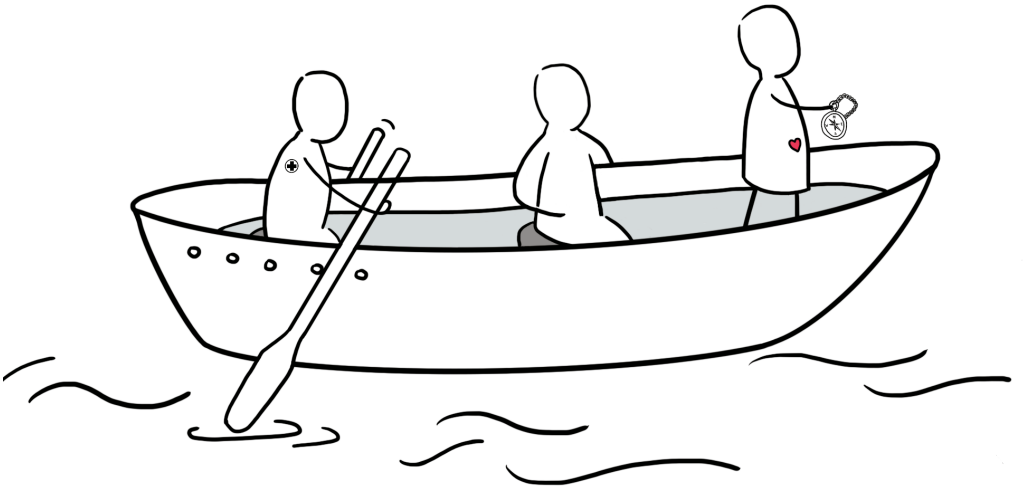
HOW TO ORGANISE PATIENT-CENTERED CARE IN EARLY PREGNANCY

MEREL VAN DEN BERG



How to organise patient-centered care in early pregnancy

Merel Marieke Johanna van den Berg

How to organise patient-centered care in early pregnancy
PhD thesis, University of Amsterdam, the Netherlands 2022

Cover design: Mandy Bos | Schetsboetiek
Printed by: Ridderprint BV | www.ridderprint.nl
Layout and design: Birgit Vredenburg | www.persoonlijkproefschrift.nl
ISBN: 978-94-6458-719-7

Printing of this thesis was supported by Stichting Gynaecologische Endocrinologie en Kunstmatige Humane Voortplanting.

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ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad van doctor

aan de Universiteit van Amsterdam

op gezag van de Rector Magnificus

prof. dr. ir. P.P.C.C. Verbeek

ten overstaan van een door het College voor Promoties ingestelde commissie,

in het openbaar te verdedigen in de Agnietenkapel

op woensdag 30 november 2022, te 10.00 uur

door Merel Marieke Johanna van den Berg

geboren te Eindhoven

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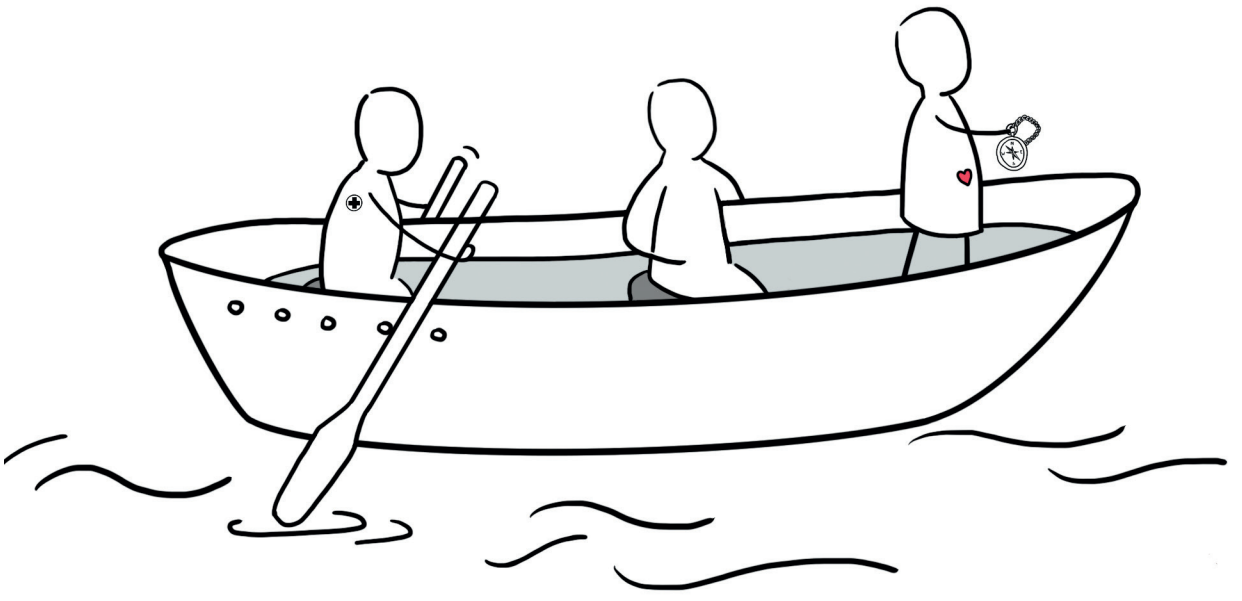

CHAPTER 1

General introduction

Patient-centered care in early pregnancy is the topic of this thesis. Patient-centered care is defined as care which is respectful of and responsive to individual patient preferences and needs and is guided by patient values. It is one of the six key dimensions of health care quality, in addition to safety, effectiveness, timeliness, efficiency and equity (Corrigan et al., 2001; Dancet et al., 2014). Patient-centered care is especially relevant in the management of complications in early pregnancy since the loss of a desired pregnancy is a major life-event for women and/or couples.

In this introduction we will describe the various complications that may occur in early pregnancy, patients' perspectives on early pregnancy care and the role of early pregnancy assessment units (EPAUs) believed to provide the best organisational structure in providing patient-centered care.

Complications in early pregnancy

In this thesis, complications in early pregnancy include miscarriage, recurrent miscarriage and ectopic pregnancy. Complaints like vaginal blood loss and/or abdominal pain commonly precede the final diagnosis.

Miscarriage is defined as a spontaneous loss of an intra-uterine pregnancy before 16 weeks of gestational age (Kolte et al., 2015). It is the most common complication in early pregnancy, as approximately 15 - 20% of all pregnancies end in a miscarriage (Wang, 2003). An incomplete miscarriage may lead to abundant vaginal blood loss. In case of hemorrhagic shock, miscarriage can even be life threatening. Septic shock is another pregnancy related cause of maternal death resulting from an infected miscarriage.

For the clinical management of miscarriage there are three options available: expectant management, medical treatment or surgery (Coomarasamy et al., 2021; NICE guideline, 2012; Guideline Dutch Society of Obstetrics and Gynecology, 2020). Expectant management, i.e. waiting for the natural release of the pregnancy tissue over a period of seven to 14 days, is the first-line treatment. Medical treatment includes misoprostol tablets administered bucally, orally or vaginally with or without mifepristone tablets orally. Surgical management includes uterine curettage or suction aspiration of pregnancy tissue. Surgery has the highest success rate, but has additional short term risks like haemorrhage, perforation of the uterine wall or infection of the uterine cavity and complications of the anaesthetic procedure. Among long term risks are Asherman's syndrome or a subsequent premature birth. Both medical treatment and surgery should be offered if expectant treatment is not acceptable to the woman or after failure of expectant management.

Recurrent miscarriage is defined as two or more miscarriages (ASRM Practice Committee, 2013). Up to 5% of all women of reproductive age will face recurrent miscarriage (Jaslow et al., 2010; Rajcan-Separovic et al., 2010). Women with recurrent miscarriage and antiphospholipid antibodies can be treated with low-dose aspirin and a prophylactic dose of low dose molecular heparin subcutaneously; women with recurrent miscarriage and hypothyroidism by levothyroxine orally; and women with recurrent miscarriage and intra-uterine abnormalities by surgery, although the evidence for the

latter is weak. Women with a history of idiopathic recurrent miscarriage, who present with vaginal blood loss in early pregnancy may benefit from the use of micronized progesterone 400 mg vaginally twice daily (Coomarasamy et al., 2019; the ESHRE guideline group on RPL, 2017).

Ectopic pregnancy is a pregnancy implanted outside the endometrial cavity, most commonly in the fallopian tube (Barnhart et al., 2009; Barnhart et al., 2011). It occurs in approximately 1 - 2% of all pregnancies (Barnhart et al., 2009). Symptoms of women with an ectopic pregnancy can be absent, mild, or severely acute due to rupture of the ectopic pregnancy presenting as a life threatening hemorrhagic shock. In women with a positive pregnancy test but without evidence of an intra-uterine pregnancy or an ectopic pregnancy on the transvaginal ultrasound scan, a tentative diagnosis of 'pregnancy of unknown location (PUL) is made. There is consensus that women with a PUL should be monitored until the final diagnosis can be made of an intra-uterine pregnancy, an ectopic pregnancy, a 'failing PUL' with an uneventful decline in serum human chorionic gonadotrophin (hCG) to undetectable levels or a 'persisting PUL' with rising or plateauing serum hCG concentrations necessitating treatment (Barnhart et al., 2011). Other, less common types of ectopic pregnancy (5 - 7%), implant outside the uterine cavity but within the uterine wall. These ectopic pregnancies include interstitial, intramural, cervical and caesarean scar pregnancies (Jurkovic and Wilkinson., 2011). An ectopic pregnancy may also implant on the ovary in 0.5 - 3.0% of all ectopic pregnancies (Singh et al., 2021). These non-tubal ectopic pregnancies are often difficult to diagnose and tend to present late with sudden rupture and /or intra-abdominal bleeding. That is why these non-tubal ectopic pregnancies are associated with significantly higher maternal morbidity and mortality rates than tubal ectopic pregnancies (Jurkovic and Wilkinson, 2011).

For the management of a tubal ectopic pregnancy or a 'persisting PUL' treatment options are expectant management, medical treatment or surgery (Mol et al., 2008). Expectant management can be offered to women who are clinically stable and without significant abdominal pain, and who have a small ectopic mass without a visible embryonic heartbeat on the transvaginal ultrasound scan and with a low serum hCG concentration (NICE guideline, 2012; Guideline Dutch Society of Obstetrics and Gynecology, 2016). Women should be able to return for follow-up for serum hCG monitoring and, if necessary, repeating the transvaginal ultrasound scan. Successful treatment is defined as an uneventful decline of serum hCG to undetectable levels without additional intervention. (NICE guideline, 2012; Guideline Dutch Society of Obstetrics and Gynecology, 2016). The most commonly used medical treatment for tubal ectopic pregnancy involves systemic methotrexate (MTX) with a single shot intramuscular (im) injection or a multiple dose im regimen in combination with folinic acid orally (Guideline Dutch Society of Obstetrics and Gynecology, 2016). MTX can be offered to women who are clinically stable without significant abdominal pain, and who have a small ectopic mass without a visible embryonic heartbeat on the transvaginal ultrasound scan and a low serum hCG concentration (NICE guideline, 2012). Follow-up after MTX is equal to the follow-up after expectant management with serum hCG monitoring to

undetectable levels. In case of inadequate declining serum hCG concentrations additional MTX injections or surgical intervention are necessary. Surgical management should be offered as a first line treatment to women with a tubal ectopic pregnancy and significant abdominal pain, and/or a large ectopic mass, and/or a visible embryonic heartbeat on the transvaginal ultrasound scan, and/or a high serum hCG concentration, and/or women who are unable to return for follow-up or have contra-indications for systemic MTX. Laparoscopic salpingectomy is the first choice, whereas in case of contralateral tubal damage salpingotomy is the preferred intervention (Mol et al.,2014; NICE guideline, 2012; Guideline Dutch Society of Obstetrics and Gynecology, 2016).

Patients' perspectives on complications in early pregnancy

The loss of a desired pregnancy is a major life-event for women and/or couples. In case of a miscarriage, women may feel that they themselves are the cause of miscarriage through something they have done, eaten or thought. This perception may lead to isolation, stress, anxiety, depression, grief and self-blame, post-traumatic stress disorder and even suicide (Coomarasamy et al., 2021). Although this psychological impact of miscarriage has now become more into view of the doctors, recommendations for prevention or treatment are still non-existent. In women and/or couples with recurrent miscarriage explorative research shows that they prefer a plan for a subsequent pregnancy, comprising one doctor showing empathy, early and regular ultrasound scans and ongoing care after a miscarriage (Musters et al., 2013; the ESHRE guideline group on recurrent pregnancy loss, 2018). The psychological impact of ectopic pregnancy and its treatment on women and/or her male partner is so far unknown.

Early pregnancy assessment units

EPAUs have been set up to enhance patient-centered care. These specialised units are staffed by healthcare professionals competent to diagnose, treat and care for women with complications in early pregnancy (Association of Early Pregnancy Units, 2020). EPAUs work according to clinical guidelines safeguarding the quality of diagnostic and treatment care for miscarriage, recurrent miscarriage and ectopic pregnancy (NICE et al., 2012; Guideline Dutch Society of Obstetrics and Gynecology, 2016; Guideline Dutch Society of Obstetrics and Gynecology, 2020). The prompt and easy access to transvaginal ultrasound scans with immediate reassurance in case of a viable intra-uterine pregnancy has rendered hospital admission obsolete and produces considerable savings in financial and staff recourses (Haider et al., 2006; Shillito and Walker, 1997; Wendt et al., 2013; Wren et al., 1997). Health care professionals working in these units are trained in sensitive communication and breaking bad news, but the available guidelines do not include patients' perspectives on complications in early pregnancy and on provided care (Newbatt et al., 2012). It is yet unknown whether EPAUs indeed provide better patient-centered early pregnancy care.

