Shared Guideline Development Experiences in Fertility Care

Elvira den Breejen

Shared Guideline Development

Experiences in Fertility Care

Elvira Martine Elise den Breejen

The research described in this thesis was partly supported by the Netherlands Organization for Health Research and Development (ZonMW) with grant no.150020015 and 150200151, The Hague.

All studies were conducted at the department of Obstetrics and Gynaecology at the Radboud university medical centre, Nijmegen.

For reasons of consistency, terminology may be changed throughout this thesis when compared to the original publications.

Publication of this thesis was generously supported by:

- Klompalberts Holding BV, Amsterdam
- Kennisinstituut van Medisch Specialisten, Utrecht
- Department of Obstetrics and Gynaecology, Radboud university medical centre, Nijmegen

Cover Design: Kees Boer, kees4arts.nl Lay-out: Ferdinand van Nispen tot Pannerden, *my*-thesis.nl Printed by: GVO Drukkers & Vormgevers

PhD Thesis, Radboud University Medical Center Nijmegen, the Netherlands ISBN: 978-94-6332-157-0

© E.M.E. den Breejen, Bussum, 2017

Shared Guideline Development

Experiences in Fertility Care

Proefschrift

ter verkrijging van de graad van doctor aan de Radboud Universiteit Nijmegen op gezag van de rector magnificus prof. dr. J.H.J.M. van Krieken, volgens besluit van het college van decanen in het openbaar te verdedigen op maandag 10 april 2017 om 12.30 uur precies

> door Elvira Martine Elise den Breejen geboren op 15 juni 1980 te Delft

Promotor	Prof. dr. J.A.M. Kremer	
Copromotoren	Dr. R.P.M.G. Hermens	
	Dr. W.L.D.M. Nelen	
Manuscriptcommissie	Prof. dr. N.M.A. Blijlevens (voorzitter)	
	Prof. dr. J.W.A. Smit	
	Prof. dr. J.S.E. Laven (Erasmus MC)	
Paranimfen	C.H. Heijmans	
	D.A. Klompalberts	

"The patient is the centre of the medical universe around which all our work revolves and towards which all our efforts tend" (William Murphy 1892-1987).

Contents

Chapter 1	General introduction.	9
Chapter 2	Added value of involving patients in the first step of multidisciplinary guideline development: a qualitative interview study among infertile patients. <i>Int J Qual Health Care</i> 2016; 28: 299-305.	23
Chapter 3	A patient-centred network approach to multidisciplinary guideline development: a process evaluation. <i>Implementation Science</i> 2014; 9: 68.	43
Chapter 4	Feasibility of a wiki as a participatory tool for patients in clinical guideline development. <i>J Med Internet Res</i> 2012; 14: e138.	67
Chapter 5	Patient partnership in guideline development: a mixed- method evaluation of an online participatory tool. <i>Submitted</i>	97
Chapter 6	Development of guideline-based indicators for patient- centredness in fertility care: what patients add. <i>Human Reproduction</i> 2013; 28: 987-996.	117
Chapter 7	General discussion	141
Chapter 8	Summary	163
	Samenvatting	171
	Dankwoord	181
	Curriculum vitae	187
	PhD theses Human Reproduction RIHS	188



Chapter 1

General introduction

General introduction

Healthcare is fragmented and does not pay enough attention to patients' needs and values. As is true of other diseases that require complex multidisciplinary care, reproductive care is generally offered by various types of independently organized professionals (e.g. general practitioners, gynaecologists, and urologists). Furthermore, the care provided is usually based on evidence or professional consensus irrespective of patients' needs and values. Well-developed clinical practice guidelines (CPGs) could be valuable tools to close the gap between this fragmented continuum of evidence-based reproductive healthcare and infertile couples' need to be in charge of their own care pathway.

However, individual professionals are traditionally the ones who define and describe optimal patient care in CPGs, as well as develop performance measurements for monitoring the quality of care [1, 2]. A reliable contribution of other stakeholders – especially infertile patients – is mostly lacking. Furthermore, guideline development methodologies mainly focus on the disease instead of on patients' clinical pathways [3]. Hence, William Murphy's statement (see the cover to this thesis) does not apply to guideline development in fertility care at all: infertile patients are not in the centre! Therefore, this thesis focuses on shifting the role of Dutch infertile patients in guideline development from the periphery towards the centre and introduces "shared guideline development" in fertility care.

This introductory chapter will start with a description of the actual prevalence of infertility and infertile patients' clinical pathways according to the treatment options that are currently available in the Netherlands. Next, the importance of patient-centredness in fertility care will be addressed. Third, the process of guideline and quality indicator development will be described and the potential role of patients in these development processes will be addressed. Fourth, an overview of guidelines and performance measurements that are currently available for Dutch fertility care will be provided and the role that patients have played in the development process will be addressed. Lastly, this introduction will end with the research questions that led to the studies performed within this thesis, as well as with a brief outline of the thesis.

Introduction

Fertility care

Fertility care concerns the infertile couple failing to conceive after at least one year of regular unprotected sexual intercourse [4]. The prevalence of infertility is estimated to range from 4–30% and affects approximately 80 million couples worldwide [5, 6]. In the Netherlands, the number of new cases of infertility in general practice is estimated at 9 per 1000 couples per year, affecting 1 out of 7 couples [5]. Dutch fertility care has been publically arranged on three levels. Primary care is provided by general practitioners and may comprise a part of an initial fertility assessment. Subsequently, a general practitioner (GP) can refer couples to a gynaecologist in a general (secondary care) or a university (tertiary care) hospital. The gynaecologist can complete this initial fertility assessment, determine a cause of infertility and define a suitable treatment plan. The initial fertility assessment generally comprises four parts: assessing ovulation, screening for Chlamydia Trachomatis, performing a semen analysis, and assessing tubal patency. Main causes of infertility in couples are: low sperm count or quality (30%), ovulatory disorders (27%), tubal damage (14%), and in smaller proportions endometriosis and decreased cervical mucus hostility [7-10]. The presence of disorders in both the female and male partner has been reported to occur in about 39% of cases [11]. However, in 8-28% of the couples, a cause of infertility cannot be identified [12]. If a severe male factor is diagnosed, couples can be referred to a urologist.

Depending on the female's age and the determined cause of infertility, couples can be treated with surgery, such as tubal reconstruction or various types of Medically Assisted Reproduction (MAR)-Techniques: Ovulation Induction (OI), Intra Uterine Insemination (IUI), In Vitro Fertilisation (IVF), and Intra Cytoplasmic Sperm Injection (ICSI), occasionally with surgically retrieved sperm [4]. Within assessments and preparations for MAR-Techniques, such as IVF, clinical chemists and embryologists are also involved. Since infertility has a high emotional and psychological impact, which also interferes with work, psychologists and occupational physicians are regularly involved in the care pathway. Dutch fertility care is organized around 13 licensed hospitals for IVF and ICSI, including: eight university hospitals, four general hospitals and one private clinic. OI and IUI are performed in all types of Dutch hospitals. OI, IUI cycles as well as the first three IVF or ICSI treatment cycles are reimbursed as part of the basic healthcare package, according to the Health Insurance Act. In the Netherlands, approximately 1 out of 38 children is born after IVF or ICSI treatment (www.nvog.nl).

11

Patient-centredness

Besides safe, effective, timely, efficient, and equal access to health care, patientcentredness represents one of the six key-dimensions of high-quality care [13]. Among the variously used definitions for patient-centredness, the Institute of Medicine (IOM) offers a well-accepted one: 'providing care that is respectful of and responsive to individual patient preferences, needs and values and ensuring that patients' values guide all clinical decisions' [13]. Patient-centredness is a multidimensional and contested concept. According to the framework for patient-centred care created by the Picker Institute, patient-centred fertility care can be divided into 10 organisational and non-organisational dimensions of patient-centredness [14, 15]. Organisational dimensions of patient-centred fertility care include: coordination and integration of care; physical comfort; transition and continuity of care; access to care; and staff competence and technical skills. Non-organisational dimensions of patient-centredness include: respect for patients' values, preferences, and needs; information, communication, and education; emotional support; partner involvement; and fertility clinic staff attitudes [14]. A number of published articles have stressed the importance of patient-centredness in fertility care. This emphasis is not surprising since infertile patients could especially benefit from patient-centred care for several reasons. Firstly, suffering from infertility is stigmatized and fertility treatments have considerable psychological impact, both of which affect quality of life. Moreover, the threat of staying childless, which unfortunately overcomes 30% of infertile couples, may mimic reactions seen in serious illness or loss of a relative [16-18]. Secondly, recent reports have confirmed that improvements in several dimensions of patient-centredness could play a major role preventing couples from deciding to drop out from infertility treatments [14, 15, 19-24]. Finally, patient-centred fertility care leads to increased patient satisfaction [25]. Thus, highly patient-centred fertility care enhances major benefits for both infertile patients and their caring professionals.

Patient-centred fertility care is increasingly encouraged by the use of innovative tools involving the Internet, which can: promote communication between doctors and infertile couples; enhance information provision, education, and emotional support; and empower infertile couples in their care process [26]. The use of Internet tools to promote patient-centredness seems especially effective for the clinical area of fertility care, as many patients represent a relatively young patient

group that heavily uses the Internet, which can provide a considerable degree of anonymity in their individual search for information and support [26].

Clinical practise guidelines

A highly valuable tool for improving the quality of fertility care could be created by clinical practice guidelines (CPGs). CPGs are defined as "statements that include recommendations intended to optimize patient care, that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options" [27]. The development process of CPGs enhances a stepwise process, which starts firstly with clarifying the target audience and selecting or prioritizing the topic of the guideline [28]. Secondly, a deliberate scoping procedure should be performed and preferably guided by a bottleneck analysis, which aims to define the objectives and boundary conditions of the guideline as well as to identify potential implementation barriers [28, 29]. Preferably a multidisciplinary CPG development group should be constituted and include all relevant stakeholders [28, 30]. Thirdly, according to the scope of the guideline, key questions are formulated, prioritized, and answered by systematically reviewing and assessing the relevant literature [30]. Fourthly, recommendations are formulated, which should include considerations of applicability in practice, patients' preferences, and cost-effectiveness [30]. Fifthly, an implementation strategy should be conceptualized and written down in the guideline. This strategy could include the development of derivative products, such as a patient version of the CPG, and address barriers for implementation in a separate section of the guideline. The sixth step includes an internal and external review procedure followed by the authorization of the final guideline. Lastly, the guideline should be disseminated and efforts to implement the guideline should be made, preferably followed by an evaluation that includes monitoring the quality of care by applying guideline-based quality indicators [31].

Application of the guideline and the development of quality indicators

To gain insight into the actual application of the guidelines and as one of the efforts to implement the guideline, the development of guideline-based quality indicators could be seen as a related product of the guideline development process. A quality indicator can be defined as: "a measurable element of practice performance for which there is evidence or consensus that can be used to assess the quality of care provided, and hence change the quality of care provided" [32]. In general, three types of quality indicators can be distinguished, which refer

to the process, outcome, and structure of care [33]. Quality indicators should preferably be developed through a systematic approach that ensures transparency [34]. Guideline-based quality indicators are generally based on selected recommendations extracted from guidelines and are comprised of a numerator (the case in which a recommendation is followed) and a denominator (all cases in which the recommendation is applicable). This step is mostly followed by a panel method to select final quality indicators and a practice test to evaluate its validity, reliability, and feasibility [1]. These last two steps are very important since judgements of quality of care based on measurements of quality indicators could have far-reaching consequences, such as when pay-to-performance models are in use.

Approaches to guideline development

In the presence of worldwide development of institutional manuals for developing CPGs, the processes described in these manuals are inconsistent and the assessed quality of the delivered guidelines is diverse [36].

Generally, two types of guidelines are currently developed: the monodisciplinary and the multidisciplinary CPG. The monodisciplinary CPG is developed and owned by an individual professional society. In addition to creating a sense of institutional ownership over the developed guideline, this approach has more disadvantages than advantages. Firstly, monodisciplinary guidelines are assessed of lower quality than multidisciplinary guidelines [38]. Furthermore, inconsistencies in recommendations for the same clinical topic in different societies' guidelines may threaten the quality of care. The more recently introduced and recommended multidisciplinary CPG is developed by a collaboration of different stakeholders. This approach intends to improve the quality of CPGs and enhance its implementation, enabling broader support and adjustment between professionals.

Although the development of CPGs has progressed enormously worldwide, unwarranted practice variation in daily care remains a problem. There are multiple reasons for these practice variations, including those on the personal, organisational, and systemic levels. However, by firstly concentrating on the approach used in the guideline development process and its consequences, several deficiencies can be identified. Among these, the lack of guideline ownership felt among the target users and the strong focus on clinical aspects rather than on the organisational and other aspects of patient-centredness of care impede full implementation [3638]. For resolving these deficiencies in the guideline development process, a new approach to multidisciplinary guideline development is necessary. Furthermore, the position of patients herein is unexplored as well.

Patients and guideline development

Patient involvement in guideline development is assumed to result in higher quality guidelines in terms of applicability, acceptability, usefulness, and enhancement of implementation [27, 38-45]. Patient involvement forms one of the key criteria of the Appraisal of Guidelines Research and Evaluation (AGREE) instrument used to assess the methodological quality of guidelines. Additionally, patient involvement is also widely advocated by institutional organisations as the National Institute for Health and Care Excellence (NICE), the National Health Service (NHS), the World Health Organization (WHO), and the Institute Of Medicine (IOM) [38]. Thus, guideline developers are increasingly urged to involve patients in the different steps of the guideline development process. Unsurprisingly, to increase the quality of care, which forms the major goal of guidelines, patients should play a considerable role. Professionals are the experts in the disease and treatment, but patients are the experts in having the disease and undergoing treatment. Nevertheless, patient involvement in guideline development is still challenging and only 25–50% of CPG developers regularly involve patients [43].

Therefore, patient involvement is not the common practice in current guideline development, which can be attributed to a number of practical difficulties. Firstly, various methods for patient involvement in CPG development could be used and practical guidance on how and when to apply these methods is lacking [40, 45-51]. Secondly, all methods are restricted to include a selected number of patients or patients' representatives and do not involve a large population of patients. Thirdly, transparently integrating patients' preferences into CPG recommendations is difficult and often unclear [2]. Fourthly, organisational (e.g. recruitment of participants), financial (e.g. costs of patients' education or for conducting focus groups), and socio-political barriers (e.g. CPG developers' resistance to including patients in the CPG group) exist [49]. Lastly, thus far, studies on the added value of patient involvement in the early stages of guideline development, as well as the effectiveness and impact of patient involvement, are limited [51]. This situation urges the development of new approaches to explore the possibilities of involving patients in the various steps of guideline development.

Patients and guideline-based quality indicator development

High-quality fertility care comprises more than just the effectiveness of care. Regardless of medical-technical quality, patient-centredness also determines the quality of fertility care [13]. The patient-centredness of care comprises various aspects, such as the coordination and integration of care and the provision of emotional support [52,53]. Furthermore, professionals in the field have been shown to be unable to adequately evaluate their performance regarding patientcentredness [54]. This inability hampers direct quality improvement regarding patient-centredness and illustrates the need for measurable elements of practice performance regarding this quality-of-care dimension. Since clinical practice guidelines recommend optimal patient care and are based on the best available evidence and consensus, guideline-based indicators are highly suitable for direct monitoring and improvement of the quality of care [13, 55, 56].

Thus far, several studies have reported on the development of guideline-based indicators within the field of fertility care [57-59]. However, in these studies, a particular focus on the patient-centredness of fertility care has been lacking. Furthermore, the involvement of patients in the guideline and indicator-development process is still not common practice [2]. Only within the field of cancer care has the development of guideline-based indicators for patient-centredness been reported [60,61]. Although patients played a minor role in these indicator-development panels, the results suggest that including patients leads to the identification of aspects of patient-centredness that may not have been considered previously. However, in these studies, the exact difference in choice of indicators between professionals and patients regarding patient-centredness remains unexplored.

Current guidelines and related indicators in fertility care

In the past, both professional societies in the fields of reproductive medicine and governmental agencies have put major efforts into the development of CPGs for infertility. These institutions include the American Society for Reproductive Medicine (ASRM), the European Society of Human Reproduction and Embryology (ESHRE), the National Institute of Clinical Excellence (NICE), and the Nordic Federation of societies of Obstetrics and Gynaecology (NFOG). By the time the studies in this thesis were conducted, the Dutch society of Obstetrics (NVOG) in the Netherlands had an extensive guideline program, including 17

Introduction

mostly monodisciplinary disease-centred CPGs that mainly refer to treatments for infertility, the National Embryo Act, and various protocols on the performance of various fertility treatments. Other allied Dutch societies that issued fertility guidelines concern the Dutch society of Clinical Embryologists (KLEM) (i.e. guideline on semen analysis), the Dutch College of General Practitioners (NHG) (i.e. standard on infertility), and the Dutch Society of Urologists (NVU) (i.e. guideline on male infertility). All Dutch guidelines on infertility had a monodisciplinary character and were mostly assessed to be of low quality by the AGREE instrument. This instrument is a 23 item-based validated instrument that assesses the methodological quality of CPGs on six domains: scope and purpose, stakeholder involvement, rigour of development, clarity and presentation, applicability, and editorial independence [39]. Remarkably, patient involvement in all these guidelines was lacking. Furthermore, guideline-based quality indicators related to any of these guidelines were absent.

Outline of this thesis

The aim of this thesis is to investigate ways to shift the role of Dutch infertile patients in developing guidelines from the outside to the centre through exploring methods for actively involving them in three different phases (e.g. scoping phase, development phase, implementation phase) of the Clinical Practice Guideline development process. Hence, we formulated the following research questions:

- 1) What value do patients add to the scope of a Dutch multidisciplinary guideline on infertility when comparing perceived key clinical issues between professionals and patients?
- 2) To what extent does a patient-centred network approach to multidisciplinary guideline development in infertility provide a feasible format regarding the actual performance of a set of guidelines, its time investments, and experiences with the approach?
- 3) To what extent does a participatory tool for Dutch infertile patients in guideline development provide a feasible tool to enhance shared guideline development, regarding its use, usability, benefits for the guideline, users' experiences with the tool, and implementability in other clinical areas?
- 4) What value do patients add to the development of guideline-based quality indicators for patient-centredness?

17

Chapter 1

In **Chapter 1** of this thesis, we describe the context of this thesis in general. In **Chapter 2**, we explore patients' value added to the scope of a Dutch multidisciplinary guideline on infertility by comparing perceived key clinical issues (clinical issues that need improvement) between professionals and patients. In **Chapter 3**, we evaluate a novel patient-centred network approach to guideline development. In **Chapter 4**, we investigate the feasibility of a wiki-based participatory tool for infertile patients in clinical guideline development. In **Chapter 5**, we evaluate the usability for both patients and guideline development. In **Chapter 6**, we explore patients' value added to the development of guideline-based quality indicators for patient-centredness by comparing suggested indicators between infertile patients and professionals. **Chapter 7** provides an overview of the main findings and their interpretation, a discussion on methodological issues, and the possible implications for clinical practice and future research.

References

- 1. Kötter T, Blozik E, Scherer M. Methods for the guideline-based development of quality indicators--a systematic review. *Implementation Science* 2012;7:21.
- Krahn M, Naglie G. The next step in guideline development: incorporating patient preferences. J Am Med Assoc 2008;300:436-8.
- 3. Gerteis, M, Edgman-Levitan S, Daley J et al. Through the Patients' Eyes: Understanding and Promoting Patient-Centered Care. San Fransisco, CA: Jossey-Bass, 1993.
- Zegers-Hochschild F, Adamson GD, de Mouzon J *et al.* The International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) Revised Glossary on ART Terminology. *Hum Reprod* 2009;24:2683-7.
- 5. Boivin J, Bunting L, Collins JA *et al*. International estimates of infertility prevalence and treatmentseeking: potential need and demand for infertility medical care. *Hum Reprod* 2007;**22**:1506–1512.
- Nachtigall RD, Castrillo M, Shah N *et al.* The challenge of providing infertility services to a low-income immigrant Latino population. *Fertil Steril* 2009;92:116-23.
- Hull MG, Glazener CM, Kelly NJ *et al.* Population study of causes, treatment, and outcome of infertility. Br Med J (Clin Res Ed) 1985;291:1693-7.
- 8. Tummon IS, Asher LJ, Martin JS *et al.* Randomized controlled trial of superovulation and insemination for infertility associated with minimal or mild endometriosis. *Fertil Steril* 1997;**68**:8-12.
- 9. Steures, P, van der Steeg JW, Hompes, PG *et al.* Effectiveness of intrauterine insemination in subfertile couples with an isolated cervical factor: a randomized clinical trial. *Fertil Steril* 2007;**88**:1692-6.
- 10. Bensdorp AJ, Cohlen BJ, Heineman MJ *et al*. Intra-uterine insemination for male subfertility. *Cochrane Database Syst Rev* 2007;CD000360.
- 11. National Institute for Health and Clinical Excellence (NICE). *Clinical Guideline on Fertility: assessment and treatment of people with fertility problems*. London, 2004.
- 12. Veltman-Verhulst SM, Hughes E, Ayeleke RO *et al.* Intra-uterine insemination for unexplained subfertility. *Cochrane Database Syst Rev* 2016;CD001838.
- 13. Institute of Medicine. *Crossing the quality Chasm. A new health system for the 21st century.* National Academy Press. Washington, DC: 2001.
- 14. Dancet EA, Nelen WL, Sermeus W *et al.* The patients' perspective on fertility care: a systematic review. *Hum Reprod Update* 2010;**16**:467-87.
- 15. Dancet EA, Van EI, Rober P *et al.* Patient-centred infertility care: a qualitative study to listen to the patient's voice. *HumReprod* 2011;**26**:827-33.
- 16. Verhaak CM, Smeenk JMJ, Evers AWM *et al*. Women's emotional adjustment to IVF: a systematic review of 25 years of research. *Hum Reprod Update* 2007;**13**:27-36.
- 17. Hammarberg K, Astbury J, Baker H. Women's experience of IVF: a follow-up study. *Hum Reprod* 2001;**16:**374-83.
- Kjaer, TK, Jensen A, Dalton SO *et al.* Suicide in Danish women evaluated for fertility problems. *Hum Reprod* 2011;26:2401-7.
- 19. Brandes M, Van Der Steen JOM, Bokdam SB *et al.* When and why do subfertile couples discontinue their fertility care? A longitudinal cohort study in a secondary care subfertility population. *Hum Reprod* 2009;**24**:3127-35.
- 20. Van den Broeck U, Holvoet L, Enzlin P *et al.* Reasons for dropout in infertility treatment. *Gynecol Obstet Invest* 2009;**68**:58-64.
- Schmidt L, Holstein BE, Boivin, J et al. High ratings of satisfaction with fertility treatment are common: findings from the Copenhagen Multi-centre Psychosocial Infertility (COMPI) Research Programme. *Hum Reprod* 2003;18:2638-46.
- 22. van Empel IW, Aarts JW, Cohlen BJ *et al.* Measuring patient-centredness, the neglected outcome in fertility care: a random multicentre validation study. *Hum Reprod* 2010;**25**:2516-26.
- van Empel IW, Nelen WL, Tepe ET *et al.* Weaknesses, strengths and needs in fertility care according to patients. *Hum Reprod* 2010,25:142-9.

- 24. Gameiro S, Boivin J, Peronace LS *et al.* Why do patients discontinue fertility treatment? A systematic review of reasons and predictors of discontinuation in fertility treatment. *Hum Reprod Update* 2012;**18**:652-69.
- Souter, VL, Penney G, Hopton JL et al. Patient satisfaction with the management of infertility. Hum Reprod 1998;13:1831-6.
- Aarts, JW, Van den Haak P, Nelen WLDM *et al.* Patient-focused internet interventions in reproductive medicine: a scoping review. *Hum Reprod Update* 2012;18:211-27.
- 27. Institute Of Medicine (IOM). *Clinical Practice Guidelines we can Trust*. Washington, DC: National Academy Press, 2011.
- Eccles, MP, Grimshaw JM, Shekelle P *et al.* Developing clinical practice guidelines: target audiences, identifying topics for guidelines, guideline group composition and functioning and conflicts of interest. *Implement Sci* 2012;7:60.
- 29. Shekelle P, Woolf S, Grimshaw JM *et al.* Developing clinical practice guidelines: reviewing, reporting, and publishing guidelines; updating guidelines; and the emerging issues of enhancing guideline implementability and accounting for comorbid conditions in guideline development. *Implement Sci* 2012;7:62.
- 30. Woolf S, Schünemann HJ, Eccles MP *et al.* Developing clinical practice guidelines: types of evidence and outcomes; values and economics, synthesis, grading, and presentation and deriving recommendations. *Implement Sci* 2012;7:61.
- 31. Grol R, Grimshaw J. From best evidence to best practice: effective implementation of change in patients' care. *Lancet* 2003;**362**:1225-30.
- 32. Lawrence M, Olesen. Indicators of quality in healthcare. Eur J Gen Pract 1997;3:103-8.
- 33. McGlynn EA, Asch SM: Developing a clinical performance measure. Am J Prev Med 1998;14:14-21.
- 34. Campbell SM, Braspenning J, Hutchinson A. Research methods used in developing and applying quality indicators in primary care. *Qual Saf Health Care* 2002;**11**:358-364.
- 35. Kotter T, Blozik E, Scherer M. Methods for the guideline-based development of quality indicators--a systematic review. *Implement Sci* 2012;7:21.
- 36. Grol, R. Has guideline development gone astray? Yes BMJ 2010;340:306.
- 37. Alonso-Coello P, Irfan A, Solà I, *et al.* The quality of clinical practice guidelines over the last two decades: a systematic review of guideline appraisal studies. *Qual Saf Health Care* 2010;**19**:e58.
- Grilli, R, Magrini N, Penna A, et al. Practice guidelines developed by specialty societies: the need for a critical appraisal. Lancet 2000;355:103-6.
- 39. Appraisal of Guidelines Research and Evaluation (AGREE) Collaboration. *The AGREE instrument*, 2001; Available from: http://www.agreecollaboration.org.
- 40. Bastian, H. Raising the standard: practice guidelines and consumer participation. *Int J Qual Health Care* 1996;**8**:485-90.
- Burgers JS, Fervers B, Haugh M *et al.* International assessment of the quality of clinical practice guidelines in oncology using the Appraisal of Guidelines and Research and Evaluation Instrument. J Clin Oncol 2004;22:2000-7.
- 42. Crawford MJ, Rutter D, Manley C *et al.* Systematic review of involving patients in the planning and development of health care. *BMJ* 2002;**325**:1263.
- 43. Gagliardi AR, Brouwers MC, Palda VA *et al.* How can we improve guideline use? A conceptual framework of implementability. *Implement Sci* 2011;**6**:26.
- 44. Nilsen ES, Myrhaug HT, Johansen M *et al.* Methods of consumer involvement in developing healthcare policy and research, clinical practice guidelines and patient information material. *Cochrane Database Syst Rev* 2006;**3**:CD004563.
- 45. van Wersch A, Eccles M. Involvement of consumers in the development of evidence based clinical guidelines: practical experiences from the North of England evidence based guideline development programme. *Qual Health Care* 2001;**10**:10-6.
- 46. Rogers WA. Are guidelines ethical? Some considerations for general practice. Br J Gen Pract 2002;52:663-8.

1

- National Institute of Clinical Excellence (NICE). The guidelines' manual. London: NICE, 2009. URL: www.nice.org.uk Archived by WebCite* at http://www.webcitation.org/65UXx2saM
- Scottish Intercollegiate Guidelines Network (SIGN). SIGN 50: A guidelines' developer handbook. Edinburgh: SIGN, 2008. URL: http://www.sign.ac.uk/pdf/sign50.pdf Archived by WebCite^{*} at http:// www.webcitation.org/65UY1tSVw
- Diaz Del Campo P, Gracia J, Blasco JA et al. A strategy for patient involvement in clinical practice guidelines: methodological approaches. BMJ Qual Saf 2011;20:779-84.
- 50. Legare F, Boivin A, van der Weijden T *et al.* Patient and public involvement in clinical practice guidelines: a knowledge synthesis of existing programs. *Med Decis Making* 2011; **31**:45-74.
- 51. Boivin A, Currie K, Fervers B *et al.* Patient and public involvement in clinical guidelines: international experiences and future perspectives. *Qual Saf Health Care* 2010;**19**:e22.
- 52. Dancet EA, Nelen WL, Sermeus *W et al.* The patients' perspective on fertility care: a systematic review. *Hum Reprod Update* 2010;**16**:467-87.
- 53. Dancet EA, Van Empel IW, Rober P *et al.* Patient-centred infertility care: a qualitative study to listen to the patient's voice. *Hum Reprod* 2011;**26**:827-33.
- 54. Aarts JW, Faber MJ, van Empel IW *et al.* Professionals' perceptions of their patients' experiences with fertility care. *Hum Reprod* 2011;**26**:1119-27.
- 55. Campbell SM, Braspenning J, Hutchinson A *et al.* Research methods used in developing and applying quality indicators in primary care. *BMJ* 2003;**326**:816-819.
- 56. Grol R, Baker R, Moss F. Quality improvement research: understanding the science of change in health care. *Qual Saf Health Care* 2002;**11**:110-1.
- 57. Haagen EC, Nelen WL, Grol RP *et al.* Variation in guideline adherence in intrauterine insemination care. *Reprod Biomed Online* 2010;**20**:533-542.
- 58. Mourad SM, Hermens RP, Nelen WL *et al.* Guideline-based development of quality indicators for subfertility care. *Hum Reprod* 2007;**22**:2665-72.
- 59. van den Boogaard E, Goddijn M, Leschot NJ *et al*. Development of guideline-based quality indicators for recurrent miscarriage. *Reprod Biomed Online* 2010;**20**:267-73.
- 60. Uphoff EP, Wennekes L, Punt CJ *et al.* Development of generic quality indicators for patient-centered cancer care by using a RAND modified Delphi method. *Cancer Nurs* 2012;**35**:29-37.
- 61. Ouwens M, Hermens R, Hulscher M *et al.* Development of indicators for patient-centred cancer care. *Supportive Care Cancer* 2010;**18**:121-30.



Chapter 2

Added value of involving patients in the first step of multidisciplinary guideline development: a qualitative interview study among infertile patients

EME den Breejen, RPMG Hermens, WH Galama, WNP Willemsen, JAM Kremer, WLDM Nelen

Int J Qual Health Care 2016; 28:299-305.

Abstract

Background: Patient involvement in scoping the guideline is emphasized, but published initiatives actively involving patients are generally limited to the writing and reviewing phase.

Objective: To assess patients' added value to the scoping phase of a multidisciplinary guideline on infertility.

Design: Qualitative interview study.

Setting and participants: We conducted interviews among 12 infertile couples and 17 professionals.

Intervention: We listed and compared the couples' and professionals' key clinical issues (=care aspects that need improvement) to be addressed in the guideline according to four domains: current guidelines, professionals, patients and organization of care.

Main outcome measures: Main key clinical issues suggested by more than three quarters of the infertile couples and/or at least two professionals were identified and compared.

Results: Overall, we identified 32 key clinical issues among infertile couples and 23 among professionals. Of the defined main key clinical issues, infertile couples mentioned eight issues that were not mentioned by the professionals. These main key clinical issues mainly concerned patient-centred (e.g. poor information provision and poor alignment of care) aspects of care on the professional and organizational domain. Both groups mentioned two main key clinical issues collectively that were interpreted differently: the lack of emotional support and respect for patients' values.

Conclusions: Including patients from the first phase of the guideline development process leads to valuable additional main key clinical issues for the next step of a multidisciplinary guideline development process and broadens the scope of the guideline, particularly regarding patient-centredness and organizational issues from a patients' perspective.

Key words: infertility, guideline development, patient-centred care, quality of care.

Introduction

Several prominent organizations have emphasized the importance of patient involvement in Clinical Practice Guideline (CPG) development [1-8]. This has been resulted in special programmes and toolkits that aim to embed patient involvement in the guideline development process, such as the NICE's Patient and Public Involvement Programme, the SIGN's patient network, the Dutch participation guide and the G-I-N PUBLIC Toolkit [9-12]. The CPG development process generally comprises several phases, i.e. defining the scope (topic selection) of the guideline, formulating key questions, systematically reviewing relevant literature and appraising its quality, formulating recommendations, writing the draft version, reviewing and finalizing the guideline [2, 13, 14].

Organizations emphasize the involvement of patients in an early phase of CPG development, but published initiatives on this topic generally focus on the writing and reviewing phase of the CPG development process or on written consultation of patient organizations when the scope has been drafted yet [6, 9-12, 15, 16]. By defining a well-constructed scope of the CPG together with a group of patients and different stakeholders, the CPG will focus on care points susceptible for improvement. This could facilitate its implementation and increase its potential benefit. Such a multidisciplinary and patient-centred approach seems especially beneficial to diseases requiring complex healthcare [3, 17-20]. For example, within fertility care, couples having problems to conceive can meet different disciplines, such as general practitioners (GPs), gynaecologists, urologists, clinical embryologists or clinical psychologists [21, 22]. Patients who are involved in such complex care paths are 'the experts of their own healthcare'; they relate it to their personal circumstances (e.g. work, comorbidity) and their needs and values, while surveying their whole care process beyond all their care providers from a different point of view and with different expectations of care [23]. Consequently, they might identify different care aspects compared with professionals that need improvement and need to be addressed in guidelines (i.e. key clinical issues) [24-30]. Therefore, this study aims to assess patients' added value to the scoping phase of a multidisciplinary guideline on infertility. For this purpose, we compared the identified key clinical issues to be addressed in this guideline between infertile patients and professionals in fertility care.

Materials and Methods

Setting

Infertility is defined as the failure to conceive after at least one year of regular unprotected intercourse [31,32]. Overall, Dutch fertility care has been publically arranged on three levels. Primary care is provided by the GP and comprises a part of an initial fertility assessment. Subsequently, the GP can refer couples to a gynaecologist in a general (secondary care) or a university (tertiary care) hospital. He/she can complete this initial fertility assessment, determine a cause of infertility and define a suitable treatment plan. If a severe male factor is diagnosed, couples can be referred to an urologist.

Study design

For assessing patients' added value to the scope of a multidisciplinary guideline on infertility, we conducted explorative semi-structured interviews among infertile couples as well as focus group interviews with professionals involved in fertility care, using a similar interview guide, developed by three authors (E.M.E.D.B., W.L.D.M.N., R.P.M.G.H.). Consensus on the topics of the final interview guide was reached through discussion.

First, eight different phases of fertility care, based on known patients' clinical care pathways, were included in a topic list: (I) initial fertility assessment by a GP and/ or (II) gynaecologist, (III) treatment with OI, or (IV) IUI, or (V) IVF or (VI) ICSI by a gynaecologist, (VII) TEsticular Sperm Extraction (TESE) by a urologist and (VIII) after care. Additionally, transitions between different phases of fertility care, such as referral from GP to gynaecologist were identified and added as topics. Furthermore, all inconsistencies within recommendations of the 11 actual Dutch monodisciplinary guidelines on infertility of the Dutch college of General Practitioners' (GP), the Dutch Society of Obstetrics and Gynaecology's (NVOG), the Dutch Society of Urologists and the Dutch Society of clinical embryologists and clinical chemists were identified and added as topics (www.nvog.nl; www.nhg. org; www.nvu.nl; www.embryologen.nl).

Interviews among patients (infertile couples)

Participating patients included infertile couples selected from all eight different phases of fertility care. These couples were consecutively invited to participate by means of an information letter, conferred while they visited a gynaecological resident working in a fertility clinic in two regions of the Netherlands (Nijmegen and Amsterdam). Potential participants, Dutch speaking infertile couples who reacted positively to the information letter, were contacted by telephone. A total of 12 couples were contacted (E.M.E.D.B.) and all of them agreed to participate in an interview. To increase the actual participation-rate and to put minimal pressure on the participants (travel requisites, possible emotional burden of confrontation with other patients), we conducted individual interviews of ~60 min at a location preferred by the couples. The structure of the individual interviews was as follows: after an explanation of the aim of the interview, namely to list key clinical issues to be addressed in a multidisciplinary guideline for fertility care and asking for participants' characteristics, we asked them for their key clinical issues perceived across their own fertility care pathway. Summaries were sent to all participants for additions and verification. The inclusion of infertile couples was discontinued when saturation of data was achieved (no new emerging themes).

Focus group interviews among professionals

We performed two focus group interviews with professionals. The first focus group consisted of a broad collaboration of mandated experts from different disciplines within the field of fertility care that assembled the guideline development group, including a gynaecologist, urologist, GP, clinical embryologist, clinical psychologist, clinical chemist, an occupational physician and two board members of 'Freya', the Dutch infertility patients' association. The focus group interview was performed during their first guideline development meeting. To broaden the view on key clinical issues in fertility care, a second focus group interview was performed including eight main professional target users of the guideline: four GPs, three gynaecologists and one urologist. All these target users were proposed by their professional societies. An independent gynaecologist not involved in the development of the guideline moderated both interviews. After an explanation of the aim of the interview, the focus group comprised both questions about participants' characteristics such as age and the level of education and questions about their experienced key clinical issues across patients' care pathway (from patients' visit to a GP to aftercare and the transitions between these care phases). Both interviews lasted ~90 min. Written interview summaries were sent to all participants for additions and consensus.

Data analysis

All interviews including additions were transcribed verbatim and anonymized. Data were managed using Kwalitan (version 5.0, Malden, the Netherlands) [33]. The data were thematically analysed in four iterative steps [34]. Two investigators (E.M.E.D.B. and W.H.G.) independently coded the transcripts, searched for themes, refined themes and defined main themes (key clinical issues) and subthemes according to the four domains derived from the framework of Cabana et al. (i.e. key clinical issues at the level of actual guidelines and at professional, patient and organizational level) [35]. After each step, the results were compared and any discrepancies were discussed until consensus was achieved. Furthermore, an experienced third researcher (W.L.D.M.N.) checked the codebook, the initial themes, the refined themes and the defined main themes and subthemes and critically looked at possible inconsistencies across the defined main themes and subthemes that were placed into the framework. Inconsistencies were jointly discussed, which resulted in refinement of the themes and replacement of one main theme in the appropriate domain of the framework. To extract the main key clinical issues, the frequency of occurrence of all key clinical issues was determined. Key clinical issues became main key clinical issues when suggested by at least two different professionals in both focus groups or in more than three quarters of the infertile couples.

Results

Participants

We interviewed 12 infertile couples and 17 professionals. Couples' characteristics are presented in Table 1. Infertile couples were selected from all different phases of care. The main characteristics of the participating professionals are summarized in Table 2. In focus group one, two-thirds of participating professionals were male, whereas in focus group two, males and females were in equal proportion.

