.05.006

192. Nguyen F, Moumjid N, Charles C, Gafni A, Whelan T, Carr??re MO. Treatment decision-making in the medical encounter: Comparing the attitudes of French surgeons and their patients in breast cancer care. Patient Educ Couns. 2014;94(2):230–7.

193. Van Audenhove C. Medische keuzes. Praktische gids voor overleg tussen zorgverstrekker en patiënt. LannooCampus; 2015. 110–115 p.

194. Frosch DL, May SG, Rendle KAS, Tietbohl C, Elwyn G. Authoritarian physicians and patients' fear of being labeled "difficult" among key obstacles to shared decision making. Health Aff. 2012;31(5):1030–8.

195. Kon AA. The shared decision-making continuum. JAMA - J Am Med Assoc. 2010;304(8):903–4.

196. Van Den Bulck SA, Hermens R, Slegers K, Vandenberghe B, Goderis G, Vankrunkelsven P. Designing a patient portal for patient-Centered care: Cross-Sectional survey. J Med Internet Res. 2018;20(10):1–14.

197. Härter M, Moumjid N, Cornuz J, Elwyn G, van der Weijden T. Shared decision making in 2017: International accomplishments in policy, research and implementation. Z Evid Fortbild Qual Gesundhwes [Internet]. 2017;123–124:1–5. Available from: http://dx.doi.org/10.1016/j.zefq.2017.05.024

198. Harwood R, Douglas C, Clark D. Decision aids for breast and nodal surgery in patients with early breast cancer: Development and a pilot study. Asia Pac J Clin Oncol. 2011;7(2):114–22.

199. Pollard S, Bansback N, Bryan S. Physician attitudes toward shared decision making: A systematic review. Patient Educ Couns [Internet]. 2015;98(9):1046–57. Available from: http://dx.doi.org/10.1016/j.pec.2015.05.004

200. EMPATHiE Consortium. Empowering patients in the management of chronic diseases (EMPATHiE): Final summary report. Brussels; 2014.

201. Perestelo-Perez L, Rivero-Santana A, Alvarez-Perez Y, Alonso-Coello P, Orrego C, Serrano-Aguilar P. Shared decision making in Spain: Supportive policies and research initiatives, trends and directions for future. Z Evid Fortbild Qual Gesundhwes [Internet]. 2017;123–124:85–90. Available from: http://dx.doi.org/10.1016/j.zefq.2017.05.002

202. Trevena L, Shepherd HL, Bonner C, Jansen J, Cust AE, Leask J, et al. Shared decision making in Australia in 2017. Z Evid Fortbild Qual Gesundhwes [Internet]. 2017;123–124:17–20. Available

from: http://dx.doi.org/10.1016/j.zefq.2017.05.011

203. The Winton Centre for Risk and Evidence Communication. Predict: Breast Cancer Version 2.2, Release 1.13. Cambridge; 2020.

204. Huldtgren A, Jonker C. User-Centered Design of Preference Elicitation Interfaces for Decision Support. In: USAB. 2010. p. 14–33.

205. Matsuyama RK, Wilson-Genderson M, Kuhn L, Moghanaki D, Vachhani H, Paasche-Orlow M. Education level, not health literacy, associated with information needs for patients with cancer. Patient Educ Couns [Internet]. 2011;85(3):e229–36. Available from: http://dx.doi.org/10.1016/j.pec.2011.03.022

206. Hoffman AS, Llewellyn-Thomas HA, Tosteson ANA, O'Connor AM, Volk RJ, Tomek IM, et al. Launching a virtual decision lab: development and field-testing of a web-based patient decision support research platform. BMC Med Inform Decis Mak [Internet]. 2014;14(1):112. Available from: http://bmcmedinformdecismak.biomedcentral.com/articles/10.1186/s12911-014-0112-8

207. Kimman ML, Dellaert BGC, Boersma LJ, Lambin P, Dirksen CD. Follow-up after treatment for breast cancer: One strategy fits all? An investigation of patient preferences using a discrete choice experiment. Acta Oncol (Madr). 2010;49(3):328–37.

208. Trenaman L, Bryan S, Bansback N. The cost-effectiveness of patient decision aids: A systematic review. Healthcare [Internet]. 2014;2(4):251–7. Available from: http://dx.doi.org/10.1016/j.hjdsi.2014.09.002

209. Butt T. Measuring the Benefits of Decision Aids for Economic Evaluation. PharmacoEconomics - Open [Internet]. 2019;3(2):143–50. Available from: https://doi.org/10.1007/s41669-018-0087-y

210. Légaré F, Thompson-Leduc P. Twelve myths about shared decision making. Patient Educ Couns. 2014;96(3):281–6.

211. Da Silva D. Helping people share decision making [Internet]. A review of evidence considering whether shared decision making is worthwhile. 2012. Available from: http://www.health.org.uk/public/cms/75/76/313/3448/HelpingPeopleShareDecisionMaking.pdf?realName=rFVU5h.pdf

212. Ara, R; Brazier, JE; Sculpher, M; Manca, A; Bjoke, L; Basarir H. A Framework for Conducting Economic Evaluations When Using Patient Decision Aids in Health Care Decision Making. Policy Res Unit un Econ Eval Heal Care Interv. 2015;Report 049:1–49.

213. Kirch W, editor. Cost-Consequence AnalysisCost-consequence analysis. In: Encyclopedia of Public Health [Internet]. Dordrecht: Springer Netherlands; 2008. p. 168. Available from: https://doi.org/10.1007/978-1-4020-5614-7_582

214. Public Health England. Cost consequence analysis: health economic studies. 2020.

215. Canadian Agency for Drugs and Technologies in Health (CADTH). Guidelines for the economic evaluation of health technologies: Canada. Vol. 4th editio. Ottawa; 2017.

216. Härter M, Van Der Weijden T, Elwyn G. Policy and practice developments in the implementation of shared decision making: An international perspective. Z Evid Fortbild Qual Gesundhwes. 2011;105(4):229–33.