Background of the thesis

When we started this thesis, women with complications in early pregnancy were seen by clinicians of various backgrounds, like general practitioners, midwives, gynaecologists, and emergency unit doctors. Despite international guidelines, women with vaginal blood loss and/or abdominal pain in early pregnancy were usually referred to and admitted to the hospital. After referral, most women who did not require emergency treatment had to wait until the appropriate tests, usually a transvaginal ultrasound scan, could be organised to confirm or refute the diagnosis of miscarriage or ectopic pregnancy. Most of these women had a viable intra-uterine pregnancy and were subsequently allowed to go home. The women who needed surgery, ie. uterine curettage or suction aspiration of pregnancy tissue or laparoscopy, often had to wait again until there was a time slot available in theatre (Bigrigg and Read, 1991).

In July 1989, the Gloucester Royal Hospital in the United Kingdom (UK) was the first hospital to introduce an EPAU to centralise early pregnancy care (Bigrigg and Read, 1991). To date, over 200 EPAUs have been raised in the UK (Association of Early Pregnancy Units, 2021). The concept of a dedicated multi professional service for women with complications in early pregnancy has also been established in Denmark, Canada and Australia (Lyoke et al., 2014).

In the Netherlands, the first EPAU opened in June 2008 in the Academic Medical Centre (AMC) in Amsterdam, now named Amsterdam University Medical Centre (Amsterdam UMC). This unit provides 24/7 care for women with acute clinical symptoms in early pregnancy. Women are referred by their general practitioner, midwife, or by the hospital's emergency department. Occasionally, self-referrals are seen. Non-pregnant women with a history of recurrent miscarriage are seen in the recurrent miscarriage clinic, an annex of the EPAU in an outpatient daytime setting in the Centre for Reproductive Medicine of the Amsterdam UMC. This consultant-led clinic provides a dedicated and focused service to women and/or couples who have experienced at least two prior miscarriages. The EPAU has set an example and in the years thereafter six hospitals in the Netherlands started working with dedicated early pregnancy outpatient clinics, although not organised as a separate unit for early pregnancy care.

Guidelines for setting up and running an EPAU have been developed by The Association of Early Pregnancy Units, the Royal College of Obstetricians and Gynaecologists (RCOG), the National Institute for Health and Clinical Excellence (NICE) in the UK and by the Ministry of Health in New South Wales (NSW) Australia (Association of Early Pregnancy Units, 2007; Ministry of Health NSW, 2012; NHS NICE, 2012; RCOG, 2008). Nevertheless, despite these guidelines, there is still considerable variation with respect to access to services and quality of care provided. For instance, in the UK, there is variation between the units in opening times, varying from five to seven days and from working hours to 24/7 and in the availability of serum hCG results varying from within one to two hours to the same day during weekdays or 48 hours during weekend days. Also, not all units are able to offer medical treatment with systemic MTX (Poddar et al., 2011).

The variation with respect to services and quality of care provided by different EPAUs is worrying from the perspective of patient-centered care in early pregnancy and therefore needs to be assessed in more detail. Quality of care can be measured by evidence-based quality indicators. Quality indicators are increasingly used to measure, monitor and evaluate health care quality by assessing particular structures, processes, or outcomes. These indicators can point to areas where the quality of care is suboptimal, subsequently allowing priorities to be set for quality improvement. Quality indicators for the care delivered by EPAUs are lacking and need to be developed to improve patient-centered care in early pregnancy delivered by EPAUs or hospitals (Campbell et al., 2003; Grol et al., 2002; Poddar et al., 2011).

Aim of this thesis

The first aim of this thesis is to study patients' perspectives on early pregnancy care. This way we hope to identify potential targets that are relevant and meaningful to women and/or couples and to improve patient-centered early pregnancy care.

The second aim of this thesis is to explore whether the establishment of the EPAU in the Amsterdam UMC has improved the quality of early pregnancy care from the doctors' perspective and to compare early pregnancy care between hospitals with and without an EPAU in the Netherlands. To do so, we developed quality indicators.

Outline of the thesis

In **chapter 2** we assess aspects on miscarriage and recurrent miscarriage care valued by women and their partners and identify potential targets for improvement in early pregnancy care by conducting a systematic review including 27 quantitative and qualitative studies.

In **chapter 3** we assess how women and their partners experience the diagnosis and treatment of an ectopic pregnancy in a qualitative study with semi-structured personal interviews which were continued until data saturation was obtained.

In **chapter 4** we present the results of an observational study in which the care provided in the EPAU in the Amsterdam UMC, the Netherlands is compared with the care provided in the period before the establishment in 2008 by measuring the care within three time periods in 2006, 2009 and 2012.

In **chapter 5** we develop a set of 19 evidence-based quality indicators to measure early pregnancy care provided by an EPAU. We do so with the help of an international expert panel in the field of early pregnancy which extracted 119 recommendations from four international guidelines using a systematic RAND-modified Delphi method.

In **chapter 6** we describe in a qualitative interview study the adherence to 19 guideline based quality indicators in four hospitals with an EPAU and in four hospitals without an EPAU in the Netherlands to assess the added value of an EPAU on patient-centered early pregnancy care.

In **chapter 7** we provide an overview of the literature to describe the logistical requirements, doctors' preferences and patients' preferences for a consultant-led recurrent miscarriage clinic.

In **chapter 8** we provide a summary of this thesis and the implications for further research.

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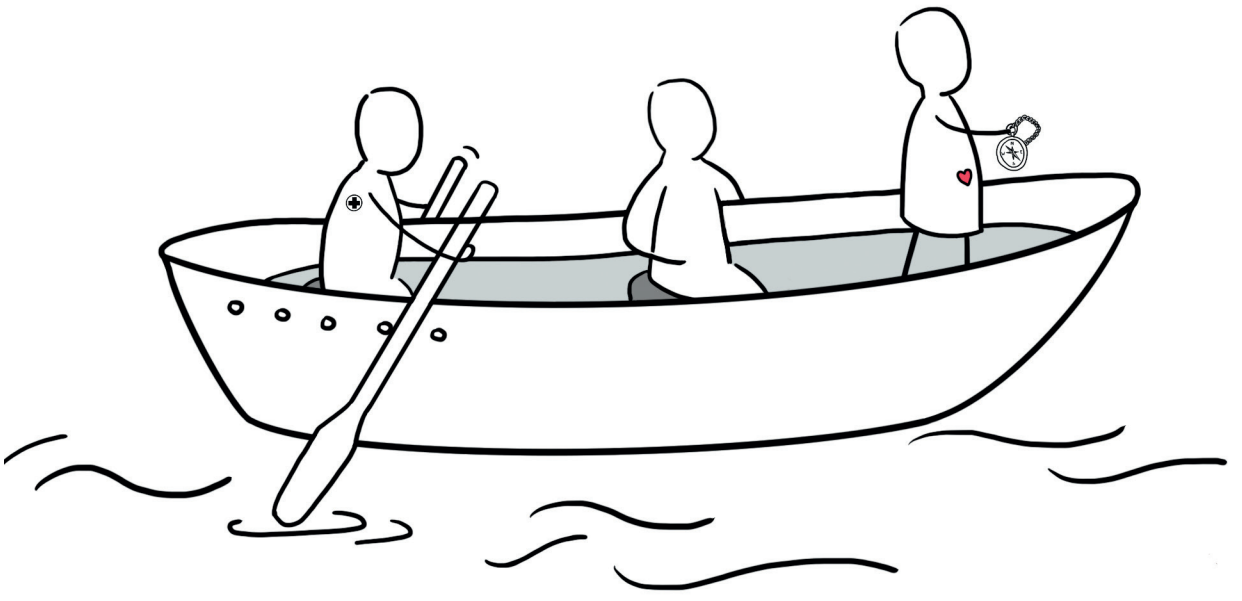

CHAPTER 2

Patient-centered early pregnancy care: a systematic review of quantitative and qualitative studies on the perspectives of women and their partners.

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Abstract

Background

Early pregnancy complications, defined as miscarriage, recurrent miscarriage or ectopic pregnancy, affect the physical and psychological well-being of intended parents. Research in this field so far has focused mainly on improving accuracy of diagnostic tests and safety and effectiveness of therapeutic management. An overview of aspects of care valued by women and/or their partners is missing.

Objective and rationale

This systematic review aims to provide an overview of aspects of care valued by women and/or their partners faced with early pregnancy complications and to identify potential targets for improvement in early pregnancy healthcare.

Search methods

We searched five electronic databases for empirical quantitative or qualitative studies on patients' perspectives of early pregnancy care in July 2017. We first identified aspects of early pregnancy care valued by women and/or their partners based on qualitative and quantitative data and organized these aspects of care according to the eight dimensions of patient-centered care. Second, we extracted the assessment of service quality from women and/or their partners on each of these aspects of care based on quantitative data. Third, we combined the findings on patients' values with the findings of service quality assessment to identify potential targets for improvement in five groups according to how likely these targets are to require improvement.

Outcomes

The search yielded 6240 publications, of which 27 studies were eligible for inclusion in this review. All included studies focused on miscarriage or recurrent miscarriage care. We identified 24 valued aspects of care, which all covered the eight dimensions of patient-centered care. The most frequently reported valued aspect was 'being treated as an individual person experiencing a significant life event rather than a common condition'. Assessment of service quality from women and/or their partners was available for 13 of the 24 identified aspects of care. Quantitative studies all documented service quality as problematic for these 13 aspects of care. We thus identified 13 potential targets for improvement in the patient-centeredness of miscarriage and recurrent miscarriage care of which none were very likely, four were likely, six were unlikely and three were very unlikely, to require improvement. The four likely potential targets for improvement were 'Understandable information provision about the etiology of pregnancy', 'Staff discussing patients' distress', 'Informing patients on pregnancy loss in the presence of a friend or partner' and 'Staff performing follow-up phone calls to support their patients after a miscarriage'.

Wider implications

It is important for clinicians to realize that women and their partners undergoing a miscarriage experience a significant live event and appreciate an individual approach. Future qualitative studies are needed to explore the identified potential targets for improvement of (recurrent) miscarriage care and to explore patients' perspectives in women suspected and treated for ectopic pregnancy.

Introduction

Patient-centeredness of care is one of the six key dimensions of healthcare quality, in addition to safety, effectiveness, timeliness, efficiency and equity (Corrigan et al., 2001). Reports on fertility care confirm that, apart from effective medical treatment, women also appreciate patient-centered care (Dancet et al., 2010; van Empel et al., 2011). According to its definition patient-centered care is respectful of and responsive to individual patient preferences and needs and is guided by patient values. The related term 'person-centered care' is especially relevant for people with co-morbidities consulting a primary healthcare setting rather than for patients with an acute complication addressed by secondary or tertiary clinics (Starfield, 2011; American Geriatrics Society Expert Panel on Person-Centered Care, 2016). Patient-centeredness is subdivided into eight dimensions (www.Pickerinstitute.org; Gerteis et al., 1993) (Table I).

Many women are faced with early pregnancy complications, including miscarriage (10–15%), recurrent miscarriage (5%) or ectopic pregnancy (1–2%) (Rai and Regan, 2006; Hajenius et al., 2007; Jaslow et al., 2010; Rajcan-Separovic et al., 2010). Apart from physical complaints, early pregnancy complications cause stress, anxiety, depression, grief and self-blame (Conway and Russell, 2000; Van and Meleis, 2003). Guidelines on early pregnancy care describe evidence-based diagnostic tests and interventions, but do not provide an overview on how to practice patient-centered care guided by the values and needs of women and/or their partners (Jauniaux et al., 2006; the Association of Early Pregnancy Units, 2007; NICE, 2012; NSW Ministry of Health, 2012; Queensland Maternal and Neonatal Clinical Guidelines Programme, 2015; Elson et al., 2016; RCOG/AEPU, 2016). The guideline of the Royal College of Obstetricians and Gynaecologists (RCOG) on recurrent miscarriage does state that all staff members should be trained in dealing with psychological aspects of early pregnancy loss and in bereavement counseling (RCOG, 2011). In the updated Queensland Clinical Guideline on early pregnancy loss, considerations are described on breaking bad news, care provision and parental support.

This systematic review aims to provide an overview of aspects of care valued by women and/or their partners faced with miscarriage, recurrent miscarriage or ectopic pregnancy and to identify potential targets for improvement in early pregnancy healthcare.

Table I. Dimensions of patient-centeredness.

Patient-centeredness	
Dimension	Considering
1. Respect to patients' values, preferences and expressed needs	Respect for the patient; focused on the individual patient; shared decision-making
2. Coordination and integration of care	Coordination and integration of clinical care; ancillary and support services and front-line patient care
3. Information, communication and education	Information on clinical status; progress and prognosis; processes of care and education
4. Physical comfort	Pain management; assistance with daily activities and living needs; hospital surroundings and environment kept in focus
5. Emotional support and alleviation of fear and anxiety	Anxiety over clinical status; treatment; prognosis; impact of the illness on themselves and family and the financial impact of illness
6. Involvement of significant other	Accommodation for social and emotional support; respect for and recognition of the patient advocate's role in decision-making; support for family members as caregivers; recognition of the needs of family and friends
7. Continuity and transition	Understandable patient information; coordinate plan after discharge; information regarding access to support
8. Access to care	Geographical accessibility; waiting times; ability to schedule appointments (when needed)

Methods

We identified and synthesized the literature on patients' perspectives on early pregnancy care by using a method based on the PRISMA statement and on previous similar reviews conducted in the fields of fertility and endometriosis care (Dancet et al., 2010, 2014). The PRISMA statement is a checklist with a set of items that should be reported in systematic reviews and meta-analyses (http://www.prisma-statement.org).

The method comprises three steps to extract and summarize the data. First, specific aspects of early pregnancy care valued by women and/or their partners were identified from the included qualitative and quantitative evidence and organized according to the eight dimensions of patient-centered care. Second, assessment of the service quality from women and/or their partners was extracted on each of these aspects of care based on quantitative evidence only. Third, the findings on patients' values were combined with the findings on the quality assessment to identify potential targets for improvement in early pregnancy healthcare.