Characteristic	Participants in-depth interviews $(n = 24)$
Median age ^a (years)	
Female	32 (25-46)
Male	35 (31-43)
Level of education ^b (%) (low/medium/high)	
Female	8/33/58
Male	0/33/67
Last treatment (n)	
GP (initial fertility assessment)	2
Initial fertility assessment by gynaecologist	4
OI	2
IUI	4
IVF	4
ICSI	6
TESE	2
Pregnancy achieved (%)	
Yes	25
No	75

 Table 1: Demographic characteristics of infertile couples

GP, General Practitioner; OI, Ovulation Induction; IUI, Intra Uterine Insemination; IVF, In Vitro Fertilization; ICSI, Intra Cytoplasmic Sperm Injection; TESE, TEsticular Sperm Extraction

^a Median age in years, range between brackets.

^b Low, primary or lower vocational education; medium, secondary or intermediate vocational education; high, higher professional education or university.

Characteristic	Participants focus Group 1 (n = 9)	Participants focus Group 2 (n = 8)
Gender		
Male	6	4
Female	3	4
Discipline		
GP	1	4
Urologist	1	1
Gynaecologist	1	3
Clinical embryologist	1	
Medical psychologist	1	
Chemist	1	
Occupational physician	1	
Members infertility patient association	2	

Table 2: Demographic characteristics of professionals

GP, General Practitioner

Key clinical issues

Overall, 32 key clinical issues among infertile couples (Table 3) and 23 key clinical issues among professionals (Table 4) were identified. The main key clinical issues (suggested by at least two different professionals in both focus groups or in more than three quarters of the infertile couples) are presented separately and per domain (i.e. key clinical issues at the level of actual guidelines (I) and at professional (II), patients (III) and organizational (IV) level). The presented main key clinical issues are accompanied by verbatim quotes taken from the interviews (Table 3).

Infertile couples' key clinical issues:

Domain I: guidelines (Table 3)

Domain II: professionals

Lack of respect and autonomy. All participants mentioned their healthcare professionals' attitude or behaviour as a key clinical issue, for example impersonal, uninterested or not serious.

... *it is all really very impersonal, you feel no more than a number.* Furthermore, the lack of partner involvement (male for GP and gynaecologist, female for urologist) was mentioned.

... everything was concentrated on her, it often felt like I did not matter.

Insufficient information provision. Information provided by professionals was mostly on a medical-technical level and lacked attention for non-medical issues. Treatment alternatives were not proposed and explanations were unclear, resulting in obscure treatment plans.

... our GP could have explained more to us, but she did not. I heard everything from the gynaecologist, I think that is a pity because our GP could have done a part of that.

Lack of emotional support. A lack of emotional support was mentioned as a key clinical issue for fertility care, delivered by both the GP and the gynaecologist. Although the need for emotional support differs among patients, it was rarely discussed in the consulting room. Furthermore, patients mentioned that the possibility of a referral to a psychologist is not enough: they clearly prefer emotional support to be embedded within daily care.

... at the advanced stage of care you are in, you will have more need for emotional support. Simply being able to talk about it may be enough, but that is lacking.

Domain III: patients

Taboo on infertility. In general, patients experienced difficulties in mentioning their infertility problem. They postponed visiting their GP and it proved difficult to discuss it with their employer.

... it is very hard to talk about it to third parties, especially if you depend on them.

Domain IV: organisation

Poor care alignment. The poor alignment of care, especially between the GP and the gynaecologist, was mentioned most often. Furthermore, communication was lacking between primary and secondary care. Regularly, GPs had no notion of the phase of care the couple being treated were in.

I think the referral letter is the only alignment between the gynaecologist and the GP... I do not think my GP knows what we are going through. ... I do not think they're communicating.

Lack of attention to work. Patients experienced problems with work, because appointments were only possible during working hours. Hence, they had to take time off or pay for their absence.

...you need to make arrangements at work, because you have to visit the hospital at very inconvenient moments.

Lack of support after treatment. Currently, there is hardly any support after treatment, particularly for patients who remain childless.

What was the support after treatment like? There was no support.

Standard treatment according to protocols. Patients did not always like to be treated according to protocols. Some couples experienced those as impersonal; others missed the liberty of having a free choice.

... at the second attempt, they came back on it and said that they had to follow a protocol, and I did not have a choice anymore.

Poor physical environment. The lack of separate waiting rooms for pregnant and infertile couples was mentioned the most. Furthermore, lack of privacy and a 'cold appearance' of the hospital were mentioned.

... That is a disadvantage of our hospital: pregnant couples and people like us are sitting next to each other in the waiting room, I found that very hard.

Time pressure. Most patients mentioned time limits during appointments as a key clinical issue.

For the ultrasound only five minutes are available, but I think they should take more time for it. It is like: five minutes, next patient please.

Domain I Characteristics of the guidelines	Domain II Characteristics of the professional	Domain III Characteristics of the patient	Domain IV Characteristics of the organization
Lack of evidence	Poor communication	Uncertain patient	Unclear distribution of tasks
Differing	Lack of respect and autonomy ^{**}	Age-related problems	Poor alignment of care*
protocolo		Desire for action	Lack of attention to work*
	not meeting expectations [*]	Taboo on infertility *	Poor quality of semen
	Lack of emotional support**	(Un)informed	analysis
		Liberty of choice	Poor insurance coverage
	Lack of medical knowledge	Patients with unrealistic	Lack of arrangements concerning work
	Lack of continuity of doctor	Need for contact with other patients Lack of contact with GP	Lack of continuity of care
			Lack of support after treatment
	Unequal policy		
	Problems with examinations		Non-fluent care path
			Standard treatment according to protocol [*]
			Difficulty making appointments
			Poor availability by phone
			Poor physical environment [*]
			Time pressure [*]

Table 3: Key clinical issues according to infertile couples

^{*} Main key clinical issues, suggested by more than three quarters of the infertile couples.

^{**} Collective main key clinical issues, suggested by both patients and professionals.

Key clinical issues among professionals

Domain I: guidelines

Unclear treatment criteria. The description of treatment criteria in actual guidelines is unclear, resulting in different policies in the various hospitals (Table 4). Some gynaecologists treat women until the age of 40 years, others until the age of 43 years, resulting in 'hospital-shopping' of patients.

... age does not mean anything. For example: a 36-year-old woman may have a high FSH and a low AFC.

Unclear treatment policy. Treatment policies are seldom clearly described in actual guidelines, or still under discussion (i.e. lifestyle advices), just as criteria for referral, especially for GPs. Moreover, interpretation of the semen analysis' results, the appropriate number of semen samples needed and best interval time to repeat them is unclear for GPs.

...if the test results of the semen analysis are poor, you have to consider the possibility of repeating the test. ...whether this is after three months, or later, I am not sure.

Lack of evidence. While on some topics research is still in progress, on others the available evidence is unclear.

There is still no consensus about the varicocele: some urologists treat it, others do not.

Domain II: professionals

Lack of respect and autonomy. Professionals mentioned the lack of partner involvement, especially by the GP, as a key clinical issue as well.

It is a classical problem, the male who is only seen as a jar of sperm.

Lack of emotional support. Overall, emotional support, offered by professionals, is lacking. Moreover, timing is unclear and attention to childless couples is limited.

The process of loss is different for every couple, they have to let go of their wishes and dreams... every professional ought to be aware of this, but it is unclear who should actually provide emotional support. *Lack of medical knowledge.* GPs and psychologists especially mentioned their inexperience in treating infertile couples.

Those psychologists do not have any expertise on childlessness.

Domain III: patients

Domain IV: organisation

Unclear distribution of tasks. The unclearness of the distribution of tasks between different professionals within fertility care is an organizational flaw. Presently, it is unclear 'who should do what'.

...sometimes patients tell me about poor information provision. That makes me wonder: who is able to pay attention to this, and where in the whole care pathway is this person who is responsible for this?

Poor quality of semen analyses. Presently, each laboratory has its own routine in performing a semen analysis (i.e. different tests, normal limits and measuring instruments), which can lead to different test results.

The laboratory, performing the semen analysis, should at least have a certification.

Domain I Characteristics of the guidelines	Domain II Characteristics of the professional	Domain III Characteristics of the patient	Domain IV Characteristics of the organization
Lack of evidence*	Poor communication	Uncertain patient	Unclear distribution of tasks ${\strut}{}^{*}$
Unclear treatment criteria [*]	Lack of respect and autonomy ^{**}	Age-related problems	Poor alignment of care
		Desire for action	Lack of attention to work
Unclear treatment policy*	Information provision not meeting expectations	Taboo on infertility	Poor quality of semen
L su k	Lack of emotional support**	Lack of motivation	analysis*
		Partner has different GP	Poor insurance coverage
	Lack of medical knowledge [*]		Lack of arrangements concerning work
	C C		Lack of continuity of care
			Policy depends on
			Ethical consequences of age- criterion

Table 4: Key clinical issues according to professionals

* Main key clinical issues, suggested by at least two different professionals in both focus groups.

^{**} Collective main key clinical issues, suggested by both infertile couples and professionals.
Patients' added value

Infertile couples mentioned eight additional main key clinical issues that were not mentioned by the professionals: expectations on information provision, taboo on infertility, poor alignment of care, lack of attention to work, lack of support after treatment, too much standard treatment according to protocols, poor physical environment and time pressure (Tables 3 and 4). Two main key clinical issues were mentioned by infertile couples and professionals collectively, but interpreted differently, namely the lack of emotional support and the lack of respect and autonomy.

Discussion

This study shows patients' added value to the scope of a multidisciplinary CPG on infertility including all different care phases. Infertile couples broadened the scope of the CPG by adding patient-centred aspects of care (i.e. expectations on information provision, taboo on infertility, poor alignment of care, lack of attention to work, lack of support after treatment, too much standard treatment according to protocols, poor physical environment and time pressure) or addressing patient-centred aspects in professionals' issues (i.e. the lack of emotional support and the lack of respect and autonomy).

To date, this is the first study that focuses on patients' added value to the scope of a multidisciplinary guideline, by comparing patients' and professionals' key clinical issues. Only two studies have reported on their positive experiences with patient involvement in an early phase of CPG development regarding anxiety, insomnia and kidney disease [16,36]. However, as these studies mainly focused on patients' subjects relevant for the CPG instead of care aspects susceptible for improvement, the actual value for the development of key questions was lacking. Furthermore, since insight into the differences between patients' and professionals' contributions were lacking, patients' added value to the scope of the guideline remained unclear. The need for emotional support, improved professional behaviour and using shared decision-making principles have been described earlier [37-46]. However, in our study the need for emotional support for professionals reveals more organizational implications, since it is especially unclear to the professionals within our sample 'who' is responsible for providing emotional support and 'when' this should be offered. For patients, this key clinical issue reflects on the lack of

enabling to discuss emotional discomfort in the consulting room during daily care. Guideline recommendations based on this key clinical issue should therefore not only focus on 'who' and 'when', but also 'how' emotional support should be embedded within daily care provided by all involved fertility care professionals. Obviously, this addition highlights the surplus value of patient involvement in an early stage of the CPG development process.

Beside different interpretations of key clinical issues, infertile couples in our study also broadened the scope of the guideline by identifying eight additional main key clinical issues that would otherwise not have been recognized. These main key clinical issues illustrate that patients do value or desire different aspects to be addressed in guidelines than their professionals. Professionals mainly consider multidisciplinary guidelines as instruments to reduce practice variation in specific cases (i.e. due to unclear treatment criteria, policy and quality of performing diagnostics), to address evidence gaps and to enhance the overall organization of multidisciplinary care on a policy level (i.e. secure distribution of tasks between different professionals). Patients enlighten aspects of patient-centred care (i.e. emotional support, information provision) as well as concrete organizational aspects focusing on the gaps in between different phases of care that professionals have not been putted forward (e.g. poor alignment of care, the lack of care after treatment) [47]. As widely discussed, complex and chronic care requires a fluent organization and central points of improvement herein may be well recognized by patients surveying their whole care process [17, 48]. This is especially illustrated by the mentioned poor alignment of care in our study that has not been addressed in the literature on guideline development before.

The main strength of our study is that both infertile couples and professionals participated in it separately, which enabled us to assess patients' added value to the scope of the guideline, covering all phases of care. Additionally, our scoping approach to CPG development provides a unique opportunity to reveal main key clinical issues, which are directly usable in formulating key questions as the next step of the CPG development process.

However, some limitations to our study need to be addressed. One may argue whether this approach can be directly translated to an international level, since for example some organizational and reimbursement aspects have been arranged differently elsewhere. However, also in other countries, different professionals treat patients, with comparable problems in patient-centred and organizational issues [37-39]. Furthermore, we acknowledge that the consecutive recruitment of

infertile couples to participate in our study can introduce a potential selection bias: we do not know if these couples are representative of the general infertile population. However, regarding the time restraints in the guideline development process and our aim of using input of patients in the first phase, we used a practical approach. The authors believe that this is a first initiative to involve patients in this first step of the guideline development process. Furthermore, the authors believe that a systematic literature search on patients' preferences for care and outcome measurements should complete patients' input in this first phase of guideline development.

The patients' and professionals' key clinical issues that resulted from this study could inform the next step of the guideline development process, namely in developing the key questions as well as form a valuable addition in defining the associated outcome measurements. Regarding the mentioned key clinical issues, this could result in key questions like: 'how to treat patients best' (attitude and partner involvement), 'how to organize information provision to infertile couples and what kind of information do patients value' and 'which place does emotional support have in fertility care and when and by whom should this be provided'.

Although the direct impact of these study results is more or less specific for fertility care, we believe that this approach could form an example for guideline developers and policy makers (inter)nationally in making multidisciplinary guidelines as well as other quality derived products (e.g. protocols in which the organization forms an important aspect) more tailored to patients. However, guideline developers may approximately need an extra month to recruit patients, conduct interviews, analyse the results and receive patients' remarks in order to precede the underpinning key questions. In the light of delivering high quality patient-centred care, the engagement of patients in an early phase of the development of products that guide the clinician, could form one of the strategies to bring this to a higher level. Finally, although suggestive, tailoring clinical guidelines to patients' perspective in this way may suggest that the guideline will be well implemented it may also interfere in a positive way with patient satisfaction, costs and improved outcomes [46]. Hence, patients' input to the scoping phase of guideline development may be worth the relatively small amount of extra time. For such, further studies on the effects on guideline implementation, the level of patient-centred care and patient satisfaction could build to the strength of the recommendation to move towards shared guideline development, from the first till the last step.

In conclusion, within this sample, evidence exists of the potential benefits of including patients in an early phase of the CPG development process: it leads to valuable additional main key clinical issues to be addressed in the next step of a multidisciplinary CPG development process and broadens the scope of the guideline, particularly regarding patient-centred and organizational aspects. Therefore, actual involvement of patients from the start of the guideline development process could make the final guideline more tailored as well as responsive to patients. Internationally, guideline developers and policy makers can use this approach. Further studies on the actual impact on guideline implementation as well as multiple aspects of the quality of care may strengthen the recommendation to involve patients in the scoping phase of guideline development.

Abbreviations: GP, General Practitioner; CPG, Clinical Practice Guideline; IUI, Intra Uterine Insemination; IVF, In Vitro Fertilization; ICSI, Intracytoplasmic Sperm Injection; OI, Ovulation Induction; TESE, Testicular Sperm Extraction.

References

- 1. The AGREE collaboration. Appraisal of Guidelines for Research and Evaluation (AGREE) instrument. Collaboration. London; 2010. www.agreecollaboration.org.
- 2. Institute Of Medicine (IOM). *Clinical Practice Guidelines we can Trust*. Washington, DC: National Academy Press, 2011.
- 3. Institute Of Medicine (IOM). Crossing the quality chasm: a new health system for the 21 st century. Washington, DC: IOM, 2001.
- 4. National Institute for Health and Clinical Excellence (NICE). *The guidelines manual*. London: NICE, 2012.
- 5. World Health Organisation (WHO). *Guidelines for WHO Guidelines. Global programm on evidence for Health Policy.* Geneva: WHO, 2003.
- 6. Boivin A, Currie K, Fervers B *et al.* Patient and public involvement in clinical guidelines: international experiences and future perspectives. *Qual Saf Health Care* 2010;**19:**e22.
- Leotsakos A, Zheng H, Croteau R et al. Standardization in patient safety: the WHO High 5s project. Int J Qual Health Care 2014;26:109-16.
- 8. Staniszewska S, Boardman F, Gunn L *et al.* The Warwick Patient Experiences Framework: patientbased evidence in clinical guidelines. *Int J Qual Health Care* 2014;**26**:151-7.
- National Institute for Health and Clinical Excellence (NICE). https://www.nice.org.uk/media/default/ About/NICE-Communities/Public-involvement/Public-involvement-programme/PIP-processguide-apr-2015.pdf, 19 January 2016, date last accessed.
- 10. Scottish Intercollegiate Guidelines Network (SIGN) http://www.sign.ac.uk/patients/network.html, 19 January 2016, date last accessed.
- G-I-N PUBLIC Toolkit: Patient and Public Involvement in Guidelines. Guidelines International Network, 2015. http://www.g-i-n.net/document-store/working-groups-documents/g-i-n-public/ toolkit/toolkit-2015, 19 January 2016, date last accessed.
- 12. The Netherlands Organisation for Health Research and Development (ZonMW). The Participation Compass. http://www.participatiekompas.nl/over-participatiekompas/english, 19 January 2016, date last accessed.
- 13. Woolf S, Schunemann HJ, Eccles MP *et al.* Developing clinical practice guidelines: types of evidence and outcomes; values and economics, synthesis, grading, and presentation and deriving recommendations. *Implement Sci* 2012;7:61.
- 14. Eccles MP, Grimshaw JM, Shekelle P *et al.* Developing clinical practice guidelines: target audiences, identifying topics for guidelines, guideline group composition and functioning and conflicts of interest. *Implement Sci* 2012;7:60.
- 15. Legare F, Boivin A, van der Weijden T *et al.* Patient and public involvement in clinical practice guidelines: a knowledge synthesis of existing programs. *Med Decis Making* 2011;**31:** E45-74.
- 16. Tong A, Lopez-Vargas P, Howell M *et al*. Consumer involvement in topic and outcome selection in the development of clinical practice guidelines. *Health Expect* 2012;**15**:410-23.
- 17. Wagner EH, Austin BT, Davis C *et al.* Improving chronic illness care: Translating evidence into action. *Health Affairs* 2001;**20**:64-78.
- Bodenheimer T, Lorig K, Holman H *et al.* Patient self-management of chronic disease in primary care. J Am Med Assoc 2002;288:2469-75.
- Kennedy A, Rogers A, Bower P. Support for self care for patients with chronic disease. BMJ 2007;335:968-70.
- Grol R, Grimshaw J. From best evidence to best practice: effective implementation of change in patients' care. *Lancet* 2003;362:1225-30.
- 21. Cooper AR, Baker VL, Sterling EW *et al.* The time is now for a new approach to primary ovarian insufficiency. *Fertil and Steril* 2011;**95:**1890-7.
- 22. van Empel IW, Aarts JW, Cohlen BJ *et al*. Measuring patient-centredness, the neglected outcome in fertility care: a random multicentre validation study. *Hum Reprod* 2010;**25**:2516-26.

- 23. Tallon D, Chard J, Dieppe P. Relation between agendas of the research community and the research consumer. *Lancet* 2000;**355**:2037-40.
- 24. Blumenthal D. Part 1: Quality of care--what is it? N Engl J Med 1996;335:891-4.
- 25. Berta W, Barnsley J, Brown A *et al*. In the Eyes of the Beholder: Population Perspectives on Performance Priorities for Primary Care in Canada. *Healthc Policy* 2008;**4**:86-100.
- Aarts JW, Faber MJ, van Empel IW *et al.* Professionals' perceptions of their patients' experiences with fertility care. *Hum Reprod* 2011;26:1119-27.
- 27. Yen L, Gillespie J, Rn YH *et al.* Health professionals, patients and chronic illness policy: a qualitative study. *Health Expect* 2011;**14**:10-20.
- van Empel IW, Dancet EA, Koolman XH *et al.* Physicians underestimate the importance of patientcentredness to patients: a discrete choice experiment in fertility care. *Hum Reprod* 2011;26:584-93.
- 29. Coulter A. Patient engagement--what works? J Ambul Care Manage 2012;35:80-9.
- 30. Nelen WLDM, Berg C, de Sutter P *et al. Manual for European Society of Human Reproduction and Embryology (ESHRE) guideline development.* Grimbergen: ESHRE, 2008.
- 31. Boivin J, Bunting L, Collins JA *et al*. International estimates of infertility prevalence and treatmentseeking: potential need and demand for infertility medical care. *Hum Reprod* 2007;**22**: 1506-12.
- 32. Gnoth C, Godehardt E, Frank-Herrmann P *et al.* Definition and prevalence of subfertility and infertility. *Hum Reprod* 2005;**20**:1144-7.
- 33. Wester F, Peters V. *Kwalitan as an aid in qualitative analysis. Paper for the ESRC Field research Seminar.* Coventry: University of Warwick, 1995.
- 34. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol 2006;3:77-101.
- Cabana MD, Rand CS, Powe NR et al. Why don't physicians follow clinical practise guidelines? A framework for improvement. J Am Med Assoc 1999;282:1458-65.
- Diaz Del Campo P, Gracia J, Blasco JA et al. A strategy for patient involvement in clinical practice guidelines: methodological approaches. BMJ Qual Saf 2011;20:779-84.
- 37. Gesell SB, Wolosin RJ. Inpatients' ratings of care in 5 common clinical conditions. *Qual Manag Health Care* 2004;**13**:222-7.
- 38. Velikova G, Keding A, Harley C *et al.* Patients report improvements in continuity of care when quality of life assessments are used routinely in oncology practice: secondary outcomes of a randomised controlled trial. *Eur J Cancer* 2010;**46**:2381-8.
- 39. Strachan PH, Ross H, Rocker GM *et al.* Mind the gap: Opportunities for improving end-of-life care for patients with advanced heart failure. *Can J Cardiol* 2009;**25:**635-40.
- 40. Dancet EA, Nelen WL, Sermeus W *et al.* The patients' perspective on fertility care: a systematic review. *Hum Reprod Update* 2010;**16**:467-87.
- Dancet EA, Van EI, Rober P *et al.* Patient-centred infertility care: a qualitative study to listen to the patient's voice. *HumReprod* 2011;26:827-33.
- 42. van Empel IW, Hermens RP, Akkermans RP *et al.* Organizational determinants of patient-centered fertility care: a multilevel analysis. *Fertil Steril* 2011;**95:**513-9.
- 43. Dancet EA, D'Hooghe TM, Sermeus W *et al.* Patients from across Europe have similar views on patient-centred care: an international multilingual qualitative study in infertility care. *Hum Reprod* 2012;**27**:1702-11.
- 44. van Empel IWH, Nelen WLDM, Tepe ET *et al.* Weaknesses, strenghts and needs in fertility care according to patients. *Hum Reprod* 2010;25:142-9.
- Cleary PD, Edgman-Levitan S. Health care quality. Incorporating consumer perspectives. J Am Med Assoc 1997;278:1608-12.
- 46. Gupta D, Rodeghier M, Lis CG. Patient satisfaction with service quality in an oncology setting: implications for prognosis in non-small cell lung cancer. *Int J Qual Health Care* 2013;**25**:696-703.
- Gerteis M. Conference overview: through the patient's eyes--improvement strategies that work. *Jt* Comm J Qual Improv 1999;25:335-42.
- 48. Kinsman L, Rotter T, James E, Snow P, Willis J. What is a clinical pathway? Development of a definition to inform the debate. *BMC Med* 2010;**8:**31.



Chapter 3

A patient-centred network approach to multidisciplinary-guideline development: a process evaluation

EME Den Breejen, MAHW Hilbink, WLDM Nelen, TJ Wiersma, JS Burgers, JAM Kremer, RPMG Hermens

Implementation Science 2014;9:68.

Abstract

Background: Guideline development and uptake are still suboptimal; they focus on clinical aspects of diseases rather than on improving the integration of care. We used a patient-centred network approach to develop five harmonized guidelines (one multidisciplinary and four monodisciplinary) around clinical pathways in fertility care. We assessed the feasibility of this approach with a detailed process evaluation of the guideline development, professionals' experiences, and time invested.

Methods: The network structure comprised the centrally located patients and the steering committee; a multidisciplinary guideline development group (gynaecologists, physicians, urologists, clinical embryologists, clinical chemists, a medical psychologist, an occupational physician, and two patient representatives); and four monodisciplinary guideline development groups. The guideline development addressed patient-centred, organizational, and medical-technical key questions derived from interviews with patients and professionals. These questions were elaborated and distributed among the groups. We evaluated the project performance, participants' perceptions of the approach, and the time needed, including time for analysis of secondary sources, interviews with eight key figures, and a written questionnaire survey among 35 participants.

Results: Within 20 months, this approach helped us develop a multidisciplinary guideline for treating infertility and four related monodisciplinary guidelines for general infertility, unexplained infertility, male infertility, and semen analysis. The multidisciplinary guideline included recommendations for the main medical-technical matters and for organizational and patient-centred issues in clinical care pathways. The project was carried out as planned except for minor modifications and three extra consensus meetings. The participants were enthusiastic about the approach, the respect for autonomy, the project coordinator's role, and patient involvement. Suggestions for improvement included timely communication about guideline formats, the timeline, participants' responsibilities, and employing a librarian and more support staff. The 35 participants spent 4497 hours in total on this project.

Conclusions: The novel patient-centred network approach is feasible for simultaneously and collaboratively developing a harmonized set of multidisciplinary and monodisciplinary guidelines around clinical care pathways for patients with fertility problems. Further research is needed to compare the efficacy of this approach with more traditional approaches. **Keywords** Clinical practice guideline development; Evaluation; Patient involvement, Clinical care pathway; Infertility

Background

Complex multidisciplinary care is often fragmented and suffers from so-called 'clinical linkage deficiencies' [1]. To resolve such deficiencies, many published reports and articles have stressed the importance of implementing integrated and patient-centred care by building bridges between the groups involved [2-6]. Clinical practice guidelines (CPGs) are potential tools for facilitating this shift in clinical care. Unfortunately, the quality of the guidelines varies, and their impact on delivering integrated and patient-centred care is still suboptimal [7-12]. Several problems still hinder CPG development and uptake, namely, inadequate management of conflicts of interest (COIs), limited panel composition, lack of patient involvement, and lack of external review [9]. Furthermore, there is still a strong focus on the single clinical aspects of diseases described in the guidelines rather than on ensuring more integrated care for patients, including attention to matters such as patient-centredness, coordination and continuity of care. Because of all this, the target users feel no affinity with the guidelines, which impedes full implementation [7,8,10].

Clinical networks are defined as collaborative, professionalized structures ranging from fully integrated service delivery systems to informal communities of practice. These networks have previously proven effective in increasing evidence-based practice and improving care models [13,14]. We aimed to resolve the deficiencies in multidisciplinary guideline (MuG) development and to re-centre the focus on the patient's overall clinical journey rather than independent contributions from each specialty or caring function. Thus, we used the network approach in a clinical area of complex multidisciplinary care, namely, fertility care. We developed a harmonized set of one MuG and four monodisciplinary guidelines (MoGs) around patient clinical pathways, including any care needed for infertile couples (such as aftercare and care given by physicians, gynaecologists, and/or urologists). We aimed to assess the feasibility of this patient-centred network approach in a detailed evaluation of the process, professionals' experiences, and the time required.

Methods

Setting

The Dutch Organization for Health Research and Development (ZonMw) funded our project, which took place within the Dutch program of Knowledge Quality and Curative Care. The program's objective was to improve the development of multidisciplinary CPGs in terms of innovation, collaboration, and efficiency.

Fertility care

Infertility is commonly defined as 'any form of reduced fertility with prolonged time of unwanted non-conception', and it affects approximately 80 million couples worldwide [15,16]. Dutch fertility care takes place on three levels. Physicians provide primary care that includes an initial fertility assessment. A physician can refer couples to a gynaecologist in a general hospital (secondary care) or a university hospital (tertiary care). The gynaecologist completes the fertility assessment, determines the cause of infertility, and defines a treatment plan. If a relevant male factor is found, the couple may be referred to an urologist. Clinical chemists and embryologists are also involved in assessments and preparation for the use of medically assisted reproductive techniques, one of which is in vitro fertilization (IVF). Because infertility has a high emotional and psychological impact that can interfere with work, psychologists and occupational physicians are regularly involved with the clinical course of the infertility problem.

The network

Our steering committee, which included five guideline experts, one implementation expert, and one project coordinator, initiated and coordinated the patient-centred network approach to MuG development. A group of gynaecologists, physicians, urologists, clinical embryologists, clinical chemists, a medical psychologist, an occupational physician, and two patient representatives from Freya (the Dutch association for people with fertility problems) assembled to collaborate in developing the guidelines in February 2008. Four MoG groups, including participants mainly from single disciplines, and one MuG group convened to develop the guidelines.

An overlap of participants from the same discipline across the groups and the project coordinator facilitated guideline harmonization. The project coordinator

was a member of all five groups and gave feedback to the steering committee. The implementation expert assured attention to the future implementation and anticipated any potential barriers to guideline implementation during all development phases. An independent researcher (MS) evaluated the project.

The network structure consisted of three organized layers comprising seven groups: the centrally located infertile patients and the steering committee, the MuG group, and four MoG groups. For our purposes, this network was to produce one patient-centred MuG on infertility and four related, mainly monodisciplinary owned guidelines. These four included a guideline on general infertility for physicians, a guideline on unexplained infertility for gynaecologists, a guideline on male infertility for urologists and gynaecologists, and a guideline on semen analysis for clinical embryologists.

Guideline development

Managing conflicts of interest (COIs)

Before starting the guideline development, all members of the groups had to declare any COIs and be officially mandated by their societies. The steering committee discussed all COIs. Participants with significant COIs were excluded from discussions or voting on recommendations for which they had COIs.

Defining the scope and key questions

We explored the care aspects in the clinical pathways of infertile patients. We paid particular attention to improvements that the patients and professionals found necessary. Various methods were used to collect data about the most relevant aspects.

We conducted 12 exploratory interviews with couples facing the spectrum of issues in the main phases of the clinical pathways in fertility care. These phases may include a physician's initial fertility assessment, a gynaecologist's fertility assessment, treatment with ovulation induction, intrauterine insemination, IVF, and/or intracytoplasmic sperm injection by a gynaecologist, a urologist's care, and aftercare (whether pregnancy occurred or not). The couples were consecutively invited to participate by means of an information letter that they received when they saw a gynaecologic resident in a fertility clinic in Nijmegen or Amsterdam. We phoned potential participants—Dutch-speaking couples with fertility problems who reacted positively to the information letter. The selection of couples

was random except for their phase in the clinical pathway. The steering committee translated care aspects that the couples said needed improvement into patient-centred key questions.

Two focus groups were conducted among members of the MuG group, including the two patient representatives, and among main target users of the guideline, including four gynaecologists, three physicians, and a urologist. The steering committee translated care aspects that the professionals said needed improvement into medical-technical, organizational, and patient-centred key questions. Example questions for these three categories, respectively, are: 'What are the indications for IVF treatment?' 'Which professionals should be part of the treatment team in a university hospital?' 'How should patients be informed about adoption?'

All key questions were given a format defined for the MuG. Then the MoG groups addressed the medical-technical questions and the MuG group addressed the organizational and patient-centred questions.

Elaborating key questions and formulating recommendations

The participants worked in pairs. They used the PICO (patient, intervention, comparison, and outcome) method to define their search strategy, conduct a systematic literature review, select relevant evidence, and summarize this evidence in formatted evidence tables. They rated (scale: 1 to 5) the evidence according to quality criteria adapted from the Centre for Evidence-Based Medicine, version 1999 [17]. The pairs of members then formulated one or more conclusions, their considerations, and one or more concept recommendations. A level of evidence (A to D) was given for each recommendation to be discussed in the particular guideline group [17]. The project coordinator was a member of all guideline groups and coordinated the entire process, which was part of a strategy for harmonizing recommendations across the groups. The project coordinator checked the rating of evidence and grading of recommendations for errors. The steering committee discussed and resolved any discrepancies. The implementation expert checked and improved the implementability of the concept recommendations and the guidelines as a whole using the items of the Guideline Implementability Appraisal (GLIA) Tool. An extensive internal review of the CPGs across the groups was used to harmonize the recommendations. Many patients also participated by formulating and prioritizing recommendations for the MuG [18].

We used advertisements and mailings over a period of seven months to invite patients with fertility problems to formulate recommendations via the Dutch online wiki-based tool at www.freyawiki.nl [18]. A patient representative and two members of the steering committee including the implementation expert modified and assessed the implementability of the patient recommendations with the GLIA Tool. Then we asked patients to select their top three or five recommendations for each wiki section (General care, General practice care, Gynaecologic care, Urologic care, and Laboratory) [18]. The guideline group assessed the eligibility of the final set of patients' recommendations within the scope of the guideline.

Integrating the guidelines

The MoGs addressed medical-technical aspects of care that needed improvement: physician care, care for patients suffering from unexplained infertility or male infertility, and fertility care given by clinical embryologists (semen analysis). The definitive MuG described the overall clinical pathway of patients with fertility problems by merging the main medical-technical, patient-centred, and organizational recommendations from the MuG and MoG groups and the prioritized patient recommendations from WikiFreya [18]. The medical-technical recommendations included transitions in fertility care and care alignment. The patient-centred recommendations dealt with respect for patients' values, preferences, and needs; information, communication, and education; emotional support; partner involvement; and the attitude of the fertility clinic staff. The organizational recommendations addressed coordination and integration of care, physical comfort, transition and continuity of care, access to care, and staff competence and technical skills. All patient recommendations obtained via WikiFreya were classed as Level P (Patient) evidence. To express patients' input in the guideline, two patient representatives reformulated patient recommendations as: 'Patients want to...' The whole project was planned to be completed in 18 months.

Evaluation

We applied a stepwise process evaluation to the feasibility of this network approach [19]. The primary outcomes were 'how' the planned project was actually carried out and 'how' participants perceived the process; the secondary outcome was 'what' time was invested. We used a mixed-method evaluation including examination of secondary resources (such as project descriptions), interviews with key figures, and a written questionnaire survey among all participants. An independent researcher (MS) conducted the interviews and collected the data.

Data collection

Examination of secondary resources

We collected all the project data from the project descriptions and minutes of meetings to determine whether the project was carried out as planned.

Interviews with key figures

We conducted eight semistructured, in-depth, telephone interviews with eight key figures: the chairpersons of the four MoG groups, four members of the MuG group, and the steering committee (one patient representative, two project leaders, and the project coordinator). We asked the interviewees to chronologically describe the guideline development and their activities in the project. We asked for comments on the overall organization, the methodology of the network approach, and the methods of patient involvement. Then we asked for suggestions to improve the approach. Full interviews took approximately 30 min each, and they were fully transcribed verbatim.

Questionnaire survey

We based our questionnaire on the interview results so that we could assess participant experiences and measure the time needed for the project. The first part of the four-part questionnaire asked about participants' background characteristics. The second part pertained to participants' involvement in the preparation and development phase and the time (excluding travel) needed for each of these phases. The third part included five open questions about the network approach (e.g., the methodology and guideline integration), patient involvement, wiki methodology, and patient contributions to the guideline. The fourth part asked participants to describe facilitators of and barriers to the approach and to suggest improvements. All participants received the questionnaire by post, after the draft guidelines were completed. A reminder was sent six weeks later.

Data analysis

We used SPSS (version 16.0 for Windows, Data Entry 4.0, SPSS, Chicago, Ill.) to perform descriptive statistics (frequencies, medians, and ranges) on participant

background characteristics and to analyse the time data. We used Kwalitan (version 5.0, Malden, The Netherlands) to qualitatively analyse the transcripts of the interviews and the free text responses from the second part of the questionnaire [20].

Project performance

Two authors (MH and RH) identified all activities and categorized them in the preparation phase or the development phase. The preparation phase included composing development groups, managing COIs, identifying care aspects to be improved, and developing WikiFreya. The development phase included attending meetings, formulating key questions, reviewing, selecting and assessing evidence, writing the guideline and formulating recommendations, harmonizing the guidelines, reviewing and revising draft guidelines, and aligning the guidelines with managing WikiFreya. We compared the actual activities with the planned activities and identified differences.

Time investments

We counted the regular and extra meetings on the attendance lists, and determined the mean meeting participation rates for each group and the steering committee. We calculated the total time the steering committee spent on the preparation phase. We computed the median actual time for the respondent meetings of each development group, total time for extra respondent meetings, and median extra time respondents spent for each development group and for each of the two phases. The total time for meetings for each group, including the project coordinator was assessed as the 'mean participation rate' x 'number of meetings' x 'median time investments.' The total extra time needed was defined as the 'number of participants for each group' x 'median extra time spent by each participant.' The values were corrected for non-responders to the questionnaire. We calculated the project coordinator's extra time separately. Our calculations totalled the time needed for the development phase.

Experiences

We analysed the data descriptively, and we used a special framework to analyse open question responses. We developed the special framework from the interview topic guide corresponding to our study objectives, which included experience with the methodology of the network approach, patient involvement, barriers to and facilitators of the approach, and suggestions for improvement [21]. Two researchers (EB and MH) studied the interviews and the open question responses independently. They identified and coded the parts of the interviewees' responses that were relevant to the study objectives. They then discussed key issues and discrepancies between their results. The key issues were structured with a view to the study objectives. The questionnaire was based on the interviews, so we only present the results of the questionnaire for each study objective, but no information found under the heading 'Organization.'

Results

Participants

Five (four MoG and one MuG) groups were installed in May 2008. None of the members of the groups declared significant COIs, and all of them were officially mandated by their societies. One of the physicians involved in the MuG group dropped out for private reasons two months later. The MuG chairperson, a physician, concurrently fulfilled this role. Overall, 32 participants were involved in the five groups (Table 1). Four participants fulfilled multiple roles: the project coordinator was a member of the steering committee and all five guideline groups; the chairperson of the MoG group for general infertility was a member of the steering committee; one project leader was a member of the steering committee and chairperson of the MuG group; and one member of the MuG group was a member of the steering committee (Table 1). All participants received the evaluation questionnaire (one patient representative was unavailable). The response rate was 79% (n = 27). Table 2 summarizes the background characteristics of the respondents. Of the 59% who were experienced in guideline development, 63% were also experienced in MuG development.