217. Goss C, Mosconi P, Renzi C, Deledda G. Participation of patients and citizens in healthcare decisions in Italy. Z Evid Fortbild Qual Gesundhwes [Internet]. 2011;105(4):277–82. Available from: http://dx.doi.org/10.1016/j.zefq.2011.04.003

218. Loh A, Härter M. Shared decision-making in diverse Healthcare systems -translating research and health policy into practice. Z Arztl Fortbild Qualitatssich. 2007;101(4):203–4.

219. Federal public health service. Symposium Kwaliteit en patiëntveiligheid. In: Mijn zorg: onze zorg! Een symposium over Shared decision making. Brussels; 2018. p. 13–4.

220. Paulus D, Van Den Heede K, Mertens R. Organisation of care for chronic patients in Belgium: Development of a position paper. 2012.

221. Adriaenssens J, Benahmed N, Eyssen M, Paulus D, Mertens R. Towards an Integrated Evidence-Based Practice Plan in Belgium - Part 1 - Literature, Belgian situation and end-users. Vol. Health Ser, Centre Fédéral d'Expertise des Soins de Santé (KCE). Brussels; 2018.

222. Don't Google it. [Internet]. Available from: http://vimeo.com/110476768

223. Gezondheid en wetenschap: Betrouwbare medische info op mensenmaat [Internet]. 2020 [cited 2020 Jul 7]. Available from: https://www.gezondheidenwetenschap.be/

224. Kom Op Tegen Kanker. Kom op tegen kanker. Vijfjarenplan 2017-2021. 2017; Available from: https://www.komoptegenkanker.be/sites/default/files/media/2018-10/vijfjarenplan.pdf

225. European Patients Forum. What is Patient Empowerment? Patients prescribe E5 for sustainable health systems. [Internet]. 2015. Available from: https://youtu.be/z91Ner8UJ60

226. Joseph-Williams N, Newcombe R, Politi M, Durand MA, Sivell S, Stacey D, et al. Toward minimum standards for certifying patient decision aids: A modified delphi consensus process. Med Decis Mak. 2014;34(6):699–710.

SUMMARY

During the last two decades, shared decision making (SDM) has been increasingly applied in multiple health care decision contexts. Within the model of SDM, a patient and physician share information regarding the benefits and risks of potential options and personal preferences. They discuss the patient's preferences for each of the available options and discuss the patient's desire for involvement in decision making. Finally, they make or defer a decision and arrange follow-up if applicable. SDM is the preferred model for medical decision making in case of preference-sensitive decisions. Within these decisions, two or more options are available, none of which is clearly superior. To facilitate the process of SDM, patient decision aids (PtDAs) can be applied. The aim of a PtDA is threefold: they make the decision explicit and provide evidence-based information on the potential options, they help patients clarify their values and preferences for the different options and they support patients to communicate their preferences to their health care provider. PtDAs exist in various formats, ranging from paper-based brochures to interactive digital applications, using audio and video elements. The International Patient Decision Aids Standards Collaboration has established a checklist for the development of PtDAs, based on 12 quality domains, covering content, development process and effectiveness of the PtDA. Internationally developed PtDAs have proven to increase patients' knowledge and accuracy of risk perception, and decrease their decisional conflict. There are multiple PtDAs available in the disease areas of breast, prostate and lung cancer, osteoarthritis and osteoporosis, end of life decisions and cholesterol-related diseases. The variety in disease areas highlights that preference-sensitive decisions occur in many different health care decision contexts. The disease area of hormone-sensitive breast cancer is particularly suitable for the implementation of a PtDA. Patients receiving adjuvant endocrine therapy undergo a very long treatment that often causes a high impact on quality of life, resulting in suboptimal treatment adherence. The available treatments, tamoxifen or aromatase inhibitors, may cause adverse events such as increased risk of blood clots or joint and muscle pain, respectively. The efficacy of both treatments is comparable, although aromatase inhibitors are considered to be the most effective option. As treatment impact varies considerably between patients, a PtDA can help to tradeoff potential benefits and adverse events to determine the optimal therapy for individual patients. Although the practice of SDM and the use of PtDAs is internationally recognized, there are currently only very few PtDAs available in Belgium and there are no examples available for patients with breast cancer.

This PhD project aimed to improve SDM for Belgian patients with hormone-sensitive breast cancer by developing a PtDA for decisions regarding switching or continuing adjuvant endocrine therapy after 2-3 years. This PtDA should meet the needs of both patient and physician, by informing patients on the

available decision options, eliciting their preferences for these options and supporting them to communicate their preferences to their treating physician. In order to meet this aim, four specific objectives were identified.

The first objective was to compare the process of decision making between patients and consumers and to identify innovative aspects of preference elicitation methods from the consumer research field. A literature review showed that the decision process between patients and consumers is highly comparable and identified five concepts from the consumer research field that might improve preference elicitation in healthcare. Preference elicitation methods that resemble real-life decision making as closely as possible, for example by providing time for self-reflection, are likely to generate the most accurate results.

The second objective was to assess the needs of both patients and physicians regarding a PtDA for breast cancer decision making. Four focus groups with 21 patients and five individual interviews with breast cancer specialists indicated that patients currently experience little involvement in their treatment decision making. Patients furthermore indicated a high need for information regarding treatment options, especially quantitative information on treatment benefits and risks. The breast cancer specialists acknowledged that SDM has become more important during the last decade but stated that it remains unclear how to implement this in clinical practice. Decisions regarding adjuvant endocrine therapy were deemed ideal for a PtDA intervention by both stakeholders as these treatments may have a high impact on quality of life and deliver limited benefits. Beneficial PtDA features were identified, such as the possibility to write down questions or to rate the impact of adverse events on daily life.

The third objective was to develop an interactive, online PtDA for patients with hormone-sensitive breast cancer switching adjuvant endocrine treatment. The combination of an in-depth literature review and stakeholder interviews were used to determine the content and design of the PtDA. Five attribute categories were identified using this approach: efficacy, adverse events, use, impact on quality of life and mechanism of action. Both patients and physicians rated potential attributes to determine the final selection, which included breast cancer mortality, risk of recurrence, treatment duration, joint and muscle pain, osteoporosis and increased thrombosis risk. The developed prototype PtDAs consists of three consecutive modules; an information module aiming to educate patients, a scenario-based module that will help patients to clarify potential impact on their everyday life and an adaptive conjoint analysis exercise to elicit patients' preferences for various treatment characteristics.