Search strategy

We identified relevant studies by searching EMBASE, MEDLINE, CENTRAL, PsychINFO and CINAHL, published from inception of the databases to 1 July 2017. We used the following search terms ((prenatal OR antenatal OR early pregnancy OR first trimester OR miscarriage OR recurrent miscarriage OR ectopic pregnancy) AND (care or counsel*)) AND ((patient* OR woman* OR women* OR female* OR mother* OR men* OR couples*) AND (patient-centered* OR patient-centered* OR patient focused* OR experience* OR perspective* OR preference*)) and MesH terms Pregnancy Trimester, First, Patient-Centered Care, Consumer Satisfaction. We performed hand searches on the reference lists of the included studies to identify other possible eligible studies (i.e. the snowball strategy).

Study selection

Two reviewers (M.M.J.vd.B. and T.E.) independently assessed the eligibility of all articles identified by the search strategy based on their title and abstract and, if indicated, full text. Articles needed to fulfill the following criteria to be eligible: (i) empirical studies, (ii) including patients with early pregnancy complications, being miscarriage, recurrent miscarriage or ectopic pregnancy and (iii) reporting on what women and/or their partners valued in the care they received and/or their assessment of service quality. How women and/or their partners valued the care they received depends on the degree of importance they assign to various aspects of care, for instance a timely diagnosis (Edwards and Elwyn, 2009). Service quality assessments generate findings on the 'service quality', which is the woman's or their partner's perception of aspects of care delivered by their doctor and/or clinic, whilst taking account of their expectations (Zeithaml et al., 1988; Parasuraman et al., 1994).

This review does not include women with an ongoing viable pregnancy but only those who have clinical symptoms such as vaginal blood loss and/or abdominal pain. We defined miscarriage as the spontaneous loss of a clinically established intra-uterine pregnancy before 24 weeks of gestation, when the fetus has yet to reach viability (Rai and Regan, 2006). Internationally, there is no consensus on the definition of recurrent miscarriage. The definition ranges from two clinical miscarriages, not necessarily consecutive, to three consecutive miscarriages (Jauniaux et al., 2006; RCOG, 2011; ASRM, 2013). For this review, we used the definition of two or more not necessarily consecutive miscarriages (van den Boogaard et al., 2010; ASRM, 2013).

We resolved initial disagreements on the eligibility of studies by discussion involving the two reviewers and, in case of continuing disagreement, their supervisors (M.G. and P.J.H.).

We evaluated the methodological quality of all eligible studies by using the COREQ checklist for reporting qualitative studies and the STROBE statement for reporting observational studies (Tong et al., 2007; Von Elm et al., 2007).

Study characteristics

We collected the following data from all included studies by standardized data extraction sheets: study population (number of patients, i.e. women and/or their partners, country of origin, gestational age and type of early pregnancy complication), methodological details (primary aim, the use of qualitative and/or quantitative methodology and evaluated outcomes of interest, differentiated as values, experiences and satisfaction) and study scope (aspects of care and dimensions of patient-centered care).

Meta-synthesis

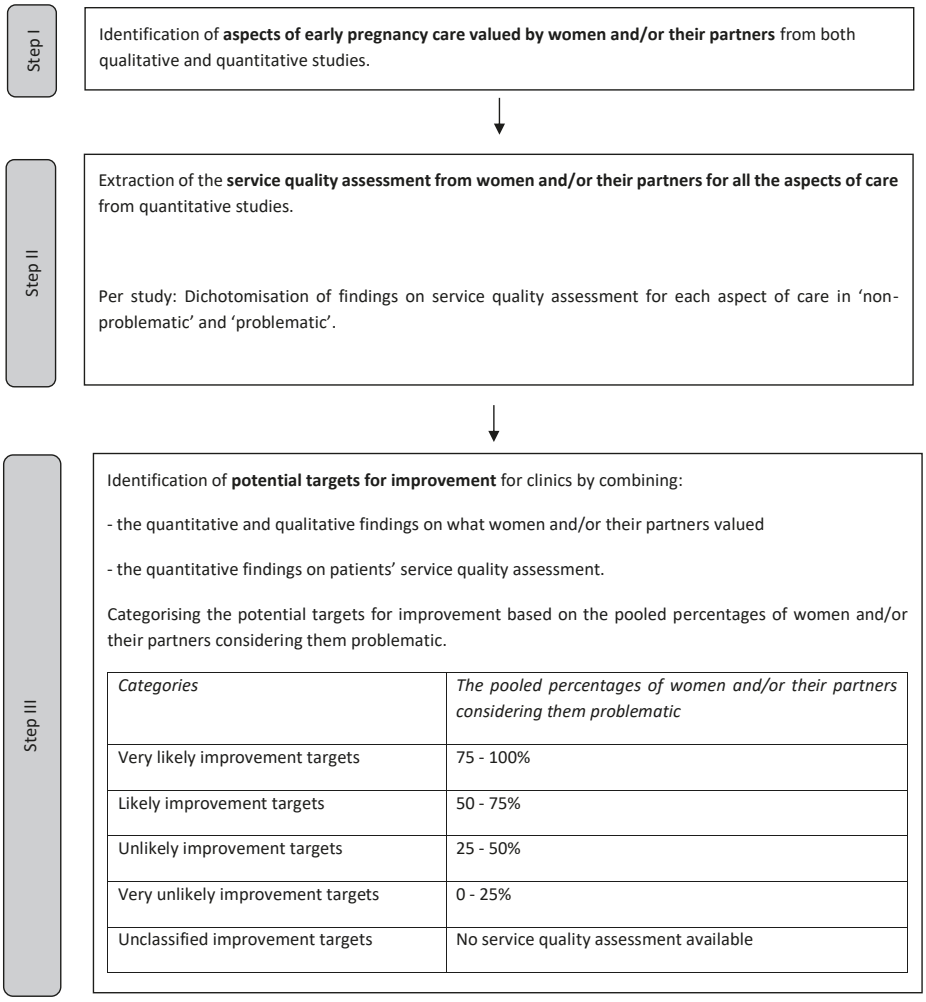
Two reviewers (M.M.J.vd.B. and T.E.) performed the meta-synthesis independently. We resolved initial disagreements by discussion involving the two reviewers and, in case of continuing disagreement, their supervisors (M.G. and P.J.H.). Figure 1 provides an overview of the steps taken in the meta-synthesis.

We first identified specific aspects of early pregnancy care valued by women and/or their partners from the included qualitative and quantitative evidence. We used the eight dimensions of patient-centered care to organize the gathered aspects of care. Both reviewers extracted the aspects of care important to at least one woman or her partner from the results section of the included studies (i.e. not the discussion section with interference or interpretation of authors). We defined aspects as important when studies used the following types of outcomes in their results section; 'important', 'helpful', 'value', 'appreciate', 'expressed their desire', 'want', 'prefer' and 'need'.

Second, for all the valued aspects of care, we extracted service quality assessment from women and/or their partners from the included quantitative evidence. We dichotomized the findings on service quality into 'non-problematic' or 'problematic'. We defined aspects of care as problematic when studies used the following types of outcomes in their results section; 'problematic', 'dissatisfaction', 'disappointed', 'inappropriate', 'poor', 'complained', 'impact negatively', 'not adequate', 'did not discuss/offer/acknowledge' and 'heightened their distress'. The dichotomized quantitative data for each specific aspect of care from each study addressing it were pooled by adding up the numerators and the denominators in each study.

Third, we combined the qualitative and quantitative findings on patients' values with the quantitative findings on patients' quality assessment to identify potential targets for improving the patient-centeredness of care (Slack, 1994; Damman et al., 2009; Dancet et al. 2010, 2012, 2014). Aspects of care 'important' to women and/or their partners according to (at least some) quantitative or qualitative data and 'problematic' to some women and/or their partners according to quantitative data were considered 'potential targets for improvement' (Damman et al., 2009; Dancet et al. 2010, 2012, 2014). We divided the targets for improvement into five groups, based on the pooled proportion of women and/or their partners considering quality assessment 'problematic'. More specifically: (i) 'very likely improvement targets', i.e. 75–100% of women and/or their partners reported a problematic quality assessment, (ii) 'likely improvement targets', i.e. 50–75% of women and/or their partners reported a problematic quality assessment, (iii)

'unlikely improvement targets', i.e. 25–50% of women and/or their partners reported a problematic quality assessment, (iv) 'very unlikely improvement targets', i.e. 0–25% of women and/or their partners reported a problematic quality assessment, (v) 'unclassified improvement targets', i.e. quality assessment not available. We divided the potential targets for improvement into likely and unlikely targets based on a 50% threshold. The likely targets for improvement include a problematic quality assessment above 50% according to the pooled proportion of women and/or their partners. Thereby, these likely targets are more apparent to receive priority for improvement.



Categories	*The pooled percentages of women and/or their partners considering them problematic*
Very likely improvement targets	75 - 100%
Likely improvement targets	50 - 75%
Unlikely improvement targets	25 - 50%
Very unlikely improvement targets	0 - 25%
Unclassified improvement targets	No service quality assessment available

Figure I. The steps taken for the outcomes of interest to this meta-synthesis.

Results

Literature search

The literature search yielded 6240 publications. We excluded 6004 studies after screening of titles and another 186 studies after screening of abstracts. We read 50 studies in full text, which led to excluding 28 studies. We searched the reference list of the 22 studies eligible for inclusion and identified another 5 studies. The reviewers had no disagreements in the assessment of studies and found 27 studies eligible for inclusion (Figure 2). The methodological quality of all 27 eligible studies was assessed and documented in Supplementary Tables I and II; Friedman, 1989; Bansen and Stevens, 1992; Cuisinier et al., 1993; Cecil, 1994; Moohan et al., 1994; Sehdev et al., 1997; Murphy, 1998; Paton et al., 1999; Wiebe and Janssen, 1999; Harvey and Moyle, 2001; Evans et al., 2002; Tsartsara and Johnson, 2002; Wong et al., 2003; Adolfsson et al., 2004; Alkazaleh et al., 2004; Nansel et al., 2005; Dalton et al., 2006; Simmons et al., 2006; Smith et al., 2006; Gerber-Epstein et al., 2009; Murphy and Merrell, 2009; Musters et al., 2011; Warner et al., 2012; Moscrop et al., 2013; Musters et al., 2013; MacWilliams et al., 2016; Meaney et al., 2017.

Study characteristics

The study populations, methodology and scope of the included studies are described in Table II.

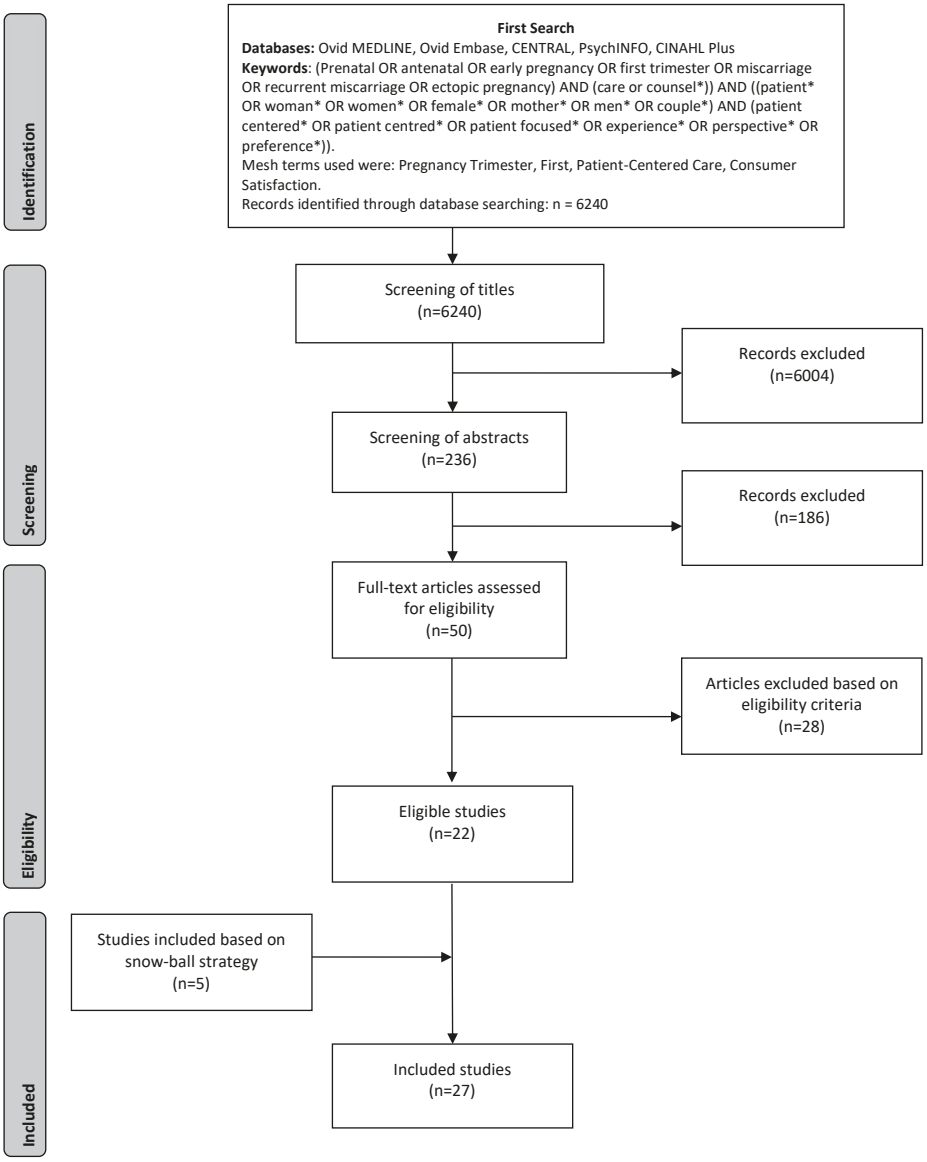


Figure 2. Flowchart literature search.