Guideline development

The project was carried out as planned, except for minor modifications needed to improve the consistency between the concepts of the guidelines. Face-to-face meetings and additional conferences calls were necessary to discuss discrepancies between recommendations concerning the cut-off points for treating infertility. These recommendations were issued by guidelines for male infertility and unexplained fertility. The cut-off points were eventually based on the existing

Professional societies	Numb	er of mem	bers in dev	elopment g	groups
	Multidisciplinary guideline	MoG: general infertility	MoG: unexplained infertility	MoG: male infertility	MoG: semen analysis
Dutch Association of Obstetrics & Gynaecology	2	1	4	2	1
Dutch National Organisation of General Practitioners	2	5	1	1	0
Dutch Urological Association	1	0	0	2	0
Dutch Society for Clinical Embryologists	1	0	0	0	2
Dutch Society for Clinical Chemistry	1	0	0	0	1
Dutch Society of Occupational Physicians	1	0	0	0	0
Dutch Association of Psychologists	1	0	0	0	0
Dutch Patient Association for Fertility Problems	2	0	0	0	0
Number of participants	11	6	5	5	4
Total number of participants = 31^{a}					

Table 1: Organizations in the guideline development groups

^aThe project coordinator took part in all working groups, which increased the total number of participants by one.

MoG = Monodisciplinary guideline.

27 respondents	n (%)
Gender	
Male	14 (52)
Female	13 (48)
Age in years	
26–35	4 (15)
36-45	9 (33)
46–55	11 (41)
>55	3 (11)
Median years of professional experience in fertility care (range)	9 (1-26)
Previous experience in guideline development ^a	
Yes	16 (59)
No	11 (41)

Table 2: Background characteristics of questionnaire respondents

MoG = Monodisciplinary guideline, MuG = multidisciplinary guideline.

^aExperience in guideline development was determined by the authorship of one or more monodisciplinary or multidisciplinary guidelines.

relevant evidence. Further, there was a lack of consensus on some recommendations in the four MoGs for life-style advices (e.g., alcohol and anabolic steroids use) issued in all four MOGs as well as lack of underlying evidence. This necessitated two additional consensus meetings, which were attended by four members of the MuG (including the chairperson) and the chairpersons of all MoG groups. These consensus meetings produced overall recommendations for life-style advice based on evidence regarding pre-pregnancy counselling. The MuG group reviewed the drafts of the MoG groups and vice versa. Then, the project coordinator initiated a conference call in order to reach consensus on the recommendations based on the expert opinion of the MoGs. Via WikiFreya, 298 patients formulated 289 recommendations, which 80 patients prioritized into 21 recommendations. These recommendations were included in the definitive guideline [18].

Resulting guidelines

One MuG and four related MoGs were developed in 20 months; all were written in Dutch: http://www.nvogdocumenten.nl/uploaded/docs/Landelijke%20netwerk richtlijn%20Subfertiliteit%20def.pdf; www.nvog.nl; www.nhg.org; www.nvu.nl; www.embryologen.nl

The definitive MuG follows the overall clinical care pathway for patients with infertility problems. It addresses patient-centred, organizational, and medical-technical issues on the clinical pathways, from first visiting the physician to completed treatment (with or without a pregnancy) and aftercare from the physician or medical psychologist (Table 3). The MuG consists of 198 recommendations based on the best available evidence or expert opinion; the level of evidence (A to D) is given for each recommendation. All recommendations were linked to the key questions formulated. Of these recommendations, 59% concerned organizational and patient-centred aspects of care (Table 4). The medical-technical recommendations for transitions in fertility care and supporting care alignment were derived from the MoGs. Twenty-one prioritized patients' recommendations, obtained via WikiFreya, were included in the MuG and graded as level P evidence [18].

Chapter 1: background	Description of the patient-centred network approach
	Composition of the guideline development groups and methods used to involve patients
	Definition of infertility and description of patients' clinical pathway
Chapter 2: organisation	Organization of fertility care
	Registration of outcomes of infertility treatments
	Care alignment
Chapter 3: physician	Basic principles in fertility care for the physician
	History, physical examination, and additional infertility assessments
	Treatment policy
	Referral
	Information provision and education
	Coordination of primary care with secondary/tertiary care
	Attendant role after referral
Chapter 4: gynaecologist	Basic principles of fertility care for the gynaecologist
	History, physical examination, and additional infertility assessments
	Treatment policy
	Treatment criteria regarding age
	Information provision and education
	Referral
	Coordination of primary care with secondary/tertiary care
Chapter 4: urologist	Basic principles of fertility care for the urologist
	History, physical examination, and additional infertility assessments
	Treatment policy
	Coordination of primary care with secondary/tertiary care
Chapter 5: semen analysis	Basic principles for semen analysis
	Collection of semen
	Analysing the semen
	Interpreting the results of a semen analysis
	Reporting the results
Chapter 6: psychologist	Basic principles in fertility care for the psychologist
	Psychological screening of patients with fertility problems
	Referral
Chapter 7: sexologist	
Chapter 8: work and	Infertility in relation to occupation
infertility	Exposure to harmful substances during work
	Participation of infertile patients in work
Chapter 9: associations for fertility problems	Opportunities and legislation for adoption

Table 3: Contents of the final version of the patient-centred multidisciplinary guideline for infertility

Medical-technical recommendations	Origin or guideline	Chapter of the MuG
The physician should only physically examine the man if his semen analysis is irregular. <i>LOE C</i>	General infertility for physicians	Family physician (physical examination)
The gynaecologist should not test ovarian reserve capacity to predict probability of pregnancy (with or without treatment). <i>LOE A</i>	Unexplained infertility	Gynaecologist (assessments)
Organizational recommendations		
The physician should order a semen analysis from an accredited laboratory (ISO15189) or from a referral hospital. <i>LOE D</i>	MuG	Organization of fertility care
In accordance with the Dutch IVF planning decree, every licensed IVF centre and their corresponding transport and satellite centres must provide annual reports on treatment outcomes for uniform national IVF registration. <i>LOE D</i>	MuG	Organization of fertility care (registration)
Patient-centred recommendations		
Both partners of the couple should be involved in the assessment and management of infertility because it is a joint problem. LOE C	MuG	Physician, gynaecologist, and urologist (basic principles)
The gynaecologist should offer couples with fertility problems psychological support throughout all phases of fertility care. $LOE D$	MuG	Gynaecologist (information provision)
Patient recommendations		
Patients want their gynaecologist to inform them about the different phases of treatment and their expected time spans. <i>LOE P</i>	MuG	Gynaecologist (information provision)
Patients want their physician to make a referral immediately after they have been trying to conceive for 1 year. <i>LOE P</i>	MuG	Physician (referral)

Table 4: Examples of recommendations integrated into the multidisciplinary guideline

MuG = Multidisciplinary Guideline, IVF = in vitro fertilization, LOE = level of evidence

Time investments

The median number of two-hour regular group meetings was 10 (range: 5 to 11). The median participation rate was 88% (range: 77 to 94%). Three additional twohour meetings were necessary for adjustment between guidelines. The steering committee needed 11 two-hour meetings for organizing the project. Seven participants (20%) were involved in the preparation phase, for which they needed 471 h in total. In the development phase, the participants spent time on meeting preparation, two-hour face-to-face meetings, and minutes of meetings; and extra time on reviewing literature, writing guidelines, and commenting on draft versions. The time all participants spent in the development phase totalled 4,497 hours, including the 281 hours the steering committee members spent organizing this phase (Table 5).

Table 5: Time investme	nts for phase 2; guideline d	levelopment					
Guideline	Mean percentage of	Median hours spent	Total hours ^a spent	Total hours in	Median extra	Total extra	Total hours ^c
development groups	participation in regular	per participant in	in regular meetings	additional meetings	hours per	hours ^b per	in the
and number of	meetings	regular meetings	per development	(number of	participant	development	development
participants	(number of meetings)	(range)	group	participants)	(range)	group	phase
MoG: General infertility; <i>n</i> = 7	92 (10)	40 (22.5–50)	258	7 (1)	58 (40-60)	348	613
MoG: Unexplained infertility; $n = 6$	85 (10)	47 (18–72)	240	15 (3)	58 (50–60)	290	545
MoG: Male infertility; <i>n</i> = 6	94 (8)	24 (12–56)	135	8 (2)	39 (18–50)	195	338
MoG: Semen analysis; $n = 5$	88 (5)	30 (10–35)	132		48 (46–50)	192	324
MuG; $n = 11$	77 (11)	30 (21–55)	254	38 (10)	31 (2–51)	310	602
Subtotal			1019	68		1335	2422
Steering committee $n = 7$	87 (11)	25 (15–77)	152	39 (4)	15 (3–52)	06	281
Project coordinator c						1794 c	1794 °
Total			1171	107		3219	4497
MoG = Monodisciplina Regular meetings are me	ry guideline, MuG = multi setings necessary for the de	idisciplinary guideline. evelopment of the guide	lines.				

Additional meetings are meetings necessary for discussing and refining the consistency of the guidelines.

Extra time investments are the hours participants needed to formulate key questions, review, select and assess evidence, write, review and revise draft guidelines, secure alignment of the guidelines and manage Wikifreya.

"Total hours for regular meetings are corrected for questionnaire non-responders (mean participation rate x number of meetings x median time investments). "fotal extra hours are corrected for questionnaire non-responders [(number of participants per development group-1) x median extra time per participant]. "The project coordinator's meeting hours are included per development group; his extra hours are given separately.

Feedback

Interviews

Most of the eight interviewees thought the guideline groups were well composed. Nevertheless, they perceived combining the role of moderating the meetings and providing clinical input for the content as unsatisfactory. The two project leaders said they underestimated the project coordinator's workload, particularly in combining the coordination tasks with writing the draft guidelines. Furthermore, views and preferences differed between the chairperson of the MuG and the project coordinator about the scope, format, and content of the guideline; this formed a time-consuming barrier.

Questionnaires

The 27 questionnaires showed that most participants perceived the methodology of the network approach on the one hand as 'the promising future of guideline development' and on the other hand as 'complex and unclear.' Positive notes included the perceived individual learning curves for guideline development, the opportunity of distributing key questions to participants with relevant knowledge, various participants' perceived respect for autonomy, and the collaborative development of the one MuG. Furthermore, participants reported that the high level of coordination required to carry out the project as planned was a potential barrier to the approach. The different opinions among the professionals caused delays and tension in finalizing the guidelines. Clear expectations about the roles of the participants and a description of the final format for the guideline were lacking.

The integration of the MoGs into the MuG was seen as 'powerful', mainly regarding 'special attention to transitions in different phases of care (alignment),' the opportunity to check possibly underexposed topics' and 'the simultaneous development of all guidelines'. The final equalization of guideline content was 'too late' (e.g., when recommendations had already been formulated), 'difficult' (due to differing opinions), and 'time consuming' (extra meetings). One respondent said integrating MoGs into the MuG was 'needless.'

Patient involvement

All MuG group respondents described the participation of patient representatives in their group as 'valuable' (e.g., influencing discussions by refocusing on the patient) and their contributions as 'beneficial to the final product' (e.g., affecting formulations of considerations or expert-based recommendations). The representatives emphasized the need for information about the components of clinical care pathways before they discussed treatment options. More than one-half of the respondents described the final patient recommendations as 'valuable' or 'eye-openers', and 'useful' in formulating professional recommendations. Some of them doubted the practical applicability of these recommendations. They questioned the fact that patients recommended that the physician immediately refer patients trying to conceive to the gynaecologist. They noted the lack of new insights in patient recommendations.

Facilitators and barriers

Facilitators for the network approach included the selection of the most competent and dedicated participants, the introduction of the project coordinator, and patient contributions. Perceived political barriers, competing professional interests of those involved, and the lack of a more detailed MuG format created barriers. Suggestions for improvement included communication of clear instructions for individual roles and responsibilities, a strict schedule including deadlines, and a clear format for the guidelines. Further, the need for supportive staff and support for literature searches were noted.

Discussion

This study provides detailed insight into the feasibility of a novel patient-centred network approach to MuG development for fertility care. This approach enabled the collaborative development of a harmonized set of one MuG and four MoGs for clinical care pathways for infertile couples. The approach helped us foresee possible barriers analogous to the US Institute of Medicine recommendations for developing trustworthy and transparent CPGs [9].

All the relevant stakeholders were included in the guideline groups. Collaboration between balanced groups of key stakeholders is an important success factor for clinical networks and may lead to a more valid method of developing guidelines [9,10]. A crossover of stakeholders from one guideline group to another helped harmonize the guideline content and distribute questions among the groups. This emphasized specific professional contributions and created a feeling of affinity with the guidelines. The development required intensive patient engagement, and the contributions of patient representatives in the MuG group and individual patients acting via WikiFreya were considered valuable [18].

The MuG follows patient clinical pathways and uses a network structure that includes all stakeholders, so that it pays much attention to the organization of the different phases of fertility care and transitions from one phase to another. This ensures better-integrated care (e.g., referral from the physician to the gynaecologist) [22]. The attention to patient preferences, needs, and values may have increased the level of patient-centredness [23]. The approach included an extensive review of the guidelines throughout the development. It used the network structure for which extra time was needed, but it enabled broader support of the guidelines and may enhance future guideline implementation [24,25].

The participants liked the approach and viewed it as a promising format for developing MuGs. Enthusiastic patients and the energetic project coordinator helped make the approach work well. Suggestions for improving the approach were reported mainly at the organizational level (e.g., previous communication about individual roles and responsibilities, a detailed time line, and a detailed format for the guidelines). This correlates with the existing literature about clinical networks, which implies that using clinical networks requires a high degree of managerial organization [13,14,22,26]. More support staff might enhance the efficiency of the network approach. Engaging a librarian to help with literature searches might accelerate guideline development and increase efficiency [27]. However, the approach seemed time consuming for developing our set of five related guidelines simultaneously. Unfortunately, it is difficult to compare our time investments with those of regular guideline development, since there is a dearth of published studies about this topic.

Strengths and limitations

Although the use of a clinical network has been suggested as an effective strategy for implementing CPGs, this is the first study that has applied this approach in developing MuGs [28-31]. Our guideline development closely paralleled the main recommendations of the US Institute of Medicine [9]. However, recommendations were not graded and to express patients' input, patients' recommendations were secondarily reformulated to a non-actionable form incongruent to the GLIA instrument. This non-actionable form could impede harmonization of patients and stakeholders generated inputs. In addition to other studies on guideline development approaches, we also evaluated the feasibility of the approach. Nevertheless, a basis for comparing time data is lacking, which is a limitation of our study and a major limitation of current study designs of guideline development. In our opinion, guideline development is time consuming and expensive. Time should always be weighed against benefits, especially for introducing new approaches. We have applied the patient-centred network approach to a MuG program for fertility care. This clinical area is characterized by the involvement of intensively collaborating professionals and responsible patients, which might be an argument against generalizability for other clinical areas. However, addressing practice change and sustaining clinical networks generally requires great motivation and is not specific to fertility care [32,33]. In this light, the level of our participants' experience may have been a success factor in realizing the project in a relatively short time, but it may also be an argument against generalizability. Nevertheless, basic knowledge of guideline development methodologies is necessary in all approaches. Moreover, not only were our participants pretty experienced in guideline development, they were also opinion leaders within their own medical specialties. This may be an important success factor for disseminating and implementing the definitive guidelines. Despite this, we realize that, because our participants are rather experienced in their own usual way of developing guidelines, they might have been more critical of such a new approach. For instance, they regarded the lack of a detailed format as a barrier. This factor may have hindered the guideline development.

Although the guidelines clearly address organizational and patient-centred aspects (altogether, in 59% of the recommendations), we did not compare the proportion of these aspects to proportions in conventionally developed guidelines. However, we expect that the proportion of patient-centred aspects is rather small in other guidelines because patient participation in guideline development is still not common practice [34]. This mechanism may also apply to the organizational aspects, which are mainly addressed in guideline-related products, such as local protocols.

Although the participating member societies and organizations are committed to disseminating the final, harmonized guidelines, our detailed process evaluation was limited to the first phases of the guideline development and did not include the dissemination and implementation phases. We assume that this approach will enhance the implementation and our network might be an effective strategy in the further efforts that are still required [28-32,35].

Conclusions and implications for further research

The novel approach of the patient-centred network is feasible for simultaneously and collaboratively developing a harmonized set of MuGs and MoGs for the clinical pathways of infertile couples. The approach is a potential strategy for developing more trustworthy and transparent guidelines. If consensus on the guideline format is reached beforehand, instructions on individual responsibilities within the network are provided, more support staff is employed, and a librarian is engaged to conduct systematic literature searches, then the network approach can be used in other guideline development programs too.

We believe that this approach may apply especially to patients who travel numerous complex pathways. Our study focuses on the network needed for patients who receive multidisciplinary fertility care and form the centre of the network. However, other patients who travel different or multiple complex clinical pathways may also profit from this approach. Multiple networks can be connected or extended where necessary. However, this approach might be less valuable when patients travel a clear monodisciplinary pathway; for example, the pathway for a simple bone fracture. Further research is needed to compare the efficacy of this approach with more traditional approaches regarding content, time investments, and actual adoption of guidelines in a pragmatic randomized controlled trial.

Abbreviations:

CPG, Clinical practice guideline; IVF, in vitro fertilization; MoG, Monodisciplinary guideline; MuG, Multidisciplinary guideline.

References

- 1. Halvorson GC. Health Care Reform Now!: A Prescription for Change. San Francisco, CA: Jossey-Bass, 2007.
- 2. Alston CPL, Halvorson G, Paget L et al.: Communicating With Patients on Health Care Evidence, Discussion Paper. Washington, DC: Institute of Medicine, 2012.
- 3. Novelli WD, Halvorson GC, Santa J. Recognizing an opinion: findings from the IOM evidence communication innovation collaborative. *J Am Med Assoc* 2012;**308**:1531–1532.
- 4. Smith M, Halvorson G, Kaplan G. What's needed is a health care system that learns: recommendations from an IOM report. *J Am Med Assoc* 2012;**308**:1637–1638.
- 5. Landon BE, Grumbach K, Wallace PJ. Integrating public health and primary care systems: potential strategies from an IOM report. *J Am Med Assoc* 2012;**308**:461–462.
- Wynia MK, Von Kohorn I, Mitchell PH. Challenges at the intersection of team-based and patientcentered health care: insights from an IOM working group. J Am Med Assoc 2012;308:1327–1328.
- Burgers JS, Cluzeau FA, Hanna SE *et al.* Characteristics of high-quality guidelines: evaluation of 86 clinical guidelines developed in ten European countries and Canada. *Int J Technol Assess Health Care* 2003;19:148–157.
- Grilli R, Magrini N, Penna A et al. Practice guidelines developed by specialty societies: the need for a critical appraisal. *Lancet* 2000;355:103–106.
- 9. Institute Of Medicine (IOM). *Clinical Practice Guidelines we can Trust*. Washington, DC: National Academy Press, 2011.
- 10. Alonso-Coello P, Irfan A, Sola *I et al.* The quality of clinical practice guidelines over the last two decades: a systematic review of guideline appraisal studies. *Qual Saf Health Care* 2010;**19**:e58.
- 11. Kung J, Miller RR, Mackowiak PA. Failure of clinical practice guidelines to meet institute of medicine standards: two more decades of little, if any, progress. *Arch Intern Med* 2012;**172**:1628–33.
- 12. Shaneyfelt TM, Centor RM. Reassessment of clinical practice guidelines: go gently into that good night. *J Am Med Assoc* 2009;**301**:868–9.
- 13. Cunningham FC, Ranmuthugala G, Plumb J *et al.* Health professional networks as a vector for improving healthcare quality and safety: a systematic review. *BMJ Qual Saf* 2012;**21**:239–249.
- Goodwin NPG, Peck E, Freeman T et al. Managing Across Diverse Networks of Care: Lessons from Other Sectors, Report to the national co-ordinating centre for NHS Service Delivery and Organisation R&D (NCCSDO). NCCSDO, 2004. http://www.sdo.nihr.ac.uk/files/adhoc/39-policy-report.pdf, 12 August 2014, date last accessed.
- Boivin J, Bunting L, Collins JA *et al*. International estimates of infertility prevalence and treatmentseeking: potential need and demand for infertility medical care. *Hum Reprod* 2007;22:1506–1512.
- 16. Gnoth C, Godehardt E, Frank-Herrmann P *et al.* Definition and prevalence of subfertility and infertility. *Hum Reprod* 2005;**20**:1144–1147.
- 17. Centre for Evidence Based Medicine (CEBM). http://www.cebm.net/index.aspx?o=4590, 12 August 2014, date last accessed.
- 18. den Breejen EM, Nelen WL, Knijnenburg JM *et al.* Feasibility of a wiki as a participatory tool for patients in clinical guideline development. *J Med Internet Res* 2012;14:e138.
- Hulscher ME, Laurant MG, Grol RP. Process evaluation on quality improvement interventions. *Qual Saf Health Care* 2003;12:40–46.
- 20. Peters V, Wester F. How Qualitative Data Analysis Software may Support the Qualitative Analysis Process. *Quality & Quantity* 2007;41:635 659.
- 21. Richie J, Spencer L. *Qualitative Data Analysis for Applied Policy Research*. In: *Analysing Qualitative Data*. Edited by Bryman A, Burgess B. London: Routledge 1994;173–194.
- 22. Cunningham FC, Ranmuthugala G, Westbrook JI *et al.* Net benefits: assessing the effectiveness of clinical networks in Australia through qualitative methods. *Implement Sci* 2012;7:108.
- 23. Institute Of Medicine (IOM). Crossing the quality chasm: a new health system for the 21 st century. Washington, DC: IOM, 2001.

- 24. Boivin A, Currie K, Fervers B, G-I-N PUBLIC *et al.* Patient and public involvement in clinical guidelines: international experiences and future perspectives. *Qual Saf Health Care* 2010;**19**:e22.
- 25. Boivin J, Domar AD, Shapiro DB *et al.* Tackling burden in ART: an integrated approach for medical staff. *Hum Reprod* 2012;**27**:941–950.
- 26. Pagliari C, Grimshaw J, Eccles M. The potential influence of small group processes on guideline development. *J Eval Clin Pract* 2001;7:165–173.
- 27. Borgonjen RJ, van Everdingen JJ, Bik CM *et al.* Prospective comparison of three guideline development methods for treatment of actinic keratosis. *BMJ Qual Saf* 2011;**20**:832–841.
- 28. Laliberte L, Fennell ML, Papandonatos G. The relationship of membership in research networks to compliance with treatment guidelines for early-stage breast cancer. *Med Care* 2005;**43**:471–479.
- 29. Ray-Coquard I, Philip T, de Laroche G *et al.* A controlled 'before-after' study: impact of a clinical guidelines programme and regional cancer network organization on medical practice. *Br J Cancer* 2002;**86**:313–321.
- 30. Tolson D, McIntosh J, Loftus L *et al.* Developing a managed clinical network in palliative care: a realistic evaluation. *Int J Nurs Stud* 2007;**44**:183–195.
- 31. Greene A, Pagliari C, Cunningham S *et al.* Do managed clinical networks improve quality of diabetes care? Evidence from a retrospective mixed methods evaluation. *Qual Saf Health Care* 2009;**18**:456–461.
- 32. Rogers S, Humphrey C, Nazareth I *et al.* Designing trials of interventions to change professional practice in primary care: lessons from an exploratory study of two change strategies. *BMJ* 2000;**320**:1580–1583.
- 33. Kaplan HC, Brady PW, Dritz MC *et al.* The influence of context on quality improvement success in health care: a systematic review of the literature. *Milbank Q* 2010;**88**:500–559.
- 34. Krahn M, Naglie G. The next step in guideline development. J Am Med Assoc 2008;300:436–438. 2008:436–438.
- 35. Grimshaw JM, Thomas RE, MacLennan G *et al.* Effectiveness and efficiency of guideline dissemination and implementation strategies. *Health Technol Assess* 2004;8:1–72.



Chapter 4

Feasibility of a Wiki as a Participatory Tool for Patients in Clinical Guideline Development

EME den Breejen, WLDM Nelen, JM Knijnenburg, JS Burgers, RPMG Hermens, JAM Kremer.

J Med Internet Res 2012; 14:138.

Abstract

Background: Patient participation is essential in developing high-quality guidelines but faces practical challenges. Evidence on timing, methods, evaluations, and outcomes of methodologies for patient participation in guideline development is lacking.

Objective: To assess the feasibility of a wiki as a participatory tool for patients in the development of a guideline on infertility determined by (1) use of the wiki (number of page views and visitors), (2) benefits of the wiki (i.e., number, content, and eligibility of the recommendations to be integrated into the guideline), and (3) patients' facilitators of and barriers to adoption, and the potential challenges to be overcome in improving this wiki.

Methods: To obtain initial content for the wiki, we conducted in-depth interviews (n = 12) with infertile patients. Transcripts from the interviews were translated into 90 draft recommendations. These were presented on a wiki. Over 7 months, infertile patients were invited through advertisements or mailings to formulate new or modify existing recommendations. After modifying the recommendations, we asked patients to select their top 5 or top 3 recommendations for each of 5 sections on fertility care. Finally, the guideline development group assessed the eligibility of the final set of recommendations within the scope of the guideline. We used a multimethod evaluation strategy to assess the feasibility of the wiki as a participatory tool for patients in guideline development.

Results: The wiki attracted 298 unique visitors, yielding 289 recommendations. We assessed the 21 recommendations ranked as the top 5 or top 3 for their eligibility for being integrated into the clinical practice guideline. The evaluation identified some challenges to improving the wiki tool, concerning its ease of use, website content and layout, and characteristics of the wiki tool.

Conclusions: The wiki is a promising and feasible participatory tool for patients in guideline development. A modified version of this tool including new modalities (e.g., automatically limiting the number and length of recommendations, using a fixed format for recommendations, including a motivation page, and adding a continuous prioritization system) should be developed and evaluated in a patient-centred design.

Keywords: Wiki, patient participation, infertility, Web 2.0, guideline development.

Introduction

Having patients participate in clinical practice guideline (CPG) development is essential but challenging [1,2]. Their participation is particularly assumed to result in higher-quality guidelines in terms of applicability, acceptability, usefulness, and enhancement of implementation [1-7]. For instance, patient participation is one of the key criteria of the Appraisal of Guidelines Research and Evaluation (AGREE) instrument [8], which is used to assess the methodological quality of guidelines. However, only 25%–50% of CPG developers regularly involve patients [9].

Several practical limitations could explain why patient participation is not common practice in CPG development. First, various methods for patient participation in CPG development can be used, such as conducting in-depth interviews or focus group meetings to explore patients' preferences, asking patients' representatives to comment on drafts of the CPG, or including patients' representatives or patients in the CPG development group [3, 6, 10-14]. However, practical guidance on how and when to apply these methods is lacking [15]. Second, all methods are restricted to including a selected number of patients or patients' representatives and do not involve a large population of patients. Third, transparently integrating patients' preferences into CPG recommendations is difficult and often unclear [16]. Fourth, organizational (e.g., recruitment of participants), financial (e.g., costs of patients' education or for conducting focus groups), and sociopolitical barriers (e.g., CPG developers' resistance to including patients in the CPG group) may impede patient participation in CPG development [13]. Finally, studies on the effectiveness and impact of patient participation are limited [15].

A new methodology for patient participation in CPG development that enables overcoming most of these drawbacks is thus necessary.

Web 2.0 tools offer opportunities to let nonorganized groups participate in a complex process such as CPG development [17-20]. In particular, a wiki, such as Wikipedia, seems to be an easily accessed tool, which enables patients to collaborate in formulating guideline recommendations directly. Ideally, to test the feasibility of such a new method for patient participation in CPG development, an Internet-using young target group such as infertile patients [21-23] is preferred. Infertility is commonly defined as "any form of reduced fertility with prolonged time of unwanted non-conception" [24] and affects approximately 80 million couples worldwide [25, 26]. In this study, we applied wiki technology as a participatory

tool for patients in the development of a multidisciplinary CPG on infertility and aimed to assess its feasibility.

Methods

Setting

Fertility Care

In the Netherlands, fertility care is mostly publically arranged and provided by various professionals. First, fertility care is provided by the general practitioner and may be part of an initial fertility assessment after a prolonged time of unwanted nonconception. Second, the general practitioner can refer couples to a gynaecologist in a general (secondary care) or a university (tertiary care) hospital to complete the fertility assessment, determine a cause of infertility, and define a suitable treatment policy. Third, if a severe male factor is diagnosed, a urologist may be consulted. Furthermore, since infertility has a high emotional and psychological impact, which also interferes with work, a psychologist and occupational physician are regularly engaged in the care pathway. In vitro fertilization and intracytoplasmic sperm injection are provided by 13 licensed hospitals (8 university hospitals, 4 general hospitals, and 1 private clinic). Ovulation induction and intrauterine insemination are performed in all Dutch hospitals. Ovulation induction, intrauterine insemination cycles, and the first three in vitro fertilization or intracytoplasmic sperm injection treatment cycles are reimbursed as part of the basic health care package according to the Health Insurance Act.

Guideline Development

In February 2008, a collaboration of stakeholders (a general practitioner, 2 gynaecologists, a urologist/sexologist, a clinical embryologist, a clinical chemical specialist, a medical psychologist, an occupational physician, 2 patients' representatives, and a researcher) was set up to develop a national multidisciplinary paper-based CPG on infertility. CPGs are defined as sets of evidence- or consensus-based recommendations describing optimal patient care to assist health care professionals and patients in clinical decision-making [2]. The aim of the CPG was to focus on organizational and patient-centred aspects of fertility care. Two representatives of the Dutch patients' association for infertility, Freya, participated
in the CPG development group. However, for direct patient participation in this guideline, we applied a wiki concurrently with this guideline development phase.

Study Objectives

The objective of this study was to assess the feasibility of the wiki as a participatory tool for patient participation in CPG development. The feasibility of the wiki was determined by three end points: (1) use of the wiki and users' characteristics (number of page views and visitors), (2) wiki content quality, particularly the assessment of various aspects of the final set of unique recommendations (i.e., number, content, and their eligibility for integration into the CPG) for high-quality fertility care, and (3) wiki system quality (i.e., patients' facilitators of and barriers to adoption of this wiki as a participatory tool for direct patient involvement in CPG development, as well as potential suggestions for improvement).

Wiki Tool Development

We developed a conventional wiki website using MediaWiki software and made accessible through the Freya website, called FreyaWIKI [27]. During the preparation phase, we first conducted in-depth interviews to obtain initial content for the wiki. Next, we structured the wiki tool according to the topics of the recommendations derived from the interviews.

Obtaining Initial Content of the Wiki Tool from In-Depth Interviews

To obtain the initial content for this wiki, we first conducted 12 semistructured in-depth interviews with infertile couples during different phases of care, from the first visit to the general practitioner, to (non)pregnant status after completing medically assisted reproduction techniques [28]. Patients visiting outpatient clinics in Nijmegen and Amsterdam were consecutively invited to participate through an information letter. Subsequently, 1 researcher (EB) obtained the final consent by telephone. Participants were asked to specify perceived bottlenecks in their fertility care pathway, using an interview guide including the main treatment stages of their fertility care pathway (e.g., treatment by a general practitioner, gynaecologist, or urologist). Interviews were audiotaped and transcribed verbatim. Next, a researcher (EB) and the chief executive of Freya (JK) independently translated these bottlenecks into draft patient recommendations. These draft recommendations were formulated as "I want my doctor to...." Consensus on the formulation of patient draft recommendations was reached through discussion.

Structuring the Wiki Tool

Division of the draft recommendations into sections and subsections determined the structure of the wiki. Draft recommendations were divided into 4 sections (EB, JK), consisting of 3 sections referring to the care delivered by the 3 most involved professionals and a general section for recommendations important to all professionals: general care, care delivered by a general practitioner, gynaecological care, and urological care. To provide more structure in the wiki, the draft recommendations in each of these 4 sections were subdivided into 8 subsections (EB, JK) based on aspects of care that are known to be important to infertile patients: 3 medical-technical aspects (i.e., examination, therapy, and referral), 4 patient-centred aspects (i.e., organization of care, information provision, communication, and staff attitudes), and 1 general aspect (i.e., general) [29]. These subsections were presented on the wiki in the following order: general (recommendations in general and those that don't apply to other care aspects), information provision (recommendations on oral and paper-based information provision), organization (recommendations on the organization of fertility care, for example, adjustment of care between different health care professionals, accessibility of care), staff attitudes (recommendations on the attitude of health care professionals toward the patient, for example, having empathy), communication (recommendations on communication between the health care professional and the patient), examination (recommendations on examinations during fertility care), therapy (recommendations on therapy, namely infertility treatment by, for example, in vitro fertilization), and referral (recommendations on referral from one health care professional to another, for example, from a general practitioner to a gynaecologist). Discrepancies in division and subdivision of the draft recommendations were resolved through discussion.

Patient Participation in CPG Development

Recruiting Participants

We recruited participants for the wiki evaluation through mailings to members of Freya, the Dutch patients' association for infertility; advertisements in Freya's quarterly journal; links on websites of Freya and the professional societies (e.g., general practitioners, gynaecologists, urologists, and clinical embryologists); and links in social media (e.g., Hyves, Twitter, and Facebook). In addition, we sent advertising posters to all 103 clinics offering fertility treatments in the Netherlands for their waiting rooms.

Obtaining Recommendations from Wiki Participants

Formulating Recommendations

From May to December 2008, we presented the draft recommendations for fertility care on the wiki. Patients were invited to modify or refine these recommendations and to add new recommendations. During this process, we asked patients to subscribe voluntarily through an email address and to provide background characteristics for study purposes. After 2 months, when the number of recommendations started to increase, patients and patients' representatives requested us to add 2 sections to the existing structure of the wiki: 1 regarding the care delivered by the laboratory (e.g., recommendations regarding semen analysis), and 1 regarding the care delivered by the remaining professionals who were not represented in a separate section (e.g., recommendations regarding the medical psychologist). Hence, we added 2 sections to the wiki: laboratory and remaining. Next, we recategorized recommendations from the general section regarding care delivered by the laboratory or care delivered by professionals other than the general practitioner, gynaecologist or urologist. After this restructuring of the wiki, the general section contained only recommendations on fertility care in general, thus not referring to the care delivered by 1 of the professionals involved.

Modifying Recommendations

After7 months, we modified the recommendations in several steps. First, we removed duplicate recommendations. Then, if necessary, we moved recommendations into the appropriate sections (EB, JK). Since all recommendations in the remaining section turned out to be more suited to other sections, we eliminated this section. Next, 2 researchers (EB, WN) and the chief executive of Freya (JK) independently assessed the implementability of all recommendations using the Guideline Implementability Appraisal (GLIA) instrument [30]. Discrepancies were discussed and resolved through consensus. Based on the results of this assessment, the recommendations were independently textually refined or modified by a researcher (EB) and the chief executive of Freya (JK). Finally, after consensus was reached on the final formulation, we re-entered the recommendations into the wiki.

Prioritizing Recommendations

All patients visiting the wiki website were invited to prioritize their top 5 (modified) recommendations in each section (for the laboratory section, we asked them to identify their top 3 due to the small number of recommendations). This prioritization was privately conducted by assigning 5, 4, 3, 2, and 1 points for the most important recommendations for determining high-quality fertility care for each of the 5 sections and independently from the subsections.

Assessing Eligibility of the Selected Recommendations

Initially, the CPG development group had intended to integrate this final top selection of patients' recommendations directly into the CPG. However, before integrating these recommendations, the entire CPG development group (n = 11) assessed the eligibility of the recommendations for inclusion in terms of the scope of the guideline.

Evaluation of the Wiki

To evaluate the feasibility of the wiki, we performed a multimethod evaluation study including three components [31]. First, to assess the ability to involve large and diverse patient populations compared with other methods such as interviews, we evaluated wiki use and users' characteristics. Second, we evaluated wiki content quality (i.e., recommendations) and, third, wiki system quality (i.e., ease of use, layout), identifying factors that could potentially influence adoption of the wiki (barriers and facilitators) as well as potential factors for improvement.

Evaluation of Wiki Use and Users' Characteristics

Data on actual use of the wiki (e.g., number of unique visitors, page views) were generated through log files on the website of the patient association (Freya). Unique visitors were determined by IP address logged and stored on the website.

Evaluation of Wiki Content Quality

To evaluate the content quality of the wiki, we assessed various aspects of the final set of unique recommendations, particularly the number of recommendations, their content, and their eligibility for integration into the CPG for high-quality fertility care.

Evaluation of Wiki System Quality

To evaluate the quality of the wiki system and to identify facilitators, barriers, and potential areas of improvement, we conducted an online questionnaire. To gain insight into the thoughts underlying the resulting factors that formed potential facilitators of or barriers to adoption of the wiki and aspects of improvement, we conducted in-depth interviews with wiki users who completed the evaluation questionnaire.

Online Evaluation Questionnaire

During the prioritization phase, patients visiting the wiki website were invited to complete an online evaluation questionnaire. This questionnaire included items regarding users' background characteristics (e.g., age, type of infertility), use of the wiki (e.g., number of visits), and factors that could potentially influence adoption of the wiki (quality of the wiki website, satisfaction, and net benefits) based on the relevant evaluation factors derived from the Human, Organization, and Technology-fit framework [32]. Questions on the potential influencing factors were grouped into 5 sections: ease of use of the wiki website, layout of the wiki website, value of the wiki methodology as a participatory tool for CPG development, content of the wiki website, and experienced privacy on the wiki website. Patients were asked to rate 22 accompanying positively formulated statements on these factors on a 5-point Likert scale from 1 (strongly disagree) to 5 (strongly agree) (Multimedia Appendix 1). After each section, patients were invited to comment. Next, patients were asked to describe their three advantages and disadvantages of the wiki website and potential areas of improvement. Finally, patients were asked for their willingness to participate again in a similar project and for their intention to recommend this wiki.

In-Depth Interviews with Wiki Users

We first summarized the identified influencing factors on adoption of the wiki website and suggested potential areas of improvement. Next, we translated these into a topic list to guide the in-depth interviews. To get both confirmation of and saturation in the thoughts underlying the facilitators of and barriers to adoption and potential areas of improvement of the wiki, 1 researcher (EB) conducted semistructured in-depth interviews with wiki users by telephone. Participants in the questionnaire survey who left their email address were randomly recruited by email. The first part of the interview consisted of open-ended questions, related to thoughts underlying the identified influencing factors on adoption and potentials for improvement of the wiki. Next, patients were asked for additional influencing factors and suggestions for improvement of the wiki. Recruitment continued until saturation of data was achieved. Regarding the starting and stopping criteria according to Francis and colleagues [33], we started with 2 interviews and aimed to repeat cycles of 2 interviews until we obtained no new data. If data saturation was achieved, an additional interview was conducted to attain data saturation.

Data Analysis

We used SPSS 16.0 for Windows, Data Entry 4.0 (IBM Corporation, Somers, NY, USA) to perform descriptive statistical tests on the background characteristics of the wiki participants and to analyse patients' top rankings of the recommendations. The final top selection of recommendations in each section was determined by identifying those with the highest sumscores derived. For analysing the results of the online evaluation questionnaire, we grouped the responses on the 5-point Likert scale into the categories agree (scores 1 and 2), neutral (score 3), and disagree (scores 4 and 5). Items were a priori identified as facilitators of adoption if >50% chose agree (scores 1 and 2) and as barriers to adoption of the wiki website if >50% of the evaluators chose disagree (scores 4 and 5). We used the reported top three advantages and disadvantages and the potential areas of improvement of the wiki to determine the frequency of occurrence of each aspect. We conducted an initial content analysis of all free-text responses to the questionnaire, to determine additional points to be improved (EB, WN).