The final objective was to test the developed PtDA in a two-stage process. First, alpha testing in a research setting yielded an average usability score of 78.75 out of 100 using the System Usability Scale.

Furthermore, content and lay-out were scored 8.9 and 8.5 out of 10 respectively by 11 patients; and quality, completeness and lay-out were scored 8.4, 8.4 and 8.2 out of 10 respectively by five health care professionals. Qualitative feedback was gathered by applying cognitive interviewing while using the PtDA and a short interview afterwards. Next, after implementing the feedback received during alpha-testing, beta testing in a clinical setting was performed using a pilot trial. Nine patients tested the PtDA in the week before their planned follow-up consultation at the university hospital of Leuven. The effect of the PtDA was assessed by determining the impact on the quality of the decision process and the decision itself using the following constructs: knowledge, values-choice agreement, feeling informed, feeling clear about values, discussing goals with health care providers, and being involved. Patient knowledge increased from 5.33 before using the PtDA to 7.78 afterwards. Decisional conflict was low after the consultation, with a score of 18.06. One month after the consultation, decisional conflict had increased significantly, with a score of 41,67. This might indicate the need for a broader support framework for patients by providing information and support them to discuss their preferences over a longer time period. Making the PtDA available after the consultation and planning follow-up consultation when needed could be potential solutions. The extent to which SDM was applied during the consultation was assessed using the SDM-9 item questionnaire. The average score of 20 out of a possibly 45 indicated that no real SDM took place, highlighting that patient directed interventions only, are not sufficient to implement SDM in clinical practice. Usability was again assessed using the System Usability Scale, resulting in a mean score of 71.25. Finally, patient preferences elicited for different treatment characteristics revealed high variability between patients, with a total of five different attributes being selected as 'the most important one' by seven patients. These results indicate the need to discuss individual treatment preferences during consultations.

Based on the information gained through the different chapters, recommendations are formulated for the future development of PtDAs in Belgium and the implementation of SDM in clinical practice.

The first set of recommendations is related to the development process of PtDAs. As the current use and development of PtDAs is very limited in Belgium, more research in other disease areas is needed to truly enable patient centred care. Stakeholder input has proven to be indispensable during the development process. Therefore, stakeholder opinions regarding PtDA design and content should be assessed using a combination of qualitative and quantitative approaches. Different formats or visual displays should be tested to meet the specific needs of the target group. Interactive, online applications offer a range of advantages regarding implementation and use. Video and audio materials can facilitate the learning process for users. Interactive features such as content control or the use of narratives may improve decision making. Furthermore, explicit preference elicitation methods that simulate real-life decision making may improve value clarification. The generated preferences weights

can open up the discussion during a consultation. More research is required to facilitate optimal implementation in Belgium. The implementation strategy for a PtDA should already be considered during the development process. A centralized platform, either for the whole of Belgium or for Flanders, may provide easy access to PtDAs. However, not all patients are familiar with an online environment, nor does everyone have internet access. The needs of the target group should be assessed to identify the best implementation approach to allow for patient-centred care.

The second set of recommendations is developed to improve SDM in Belgium. The main recommendation here is to create awareness for SDM and to support implementation in clinical practice. A combination of clinical guidelines and practical measures such as logistic and financial support are needed. More research is needed to identify and address the barriers of Belgian health care professionals for SDM implementation. An example can be financial support to reimburse physicians for the time spent on the conduct of true SDM, for example in analogy to the compensation pharmacists can receive for performing counselling on the use of diabetes or asthma medicines. Moreover, financial support will be required to stimulate research on the development of PtDAs and the implementation of SDM. Furthermore, initiatives from various stakeholders and organizations should be harmonized in one collective approach. We should capitalize on the knowhow built up during international research, especially from countries with a comparable health care system such as the Netherlands. Care pathways in both primary and secondary care might need to be revised, to allow patients the necessary time to inform themselves and participate in decision making. More quality measures are needed to monitor the extent of SDM in clinical practice and to improve where needed. Another important recommendation is to apply trainings in SDM for health care professionals. If we truly want to implement SDM in routine clinical practice, a change of culture and mindset is needed. Only focusing on patient directed interventions will not suffice to accomplish this. Finally, public awareness for the right to engage in SDM should be raised. Patients should know where to find relevant information regarding their medical condition and available options at all times. More patient directed interventions such as PtDAs should be made available, either by developing new interventions or by translating and adapting PtDAs from the international scene.

By implementing these recommendations, we could truly start our journey towards patient-centred care.