Table II. Study populations, methodology and scope of the included studies

	Study population*	Methodological details			Scope	
	Number of patients/ country of origin/maximum gestational age/early pregnancy complication	Primary aim**	Methodology***	Evaluated outcome	Evaluated component of care	Evaluated dimension of patient-centeredness ****
Friedman et al, 1989	67 women/UK/12 wks/ sporadic and recurrent miscarriage	Yes	Semi-structured Interview (QID)	Satisfaction, Experience	Miscarriage care and follow-up counselling	Respect; Information; Support; Involvement; transition
Bansen et al, 1992	10 women/USA/15 wks/n.r.	Yes	Semi-structured Interview (QID)	Experience	Miscarriage care	Comfort; Support; Involvement; Professionals
Cuisiner et al, 1993	143 women/the Netherlands/ 20 wks/ n.r.	Yes	Questionnaire (QSD)	Satisfaction, Experience	Miscarriage care	Information; Support, Transition; Skills
Cecil, 1994	50 women/Northern Ireland/13 wks/sporadic and recurrent miscarriage	Yes	Questionnaire and semi-structured interview (QID)	Experience	Miscarriage care and management, and follow-up counselling	Coordination; Comfort; Support; Transition
Moohan et al, 1994	74 women/Northern Ireland/< 12 wks/sporadic and recurrent miscarriage	Yes	Questionnaire (QNSD)	Satisfaction	Miscarriage care	Respect; Information; Skills
Sehdev et al, 1997	6 women+4 partners/ UK/n.r./n.r.	No	Unstructured interview (QID)	Experience	Miscarriage care	Respect; Information; Support; Involvement
Murphy et al, 1998	5 men/UK/-/sporadic and recurrent miscarriage	No	Unstructured interview (QID)	Experience	Miscarriage care	Respect; Support
Wiebe et al, 1999	59 women/Canada/ 12 wks/n.r.	Yes	Questionnaire (QSD and QNSD)	Satisfaction, Experience	Miscarriage care	Access; Information; Comfort; Support

Table II. Continued.

	Study population*	Methodological details			Scope	
Paton et al, 1999	79 women/UK/n.r./sporadic and recurrent miscarriage	Yes	Questionnaire and structured interview (QNSD)	Satisfaction	Miscarriage care and follow-up counselling	Coordination; Information; Support; Transition; Professionals
Harvey et al, 2001	3 women/Australia/ 11 wks/ Sporadic miscarriage	Yes	Unstructured interview (QID)	Experience	Miscarriage care	Information; Support
Evans et al., 2002	10 women/Australia/12 wks/ sporadic and recurrent miscarriage	Yes	Questionnaires and semi-structured interview (QNSD)	Satisfaction, Experience	Miscarriage care	Access; Continuity; Comfort; Information; Involvement; Support
Tsartsara et al, 2002	6 women/UK/up to 16 wks/ sporadic and recurrent miscarriage	Yes	Semi-structured interview (QID)	Satisfaction, Experience	Miscarriage care	Access; Coordination; Information; Support; Transition
Wong et al, 2003	100+22 women/UK/n.r./n.r.	Yes	Questionnaires and semi-structured interview (QID)	Experience	Miscarriage management and follow-up	Information; Support; Transition; Skills
Alkazaleh et al, 2004	117 women/Canada/n.r.	Yes	Questionnaire (QNSD)	Experience, values	Presenting abnormal ultrasound news	Access; Information; Comfort; Support; Involvement
Adolfsson et al, 2004	15 women/Sweden/12 wks/ sporadic and recurrent miscarriage	Yes	Semi-structured interview (QID)	Experience	Miscarriage management in the emergency ward and telephone counselling	Access; Respect; Information; Support; Involvement; Transition; Professionals
Nansel et al, 2005	80 women/USA/ 11 wks/ sporadic and recurrent miscarriage	No	Questionnaire (QSD)	Experience	Medical management of early pregnancy failure with misoprostol	Respect; Information; Comfort; Skills

Table II. Continued.

	Study population*	Methodological details			Scope	
Dalton et al, 2006	165 women/USA/13 wks/ sporadic and recurrent miscarriage	Yes	Questionnaire (QNSD)	Satisfaction, values	Office- vs operating-based procedures for early pregnancy failure	Comfort; Respect
Simmons et al, 2006	172 women/UK/n.r./sporadic and recurrent miscarriage	Yes	Questionnaire (QSD and QNSD)	Experience	Miscarriage medicalisation and follow-up	Respect; Coordination; Information; Support; Transition
Smith et al, 2006	72+47+8 women/UK/ sporadic and recurrent miscarriage	Yes	Semi-structured Interview and focus group (QID)	Experience	Medical, surgical or expectant management of miscarriage	Respect; Information; Comfort; Support
Murphy et al, 2009	8 women/UK/14 wks/n.r.	Yes	Unstructured interview (QID)	Experience	Miscarriage management and hospitalization	Respect; Coordination; Information; Transition
Geber-Epstein et al, 2009	19 women/Israel/6-15 wks/n.r.	Yes	Semi-structured interview (QID)	Experience	Miscarriage care	Access; Support; Involvement
Musters et al., 2011	17 women/the Netherlands/5-17 wks/ recurrent miscarriage	Yes	Semi-structured interview (QID)	Experience, values	Recurrent miscarriage care	Comfort; Continuity; Coordination; Information; Involvement; Support
Warner et al, 2012	16 women/Australia/20 wks/n.r.	Yes	Semi-structured interview (QID)	Experience	Early pregnancy care in Emergency department	Access; Respect; Information; Support; Transition
Moscrop et al, 2013	57 women/UK/ 16 wks/n.r.	No	Questionnaire (QNSD)	Experience	Follow-up appointment after miscarriage	Transition; Information

Table II. Continued.

	Study population*	Methodological details			Scope	
Musters et al., 2013	174 women/ the Netherlands/ 4-38 wks/ recurrent miscarriage	Yes	Questionnaire (QNSD)	Experience, values	Recurrent miscarriage care	Comfort; Continuity; Coordination; Information; Involvement; Support
MacWilliams et al., 2016	8 women/Canada/5-14wks/ miscarriage	Yes	Semi-structured interview (QID)	Experience	Miscarriage care in Emergency Department	Information; Involvement; Respect; Support
Meaney et al., 2017	10 women and 6 men/ Ireland/5-16 wks/recurrent miscarriage	Yes	Semi-structured interview (QID)	Experience	Recurrent miscarriage care	Comfort; Information

*N, respondents/country/miscarriage at week of gestation

** (Yes) primary aim is patients' perspective (No) primary aim is not patients' perspective

****QID: qualitative interview data, QSD: qualitative survey data, QNSD: quantitative survey data, [percentages from quantitative studies]

****(Access) access to care, (respect) respects for patients' values, preferences, needs, (coordination) coordination and integration of care, (information) information, communication and education, (comfort) physical comfort, (support) emotional support and alleviation of fear and anxiety, (involvement) involvement of family and friends, (transition) transition, (professionals) professionals, (skills) technical skills (number of dimensions).

n.a.: not applicable; n.r.: not reported

Study populations

The sample size of the included studies varied from 3 to 174 patients. In total, 24 studies explored the perspective of women on their care, one study explored the perspective of men and two studies explored the perspective of couples. The studies were conducted in eight countries: UK (n = 10), USA (n = 3), Ireland (n = 3), Canada (n = 3), the Netherlands (n = 3), Sweden (n = 1), Australia (n = 3) and Israel (n = 1).

Of the 27 studies, one study included pregnant women with ultrasound findings in the first trimester related with suspected miscarriage or ectopic pregnancy (Alkazaleh et al., 2004). Another study included pregnant women reporting on their experience of early pregnancy care in general. These women had presented with vaginal blood loss and/or abdominal pain and/or abnormal ultrasound findings in the first trimester related with miscarriage or ectopic pregnancy (Warner et al., 2012). The remaining 25 studies that included women and/or their partners having experienced a miscarriage. This could involve either sporadic and/or recurrent miscarriage (n = 13), only sporadic miscarriage (n = 2) or only recurrent miscarriage (n = 2), whereas in some studies the number of previous miscarriages was not mentioned (n = 8). In 19 studies, the duration of pregnancy at which the miscarriages occurred was reported and varied between 5 and 20 weeks gestational age. None of the studies reported on the perspectives of women and/or their partners having experienced an ectopic pregnancy.

Methodology of the studies

Fourteen studies collected their data with one qualitative interview per woman, man or couple. These interviews were either semi-structured (n = 10) or unstructured (n = 4). Nine studies used a questionnaire. These questionnaires comprised open ended questions (n = 3), closed questions using Likert-type response scales (n =7), or both (n = 1). Four studies used a mixed method design both an interview and questionnaire. The studies assessed one or more of the following outcomes: experience (n = 19), experience and satisfaction (n = 5) and satisfaction (n = 3).

Scope of the studies

Fourteen studies assessed patients' perspectives on actual care related to their miscarriage and a further six studies also included follow-up care. Another three studies focused on care related to specific interventions to which women were randomized, e.g. surgery versus misoprostol. Two studies focused on a specific component of care such as hospitalization at the emergency ward, one study focused on breaking bad news and one study assessed on telephone counseling.

The studies reported on two to seven of the eight dimensions of patient-centered care. The most commonly assessed dimensions were 'emotional support and alleviation of fear and anxiety' and 'information, communication and education', which were each assessed by 22 of the 25 studies.

Meta-synthesis

Based on data on patients' values, we identified 24 important aspects of care (Table III). These 24 aspects of care covered the eight dimensions of patient-centered care (one to six aspects of care per dimension). Nineteen aspects of care were evaluated by both qualitative and quantitative studies and five were assessed by qualitative studies. The most frequently reported aspect of care was 'being treated as an individual person experiencing a significant life event rather than a common condition', which is part of the patient-centered care dimension 'respect for patients' values, preferences and needs'.

Assessment of the service quality from women and/or their partners was available for thirteen identified aspects of care. The quantitative studies all documented problematic service quality for these thirteen aspects of care.

We thus identified thirteen potential targets improving the patient-centeredness of miscarriage and recurrent miscarriage care of which none was categorized as very likely, whereas four were categorized as likely, six were unlikely and three were very unlikely (Table IV).

Table III. Aspects of early pregnancy care organised per dimension of patient-centeredness, methodology and references

Dimension	Aspects of early pregnancy care (n =24)	Methodological design*	Important patients values (references)	Problematic quality assessment (references)
1.Respect for patients' values, preferences and needs	Being treated as an individual person experiencing a significant live event rather than a common condition	QID	A;H;M;K;P;U;Y;ZZ	na
		QSD	E;V;Z	
		QNSD	B	T [33%,26/79]
	Appraising patient as exceptional rather than one of many	QID	K	na
		QSD	E	
		QNSD		T[23%,17/75]
	Staff acknowledging human nature of the fetus rather than using distant medical terms	QID	D;Y;ZZ	na
		QSD	E;V	
		QNSD		
2.Coordination and integration of care	Performing an ultrasound scan confirming the viability of their pregnancy during each acute visit to the clinic	QID	Q;X	na
		QSD	V	
		QNSD	R	
	To appraise patient as urgent rather than adding patient to the queue	QID	P;Y	na
		QSD		
		QNSD		

Table III. Continued.

Dimension	Aspects of early pregnancy care (n =24)	Methodological design*	Important patients values (references)	Problematic quality assessment (references)
3.Information, communication and education	Understandable information provision and communication	QID	D;H;K;Q;U;Y;ZZ	na
		QSD		
		QNSD	B;M;R	
	Information provision about the degree of pain and bleeding to expect while awaiting spontaneous miscarriage	QID	A;K;L:W	na
		QSD	Z	
		QNSD	R	M[45%,33/74]; Z[38%,19/50]
	Information provision about the aetiology of pregnancy loss	QID	A;C;D;K;X;ZZ	na
		QSD	V	
		QNSD		G[58%,63/109]; V[77%,132/172]
	Information provision about care aspects to expect after pregnancy loss	QID	X;Z	na
		QSD	V	
		QNSD	N	
	Information provision about planning future pregnancies	QID	D;H;L;U;Y;ZZ	na
		QSD		
		QNSD	B	M[32%,24/74]; Z[72%,36/50]
	Information provision about support groups	QID	Q	na
		QSD		
		QNSD	G;R	G[43%,47/109]
	Providing written information	QID		na
		QSD	Z	
		QNSD		

Table III. Continued.

Dimension	Aspects of early pregnancy care (n =24)	Methodological design*	Important patients values (references)	Problematic quality assessment (references)
4.Physical comfort	Recognition of patient's physical pain	QID	C;W	na
		QSD		
		QNSD	F	
	Being given time in a private room to cope with diagnosis of pregnancy loss	QID	L;Y	na
		QSD	V	
		QNSD	B;F	G[25%,27/109]
	Not sharing a waiting room with women awaiting a routine pregnancy scan	QID	D;L;Q;X	na
		QSD	V	
		QNSD	R	
	Allocating patients to a bed in a quiet room during acute visits to the clinic	QID	D;Y	na
		QSD		
		QNSD		
	Providing sufficient analgesia during curettage	QID		na
		QSD	Z	
		QNSD	F	
5.Emotional support and alleviation of fear and anxiety	Staff discussing patients' distress	QID	A;D;I;Q	na
		QSD		
		QNSD	R	G[60%,65/109]
	Staff discussing patients' grief	QID	A;D;I	na
		QSD		
		QNSD		
	Staff showing empathy for patients' emotional pain	QID	A;C;I;L;O;Q;X;ZZ	na
		QSD	E;V;Z	
		QNSD	R	G[25%,27/109]; M[23%,17/74]; T[23%,17/75]; V[70%,120/172]; Z[8%,4/50]
6.Involvement of significant other	Informing patients on pregnancy loss in the presence of a partner or friend (significant other)	QID	A;K;Q	na
		QSD		
		QNSD	B;R	G[62%,68/109]

Table III. Continued.