Qualitative Analysis of the Interviews

All interviews were audiotaped and transcribed verbatim. Data were analysed iteratively and thematically across accounts (EB, JK) [34], according to the relevant factors of the evaluation framework, as used in the questionnaire to identify barriers to and facilitators of adoption and potential areas of improvement of the wiki [32]. Another researcher (WN) independently checked the coding framework and analysis.

Results

Wiki Tool Development

In-Depth Interviews

From the transcripts of 12 in-depth interviews with infertile patients, we translated the perceived bottlenecks into a set of 90 draft patient recommendations and entered them into the wiki (Figure 1).

Figure 1: The process of obtaining recommendations for CPG development



For example, patients perceived a bottleneck in that appointments were possible only during working hours instead of also during the evening, which resulted in difficulties with work. The resulting draft recommendation was formulated as "I want the hospital to provide possibilities to make appointments during evening hours." Other examples of the bottlenecks mentioned were the variation between hospitals' laboratories in performing a semen analysis, unavailability of separate waiting rooms for pregnancy and infertility consultations, and gynaecologists' lack of empathy.

Structure of the Wiki

FreyaWIKI was structured through the division of recommendations into 6 sections. Each of these sections was subdivided into 8 subsections (Figure 2 and 3).

Figure 2: Screenshot of recommendations on FreyaWIKI



@ @ - M F ALLERI OF STREYA Watter 1000 FrevaWiki:Aanbevelingen FREYA Ik ben nieuw hier Wanneer a voor de eestte keer de aanbevelingen wii gaan veranderen, aanvuijonde gegevans in te vuijen. Kiik hiervoor op de volgende link (1) Geef uw mening Kilk Mercadar og het traject verar ta ov menning ever witt geven. Het ta bijserned ere ansheeling vor de hurant, skil dan op fulsam en kijk of levend ov anteving å opgeven keel. Zo nen, dan kan a hen actre lanel Net ta ena port fat vor de gehei zor gield, dan kan u hen gladber in Algemme zorg. Als u een andereling keel, maar a west nel bij welk tapect bij pet, dan han ta dez song doch, der het song de geheel tapect song andereling keel. DK Zoeken Traject · ALGEMENE ZORG · HUISARTS · GYNAECCR.00G · LIROLOOK er Fwe CHREVA-Intern

Figure 3: Screenshot of the FreyaWIKI homepage

Patient Participation in CPG Development

Wiki Use and Users' Characteristics

During 7 months of access, 36,473 wiki pages were viewed. We identified 289 unique users, including 81 registered users who provided background characteristics (Figure 4). The majority of them were female 78/81 (96%), highly educated 54/81(67%), and middle aged (mean 33 years). Median duration of infertility was 30 months (range 0–71 months). More than half 43/81(53%) underwent medically assisted reproduction techniques during the period of their visit. Another 14% (n = 11) stayed childless despite treatment.



Figure 4: Flow of wiki participants trough the study

Wiki Content Quality

Overall, we collected 265 recommendations and modified them into 289 unique recommendations (Figure 1). After patients (n = 80) prioritized the

recommendations by ranking the top 5 or top 3 in each section (we had eliminated the remaining section) according to their importance to high-quality fertility care, we selected 23 recommendations (4 sets of top 5 and 1 set of top 3) for eligibility assessment by the CPG development group (Table 1). We excluded 2 insurance-related recommendations, since they did not meet the scope of the CPG. The CPG development group accepted all of the remaining 21 recommendations, which were integrally integrated into the CPG. More than half (n = 11) of the final set of recommendations concerned the organization of care. Similar to the quality assessment scale used in evidence-based recommendations (levels of evidence A–D) [35], a level of P (patients) was provided for the patients' recommendations and formulated as "Patients would like to...". Participants were informed by email, on the wiki website, and through the websites of Freya and the professional associations of the final CPG that included the literally eligible recommendations of the patients.

Evaluation of Wiki System Quality

Online Evaluation Questionnaire

Of the 80 patients who participated in the prioritization, 45 completed the questionnaire. Of these, 53% (n = 24) visited FreyaWIKI at first while completing the questionnaire, and 93% (n = 42) had never worked with a wiki, other than this one, before. Other background characteristics of the respondents are presented in Table 2. Facilitators of adoption of the wiki, defined as >50% of respondents agreeing (scores 1 and 2) to the relevant statements, were not identified. Barriers, defined as >50% disagreeing (scores 4 and 5) to the relevant statements, were identified in 3 of the 5 sections: ease of use, content of the website, and value of the wiki methodology (Table 3). In decreasing order of the proportion of evaluators who disagreed with the relevant statement, the main identified barriers concerned the findability (82%) and accessibility (78%) of the website, and the suitability of this wiki for obtaining recommendations for CPG development (71%).

Reported advantages of the wiki were the privacy they experienced on the website, the structure of the website linking recommendations to sections on care delivered by fertility professionals, ease of navigation through the website, and the additional value of the wiki website as a source of information and as an opportunity to provide feedback to the care services.

Reported disadvantages of the wiki concerned the content of the wiki website, in terms of the unstructured recommendations not being formulated in a similar way, too much content being visible on one screen, and the nonattractive layout of the wiki website.

The main potential areas of improvement were providing information on treatment options and causal factors of infertility on the wiki website, broadening the marketing of the wiki by placing advertisements in commercial magazines, and communicating information on related activities (Table 4). Overall, 98% of the patients said they would recommend the website and 84% would participate again in a similar project.

Table 1. Final set of the patients' top-5 and top-3 recommendations (n = 23) for the 5 sections, ranked by importance to the quality of fertility care as formulated on the wiki website.

Section	Subsection (aspect of care) ^a	
Genera	al care	
1	I want insurance companies to reimburse six attempts at in vitro fertilization ^b	General
2	I want insurance companies to start counting in vitro fertilization attempts only after oocyte retrieval or even after embryo transfer has been performed ^b	General
3	I want my doctor to practice empathy, instead of only working on the technical or financial part	Staff attitudes
4	I want the hospital to have separate waiting rooms for pregnant women and couples being treated for infertility	Organization
5	I want to be able to arrange appointments during the daytime as well as in the evenings	Organization
Genera	al practice care	
1	I want my gynaecologist and GP ^c to have good communication, so my GP knows what is going on with us	Referral
2	I want my GP to make a referral immediately after we have been trying to conceive for a year	Referral
3	I want to have my first medical consultation with my gynaecologist within 1 month after referral	Organization
4	I want my GP to be informed of possible causes of infertility, in both women and men	General
5	I want my GP to pay attention to nonmedical issues, such as stress, anxiety, relational problems, and sexuality	Communication
Gynae	cologic care	
1	I want also to be able to receive treatments on weekends (Saturdays and Sundays)	Organization
2	I want all members of the fertility treatment team to apply one policy regarding my infertility treatment	Organization
3	I want my gynaecologist to inform me of all possible fertility treatment options, even if these are outside the hospital	Information provision
4	I want my gynaecologist to inform me about the different phases of treatment and their expected time span	Information provision
5	I want assisted hatching to be possible or available in the Netherlands	Therapy
Urolog	ric care	
1	I want my urologist and gynaecologist to have good communication	Organization
2	I want to be informed of the investigations that are to be performed by the urologist	Examination
3	I want to have a permanent urologist who is specialized in infertility	Organization
4	I want to have a consultation with a urologist within 1 month after referral	Organization
5	I want my urologist to involve my partner in the conversation	Communication
Labora	atory	
1	I want to be informed as soon as possible when our embryos do not divide correctly	Organization
2	I want Dutch laboratories to share protocols and learn from each other's experiences	Organization
3	I want to be informed of the causes of nonviability of our frozen embryos, if appropriate	Organization

^a Subsections were derived from the website's structure and located by the user.

^b Recommendation was excluded, since it fell out of the scope of the clinical practice guideline.

^c General practitioner.

<u> </u>	1		
Characteristic	Data		
Gender, n (%)			
Male	0 (0%)		
Female	45 (100%)		
Age (years), mean (SD)	35 (5.24)		
Type of infertility, n (%)			
Primary	15 (33%)		
Secondary	30 (67%)		
Duration of infertility (months), median (range)	36 (0-71)		
Current phase in fertility care, n (%)			
Gynaecologic	19 (42%)		
No pregnancy after fertility treatment	8 (18%)		
Pregnant achieved by fertility treatment	4 (9%)		
Unknown	14 (31%)		
Level of education, n (%)			
Low	0 (0%)		
Intermediate	14 (31%)		
High	31 (69%)		
Membership in Freya, n (%)	24 (53%)		

Table 2: Background characteristics of respondents (n = 45) to the evaluation questionnaire.

Table 3: Patients' barriers to adoption of the wiki (n = 45).

Factor influencing adoption of the wiki	Proportion disagreeing with the factor ^a		
	n	%	
Ease of use of the website			
Findability of the website	37	82%	
Accessibility of the website	35	78%	
Clarity of log-in location on the website	27	60%	
Clarity on the goal of the website	28	62%	
Clarity on instructions for using the website	24	53%	
Efficiency of the website (i.e., speed at which the website enabled users to accurately and successfully add and modify recommendations)	24	53%	
Content of the website			
Comprehensiveness of the clarifying text on the website	30	66%	
Satisfaction with the content of the formulated recommendations	25	56%	
Usefulness of clustering recommendations into sections in searching for existing recommendations	23	51%	
Similarity between formulated recommendations and participants' actual opinions on fertility care	23	51%	
Value of using the wiki			
Suitability of the wiki for obtaining recommendations for clinical practice guideline development	32	71%	
Ease of using the wiki	24	53%	
Accessibility of the wiki	27	60%	

^a Number (%) of participants who rated the positively formulated statements on the evaluation factors as disagree (scores 4 or 5).

In-Depth Interviews

Overall, 11 of the 30 patients who gave their email address in the evaluation questionnaire agreed to participate in the interviews. We conducted 3 interviews. All 3 interviews confirmed barriers to adoption as well as suggestions to improve the wiki, and saturation of the related underlying thoughts was reached (Table 4). All patients reported problems with formulating a recommendation and expressed their wish to add a personal touch to the recommendation (e.g., to explain why something should be done). The introduction of a motivation page, where patients are able to describe why they formulated a recommendation might meet this request. Patients also embraced the missing community feeling as mentioned in the evaluation questionnaire. Introducing a monthly newsletter and automatically sending an email to the person who made the recommendation were suggested.

Aspect of improvement	Respondents suggesting the aspect		Sample translated quotes from in-depth interviews (I) and online questionnaires (Q)
	n	%	
Usability of the website			
Findability of the website	10	22%	Q: Hard to find Q: I think it is awkward that the website is only findable through the Freya website I: I wouldn't know how to find the website, unless through the Freya website
Accessibility of the website	2	4%	I: I was unable to find the log-in location or request a new password
Content of the website			
Comprehensiveness of clarifying text	1	2%	Q: Unclear
Clearness of description of the goal of the wiki	4	8%	I: The description is a bit unclear; therefore, I previously thought to check it more precisely, but I still haven't done this I: I had not concluded that the recommendations were directly integrated in a professional guideline
Clearness of instructions for use	1	2%	
Satisfaction with formulated recommendations	8	16%	I: but there are recommendations I am not satisfied with, I would suggest that participants can prioritize recommendations that they are satisfied with in an earlier stage, then you only have to list the most important recommendations in one screen
Similarity between actual preferences and recommendations	4	8%	Q: I would like to see why a specific recommendation was formulated, separately from the recommendation I: There are too many recommendations on the website, but there are recommendations I am not satisfied with. I would suggest that participants can prioritize recommendations that they are satisfied with

Table 4: Participants' (n = 45^a) suggestions for improving the wiki website.

Table 4: Continued

Aspect of improvement	Respondents suggesting the aspect		Sample translated quotes from in-depth interviews (I) and online questionnaires (Q)	
	n	%		
Content of the website				
Clarity of the structure in which recommendations are placed on the website	30	66%	I: Structure is good but the provided sections are incomplete, for example the care provided by a psychologist or other forms of mental counselling. Psychosocial concerns are always underestimated in fertility care Q: The used structure is good, but for searching an existing recommendation it would be valuable to add a search function to the website	
Relationship between length and number of recommendations and their presentation on one screen	32	71%	Q: There are too many recommendations on the website I: Recommendations are too long, sometimes it's more like a story, which is very interesting, but I wonder if the doctors are taking this as serious input to a guideline Q: The prioritization is hard due to the large number of recommendations	
Education provision on the website	19	42%	 Q: It might be valuable if the website provides usable links to high-quality websites Q: Information on treatment options might enrich the website Q: I would like to find information on causal factors of infertility Q: Practical information about compensations for treatment per insurance company, regional psychological services, plural miscarriages, infertility, and referral 	
Characteristics of the wiki				
Usability of wiki methodology	6	13%	Q: The website is not user friendlythe number of visible recommendations makes it unclear Q: Recommendations given contain too many words I: I really don't have a clue about what constitutes a high- quality recommendation I: It would be valuable to apply an automatic program, through which patients are able to formulate recommendations	
Accessibility of wiki methodol	ogv			
Efficiency of wiki methodology	5	11%	Q: Prioritizing is hard and not efficient in this stage; the list of recommendations is too long I: The efficiency might be improved if you ask patients immediately after formulating a recommendation to prioritize the most important recommendations	
Layout of the website				
Impression of the layout	33	73%	Q: Nonattractive/not a modern/not a fashionable website Q: The layout is not from today Q: Looks unprofessional	
Communication with wiki use	rs			
Marketing	6	13%	Q: This good initiative requires a better marketing approach to reach more participants	
Community feeling of the wiki	3	6%	I: More communication on related activities and results will increase the number of patients that will come back Q: Effect of the recommendations on the guideline is unclear	

^a45 participants completed the online evaluation questionnaire, of whom 3 participated in the in-depth interviews.

All 3 interviewees regarded the website as a valuable source of information, rather than as a tool for modifying recommendations for CPG development. They mentioned that the content of the wiki had been helpful to them in searching for information on experiences regarding infertility treatment and in searching for recognition of their own experiences. Suggestions to improving the awareness of essence of use were suggested within improving the clearness of instructions.

Discussion

Principal Results

In this study, we showed that the wiki is a feasible tool to ensure active patient participation in the development of a Dutch multidisciplinary CPG on infertility. The high numbers of page views (36,473), unique visitors (298), and recommendations formulated (289) implies patients' willingness and ability to contribute to CPGs through a wiki-based method. We also showed that such a wiki is a useful information source for patients.

Second, we gained a final set of 21 selected recommendations, which were assessed as being eligible to be integrated directly and transparently into the CPG. Third, patients had positive views on the experienced privacy, ease of navigation, divisional structure of the wiki, and its potential befits. A total of 98% of the patients would recommend the website and 84% would participate again in a similar project. This study also provided some important suggestions to improve this participatory tool for patients in the development of CPGs, concerning ease of use, content and layout of the website, and characteristics of the wiki tool.

Comparison with Existing Techniques

Several studies on specialized medical wikis (e.g., wikis that fall outside the scope of a general encyclopaedia) have been published, but most particularly focus on education of medical students [36] or collaboration between health care professionals [37,38], rather than on patients, and did not include a process evaluation. Only Gupta and colleagues [39] and Archambault [40] involved a group of preselected patients as well as professionals in the development of an asthma action plan through a wiki. However, results are premature, since this study was conducted over a very short time period (weeks), and a wiki needs more time to build content (approximately 7–8 months) [41]. Furthermore, their evaluation of

the wiki tool was not focused on patients' experiences and was less extensive than our multifaceted approach to gaining insight into patients' barriers to adoption of our wiki. In this study, we involved a large number of patients (298), which cannot be realized using traditional methods, such as focus groups, in which participation is generally restricted to a maximum of 8 participants [42]. We even assessed the final selection of top recommendations for their eligibility for direct integration into the CPG. Thus, the patients' contribution to the CPG was clearly illustrated by integrating their recommendations in their entirety, indicated by the new P level (Patients). We also addressed other practical limitations of the methods used to enhance patient participation in CPG development, such as organizational (e.g., recruitment of participants), financial (e.g., travel costs), and socio-political (e.g., professional resistance to including patients in CPG development group) constraints.

Professionals and patients' representatives could also use the wiki and had the opportunity to informed themselves about patients' views and to bring up content for discussion in the CPG development group. According to the results of the evaluation questionnaire and the interviews, this content was also helpful to patients as an information source, which may also explain the relatively large number of page views. Although providing information was not the initial goal of this wiki, its relevance is in agreement with published literature on conventional wikis [19] and with European patients' perception of the importance of the Internet as a source of information [43]. Hence, this unintended but solid flaw concurrently yields challenges for improvement and might be aided by providing clearer instructions for use and description of the goal of the wiki, but also addresses important implications for future studies in this field. Next to the informational value of formulated recommendations for high-quality care, attention should be paid to useful links to relevant websites that may potentially attract more patients to the wiki website and increase the chances for adoption of an improved version of the wiki.

Although drawbacks to active patient participation methods were reduced, this study drew attention to some other potential implications derived from patients' suggestions that might improve the use of a future medical dedicated wiki for this purpose exclusively. First, structuring recommendations and limiting the number and length of recommendations to presentation on one screen may improve usability [44]. Second, using a fixed format in the formulation of recommendations, based on relevant items of the GLIA instrument, may not only improve usability

and accessibility of the wiki [30,44], but may also improve the efficiency of the wiki and the usefulness of recommendations in being integrated directly into the CPG. Introducing a motivation page might give patients the opportunity to add a personal touch to the recommendation. Third, a prioritization system, continuously refining the similarity between patients' perspectives and the top5 recommendations (e.g., by rating recommendations after every contribution), could improve the tools' efficiency by avoiding separate prioritization of recommendations and could improve patients' satisfaction with the highest-rated recommendations. This modality would also allow more flexible use by CPG developers at the time of their choosing. In addition to the suggested modalities, some known refinements in overall usability (e.g., findability, prominent log-in location), content (comprehensiveness of text), and layout of the website might improve use of the wiki and would be reduced by repeated cycles of design, evaluation, and redesign [45,46]. Furthermore, a user-centred design, in which patients codevelop such new modalities, may improve future implementability and provide chances for local adaptation of a redesigned wiki website [47,48].

Both the feasibility of a wiki as a participatory tool for patients in the development of CPGs and the recommendations for future wiki-based initiatives illustrate the value of eHealth. With this in mind, numerous participatory applications based on wikis are conceivable and may be valuable in various fields of research. In the field of guideline development, guideline-derived initiatives actively involving patients in the development of patient information leaflets or treatment action plans, in addition to fully online-based CPGs, may also benefit from our results. Finally, our results add to the knowledge base about wikis in health care [49].

Limitations

This wiki has been tested in the field of infertility care, representing a relatively young target group [50]. More than 98% of this group use the Internet [21]. This participant characteristic is associated with more frequent health-related Internet use [51-53]. Therefore, the participants in our study were an ideal subgroup for testing and evaluating a wiki-based method, which argues against the generalizability of our findings to other patient groups. Nevertheless, health-related Internet use in Europe is increasing over time [54]. Hence, it seems to be a question of time until older people or their caregivers, or both, will be using such tools [55]. Furthermore, this feasibility study provided an important exploratory evaluation component, which resulted in valuable information for future studies

in this field but also had certain limitations. First, based on the results of a recent systematic review from Gagnon and colleagues [56], we acknowledge that the items used in our evaluation questionnaire might be incomplete. However, the results of our study add to those from the limited number of previously published studies on patients' facilitators of and barriers to adoption of eHealth applications [57,58]. Second, the heuristics used were not based on a validated questionnaire and were too limited for drawing conclusions on the usability that patients perceived. Therefore, a next step in future development of a wiki-based participatory tool for patients in CPG development should be to include a broader evaluation of the potentially influencing factors on adoption, including more organizational factors and a heuristic evaluation.

Third, the participation rate in the evaluation of the wiki might have subjected our study to a participation bias of potentially the most motivated wiki users. However, this is a known limitation in the active use of wikis in general: the most motivated users provide most of the content [19]. Finally, this feasibility study did not assess the representativeness of either the participants or the final set of recommendations in the wiki.

Conclusions

The wiki is a promising and feasible tool to actively involve patients in CPG development. To improve the tool's ease of use and practical aspects to enhance direct integration of recommendations into the CPG, a more specialized and refined wiki should be developed. This should include new modalities, such as automatically shortening the number and length of recommendations, using a fixed format for formulation of recommendations, using a continuous prioritization system for selection of the most important recommendations, and including a separate motivation page. Furthermore, in the development, attention should be paid to the informational character of such a wiki. To improve future implementability, a modified tool should preferably be codeveloped and evaluated by patients in a user-centred design study. Furthermore, representativeness of patients and recommendations should be integrated into this next phase.

Abbreviations: AGREE, Appraisal of Guidelines Research and Evaluation; CPG, clinical practice guideline; GLIA, Guideline Implementability Appraisal

Reference list

- 1. Nilsen ES, Myrhaug HT, Johansen M *et al.* Methods of consumer involvement in developing healthcare policy and research, clinical practice guidelines and patient information material. *Cochrane Database Syst Rev* 2006;**3**:CD004563.
- 2. Institute Of Medicine (IOM). *Clinical Practice Guidelines we can Trust*. Washington, DC: National Academy Press, 2011.
- 3. van Wersch A, Eccles M. Involvement of consumers in the development of evidence based clinical guidelines: practical experiences from the North of England evidence based guideline development programme. *Qual Health Care* 2001;**10**:10-6.
- Crawford MJ, Rutter D, Manley C *et al.* Systematic review of involving patients in the planning and development of health care. *BMJ* 2002;**325**:1263.
- Burgers JS, Fervers B, Haugh M *et al.* International assessment of the quality of clinical practice guidelines in oncology using the Appraisal of Guidelines and Research and Evaluation Instrument. J Clin Oncol 2004;22:2000-7.
- 6. Bastian H. Raising the standard: practice guidelines and consumer participation. *Int J Qual Health Care* 1996;**8**:485-90.
- 7. Gagliardi AR, Brouwers MC, Palda VA *et al.* How can we improve guideline use? A conceptual framework of implementability. *Implement Sci* 2011;**6**:26.
- AGREE Collaboration. Appraisal of Guidelines Research and Evaluation (AGREE Instrument). London, 2001. URL: http://www.agreetrust.org Archived by WebCite* at http://www.webcitation. org/65UXoyUUk
- 9. Schunemann HJ, Fretheim A, Oxman AD. Improving the use of research evidence in guideline development: 10. Integrating values and consumer involvement. *Health Res Policy Syst* 2006;4:22.
- 10. Rogers WA. Are guidelines ethical? Some considerations for general practice. Br J Gen Pract 2002;52:663-8.
- 11. National Institute of Clinical Excellence (NICE). The guidelines' manual. London: NICE, 2009. URL: www.nice.org.uk Archived by WebCite* at http://www.webcitation.org/65UXx2saM
- Scottish Intercollegiate Guidelines Network (SIGN). SIGN 50: A guidelines' developer handbook. Edinburgh: SIGN, 2008. URL: http://www.sign.ac.uk/pdf/sign50.pdf Archived by WebCite^{*} at http:// www.webcitation.org/65UY1tSVw
- 13. Diaz Del Campo P, Gracia J, Blasco JA *et al.* A strategy for patient involvement in clinical practice guidelines: methodological approaches. *BMJ Qual Saf* 2011;**20**:779-84.
- 14. Legare F, Boivin A, van der Weijden T *et al.* Patient and public involvement in clinical practice guidelines: a knowledge synthesis of existing programs. *Med Decis Making* 2011;**31**:E45-74.
- 15. Boivin A, Currie K, Fervers B *et al.* Patient and public involvement in clinical guidelines: international experiences and future perspectives. *Qual Saf Health Care* 2010;**19**:e22.
- 16. Krahn M, Naglie G. The next step in guideline development: incorporating patient preferences. *J Am Med Assoc* 2008;**300**:436-8.
- 17. Cross M. How the internet is changing health care. BMJ 2008;337:a883.
- 18. Giustini D. How Web 2.0 is changing medicine. BMJ 2006;333:1283-84.
- 19. Heilman JM, Kemmann E, Bonert M *et al.* Wikipedia: a key tool for global public health promotion. *J Med Internet Res* 2011;**13**:e14.
- 20. Trevena L. WikiProject medicine. BMJ 2011;342:d3387.
- 21. Haagen EC, Tuil W, Hendriks J *et al.* Current Internet use and preferences of IVF and ICSI patients. *Hum Reprod* 2003;**18**:2073-8.
- 22. Weissman A, Gotlieb L, Ward S *et al.* Use of the internet by infertile couples. *Fertil Steril* 2000;**73**:1179-82.
- 23. Wischmann T. Implications of psychosocial support in infertility--a critical appraisal. J *Psychosom Obstet Gynaecol* 2008;**29:**83-90.
- 24. Gnoth C, Godehardt E, Frank-Herrmann P *et al.* Definition and prevalence of subfertility and infertility. *Hum Reprod* 2005;**20**:1144-7.

- 25. Taylor A. ABC of subfertility: extent of the problem. BMJ 2003;327:434-6.
- 26. Nachtigall RD. International disparities in access to infertility services. Fertil Steril 2006;85:871-5.
- 27. UMC St Radboud, 2008. FreyaWIKI URL: http://www.freyawiki.nl. Archived by WebCite^{*} at http:// www.webcitation.org/65UYXww7d
- 28. Zegers-Hochschild F, Adamson GD, de Mouzon *J et al. International* Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) revised glossary of ART terminology, 2009. *Fertil Steril* 2009;**92**:1520-4.
- 29. Dancet EA, Nelen WL, Sermeus *W et al.* The patients' perspective on fertility care: a systematic review. *Hum Reprod Update* 2010;**16**:467-87.
- 30. Shiffman RN, Dixon J, Brandt C *et al.* The GuideLine Implementability Appraisal (GLIA): development of an instrument to identify obstacles to guideline implementation. *BMC Med Inform Decis Mak* 2005;**5:**23.
- 31. Arain M, Campbell MJ, Cooper CL *et al.* What is a pilot or feasibility study? A review of current practice and editorial policy. *BMC Med Res Methodol* 2010;**10**:67.
- 32. Yusof MM, Kuljis J, Papazafeiropoulou A et al. An evaluation framework for Health Information Systems: human, organization and technology-fit factors (HOT-fit). Int J Med Inform 2008;77:386-98.
- 33. Francis JJ, Johnston M, Robertson C *et al.* What is an adequate sample size? Operationalising data saturation for theory-based interview studies. *Psychol Health* 2010;**25**:1229-45. PMID:20204937
- 34. Silverman D. Doing qualitative research. 3rd edition. London: Sage Publications Ltd, 2009.
- Phillips B, Sackett D, Badenoch D et al. Levels of Evidence. Centre for evidence based medicine, 2009. URL: http://www.cebm.net/index.aspx?o=4590 Archived by WebCite* at http://www.webcitation. org/68aRCTclX
- 36. Jalali A, Mioduszewski M, Gauthier M *et al.* Wiki use and challenges in undergraduate medical education. *Med Educ* 2009;**43**:1117.
- 37. Naik AD, Singh H. Electronic health records to coordinate decision making for complex patients: what can we learn from wiki? *Med Decis Making* 2010;**30**:722-31.
- 38. Archambault PM, Legare F, Lavoie A, *et al.* Healthcare professionals' intentions to use wiki-based reminders to promote best practices in trauma care: a survey protocol. *Implement Sci* 2010;5:45.
- 39. Gupta S, Wan FT, Newton D *et al.* WikiBuild: A New Online Collaboration Process For Multistakeholder Tool Development and Consensus Building. *J Med Internet Res* 2011;**13**:e108.
- 40. Archambault PM. WikiBuild: a new application to support patient and health care professional involvement in the development of patient support tools. *J Med Internet Res* 2011;**13**:e114
- 41. Hansen DL. Knowledge Sharing, Maintenance, and use in Online Support Communities: The University of Michigan, 2007. URL:http://deepblue.lib.umich.edu/bitstream/2027.42/57608/2/shakmatt_1.pdf Archived by WebCite* at http://www.webcitation.org/68aQHFxWs
- 42. Pope C, van Royen P, Baker R. Qualitative methods in research on healthcare quality. *Qual Saf Health Care* 2002;**11**:148-52.
- 43. Kummervold PE, Chronaki CE, Lausen B *et al.* eHealth trends in Europe 2005-2007: a populationbased survey. *J Med Internet Res* 2008;**10:**e42.
- 44. Spyridakis JH. Guidelines for Authoring Comprehensible Web Pages and Evaluating Their Success. *Technical Communication* 2000;47:359-82. URL:http://www.ingentaconnect.com/content/ stc/tc/2000/00000047/00000003/art00008 Archived by WebCite^{*} at http://www.webcitation. org/65UYhsQro
- 45. Gustafson DH, Wyatt JC. Evaluation of ehealth systems and services. BMJ 2004;328:1150.
- 46. Kushniruk A. Evaluation in the design of health information systems: application of approaches emerging from usability engineering. *Comput Biol Med* 2002;**32:**141-9.
- 47. Taylor HA, Sullivan D, Mullen C *et al.* Implementation of a user-centered framework in the development of a web-based health information database and call center. *J Biomed Inform* 2011;44:897-908.
- 48. Roehrer E, Cummings E, Ellis L *et al.* The role of user-centred design within online community development. *Stud Health Technol Inform* 2011;**164**:256-60.
- 49. Archambault PM, van de Belt TH, Grajales FJ *et al.* Wikis and collaborative writing applications in health care: a scoping review protocol. *JMIR Res Protoc* 2012;1:e1.

- 50. Brandes M, Hamilton CJ, Bergevoet KA *et al.* Origin of multiple pregnancies in a subfertile population. *Acta Obstet Gynecol Scand* 2010;**89:**1149-54.
- 51. Atkinson NL, Saperstein SL, Pleis J. Using the internet for health-related activities: findings from a national probability sample. *J Med Internet Res* 2009;11:e4.
- 52. Baker L, Wagner TH, Singer *S et al.* Use of the Internet and e-mail for health care information: results from a national survey. *J Am Med Assoc* 2003;**289**:2400-6.
- 53. Cotten SR, Gupta SS. Characteristics of online and offline health information seekers and factors that discriminate between them. *Soc Sci Med* 2004;**59**:1795-806.
- 54. Andreassen HK, Bujnowska-Fedak MM, Chronaki *et al.* European citizens' use of E-health services: a study of seven countries. *BMC Public Health* 2007;7:53.
- 55. Karunanithi M. Monitoring technology for the elderly patient. Expert Rev Med Devices 2007;4:267-77.
- Gagnon MP, Desmartis M, Labrecque M *et al.* Systematic review of factors influencing the adoption of information and communication technologies by healthcare professionals. *J Med Systems* 2012;36:241-77.
- 57. Chhanabhai P, Holt A. Consumers are ready to accept the transition to online and electronic records if they can be assured of the security measures. *Med Gen Med* 2007;**9**:8.
- 58. Gagnon MP, Shaw N, Sicotte C *et al*. Users' perspectives of barriers and facilitators to implementing EHR in Canada: a study protocol. *Implement Sci* 2009;**4**:20.

Multimedia Appendix 1: Constructs of the online evaluation questionnaire

Statements (n=22) rated on a 5-point Likert scale (1= strongly agree, 5= strongly disagree)

Ease of Use of the website

- I am able to find the website easily
- The website has a good availability
- The website has a clear place for login
- The goal of the website is clear to me
- The instructions for use of the website are clear to me
- The instructions for modifying previously formulated recommendations and adding new recommendations are clear to me
- The use of the website is efficient
- (speed at which the website enables a user to accurately and successfully add and modify recommendations)
- Navigating through the website is easy
- The links on the website are functional
- It is clear to me where to ask questions and/or report problems with the website

Layout of the website

- The used layout makes the website accessible
- The used layout encourages the use of the website
- The layout of the website is conveniently arranged

Content of the website

- The content on the website is well organized
- The clarifying text on the website is easily understandable
- I am satisfied with the content of the recommendations formulated on the website
- The clustering of recommendations into different sections on the website is useful to search recommendations (general care, gynaecologic care etc.)
- The recommendations formulated on the website are in agreement with my actual opinion on fertility care in the Netherlands

Value of the used wiki

- The used wiki is a suitable way of gaining recommendations for a national guideline
- The used wiki is easy in use
- The used wiki is easy accessible

Privacy on the website

• I am not afraid for abuse of my personal data on the website

Additional open questions

- Can you provide the three advantages of the website?
- Can you provide the three disadvantages of the website?
- o Can you provide potentials for improvement of the wiki-website?
- Would you recommend wikifreya to others?
- o Would you re-participate in a similar project in the future?
- Do you have any additions to his questionnaire?
- = statement
- o = open question



Chapter 5

Patient partnership in guideline development: a mixed-method evaluation of an online participatory tool

EME den Breejen, RPMG Hermens, FAM Kersten, JM Knijnenburg, WLDM Nelen, JAM Kremer.

Submitted

Abstract

Background: Participation of patients in guideline development is advocated, but transparent approaches to facilitate this have hardly been practiced. A collaborative writing tool such as a wiki is promising for such participation, but needs customization.

Objective: To evaluate the use and benefits of a specialized online participatory tool to facilitate patient partnership in guideline development.

Methods: A specialized online participatory tool was developed based on (dis) advantages that resulted from a previous pilot study of a wiki tool. We used a mixed method to evaluate its use and benefits. Outcome measurements for use included: actual use of the tool (number of unique visitors, registered participants, and visits), the usability of the tool measured on a SUS-scale (0–100), and representativeness of visitors compared to a valid representative Dutch hospital cohort. Outcome measurements for benefits on guideline development included: number of newly generated and modified recommendations, number of prioritizations, and the change over time of the top five recommendations.

Results: In 12 months, the tool welcomed 3028 unique visitors, of which 87 were registered participants. The tool enabled a broad and representative (age (P=0.39), type of infertility (P=0.31), and percentage of childlessness (p=0.71)) female target group (n=75) compared to a hospital group (n=200) to participate. Participants delivered a set of 50 clear and prioritized recommendations for clinical guidelines on Dutch fertility care. Overall, 39 out of 45 registered participants for the evaluation qualified the tool as highly usable (median SUS-score=82.5).

Conclusions: Using this specialized online participatory tool is a feasible method of involving a broad group of representative infertile patients in guideline development. This paper can be used as a practical guide for policymakers, guideline developers, and patients' organizations that are willing to facilitate patient partnership in guideline development in any healthcare setting.

Key words: patient-partnership, patient-centredness, wiki, guideline development, infertility, E-Health.

Introduction

To pave the way to patient-centred care, patient partnership as a basic principle of healthcare should be firmly embedded [1–4]. The Internet plays a crucial role herein. Patients become active partners in their own treatment by using online decision-making tools, accessing and writing patient information, accessing their personal health record, and even connecting to medical doctors or professionals via online communities [5–10]. However, in clinical guideline development, which can be seen as the basis for optimizing high-quality patient-centred care, patient partnership is still underdeveloped. Determining factors in choosing whether to more or less actively involve patients in the clinical guideline development process can probably be identified as practical barriers. These barriers include the various methods that exist for patient involvement in guideline development, the haziness in how and when to apply these methods most effectively, the difficulty in transparently integrating patients' preferences into guideline recommendations, the representativeness of participating patients, and costs [11–19]. Likely, online tools are relatively new in this field, but may overcome these barriers and facilitate patient partnership in guideline development. Publications regarding the use and evaluation of collaborative online writing tools to involve patients in the development of quality instruments are scarce, but promising [20, 21].

A previous pilot study showed that a wiki is a promising and feasible tool for the participation of a broad group of non-organized infertile patients in Clinical Practice Guideline (CPG) development [20]. However, this tool still needs customization to bridge patients' preferences for its use and the goal of directly collecting prioritized, authentic patient recommendations for CPGs [20]. Additionally, the lack of transferability of this tool to other target groups is a potential drawback.

Therefore, we developed and implemented a specialized online participatory tool that can be adapted to various healthcare areas (in this study, fertility care) and that is tailored to the (dis)advantages that resulted from the pilot study. This preliminary tool presented in the pilot study includes a basic wiki tool for formulation and prioritization of patients' recommendations. We evaluated this specialized online participatory tool for patients regarding its use and benefits for CPG development.

Methods

Setting: Dutch fertility care

Infertility is estimated to affect 80 million couples worldwide [22,23]. It is defined as the couples' inability to achieve pregnancy after having at least one year of regular unprotected sexual intercourse [24]. In the Netherlands, fertility care has been publicly arranged on three levels. Primary care is provided by general practitioners (GPs) and may comprise part of an initial fertility assessment. If necessary, a GP can refer couples to a gynaecologist in a general (secondary care) or a university (tertiary care) hospital, who can complete this initial fertility assessment, determine a cause of infertility, and define a suitable treatment plan. If a severe male factor is diagnosed, couples are also referred to a urologist. Nurses, biochemists, and clinical embryologists are also involved in assessments and preparations for Medically Assisted Reproductive (MAR) techniques, such as In Vitro Fertilization (IVF). Since infertility has a high emotional and psychological impact, which may also interfere with people's jobs, medical psychologists and occupational physicians are regularly involved in patients' clinical care pathways [25]. The complexity of this condition affecting young couples and its multidisciplinary care pathway possibly elucidates the active form in which Freya, the Dutch patients' association for infertility, supports infertile patients (www.freya.nl).

Development of the tool

The principles guiding the initial design of the specialized online participatory tool for patients in CPG development were derived from a previous feasibility study on a basic wiki as a participatory tool for Dutch fertility patients in CPG development [20]. Based on these results, a prototype of the specialized online participatory tool for CPG development that can be adapted to every healthcare setting and usable for both end-users (i.e. guideline developers and patients) was developed and pilot tested.

Prototype development and pilot test

In January 2010, a multidisciplinary team (two clinical guideline developers, two gynaecologists, a website developer, and a board member of Freya) was assembled to develop a prototype of the specialized online participatory tool. Goals for improving the basic wiki tool included lowering the level of moderation of patients' recommendations needed and increasing the direct usability of patients'

recommendations for uptake in the guidelines. Facilitating the formulation of these recommendations by patients using a standardized format as well as creating the ability to continuously prioritize recommendations introducing a star-rating system were other important improvement goals. The initial prototype of the specialized online participatory tool was pilot tested and re-designed by two expert panels including the two types of end-users of the tool: one patients' panel (n=8) and one clinical guideline developers' panel (n=6), including one web designer. The tool was successively re-designed through the input of both panels through three steps: 1) redesign of the homepage and registration page; 2) redesign of the recommendations pages, including the prioritization of recommendations; and 3) final assessment of the re-designed tool. In each round, both types of end-users provided their suggestions for improvement as a whole by completing a written questionnaire regarding their perceived advantages and disadvantages as well as their suggestions for improvement. This questionnaire was based on the relevant items of the framework of Yusof and colleagues for the evaluation of e-health initiatives [26]. Items included: ease of use of the tool, layout of the tool's website, value of the participatory tool for CPG development, content of the tool's website, and experienced privacy on the tools' website. Additionally, the first and the last step included an assessment of the usability of the tool by using the System Usability Scale (SUS) questionnaire [27].