SAMENVATTING

In de voorbije 20 jaar is gedeelde besluitvorming (GB) in toenemende mate toegepast in verschillende contexten binnen de gezondheidszorg. In het model van GB delen een patiënt en arts informatie over de voordelen en risico's van mogelijke opties en hun persoonlijke voorkeur. Ze bespreken de voorkeuren van de patiënt voor elk van de beschikbare opties en bespreken de wens van de patiënt om bij de beslissing te worden betrokken. Tot slot nemen ze een beslissing, of ze stellen de beslissing uit en maken afspraken over een eventuele follow-up. GB is het beslissingsmodel bij uitstek in het geval van voorkeursgevoelige beslissingen. Bij dit soort beslissingen zijn er twee of meer opties beschikbaar, waarbij geen van beide duidelijk beter is dan de andere. Om het proces van GB te vergemakkelijken, kunnen beslishulpen voor patiënten worden gebruikt. Het doel van een beslishulp is drieledig: ze maken duidelijk dat er een beslissing genomen moet worden en bieden wetenschappelijke info over de mogelijke opties, ze helpen patiënten hun mening over de verschillende opties te verduidelijken en ze ondersteunen patiënten om hun voorkeuren aan hun zorgverlener te communiceren. Beslishulpen komen voor onder verschillende vormen, variërend van papieren brochures tot interactieve digitale applicaties, waarbij audio- en videomateriaal wordt gebruikt. De *International Patient Decision Aids Standards Collaboration* heeft een checklist opgesteld voor de ontwikkeling van beslishulpen. Deze is gebaseerd op 12 kwaliteitsdomeinen, verdeeld over drie categorieën: inhoud, ontwikkelingsproces en effectiviteit van de beslishulp. Onderzoek heeft aangetoond dat internationaal ontwikkelde beslishulpen de kennis en risicoperceptie van patiënten verbeteren en hen minder doet twijfelen over hun beslissing. Er zijn verschillende beslishulpen beschikbaar in het domein van borst-, prostaat- en longkanker, osteoartritis en osteoporose, beslissingen rond het levenseinde en cholesterol-gerelateerde ziekten. De grote verscheidenheid aan toepassingsgebieden toont aan dat voorkeursgevoelige beslissingen in vele domeinen van onze gezondheidszorg voorkomen. Het ziektegebied van hormoongevoelige borstkanker is uitermate geschikt voor de implementatie van een beslishulp. Patiënten die adjuvante endocriene therapie krijgen, ondergaan een zeer lange behandeling die vaak een grote impact heeft op hun levenskwaliteit, wat resulteert in een niet-optimale therapietrouw. De beschikbare behandelingen, tamoxifen of aromataseremmers, kunnen bijwerkingen veroorzaken zoals, respectievelijk, een verhoogd trombose risico of spier- en gewrichtspijn. De werkzaamheid van beide behandelingen is vergelijkbaar, hoewel aromataseremmers als de meest effectieve optie worden beschouwd. Aangezien de impact van de behandeling erg verschilt van patiënt tot patiënt, kan een beslishulp helpen om mogelijke voordelen en bijwerkingen af te wegen om zo de optimale behandeling voor een individuele patiënt te bepalen. Hoewel de praktijk van GB en het gebruik van beslishulpen internationaal erkend wordt, zijn er momenteel heel

weinig beslishulpen beschikbaar in België. Er zijn op dit moment geen beslishulpen beschikbaar voor patiënten met borstkanker.

Het doel van dit doctoraat was om GB te verbeteren voor Belgische patiënten met hormoongevoelige borstkanker, door een beslishulp te ontwikkelen die beslissingen over het mogelijk veranderen van adjuvante endocriene therapie na 2-3 jaar behandeling kan ondersteunen. Deze beslishulp moet beantwoorden aan de noden van zowel de patiënt als de arts, door patiënten te informeren over de beschikbare behandelingsopties, hun voorkeuren voor deze opties te meten en hen te ondersteunen bij het bespreken van deze voorkeuren met hun behandelende arts. Om dit algemene doel te bereiken, werden vier specifieke doelstellingen bepaald.

Het eerste doel was om het beslissingsproces tussen patiënten en consumenten te vergelijken en om innovatieve elementen te identificeren in methoden voor het meten van voorkeuren uit het domein van consumentenonderzoek. Een literatuuronderzoek toonde aan dat het beslissingsproces tussen patiënten en consumenten sterk vergelijkbaar is en er werden vijf concepten geïdentificeerd uit consumentenonderzoek die het meten van voorkeuren in de gezondheidszorg zouden kunnen verbeteren. Methoden om voorkeuren te meten die een echt beslissingsproces zo goed mogelijk nabootsen, leveren waarschijnlijk de meest nauwkeurige resultaten op. Een voorbeeld van dergelijke methode is het aanmoedigen van zelfreflectie over persoonlijke voorkeuren bij de deelnemers.

Het tweede doel was om de noden en wensen van patiënten en artsen in kaart te brengen in verband met het gebruik van een beslishulp om GB te faciliteren in borstkanker. Vier focusgroepen met 21 patiënten en vijf individuele interviews met borstkankerspecialisten gaven aan dat patiënten momenteel weinig betrokken worden bij beslissingen over hun behandeling. Patiënten gaven bovendien aan een grote behoefte te hebben aan informatie over de mogelijke behandelingsopties, meer specifiek kwantitatieve informatie over voordelen en risico's van de verschillende opties. De borstkankerspecialisten erkenden dat GB het afgelopen decennium belangrijker is geworden, maar gaven aan dat het onduidelijk blijft hoe dit best in de klinische praktijk wordt geïmplementeerd. Beslissingen over adjuvante endocriene therapie werden door beide partijen als een ideaal onderwerp voor een beslishulp beschouwd, aangezien deze behandelingen een grote impact kunnen hebben op de levenskwaliteit en soms relatief beperkte voordelen opleveren. Nuttige eigenschappen van een beslishulp werden geïdentificeerd, zoals de mogelijkheid om vragen te noteren of om de huidige impact van bijwerkingen op het dagelijks leven aan te geven.

Het derde doel was om een interactieve, online beslishulp te ontwikkelen voor patiënten met hormoongevoelige borstkanker die in aanmerking komen om te veranderen van adjuvante endocriene therapie. Een literatuuronderzoek gecombineerd met interviews met patiënten en artsen werd

gebruikt om de inhoud en het design van de beslishulp te bepalen. Op deze manier werden vijf categorieën met attributen geïdentificeerd: werkzaamheid, mogelijke bijwerkingen, gebruik, impact op levenskwaliteit en werkingsmechanisme. Mogelijke attributen werden gerangschikt door patiënten en artsen om de uiteindelijke selectie te bepalen. Onder andere volgende attributen werden weerhouden: sterfte aan borstkanker, risico op herval, duur van de behandeling, spier- en gewrichtspijn, osteoporose en risico op trombose. Het prototype beslishulp bestaat uit drie opeenvolgende modules; een informatiemodule om patiënten te informeren over mogelijke opties, een scenario module die patiënten kan helpen om de mogelijke impact van de opties op hun dagelijks leven in te schatten en een *adaptive conjoint analysis* oefening om de voorkeur van patiënten voor verschillende eigenschappen van de behandelingen te meten.