Dimension	Aspects of early pregnancy care (n =24)	Methodological design*	Important patients values (references)	Problematic quality assessment (references)
7.Continuity and transition	Staff performing follow-up phone calls to support their patients after a miscarriage	QID	C;X;Y	na
		QSD	E;V;Z	
		QNSD	G;N	G[85%, 34/65]; T[52%,34/65]
	The offer of a follow-up medical consult after pregnancy loss	QID	A;C;D;I;Q;X;Y	na
		QSD	E;Z	
		QNSD	R	G[20%,22/109]
8.Access to care	Limit the duration of waiting times in waiting rooms	QID	A;H;Y	na
		QQD		
		QNSD		G[20%,22/109]

*QID: qualitative interview data, QSD: qualitative survey data, QNSD: quantitative survey data, [percentages from quantitative studies, n/n], na = not applicable

A= Adolfsson et al.,2004;B= Alkazaleh et al.,2004; C= Bansen and Stevens,1992;D= Cecil, 1994;E= Cuisinier et al.,1993;F= Dalton et al., 2006;G= Evans et al., 2002;H= Friedman,1989;I= Gerber-Epstein et al., 2009;J= Harvey et al., 2001;K=MacWilliams et al., 2016; L=Meaney et al., 2017;M= Moohan et al., 1994;N= Moscrop et al., 2013;O= Murphy,1998;P= Murphy and Merrell, 2009;Q= Musters et al., 2011;R= Musters et al., 2013;S= Nansel et al.,2005;T= Paton et al., 1999;U= Sehdev et al., 1997;V= Simmons et al., 2006;W= Smith et al.,2006;X= Tsartsara and Johnson, 2002;Y= Warner et al., 2012;Z= Wiebe and Janssen, 1999;ZZ= Wong et al., 2003

Table IV. Potential targets for improvement in the patient-centeredness of early pregnancy care organised per dimension of patient-centeredness

Target	**Dimension of patient-centeredness** Patients' values [pooled percentages]
Very likely improvement targets (75-100% of women and/or their partners reported a problematic quality assessment)	Non identified
Likely improvement targets (50 - 75% of women and/or their partners reported a problematic quality assessment)	*Information, communication & education* Understandable information provision about the aetiology of pregnancy loss [69] *Emotional support and allevation of fear and anxiety* Staff discussing patients' distress [60] *Involvement of significant other* Informing patients on pregnancy loss in the presence of friend or partner (significant other) [62] *Continuity and transition* Staff performing follow-up phone calls to support their patients after a miscarriage [52]
Unlikely improvement targets (25 - 50% of women and/or their partners reported a problematic quality assessment)	*Respect for patients' values, preferences & needs* Treating patients as an individual person experiencing a significant live event rather than a common condition [33] *Information, communication and education* Information provision about the expected degree of pain and bleeding while awaiting spontaneous miscarriage [42]; Information provision about planning future pregnancies [48]; Information provision about support groups [43] *Physical comfort* Being given time in a private room to cope with diagnosis of pregnancy loss [25] *Emotional support and allevation of fear and anxiety* Staff showing empathy for patients' emotional pain [39]
Very unlikely improvement targets (0 - 25% of women and/or their partners reported a problematic quality assessment)	*Respect for patients' values, preferences & needs* Appraising the patient as exceptional rather than one of many [23] *Continuity and transition* The offer of a follow-up medical consult after pregnancy loss [20] *Access to care* Limit the duration of waiting times in waiting rooms [20]

Table IV. Continued.

Target	Dimension of patient-centeredness Patients' values [pooled percentages]
Unclassified potential improvement targets (Quality assessment not available)	*Respect for patients values, preferences & needs* Staff acknowledging human nature of the fetus rather than using distant medical terms *Coordination and integration of care* Performing an ultrasound scan confirming the viability of their pregnancy during each acute visit to the clinic; To appraise the patient as urgent rather than adding the patient to the queue *Information, communication and education* Understandable information provision and communication; Information provision about care aspects to expect after pregnancy loss; Providing written information *Physical comfort* Recognition of patient's physical pain; Not sharing a waiting room with women awaiting a routine pregnancy scan; Allocating patients to a bed in a quiet room during acute visits to the clinic; Providing sufficient analgesia during curettage *Emotional support and allevation of fear and anxiety* Staff discussing patients' grief

The aspects of early pregnancy care per dimension of patient-centeredness with exemplifying quotations from participants in the included studies are discussed below.

Respect for patients' preferences and needs

Patients valued being treated as an individual person who experienced a significant life event rather than a common condition (unlikely improvement target). *'Most people treat miscarriage as not very important 'everybody has them' etcetera, but it was very traumatic for me'* (Simmons et al., 2006). Patients also missed being treated as exceptional rather than one of many (very unlikely improvement target). Furthermore, patients found it important that clinicians referred to 'the baby' rather than hearing them use an impersonal medical term like 'the fetus' (unclassified potential improvement target) (Warner et al., 2012).

Coordination and integration of care

Patients wanted to know if they still had a viable pregnancy when they experienced first trimester vaginal blood loss and/or abdominal pain. Patients found it important to undergo an ultrasound scan to confirm viability and assessed this aspect of care as problematic. *'I spotted continually throughout the 10 weeks of pregnancy—very upsetting and stressful. I kept doing home pregnancy tests because I was paranoid that I was losing the baby. Doc wouldn't send me for an early scan until I pleaded at 10 weeks'* (Simmons et al., 2006).

Also, patients valued being appraised as urgent instead of being added to the queue before being seen by a clinician. *'I mean, I sat on the ambulance gurney for five hours before I was put in a room. I saw no hospital member of staff. I had the ambulance men there and that was that'* (Warner et al., 2012). All these aspects of care are unclassified potential improvement targets.

Information, communication and education

Patients valued understandable information and communication and reported problematic experiences in this respect in qualitative studies only (unclassified potential improvement target). Patients liked to receive information on the degree of pain and blood loss to expect while awaiting a spontaneous miscarriage (unlikely improvement target). *'I was not expecting that sort of thing to happen and was scared and embarrassed and uncertain if I would ever stop bleeding. I did, of course, but I could have been better prepared, i.e. told what to expect'* (Wiebe and Janssen, 1999).

Patients appreciated being informed on the etiology of the pregnancy loss (likely improvement target), the healthcare which would be provided after a pregnancy loss (unclassified potential improvement target), support groups and when to plan a future pregnancy (unclassified or unlikely improvement targets). *'I was given advice on future pregnancies by most of the doctors and nurses. Some said to wait 3 months, some said 4 months. I went back to see my GP and he said 8 months. This left me feeling quite confused'* (Sehdev et al., 1997). Patients valued the provision of written information on pregnancy loss to assist them with their understanding and grieving (unclassified potential improvement target).

Physical comfort

Patients valued privacy after receiving bad news about having a miscarriage and some patients assessed this aspect of care as problematic (unlikely improvement target). A patient said: *'They put me in a plaster room with people coming in and out. It was a public thoroughfare. I was just mortified'* (Warner et al., 2012).

Patients found queuing amongst other pregnant patients, while miscarrying, the most upsetting of all (unclassified potential improvement target) because they were going through a painful process in contrast to other 'healthy' pregnant women who were awaiting a routine pregnancy scan (Tsartsara and Johnson, 2002). The provided analgesia during the curettage was described as problematic by patients (unclassified potential improvement target) as several patients reported pain, besides grief, during the procedure (Tsartsara and Johnson, 2002).

Emotional support and alleviation of fear and anxiety

Patients valued treatment with sensitivity and compassion by hospital staff who is able and willing to discuss patients' distress (likely improvement target) and grief (unclassified potential improvement target). Negative assessment of provided care occurred when hospital staff did not recognize or mentioned the emotional pain (unlikely improvement

target). A patient said*: 'Emphasize this aspect, that it is all right to mourn, know how to say it to people—perhaps it is difficult, one patient may need more time and another less. The professionals also must emphasize to these mothers, these women, that they are not alone, or that they are not freaks'* (Gerber-Epstein et al., 2009).

Involvement of significant others

Patients valued the presence of their partner when being informed on pregnancy loss (likely improvement target). Patients reported unwelcoming attitudes from medical staff to the presence of a partner or friend. *'I wanted my husband with me. They phoned him, butas he arrived on the ward, one of the nurses stopped him and said 'what are you doing?' sort of thing. He was quite upset that, he just wanted to see me'* (Adolfsson et al., 2004).

Continuity and transition

Patient valued medical follow-up or a repeat consultation after a pregnancy loss (very unlikely improvement target). Patients who were visited at home by their general practitioner were very grateful for that (Cuisinier et al., 1993). *'I think the offer of counseling was great because you are in and out and gone, so follow-up is important'* (Warner et al., 2012).

Many patients stated that they felt left alone after leaving the hospital and would have appreciated a follow-up phone call (likely improvement target). Many patients felt frustrated because they had received no further professional support or information.

Access to care

Long waiting times in the waiting room was assessed as problematic by some patients (very unlikely improvement target). A patient said: *'First, I waited for over 5 h and there was a sign if you are presenting with a 'pregnancy related issue to let them know so I did that straight away but I was not even called to see the triage nurse for the first 2 h'* (Warner et al., 2012).

Discussion

This systematic review has provided insight in the aspects of care valued by women and/or their partners who experience a miscarriage and/or recurrent miscarriage and identified targets for improvement of patient-centered miscarriage care.

We identified 24 aspects of care valued by women and/or their partners who experienced a miscarriage or recurrent miscarriage. The perspective of the (male) partner was examined in only three studies. There were no studies on patients' perspectives on ectopic pregnancy care. The most frequently reported aspect of care was 'being treated as an individual person experiencing a significant live event rather than a common condition', which is part of the dimension 'respect for patients' values, preferences and needs' in patient-centered care. In 13 aspects of care, quality assessment was reported as 'problematic' and these aspects were thus identified as potential targets for

improvement. 'Understandable information provision about the etiology of pregnancy', 'Staff discussing patients' distress', 'Informing patients on pregnancy loss in the presence of friend or partner' and 'Staff performing follow-up phone calls to support their patients after a miscarriage' were categorized as likely targets for improvement.

In our meta-synthesis, we considered an aspect of care relevant to patient-centered care as soon as it became clear from a study's results section that one or more patients valued this aspect. This is in line with patient-centered care which is guided by individual patient's values rather than guided by the values shared by a larger group (Corrigan et al., 2001). However, this method has the disadvantage of resulting in many aspects of care to be taken into account. We report in our meta-synthesis exactly which proportion of patients from quantitative studies assessed an aspect of care as problematic. This allowed us to order the abundance of valued aspects of care for their likeliness to require improvement, based on how often these aspects were considered problematic. To limit the influence of interpretation of the original authors on our findings, two authors (M.M.J.vd.B. and T.E.) performed the classification of aspects of care as important and problematic on clear pre-defined rules, consulting their supervisors (M.G. and P.J.H.) in case of disagreement.

Our findings on patient-centered early pregnancy care can be generalized to Western countries as we included studies from eight different Western countries. Furthermore, we do not expect women to differ in aspects of care valued as fertility patients from different European countries valued surprisingly similar aspects of care (Dancet et al., 2012).

Patient-centered care is important for providing high quality healthcare. This has recently been reinforced by a group of patients drawing a miscarriage code of care (http://www.mumsnet.com/campaigns/miscarriage-code-of-care). The five principles in this miscarriage code, that calls for improvements of NHS care, are supportive staff, access to ultrasound scanning, safe and appropriate places for treatment, good information and effective treatment and joined-up care.

The introduction of early pregnancy units and recurrent miscarriage clinics has been a first step towards a more patient-centered approach for women facing early pregnancy complications, especially in the organization of care with a dedicated multi-professional service providing sometimes even 24/7 access. This review additionally informs the staff working in these units and clinics on what a patient-centered approach should entail. Women with a miscarriage or recurrent miscarriage also need to be treated as individual persons who experience a significant live event in addition to getting the best possible medical care. More specifically, women want respect, information, physical comfort, emotional support, involvement of their partner, friend or family, continuity and easy access to care. The problematic experiences with communication could be improved by providing understandable information by way of decision aids, such as Option Grids (Elwyn et al., 2013; http://optiongrid.org). Thus far, option grids have not been published on early pregnancy complications and therefore should be developed.

Our overview of targets for improvement can be used by clinicians to improve the patient-centered approach of women and/or their partners facing miscarriage or recurrent miscarriage. The likely targets for improvement include a problematic quality assessment above 50% according to the pooled proportion of women and/or their partners and thereby need to receive more priority in improvement than the unlikely targets. Future qualitative studies are needed to explore how to improve the identified potential targets for improvement of (recurrent) miscarriage care and to explore the perspectives of women and/or their partners treated for ectopic pregnancy.