Description of the specialized online participatory tool

The final version of the specialized online participatory tool was fully based on open-source software and made accessible over 12 months at www.freyawiki.nl. The homepage included a description of the tools' goals and a navigation menu for linking to five main pages: the recommendations page, the discussion page, the chat page, the frequently asked questions page, and the registration page (Figure 1). On the recommendations page, visitors could define or modify recommendations according to the statements of the GuideLine Implementability Appraisal (GLIA) instrument [28]. To help patients formulate clear recommendations as supported by this instrument, a template was used to address the following questions: (1) under what circumstances?, (2) has who?, (3) with what level of obligation?, (4) to do what?, (5) to whom?, and (6) how? Controlled natural language was applied to create and populate a template for recommendations (Figure 2). The question 'why' was posed on a linked, but separate, motivation page to enable patients to express their motivation for their recommendation. By using the template,



Figure 1: Screenshot of the homepage of the specialized online participatory tool

Figure 2: Screenshot of the recommendations' page



participants were also able to modify existing recommendations. The specialized online participatory tool was firstly populated with 21 initial recommendations based on the prioritized patients' recommendations included in the Dutch network guideline on subfertility [20,29]. These initial recommendations for high-quality fertility care were distributed according to seven different phases of fertility care: General care (n=3), General practitioner care (n=5), Gynaecologic care (n=5), Urologic care (n=5), and Laboratory phase (n=3). To help participants search existing recommendations, a search engine was added to each page of the website. Furthermore, participants were asked to rate (1–5 stars) the existing recommendations, including their own recommendation(s), according to each one's level of importance for high-quality fertility care. The actual top five per care phase were illustrated on the individual recommendation pages. A discussion forum page and a chat page provided visitors the opportunity to discuss the recommendations with co-users of the tool.

Evaluation of the tool

Study population

Potential participants for the evaluation of the tool were invited through an advertisement on the website of the previous pilot version of the basic wiki tool [20]. Furthermore, they were invited through mailings to members of Freya, advertisements in Freya's quarterly journal, links on Freya's website, links on websites of allied professional societies (i.e. general practitioners, gynaecologists, urologists, and clinical embryologists), and links on social media channels (i.e. Twitter and Facebook). In addition, we sent advertising posters and business cards to all 103 Dutch clinics offering fertility treatments in the Netherlands for their waiting rooms at the departments of urology and gynaecology.

Evaluation design of the tool

We evaluated the tool with automatically generated data and questionnaires regarding its use and benefits for CPG development. Outcome measurements for use included: actual use of the tool (number of unique visitors, registered participants, and visits), the usability of the tool, and representativeness of participants. Outcome measurements to evaluate its benefits for CPG development included: number of newly developed and modified recommendations, number of performed prioritizations (total and per care phase), and the change over time of the top five recommendations (overall and per care phase).

Data collection

Use of the tool

Actual use

On the homepage, all visitors were asked to create a nickname and password, which was mandatory for actively using the tool. Additionally, visitors were asked to voluntarily fill out a registration form for study purposes. This registration form consisted of two parts, including questions on: 1) conventional background characteristics (i.e. age, gender, and level of education) and 2) infertility-related variables (i.e. source of infertility (primary/secondary), having a living child (yes/ no), duration of infertility (months), and last treatment phase). Additionally, participants were asked to provide their email address for receiving a monthly newsletter. To assess the use of the tool, the number of unique visitors, registered participants, and visits were recorded. Members of the project were excluded from participation. Data were automatically generated on the website and collected.

Usability of the tool

For assessing the usability of the tool, we used the validated ten-item System Usability Scale (SUS), which has a high level of face validity for measuring usability of software or information technology [27]. With this SUS all registered participants of the specialized online participatory tool were asked to score 10 usability statements on a five-point Likert scale. The statements covered a variety of aspects of system usability (such as the need for support, training, and complexity) measured with scores from 0 to 100. The target SUS score was >70, representing 'good' usability [30]. The link to this survey was included in the monthly newsletters, which are sent to all registered participants who provided their email address as willing participants in the evaluation of the tool.

Representativeness of users

To assess the representativeness of the registered participants, their background characteristics were compared to the characteristics of a valid representative Dutch hospital cohort of female infertile patients [31]. The sample size of this hospital population was calculated at 170 by applying the formula on a precise estimate of a proportion: $N=(p^*(1-p) *Z^2_{a/2})/d^2$, using an estimated proportion of p=0.5, a proportion of error of d=0.075, and a degree of confidence of $Z^2_{a/2}$ =1.96.

Considering the possibility of missing data, the N was enlarged to 200 patients. Based on the results of the cohort study of Brandes and colleagues, the hospital group was distributed between patients in an IVF clinic and a satellite clinic into a 2:3 ratio [31]. Accordingly, we used background characteristics of 80 patients visiting the regional IVF clinic and 120 female infertile patients visiting the regional satellite clinic. Both clinics were based in the east region of the Netherlands. Data of the hospital group were collected from patients' electronic and written health records. Patients' education level was derived from their occupations, since education level was not registered. If their occupation did not refer to the education level directly, data were recorded as missing.

Benefits of the tool

Recommendations

To collect data on newly developed and modified recommendations, the following aspects were automatically generated on and collected from the website: (1) the total number of unique patients' recommendations, (2) the total number of modifications to these recommendations, (3) the total number of prioritizations on these recommendations, (4) the change over time of the top five recommendations and (5) total number of performed prioritizations. Next, we collected all final top 3 or top 5 rankings per care phase and compared them with the initial 21 recommendations used to populate the tool at the start of the project. Additionally, we identified differences in the top fives of recommendations per care phase over time.

Data analysis

All data collected from the website (participants' background characteristics, number of new and modified recommendations, number of prioritizations) and scores on the items of the SUS were descriptively analysed using SPSS 16.0. For calculating the SUS score, we firstly summed the score contributions of each item (0-4). For items 1, 3, 5, 7, and 9, the score contribution was calculated as the scale position minus 1. For items 2, 4, 6, 8, and 10, the contribution is 5 minus the scale position. Finally, the sum of the scores was multiplied by 2.5 to obtain the overall value of System Usability ranging from 0-100 [27–30]. For comparisons between users' characteristics and the characteristics of the representative Dutch hospital population, we statistically analysed the data using the unpaired t-test (i.e.

age, infertility duration, and total treatment duration) and the chi-square test (i.e. education level, primary/secondary infertility, childless, and type of treatment). All reported P values were two sided, with P<0.05 considered to be significant.

Results

Use of the tool

Actual Use

In 12 months, the specialized online participatory tool welcomed 3028 unique Dutch visitors. Of these visitors, 95 visitors completed a registry form. Of the registered participants, eight participated in the project and were therefore excluded. The remaining 87 registered participants included 12 men and 75 women. Those 3028 visitors viewed 11.658 pages and 649 (21%) of them visited the tool more than once. Visitors viewed on average 3.28 pages per visit. Overall, visitors spent a mean time of 2 minutes and 26 seconds on the tool, new visitors 1 minute and 36 seconds, and recurrent visitors 5 minutes and 36 seconds per visit. Of all visitors, 23% visited the tool directly. Other landing pages included the website of the previous basic wiki tool (50%), Google (13%), Twitter (13%), and other (1%).

Usability of the tool

Of the 87 registered participants, 45 (52%) indicated on the registry form that they were willing to participate in the SUS evaluation of the tool. Of these 45 potential participants for the evaluation that received the link to the questionnaire by email, 39 (87%) performed the SUS evaluation of the tool. The median overall score was 82.5, ranging from 70 to 90, corresponding with good usability for the tool.

Representativeness of users

Female active registered participants (n=75) of the specialized online participatory tool were representative regarding their age (P=0.39), type of infertility (i.e. primary/secondary) (P=0.31), and percentage of childlessness (P=0.71) compared to a valid hospital group. They had a significantly longer duration of infertility and treatment period, were within a more advanced treatment phase, and were more highly educated than the hospital group (Table 1).
Characteristics	Participants (n=75)	Hospital cohort (n=200)	
	Median [Range] or (%)	Median [Range] or (%)	Р
	Ť	·	value
Age (years)	34 [19-51]	32 [21-43]	0.06ª
<25	4 (6%)	10 (5%)	
25-35	45 (62%	142 (71%)	0.39ª
>35	23 (32%)	48 (24%)	
Missing	3	0	
Education level ^b			< 0.01°
Low	1 (1.5%)	37 (20%)	
Middle	14 (21%)	58 (32%)	
High	52 (77.5%)	90 (48%)	
Missing	8	15	
Type of infertility ^d			0.31°
Primary	39 (54%)	122 (61%)	
Secondary	33 (46%)	78 (39%)	
Missing	3	0	
Childless			0.71°
Yes	41 (69.5%)	144 (72%)	
No	18 (30.5%)	56 (28%)	
Missing	16	0	
Duration of infertility (months) ^e	38 [12-228]	24 [1-116]	<0.01ª
0-2 years	4 (8%)	98 (49%)	
2-4 years	26 (51%)	72 (36%)	< 0.01°
>4 years	21 (41%)	30 (15%)	
Missing	24	0	
Total duration under treatment (months)	24 [0-144]	6 [0-58]	<0.01 ^a
Treatment phase			< 0.01°
Initial examination	6 (12%)	50 (25%)	
OI/IUI	7 (15%)	86 (43%)	
IVF/ICSI	19 (40%)	50 (25%)	
Pregnant	4 (8%)	4 (2%)	
After/No treatment	12 (25%)	10 (5%)	
Missing	27	0	

Table 1: Characteristics of registered female participants of the specialized online participatory tool

^a Independent t-test

^b Low: primary or lower vocational education; Middle: secondary or intermediate vocational education; High: higher professional education or university

° Chi-square test

^d Type of infertility was determined

^e Duration of infertility defined as the period between the start of regular unprotected sexual intercourse and date filled out the registry form

Benefits of the tool

Recommendations

In 12 months, 50 new recommendations were generated within the different care phases (Table 2). Of these new recommendations, 37 (74%) were generated within the gynaecologic section of the tool. Of the 21 initial recommendations, 3 were modified and the other 18 initial recommendations remained unaffected.

Care phase	Recommendations (n)	Total ratings (n) ^a
General care		6 ()
Total	6	45
newly generated	3	
modified	2	
unaffected	1	
General Practice care		
Total	7	40
newly generated	2	
modified	1	
unaffected	4	
Gynaecologic care		
Total	42	479
newly generated	37	
modified	-	
unaffected	5	
Urologic care		
Total	5	6
newly generated	-	Ũ
modified	-	
unaffected	-	
Laboratory		
Total	4	19
newly generated	ī	
modified	-	
unaffected	3	
Psychologic care		
Total	3	40
newly generated	3	10
modified	-	
unaffected	-	
Occupational Physician's care		
Total	3	17
newly generated	3	17
modified	-	
unaffected	-	
Remaining care		
Total	1	2
newly generated	1	-
modified	-	
unaffected	-	

Table 2: Recommendations and their ratings

^a Total number of ratings within 12 months on the specialized online participatory tool

The total number of modifications in all recommendations (n=71) was 37 (Table 2). Modifications mainly concerned the elimination of grammatical errors or making the recommendation more specific. Regarding the prioritizations, 71 recommendations were ranked with stars 642 times, of which 479 rankings were awarded within the gynaecologic section (Table 2). Regarding the comparison of the top five rankings between the start and the end of the project, the top five of the gynaecologic section had changed the most and consisted of completely different

recommendations. The top fives of recommendations within the laboratory and urologic care sections remained unaltered. Table 3 provides an overview of the two main recommendations per care phase.

Main patients' recommendations Care phase General care I want the Dutch government to educate and explain to the broader public what the law entails regarding artificial donor insemination. I want the Dutch government to reimburse fertility treatments in all cases. General practitioner's care I want my GP to provide a clear transferral to the gynaecologist. I want my GP to take the information given to her/him seriously and consider this in determining the time of referral. I want my gynaecologist to schedule an appointment within 15 days Gynaecologic care after a failed IUI/IVF/ICSI attempt to discuss the treatment plan. I want my gynaecologist to provide me during my first appointment with a general brochure explaining how I can increase the chance of pregnancy. Urologic care I want my urologist to engage my partner in the conversation. I want my urologist to enable patients to make an appointment in the first month after referral. Laboratory I want the laboratory's staff to inform patients as soon as possible when embryos are not dividing. I want the laboratory's staff to inform patients of how many embryos _ developed the day before the embryo transfer instead of by the time of the embryo transfer. Psychologic care I want the healthcare system to enable quick and adequate care in case of problems due to unwanted childlessness. I want my psychologist or sexologist to be present during the first intake as a standard operating procedure. **Occupational Physicians'** I want the occupational physician to educate employers and provide tools for employees receiving fertility treatments. care I want employers to give every patient the opportunity to have fertility treatments during working hours. Remaining care I want the insurance company to offer patients the opportunity to insure for a fourth IVF/ICSI attempt if the third attempt has not resulted in a pregnancy.

Table 3: Main recommendations per treatment phase

GP=General practitioner

Discussion

This study shows that a specialized online participatory tool enables patient partnership in CPG development in the case of Dutch infertile patients. The tool enabled a broad and representative target group that participated in the clinical guideline development process by delivering a clear and prioritized set of recommendations that meet the statements of the GLIA instrument. Furthermore, according to the relatively high SUS scores, participants qualified the tool as highly usable. We expect that this specialized online participatory tool has generic characteristics and could be adapted to every healthcare setting.

Our original wiki-inspired tool was developed and based on the results of a previous evaluation study, as well as custom fit to clinical guideline development in general and to the partners in the clinical guideline development process, particularly the patients [20]. Thus far, with the exception of our previous pilot study, this is the first study that presents a feasible tool for facilitating patient partnerships in clinical guideline development by enabling a collaborative of patients to actively participate by delivering prioritized high-quality recommendations for Dutch clinical guidelines on infertility.

Both research on wiki-inspired tools and on other online tools to facilitate patient partnership still mainly focus on (guideline-derived) quality products, such as information leaflets and shared decision-making tools [5–10, 21].

With respect to the engagement of patients in the guideline development process, the use of other instruments such as focus groups or individual interviews has been described previously [11–19,32]. However, apart from the usability of these instruments in previous stages of the clinical guideline development process (i.e. shaping the key questions, defining/selecting related outcome measurements, and considerations), the actual usability of these kinds of instruments in the formulation of recommendations can be debated. Firstly, the outcomes of these interviews cannot be translated into clear recommendations directly. Secondly, members of the guideline development groups are challenged to transform patients' input into recommendations that correspond to patients' views. Furthermore, the tool presented in this study engages far more patients compared to the restricted number of patients involved in interviews or focus groups, which can also be time consuming, laborious, and bias sensitive.

These barriers may also apply when patients' representatives participate in the guideline development group. These patients need to represent all patients who

the guideline is focussed on. Our specialized online participatory tool could form an excellent aid to represent the views of a broad group of patients and to take a stronger position in the guideline development group for involved patients' representatives. Another strength of this tool is that moderating and prioritizing recommendations is continuously performed by patients themselves, which could minimalize efforts. We especially believe that our participatory tool is highly usable in guideline topics for which the body of evidence is rapidly growing and needs a nearly continuous update process.

Nevertheless, some limitations to this study should be mentioned. Firstly, we acknowledge that the level of participation (i.e. 95 of the 3028 visitors) is low, as is the willingness to fill out a usability questionnaire (i.e. 45 of the 95). The fact that registration was mandatory for using the tool and the introduction of a new tool could have played a significant role herein. Secondly, we conclude that registered female participants of this study are representative for the Dutch infertile population regarding important patients' characteristics, but we must acknowledge that participants still represent a specific subgroup that is in a more advanced treatment phase, have a longer duration of infertility, and are more highly educated. One might argue whether patients who are starting an infertility care pathway can shape specific recommendations for high-quality fertility care since they are unable to predict the forthcoming steps of their care pathway. This inability could explain the fact that registered participants form specific subgroups regarding the high duration of treatment and the more advanced treatment phase they are in. Moreover, the authors acknowledge challenges in the generalizability of the tool to other healthcare fields and in international settings. The level of uptake of this tool by health policy organizations might play a crucial role therein. This could motivate professional associations and clinical guideline development organizations to implement it in the guideline development process. Support from patients' associations by increasing their role in guideline development is recommended. Furthermore, it is assumed that the implementation of the tool in guideline development practice and using patients' recommendations directly in the guideline can lead to a variety of discussions on financial and political levels (i.e. these might be contradictory to professionals' recommendations). Therefore, clear arrangements on this point should be made. Finally, as with all other forms of patient involvement in clinical guideline development, concrete evidence of the impact of patient involvement on the quality of care is still lacking.

Our tool might be implementable in healthcare settings other than infertility, but

it requires uptake in clinical guideline development programs by health policy organizations, which would thus motivate allied stakeholders. Furthermore, clear guidelines on how to use this tool in practice need to be set.

In conclusion, using a specialized online participatory tool is a feasible method of involving a broad group of representative infertile patients in CPG development. This study adds to current knowledge using online tools to facilitate patient partnership in clinical guideline development. This paper can be used as a practical guide for policy organizations, guideline developers, and patients' organizations that are interested in interventions to facilitate patient partnership in clinical guideline development in any healthcare setting. Furthermore, using the tool for facilitating patient partnership in other components of the clinical guideline development process – such as defining the scope of a guideline, defining important outcome measurements for patients herein, and prioritizing guideline topics by patients – could broaden the value of the tool in the future.

References

- 1. Hibbard JH, Greene J. What the evidence shows about patient activation: better health outcomes and care experiences; fewer data on costs. *Health Aff* 2011;**32**:207-214.
- 2. Greene J, Hibbard JH, Sacks R *et al.* Engagement: When Patient Activation Levels Change, Health Outcomes And Costs Change, Too. *Health Aff* 2015;**34**:3431-437.
- 3. Richards T, Godlee F. The BMJ's own patient journey. BMJ 2014;348:3726.
- 4. Richards T, Montori VM, Godlee F et al. Let the patient revolution begin. BMJ 2013;346:2614
- Tuil WS, Verhaak CM, Braat DD et al. Empowering patients undergoing in vitro fertilization by providing Internet access to medical data. Fertil Steril 2007;88:361-368.
- 6. Samoocha, D, Bruinvels DJ, Elbers NA *et al*. Effectiveness of web-based interventions on patient empowerment: a systematic review and meta-analysis. *J Med Internet Res* 2010;**12**:23.
- 7. Irizarry T, DeVito Dabbs A, Curran CR. Patient Portals and Patient Engagement: A State of the Science Review. *J Med Internet Res* 2015;**17**:148.
- 8. van der Eijk, M, Faber MJ, Aarts JW *et al.* Using online health communities to deliver patient-centered care to people with chronic conditions. *J Med Internet Res* 2013;15:115.
- 9. Archambault PM, van de Belt TH, Grajales III *et al.* Wikis and collaborative writing applications in health care: a scoping review. *J Med Internet Res* 2013;**15:**210.
- 10. Archambault PM. WikiBuild: a new application to support patient and health care professional involvement in the development of patient support tools. *Journal of medical Internet research* 2011;**13**:114.
- 11. Nilsen ES, Myrhaug HT, Johansen M *et al.* Methods of consumer involvement in developing healthcare policy and research, clinical practice guidelines and patient information material. The *Cochrane Library* 2006;**3**:1-25.
- 12. Institute Of Medicine (IOM). *Clinical Practice Guidelines we can Trust*. Washington, DC: National Academy Press, 2011.
- 13. van Wersch A, Eccles M. Involvement of consumers in the development of evidence based clinical guidelines: practical experiences from the North of England evidence based guideline development programme. *Qual Health Care* 2001;**10**:10-16.
- 14. Bastian H. Raising the standard: practice guidelines and consumer participation. *Int J Qual Health Care* 1996;**8**:485-490.
- 15. Rogers WA. Are guidelines ethical? Some considerations for general practice. Br J Gen Pract 2002;52:663-668.
- 16. Diaz Del Campo P, Gracia J, Blasco JA *et al.* A strategy for patient involvement in clinical practice guidelines: methodological approaches. *BMJ Qual Saf* 2011;**20**:779-84.
- 17. Legare F, Boivin A, van der Weijden T *et al.* Patient and public involvement in clinical practice guidelines: a knowledge synthesis of existing programs. *Med Decis Making* 2011;**31**:45-74.
- 18. Boivin A, Currie K, Fervers B *et al.* Patient and public involvement in clinical guidelines: international experiences and future perspectives. *Qual Saf Health Care* 2010;**19**:e22.
- 19. 34. Krahn M, Naglie G. The next step in guideline development. J Am Med Assoc 2008;300:436-438.
- 20. den Breejen EM, Nelen WL, Knijnenburg JM *et al.* Feasibility of a wiki as a participatory tool for patients in clinical guideline development. *J Med Internet Res* 2012;14:e138.
- Gupta D, Rodeghier M, Lis CG. Patient satisfaction with service quality in an oncology setting: implications for prognosis in non-small cell lung cancer. Int J for Qual in Health Care 2013;25:696-703.
- 22. Nachtigall RD, Castrillo M, Shah N *et al.* The challenge of providing infertility services to a low-income immigrant Latino population. *Fertil Steril* 2009;**92**:116-23.
- Boivin J, Bunting L, Collins JA *et al*. International estimates of infertility prevalence and treatmentseeking: potential need and demand for infertility medical care. *Hum Reprod* 2007;22:1506–1512.
- 24. Zegers-Hochschild F, Adamson GD, de Mouzon J *et al.* The International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) Revised Glossary on ART Terminology. *Hum Reprod* 2009;**24**:2683-7.

- 25. Verhaak CM, Smeenk JMJ, Evers AWM *et al*. Women's emotional adjustment to IVF: a systematic review of 25 years of research. *Hum Reprod Update* 2007;**13**:27-36.
- 26. Yusof, MM, Kuljis J, Papazafeiropoulou A *et al.* An evaluation framework for Health Information Systems: human, organization and technology-fit factors (HOT-fit). *International J Med Informatics* 2008;77:386-398.
- 27. Jordan PW, Thomas B, Weerdmeester BA *et al. A quick and dirty usability scale*. In: Usability evaluation in industry. London: Taylor and Francis, 1986.
- Shiffman RN, Dixon J, Brandt C, et al. The GuideLine Implementability Appraisal (GLIA): development of an instrument to identify obstacles to guideline implementation. BMC Med Inform Dec Making 2005;5:23.
- 29. Den Breejen EM, Hilbink MA, Nelen WL *et al.* A patient-centered network approach to multidisciplinary-guideline development: a process evaluation. *Implementation Science* 2014;**9**:1.
- 30. Bangor A, Kotum P, Miller J. Determining what individual SUS scores mean: adding an adjective rating scale. *J Usability Stud* 2009;4:114–23.
- 31. Brandes M, Hamilton CJCM, van der Steen JOM *et al.* Unexplained infertility: overall ongoing pregnancy rate and mode of conception. *Human Reproduction* 2011; **26**:360-368.
- 32. den Breejen EM, Hermens RP, Galama WH *et al.* Added value of involving patients in the first step of multidisciplinary guideline development: a qualitative interview study among infertile patients. *Int J Qual Health Care* 2016;**28**:299-305.



Chapter 6

Development of guideline-based indicators for patient-centredness in fertility care: what patients add

EME den Breejen, WLDM Nelen, SFE Schol, JAM Kremer, RPMG Hermens

Human Reproduction 2013;28:987-996.

Abstract

Study question: What value can patients add to the development of guideline-based quality indicators for patient-centredness in fertility care?

Summary answer: Infertile patients mainly select different indicators and value different dimensions of patient-centredness (e.g. information and communication and access to care) than professionals (e.g. coordination and integration of care) during an indicator development process.

What is known already: Patient-centredness is an important dimension for the quality of fertility care. However, this dimension is not adequately evaluated by professionals, due to a lack of quality indicators. Furthermore, it is suggested that patients select different indicators for patient-centredness than professionals, although exact differences are unknown.

Study design, size and duration: The RAND-modified Delphi method (a twostep systematic consensus method) was used to develop two sets of quality indicators for patient-centredness. Similarities and differences in the indicators as well as in aspects of patient-centredness between patients' and professionals' sets of indicators were analysed descriptively.

Participants, setting, methods: The development of quality indicators for patientcentredness was based on the national multidisciplinary Network Guideline on infertility. Two panels participated: One patients' panel (n=19) and one multidisciplinary professionals' panel (n=15).

Main results and the role of chance: From 119 formulated potential indicators of patient-centredness, the patients' panel selected a representative set of 16, while the professionals' panel selected 18. Five indicators were included in both sets. These regarded the need to: perform IUI at least 6 days a week; report on treatment outcomes and complications; report on results of semen analyses in a standardized way; counsel infertile couples about the positive effects on their chance of pregnancy of the elimination of a harmful lifestyle and provide information on the negative consequences for achieving a pregnancy in case of a high BMI. Both patients and professionals put highest value on potential indicators of information and communication in fertility care. Patients also emphasized accessibility of care, whereas professionals emphasized coordination and integration as important quality measures for patient-centredness in fertility care.

Limitations, reasons for caution: First, the total number of developed indicators in the final set is relatively large (n=29), which could be a first potential limitation in

its use for accreditation and quality monitoring. Second, although panel members were asked to take reliability into account during the selection procedure, the indicators still need an evaluation of the measurability and the intra- and interobserver reliability.

Wider implications of the findings: The final guideline-based indicator set consisting of 29 indicators represents a balanced set that is based on the expertise of all stakeholders, including patients. A next step should be the application of this set in a future practice test to assess the feasibility in daily practice. In our opinion, most quality indicators for patient-centredness could be used for monitoring and improving the quality of fertility care internationally, occasionally by a more broad interpretation (e.g. by replacing the general practitioners with other healthcare professionals engaged in the care process).

Study funding/competing interest(s): This study was supported by a research grant (number 150020015) from the Dutch Organisation for Health Research and Development (ZonMw) in a research programme on broadening and acceleration in multidisciplinary guideline development. The authors have no conflicts of interest to declare.

Key words: infertility, monitoring healthcare, quality indicator, quality of care, patient-centredness.

Introduction

The quality of fertility care is usually monitored by outcome measurements such as live birth rates [1]. However, high quality fertility care comprises more than just the effectiveness of care. Regardless of medical-technical quality, patientcentredness described as 'providing care that is respectful of and responsive to individual patient preferences, needs, and values and ensuring that patients' values guide all clinical decisions' also determines the quality of fertility care [2]. The multidimensional concept of patient-centredness comprises various aspects, such as the coordination and integration of care as well as the provision of emotional support [3, 4]. Recent reports have confirmed that infertile patients long for patient-centred care and that improvements in several dimensions of patient-centred fertility care could play a crucial role in deciding to drop out from fertility treatments [3-8]. Moreover, patient-centred fertility care is associated with increased patient satisfaction [6,9]. Regrettably, professionals are unable to adequately evaluate their performance regarding patient-centredness [10]. This hampers the direct quality improvement regarding patient-centredness. It also illustrates the need for measurable elements of practice performance derived from evidence-based guidelines regarding this quality of care dimension [11-13].

So far, several studies have reported on the development of guideline-based indicators within the field of fertility care [14-16]. However, in these studies a particular focus on patient-centredness in fertility care is lacking. This could be because the involvement of patients in the guideline and indicator development process is still not common practice [17,18]. The development of guideline-based indicators for patient-centredness has only been reported within the field of cancer care [19, 20]. Although patients played a minor role in these indicator development panels, the results suggest that including patients will lead to the identification of aspects of patient-centredness that may not have been considered previously. However, in these studies the exact difference in choice of indicators between professionals and patients regarding patient-centredness remains unknown.

Therefore, as a first step in improving and monitoring patient-centredness in fertility care, our aim was to get insight into what patients could add to the indicator development by developing two sets of guideline-based quality indicators for patient-centredness: one from the patients' and one from the professionals' perspective, and comparing the content of these two sets.

Materials and Methods

Setting

In this study, the development of quality indicators for patient-centredness was based on a recently developed national multidisciplinary Network Guideline (NG) on infertility (www.nvog.nl). The guideline's cornerstones consisted of a multidisciplinary approach to ensure proper alignment and special attention to patient-centredness of care. For this purpose, this NG was initially based on infertile patients' clinical pathways and consisted of separate sections subject to different phases of care (e.g. care provided by General Practitioners (GPs), gynaecologists, urologists, psychologists and after-care). Next, apart from the involvement of patients' representatives in the guideline development group, a large group of infertile patients was involved in the development process. They contributed to this process through their input in the formulation of key questions and through directly formulating and prioritizing recommendations on a wiki-based website [21]. Finally, the prioritized patients' recommendations were literally integrated into the final guideline and provided with a level P (Patients) evidence.

Dutch Fertility care

Overall, the Dutch fertility care has been publically arranged on three levels. Primary care is provided by GPs and may comprise a part of an initial fertility assessment. Subsequently, a GP can refer couples to a gynaecologist in a general (secondary care) or a university (tertiary care) hospital, who could then complete this initial fertility assessment, determine a cause of infertility and define a suitable treatment plan. If a severe male factor is diagnosed, couples can be referred to a urologist. Nurses, clinical biochemists and embryologists are also involved in assessments and preparations for Medically Assisted Reproductive (MAR)-techniques, for instance IVF. In the Netherlands, IVF is carried out in 13 licensed clinics: 8 university hospitals, 4 general hospitals, and 1 private clinic. In clinics without an IVF-license (e.g. satellite clinics), professionals have the possibility to start up and monitor ovarian stimulation, but they have to refer to a licensed clinic for the retrieval of oocytes and embryo transfers. Additionally, in transport clinics, the ovarian stimulation and retrieval of oocytes can be performed initially, but retrieved oocytes have to be transported to the central IVF laboratory of a licensed clinic. Since infertility has a high emotional and psychological impact, which may also interfere with people's jobs, psychologists and occupational physicians are regularly involved in the clinical pathway.

Indicator development

The RAND-modified Delphi method (a two-round systematic consensus method using expert panels) was used to develop two sets (i.e. one from the patients' and one from the professionals' perspective) of quality indicators for patient-centredness [22]. The indicator development process comprised three consecutive steps: (1) extraction and classification of NGs' key recommendations; (2) written questionnaire survey and (3) consensus round by email.

Participants

One patients' panel and one multidisciplinary professionals' panel were formed in order to develop two sets of quality indicators for patient-centredness of fertility care. For the patient panel, infertile patients were recruited through a call for participation at 'Freyawiki' (the tool used for patient involvement in the NG), social media channels and mailings from Freya, the Dutch Patients' Association for infertility. Eligibility criteria included (previous) homologous treatment with MAR-techniques. Furthermore, two executives of Freya, involved in the development of the NG, were added to the patient panel.

Professionals were recruited by a letter signed by the coordinator (EB), the project leader (JK) and the implementation and performance measurements expert (RH) of the NG. In this letter, professional societies were asked to officially nominate professionals experienced in fertility care as well as in performance monitoring. The societies of gynaecologists, urologists and GPs were asked to nominate three professionals. For the participation of clinical embryologists, occupational physicians, clinical psychologists, and clinical biochemists, each particular professional society was asked to nominate two professionals. The intended number of participants for inclusion in both panels was 15-17 participants. This was based on previously published studies describing the number of participants in multidisciplinary expert panels [22, 23]. The rough balance between different stakeholders was chosen in proportion to the extent of their key role in fertility care.

Step 1: extraction and classification of NGs' recommendations

First, all listed recommendations were extracted from the NG (E.B.). Next, the extracted recommendations were classified into two quality domains (i.e. medical-technical and patient-centredness of care) by three researchers independently (E.B., W.N. and R.H). The inclusion criteria for the patient-centredness domain

were recommendations concerning the 10 dimensions of patient-centredness in fertility care according to Dancet *et al.* (2010) or recommendations provided by a level P [3]. Discrepancies in this division of recommendations were easily solved through discussion. Furthermore, all recommendations regarding the medical-technical quality of care were excluded, since these were not a subject of research of this study. Lastly, in the final set of indicators a balance was needed between organizational indicators (i.e. coordination and integration of care; physical comfort; transition and continuity of care; access to care; staffs' competence and technical skills) and non-organizational indicators (i.e. respect for patients' values, preferences and needs; information, communication and education; emotional support; partner involvement; attitude fertility clinic staff) for patient-centredness in fertility care. To achieve this, the extracted recommendations were subdivided as described. Level P recommendations, directly formulated by patients through 'Wikifreya', represent *par excellence* patients' personal needs and are therefore classified as non-organizational indicators [21].

Discrepancies in this division of recommendations were again resolved through discussion. Next, all recommendations for patient-centredness (organizational and non-organizational aspects) were formulated into potential indicators (E.B.) and checked and eventually adjusted independently by a second researcher (R.H.). After reaching consensus on their formulation, the potential indicators were included in a written questionnaire and formulated as follows: *'The healthcare provider (e.g. gynaecologist, urologist) should...'* or *'Patients would like to...'*.

Step 2: written questionnaire round

The written questionnaire was sent to the members of both panels by post. The first part of the questionnaire comprised questions about background characteristics (e.g. age, sex). Secondly, panel members were asked to rate the relevance of all potential indicators for patient-centredness on a nine-point Likert-scale ranging from 1 (=completely irrelevant) to 9 (=extremely relevant), with respect to their usefulness as a measure for the quality of patient-centredness in fertility care [11]. Both categories (i.e. organizational and non-organizational) of indicators for patient-centredness were presented separately and according to the structure of the NG following infertile patients' clinical pathways (e.g. general care by GPs, fertility assessments and treatment by GPs, gynaecologists and urologists as well as aftercare). All potential indicators within the professionals' questionnaire were supplemented with levels of evidence to facilitate decision-making. The evidence underlying the recommendations was classified into five levels: I, systematic review/Randomized Controlled Trials (RCT); II, RCT; III, comparative studies; IV, case studies or expert opinion and level P, patients' opinion [24]. In collaboration with Freya, the patients' questionnaire was supplemented with additional laymen's information to clarify the jargon used. Thirdly, for the organizational as well as the non-organizational potential indicators, all panel members were asked to give a top five ranking to promote the discrimination between indicators with a high Likert score [16, 25]. Finally, all panel members were invited to rephrase the proposed indicators and to add comments. Reminders were sent by email to non-responders after 2 and 4 weeks.

Data analysis: step 2

Campbell's criteria and the top five ranking method were used to analyse the results of the questionnaire surveys of step 2 [26]. Therefore, per potential indicator, we calculated an overall panel median score and an overall ranking score for each panel. To calculate the overall ranking score, a potential indicator ranked first, second, third, fourth or last in the top five received 5,4,3,2 or 1 point respectively. The overall ranking score was expressed as the percentage of the maximum top five score that could be obtained (0-100%). A potential indicator was associated with face validity and proposed for 'selection' in this consensus round if it matched the following criteria: (i) an overall panel median score of 8 or 9 combined with a top five ranking $\geq 10^{\text{th}}$ percentile of the percentage of the maximum top five score and (ii) an agreement between the ratings of the independent panel members. The agreement was reached if 70% or more of ratings within a panel was in the highest tertile (7, 8, 9). A potential indicator was 'rejected' if none of these criteria were met. A potential indicator was considered 'equivocal' or open to discussion if it matched an overall panel median score of 8 or 9 with agreement, but with low or no top five ranking score.

Step 3: consensus round

After rephrasing, the organizational and non-organizational 'selected' and 'equivocal' indicators were presented separately in a second questionnaire intended for all panel members for commented written approval. In this questionnaire, the 'selected' and 'equivocal' indicators were presented along with the comments provided by the particular panel (e.g. patients and professionals), the frequency distribution of scores within the panel, the overall median score of the panel as well as the individual panellists' score for each particular indicator. Both panels, including the non-responders of step 2, were asked for their approval (yes or no) of the 'selected' indicators and to indicate which 'equivocal' indicators, if any, should be part of the final set of indicators as well. The questionnaire was sent by email. Reminders were sent by email to non-responders after 2 and 4 weeks.

Defining final sets of indicators (data analysis step 3)

To gain patients' and professionals' final sets of indicators, the approved initially 'selected' indicators were supplemented with the accepted 'equivocal' indicators (i.e. consensus round) and rephrased or merged at the request of the panel members. An 'equivocal' indicator was accepted if >50% of the panellists were in favour.

Comparison of the two final sets of indicators

The selected quality indicators for patient-centredness from the patients' and the professionals' perspective were compared and checked for corresponding indicators. Furthermore, individual indicators of both sets were descriptively analysed by the frequency distribution of the 10 dimensions of patient-centredness for fertility care according to Dancet *et al.* (2010): coordination and integration of care; physical comfort; transition and continuity of care; access to care; competence and technical skills of staff; respect for patients' values, preferences and needs; information, communication and education; emotional support; partner involvement; attitude of the fertility clinic staff [3].

Main outcome measures

Primary outcome measures were two final sets of quality indicators for patientcentredness, i.e. one from the patients' and one from the professionals' perspective. Secondary outcome measures were the differences in the distribution over the 10 dimensions of patient-centredness between the two sets of quality indicators.

Results

Participants

The patient panel included 19 infertile patients. The professional panel included 15 professionals nominated from different specialities: 3 gynaecologists, 3 urologists, 2 GPs, 2 clinical biochemists, 2 occupational physicians, 2 clinical psychologists, and 1 clinical embryologist. The society of GPs as well as the society of clinical embryologists mandated two and one professionals respectively, instead of the requested three and two professionals. Eight professionals (53%) were previously involved in the development of the NG on infertility.

Indicator development

Step 1: extraction and classification of NGs' recommendations

The NG on infertility contained 201 evidence-based or consensus-based recommendations for optimal quality of fertility care. The recommendations were classified into 81 medical-technical and 120 recommendations for patient-centredness. All 81 recommendations regarding the medical-technical quality of fertility care were discarded (Figure I). By formulating the 120 recommendations into potential indicators for patient-centredness, two recommendations, both regarding the indications for referral to a social worker, were merged into one potential indicator. Of these 119 potential quality indicators for patient-centredness, 58 indicators concerned organizational aspects: 12 supported by levels I, II or III and 46 by a level IV of evidence. Sixty-one potential indicators concerned non-organizational aspects, of which 23 were supported by levels I, II or III, 14 by a level IV of evidence and 24 by a level P.