Het vierde en laatste doel was om de ontwikkelde beslishulp te testen in een tweeledig proces. Ten eerste werd een alfatest uitgevoerd in een onderzoeksomgeving, wat een gemiddelde gebruiksvriendelijkheid van 78,75 op 100 opleverde, gemeten met de *System Usability Scale*. Verder werden de inhoud en lay-out beoordeeld door 11 patiënten, wat scores opleverde van respectievelijk 8,9 en 8,5 op 10. De kwaliteit, volledigheid en lay-out werden door vijf zorgprofessionals respectievelijk 8,4; 8,4 en 8,2 op 10 gescoord. Kwalitatieve feedback werd verzameld door cognitieve interviews af te nemen tijdens het gebruik van de beslishulp en een kort interview na gebruik. Na het implementeren van de verkregen feedback, werd een pilootstudie uitgevoerd als bètatest in een klinische setting. Negen patiënten testten de beslishulp in de week voor hun geplande consultatie in het universitair ziekenhuis van Leuven. Het effect van de beslishulp werd beoordeeld door het effect op de kwaliteit van het beslissingsproces en het effect op de kwaliteit van de beslissing zelf te bepalen. Dit werd gedaan aan de hand van volgende concepten: kennis, overeenkomst tussen voorkeuren en keuze, zich geïnformeerd voelen, zeker zijn over voorkeuren, doelen bespreken met zorgverleners, en betrokken zijn. De kennis van de patiënten nam toe van 5,33 voor het gebruik van de beslishulp tot 7,78 na het gebruik. Het beslissingsconflict van de patiënten was laag na de consultatie, met een score van 18,06. Eén maand na de consultatie wad het beslissingsconflict van de patiënten significant gestegen, met een score van 41,67. Dit zou kunnen wijzen op een nood aan langdurige ondersteuning voor patiënten, zowel wat informatie als het bespreken van voorkeuren betreft. De beslishulp ook nog beschikbaar stellen na de consultatie en het inplannen van een follow-up consultatie indien nodig, zouden mogelijke oplossingen kunnen zijn hiervoor. De mate waarin GB werd toegepast tijdens de consultatie werd beoordeeld met behulp van de SDM-9 item vragenlijst. De gemiddelde score van 20 op 45 gaf aan dat er geen echte GB plaatsvond, wat erop wijst dat interventies die enkel gericht zijn op de patiënt, niet voldoende zijn om GB in de klinische praktijk te implementeren. De gebruiksvriendelijkheid werd opnieuw beoordeeld met de *System Usability Scale*, wat een gemiddelde

score van 71,25 opleverde. Ten slotte bleek er een hoge variabiliteit te zijn in de voorkeuren van de patiënten voor verschillende eigenschappen van behandelingen, waarbij in totaal vijf verschillende eigenschappen door zeven patiënten als 'de belangrijkste' werden aangeduid. Deze resultaten tonen de noodzaak aan om individuele voorkeuren te bespreken tijdens consultaties.

Op basis van de informatie verkregen uit de verschillende hoofdstukken, werden aanbevelingen geformuleerd voor de toekomstige ontwikkeling van beslishulpen in België en de implementatie van GB in de klinische praktijk.

De eerste reeks aanbevelingen heeft betrekking op het ontwikkelingsproces van beslishulpen. Aangezien het huidige gebruik en de ontwikkeling van beslishulpen in België zeer beperkt is, is er meer onderzoek nodig, ook in andere ziektedomeinen, om echt patiëntgerichte zorg mogelijk te maken. De inbreng van verschillende partijen tijdens het ontwikkelproces van een beslishulp is erg belangrijk gebleken. Daarom kan er best gebruik gemaakt worden van een combinatie van kwalitatieve en kwantitatieve methoden om de meningen van verschillende partijen over de inhoud en het design van een beslishulp in kaart te brengen. Verschillende vormen en visuele voorstellingen moeten worden getest om aan de specifieke noden van de doelgroep tegemoet te komen. Interactieve, online applicaties bieden tal van voordelen wat betreft implementatie en gebruik. Video- en audiomateriaal kan het leerproces voor gebruikers vergemakkelijken. Interactieve functies zoals controle over de inhoud of het gebruik van verhalen kunnen het beslissingsproces verbeteren. Bovendien kunnen methoden voor het meten van voorkeuren die een echt beslissingsproces simuleren, ervoor zorgen dat gebruikers meer inzicht krijgen in hun persoonlijke voorkeur. Een overzicht van de gekwantificeerde voorkeuren kan gebruikt worden om het gesprek te openen tijdens een consultatie. Meer onderzoek is echter nodig om een optimale implementatie in België mogelijk te maken. De implementatiestrategie voor een beslishulp kan best al tijdens het ontwikkelingsproces worden bepaald. Een gecentraliseerd platform zou patiënten in België of Vlaanderen op een eenvoudige en gebruiksvriendelijke manier toegang kunnen verlenen tot een beslishulp. Niet alle patiënten zijn echter bekend met een online omgeving, noch heeft elke patiënt toegang tot het internet. De noden van de doelgroep moeten in kaart worden gebracht om de beste implementatiestrategie te bepalen om patiëntgerichte zorg mogelijk te maken.

De tweede reeks aanbevelingen is ontwikkeld om GB in het algemeen in België te verbeteren. De belangrijkste aanbeveling hier is om bewustzijn voor GB te creëren en de implementatie in de klinische praktijk te ondersteunen. Een combinatie van klinische richtlijnen en praktische maatregelen zoals logistieke en financiële ondersteuning is vereist. Meer onderzoek is verder nodig om de factoren die de implementatie van GB bij Belgische gezondheidszorgmedewerkers bemoeilijkt, te adresseren. Een mogelijk voorbeeld van een praktische maatregel is financiële ondersteuning om artsen te vergoeden