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Supplementary table I. COREQ criteria for qualitative studies

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y
Domain 1: Research team and reflexivity																									
1. Which author conducted the interview or focus group?	0	-	0	0	-	-	0	0	0	0	-	-	1	0	1	-	-	0	1	-	0	1	1	-	1
2. What were the researcher's credentials?	0		0	0			0	0	0	0			0	0	1			0	1		0	1	1		1
3. What was their occupation at the time of the study?	0		0	0			0	0	0	0			0	0	0			0	1		0	0	1		1
4. Was the researcher male or female?	0		0	0			0	0	0	0			0	0	1			0	0		0	0	0		1
5. What experience or training did the researcher have?	0		0	0			1	0	0	0			0	0	0			0	0		0	0	1		1
6. Was a relationship established prior to study commencement?	1		0	0			0	0	0	0			0	0	1			0	0		0	0	0		0
7. What did the participants know about the researcher?	1		0	0			0	0	0	0			0	0	0			0	0		0	0	0		0
8. What characteristics were reported about the interviewer?	0		0	0			0	0	0	0			0	0	0			0	0		0	0	0		1
Domain 2: study design																									
9. What methodological orientation was stated to underpin the study?	0		1	0			1	0	1	0			1	1	1			1	1		1	1	1		1
10. How were participants selected?	1		1	1			1	1	1	1			1	1	1			1	0		1	1	1		1
11. How were participants approached?	1		1	1			1	1	1	1			1	1	1			1	0		1	1	1		1
12. How many participants were in the study?	1		1	1			1	1	1	1			1	1	1			1	1		0	1	1		1
13. How many people refused to participate or dropped out? Reasons?	1		1	1			1	1	0	1			0	0	1			1	0		1	0	0		1
14. Where was the data collected?	1		0	1			1	1	1	1			0	1	0			1	0		1	1	1		0
15. Was anyone else present besides the participants and researchers?	0		0	0			0	0	0	0			0	0	1			0	0		1	0	1		0
16. What are the important characteristics of the sample?	1		1	1			0	1	1	1			1	1	1			1	0		1	1	1		1

Supplementary table I. Continued.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y
17. Were questions, prompts, guides provided by the authors? Was it pilot tested?	1		1	1			1	0	1	1			1	1	0			1	0		0	1	1		1
18. Were repeat interviews carried out?	1		1	1			0	0	0	0			0	1	1			0	0		1	0	0		0
19. Did the research use audio or visual recording to collect the data?	1		1	1			0	0	1	1			1	0	1			1	1		1	1	0		1
20. Were field notes made during and/or after the interview or focus group?	0		1	1			1	0	0	1			0	1	1			0	0		1	1	1		1
21. What was the durarion of the interview or focus group?	1		1	1			1	0	1	1			1	1	1			0	0		0	1	0		1
22. Was data saturation discussed?	0		0	0			0	0	0	0			0	0	1			0	0		1	0	0		0
23. Were transcripts returned to participants for comment and/or correction?	0		0	0			0	0	0	0			0	0	0			0	0		0	0	0		1
Domain 3: analysis and findings																									
24. How many data coders coded the data?	1		1	1			0	0	1	1			0	0	1			0	1		1	1	1		1
25. Did authors provide a description of the coding tree?	0		1	0			0	0	1	1			0	1	1			0	0		0	0	0		1
26. Were themes identified in advance or derived from the data?	0		0	1			1	0	1	0			0	1	1			0	1		1	1	1		1
27. What software, if applicable, was used to manage the data?	0		0	0			0	0	1	1			1	1	1			0	0		1	0	0		0
28. Did participants provide feedback on the findings?	0		0	0			0	0	1	0			0	0	1			0	0		0	0	0		0
29. Were participant quotations presented to illustrate the themes / findings?	1		1	1			0	0	1	0			1	1	1			1	1		1	1	1		1
30. Was there consistency between the data presented and the findings?	1		1	1			1	0	1	1			1	1	1			1	1		1	1	1		1

Supplementary table I. Continued.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y
31. Were major themes clearly presented in the findings?	1		1	1			1	1	1	1			1	1	1			1	1		1	1	1		1
32. Is there a description of diverse cases or discussion of minor themes?	1		1	1			1	1	0	1			1	1	1			1	1		1	1	1		1

A= Adolfsson et al.,2004;B= Alkazaleh et al.,2004; C= Bansen and Stevens,1992;D= Cecil, 1994;E= Cuisinier et al.,1993;F= Dalton et al., 2006;G= Evans et al., 2002;H= Friedman,1989;I= Gerber-Epstein et al., 2009;J= Harvey et al., 2001;K= Moohan et al., 1994;L= Moscrop et al., 2013;M= Murphy,1998;N= Murphy and Merrell, 2009;O= Musters et al., 2011;P= Musters et al., 2013;Q= Nansel et al.,2005;R= Paton et al., 1999;S= Sehdev et al., 1997;T= Simmons et al., 2006;U= Smith et al.,2003;V= Tsartsara and Johnson, 2002;W= Warner et al., 2012;X= Wiebe and Janssen, 1999;Y= Wong et al., 2003

Supplementary table II. STROBE statement for observational studies

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y
Introduction																									
1a. Indicate the study's design with commonly used terms in the title or abstract 1b. provide in the abstract an informative and balanced summary of what was done and what was found	-	1	-	0	0	1	1	-	-	-	1	1	-	-	-	1	1	1	-	1	-	-	-	1	1
2. Explain the scientific background and rationale for the investigation being reported		1		1	0	1	1				1	1				1	1	1		1				1	1
3. State specific objectives, including any prespecified hypotheses		1		1	1	1	1				1	1				1	1	1		1				1	1
Methods																									
4. Present key elements of study design early in paper		1		1	1	1	1				1	1				1	1	1		1				1	1
5. Describe the setting, locations, and relevant dates		1		1	0	1	1				1	1				1	1	1		1				1	1

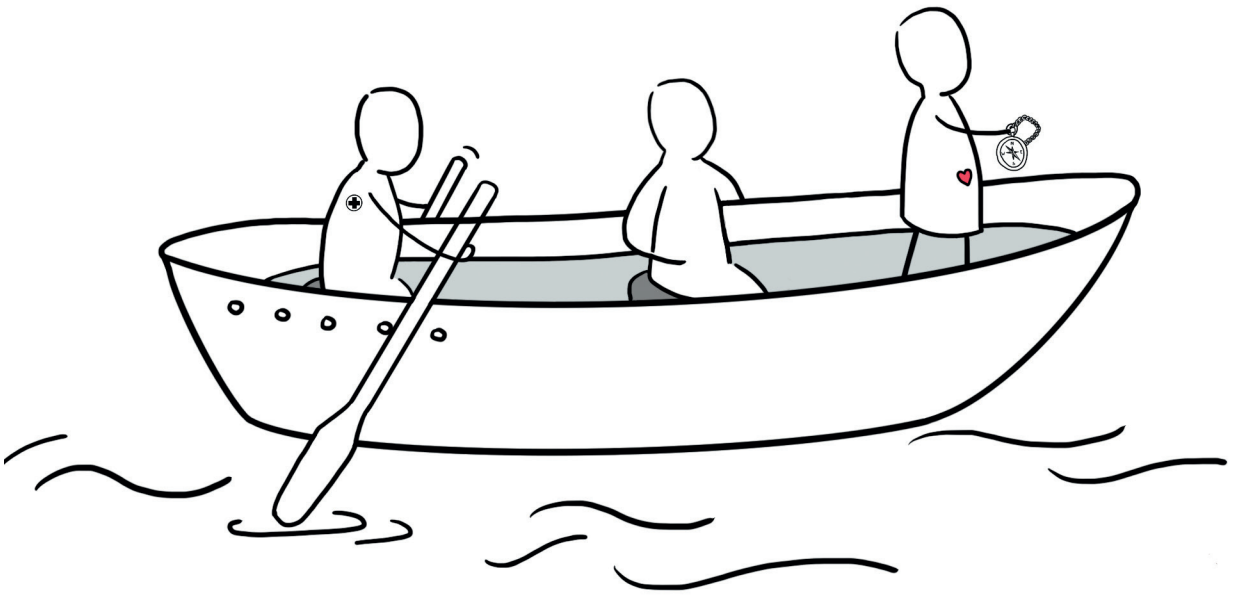
Supplementary table II. Continued.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y
6a. Give the eligibility criteria, and the sources and methods of selection of participants 6b. For matched studies, give matching criteria and number of exposed and unexposed		1		1	0	1	1				1	1				1	1	1		1				1	1
7. Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers		0		0	0	1	0				0	0				1	1	0		1				1	1
8. For each variable of interest, give sources of data and details of methods of assessment		1		0	1	1	0				0	1				1	1	0		1				0	0
9. Describe any efforts to address potential sources of bias		0		0	0	0	0				0	0				1	1	0		1				1	1
10. Explain how the study size was arrived at		0		1	1	1	1				0	1				1	1	1		1				1	1
11. Explain how quantitative variables were handled in the analyses		0		0	1	1	1				0	1				1	1	1		1				0	1
12a. Describe all statistical methods 12b. Describe any methods used to examine subgroups and interactions 12c. Explain how missing data were addressed 12d. If applicable, explain how loss to follow-up was addressed 12e. Describe any sensitivity analyses		0		1	1	1	1				1	1				1	1	0		1				0	1
Results																									
13a. Report numbers of individuals at each stage of study 13b. Give reasons for non-participation at each stage 13c. Consider use of a flow diagram		1		1	1	1	1				1	1				1	1	1		1				1	1
14a. Give characteristics of study participants 14b. Indicate number of particpants with missing data for each variable of interest		0		1	1	1	1				1	1				1	1	1		1				1	1

Supplementary table II. Continued.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y
15. Report number of outcome events or summary measures over time		1		0	1	1	1				1	1				1	1	1		1				1	1
16a. Report the numbers of individuals at each stage of the study. 16b. Give reasons for non-participation at each stage 16c. Consider use of a flow diagram		1		1	1	1	1				1	1				1	1	1		1				1	1
17. Report other analysis done		0		0	0	1	0				0	0				1	1	0		0				0	0
Discussion																									
18. Summarise key results with reference to study objectives		1		0	1	1	1				1	1				1	1	1		1				1	1
19. Discuss limitations of the study		1		1	1	1	1				1	1				1	1	1		1				1	1
20. Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence		1		1	1	1	1				1	1				1	1	1		1				1	1
21. Discuss the generalisablity of the study results		1		1	1	1	1				1	1				1	1	1		1				1	1
Other information																									
22. Give the source of funding and the role of the funders for the present study		1		1	0	0	0				0	1				1	0	0		1				0	1

A= Adolfsson et al.,2004;B= Alkazaleh et al.,2004; C= Bansen and Stevens,1992;D= Cecil, 1994;E= Cuisinier et al.,1993;F= Dalton et al., 2006;G= Evans et al., 2002;H= Friedman,1989;I= Gerber-Epstein et al., 2009;J= Harvey et al., 2001;K= Moohan et al., 1994;L= Moscrop et al., 2013;M= Murphy,1998;N= Murphy and Merrell, 2009;O= Musters et al., 2011;P= Musters et al., 2013;Q= Nansel et al.,2005;R= Paton et al., 1999;S= Sehdev et al., 1997;T= Simmons et al., 2006;U= Smith et al.,2003;V= Tsartsara and Johnson, 2002;W= Warner et al., 2012;X= Wiebe and Janssen, 1999;Y= Wong et al., 2003



CHAPTER 3

Womens' experiences on ectopic pregnancy care: in-depth interviews

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Manuscript in preparation

Abstract

Research Question

How do women experience diagnosis, treatment and follow-up of ectopic pregnancy care?

Design

Between April and November 2021 eight women were interviewed who had been diagnosed and treated for ectopic pregnancy in the Amsterdam University Medical Centres (Amsterdam UMC; the Netherlands) in the preceding 12 months. Women were asked to share their experiences of diagnosis, treatment and follow-up of their ectopic pregnancy and we explored which aspects of care they valued. In-depth interviews were subjected to deductive and inductive content analysis.

Results

Women valued specific information on diagnosis and treatment of ectopic pregnancy and on implications for their fertility in both oral and written format. Women also appreciated sharing decisions with an empathic clinician who provided clear information. Women shared negative experiences with the waiting time after referral for a pregnancy test and/or an ultrasound scan and preferred to be seen directly by a gynaecologist instead of a general practitioner or staff from the emergency room. All women shared that adequate communication would have lowered their level of frustration around waiting times.

Conclusions

Patient-centeredness of ectopic pregnancy care needs to be improved in particular by direct referral to an early pregnancy assessment unit. Staff working in the EPAU should adhere to recent evidence-based guidelines, and should be trained in communication skills to regularly discuss the rationale for and duration of inevitable waiting time.

Introduction

Evidence based guidelines regarding miscarriage and ectopic pregnancy emphasize the importance of good communication skills and emotional support (Dutch Society of Obstetrics and Gynecology, 2016; Dutch Society of Obstetrics and Gynecology, 2020; NICE guideline, 2019; Po et al., 2021). These guidelines recommend the training of staff in breaking bad news and in supporting women dealing with the psychological aspects of pregnancy loss (Dutch Society of Obstetrics and Gynecology, 2016; Dutch Society of Obstetrics and Gynecology, 2020; NICE guideline, 2019; Po et al., 2021).

Miscarriage can trigger mental health problems (i.e. anxious reactions, depression, post-traumatic stress disorder, and even suicide attempts) but screening instruments are non-existent (Coomarasamy et al., 2021; Quenby et al., 2021). A systematic literature review highlighted to clinicians that women and their partners appreciate an individual approach, whilst experiencing a miscarriage, being the significant life event it is. (van den Berg et al., 2018). Data on these topics in women and partners experiencing an ectopic pregnancy are non-existent. This study, therefore, aimed to explore how women experience diagnosis, treatment and follow-up of ectopic pregnancy.

Material and Methods

Design

We performed a qualitative study with in-depth interviews. We subjected these interviews to a combination of deductive and inductive content analysis. We took the 'Consolidated Criteria for Reporting Qualitative Studies (COREQ) criteria into account for the write-up of this manuscript (Tong et al, 2007).

Participants & setting

Women who had been treated for an ectopic pregnancy in the Amsterdam University Medical Centres (AUMC, the Netherlands) in the preceding 12 months were eligible.

Ethics

The Institutional Review Board (IRB) of the AUMC concluded that this interview study was not subject to the Dutch 'Medical Research Involving Human Subjects Act' the study did not require additional medical investigations or treatments. Therefore, meaning that no formal IRB approval was needed. Women were informed orally and in writing about the aim and the format of the study and confirmed their consent for participation in writing.

Recruitment

We identified eligible women through the financial registry of the Early Pregnancy Assessment Unit (EPAU) of the AUMC. Eligible women received a telephone call from their treating clinician in which he/she explained the aim and format of the study. Thereafter, written patient information and a consent letter was sent to interested women and they were asked to confirm their consent in writing. Afterwards, consenting women were contacted by the researcher (MvdB) to schedule the in-depth interview.

We encouraged all women to involve their partner in the interview. Partners who took part in the interview also confirmed their consent in writing.

A pilot face-to-face interview was conducted by the female senior researcher (ED) experienced in qualitative research together with the more junior female researcher (MvdB), both not involved in clinical care. MvdB conducted all subsequent interviews between April and November 2021 by video call (Microsoft Teams) due to the COVID-19 pandemic.

The interview was preceded by a short questionnaire to collect background characteristics regarding age, obstetric history, and management of the ectopic pregnancy. The interview started with open questions on the most positive and most negative care experiences during diagnosis, treatment and follow-up. The interviewer followed the story line of the women and asked probing questions by means of a topic list (Table I), based on all aspects of care valued by women experiencing a miscarriage (van den Berg et al., 2018). The interviews were audio-recorded and transcribed verbatim. Data collection and analysis were intertwined to ensure that novel findings could be checked in subsequent interviews. The sample size was determined by data-collection saturation and inductive thematic saturation (Polit and Beck, 2004; Saunders et al., 2018).