Step 2: written questionnaire round

From the patient panel 12 out of 19 (63%) and from the professional panel 14 out of 15 (93%) of the questionnaires were returned. Of the responding all female patients, 75% (n=9) suffered from secondary infertility, and had a median age of 37 years (range 28-39). Of these women, 67% (n=8) were highly educated. The median duration of infertility was 49 months (range 30-77). Most respondents (92%) received treatment (n=3) or had been treated (n=8) with MAR-techniques. Reasons for drop out included: time restraints (2), emotional distress during infertility treatment at the time (3), having difficulty to assess the indicators (1)



Figure 1: Development process of quality indicators for patient-centredness in fertility care

* Two recommendations for patient-centredness were merged into one potential indicator. ** After rephrasing and merging the potential indicators of both the patients' and the professionals' set, the number of indicators was reduced

and unknown (1). Most of the professionals (79%, n=11) were attached to general or academic teaching hospitals and 57% (n=8) of them were male.

The patients rated 15 of the 119 potential indicators face valid, including seven organizational and eight non-organizational aspects of care. Fifty potential indicators were rated 'equivocal' and 54 potential indicators were rejected. The professionals rated 13 of the 119 potential indicators face valid, i.e. five organizational and eight non-organizational aspects of care. Of the remaining potential indicators, 20 were considered 'equivocal' and 86 were rejected.

Chapter 6

The members of the patient panel proposed to merge four organizational indicators regarding the provision of annual reports on treatment outcomes and complications of different MAR-techniques for registration as well as to merge two indicators on staff's composition of transport and satellite clinics. The members of the professional panel proposed to rephrase 12 non-organizational indicators by merging 3 indicators on partner involvement by the gynaecologist, urologist and GP and by merging 3 sets of 3 indicators on the information provision regarding the influence of obesity, smoking cessation and alcohol use on fertility respectively. All these suggestions for rephrasing the indicators were adopted for the patients as well as the professionals. Accordingly, patients' 'equivocal' indicators were reduced with 12 indicators. Professionals' selected' and 'equivocal' indicator was merged with two and six indicators.

Step 3: consensus round

From the patient panel 10 out of 19 (53%) and from the professional panel nine out of 15 (60%) of the second questionnaires were returned. All responding patients and professionals gave their approval for the rephrased selected set of 15 and 11 indicators resulting from step I, respectively. Among the 38 rephrased patients' equivocal' indicators, only one non-organizational indicator was selected by more than 50% of the panel. Among the 14 rephrased 'equivocal' indicators (i.e. eight organizational and six non-organizational) of the professionals, yet four organizational and three non-organizational indicators were selected by more than 50% of the panel.

Final sets of indicators for patient-centredness

The patients' final set consisted of 16 key indicators, including 7 organizational and nine non-organizational indicators (Table 1). All were supported by a level IV-evidence or a level P (Patients).

The professionals' final set consisted of 18 key indicators, including nine organizational and nine non-organizational indicators (Table 2). All professionals' key indicators were supported by a level III- or IV-evidence.

Patients' final set of 16 quality indicators for patient-centredness (PC)	Sub-dimension of PC	Dimension of PC
Composition of the infertility treatment team in licensed IVF- clinics as well as transport- or satellite clinics should be according to the NVOG quality norm 'IVF'	Quality management	Staffs' competence and technical skills
Fertility clinics (licensed and non-licensed) should have the possibility to perform IUI at least 6 days a week ^a	Accessibility outside traditional working hours	Access to care
In accordance with the Dutch IVF planning decree, every licensed IVF centre and their corresponding transport and satellite centres must provide annual reports on treatment outcomes and complications (OI, IUI, IVF) for uniform national IVF registration (NVOG) ^a	Quality management	Staffs' competence and technical skills
The gynaecologist should: complete or perform the initial fertility assessment, give information on possible causes of infertility, consult a urologist in case of urological problems and start treatment if it enhances pregnancy-probabilities (demarcation of first, second and third line's professionals 'roles)	Role demarcation	Coordination and integration of care
The gynaecologist should preferably accommodate daily monitoring in ovulation induction cycles in order to assess the individual response as well as to reduce complication risks	Accessibility	Access to care
The gynaecologist should keep up detailed correspondence with the GP regularly	Continuity in policy	Transition and continuity of care
Regarding the semen analysis, the laboratory officer should at least report on: the test-criteria used, the results including normal limits, the calculated total motile sperm count, the completeness of the sample, the time span between production and analysis and an overall conclusion ^a	Providing adjusted professional information	Transition and continuity of care
Each fertility professional should counsel infertile couples about the potential positive effects of eliminating harmful lifestyle choices on pregnancy-chances ^a	Information on helping themselves	Information, Communication & Education
Patients would like to have a consult with a gynaecologist within 1 month after referral by a GP	Accessibility	Access to care
Patients visiting a fertility clinic would like to have separate waiting rooms from pregnant women	Accommodation of clinic	Physical comfort
Patients would like to be able to visit a fertility clinic during daytime as well as in the evening.	Accessibility outside traditional working hours	Access to care
Patients would like to have the possibility of receiving treatments on weekends	Accessibility	Access to care
Regarding infertility treatment, patients would like to see all members of the infertility treatment team following the same policy	Continuity in policy	Transition and continuity of care
With respect to the IVF laboratory phase, patients would like to be informed in case their embryos do not divide any further as soon as possible	Sufficiency of information	Information, Communication and Education

Table 1: Patients' final set of quality indicators for patient-centredness

Table 1: Continued

Patients' final set of 16 quality indicators for patient-centredness (PC)	Sub-dimension of PC	Dimension of PC
Patients would like their gynaecologist to provide them with information on all possible infertility treatments	Information on alternatives	Information, Communication and Education
Each fertility professional should inform infertile couples on the negative influences and consequences of a high BMI (>29) regarding pregnancy-chances and if anovulatory, that losing weight increases the pregnancy-chances ^a	Information on helping themselves	Information, Communication and Education

IVF, in vitro fertilization; OI, ovulation induction; IUI, intrauterine insemination; GP, General Practitioner; NVOG, Dutch society of Obstetrics and Gynaecology.

^a Similar indicators in patients' and professionals' final set.

Professionals' final set of 18 quality indicators for	Sub-dimension	Dimension of
patient-centredness (PC)	of PC	PC
In accordance with the Dutch IVF planning decree, every licensed IVF centre and their corresponding transport and satellite clinics must provide annual reports on treatment outcomes and complications (OI, IUI, IVF) for uniform national IVF registration (NVOG) ^a	Quality management	Staffs' competence and technical skills
The GP should conduct an initial fertility assessment comprising a semen analysis in men and screening for Chlamydia trachomatis and when in doubt of an ovulatory cycle a single basal body temperature chart in women	Role demarcation	Coordination and integration of care
The GP should perform a semen analysis in an accredited laboratory (ISO 15189) or in a referral hospital	Quality management	Staffs' competence and technical skills
The GP should refer an infertile couple to a gynaecologist if there are indications for tubal pathology, such as a positive chlamydia antibody test and/or a medical history of (recurrent) abdominal infections or abdominal surgery	Transition of care	Coordination and integration of care
Regarding the semen analysis, the laboratory officer should at least report on the test-criteria used, the results including normal limits, the total motile sperm count, the completeness of the sample, the time span between production and analysis and an overall conclusion ^a	Providing adjusted professional information	Transition and continuity of care
Fertility clinics (licensed and non-licensed) should at least have the possibility to perform IUI 6 days a week $^{\rm a}$	Accessibility	Access to care
The GP should immediately refer an infertile couple with ovulations abnormalities to a gynaecologist	Transition of care	Coordination and integration of care
The gynaecologist should refer the infertile couple with sexual dysfunction, male genital abnormalities or azoospermia to a urologist	Transition of care	Coordination and integration of care
The laboratory officer (and not the gynaecologist) should ask and report the time-span of production and the completeness of the semen sample by accepting it	Role demarcation	Coordination and integration of care
Each fertility professional should counsel infertile couples about the potential positive effects of eliminating harmful lifestyle choices on pregnancy-chances ^a	Information on helping themselves	Information, Communication and Education

Table 2: Professionals' final set of quality indicators for patient-centredness

Professionals' final set of 18 quality indicators for patient-centredness (PC)	Sub-dimension of PC	Dimension of PC
Both partners of the infertile couple should be involved in the assessment and management of infertility because it is a joint problem	Involving the partner	Partner involvement
The GP should provide a couple experiencing problems in conceiving, but with normal preliminary test results, with specific information on the fertile period	Information on helping themselves	Information, Communication and Education
The GP should offer infertile couples the opportunity to talk about their experiences and expectations throughout all phases of fertility care	Provision of emotional support	Emotional support
The gynaecologist should offer infertile couples moral and psychosocial support throughout all phases of fertility care.	Provision of emotional support	Emotional support
With respect to adoption, all fertility professionals should give information on: the age limit of 41 years for both adoptive parents (as opposed to foster care, i.e. no age limit), lengthy waiting times (3-6 years), websites for additional information and make a comparison with foster care	Concrete information	Information, Communication and Education
Each fertility professional should inform infertile couples on the influences and consequences of a high BMI (>29) regarding pregnancy-chances and if anovulatory, that losing weight increases the pregnancy-chances ^a	Information on helping themselves	Information, Communication and Education
Each fertility professional should inform infertile men who smoke, or use more than 20 glasses of alcohol per week, use drugs and or anabolic steroids on the negative influence of this lifestyle on the semen quality and fertility	Information on helping themselves	Information, Communication and Education
Each fertility professional should inform infertile females, who smoke and/or use alcohol on the negative influence on fertility as well as motivate them to preventively quit the smoking ore use of alcohol	Information on helping themselves	Information, Communication and Education

IVF, in vitro fertilization; OI, ovulation induction; IUI, intrauterine insemination; GP, General Practitioner; NVOG, Dutch Society of Obstetrics and Gynaecology

^a Similar indicators in patients' and professionals' final set.

Table 2: Continued

Comparison of the two final sets of indicators

Five indicators were included in both the patients' and the professionals' final sets. These concerned the need to: perform IUI at least 6 days a week; report on treatment outcomes and complications; report the results of a semen analysis in a standardized way; counsel infertile couples about positive effects on pregnancy chances regarding the elimination of a harmful lifestyle; provide information on the negative consequences for achieving a pregnancy in case of a high BMI. Both sets comprised a variety of dimensions of patient-centredness. Of the six included dimensions for patient-centredness in the patients' final set of indicators (n=16), access to care (31%) and information and communication (25%) were

valued mostly. Meanwhile, patients valued transition and continuity of care (19%), staffs' competence and technical skills (13%), coordination and integration of care (6%) and physical comfort (6%). Among the professionals' final set of indicators (n=18), information and communication (33%) was one of the key dimensions of patient-centredness along with the dimension coordination and integration of care (27%). In addition to both these dimensions, professionals also valued staffs' competence and technical skills (11%), transition and continuity of care (6%), access to care (6%) partner involvement (6%) and emotional support (11%). Overall, two dimensions of patient-centredness were absent from both sets: respect for patients' values, preferences and needs as well as the attitude of the fertility clinic staff (Figure 2, Table 1 and 2).

Figure 2: Indicators of patient-centredness in various dimensions as a percentage of the total number of indicators selected by patients (16 indicators) and professionals (18 indicators)



Classification according to the 10 dimensions of patient-centred fertility care as described by Dancet et al. (2011 a, b).

Discussion

This study shows that the quality indicator development process regarding patientcentredness is affected by patient involvement. Only five indicators were included in both the patients' and professionals' final sets of indicators. Although both patients and professionals valued information and communication in fertility care most prominently, patients also emphasized the importance of access to care, whereas professionals emphasized the importance of coordination and integration of fertility care.

So far, within fertility care this is the first study that focuses on the development of guideline-based quality indicators for measuring and monitoring patientcentredness. Moreover, this is the first study on separately developing indicators among patients as well as a multidisciplinary professional panel. Generic and specific guideline-based quality indicators for fertility care have been developed previously [14-16]. However, as these studies mainly focused on the medicaltechnical quality of fertility care, indicators for patient-centredness were scant. Remarkably, since only gynaecologists were involved in the development process, instead of patients or other fertility care professionals, the selected indicators regarding patient-centredness of care mainly focused on information and communication. This is in line with the high percentage of indicators in the professionals' set (33%) on information and communication in our study. Although indicators for patient-centredness have previously been developed in the field of cancer care, they were not exclusively guideline-based and patients played a minor role in the development panel [19, 20]. These studies resulted in largely merged indicators that also mainly focused on information and communication regarding generic patient-centred cancer care. In one of these studies, patients actually got the opportunity to contribute in a face-to-face consensus round, without being snowed under by professionals in the development panel. Remarkably, they then selected additional indicators regarding access to care and information as well as communication, which is in line with our study results [20]. The latter might not only suggest uniformity in importance on dimensions of patient-centredness according to patients, but also underlines the need to involve patients in such a way that they are actually able to contribute to the entire development process.

Within the field of fertility care, other studies also aimed at measuring the level of patient-centredness through patients' experience surveys [4-6, 9, 27]. These studies evaluated patient-centredness in fertility care, but were not supported by

critically appraised evidence or consensus in a broad multidisciplinary group of professionals, which may hamper the likeliness of associated quality improvement initiatives to succeed. In addition, these studies only evaluated the patient-centredness of the clinical treatment phase within fertility care; other phases within patients' clinical pathways, such as care by GPs, urologists and after-care were omitted. Our study emphasises that the importance of including patients' clinical pathways with regard to the high percentage of indicators on coordination and transition in professionals' and access to care in patients' final set of indicators. Recently, studies have also reported on this close linkage between organisational determinants of care and other dimensions of patient-centredness as well as the need to apply a multidisciplinary approach in fertility care [4, 7, 27, 28].

By comparing the dimensions of patient-centredness between these nonguideline based instruments and our developed indicator sets, similarities but also noteworthy differences can be identified. The importance of information provision and communication for measuring patient-centredness is also underlined by the results of non-guideline based instruments and even assigned to be top priority in quality improvement initiatives [4-6, 9, 29]. Even so, the accessibility, coordination and integration of fertility care appeared to be proportionally underexposed dimensions of patient-centredness [4-6, 9, 27].

The main strength of our study is the involvement of infertile patients and different professionals from various phases in fertility care. Furthermore, by separately developing the two sets of quality indicators, we were able to get insight into patients' actual contribution and describe the differences in the selected indicators as well as dimensions of patient-centredness between patients and professionals.

However, by respecting different perspectives on patient-centred fertility care, one might argue against the development of two separate sets of quality indicators. Although mandatory to the aim of our study, three arguments for this approach need to be addressed. First, patients are the ultimate experts in patient-centredness of care, thus patients' involvement is necessary [13]. Secondly, to create a high level of support and ownership for the developed indicators, professionals also need to play a major role in the development process from the start. Finally, this increases the chances to use the indicators for actually monitoring and improving the quality of patient-centred fertility care [18, 30, 31]. Nevertheless, due to the lack of agreement between patients' and professionals' selected indicators, our approach results in a relatively large aggregated indicator set (n=29), which could become an obstacle in the use for accreditation and quality monitoring goals. An option to

reduce the set is to integrate them in a further consensus procedure. However, we think that the integration of the two developed sets in a further consensus process should be considered carefully: there is a risk of patients being "snowed under" in the discussion and most of the indicators developed by professionals would dominate the final indicator set. Another option is to only use the five similar indicators within both final sets in practice. We do think that these five indicators are important for quality improvement initiatives, but they do not include the whole concept of patient-centredness. In our opinion, the final indicator set consisting of 29 indicators represents a balanced set that is based on the expertise of all stakeholders, including patients. A next step should be the application of this set in a future practice test to assess the feasibility in daily practice. By evaluating its measurability and the intra- and inter-observer reliability the core set of indicators might be reduced with 10-20% [11, 32, 33].

Besides, we also need to address some other potential methodological limitations of this study. First, the worldwide used RAND-modified Delphi method has previously proved its effectiveness for developing quality indicators, but the influence of the panel composition and type of feedback on the legitimacy of the results have been questioned regularly [11, 18, 34, 35]. However, in this study we included a balanced group of fertility care professionals mandated by their professional societies and reliably reflecting the opinions of all Dutch professionals involved in fertility care. Regarding the type of feedback, panel members in our study received overall and individual scores, which ensured good consensus formation within the panels. Additionally, panellists received written feedback instead of face-to-face feedback, which may have minimized the influence on the selection of indicators in step 2 by intimidation [11, 35]. In addition, regarding the patient panel, we do not know if these patients are representative of the general infertile population. The majority of all female members suffered from secondary infertility, which may explain the relatively high median age and duration of infertility compared with the used and valid Dutch cohort of infertile patients described by Brandes and colleagues [36]. Nevertheless, both age and duration of infertility are comparable with a larger group used in a study to assess patient-centredness in Europe [29]. Moreover, they are eligible since they have completed one or more phases within the clinical pathway of fertility care, enabling them to appraise indicators regarding different phases of fertility care. Finally, the number of patients' participants might be small, but comparable to panels used in other studies developing quality indicators and larger than the involvement of one

or two patients in previously described methods [18, 22, 23]. Another discussion point is the attrition of the members of both panels over the course of the study, which is considerably high, especially of the professional panel members in the third step of our study. A plausible explanation for this might be found in the fact that indicator development (rating and ranking 120 indicators) is time-consuming and within a second round, professionals may feel less urge in adding important points to the final set of indicators.

Finally, some considerations for the use of these indicators in daily practice have to be addressed. First, the developed indicators in this study were based on a national multidisciplinary guideline on infertility, in which patient-centredness represented the primary goal in the development phase. This resulted in a high number of recommendations (n=120) for patient-centredness. Although patientcentredness is becoming increasingly important in the field of infertility care, it could be questioned if this approach can be performed similarly in all existing guidelines, since patient involvement in guideline development is still not common practice and the number of recommendations regarding patient-centredness might be rather small [17]. Furthermore, we are aware of the fact that some of the selected indicators, mainly regarding the access to care, may be specific for the Dutch setting (e.g. the unique role of the Dutch GP) and that this might have influenced the choice of indicators. However, this guideline was also based on international evidence, which implies that most of the developed indicators are more or less applicable in other care models as well, occasionally by a broader interpretation of the indicators (e.g. by replacing the GP with other engaged healthcare professionals). Moreover, evidence suggests that European patients have a similar generic view on patient-centredness of fertility care [27].

Additionally, with regard to the use of indicators for patient-centredness to monitor the quality of patient-centred fertility care, we think that professionals do not need to set up a quality assurance system for patient-centredness separately, since most of the performance measures can be collected by simply asking the patient directly or by introducing a periodic questionnaire to be completed. A good example of such a questionnaire may be found in the ENDOCARE-questionnaire [27].

Conclusion and implications

This study describes the systematic, stepwise development of patients' and professionals' guideline-based quality indicators for patient-centredness in fertility care and provides an insight into the differences in selection of quality indicators

for patient-centredness, especially regarding the accessibility dimension, between patients and professionals. Moreover, our results reinforce the importance of involving patients - the ultimate experts in patient-centred fertility care - in these indicator development processes. The presented final set of quality indicators for patient-centredness can be used to monitor and improve the quality of fertility care.

References

- 1. Min JK, Breheny SA, MacLachlan V *et al.* What is the most relevant standard of success in assisted reproduction? The singleton, term gestation, live birth rate per cycle initiated: the BESST endpoint for assisted reproduction. *Hum Reprod* 2004;**19**:3-7.
- 2. Institute Of Medicine (IOM). *Crossing the Quality Chasm: A New Health System for the 21st Century.* National Academy Press, Washington, DC: National Academy Press, 2001.
- 3. Dancet EA, Nelen WL, Sermeus W *et al.* The patients' perspective on fertility care: a systematic review. *Human reproduction update* 2010;**16**:467-487.
- 4. Dancet EA, Van Empel IW, Rober P *et al.* Patient-centred infertility care: a qualitative study to listen to the patient's voice. *Hum Reprod* 2011a;**26**:827-33.
- Schmidt L, Holstein BE, Boivin J *et al.* A. High ratings of satisfaction with fertility treatment are common: findings from the Copenhagen Multi-centre Psychosocial Infertility (COMPI) Research Programme. *Hum Reprod* 2003;18:2638-2846.
- 6. van Empel IW, Aarts JW, Cohlen BJ *et al.* Measuring patient-centredness, the neglected outcome in fertility care: a random multicentre validation study. *Hum Reprod* 2010;**25**:2516-2526.
- 7. van Empel IW, Hermens RP, Akkermans RP *et al.* Organizational determinants of patient-centered fertility care: a multilevel analysis. *Fertil Steril* 2011;**95**:513-519.
- 8. Gameiro S, Boivin J, Peronace L *et al.* Why do patients discontinue fertility treatment? A systematic review of reasons and predictors of discontinuation in fertility treatment. *Human reproduction update*, 2012;**18**:652-669.
- Souter VL, Penney G, Hopton JL et al. A. Patient satisfaction with the management of infertility. Hum Reprod 1998;13:1831-1836.
- 10. Aarts JW, Faber MJ, van Empel IW *et al.* Professionals' perceptions of their patients' experiences with fertility care. *Hum Reprod* 2011;**26**:1119-27.
- 11. Campbell SM, Braspenning J, Hutchinson A *et al.* Research methods used in developing and applying quality indicators in primary care. *BMJ* 2003;**326**:816-19.
- 12. Grol R, Baker R, Moss F. Quality improvement research: understanding the science of change in health care. *Qual Saf Health Care* 2002;**11**:110-111.
- 13. Institute Of Medicine (IOM). *Clinical Practice Guidelines we can trust*. 2011. National Academy Press, Washington, DC: National Academy Press, 2011.
- 14. Haagen EC, Nelen WL, Grol RP *et al.* Variation in guideline adherence in intrauterine insemination care. *Reprod Biomed Online* 2010;**20**:533-542.
- 15. Mourad SM, Hermens RP, Nelen WL *et al.* Guideline-based development of quality indicators for subfertility care. *Hum Reprod* 2007;**22**:2665-72.
- 16. van den Boogaard E, Goddijn M, Leschot NJ *et al*. Development of guideline-based quality indicators for recurrent miscarriage. *Reprod Biomed Online* 2010;**20**:267-273.
- 17. Krahn, M, Naglie G. The next step in guideline development: incorporating patient preferences. *J Am Med Assoc* 2008;**300**:436-38.
- 18. Kotter T, Blozik E, Scherer M. Methods for the guideline-based development of quality indicators--a systematic review. *Implement Sci* 2012;7:21.
- 19. Ouwens M, Hermens R, Hulscher M *et al.* Development of indicators for patient-centred cancer care. *Supportive Care in Cancer* 2010;18:121-130.
- 20. Uphoff EP, Wennekes L, Punt CJ *et al.* Development of generic quality indicators for patient-centered cancer care by using a RAND modified Delphi method. *Canc Nursing* 2012;**35**:29-37.
- 21. den Breejen EM, Nelen WL, Knijnenburg JM *et al.* Feasibility of a wiki as a participatory tool for patients in clinical guideline development. *J Med Intern Res* 2012;**14**:e138.
- 22. Fitch K, Bernstein S, Aguilar M. The RAND/UCLA *Appropriateness Method User's Manual*. Santa Monica, CA: RAND, 2001.
- 23. Boulkedid R, Abdoul H, Loustau M *et al.* Using and Reporting the Delphi Method for Selecting Healthcare Quality Indicators: A Systematic Review. *PLoS ONE* 201;6:e20476.

- 24. National Institute of Clinical Excellence (NICE). The guidelines' manual. London: NICE, 2009. URL: www.nice.org.uk Archived by WebCite^{*} at http://www.webcitation.org/65UXx2saM
- 25. Hermens RP, Ouwens MM, Vonk-Okhuijsen SY, van der Wel Y *et al.* Development of quality indicators for diagnosis and treatment of patients with non-small cell lung cancer: a first step toward implementing a multidisciplinary, evidence-based guideline. *Lung Cancer* 2006;**54**:117-24.
- Campbell SM, Cantrill JA, Roberts D. Prescribing indicators for UK general practice: Delphi consultation study. BMJ 2000;321:425-428.
- 27. Dancet EA, Ameye L, Sermeus *et al.* The ENDOCARE questionnaire (ECQ): a valid and reliable instrument to measure the patient-centeredness of endometriosis care in Europe. *Hum Reprod* 2011b;**26**:2988-99.
- 28. Boivin J, Domar AD, Shapiro DB *et al.* Tackling burden in ART: an integrated approach for medical staff. *Hum Reprod* 2012; **27**:941-50.
- 29. Dancet EA, D'Hooghe TM, Sermeus W *et al.* Patients from across Europe have similar views on patient-centred care: an international multilingual qualitative study in infertility care. *Hum Reprod* 2012;**27**:1702-1711.
- Alexander JA, Hearld LR. The science of quality improvement implementation: developing capacity to make a difference. *Medical care* 2011;49:S6-20.
- 31. Kaplan HC, Brady PW, Dritz MC *et al.* The influence of context on quality improvement success in health care: a systematic review of the literature. *The Milbank quarterly* 2010;**88**:500-559.
- 32. Scinto JD, Galusha DH, Krumholz HM *et al.* The case for comprehensive quality indicator reliability assessment. *J Clin Epidem* 2001;54:1103-1111.
- 33. Wollersheim H, Hermens R, Hulscher M *et al.* Clinical indicators: development and applications. *The Netherlands J Med* 2007;**65**:15-22.
- 34. Jones J, Hunter D. Consensus methods for medical and health services research. BMJ 1995;311:376-80.
- 35. Campbell SM, Shield T, Rogers A *et al.* How do stakeholder groups vary in a Delphi technique about primary mental health care and what factors influence their ratings? *Qual Saf Health Care* 2004;**13**:428-34.
- 36. Brandes M, Hamilton CJ, de Bruin JP *et al.* The relative contribution of IVF to the total ongoing pregnancy rate in a subfertile cohort. *Hum Reprod* 2010;**25**:118-126.



Chapter 7

General discussion

General discussion

This thesis focused on our first experiences with the participation of Dutch infertile couples in 'shared guideline development'.

First, we explored the added value of patients to various phases of the guideline development process (i.e. defining the guideline's scope, formulating the guideline's recommendations, and defining performance measurements). Next, we introduced a novel network approach to multidisciplinary guideline development, in which the infertile couple plays a crucial role. Finally, this thesis described the development, evaluation, and potentials for wider implementation of an online participatory tool for patients in guideline development.

In the first part of this final chapter, we present answers to the research questions as posed in the general introduction. Next, the main findings from the studies included in this thesis are discussed in the light of available literature and recent policy. Then some methodological considerations are addressed and discussed. Finally, this chapter concludes with recommendations for future research, implications for practice, and an overall conclusion.

Answers to the research questions:

The following answers to the research questions posed in Chapter 1 can be formulated from the studies described in this thesis.

1. What value do patients add to the scope of a Dutch multidisciplinary guideline on infertility when comparing perceived key clinical issues between professionals and patients? (Chapter 3)

Including patients in the scoping phase of the guideline development process leads to valuable additional main key clinical issues (defined as care aspects that need improvement) for the next step of a multidisciplinary guideline development process. Infertile couples broadened the scope of the guideline by adding eight main key clinical issues regarding patient-centred (e.g. information provision not meeting expectations) and organizational (e.g. poor care alignment) aspects of care. Infertile patients and professionals mentioned only two main key clinical issues collectively: the lack of emotional support and the lack of respect and autonomy. Nevertheless, patients posed different interpretations of these issues than professionals, which resulted in more patient-centred care aspects to be addressed in a multidisciplinary guideline on infertility.
2. To what extent does a patient-centred network approach to multidisciplinary guideline development in infertility provide a feasible format regarding the actual performance of a set of guidelines, its time investments, and experiences with the approach? (Chapter 2)

The novel patient-centred network approach is a feasible format for simultaneously and collaboratively developing a harmonized set of multidisciplinary and monodisciplinary guidelines around clinical care pathways for patients with fertility problems. Although comparisons of the actual time investments (20 months) are barely noted in the published literature on this topic, if converted into euros, it seems at least comparable to other published multidisciplinary guideline development initiatives. Moreover, multiple stakeholders reached agreement on the clinical content and perceived the network approach as positive and promising for developing multidisciplinary guidelines.

3. To what extent does a participatory tool for Dutch infertile patients in guideline development provide a feasible tool to enhance shared guideline development, regarding its use, usability, benefits for the guideline, users' experiences with the tool, and implementability in other clinical areas? (Chapters 4 & 5)

In this thesis two interrelated types of participatory tools are described and investigated. Chapter 4 answers the question posed for a preliminary wiki-based participatory tool and Chapter 5 answers the question posed for a specialized online participatory tool.

The wiki-based tool (Chapter 4) is a promising and feasible participatory tool for patients in guideline development. The evaluation of this tool led to suggestions for new modalities (e.g. automatic limitation of the number and length of recommendations, the use of a fixed format for recommendations, inclusion of a motivation page, and addition of a continuous prioritization system). Furthermore, attention should be paid to the informational character of such a wiki. To improve future implementability, a modified tool should preferably be co-developed and evaluated by patients themselves in a user-centred design study. Furthermore, representativeness of participating patients should be evaluated. These recommendations for improvement were used to develop the next specialized online participatory tool (Chapter 5). This specialized online tool is a usable and suitable participatory tool for guideline development on infertility. This tool might be implementable in clinical areas other than infertility, but requires cooperation from related professional societies and active patients' associations.

4. What value do patients add to the development of guideline-based quality indicators for patient-centredness? (Chapter 6)

The involvement of patients in the development of guideline-based indicators had an added value. Patients mainly select different quality indicators than do professionals involved in fertility care. Within professionals' and patients' final sets of 18 and 16 quality indicators, respectively, only 5 indicators were similar. Although both patients and professionals most prominently valued information and communication in fertility care, patients also emphasised the importance of access to care. Professionals emphasised the importance of coordination and integration of fertility care.

Discussion of main findings

The studies performed within the span of this thesis revealed that 'shared guideline development' adds value to current guideline development programmes with scarce patient participation. Patients, professionals, guideline developers, and policy directors should act upon these gathered experiences and shift the role of patients from the periphery towards the centre of the guideline development process.

Box 1: Clinical Practice Guidelines

Clinical Practice Guidelines (CPGs) are now ubiquitous. Although CPGs have a relatively short history, the goals and development process have evolved dramatically. From the mid-1970s practice variation and the appropriateness of medical procedures have been questioned as a result of the evidence-based movement. Since then, guideline production has accelerated and the development has been increasingly centrally organized [1]. The increase in international publications within the field of CPGs gives an indication of the rapid rise of their development. In 1993, the Medical Subject Heading (MeSH) 'practice guideline' was added to MEDLINE as a topic, and 444 articles were classified under that heading. In subsequent years, there has been an increase in the number of articles classified per year under the 'practice guideline's MeSH', to a total of 90.922 articles in 2016 (www.pubmed.com). Of these published articles, 21.473 articles included the description of CPGs and yet a plethora of CPGs has been produced.

Clinical practice guidelines are actually designed to support the decision-making processes in patient care and reduce inappropriate practice variation [2]. Published data confirmed that CPGs can substantially improve daily clinical practice, but low-quality guidelines may harm patients [3,4].

It is therefore not surprising that in the past 10 years the elements of the guideline development process and the quality of the guidelines have been issued and criticized nationally and internationally [2, 5–9]. In 2003 The Appraisal of Guidelines for Research and Evaluation (AGREE) Collaboration issued criteria to assess the quality of guidelines [10]. This collaboration developed a generic instrument to assess the methodological quality of Clinical Practice Guidelines using 23 key items grouped in 6 domains: scope and purpose, stakeholder involvement, rigour of development, clarity and presentation, applicability, and editorial independence. Worldwide, this initiative has led to the development of guideline programs and manuals by leading institutes, in which the elements and crucial steps have become a more standardized process; quality assessment according to the items of the AGREE instrument played a major role in the development of this process [11–14]. In 2009 in the Netherlands, 'the regieraad' was issued by The Dutch Ministry of *Health to overcome major problems in the development, uptake, and quality of* guidelines. In 2010, they published the first version of a general guideline manual, which included minimal quality requirements for guidelines, called guidelines for guidelines. This document was updated twice in 2011 and 2012 [15]. In addition, in 2011 the first version of 'medical specialists' guidelines 2.0' was published and endorsed by all 32 Dutch Medical Specialty societies [16]. The latter included a broader scope, including the minimal requirements regarding the guideline development process.

The guideline development process generally enhances several elements including topic selection, definition of the scope, formulation of key questions, answering the key questions by systematically reviewing the relevant literature and assessing its quality, formulation of conclusions and considerations, formulation of recommendations, reviewing the draft guideline (internal and external), and authorization and dissemination by relevant stakeholders. In addition, the 'medical specialists' guidelines 2.0' recommends that an implementation strategy should be conceptualized since guidelines do not implement themselves [3,17,18]. Preferably, the last step should be followed by an evaluation, including the monitoring of the quality of care when applying guideline-based quality indicators [19,20].

Guideline development approaches

As highlighted in Box 1, CPG development has been rapidly evolving over the past 10 years. Despite of all efforts that have been made, the appraised quality of the guidelines and the development methods still vary or do not meet the basic quality criteria, including the involvement of patients [2,5–9]. Furthermore, patients are not in the centre of the guideline development process, which may hinder further improvement of the quality of care, which is one of the key goals of CPGs. Finally, several reported problems still hinder CPG development and uptake, namely inadequate management of conflicts of interest (COIs), limited panel composition, lack of patient involvement, and lack of external review [6]. These problems also seem to play a crucial role in the implementability of the CPGs.

One may conclude that healthcare is still fragmented. This conclusion is illustrated by a strong focus on the single clinical aspects of diseases issued in the guidelines rather than on ensuring more integrated care for patients, including attention to matters such as patient-centredness, coordination, and continuity of care. These problems are not specific for guideline development and also play a crucial role in the efforts to improve the healthcare system worldwide. Different international published perspectives on re-designing healthcare have put forward these arguments and have strived for integrated and patient-centred care [21-28]. If well implemented, CPGs could be the ultimate tools to achieve this shift in healthcare, although essential elements in the approach are still lacking. Therefore, the target users feel no affinity with the guidelines, which impedes full implementation. Extensive collaboration among stakeholders seems to be a determining factor in bringing the quality of care to a higher level. Monodisciplinary guidelines, or separate multidisciplinary guidelines on the same topic, may not help policymakers, professionals, or patients to strive for integrated and patient-centred care. Solutions may be found in clustering the guideline development, such as clustering care in terms of integrated care and organizing the care with the patient in the centre. The use of such clinical networks has previously proven to be effective in increasing evidence-based practice and improving care models [29,30]. Therefore, the specific aim of the study described in Chapter 2 was to assess the feasibility of a patient-centred network approach to guideline development in fertility care. The network approach provides a feasible format for guideline developers to bring patients and other relevant stakeholders together. The efficiency of this approach would benefit from a rigid structure and a supportive organization. Additionally,

Discussion

this approach could be investigated in further detail by organizations that support, fund, or initiate the development of CPGs.

In the Netherlands, the first step has already been taken towards more multidisciplinary thinking in the development of CPGs. Recently, the Dutch Ministry of Health established the Dutch Quality Institute, which aims to bring the quality of CPGs and their development processes to a higher level (www. zorginstituut.nl). This Dutch quality institute has made significant strides in defining CPGs as part of 'quality'; for example, in documents, they replaced the term 'professional standard' as defined in the Dutch Health Insurance Act with 'quality standards'. This term is now used to refer to a broader spectrum of quality documents (i.e. clinical practice guidelines, [care] standards, best practices, and quality indicators), which should concern the whole care process (www. glossarium.zorginstituutnederland.nl). Although the term 'quality standard' may refer to a multidisciplinary development process of the underlying documents, it still does not imply that patients play a substantial role therein.

In addition to the development and authorization of CPGs, the 32 Dutch associations of medical specialists have developed a jungle of (un)related and undefined quality documents: protocols, (care) standards, and national cooperation agreements. The ability of all these documents to actually contribute to the quality of care seems questionable, especially when their content is unrelated or even contradictory. To bring the quality of care to a higher level, patients, health policymakers, guideline developers, and other allied stakeholders need to collaborate on scoping, prioritizing, defining, developing, and maintaining clinical practice guidelines. Furthermore, it seems time to develop a uniform vision for the definition and the development process of related quality documents to achieve this ultimate goal. We are convinced that our format could help these organizations further ensure collaboration and patient-centredness in clinical guideline development, broadening quality standards, and actualizing content.

Patients and guidelines

When planning to transform the healthcare system from a disease-driven system into an integrated and patient-centredness-driven system, it seems logical that patients would play a key role in shaping and improving its quality. Corresponding with the ultimate goal of CPGs, patients should also play a key role in their development process. Although patient involvement in the main phases of Clinical Practice Guideline development has been urged internationally, implementing this involvement still remains a challenge. Several underlying challenges regarding the involvement of patients in the main phases of the clinical guideline development process have been reported in published literature [2,31–33]. In Chapters 3, 4, and 5, we aimed to assess the added value of patients in scoping and writing clinical guidelines, as well as in developing guideline-based indicators, which facilitate the adherence to clinical practice guidelines.

Patients' role in scoping the guideline

Scoping the guideline is the first and most crucial step of the guideline development process. In this step the guideline development group defines what should and should not be addressed in a new or revised guideline. Various approaches are applied to scope a guideline and identify clinical issues that need improvement, including focus groups or workshops with various allied stakeholders in the topic of the guideline, written questionnaires, discussion within the guideline development group itself, and a written consultation phase to comment on the scope of the draft [34,35]. Although several institutes use patient focus groups to gather input for guidelines, their impact on the scope remains unclear or is not the primary goal [34,35]. Most published initiatives on patient involvement focussed on the writing and reviewing phase of the guideline development process or on written consultation when the scope has already been drafted [35-39]. One can question whether patients are able to have any influence on the scope when they are not involved until after the scope has been drafted. In Chapter 3, we aimed to assess the added value of patients in scoping a Dutch guideline on infertility. This study demonstrated that patients can broaden the scope of a guideline on infertility, as they suggested different key clinical issues (e.g. issues that need improvement and should be addressed in the clinical guideline) than did the professionals. Furthermore, patients addressed patient-centred aspects of professionals' key clinical issues (Figure 1). This finding corresponds to the results of other studies on the assessment of the quality of fertility care, which have shown that patient-centredness is one of the key aspects among all six aspects that define the quality of care as proposed by the Institute of Medicine (IOM) [2,40–42]. However, professionals working in fertility care still overestimate their level of patient-centredness, demonstrating a poor correlation between patients' and physicians' perceptions of the quality of care [42]. This phenomenon has also been seen in healthcare areas other than fertility care [43–45].