voor de tijd besteed aan het uitvoeren van echte GB tijdens een consultatie. Dit zou, bijvoorbeeld, in analogie kunnen gebeuren aan de vergoeding die apothekers krijgen voor de begeleidingsgesprekken bij het gebruik van diabetes- of astmamedicijnen. Financiële steun zal verder ook nodig zijn om onderzoek naar de ontwikkeling van beslishulpen en de implementatie van GB te stimuleren. Bovendien moeten initiatieven van verschillende organisaties geharmoniseerd worden in één collectieve aanpak. We moeten gebruik maken van de kennis die is opgebouwd in internationaal onderzoek, vooral uit landen met een vergelijkbare gezondheidszorg, zoals Nederland. Zorgtrajecten in zowel de eerste als de tweede lijn moeten worden herzien om patiënten de nodige tijd te geven om zichzelf te informeren en deel te nemen aan de besluitvorming. Verder zijn er meer kwaliteitsindicatoren nodig om GB in de klinische praktijk te monitoren en waar nodig te verbeteren. Een andere belangrijke aanbeveling is om trainingen in GB beschikbaar te maken voor zorgprofessionals. Als we GB echt willen implementeren in de dagelijkse klinische praktijk, is er een verandering van zowel cultuur als mentaliteit vereist. Enkel focussen op interventies op maat van de patiënt is hierbij niet voldoende. Ten slotte moet de bevolking bewust worden gemaakt van het recht op inspraak in medische beslissingen. Patiënten moeten ten allen tijde weten waar ze relevante informatie over hun ziekte en beschikbare screenings- of behandelingsopties kunnen vinden. Er zouden meer patiëntgerichte interventies zoals beslishulpen beschikbaar moeten worden gemaakt; hetzij door nieuwe interventies te ontwikkelen, hetzij door beslishulpen van het internationale toneel te vertalen en aan te passen aan de Belgische context.

Door deze aanbevelingen te implementeren, zouden we de weg kunnen aanvatten naar echt patiëntgerichte zorg.

SUPPLEMENTARY MATERIAL

PART A: Online supplementary materials

Electronic supplementary materials have been uploaded to a Google Drive.

Appendix A

https://drive.google.com/file/d/1Pno_4qI7dL39e1iMB1h0j_jXtKaKOf65/view?usp=sharing

Appendix C

https://drive.google.com/file/d/1HgWOXfkRGNS281zIMlgvQOpx0S9oqeRG/view?usp=sharing

Appendix D

https://drive.google.com/file/d/11KuUs9UlCaaBOcZkudr18gD68a-Pyq0r/view?usp=sharing

Appendix F

https://drive.google.com/file/d/1YnhEUILt4xCK2O1Z6W1w8D5pTmYBUwl8/view?usp=sharing

PART B: Other supplementary materials

Other supplementary materials (appendix B, E and G) are included on the following pages.

Appendix B: International Patient Decision Aid Standards (IPDAS) Minimal criteria (version 4.0) [215]
Criteria for patient decision aids (PtDAs) regarding screening or testing were omitted

	Developed PtDA
Qualifying criteria	
1 Describes health condition or problem for which index decision is required	✓
2 Explicitly states the decision that needs to be considered (index decision)	✓
3 Describes the options available for the index decision	✓
4 Describes the positive features of each option	✓
5 Describes the negative features of each option	✓
6 Describes what it is like to experience the consequences of the options (eg physical, psychological, social)	✓
Certification criteria	
1 Shows positive and negative features of options with equal detail	✓
2 Provides citations to the evidence selected	–
3 Provides a production or publication date	✓
4 Provides information about update policy	–
5 Provides information about the level of uncertainty around outcome probabilities	✓
6 Provides information about the funding source used for development	–[a]
Quality criteria	
1 Describes the natural course of the health condition or problem, if no action is taken (when appropriate)	–
2 Makes it possible to compare the positive and negative features of the available options	✓
3 Provides information about outcome probabilities associated with the options	✓
4 Specifies the defined group of patients for whom the outcome probabilities apply	✓
5 Specifies the event rates for the outcome probabilities	✓
6 Allows user to compare outcome probabilities across options using the same time period (when feasible)	✓
7 Allows the user to compare outcome probabilities across options using the same denominator	✓
8 Provides more than 1 way of viewing the probabilities (eg words, numbers, and diagrams)	✓
9 Asks patients to think about which positive and negative features of the options matter most to them (implicitly or explicitly)	✓
10 Provides step by step way to make decision	✓
11 Includes tools to use when discussing options with practitioner	✓
12 Development process included a needs assessment with clients or patients	✓
13 Development process included a needs assessment with health professionals	✓
14 Development included review by patients not involved in producing the PtDA	✓[b,c]
15 Development included review by professionals not involved in producing the PtDA	✓[c]
16 PtDA was field tested with patients who were facing the decision	✓[c]
17 PtDA was field tested with practitioners who counsel patients who face the decision	✓[c,d]
18 Describes how research evidence was selected or synthesized	–
19 Describes the quality of research evidence used	–
20 Includes author/developers credentials or qualifications	–
21 Reports readability levels	–
22 There is evidence that the PtDA improves the match between the preferences of the informed patient and the option that is chosen	–[e]
23 There is evidence that the PtDA helps patients improve their knowledge about options' features	✓

a. *Information was provided on the website that included the PtDA for beta testing, not in the PtDA itself*
b. *Patients that also participated in the needs assessment were asked to review the PtDA during alpha testing, these patients were not involved in the production of the PtDA*
c. *Criterium fulfilled after performing alpha and beta testing*
d. *The PtDA was only alpha tested with practitioners as patients consulted the PtDA before consultation during beta testing*
e. *Beta testing indicated that values-clarification might improve by using the PtDA, however, there is no conclusive evidence at this time.*

Appendix E - part 1

Patients original and converted scores on the system usability scale during alpha testing. SD: Standard deviation