Analysis

Two researchers (MvdB, MR) analysed the interviews and achieved agreement through negotiated consensus to ensure reliability. The interviews were analysed immediately after each interview to ensure that novel findings could be checked in subsequent interviews. The analysis started after thoroughly reading each interview transcript several times (Graneheim and Lundman, 2004).

We first performed a deductive content analysis (Elo & Kyngäs, 2008). This is a structured matrix analysis based on all aspects of patient-centered care valued by women with a miscarriage organised by the eight dimensions of patient-centered care (Table I, van den Berg et al., 2018). We added one novel dimension 'competence of medical staff members', which was previously proven important to subfertility patients (Dancet et al., 2011).

Patient-centered care dimensions have been divided in six system and four human factors that can be improved by organisational decisions and by staff training respectively (Dancet et al., 2011). We divided the literature-based dimension 'information, communication and education' into the system factor 'information provision' and the human factor 'communication skills' (van den Berg et al., 2018).

Next, we subjected the data that did not fit the deductive matrix analysis to inductive content analysis. We checked whether specific novel care aspects could be allocated to one of the eight dimensions of patient-centered care or required the development of a novel dimension (Hsieh & Shannon, 2005; Elo & Kyngäs, 2008). The inductive content analysis also explored the interaction between dimensions of patient-centered care or patterns in narrative data (Dancet et al., 2011).

Table I. The eight dimensions of patient-centeredness and aspects of ectopic pregnancy care

1.Respect for patients' values, preferences and needs	Being treated as an individual person experiencing a significant live event rather than a common condition
	Appraising the patient as exceptional rather than one of many
	Staff acknowledging human nature of the embryo rather than using distant medical terms
2.Coordination and integration of care	Performing an ultrasound scan establishing the location of the pregnancy during each acute visit to the clinic
	To appraise the patient as urgent rather than adding the patient to the queue
3.Information, communication and education	Understandable information provision and communication
	Information provision about the degree of abdominal pain and vaginal bleeding to expect while awaiting expectant or medical treatment for ectopic pregnancy
	Information provision about the aetiology of ectopic pregnancy
	Information provision about care aspects to expect for the management of ectopic pregnancy
	Information provision about planning future pregnancies
	Information provision about support groups
	Providing written information
4.Physical comfort	Recognition of patient's physical pain
	Being given time in a private room to cope with diagnosis of pregnancy loss
	Not sharing a waiting room with pregnant women awaiting a routine ultrasound scan or antenatal visit
	Allocating patients to a bed in a quiet room during acute visits to the clinic
	Providing sufficient analgesia during surgical treatment
5.Emotional support and alleviation of fear and anxiety	Staff discussing patients' distress
	Staff discussing patients' grief
	Staff showing empathy for patients' emotional pain
6.Involvement of significant other	Informing patients on ectopic pregnancy in the presence of a partner or friend (significant other)
7.Continuity and transition	Staff performing follow-up phone calls to support their patients after treatment of an ectopic pregnancy
	Follow-up with a face to face consultation after treatment of an ectopic pregnancy
8.Access to care	Limit the duration of waiting times in the waiting room and for installing treatment

Results

Participants

We reached data collection saturation and thematic saturation regarding the dimensions of patient-centered care after seven interviews and this was confirmed by the eighth interview. Therefore, we included eight women and in three interviews their partners (all men) were present. These men were regularly asked by the interviewer to reinforce or challenge womens' narratives. The interviews lasted 60 to 90 minutes. The background characteristics of the women are presented in Table II. Six women had been treated surgically by laparoscopic salpingotomy and two women with systemic single dose methotrexate (MTX).

Table II. Background characteristics of the eight participants

Characteristic		
Age (range in years)		33 to 38
Parental status		**n**
	Primi gravid	2
	Nulli para (previous miscarriage)	3
	Para (offspring)	3
Conception		
	Natural conception	5
	Intra-uterine insemination	2
	In vitro fertilisation	1
Presenting symptoms		
	Vaginal bleeding	2
	Abdominal pain	0
	Vaginal bleeding and abdominal pain	5
	Abnormal ultrasound scan at intake	1

The dimensions of patient-centered ectopic pregnancy care

Deductive content analysis (supplementary table)

System factors

1. Provision of information

Women wanted to receive concrete and clear information, especially on diagnosis, treatment (i.e. surgical and medical interventions) and on implications for their future fertility. They appreciated the face-to-face explanations from clinicians to be repeated in reliable and step-by-step written information. When this information did not fully cover what could be expected, women searched the internet which only made them more confused and worried as exemplified in the following interview quotation: 'The doctor did not tell me when my period could start after surgery. I got my period two

weeks after the surgery. I was worried because I've read on the internet that you are supposed to have your period after six or even eight weeks. I thought the blood loss was a complication of the treatment.' (interview I).

2. Access to care

The referral time to the EPAU within and outside working hours was important to women. Several women had to wait for pregnancy testing and / or a transvaginal ultrasound scan. One woman stated: 'My initial ultrasound was scheduled for over one week. When I started to bleed I called the unit and asked for an ultrasound in the morning because I was worried. However, the woman on the phone said that it was very busy and that it was not possible to come that day. When I insisted she said eventually that I could come for an appointment in the afternoon.' (interview II).

3. Coordination and integration of care

Several women felt that time had been wasted while awaiting anxiously before a final diagnosis was reached and treatment was started after coping with the bad news, as exemplified in the following interview quotation: 'I was admitted to the hospital at 9 am and went for surgery at 3 am…' (interview VI).

Whilst waiting, women appreciated not having to share a waiting room with pregnant women scheduled for a routine ultrasound scan or antenatal visit.

4. Competence of medical staff

Some women doubted the expertise of their doctor as they themselves had to insist on receiving an ultrasound scan and/or as they had initially been erroneously diagnosed as having a miscarriage, as exemplified in the following interview quotation: 'They cancelled my ultrasound scan for the next day because they thought it was a miscarriage, however because I was not reassured, I insisted that I could come for that scheduled ultrasound scan the next day. During that ultrasound it became clear that I had an ectopic pregnancy which needed surgery. I felt unsafe after this diagnosis and did not want to think about the consequences had I not insisted on getting this ultrasound' (interview I).

Women would have appreciated being referred directly to a gynaecologist instead of a general practitioner or staff in the emergency room, as exemplified: 'I was first seen by my general practitioner and then referred to the emergency room and investigated by the surgeon. He, eventually, referred me to a gynaecologist who was working at another location of the hospital. Because I did not trust the diagnosis I contacted the Amsterdam UMC for an ultrasound because I had received fertility treatment there. They diagnosed me with an ectopic pregnancy' (interview IV).

5. Physical comfort

All women appreciated adequate pain relief. Additionally, the six women who had undergone surgery appreciated being able to see their partner or significant other immediately after surgery. These women had also struggled with having to remain

sober for a long period of time whilst waiting for surgery. Some women had to ask for something to eat, as exemplified: 'I had been sober for 24 hours and heard that they were not able to schedule the surgery that night. After that news I, myself, had to ask the nurses whether I could eat something' (interview I).

Women shared their negative experience with staying in a room without any windows whilst awaiting surgery and coping with the bad news of having an ectopic pregnancy, as exemplified: 'It was really the environment, there was no distraction. We just sat there, looking at each other, no day light, no possibility to look outside.' (interview IV).

6. Continuity and transition of care

Women would have appreciated being seen by the same clinician as exemplified: 'I've seen many different faces which gave me the feeling that nobody really cared about me, I felt like a number'' (interview V).

During the follow-up after discharge of the hospital, most women wanted at least one telephone consultation, but they would prefer to have a face-to-face consultation at the outpatient clinic.

Human factors

1. Respect for patients' values, preferences and needs

Women liked to be involved in shared-decision making and appreciated clinicians being open to their opinion. Women shared negative experiences on not being heard and respected and on clinicians talking about rather than with them. One woman shared: 'I asked the doctors a question during the ultrasound. They, however, did not even hear me because they were busy discussing [with each other] what they observed' (interview II).

2. Communication skills

Women preferred face-to-face explanations, adapted to their level of health literacy, regarding what to expect during their entire diagnostic, treatment and follow-up trajectory. Women also valued communication skills of clinicians. Women would have liked having exchanged proper introductions with all staff members involved in the management of their ectopic pregnancy. Women wanted clinicians to be accessible, to take their time, to listen carefully, to be decisive and direct and to ask how they could help. In addition, being friendly, good tempered, sensitive, empathic and paying attention to their emotional needs was considered important. The combination of being direct and showing empathy was very much appreciated, as exemplified: 'When the doctor made the ultrasound she immediately said: I see a heartbeat but unfortunately not in the right place. Beautifully said.' (interview II).

3. Emotional support

During the diagnostic and treatment trajectory, the main focus of women and their partners was on their physical health, rather than on having lost a pregnancy, as

exemplified: 'Especially my husband was not worried about the loss of the pregnancy. He was worried that he would lose me because of his wish for a child' (interview V).

Women, especially the three women who got pregnant after artificial reproductive techniques (ART), found coping with their pregnancy loss after treatment of their ectopic pregnancy challenging. Women expected emotional support from their clinicians, for example taking account of women's ambiguity prior to diagnosis. Only two women indicated that they would have preferred additional support from a mental health professional.

4. Involvement of partners & significant others & privacy

Despite the COVID-19 pandemic, all partners present were involved in the diagnostic process and they all appreciated that. Unfortunately, not all women were given time alone with their partner or significant other in a separate room to cope with the bad news of the ectopic location of their pregnancy. This was something that they had missed, as exemplified: 'After the doctor informed us about the diagnosis we were directly moved to another department, this overwhelmed me. Me and my partner did not even have time to comfort each other.' (interview VII).

Inductive content analysis

The narratives of the eight women showed a key role for the dimension 'communication skills'. Communication of staff could compensate for negative experiences, but occasionally made the negative experiences even worse.

1. Communication – Information provision

Women appreciated their time with the clinician to ask questions about aspects not covered by the written patient information leaflet. One woman stated: 'I had the opportunity to ask the anesthesiologist some questions about the anesthesia during the surgery, this made me feel more safe' (interview VI).

2. Communication - Competence of clinicians

Clinicians who were inexperienced and too quick to congratulate women with their pregnancy prior to performing an ultrasound scan gave rise to negative experiences, as exemplified: 'Two young doctors came up to me and congratulated me with my pregnancy before they even made an ultrasound scan. I said to them: well that's is not possible because I had my period. They made an ultrasound and said that they saw a yolk sac in the uterus and that I should come back in two weeks to determine whether it was a viable pregnancy. I was not reassured and asked the doctor about my abdominal pain. He said that I was just constipated' (interview VII).

The three women who had been misdiagnosed by their general practitioner as having a miscarriage shared that this could have been prevented if the clinicians would have listened more carefully to the story they shared over the phone.

3. Communication - Coordination and integration of care

Women wanted to be told why repeat ultrasounds were required, as exemplified: 'I was asked to come back after two days for a new ultrasound scan because they could not make a final diagnosis, I was confused, should they see something in the uterus then or not? Why these two days?' (interview III). Women understood that they could not immediately have surgery or medication, but shared that regular updates on the waiting time for starting treatment could have lowered their frustration.

4. Communication – Access to care

Women felt unheard by the clinicians when they asked for a prompt ultrasound. A woman shared that being explained why an early ultrasound is not always informative this would have prevented her from feeling unwelcome, as exemplified: 'The doctor explained that you can't see a pregnancy in the uterus in the early stage of a pregnancy which made it clear to me why they were not keen on scheduling the ultrasound on an earlier date.' (interview VII).

5. Communication - Continuity and transition of care

Communication was key during the follow-up period after diagnosis and treatment. Women shared that they had forgotten the explanations given during the diagnostic and treatment trajectory as they were so emotionally overwhelmed. Women expressed their need to communicate with clinicians about the medical management and emotional impact of an ectopic pregnancy in order to be able to cope and to move on with their life. A woman shared: 'After the diagnosis a lot happened, a nurse moved us to the early pregnancy unit to swiftly start medical treatment. We arrived at the unit and my head was full of questions and emotions and then I just broke down. Luckily, a nurse allocated us to a room and took the time to listen to me and answer my questions' (interview III).

6. Communication - Physical comfort

Women who had to stay sober for (too) long felt that the clinicians did not update them enough on the (reasons for) the waiting time for surgery as exemplified: 'I had been sober for 24 hours and had to ask for updates about the delay in surgery during that entire period' (interview I).

Perspectives shared by the partners only

The three partners shared that due to the COVID-19 pandemic, they were not allowed to be present during the first visit in the EPAU and this was difficult for them. One man stated: 'the most difficult part is that I could not be present during all the appointments, especially during the appointment in which the ectopic pregnancy was diagnosed.' (interview II).

All men were involved in the diagnostic process immediately after the transvaginal ultrasound scan. Men felt that their presence was important during the diagnostic and treatment trajectory. Men would have appreciated being informed on the progress of

the surgical procedure. Although preoperatively the clinicians had given an indication of the duration of the procedure, men felt worried if the surgical procedure took longer.

Discussion

This study on women's experiences of the management of their ectopic pregnancy revealed that clear and emphatic communication by clinicians is the key for quality of care. Women valued concrete information both face-to-face and in writing on diagnosis, treatment and implications for future fertility. They also appreciated shared-decision making with clinicians who were open to input of the woman. Long waiting times, both for reaching the final diagnosis and for starting treatment were frustrating experiences. All women agreed that communication on the duration and reasoning behind the delays would have lowered their level of frustration.

The strength of our study is that we relied on in-depth interviews and content analysis, which previously proved to deepen one's understanding of patient-centered care (Dancet et al. 2011; Dahhan et al., 2021). The rigor of the study was increased by relying on an interview guide and topic (Dancet et al., 2011; Polit and Beck, 2014).

Regrettably, this study does not represent the experience of women managed expectantly for their ectopic pregnancy. A randomised trial has shown that women treated with single dose MTX or expectant management had similar levels of health-related quality of life assessed at four-time points; before randomisation and during the follow-up visits one, four and twelve weeks after treatment (Mello et al., 2015). We therefore feel that we may generalise the experiences of women who had a therapeutic intervention to women who are managed expectantly. However, we need future studies to confirm this hypothesis.