This finding strengthens our recommendation to enable patients to play a key

role in scoping guidelines. As guidelines are currently being transformed from 'cookbooks' to documents based on clinical issues that need improvement while, for example, reducing practice variation or optimizing patient care or patient safety, the involvement of patients in this phase may help to ensure guidelines address issues that are relevant and important to them too. The study presented in Chapter 3 shows that actual involvement of patients from the start of the scoping process can make the guideline more tailored and responsive to patients in terms of key questions and defined outcomes regarding fertility care. We therefore suggest that guideline developers and policymakers use this approach in other areas as well. In the era of high-quality patient-centred care, this approach may positively impact patient satisfaction, care costs, and improved outcomes [46]. Future studies on the actual impact on the implementability of guidelines and on the quality of care may support our recommendation to use this approach systematically. Finally, this approach could be used to identify patients' needs for tailored information or to select important questions for developing tools that facilitate shared decisionmaking in the clinical setting.



Figure 1: Shared guideline development: the scoping process (Chapter 3)

Patients' role in writing the guideline

Both in the Dutch guideline manual and international manuals, the role of patients in the guideline development process is unstructured, lacking in transparency, and sometimes unclear. Although patient participation in clinical guideline development is emphasized, it faces practical challenges [32,33]. Firstly, several methods have been suggested and the level of participation of patients varies from very low and passive (i.e. exploring patients' preferences in interviews or focus groups, asking patients' representatives to comment on draft guidelines) to higher and more active (i.e. including patients or patients' representatives in the guideline development group) [34,35,47-51]. Secondly, 'golden rules' on how and when to apply these methods most effectively are lacking [37,38]. Thirdly, all these methods are restricted to including a selected number of patients or patients' representatives. Fourthly, integrating patients' preferences into guideline recommendations is difficult and the result of their input is often unclear [52]. Fifthly, important organizational (i.e. recruitment of participants), financial (i.e. costs of patients' education or for conducting focus groups), and socio-political barriers (i.e. guideline developers' resistance to including patients in the guideline development group) also impede patient participation in guideline development [50]. Finally, studies on the effectiveness and impact of patient participation are limited [32,37]. These challenges are determining factors in choosing the extent of involving patients in the clinical guideline development process. In Chapters 4 and 5, we assessed the feasibility of two interrelated participatory online tools to facilitate patient participation in clinical guideline development.

Using online participatory tools to involve patients

The Internet has been rapidly evolving from a 'one-way download medium' to a 'participatory medium' in which consumers are now playing a more active role. This evolution has a considerable impact on the healthcare system and Web 2.0 technologies are now increasingly used to empower patients. For example, patients can become active partners in their own treatment by using online decision-making tools, accessing and writing patient information, accessing their personal health record, and even connecting to medical doctors or professionals via online communities [53–59]. Using an online participatory tool may solve most of the challenges regarding patient participation in clinical guideline development. In Chapter 4 we concluded that a conventional wiki as a participatory tool for patients in guideline development for Dutch fertility care is feasible considering the high

Discussion

number of unique visitors and recommendations obtained, although it is also a laborious method. In Chapter 5 we discussed the evaluation of a more specialized and refined online participatory tool that focussed on the successful improvement of the usability for patients and guideline developers. Both chapters add to the knowledge on empowering patients in the development of clinical guidelines. The specialized online participatory tool described in Chapter 5 may be implementable in clinical areas other than infertility, although this would require cooperation from related professional societies and active patients' associations. Therefore, we recommend that policy organizations introduce the tool to guideline development programs and support their use of it. This approach could motivate professional associations to implement this tool in the guideline development process and support patients' associations in increasing their role in guideline development. Chapter 4 also acknowledged that the Internet has an important role in finding helpful information for patients' clinical pathways. As such, it seems important that reliable information is guideline based and digitized in the same place as the guideline. Our tool could also be used to identify patients' priorities in research and informational needs. In the Netherlands, most decisions on how to involve patients in the guideline development process are generally made by the guideline development institutes and/or the medical specialty associations. We acknowledge that time and cost restrictions play an important role herein. With the recent introduction of the national guideline database and the handin-hand development of guidelines in sections dedicated to one key question, these challenges might play a more prominent role (www.richtlijnendatabse. nl). Furthermore, there are also the risks that patients' associations will be overwhelmed and unable to meet requests to participate or will need to decide which sections they will participate in and which sections they will not. By having a set of recommendations, which are continuously updated by patients already developed, the use of an online participatory tool could help patients' associations and guideline developers gather input on a specific subject without losing time. We therefore suggest that guideline development institutes together with the Dutch Federation of Patients continue to explore patient participation in the guideline development process using tools such as our participatory tool.

Patients' role in developing measures to guideline adherence

In addition to clinical effectiveness, safety, and cost effectiveness, patientcentredness is another important dimension of the quality of care [2]. The ultimate goal of clinical practice guidelines is to optimize the quality of care and guidelinebased indicators are being developed to monitor the adherence to them. Quality indicators can focus on the process, structure, or outcome of care, including important domains of the patient-centredness of care. However, patients are, for the most part, surprisingly not involved in the development process of guidelinebased quality indicators. Guideline-based indicators are usually developed by panels of experts, who may be unable to adequately evaluate their performance regarding patient-centredness [41].

The study in Chapter 6 showed that infertile patients can broaden a set of guidelinebased quality indicators for fertility care by selecting different indicators representing different domains of patient-centred care (e.g. accessibility, coordination, and integration of care) than professionals select, which appeared earlier as underexposed dimensions of patient-centredness [60–65]. This finding strengthens the recommendation to involve patients in the guideline indicator development process. Following this recommendation is even more important in complex chronic conditions where a high adherence to treatment is inevitable. Nevertheless, there is still not an existing uniform methodological gold standard for patient involvement in the development process of quality indicators [66]. Additionally, the Netherlands is still facing challenges in measuring quality indicators, since adequate registration is lacking, and in determining responsibilities in the registration process. Furthermore, there is a tendency to develop all kinds of instruments to measure quality of care and, consequently, healthcare professionals may face a huge burden in registration load. To alleviate this burden, the effective use of existing data and education on the importance of registering data and its value in improving the quality of care should be considered to be key factors in motivating professionals to pave the way to continuously improving the quality of care [67].

Methodological considerations

Setting of the studies

The majority of the studies included in this thesis were conducted within a national project aiming to innovate, broaden collaboration, and improve the level of patient-centredness in guideline development. This setting could influence the results of our studies since participants were more committed to collaborate at first.

Study design

This thesis consists of mainly qualitative exploratory and feasibility studies. In Chapter 2, we used qualitative research methods and data analysis to explore and compare patients' and professionals' perceived key clinical issues. The value of qualitative methods has been widely proven in exploratory studies [68]. In our first study, for practical reasons, we used two types of qualitative research methods, namely semi-structured interviews with infertile couples and focus group interviews among professionals involved in fertility care. Research has been previously suggested that social desirability plays an important role in focus group discussions, which could have restricted the number of and variety in key clinical issues [69]. Nevertheless, various key clinical issues were addressed.

In Chapters 3, 4, and 5 we performed feasibility studies. The term 'feasibility study' is still a contested term that refers to the exploration of new methodologies or interventions [70]. Traditionally part of feasibility studies, experience with a new approach or intervention, barriers and facilitators, and suggestions for improvement are important outcome measures and input for further study [70]. In this thesis, we used a mixed-method evaluation. Mixed methods are frequently used to quantify predefined qualitative outcome data and are therefore highly applicable to our described studies. However, potential disadvantages of this methodology regarding our studies include potential sampling bias and the low response rates on the written questionnaires described in Chapter 5. Furthermore, we used interviews as input for designing a written questionnaire while saturation of data was not reached.

In Chapter 6 we described the development of guideline-based quality indicators for patient-centredness using a RAND modified Delphi method. This method has been widely used in the development of quality indicators in healthcare [66,71]. While this method is a useful approach to facilitating consensus, the influence of the panel composition and type of feedback on the legitimacy of the results have been questioned regularly [66,72–74]. However, in our study, a balanced group of stakeholders mandated by their professional societies participated. Furthermore, the panel members received written feedback instead of face-to-face feedback, which may have minimized intimidation factors while selecting potential indicators [73,74].

Outcome

The main goal of developing quality instruments is monitoring and finally improving the quality of care. However, there is still no direct, sufficient evidence that patient

involvement in guideline development leads to a higher quality of care. This thesis focussed on the added value of the involvement of patients in the scoping and writing phase of guideline development and the indicator development process (i.e. key clinical issues as input on key questions and recommendations being part of a Dutch national guideline on infertility and on quality indicators for patient-centredness). We focussed particularly on the evaluation of a new approach in terms of barriers, facilitators, suggestions for improvement, and the feasibility of a participatory tool to involve patients in the guideline development process. Among these outcomes, the effect on the implementability of the guideline and on the quality of care have not been evaluated in the studies as presented in this thesis. These final outcomes need to be a topic of future studies.

Discussion of future research

In this thesis, we explored the added value of patients in several phases of the guideline development process. However, some questions remain unanswered, namely the impact of the level of patient involvement in guideline development on both the implementability of the guideline and on the quality of care. Firstly, to evaluate the impact on implementability, The Guideline Implementability Appraisal (GLIA) instrument can be used [75]. This instrument is based on a set of guideline characteristics that predict potential challenges of effective implementation. However, implementation is determined by both intrinsic and extrinsic factors, and the latter is not included in this instrument [76]. Studies to compare the level of implementation of guidelines developed with a high level of patient involvement to guidelines developed without involving patients are generally impossible. The content of the guidelines would not be comparable since patients can broaden the scope of the guideline and add recommendations. Furthermore, extrinsic factors that determine implementation, such as differences in the organization of healthcare professionals between hospitals, would make it bias sensitive.

Next, to evaluate interventions for healthcare improvement, performing a randomised controlled trial (RCT) is considered the gold standard in implementation research. However, it could be debated whether the impact of patient involvement on the quality of care could be captured within a study design as a (clustered) RCT. In practice, developing two types of guidelines crosses ethical barriers (i.e. stakeholders' participation could have been pointless in one of the guidelines). Furthermore, developing CPGs include whole-intensive processes, which costs time and commitment from stakeholders. The differences in the content and structure of the final guidelines would also make them noncomparable in the baseline. Finally, performing a budget-impact analysis on the network approach to multidisciplinary guideline development could be considered as well.

Implementation and evaluation of the participatory tool for patients in guideline development within other clinical areas (predominantly within other complex multidisciplinary diseases, such as cancer) should be the next step.

The developed indicators for patient-centredness should be followed by a further practice test to assess its feasibility in daily practice. By evaluating its measurability and the intra- and inter-observer reliability, the core set of 29 indicators for patient-centredness could be reduced by 10–20% [73,77,78]. Finally, its effects on the quality of patient-centred care needs to be investigated and compared to other instruments that have been developed to improve patient-centred care, such as Patient Reported Outcome Measurements for infertility (i.e. the FertiQol, QPP-IVF instrument, and the PCQ infertility) [41,62,79].

Key implications for future research:

- To evaluate the impact on the implementability of guidelines with a high level of patient involvement is generally impossible since implementation is determined by intrinsic and extrinsic factors.
- It could be debated whether the impact of patient involvement on the quality of care could be captured within a study design such as a (clustered) RCT since ethical barriers, commitment of stakeholders, and costs play a crucial role.
- A budget-impact analysis on the network approach to multidisciplinary guideline development could be considered.
- Implementation and evaluation of the participatory tool for patients in guideline development within other clinical areas (predominantly within other complex multidisciplinary diseases, such as cancer) should be the next step.
- The developed indicators for patient-centredness should be followed by a further practice test to assess its feasibility in daily practice.
- The effects of the developed set of indicators for patient-centredness on the quality of patient-centred care needs to be investigated and compared to

other instruments, such as Patient Reported Outcome Measurements for infertility (i.e. the FertiQol, QPP-IVF instrument, and the PCQ infertility).

Key implications for policy and practice

Implications for professionals' associations and policymakers:

- Clinical Practice Guidelines should focus on clinical issues, which are relevant to all stakeholders, including patients.
- Facilitate patients to play a key role in scoping the guideline.
- The development of monodisciplinary guidelines, even those developed by a multidisciplinary development group, should not be permitted anymore.
- Explore patient-centred approaches, such as our network approach to enhance shared guideline development.
- Collaborate with patients, health policymakers, guideline developers, and all allied stakeholders in prioritizing, scoping, developing, and maintaining clinical practice guidelines.
- Change the introduced term 'quality standards' into collaborative standards since patients and all relevant stakeholders should be involved as well.
- Develop a uniform vision for the definition and development process of all quality documents that are part of quality standards.
- Ideally, include patients in the scoping phase to identify their needs for tailored information and to select important questions for developing tools that facilitate shared decision-making in the clinical setting.
- Introduce the online participatory tool to guideline development programs, further explore its possibilities regarding major clinical issues (first with the Dutch Federation of Patients), and assure the cooperation of professional associations.
- Involve patients in the guideline-indicator development process.
- Create an efficient infrastructure for measuring quality indicators, including the level of patient-centredness.
- Educate professionals on the importance of registering data on the quality of care and their value in improving the quality of care.
- Stress the importance of patient involvement in all different phases (i.e. scoping, writing, and developing quality indicators) of the guideline development process and encourage associations' members to be actively involved in guideline development to implement this approach.

Key implications for patients and patients' associations:

- Encourage patients and patients' associations to contribute to the guideline development process since their involvement will help enhance the level of patient-centredness of clinical practice guidelines.
- Collaborate with health policymakers, guideline developers, and all allied stakeholders in prioritizing, defining, developing, and maintaining clinical practice guidelines.
- Take a key role in scoping a clinical practice guideline.
- Introduce and implement tools, such as an online participatory tool, to facilitate patient participation in guideline development programs and to further explore its possibilities regarding major clinical issues.
- Involve patients in the guideline-indicator development process.
- Stress the importance of involvement in all different phases (i.e. scoping, writing, and developing quality indicators) of the guideline development process and encourage associations' members to be actively involved in guideline development to implement this approach.

Final conclusions and remarks

This thesis demonstrates the added value of involving patients in all phases of the guideline development process and of using a patient-centred approach therein; 'shared guideline development' is the future of guideline development. In fact, all involved healthcare professionals, their associations, patients, and policymakers are now in the lead to collaborate on implementing this concept. Online participatory tools could contribute to bringing shared guideline development to a higher level while transparently using patients' input in the guideline development process.

References

- 1. Weisz G, Cambrosio A, Keating P *et al.* The emergence of clinical practice guidelines. *Milbank Q* 2007;85:691–727.
- Institute of Medicine (IOM). Crossing the quality Chasm. A new Health System for the 21st century. Washington D.C.: National Academy Press, 2001.
- 3. Grimshaw J, Thomas R, MacLennan G *et al*. Effectiveness and efficiency of guideline dissemination and implementation strategies. *Health Technol Assess* 2004;**8**:1–72.
- Grol R, Wensing M, Eccles M. Improving Patient care. The implementation of change in clinical practice. Oxford, UK: Elsevier Butterworth Heinemann, 2005.
- Burgers JS, Cluzeau FA, Hanna SE *et al.* Characteristics of high-quality guidelines: evaluation of 86 clinical guidelines developed in ten European countries and Canada. *Int J Technol Assess Health Care* 2003;19:148–157.
- Grilli R, Magrini N, Penna A *et al.* Practice guidelines developed by specialty societies; the need for a critical appraisal. *Lancet* 2000;355:103–106.
- 7. Alonso-Coello P, Irfan A, Sola I *et al.* The quality of clinical practice guidelines over the last two decades: a systematic review of guideline appraisal studies. *Qual Saf Health Care* 2010;**19**:e58.
- 8. Kung J, Miller RR, Mackowiak PA. Failure of clinical practice guidelines to meet institute of medicine standards: two more decades of little, if any, progress. *Arch Intern Med* 2012;**172**:1628–1633.
- Shaneyfelt TM, Centor RM. Reassessment of clinical practice guidelines: go gently into that good night. J Am Med Assoc 2009;301:868–869.
- Terrace, L. Development and validation of an international appraisal instrument for assessing the quality of clinical practice guidelines: the AGREE project. *Qual Saf Health Care* 2003;12:18-23.
- Burgers JS, Fervers B, Haugh M *et al.* International assessment of the quality of clinical practice guidelines in oncology using the Appraisal of Guidelines and Research and Evaluation Instrument. J Clin Oncol 2004;22:2000-2007.
- 12. National Institute of Clinical Excellence (NICE). The guidelines' manual. London: NICE, 2009. URL: www.nice.org.uk Archived by WebCite* at http://www.webcitation.org/65UXx2saM
- Scottish Intercollegiate Guidelines Network (SIGN). SIGN 50: A guidelines' developer handbook. Edinburgh: SIGN, 2008. URL: http://www.sign.ac.uk/pdf/sign50.pdf Archived by WebCite^{*} at http:// www.webcitation.org/65UY1tSVw
- 14. Appraisal of Guidelines for Research & Evaluation (AGREE) Next Steps Consortium. AGREE II Instrument, 2009. www.agreetrust.org.
- 15. Werkgroep richtlijnen voor richtlijnen. *Richtlijn voor richtlijnen*. Den Haag: Regieraad Kwaliteit van Zorg, 2012.
- 16. Medisch Specialistische richtlijnen 2.0.: http://www.kwaliteitskoepel.nl/assets/structured-files/2012/ Eindrapport_adviescommissie_richtlijnen_okt20111.pdf.
- 17. Grol, R. Personal paper. Beliefs and evidence in changing clinical practice. BMJ 1997; 315:418.
- 18. Bero LA, Grilli R, Grimshaw JM *et al.* Getting research findings into practice: Closing the gap between research and practice: an overview of systematic reviews of interventions to promote the implementation of research findings. *BMJ* 1998;317:465.
- 19. Grol, R., Grimshaw, J. From best evidence to best practice: effective implementation of change in patients' care. *Lancet* 2003;**362**:1225-30.
- 20. Nelen WLDM, Hermens RPMG, Mourad SM *et al.* Monitoring reproductive health in Europe: what are the best indicators of reproductive health? A need for evidence-based quality indicators of reproductive health care. *Human Reprod* 2007; **22**:916-918.
- 21. Alston CPL, Halvorson G, Paget L et al. Communicating With Patients on Health Care Evidence, Discussion Paper. Washington, DC: Institute of Medicine, 2012 [http://www.iom.edu/evidence].
- 22. Halvorson GC. Health Care Reform Now!: A Prescription for Change. San Francisco, CA: Jossey-Bass, 2007.
- 23. Landon BE, Grumbach K, Wallace PJ. Integrating public health and primary care systems: potential strategies from an IOM report. *J Am Med Assoc* 2012;**308**:461–462.

- 24. Novelli WD, Halvorson GC, Santa J. Recognizing an opinion: findings from the IOM evidence communication innovation collaborative. *J Am Med Assoc* 2012;**308**:1531–1532.
- 25. Porter, Michael E. "A strategy for health care reform—toward a value-based system." *New England Journal of Medicine* 2009;**361**:109-112.
- 26. Porter, Michael E, Thomas H Lee. "Why strategy matters now." New England Journal of Medicine 2015;372:1681-1684.
- 27. Smith M, Halvorson G, Kaplan G. What's needed is a health care system that learns: recommendations from an IOM report. *J Am Med Assoc* 2012;**308**:1637-1638.
- Wynia MK, Von Kohorn I, Mitchell PH. Challenges at the intersection of team-based and patientcentered health care: insights from an IOM working group. J Am Med Assoc 2012;308:1327-1328.
- 29. Cunningham FC, Ranmuthugala G, Plumb J *et al.* Health professional networks as a vector for improving healthcare quality and safety: a systematic review. *BMJ Quality Safety* 2012;**21**:239-249.
- Goodwin N, Peck E, Freeman T et al. Managing across diverse networks of care: lessons from other sectors. Report to the NHS SDO R&D Programme. Birmingham: Health Services Management Centre, University of Birmingham, 2004.
- 31. Schünemann HJ, Fretheim A, Oxman AD. Improving the use of research evidence in guideline development: 10. Integrating values and consumer involvement. *Health Res Policy Syst* 2006;4:22.
- 32. Nilsen ES, Myrhaug HT, Johansen M *et al.* Methods of consumer involvement in developing healthcare policy and research, clinical practice guidelines and patient information material. *Cochrane Database Syst Rev* 2006;**3**:CD004563.
- 33. Graham RL, Mancher M, Wolman DM *et al. Clinical Practice Guidelines We Can Trust.* Washington, DC: National Academies Press, 2011.
- National institute for health and clinical excellence (NICE). https://www.nice.org.uk/media/default/ About/NICE-Communities/Public-involvement/Public-involvement-programme/PIP-processguide-apr-2015.pdf. 19 January 2016, date last accessed.
- Scottish Intercollegiate Guidelines Network (SIGN). http://www.sign.ac.uk/ patients/network.html, 19 January 2016, date last accessed.
- 36. The Netherlands Organisation for Health Research and Development (ZonMW). *The Participation Compass.* http://www.participatiekompas. nl/over-participatiekompas/english, 19 January 2016, date last accessed.
- 37. Boivin A, Currie K, Fervers B *et al.* Patient and public involvement in clinical guidelines: international experiences and future perspectives. *Qual Saf Health Care* 2010;**19**:e22.
- 38. Legare F, Boivin A, van der Weijden T *et al.* Patient and public involvement in clinical practice guidelines: a knowledge synthesis of existing programs. *Med Decis Making* 2011;**31**:E45–74.
- 39. Tong A, Lopez-Vargas P, Howell M *et al.* Consumer involvement in topic and outcome selection in the development of clinical practice guidelines. *Health Expect* 2012;**15**:410–23.
- 40. Dancet EA, Nelen WL, Sermeus *W et al.* The patients' perspective on fertility care: a systematic review. *Hum Reprod Update* 2010;**16**:467-87.
- Aarts, JWM, Huppelschoten AG, van Empel IWH *et al.* How patient-centred care relates to patients' quality of life and distress: a study in 427 women experiencing infertility. *Hum Reprod* 2012;27:488-495.
- 42. van Empel IW, Dancet EA, Koolman XH *et al.* Physicians underestimate the importance of patientcentredness to patients: a discrete choice experiment in fertility care. *Hum Reprod* 2011;**26**:584-593.
- Hall JA, Stein TS, Roter DL et al. Inaccuracies in physicians' perceptions of their patients. Medical Care 1999;37:1164-1168.
- 44. Jung HP, Wensing M, Olesen F *et al.* Comparison of patients' and general practitioners' evaluations of general practice care. *Qual Saf Health Care* 2002;**11**:315-319.
- 45. Zandbelt LC, Smets E, Oort FJ *et al.* Satisfaction with the outpatient encounter. *J Gen Intern Medicine* 2004;**19:**1088-1095.
- 46. Gupta D, Rodeghier M, Lis CG. Patient satisfaction with service quality in an oncology setting: implications for prognosis in non-small cell lung cancer. *Internat J Qual Health Care* 2013;25:696-703.

- 47. van Wersch A, Eccles M. Involvement of consumers in the development of evidence based clinical guidelines: practical experiences from the North of England evidence based guideline development programme. *Qual Health Care* 2001;**10**:10-16.
- 48. Bastian H. Raising the standard: practice guidelines and consumer participation. *Int J Qual Health Care* 1996;**8**:485-490.
- 49. Rogers WA. Are guidelines ethical? Some considerations for general practice. Br J Gen Pract 2002;52:663-668.
- Diaz Del Campo P, Gracia J, Blasco JA et al. A strategy for patient involvement in clinical practice guidelines: methodological approaches. BMJ Qual Saf 2011;20:779-84.
- 51. Legare F, Boivin A, van der Weijden T *et al.* Patient and public involvement in clinical practice guidelines: a knowledge synthesis of existing programs. *Med Decis Making* 2011;**31**:E45-74.
- Krahn, M, Naglie G. The next step in guideline development: incorporating patient preferences. J Am Med Assoc 2008;300:436-38.
- 53. Tuil WS, Verhaak CM, Braat DD *et al.* Empowering patients undergoing in vitro fertilization by providing Internet access to medical data. *Fertil Steril* 2007;**88**:361-368.
- 54. Samoocha, D, Bruinvels DJ, Elbers NA *et al*. Effectiveness of web-based interventions on patient empowerment: a systematic review and meta-analysis. *J Med Internet Res* 2010;**12**:23.
- 55. Irizarry T, DeVito Dabbs A, Curran CR. Patient Portals and Patient Engagement: A State of the Science Review. *J Med Internet Res* 2015;**17**:e148.
- 56. van der Eijk, M, Faber MJ, Aarts JW *et al.* Using online health communities to deliver patient-centered care to people with chronic conditions. *J Med Internet Res* 2013;15:115.
- 57. Aarts JWM, Vennik F, Nelen WL *et al.* Personal health communities: a phenomenological study of a new health-care concept. *Health Expectations* 2015;**18**:2091-2106.
- 58. Archambault PM, van de Belt TH, Grajales III *et al.* Wikis and collaborative writing applications in health care: a scoping review. *J Med Internet Res* 2013;**15:**210.
- 59. van de Belt TH, Faber MJ, Knijnenburg JM *et al.* Wikis to facilitate patient participation in developing information leaflets: first experiences. *Informatics for Health and Social Care* 2014;**39**:124-139.
- 60. Souter VL, Penney G, Hopton JL *et al.* A. Patient satisfaction with the management of infertility. *Hum Reprod* 1998;**13**:1831-1836.
- Schmidt L, Holstein BE, Boivin J *et al.* High ratings of satisfaction with fertility treatment are common: findings from the Copenhagen Multi-centre Psychosocial Infertility (COMPI) Research Programme. *Human Reprod* 2003;18:2638-2646.
- 62. van Empel IW, Aarts JW, Cohlen BJ *et al.* Measuring patient-centredness, the neglected outcome in fertility care: a random multicentre validation study. *Human Reprod* 2010;**25**:2516-2526.
- 63. Dancet EA, D'Hooghe TM, Sermeus W *et al.* Patients from across Europe have similar views on patient-centred care: an international multilingual qualitative study in infertility care. *Hum Reprod* 2012;**27**:1702-1711.
- 64. Schleedoorn MJ, Nelen WLDM, Dunselman GAJ *et al.* Selection of key recommendations for the management of women with endometriosis by an international panel of patients and professionals. *Human Reprod* 2016;**31**:1208-18.
- 65. Uphoff EP, Wennekes L, Punt CJ *et al.* Development of generic quality indicators for patient-centered cancer care by using a RAND modified Delphi method. *Canc Nursing* 2012;**35**:29-37.
- 66. Kotter T, Blozik E, Scherer M. Methods for the guideline-based development of quality indicators--a systematic review. *Implement Sci* 2012;7:21.
- 67. Dutch Federation of University Medical Centres (NFU). *Registratie aan de bron. Visie op documentatie en gebruik van zorggegevens* 20132020. Utrecht: NFU, 2013.
- 68. Silverman D. Doing qualitative research. 3rd edition. London: Sage Publications Ltd, 2009.
- 69. Fitzpatrick R, Boulton, M. Qualitative methods for assessing health care. *Quality Health Care* 1994;**3:**107.
- 70. Arain M, Campbell MJ, Cooper CL *et al.* What is a pilot or feasibility study? A review of current practice and editorial policy. *BMC Med Res Methodology* 2010;**10**:67.

- 71. Boulkedid R, Abdoul H, Loustau M *et al.* Using and Reporting the Delphi Method for Selecting Healthcare Quality Indicators: A Systematic Review. *PLoS ONE* 201;6:e20476.
- 72. Green B, Jones M, Hughes D *et al.* Applying the Delphi technique in a study of GPs' information requirements. *Health Social Care Community* 1999;7:198-205.
- 73. Shield T, Campbell S, Rogers A *et al.* Quality indicators for primary care mental health services. *Qual Saf Health Care* 2003;**12**:100-106.
- 74. Campbell SM, Shield T, Rogers A *et al.* How do stakeholder groups vary in a Delphi technique about primary mental health care and what factors influence their ratings? *Qual Saf Health Care* 2004;**13**:428-34.
- 75. Kashyap N, Dixon J, Michel G *et al. GuideLine implementability appraisal v. 2.0*. New Haven, CT: Yale Center for Medical Informatics, 2011.
- 76. Shiffman RN, Dixon J, Brandt C, *et al.* The GuideLine Implementability Appraisal (GLIA): development of an instrument to identify obstacles to guideline implementation. *BMC Med Inform Dec Making* 2005; **5:**23.
- 77. Scinto JD, Galusha DH, Krumholz HM *et al.* The case for comprehensive quality indicator reliability assessment. *J Clin Epidem* 2001;**54**:1103-1111.
- Wollersheim H, Hermens R, Hulscher M *et al.* Clinical indicators: development and applications. *The Netherlands J Med* 2007;65:15-22.
- Holter H, Sandin-Bojö AK, Gejervall AL *et al.* Quality of care in an IVF programme from a patient's perspective: development of a validated instrument. *Human Reprod* 2014;29:534-547.



Chapter 8

Summary

English Summary

Healthcare is fragmented and does not pay enough attention to patients' needs and values. As is true of other diseases that require complex multidisciplinary care, reproductive care is generally offered by various types of independently organized professionals (e.g. general practitioners, gynaecologists, and urologists). Furthermore, the care provided is usually based on evidence or professional consensus irrespective of patients' needs and values. Well-developed clinical practice guidelines (CPGs) could be valuable tools to close the gap between this fragmented continuum of evidence-based reproductive healthcare and infertile couples' need to be in charge of their own care pathway.

However, reliable contributions of other stakeholders – especially infertile patients – are mostly lacking. Furthermore, guideline development methodologies mainly focus on the disease instead of on patients' clinical pathways. Therefore, we have attempted to put the patients in the centre of the various stages of the guideline development process. This thesis focuses on the experiences with shifting the role of Dutch infertile patients in guideline development from the periphery towards the centre and introduces 'shared guideline development' in fertility care.

The aim of this thesis, as outlined in **Chapter 1**, was to answer four specific questions.

Chapter 2 focuses on the first question:

What value do patients add to the scope of a Dutch multidisciplinary guideline on infertility when comparing perceived key clinical issues between professionals and patients?

To answer this question a qualitative interview study was performed among 12 infertile couples and 17 professionals. We listed and compared the couples' and professionals' key clinical issues (i.e. care aspects that need improvement) to be addressed in the guideline according to four domains: current guidelines, professionals, patients, and organization of care. Main Outcome Measures of this study included the main key clinical issues, which were the key clinical issues suggested by more than three-quarters of the infertile couples and/or at least two professionals.

Overall, we identified 32 key clinical issues among infertile couples and 23 among professionals. Of the defined main key clinical issues, infertile couples mentioned

eight issues that were not mentioned by the professionals. These main key clinical issues mainly concerned patient-centred aspects of care on the professional and organizational domain (e.g. poor information provision and poor alignment of care). Both groups mentioned two main key clinical issues collectively that were interpreted differently: the lack of emotional support and respect for patients' values.

We concluded that including patients in the guideline development process beginning in the first phase leads to the identification of valuable additional main key clinical issues for the next step of a multidisciplinary guideline development process and broadens the scope of the guideline, particularly regarding patientcentredness and organizational issues from a patients' perspective.

Chapter 3 focuses on the second question:

To what extent does a patient-centred network approach to multidisciplinary guideline development in infertility provide a feasible format for multidisciplinary guideline development regarding the actual performance of a set of guidelines, its time investments, and experiences with the approach?

To answer this question a feasibility study was performed, including a detailed process evaluation of the guideline development process, professionals' experiences with the network approach, and time invested. We used a patient-centred network approach to develop five harmonized guidelines (one multidisciplinary and four monodisciplinary) around clinical pathways in fertility care.

The network structure comprised the centrally located patients and the steering committee; a multidisciplinary guideline development group (gynaecologists, physicians, urologists, clinical embryologists, clinical chemists, a medical psychologist, an occupational physician, and two patient representatives); and four monodisciplinary guideline development groups. The guideline development addressed patient-centred, organizational, and medical-technical key questions derived from interviews with patients and professionals. These questions were elaborated and distributed among the groups. We evaluated the project performance, participants' perceptions of the approach, and the time needed, including time for analysis of secondary sources, interviews with eight key figures, and a written questionnaire survey among 35 participants.

Within 20 months, this approach helped us develop a multidisciplinary guideline for treating infertility and four related monodisciplinary guidelines for general

infertility, unexplained infertility, male infertility, and semen analysis. The multidisciplinary guideline included recommendations for the main medicaltechnical matters and for organizational and patient-centred issues in clinical care pathways. The project was carried out as planned except for minor modifications and three extra consensus meetings. The participants were enthusiastic about the approach, the respect for autonomy, the project coordinator's role, and patient involvement. Suggestions for improvement included timely communication about guideline formats, the timeline, participants' responsibilities, and employing a librarian and more support staff. The 35 participants spent 4497 hours in total on this project. We concluded that the novel patient-centred network approach is feasible for simultaneously and collaboratively developing a harmonized set of multidisciplinary and monodisciplinary guidelines around clinical care pathways for patients with fertility problems. Further research is needed to compare the efficacy of this approach with more traditional approaches.

Chapter 4 and Chapter 5 both focus on the third question:

To what extent does a participatory tool for Dutch infertile patients in guideline development provide a feasible tool to enhance shared guideline development, regarding its use, usability, benefits for the guideline, users' experiences with the tool, and implementability in other clinical areas?

To answer this question two feasibility studies were performed. In **Chapter 4** the feasibility of a basic wiki as a participatory tool for patients in the development of a guideline on infertility was assessed. A multimethod evaluation strategy was used to assess the feasibility of the wiki as a participatory tool for patients in guideline development.

The evaluation included (1) the use of the wiki (number of page views and visitors), (2) benefits of the wiki (i.e. number, content, and eligibility of the recommendations to be integrated into the guideline), and (3) patients' facilitators of and barriers to adoption, as well as the potential challenges to be overcome in improving this wiki.

To obtain initial content for the wiki, we conducted in-depth interviews (n = 12) with infertile patients. Transcripts from the interviews were translated into 90 draft recommendations. These were presented on a wiki. Over 7 months, infertile patients were invited through advertisements or mailings to formulate new or modify existing recommendations. After modifying the recommendations, we

asked patients to select their top five or top three recommendations for each of the five sections on fertility care. Finally, the guideline development group assessed the eligibility of the final set of recommendations within the scope of the guideline. The wiki attracted 298 unique visitors, yielding 289 recommendations. We assessed the 21 recommendations ranked as the top five or top three for their eligibility for being integrated into the clinical practice guideline. The evaluation identified some challenges needed to be met to improve the wiki tool, namely its ease of use, website content and layout, and characteristics of the wiki tool.

We concluded that the wiki is a promising and feasible participatory tool for patients in guideline development. A modified version of this tool, including new modalities (e.g. automatically limiting the number and length of recommendations, using a fixed format for recommendations, including a motivation page, and adding a continuous prioritization system), should be developed and evaluated in a patient-centred design.

In **Chapter 5** the use and benefits of a specialized online participatory tool to facilitate patient partnership in guideline development were evaluated. This specialized tool was developed and based on the barriers and facilitators that resulted from a previous pilot study on a wiki tool as described in Chapter 4. To answer the question a mixed method evaluation was applied. Outcome measurements for use included: actual use (number of unique visitors, number of registries, and number of visits), the usability of the tool measured on a SUS-scale (0–100), and representativeness of users compared to a valid representative Dutch hospital cohort. Outcome measurements for benefits on guideline development included: number of new and modified recommendations, number of prioritizations, and the change over the time period (months) of the top five recommendations.

In 12 months, the specialized participatory tool welcomed 3028 unique visitors, of which 87 registered. The tool enabled a broad and mostly representative target group regarding their age, type of infertility, and duration of childlessness compared to a hospital group. The visitors delivered a set of 50 clear and prioritized recommendations for guidelines on Dutch fertility care. According to 39 out of 45 registries the tool was qualified as highly usable.

We concluded that the specialized online participatory tool is a feasible method to involve a broad group of generally representative infertile patients in guideline development. This study adds to current knowledge using online tools to facilitate patient partnership in clinical guideline development. This thesis can be used as a practical guide for policy organizations, guideline developers, and patient organizations that are interested in interventions to facilitate patient partnership in clinical guideline development in any clinical setting.

Chapter 6 focuses on the fourth question:

What value do patients add to the development of guideline-based quality indicators for patient-centredness?

To answer this question the RAND-modified Delphi method (a two-step systematic consensus method) was used to develop two sets of quality indicators for patientcentredness. The development of these quality indicators for patient-centredness was based on the national multidisciplinary Network Guideline on infertility. Two panels participated: one patients' panel (n=19) and one multidisciplinary professionals' panel (n=15). Similarities and differences in the indicators and in aspects of patient-centredness between patients' and professionals' sets of indicators were analysed descriptively. From 119 formulated potential indicators of patient-centredness, the patients' panel selected a representative set of 16, while the professionals' panel selected 18. Five indicators were included in both sets. These indicators regarded the need to perform IUI at least six days a week, report on treatment outcomes and complications, report on results of semen analyses in a standardized way, counsel infertile couples about the positive effects on their chance of pregnancy of the elimination of a harmful lifestyle, and provide information on the negative consequences of achieving a pregnancy when the patient has a high BMI. Both patients and professionals put the highest value on potential indicators of information and communication in fertility care. Patients also emphasized accessibility of care, whereas professionals emphasized coordination and integration as important quality measures for patient-centredness in fertility care. Infertile patients mainly select different indicators and value different dimensions of patient-centredness (e.g. information, communication, and access to care) than professionals (e.g. coordination and integration of care) during an indicator development process.

Therefore, we concluded that infertile patients add value to the development of guideline-based quality indicators for patient-centredness. The final guideline-based indicator set, consisting of 29 indicators, represents a balanced set that is based on the expertise of all stakeholders, including patients. A next step should

be the application of this set in a future practice test to assess the feasibility in daily practice. In our opinion, most quality indicators for patient-centredness could be used for monitoring and improving the quality of fertility care internationally, occasionally by a broader interpretation (e.g. by replacing the general practitioners with other healthcare professionals engaged in the care process).

Chapter 7 discusses the main findings from the studies included in this thesis in the light of available literature and recent policy relating to the main phases of the guideline development process. Furthermore, some methodological considerations regarding the exploratory studies performed within the span of this thesis were addressed and discussed.

We concluded that this thesis demonstrates the added value of involving patients in all phases of the guideline development process, as well as of using a patientcentred approach therein; 'shared guideline development' is the future of guideline development. In fact, all involved healthcare professionals, their associations, patients, and policymakers are now in the lead to collaborate on implementing this concept. Online participatory tools could contribute to bringing shared guideline development to a higher level while transparently using patients' input in the guideline development process.