	Patients											Mean (SD)
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	
Participants' original scores												
1. I think that I would like to use this system frequently.	3	4	5	4	4	4	4	4	5	5	1	3,91 (1,14)
2. I found the system unnecessarily complex.	1	2	1	2	2	2	1	2	4	1	1	1,73 (0,90)
3. I thought the system was easy to use.	5	3	4	4	3	3	4	4	4	1	3	3,45 (1,04)
4. I think that I would need the support of a technical person to be able to use this system.	1	2	1	3	2	1	1	4	1	1	1	1,64 (1,03)
5. I found the various functions in this system were well integrated.	4	4	5	4	4	3	4	5	3	2	5	3,91 (0,94)
6. I thought there was too much inconsistency in this system.	1	1	1	1	2	1	1	1	1	1	1	1,09 (0,30)
7. I would imagine that most people would learn to use this system very quickly.	4	4	5	4	3	3	4	4	3	2	2	3,45 (0,93)
8. I found the system very cumbersome to use.	1	1	1	2	2	2	1	1	1	1	1	1,27 (0,47)
9. I felt very confident using the system.	4	3	5	4	3	3	4	4	3	1	4	3,45 (1,04)
10. I needed to learn a lot of things before I could get going with this system.	1	1	1	3	3	1	2	2	1	1	1	1,55 (0,82)
Participants' converted scores												
1. I think that I would like to use this system frequently.	2	3	4	3	3	3	3	3	4	4	0	2,91 (1,14)
2. I found the system unnecessarily complex.	4	3	4	3	3	3	4	3	1	4	4	3,27 (0,90)
3. I thought the system was easy to use.	4	2	3	3	2	2	3	3	3	0	2	2,45 (1,04)
4. I think that I would need the support of a technical person to be able to use this system.	4	3	4	2	3	4	4	1	4	4	4	3,36 (1,03)
5. I found the various functions in this system were well integrated.	3	3	4	3	3	2	3	4	2	1	4	2,91 (0,94)
6. I thought there was too much inconsistency in this system.	4	4	4	4	3	4	4	4	4	4	4	3,91 (0,30)
7. I would imagine that most people would learn to use this system very quickly.	3	3	4	3	2	2	3	3	2	1	1	2,45 (0,93)
8. I found the system very cumbersome to use.	4	4	4	3	3	3	4	4	4	4	4	3,73 (0,47)
9. I felt very confident using the system.	3	2	4	3	2	2	3	3	2	0	3	2,45 (1,04)
10. I needed to learn a lot of things before I could get going with this system.	4	4	4	2	2	4	3	3	4	4	4	3,45 (0,82)
Sum converted scores/40	**35**	**31**	**39**	**29**	**26**	**29**	**34**	**31**	**30**	**26**	**30**	**30,91 (3,86)**
Converted score/100	**88**	**78**	**98**	**73**	**65**	**73**	**85**	**78**	**75**	**65**	**75**	**77,27 (9,65)**

Appendix E - part 2

Health care providers original and converted scores on the system usability scale during alpha testing.

SD: Standard deviation

	Health care providers					Mean (SD)
	1	**2**	**3**	**4**	**5**	
Participants' original scores						
1. I think that I would like to use this system frequently.	4	4	5	4	4	4,20 (0,45)
2. I found the system unnecessarily complex.	1	2	1	2	1	1,40 (0,55)
3. I thought the system was easy to use.	5	4	5	4	4	4,40 (0,55)
4. I think that I would need the support of a technical person to be able to use this system.	3	1	1	2	1	1,60 (0,89)
5. I found the various functions in this system were well integrated.	4	4	4	4	4	4,00 (0,00)
6. I thought there was too much inconsistency in this system.	1	1	1	1	1	1,00 (0,00)
7. I would imagine that most people would learn to use this system very quickly.	4	3	4	4	5	4,00 (0,71)
8. I found the system very cumbersome to use.	3	4	1	3	1	2,40 (1,34)
9. I felt very confident using the system.	4	3	4	4	4	3,80 (0,45)
10. I needed to learn a lot of things before I could get going with this system.	2	1	1	1	1	1,20 (0,45)
Participants' converted scores						
1. I think that I would like to use this system frequently.	3	3	4	3	3	3,20 (0,45)
2. I found the system unnecessarily complex.	4	3	4	3	4	3,60 (0,55)
3. I thought the system was easy to use.	4	3	4	3	3	3,40 (0,55)
4. I think that I would need the support of a technical person to be able to use this system.	2	4	4	3	4	3,40 (0,89)
5. I found the various functions in this system were well integrated.	3	3	3	3	3	3,00 (0,00)
6. I thought there was too much inconsistency in this system.	4	4	4	4	4	4,00 (0,00)
7. I would imagine that most people would learn to use this system very quickly.	3	2	3	3	4	3,00 (0,71)
8. I found the system very cumbersome to use.	2	1	4	2	4	2,60 (1,34)
9. I felt very confident using the system.	3	2	3	3	3	2,80 (0,45)
10. I needed to learn a lot of things before I could get going with this system.	3	4	4	4	4	3,80 (0,45)
Sum converted scores/40	**31**	**29**	**37**	**31**	**36**	**32,80 (3,49)**
Converted score/100	**77,5**	**72,5**	**92,5**	**77,5**	**90**	**82,00 (8,73)**

Appendix G

Patients original and converted scores on the system usability scale during alpha testing.

SD: Standard deviation	Patients									
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	
Participants' original scores										
1. I think that I would like to use this system frequently.	4	3	2	4	2	3	3	4	3	
2. I found the system unnecessarily complex.	2	2	2	1	3	2	3	2	2	
3. I thought the system was easy to use.	2	4	4	5	5	4	4	4	3	
4. I think that I would need the support of a technical person to be able to use this system.	1	1	1	5	3	1	1	1	3	
5. I found the various functions in this system were well integrated.	4	4	3	5	4	5	4	5	3	
6. I thought there was too much inconsistency in this system.	3	2	1	1	2	1	2	2	3	
7. I would imagine that most people would learn to use this system very quickly.	4	3	4	4	4	3	4	3	3	
8. I found the system very cumbersome to use.	2	2	2	1	3	1	2	1	2	
9. I felt very confident using the system.	3	3	3*	3	4	3	3	4	3	
10. I needed to learn a lot of things before I could get going with this system.	1	1	1	1	2	4	1	1	3	
Participants' converted scores										
1. I think that I would like to use this system frequently.	3	2	1	3	1	2	2	3	2	
2. I found the system unnecessarily complex.	3	3	3	4	2	3	2	3	3	
3. I thought the system was easy to use.	1	3	3	4	4	3	3	3	2	
4. I think that I would need the support of a technical person to be able to use this system.	4	4	4	0	2	4	4	4	2	
5. I found the various functions in this system were well integrated.	3	3	2	4	3	4	3	4	2	
6. I thought there was too much inconsistency in this system.	2	3	4	4	3	4	3	3	2	
7. I would imagine that most people would learn to use this system very quickly.	3	2	3	3	3	2	3	2	2	
8. I found the system very cumbersome to use.	3	3	3	4	2	4	3	4	3	
9. I felt very confident using the system.	2	2	2*	2	3	2	2	3	2	
10. I needed to learn a lot of things before I could get going with this system.	4	4	4	4	3	1	4	4	2	**Mean (SD)**
Sum converted scores/40	**28**	**29**	**29**	**32**	**26**	**29**	**29**	**33**	**22**	**30,91 (3,86)**
Converted score/100	**70**	**72,5**	**72,5**	**80**	**65**	**72,5**	**72,5**	**82,5**	**55**	**71,39 (8,01)**

PROFESSIONAL CAREER

Background

2016 – 2020	**KU Leuven - ISMS - MindBytes, Belgium** PhD Researcher Baekeland mandate holder, awarded by Flanders Innovation and Entrepreneurship (VLAIO)
2014 – 2016	**KU Leuven, Belgium** Master of Pharmaceutical Care Master thesis: Assessing the public's knowledge and opinion on the use of benefit-risk assessments for medicinal products
2011 – 2014	**KU Leuven, Belgium** Bachelor of Pharmaceutical Sciences

Publications in international peer-reviewed journals

Ver Donck N., Vander Stichele G., Huys I. Improving patient preference elicitation by applying concepts from the consumer research field: Narrative literature review. Interactive Journal of Medical Research (2020)

Manuscripts in preparation

Ver Donck N., Reymen M., Neven P., Buffel C.*, Huys I.* Assessing patients' and physicians' unmet need and preferences for the development of a breast cancer decision aid. (chapter 2)

Ver Donck N., Verschueren S., Buffel C., Vander Stichele G.*, Huys I.* Development of a web-based patient decision aid for patients with hormone-sensitive breast cancer eligible for switching or extending adjuvant endocrine treatment. (chapter 3)

Ver Donck N., Huys I. Alpha testing of a patient decision aid for patients deciding on adjuvant endocrine treatment during breast cancer aftercare: a mixed methods approach. (chapter 4)

Ver Donck N., Van Cauwenberge J., Neven P., Huys I. Beta testing of a patient decision aid for patients deciding on switching adjuvant endocrine treatment during breast cancer follow up: a pilot study. (chapter 5)

Verschueren S., **Ver Donck N.**, Pinto C., Kihlbom U., Buffel C., Huys I., Vander Stichele G. Optimal educational instrument features to support patient decision-making: Review of regulatory and health technology assessment requirements and development of an interactive tool to support researchers and developers (EDU-GRID)

Scientific presentations & published abstracts

Ver Donck N., Vandersmissen I., Huys I., Vander Stichele G. Aligning drug development with future patient-specific HTA requirements. Knowledge for Growth 2017, Ghent (poster presentation)

Ver Donck N., Vander Stichele G., Huys I. Learnings from consumer research for patient preference research. ISPOR 2018, Glasgow (poster presentation)

ACKNOWLEDGEMENT, PERSONAL CONTRIBUTION AND CONFLICT OF INTEREST STATEMENTS

SCIENTIFIC ACKNOWLEDGEMENTS

Chapter 1-5

This research project was funded by VLAIO, Flanders Innovation and Entrepreneurship, under the form of a Baekeland mandate for doctoral research. The project was further supported by ISMS, Mindbytes and the University of Leuven.

Chapter 2

The authors wish to thank Sarah Verschueren for proofreading the manuscript and Silke De Roover and Lore Goethals for transcribing the interviews.

Chapter 3

The authors wish to thank all the patients and clinicians that participated in the focus groups and individual interviews. Furthermore, the authors wish to thank Elske Van Den Akker-Van Marle for her scientific expertise regarding the development of the ACA exercise and professor Patrick Neven and Melissa Reymen for their valuable input throughout this study.

Chapter 4

The authors wish to thank all the patients and HCPs that have participated in this study and Sarah Verschueren for proofreading the manuscript.

Chapter 5

The authors wish to thank all patients and health care professionals that participated in this pilot study. Furthermore, the authors wish to thank Rudi Ver Donck for the development and maintenance of the study website and Martial Luyts for his input regarding statistical analyses.

Chapter 1

NVD determined the search strategy that was subsequently approved by all authors. Title-abstract screening, full text screening and data extraction was performed by NVD. Data extraction was reviewed by GVS and IH. The first draft of the manuscript was prepared by NVD and subsequently reviewed by IH and GVS. All authors approved the final manuscript.

Chapter 2

NVD designed the study, conducted the interviews, performed the qualitative analysis, and drafted the manuscript. MR, CB and PN provided feedback on the study design and revised the manuscript. IH designed the study, revised the analysis, and revised the manuscript. All authors approved the final manuscript.

Chapter 3

NVD, GVS and IH designed the study. SV and CB provided feedback on the study design. NVD performed the literature review, conducted the qualitative research and performed the analyses, which were all reviewed by IH. The first version of the manuscript was drafted by NVD. The manuscript was afterwards revised by all authors, who approved the final manuscript.

Chapter 4

NVD and IH designed the study. NVD conducted and transcribed all the interviews, and performed both qualitative and quantitative analyses. NVD drafted the first version of the manuscript, IH refined the manuscript. Both authors approved the final manuscript.

Chapter 5

NVD and IH designed the pilot study. NVD designed the study website and drafted the study information and communication materials, which were subsequently revised by all the authors. Patient recruitment was performed by JVC. After recruitment, all email communications were performed by NVD. The analysis was conducted by NVD and revised by IH. NVD produced the first draft of the paper, which was subsequently revised and finalized with all authors.

CONFLICT OF INTEREST STATEMENT

This research was funded by VLAIO, Flanders Innovation and Entrepreneurship, under the form of a Baekeland mandate for doctoral research. The project was further supported by the companies ISMS and MindBytes, and the University of Leuven.

The research from chapters 3, 4 and 5 was further funded by Sawtooth Software, who awarded NVD with an academic grant to perform the studies. For the development of the value clarification method in the third module of the patient decision aid (an adaptive conjoint analysis exercise), Lighthouse Studio by Sawtooth Software was used. For the execution of the pilot trial, Sawtooth Software online hosting services were used.

NVD was employed by ISMS, a pharmaceutical consultancy firm, during the four years of her PhD research. NVD has no other conflicts of interest to report. Sarah Verschueren, the industrial promotor of this PhD project, was employed by MindBytes during the course of this project. Isabelle Huys, the scientific promotor, has no conflict of interest to report. She advised and supervised on all major research decisions.