Samenvatting

Nederlandse samenvatting

De gezondheidszorg is versnipperd en houdt nog te weinig rekening met de behoeften en waarden van patiënten. Zoals bij andere aandoeningen die complexe zorg behoeven, wordt ook de voortplantingsgeneeskundige zorg verleend door meerdere onafhankelijk opererende medische professionals, zoals huisartsen, gynaecologen en urologen. Daarnaast is de inhoud van de geleverde zorg meestal gebaseerd op wetenschappelijk bewijs of op professionele consensus, die onafhankelijk zijn van de behoeften en waarden van patiënten. Richtlijnen, mits op de juiste manier ontwikkeld, kunnen waardevolle instrumenten zijn om het gat te dichten tussen de voortplantingsgeneeskundige zorg gebaseerd op wetenschappelijk bewijs en gebaseerd op de behoeften van paren met vruchtbaarheidsproblemen die de leiding hebben in hun eigen af te leggen zorgpad. Echter, een aanzienlijke bijdrage van andere belanghebbenden, bij uitstek die van subfertiele patiënten, ontbreekt vooralsnog in richtlijnontwikkeling. Verder beperkt de aanpak van richtlijnontwikkeling zich meestal tot de aandoening zelf, in plaats van dat ze gericht is op het totale zorgpad dat patiënten afleggen.

Daarom hebben wij getracht patiënten in het middelpunt van de verschillende ontwikkelingsstadia van het richtlijnontwikkelingsproces te positioneren. Dit proefschrift richt zich op de ervaringen met het verplaatsen van de positie van de patiënt van de zijlijn naar het middelpunt en introduceert het concept 'gezamenlijke richtlijnontwikkeling' in de voortplantingsgeneeskunde.

Het doel van dit proefschrift, zoals uiteengezet in **Hoofdstuk 1**, is om vier specifieke vragen te beantwoorden.

Hoofdstuk 2 richt zich op de eerste vraag:

Wat is de toegevoegde waarde van de belangrijkste klinische knelpunten zoals ervaren door patiënten vergeleken met die van professionals voor het vaststellen van het bestek van een Nederlandse multidisciplinaire richtlijn subfertiliteit?

Om deze vraag te beantwoorden, is een kwalitatieve studie verricht met behulp van interviews onder twaalf subfertiele paren en zeventien professionals. Op basis van deze interviews zijn twee lijsten samengesteld met de in de richtlijn op te nemen klinische knelpunten (aspecten van de zorg die verbetering behoeven) die aangedragen zijn door zowel patiënten als door professionals binnen de vier domeinen (huidige richtlijnen, professionals, patiënten en organisatie van zorg). Door beide lijsten met elkaar te vergelijken, zijn de belangrijkste klinische knelpunten naar voren gekomen zoals gedefinieerd door meer dan drie kwart van de subfertiele paren en/of ten minste twee professionals.

In totaal hebben subfertiele paren 32 klinische knelpunten aangedragen en professionals 23. Van de belangrijkste klinische knelpunten zijn acht aangedragen door de subfertiele paren die de professionals niet hebben genoemd. Deze belangrijkste klinische knelpunten betreffen hoofdzakelijk de patiëntgerichte aspecten van zorg op het domein van de professional en de organisatie. De groepen hebben gezamenlijk twee belangrijke klinische knelpunten aangedragen, hoewel ze deze knelpunten echter anders interpreteren: enerzijds het gebrek aan emotionele steun en anderzijds het gebrek aan respect voor de waarden van patiënten.

Hieruit is geconcludeerd dat het betrekken van patiënten vanaf de eerste fase van het richtlijnontwikkelingsproces tot waardevolle en aanvullende belangrijke klinische knelpunten leidt, die als input kunnen dienen voor de volgende stap van het multidisciplinaire richtlijnontwikkelingsproces. Bovendien breidt dit het bestek van de richtlijn uit, met name ten aanzien van patiëntgerichte en organisatorische onderwerpen vanuit het perspectief van de patiënt.

Hoofdstuk 3 is gericht op de tweede vraag:

In hoeverre is in geval van subfertiliteit een netwerkbenadering waarin de patiënt centraal staat een haalbaar format voor multidisciplinaire richtlijnontwikkeling ten aanzien van daadwerkelijke ontwikkeling van een set van richtlijnen, de tijdsinvestering en de ervaringen met deze benadering?

Om deze vraag te beantwoorden, is een haalbaarheidsstudie uitgevoerd bestaande uit een gedetailleerde procesevaluatie van het richtlijnontwikkelingsproces, de ervaringen van professionals met de netwerkbenadering en de daarmee gemoeide tijdsinvesteringen.

Hierbij is gebruikgemaakt van een netwerkbenadering waarin de patiënt centraal staat om vijf op elkaar afgestemde (een multidisciplinaire en vier monodisciplinaire) richtlijnen te ontwikkelen rondom de klinische zorgpaden binnen de voortplantingsgeneeskundige zorg. De netwerkstructuur bestond hierbij uit: de centraal gepositioneerde patiënt en de adviescommissie; een werkgroep ten behoeve van de ontwikkeling van een multidisciplinaire richtlijn (gynaecologen, Chapter 8

huisartsen, urologen, klinische embryologen, klinisch chemici, een medisch psycholoog, een arbeidsgeneeskundige en twee patiëntafgevaardigden); en tot slot vier werkgroepen ten behoeve van de ontwikkeling van vier monodisciplinaire richtlijnen. De volledige richtlijn is gericht op patiëntgerichte, organisatorische en medisch-technische uitgangsvragen die naar voren gekomen zijn uit de interviews met patiënten en professionals. Deze uitgangsvragen zijn uitgewerkt en verdeeld over de werkgroepen. Vervolgens zijn de projectprestaties, de deelnemerservaringen met deze benadering en de benodigde tijdsinvestering ook geëvalueerd. Deze evaluatie baseerde zich op de analyse van secundaire bronnen, interviews met acht sleutelfiguren en een schriftelijk vragenlijstonderzoek onder alle 35 deelnemers.

Binnen twintig maanden zijn met deze benadering een multidisciplinaire richtlijn subfertiliteit en vier gerelateerde monodisciplinaire richtlijnen (een voor subfertiliteit in het algemeen, een voor onverklaarde subfertiliteit, een voor mannelijke subfertiliteit en een voor semenanalyse) ontwikkeld. De multidisciplinaire richtlijn bestaat uit aanbevelingen voor de belangrijkste medischtechnische onderwerpen en uit organisatorische en patiëntgerichte thema's die onderdeel zijn van het klinische zorgpad. Het project is verlopen zoals gepland, met uitzondering van kleine aanpassingen en drie extra consensusbijeenkomsten. De deelnemers waren enthousiast over de toegepaste benadering, het respect voor de autonomie, de rol van de projectcoördinator en de betrokkenheid van patiënten. Verbeteringssuggesties waren tijdige communicatie over het format van de richtlijnen, de tijdslijnen van het project, de verantwoordelijkheden van de deelnemers, het aanstellen van een medisch bibliothecaresse en meer ondersteuning. De 35 deelnemers hebben in totaal gezamenlijk 4497 uur aan dit project besteed.

Hieruit is geconcludeerd dat de nieuwe netwerkbenadering waarin de patiënt centraal staat, geschikt is voor het gelijktijdig en gezamenlijk ontwikkelen van een op elkaar afgestemde set richtlijnen bestaande uit een multidisciplinaire richtlijn en monodisciplinaire richtlijnen rondom het klinische zorgpad van patiënten met voortplantingsgeneeskundige problemen. Verdiepend onderzoek is nodig om de efficiëntie van deze benadering te vergelijken met traditionelere benaderingen.

Hoofdstuk 4 en Hoofdstuk 5 richten zich allebei op de derde vraag:

In hoeverre is een participatie-instrument voor Nederlandse patiënten geschikt om gezamenlijke richtlijnontwikkeling te bewerkstelligen ten aanzien van het gebruik, de gebruiksvriendelijkheid, de meerwaarde voor de richtlijn, de ervaringen met het instrument en de toepasbaarheid ervan in andere klinische aandachtsgebieden binnen de zorg?

Om deze vraag te beantwoorden, zijn twee haalbaarheidsstudies verricht. Hoofdstuk 4 gaat in op de eerste haalbaarheidsstudie naar het gebruik van een basiswiki (zoals Wikipedia) als een participatie-instrument voor patiënten in de ontwikkeling van een richtlijn subfertiliteit. Hierbij is gebruikgemaakt van een evaluatiestrategie bestaande uit verschillende toegepaste methoden. Hierbij is gekeken naar (1) het gebruik van de wiki (aantal pagina bezoeken en bezoekers), (2) de voordelen van de wiki (aantal, inhoud en de directe toepasbaarheid van de aanbevelingen voor opname in de richtlijn en (3) de voor- en nadelen volgens patiënten voor ingebruikneming van de wiki en de potentiële uitdagingen om de wiki te verbeteren. Om de wiki te vullen, zijn twaalf diepte-interviews onder subfertiele patiënten afgenomen. Uitwerkingen van de interviews zijn vertaald in negentig conceptaanbevelingen, die vervolgens op de wiki zijn gepresenteerd. Gedurende zeven maanden zijn subfertiele patiënten uitgenodigd via advertenties en e-mails om nieuwe aanbevelingen te formuleren of bestaande aanbevelingen aan te passen. Na aanpassing van de aanbevelingen zijn de patiënten gevraagd om hun top 5 of top 3 uit de aanbevelingen te geven voor elk van de vijf onderdelen van de voortplantingsgeneeskundige zorg. Uiteindelijk heeft de richtlijnontwikkelingsgroep de inpasbaarheid van de uiteindelijke set aanbevelingen beoordeeld ten aanzien van het bestek van de richtlijn. De wiki heeft 298 unieke bezoekers getrokken en omvatte 289 aanbevelingen. Daarvan zijn 21 aanbevelingen door patiënten geprioriteerd in de top 5 en top 3-lijsten op hun inpasbaarheid in de klinische richtlijn. Uit de evaluatie zijn uitdagingen naar voren gekomen ter verbetering van de wiki, onder andere met betrekking tot het gebruikersgemak, de inhoud en lay-out van de website en de karakteristieken van het wiki-instrument.

Uiteindelijk is geconcludeerd dat de wiki een veelbelovend en geschikt instrument is voor patiëntparticipatie in richtlijnontwikkeling. Een aangepaste versie van dit instrument dient ontwikkeld en geëvalueerd te worden, die vormgegeven moet worden op een wijze waarbij de patiënt centraal staat. Hierbij moeten nieuwe modaliteiten worden meegenomen, zoals het aantal aanbevelingen en de lengte ervan automatisch beperken, een vast format voor aanbevelingen instellen, een motivatie-pagina inbedden en een continu prioriteringssysteem toevoegen.

In **hoofdstuk 5** zijn het gebruik en de baten geëvalueerd van een gespecialiseerd online-instrument om patiëntpartnerschap in richtlijnontwikkeling te vergemakkelijken. De ontwikkeling van dit gespecialiseerde instrument is gebaseerd op de voor- en nadelen die naar voren gekomen zijn uit een voorgaande pilotstudie over een op wiki gebaseerd instrument, zoals beschreven in hoofdstuk 4. Om de specifieke vraag te beantwoorden, is een evaluatie verricht met behulp van verschillende methoden. Uitkomstmaten voor het gebruik betreffen: het daadwerkelijke gebruik (het aantal unieke bezoekers, het aantal geregistreerde bezoekers en het aantal bezoeken), de gebruiksvriendelijkheid van het instrument gemeten op een gebruiksvriendelijkheidsschaal (0-100) en de representativiteit van de bezoekers vergeleken met een representatief valide Nederlands ziekenhuiscohort. Uitkomstmaten voor de meerwaarde voor richtlijnontwikkeling betreffen: het aantal nieuwe en aangepaste aanbevelingen, het aantal prioriteringen en de veranderingen in de top-5 geprioriteerde aanbevelingen per maand en over de gehele periode van de studie. Gedurende twaalf maanden heeft het gespecialiseerde participatie-instrument 3028 unieke bezoekers getrokken, waarvan 87 bezoekers zich hebben geregistreerd. Via het instrument heeft een brede en, vergeleken met een ziekenhuiscohort, voornamelijk representatieve doelgroep geparticipeerd met betrekking tot leeftijd, type subfertiliteit en duur van kinderloosheid. De participanten hebben een set van vijftig duidelijke en geprioriteerde aanbevelingen voor richtlijnen over de Nederlandse voortplantingsgeneeskundige zorg opgeleverd. Volgens 39 van de 45 geregistreerde bezoekers is het instrument zeer goed bruikbaar.

Uiteindelijk is geconcludeerd dat het gebruik van een gespecialiseerd online participatie-instrument een haalbare methode is om een brede en representatieve groep subfertiele patiënten te laten participeren in richtlijnontwikkeling. Deze studie draagt bij aan de huidige kennis over de inzetbaarheid van online instrumenten om patiëntpartnerschap in richtlijnontwikkeling te vergemakkelijken. Deze publicatie kan worden gebruikt als praktische richtlijn voor beleidsinstanties, richtlijnontwikkelaars en patiëntenorganisaties in alle takken van klinische zorg die geïnteresseerd zijn in interventies om patiëntpartnerschap in richtlijnontwikkeling vorm te geven.

Hoofdstuk 6 richt zich op de vierde vraag:

Wat is de toegevoegde waarde van patiënten bij de ontwikkeling van op richtlijngebaseerde kwaliteitsindicatoren voor patiëntgerichtheid?

Om deze vraag te beantwoorden, is de aangepaste RAND Delphi-methode (een systematische consensus methode bestaande uit twee stappen) gebruikt om twee sets van kwaliteitsindicatoren voor patiëntgerichtheid te ontwikkelen. De ontwikkeling van deze kwaliteitsindicatoren voor patiëntgerichtheid is gebaseerd op de Landelijke multidisciplinaire netwerkrichtlijn subfertiliteit. Twee panels hebben hierin geparticipeerd: een panel met patiënten (n=19) en een multidisciplinair samengesteld panel met professionals (n=15). Vervolgens zijn de indicatorensets voor patiëntgerichtheid van de patiënten en van de professionals vergeleken op indicatorniveau en op aspecten van patiëntgerichtheid en zijn beschrijvend geanalyseerd. Uit de 119 geformuleerde potentiële indicatoren heeft het patiëntenpanel een representatieve set van 16 indicatoren geselecteerd en de professionals een set van 18. Vijf indicatoren kwamen voor in beide sets. Deze omvatten de noodzaak om zes dagen per week Intra Uteriene Inseminatie (IUI) uit te voeren, om behandelingsuitkomsten en complicaties te rapporteren, om de resultaten van een semenanalyse op een gestandaardiseerde wijze te rapporteren en om subfertiele paren te counselen ten aanzien van de positieve effecten op de zwangerschapskansen bij vermijding van een slechte leefstijl en om subfertiele paren te informeren over de negatieve effecten van een verhoogde Body Mass Index (BMI) op de zwangerschapskansen. Zowel patiënten als professionals kennen de meeste waarde toe aan potentiële indicatoren over communicatie en informatie in de voortplantingsgeneeskundige zorg. Patiënten benadrukken tevens de toegankelijkheid van zorg, terwijl professionals juist zorgcoördinatie en -integratie als cruciale kwaliteitsmaten voor patiëntgerichtheid in de voortplantingsgeneeskundige zorg bestempelen. Hieruit is gebleken dat subfertiele patiënten over het algemeen andere indicatoren selecteren en waarde toekennen aan andere aspecten van patiëntgerichtheid (met name informatie, communicatie en de toegankelijkheid van zorg) dan professionals (coördinatie en integratie van zorg) tijdens het indicatoren-ontwikkelingsproces. Daarom concluderen de onderzoekers dat subfertiele patiënten waarde toevoegen aan de ontwikkeling van op richtlijn gebaseerde kwaliteitsindicatoren voor patiëntgerichtheid.

De uiteindelijke op richtlijnen gebaseerde set van 29 indicatoren vertegenwoordigt een gebalanceerde set die gebaseerd is op de expertise van alle belanghebbenden, Chapter 8

inclusief patiënten. Een volgende stap kan bestaan uit het onderwerpen van deze set aan een praktijktest, om zo de haalbaarheid in de dagelijkse praktijk te onderzoeken. Naar onze mening zouden, eventueel met een bredere interpretatie (bijvoorbeeld door huisartsen door andere medische professionals te vervangen die onderdeel uitmaken van het zorgproces), de meeste kwaliteitsindicatoren voor patiëntgerichtheid gebruikt kunnen worden om de kwaliteit van de voortplantingsgeneeskundige zorg op internationaal niveau te monitoren en te verbeteren.

Hoofdstuk 7 gaat aan de hand van de verschillende fasen van het richtlijnontwikkelingsproces in op de belangrijkste bevindingen uit de studies van dit proefschrift in het kader van de beschikbare literatuur en de beleidsmatige ontwikkelingen. Tevens worden een aantal methodologische overwegingen ten aanzien van de verkennende studies van dit proefschrift aangehaald en besproken. Dit proefschrift laat de toegevoegde waarde zien van actief betrokken patiënten en het gebruik van een benadering waarin de patiënt centraal staat bij alle fasen van het richtlijnontwikkelingsproces; het concept 'gezamenlijke richtlijnontwikkeling' representeert de toekomst van richtlijnontwikkeling.

Vanaf heden zijn alle betrokken gezondheidszorgprofessionals, de medisch wetenschappelijke beroepsverenigingen, patiënten en beleidsmakers aan zet om samen dit concept te implementeren. Online participatie-instrumenten kunnen een bijdrage leveren om dit concept van gezamenlijke richtlijnontwikkeling nog beter ten uitvoer te brengen en kunnen helpen om op transparante wijze gebruik te maken van de geleverde input van patiënten in het richtlijnontwikkelingsproces.


Dankwoord

Dankwoord

Wanneer een project als dit proefschrift na dik acht jaar voltooid is, kan het niet anders dan dat heel veel mensen hier op diverse manieren een bijdrage aan geleverd hebben. Graag maak ik dan ook van de gelegenheid gebruik om iedereen te bedanken en de volgende mensen in het bijzonder.

In de eerste plaats wil ik alle patiënten die meegewerkt hebben aan de totstandkoming van de publicaties uit dit proefschrift bedanken voor de tijd en moeite die zij gestoken hebben in interviews of het invullen van vragenlijsten. Jullie verhalen hebben mij doen beseffen hoe belangrijk het nastreven van patiëntgerichte zorg is en de enorme meerwaarde die patiënten kunnen bieden in het richtlijnontwikkelingsproces. Mijn ambitie dit te benadrukken zal ik mijn gehele verdere loopbaan uitdragen, met jullie leerzame verhalen in mijn achterhoofd.

Professor J.A.M. Kremer, beste Jan. Door jouw enthousiasme en visie verruilde ik het Amsterdamse voor het Nijmeegse. Jouw kritische 'helikopterview' zette mij altijd aan het denken. Soms raakte ik de draad kwijt en dan was jij daar om het te versimpelen in woord en beeld. Jij zorgde ervoor dat ik focus hield. Je steunde mij in moeilijke tijden, gaf mij vertrouwen en hielp mij op geweldige wijze door de allerlaatste fase heen. Ongelofelijk veel dank daarvoor! Ik hoop dat onze wegen nog vaak mogen kruisen.

Dr. R.P.M.G. Hermens, lieve Rosella. Jij hebt mij al die tijd gesteund en tot op het laatste moment geholpen om de eindstreep voor ogen te blijven zien. '24/7' stond jij voor mij klaar. Jouw kritische blik, hielp mij dit proefschrift te verbeteren. Als copromotor, was jij een kundig en zeer meelevend persoon en steunde je mij door dik en dun. Ik draag je een zeer warm hart toe en ben je heel veel dank verschuldigd. Ik hoop nog vele fijne momenten met je mee te mogen maken!

Dr. W.L.D.M. Nelen, lieve Willianne. Als ik na hard zwoegen mijn stuk wat gekleurder terugkreeg, wist ik in ieder geval dat jij er kritisch naar gekeken had en dat het er vele malen beter op geworden was. Jouw up-to-date referentiedatabase voor de fertiliteitzorg is altijd van enorme meerwaarde voor mij geweest. In al die jaren hebben jouw zorg en medeleven mij bijzonder geraakt. Ik ben je heel veel dank verschuldigd! Ik hoop dat onze wegen nog mogen blijven kruisen!

Patiëntvertegenwoordigers van Freya, beste Jose Knijnenburg en Marjolein Grömminger. Ongelofelijk veel dank voor jullie tomeloze inzet en hulp bij het verwoorden van de wensen en behoeften van patiënten met vruchtbaarheidsproblemen! Als iemand weet hoe een achterban te vertegenwoordigen, dan zijn jullie dat! Ik ben jullie zeer dankbaar!

De leden van het projectteam van de landelijke netwerkrichtlijn subfertiliteit, beste Sander Flikweert (in memoriam), dank voor jouw creatieve en verbindende geest. Onze samenwerking was veel te kort, maar zeer waardevol... Beste Elske Faber, Tjerk Wiersma en Jacintha van Balen, dank voor jullie hulp en vooruitstrevende blik. Ik had de samenwerking met jullie niet willen missen!

Alle medeauteurs, beste Jako Burgers, Wim Willemsen, Miriam Hilbink en alle andere medeauteurs. Heel veel dank voor jullie hulp bij de totstandkoming van de artikelen!

Mijn (toen nog) stagiaires, beste, Suzanne, Wienke, en Fleur. Dank voor jullie inzet en hulp!

Beste (oud) kantoortuin-collegae, het was fijn om met jullie te mogen sparren, te genieten van gezellige taartmomenten en hilarische onderzoekersweekendjes. Annemijn, Inge, Selma, Bea, Gwendolyn, Helga Dana, Angelique en Fleur, veel dank voor jullie gezelligheid en hulp toen nog vanuit ons VPG-eilandje in de tuin, maar ook tijdens de laatste loodjes van de afronding van dit proefschrift! Fleur, zet hem op: veel succes met de afronding van jouw proefschrift!

Beste leden van de promotiecommissie, dank voor het kritisch doorlezen en beoordelen van mijn proefschrift en jullie aanwezigheid bij mijn verdediging.

Dr. K.Boer, beste Kees. Wat is het een eer om na jaren weer eens met jou samen te mogen werken, maar dan nu op een heel ander vlak. Veel dank voor jouw tijd, creativiteit en inspiratie. Dankzij jou is de kaft van mijn proefschrift prachtig geworden. Lieve Caroline, lieve 'Car'. Dank voor jouw onvoorwaardelijke steun en hechte vriendschap. Wat is het bijzonder mooi om te zien dat onze bijzondere vriendschap ook nog kan uitvloeien in een mede door jou kritische blik vormgegeven proefschrift. Onze eerste kennismaking stamt uit onze entree op de Gooische Hockeyclub en is sindsdien alleen maar hechter geworden. Ik vind het een enorme eer dat jij mijn paranimf wil zijn en had mij geen betere kunnen wensen!

Beste collegae van het Kennisinstituut van Medisch Specialisten en de Federatie Medisch Specialisten, dank voor jullie begrip en steun, vooral in de laatste fase van de afronding van dit proefschrift. Saskia, Joppe en Dunja: zet hem op! Straks ligt er van jullie ook zo'n mooi eindresultaat!

Beste Kristie, veel succes met het uitzetten van een mooie onderzoekslijn! Beste Marjolein, eindelijk heb ik straks weer meer tijd om het kennisforum 'patient empowerment' samen met jou en Kristie verder vorm te geven, daar kijk ik enorm naar uit! Beste Joyce, ik hoop dat onze leerzame samenwerking op het gebied van patiëntenparticipatie in richtlijnontwikkeling samen met de Patiëntenfederatie nog lang zo blijft bestaan. Dank voor jouw steun!

Beste Teus, Margreet, Annefloor, Pieter, Marleen en Dunja, dank voor jullie steun en begrip in de afgelopen periode!

Beste collegae van de Nederlandse Vereniging voor Obstetrie en Gynaecologie, in het bijzonder de commissie kwaliteitsdocumenten, Esther van Wissen en Veronique van Dooren. Dank voor jullie begrip en steun. Ik kan me nog goed mijn introductie als kandidaat-promovenda door Ben Willem Mol herinneren. Sindsdien ben ik altijd nauw betrokken geweest bij jullie vereniging. Dank voor de leerzame tijd! Ik hoop nog lang onderdeel te mogen uitmaken van jullie vereniging.

Beste collegae van de Nederlandse Vereniging voor Kindergeneeskunde. Jullie interesse in de afronding van mijn proefschrift en medeleven heeft mij enorm gesteund! Dank daarvoor! Ik hoop nog lang onderdeel te mogen uitmaken van jullie vereniging.

Liefste vriendinnetjes en hockeyteamgenootjes, in het bijzonder Marieke, Shemara, Uschi en Jasmijn en Jill. Wat ben ik jullie allemaal dankbaar voor jullie steun en fijne hechte momenten in de afgelopen jaren. Ondanks dat ik af en toe te weinig tijd voor jullie heb gehad, zijn jullie mij blijven steunen en altijd geïnteresseerd geweest in de voortgang van dit proefschrift. Vaak hebben jullie jezelf afgevraagd of dit proefschrift nog af zou komen. Vanaf nu zullen de koffie-momentjes er niet meer onder leiden. Ook zal ik niet meer de grote afhaker zijn bij de hot yoga tijdens de winterstop! Dank voor jullie steun door dik en dun!

Mijn schoonouders, lieve Rob en Ria, Dank voor jullie oprechte interesse en steun.

Mijn zussen, lieve Marije en Laetitia. Ook al hebben jullie niet altijd evenveel inzage in waar ik de afgelopen jaren mee bezig geweest ben, jullie medeleven, begrip en steun hebben mij mede geholpen dit boekje af te ronden. Dank dat jullie er altijd voor mij zijn, in het bijzonder tijdens de intense en zeer hechte afgelopen twee jaar! Ik ben supertrots dat jullie mijn zussen zijn; ik vind jullie geweldig! Nu snel op naar ons zussen-weekend!

Lieve Maarten en Robert, dank je wel dat jullie er altijd voor mij en mijn zussen zijn en onderdeel uitmaken van mijn familie!

Mijn Vader; lieve papa, dankzij jouw onvoorwaardelijke liefde, steun en vertrouwen heb ik bereikt wat ik voor ogen had. Ik heb diep respect voor hoe jij weer een nieuwe modus hebt gevonden na het overlijden van mama. Dat je je dan ook nog kunt bekommeren over de laatste loodjes van de afronding en hulp biedt waar nodig is kenmerkend voor hoe jij in het leven staat. Ik hoop nog vele jaren te kunnen genieten met jou als vader en 'lieve opa' van mijn kindjes!

Mijn Moeder; de allerbelangrijkste vrouw in mijn leven, mijn lieve schat. Helaas heb je de eindstreep niet meer mogen meemaken... Zelfs tot op het laatste moment kon jij je interesseren voor de voortgang van dit proefschrift en zag je mij worstelen. Als iemand een ongekend doorzettingsvermogen had om iets af te ronden was jij het wel. Daar heb ik veel van geleerd. Ook heb ik door jouw intensieve ziekteperiode geleerd dat je moet genieten van de kleine dingen in het leven. En dat is wat ik nu nog meer dan ooit ga doen!

Sophie, Pepijn en Annefleur; mijn allerliefste en mooiste kindjes. Dankzij jullie werd ik er al die tijd herinnerd aan wat echt belangrijk is in het leven. Het veelbesproken 'boekje' is nu eindelijk echt af! Nu heeft mama nog meer tijd om te genieten van leuke dingen samen. Daar kijk ik enorm naar uit! Dennis, liefste en maatje. Wat ben ik gelukkig met jou! Jouw onvoorwaardelijke steun heeft mij gebracht tot waar ik nu ben gekomen. Hoewel de opvoeding van 3 kinderen, het opzetten van een bedrijf een drukke baan en in de laatste fase de zorg voor mijn zieke moeder naast het afronden van een proefschrift wat ambitieus bleek, voelde ik mij door jou altijd gesteund. Ik ben trots en dankbaar dat we samen op deze wijze een hoofdstuk kunnen afsluiten. Dank je wel dat jij mijn paranimf bent.

Ik hou ongelofelijk veel van jou!

Curriculum vitae

De auteur van dit proefschrift zag op 3 Juni 1980 het levenslicht in Delft. Zij groeide haar eerste levensjaren op in Delft en verhuisde op 3-jarige leeftijd naar Rotterdam. Zij was de oudste van drie kinderen. Zij genoot samen met haar 2 zussen van een onbezorgde en vrolijke jeugd. Zij behaalde haar vwo-diploma aan het Zadkine College te Capelle aan den IJssel. Op haar 18 jarige leeftijd leerde zij haar vriend en maatje Dennis kennen en vanaf dat moment waren zij onafscheidelijk. In 2000 begon zij haar studie geneeskunde aan de Vrije Universiteit van Amsterdam. Tijdens haar studie verrichte zij wetenschappelijk onderzoek naar de effecten van enterale glutaminesuppletie bij te vroeg of te klein geboren neonaten (Begeleiding Dr. A. van den Berg, neonatologie VUMC) en naar de behandeling van het androgenitaal syndroom (Begeleiding professor H.A. Heij, kinderchirurg VU Medisch Centrum). Zij werd in het kader van dit laatste onderzoek genomineerd voor de studentenonderzoeksprijs van het VUMC. Tijdens haar extra lange wetenschappelijke stage verrichte zij onderzoek naar de invloed van het opleidingsklimaat onder studenten geneeskunde. (Begeleiding Dr. K. Boor en Prof. Dr. F. Scheele). Haar keuze, en oudste- coschappen volgde zij op de afdeling Obstetrie en Gynaecologie in het Sint Lucas Andreas Ziekenhuis te Amsterdam en de afdeling Voortplantingsgeneeskunde van het VU Medisch Centrum. Het artsexamen met profiel Voortplanting, Endocrinologie en Metabolisme werd behaald in 2006. In datzelfde jaar startte zij als ANIOS Obstetrie en Gynaecologie in de Isala Klinieken te Zwolle. In 2007 startte zij als ANIOS Obstetrie en Gynaecologie van het AMC te Amsterdam. In 2008 verruilde zij het Amsterdamse voor het Nijmeegse en begon zij haar promotieonderzoek aan het Radboud Universitair Medisch Centrum op de afdeling voortplantingsgeneeskunde onder supervisie van Prof. dr. Jan Kremer. In 2013 startte zij als adviseur bij de toenmalige 'Orde van Medisch Specialisten.' Inmiddels is zij werkzaam als Senior-adviseur kwaliteit/ teamleider en tevens trekker van het kennisforum 'patient empowerment' bij het Kennisinstituut van Medisch Specialisten, te Utrecht. Tevens is zij 1 dag per week werkzaam als Senior-beleidsadviseur bij de Nederlandse Vereniging voor Kindergeneeskunde (NVK) en sinds de start van haar promotieonderzoek lid van de commissie kwaliteitsdocumenten van de Nederlandse Vereniging voor Obstetrie en Gynaecologie (NVOG).

De auteur woont samen met Dennis Klompalberts en zij hebben samen 3 fantastische kinderen: Sophie (8jaar), Pepijn (5 jaar) en Annefleur (3jaar).

PhD theses Human Reproduction RIHS

07-02-2000	Els van der Molen Disturbed homocysteine metabolism endothelial dysfunction and placental vasculopathy
29-06-2000	Willianne Nelen Risk factors for recurrent early pregnancy loss. Hyperhomocysteinaemia, thrombophilia and impaired detoxification
05-09-2000	Ina Beerendonk Sodium and ovarian hyperstimulation. Some clinical and psychological aspects
04-12-2000	Anne-Marie van Cappellen van Walsum Cerebral metabolism of hypoxic fetal sheep by NMR spectroscopy
18-12-2000	Friso Delemarre Vascular aspects of human pregnancy. Clinical studies on sodium restriction and angiotensin infusion
2001	
10-01-2001	Way Yee Wong Male factor subfertility. The impact of lifestyle and nutritional factors
05-06-2001	Petra Zusterzeel Biotransformation enzymes and oxidative stress in preeclampsia
05-10-2001	Cathelijne van Heteren Development of habituation and memory in the human fetus
10-10-2001	Michael Gaytant Cytomegalovirus and herpes simplex virus infections in pregnancy

2002	
25-01-2002	Ron van Golde
	Male subfertility and genetics
21-05-2002	Tanja de Galan-Roosen
	Perinatal Mortality
2003	
08-01-2003	Maarten Raijmakers
	Oxidative stress and detoxification in reproduction with emphasis on glutathione and preeclampsia
18-2-2003	Sabine de Weerd
	Preconception counselling. Screening & periconceptional health
22-4-2003	Iris van Rooij
	Etiology of orofacial clefts. Gene-environment interactions and folate
17-12-2003	Chris Verhaak
	Emotional impact of unsuccessful fertility treatment in women
2004	
14-01-2004	Liliana Ramos
	The quality of epididymal sperm in azoospermia
04-10-2004	Pascal Groenen
	Nutritional and environmental factors in human spina bifida. An emphasis on myo-inositol
24-11-2004	Tanya Bisseling
	Placental function in maternal disease. Ex vivo assessment of
	foetoplacental vascular function and transport in diabetes and preeclampsia

15-12-2004	Eva Maria Roes Oxidant-antioxidant balance and maternal health in preeclampsia and HELLP syndrome
2005	
01-06-2005	Marieke Rijnsaardt-Lukassen Single Embryo Transfer: clinical and immunological aspects
10-11-2005	Ingrid Krapels The etiology of orofacial clefts. An emphasis on lifestyle and nutrition other than folate
2006	
14-06-2006	Reini Bretveld Fertility among greenhouse workers
09-11-2006	Jesper Smeenk Stress and IVF. Clinical consequences
2007	
08-02-2007	Inge Ebisch Human subfertility: explorative studies on some pathophysiologic factors in semen and follicular fluid
01-11-2007	Alwin Derijck The transmission of chromatin and DNA lesions by sperm and their fate in de zygote(1)
01-11-2007	Godfried van der Heijden The transmission of chromatin and DNA lesions by sperm and their fate in de zygote(2)
03-12-2007	Kirsten Kluivers On the measurement of recovery following hysterectomy

10-12-2007	Rene Kok
	Proton Magnetic Resonance Spectroscopy of Human fetal brain
2008	
10-12-2008	Trudie Gerrits
	Clinical encounters: Dynamics of patient-centred practices in a
	Dutch fertility clinic
12-12-2008	Wouter Tuil
	IVF and Internet
2009	
06-03-2009	Ineke Krabbendam
	Venous reserve capacity & autonomic function in formerly
	preeclamtic women
03-09-2009	Arno van Peperstraten
	Implementation of single embryo transfer
07-10-2009	Wilson Farid Abdo
	Parkinsonism: possible solutions to a diagnostic challenge
2010	
10-03-2010	Suzan Broekhuis
	Dynamic MR imaging in female pelvic floor disorders
12-03-2010	Bea Lintsen
	IVF in the Netherlands: success rates, lifestyle, psychological factors
	and costs
21-04-2010	Selma Mourad
	Improving fertility care: the role of guidelines, quality indicators
	and patients

2011	
24-02-2011	Monique Brandes Observational studies in reproductive medicine
04-04-2011	Marijn Brouwers Why foetal development of the male reproductive structures sometimes fails. An epidemiologic study on hypospadias and undescended testis with a focus on endocrine disruptors.
22-06-2011	Marian Spath Risk estimate for fragile X-associated primary ovarian insufficiency: Genetic, environmental and reproductive factors
30-06-2011	Inge van Empel Patient-centredness in fertility care
18-11-2011	Gwendolyn Woldringh ICSI children. Follow-up after ICSI with ejaculated or non- ejaculated sperm
17-06-2011	Tiny de Boer Aspects of surgery for pelvic organ prolapse and its relation to overactive bladder symptoms
2012	
20-01-2012	Esther Haagen Guidelines in IUI care. Implications for quality improvement
17-02-2012	Loes van der Zanden Aetiology of hypospadias. From genes to environment and back
11-04-2012	Reda Z Mahfouz Oxidative stress and apoptotic biomarkers in human semen

06-06-2012	Marleen van Gelder The role of medical and illicit drug use in the etiology of birth defects.
	Epidemiological studies and methodological considerations.
12-09-2012	Annemijn Aarts Personalized fertility care in the Internet era
17-09-2012	Eline Dancet Bridging the gap between evidence based and patient-centred infertility and endometriosis care in Europe
09-10-2012	Bertho Nieboer Minimally invasive surgery: patients and doctors perspectives
25-10-2012	Sanne van Leijsen The value of urodynamics prior to surgery for stress urinary incontinence
21-12-2012	Marieke de Vries A cytological exploration of human spermatogenesis in non- obstructive azoospermia patients: an analysis of variation
16-01-2013	Jacqueline Pieters Incidental Findings of Sex Chromosomal Aneuploidies in Routine Prenatal Diagnostic Procedures
04-09-2013	Ellen Lensen Surgery for pelvic organs prolapse with emphasis on the anterior compartment
16-12-2013	Renne Gerritse Cryopreservation of an intact ovary

2014	
23-01-2014	Dana Huppelschoten Improving patient-centredness of fertility care
07-02-2014	Tom van de Belt #HCSM Social media en wiki's in de gezondheidszorg
19-02-2014	Lucie Martijn Patient safety in primary midwifery care
25-02-2014	Kim van Delft Levator ani muscle avulsion following childbirth
04-04-2014	Karin Lammers Pelvic organ prolapse and a magnetic resonance imaging view on pubovisceral muscle avulsions
22-08-2014	Joris van Drongelen Vascular adaptation to pregnancy and relaxin
19-09-2014	Yvette Geels Improved Identification of High Risk Endometrial Carcinoma
23-09-2014	Lobke Bastings Improving female fertility preservation care
14-11-2014	Kim Meeuwis Clinical studies on genital psoriasis and HPV-related lesions: a multidisciplinary approach
20-11-2014	Anika Dam (Partial) Globozoospermia, an allround study on what is not all round
02-12-2014	Remko Bosgraaf Improving cervical cancer screening in the HPV era

18-12-2014	Carline Roos
	Maintenance tocolysis with nifedipine in treatened preterm labor
2015	
19-10-2015	Droïma Stevens
	Decidual vasculopathy in Preeclampsia
01-12-2015	Martijn van der Eijk
	Patient-centered care in Parkinson's disease
2016	
12-01-2016	Joanne in 't Hout
	On trees and forests. Meta-analysis and between-study heterogeneity
	in practice
14-01-2016	Loes van den Einden
	Improving care for women with vulvar squamous (pre)malignicies
05-02-2016	Renée Detollenaere
	Uterus preservation versus hysterectomy in surgical treatment of
	uterine prolapse
29-06-2016	Marloes Hessel
	Diagnosis, treatment and outcome in non-obstructive azoospermia
10-11-2016	Aukje Meijerink
	safety and efficacy of assisted reproductive techniques in male
	infertility