We divided the dimensions of patient centered care into system and human factors which makes it easier for clinicians to see on which level changes should be made, i.e. on an organisational or a personnel level. Improving human factors is much more challenging than improving system factors. An example of a system factor that needs attention is that some women mentioned that they had missed time alone in a separate room to cope with the bad news. This is in line with our findings on women diagnosed with (recurrent) miscarriage (van den Berg et al., 2018).

In the set-up of an EPAU it is recommended that the EPAU is fitted with a separate room, the so called blue room, for women and their partners to be able to withdraw and have some time alone to cope with bad news (Association of Early Pregnancy Units, 2007; NICE guideline, 2019; RCOG, 2008). The EPAU in the AUMC does have a separate blue room, but it was not always used because most of the time women stay in the same room during the diagnostic procedure and are afterwards either sent home or referred to the ward for admission. This originates from the preconceived idea with doctors that women wish to start an intervention as soon as possible. Our study shows that this is not the case since women don't want to be rushed into treatment and prefer some time to cope with the news after diagnosis. Existing guidelines for running an EPAU which

already emphasize this, should thus be followed to improve patient-centered ectopic pregnancy and miscarriage care.

Another system factor that needs attention is the follow-up after treatment of the ectopic pregnancy. We recommend to schedule a follow-up appointment, preferably in person, to address the loss of a desired pregnancy, especially for those women pregnant after ART, as women faced with ectopic pregnancy initially focus on how to get better and to regain health again in contrast to women experiencing a miscarriage (van den Berg et al., 2018). One of the human factors that needs attention is the communication skills from the clinicians. This is also in line with our review on patient-centered (recurrent) miscarriage care which identified that women valued treatment with sensitivity and compassion by clinicians who are willing to discuss patients' distress (van den Berg et al., 2018). Although current guidelines underline the importance of adequate communication skills of staff members working with women with early pregnancy complications, this study on women's experience identified that communication skills of staff need improvement. Clinicians should be aware of and follow recent evidence-based guidelines. Guidance of women diagnosed with an ectopic pregnancy needs attention for a better patient-centered approach.

In conclusion, patient-centeredness of ectopic pregnancy care needs to be improved in particular by direct referral to an early pregnancy assessment unit. Staff working in the EPAU should adhere to recent evidence-based guidelines, and should be trained in communication skills to regularly discuss the rationale for and duration of inevitable waiting time.

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Supplementary table. Patient-centeredness of ectopic pregnancy care

Code		n*
SYSTEM FACTORS		
1.	**Provision of information**	
1.1	*Concrete information needs*	
1.1.1	General information on...	
	- vaginal blood loss and/or abdominal pain with a positive pregnancy test	1
	- diagnosis of ectopic pregnancy	5
	- degree of abdominal pain and vaginal blood loss to expect during expectant or medical treatment	1
	- risk of complications during treatment	2
	- implications for future fertility	8
	- risk of ectopic pregnancy after fertility treatment	2
	- aetiology of ectopic pregnancy	3
	- complications of different treatment options	2
	- pain relief	3
	- surgical treatment	5
1.2	*Form/canal of information*	
1.2.1	Telephone	1
1.2.2	Face to face	
	- one-on-one	8
1.2.3	Information on media	
	- written information	2
	- visual information	2
	- book or references	0
	- online information	3
1.3	*Nature of information*	
1.3.1	Conflicting information	
	- advantage	1
	- disadvantage	0
1.3.4	Timelines of the information	1
2.	**Access to care**	
2.1	*Telephone accessibility*	
2.1.1	Within traditional working hours	
	- how easy to get connected	3
	- possibility to ask clinical questions by telephone	0
2.1.2	Outside traditional working hours	3
2.1.3	Wrong diagnosis	2

Supplementary table. Patient-centeredness of ectopic pregnancy care

Code		n*
2.2	*Access to care*	
2.2.1	Reffered to the gynaecology department instead to the general practioner or emergency department	4
2.2.2	Reffered to the general practioner or emergency department	2
3.	**Coordination and integration of care**	
3.1	*Waiting times and waiting lists*	
3.1.1	Importance of not wasting time	3
3.1.2	Waiting times…	
	- for pregnancy test	2
	short waiting times	1
	long waiting times	
	- for ultrasound	2
	short waiting times	
	long waiting times	3
	- for diagnosis	1
	short waiting times	6
	long waiting times	
	- treatment	
	short waiting times	0
	long waiting times	7
3.1.3	Waiting time in waiting room	
	short waiting times	2
	long waiting times	4
3.1.4	Not sharing waiting room with women awaiting a routine pregnancy scan	5
3.2	*Smooth organization*	
3.2.1	Fluent processes	
	- long waiting times for the availability of methotrexate	2
3.2.2	Coordination between different departments within the hospital	3
3.2.3	Offering the option of admission to the hospital while waiting for medical treatment	1
4.	**Competence of medical staff members**	
4.1	*Timely referred*	
4.1.1	Timely referred for pregnancy test	
	- negative experience	3
	- positive experience	1
4.1.2	Timely referred for ultrasound	5
	- negative experience	1
	- positive experience	

Supplementary table. Patient-centeredness of ectopic pregnancy care

Code		n*
4.2	*Clinical Expertise*	
4.2.1	Thorough diagnostic phase	4
4.2.2	Good medical follow-up	4
	positive experience	1
	negative experience	
4.2.3	No unnecessary appointments	1
4.2.4	Misdiagnosis	2
4.3	*Competence of staff*	
4.3.1	Experienced medical staff (divided opinions?)	
	- advantage	3
	- disadvantage	0
4.3.2	Expert medical staff	
	- expertise is positive	3
	- lack of expertise is negative	2
	- difference in expertise between medical staff	3
	- Students or clinicians in training under supervision	1
5.	**Physical comfort**	
5.1	*Pain medication*	1
5.2	*Accommodation*	
5.2.1	Accommodation which offers privacy	1
5.2.2	Comfort of the accommodation	1
	- comfortable room awaiting treatment	1
5.3	*Specifically for surgical treatment*	
5.3.1	Unnecessary staying sober to long	6
5.3.3	Providing food after a period of staying sober had to ask for	2
5.3.4	Comfort after surgery	4
6.	**Continuity and transition of care**	
6.1	*Continuity of medical staff*	
6.1.1	Always the same staff member	
	- not necessary	0
	- necessary	2
6.2	*Transition*	
6.2.1	Follow-up care	
	- after treatment (by phone)	7
	- after treatment (consultation)	3

Supplementary table. Patient-centeredness of ectopic pregnancy care

Code		n*
HUMAN FACTORS		
7.	**Respect for patients' values, preferences and needs**	
7.1	*Attitude*	
7.1.1	Positive attitudes	
	- friendly	8
	- empathic	8
	- careful (with care and attention)	8
	- protective	0
	- helpful	5
	- correct	1
	- understanding	5
	-unprejudiced	0
	- decisive	4
	- supportive	5
	- good tempered	1
	- accessible	2
	- respectful	7
	- engaged	1
	- empathic & clear communication	4
7.1.2	Negative attitudes	
	- unstable/unpredictable mood	0
	- to patronize/ cavil	0
	- care provider shows frustration	0
	- inaccessible	2
	- disrespectful	0
	- not interested	1
	- unengaged	1
	- talking over instead of to the patient	1
7.2	*Professional appearance*	2
8.	**Communication skills**	
8.1	*Importance of communication*	2
8.2	*Time for patient*	
8.2.1	Opportunity to ask questions	1
8.2.2	Time taken for patient	5
8.2.3	Ask the question 'How can I help you?	4

Supplementary table. Patient-centeredness of ectopic pregnancy care

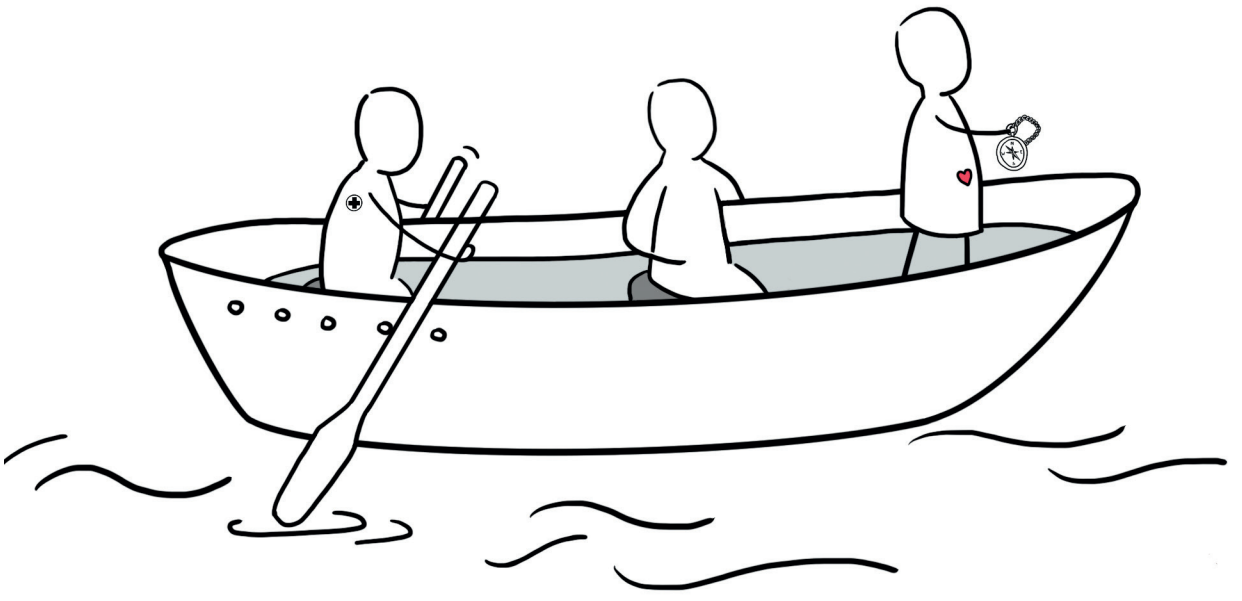
Code		n*
8.3	*Information on time schedule*	
8.3.1	On waiting time in waiting room	1
8.3.2	On waiting times for diagnostic test	1
8.3.3	Concerning waiting time telephone	0
8.3.4	On waiting times for surgical intervention	5
	- negative experience	1
	- positive experience	
8.4	*Concrete information skills*	
8.4.1	Introduce yourself	2
8.4.2	Look at patient	3
8.4.3	Courtesy	0
8.4.4	Address patient with first name	0
8.4.5	Listen	4
8.4.6	Be sensitive	5
8.4.7	Providing information spontaneous instead of pulling out information	3
8.4.8	Skills for bad news conversation	
	- through appropriate information channel	2
	- allow time to cope	3
	- know what to say	0
	- provide coaching and guidance	2
	- show empathy	5
	- provide follow-up consultation	1
	- do not make inappropriate remarks	0
	- straight to bad news	3
8.4.9	Non-verbal communication	1
8.4.10	Pay attention / open to patients' 'not feeling good' feeling	4
8.4.11	Referring to the ectopic pregnancy as a foetus and not using technical names	1
8.5	*Unprofessional communication*	1
8.6	*Tell the patient what will happen*	
8.6.1	Clear appointments	3
8.6.2	Expectation management	
	- concerning what treatment entails	2
	negative experience	2
	positive experience	
	- concerning chances of success	3
	- concerning waiting times for treatment	8
8.6.3	To the point	5

Supplementary table. Patient-centeredness of ectopic pregnancy care

Code		n*
8.6.4	Honest (divided opinions)	
	- advantage	4
	- disadvantage	1
8.6.5	Reliable information	6
8.6.6	Introduce every clinician who will be involved during the procedure - didn't do that - did do that	3 1
8.6.7	Information about the performed surgery	2
8.7	*Understandable explanation*	
8.7.1	Explanation at level of the patient	2
8.7.2	Understandable language	1
8.8	*Explanation from nurses* positive experience negative experience	1
9.	**Emotional support**	
9.1	*Type of care provider providing emotional support*	1
9.2	*Emotional support from clinical care provider*	
9.2.1	Provision of emotional support	7
9.2.2	Attention to emotional well-being	6
9.2.3	Attention to the loss of a wanted pregnancy	1
9.2.4	Attention to the insecurity of the diagnostic phase	4
9.3	*Emotional support from specialised care providers (e.g. psychologist)*	
9.3.1	Offering this kind of support	2
9.3.2	Benefit from it	2
9.4	*Concrete needs for emotional support*	
9.4.1	Concrete moments on which emotional support should be offered	
	- during bad news consultation during treatment (e.g. at time of diagnosis, during treatment)	1
	- support at end of treatment	1
9.4.3	Focus on getting better instead of the loss of a wanted pregnancy	6
10.	**Patient and involvement of significant other and privacy**	
10.1	*Autonomy*	
10.1.1	Decision-making process	
	- shared decision-making	4
	- contribution to informed decision	1
10.1.2	Open for patient	
	- open for input patient	4
	- open for critical reflections patients	1

Supplementary table. Patient-centeredness of ectopic pregnancy care

Code		n*
	- take into account patient remarks	0
	- personalised care (adapted to individual case)	1
	- involve patient	1
	- equal partner	1
	- equal possibilities irrespective of assertiveness patient	0
10.1.3	Possibility to indicate preferred sex of care provider	0
10.2	*Involvement partner*	
10.2.1	Actual involvement partner	
	- active involvement when present	7
	- invite partner	8
	- partner informed concerning results diagnostic tests	2
	- in decision-making	0
	- option for face time with partner (because of COVID-19 restrictions)	3
	- Partner / family involvement during / after surgery	4
10.2.3	Looking after ('caring for') partner	1
10.2.4	Partner is being recognised for role	5
10.3	*Privacy*	
10.3.1	Specific times and place important for privacy	
	- privacy after hearing bad news	3
10.3.2	Amount of care providers	
	- acceptable number of care providers	1
	- unnecessary presence of students	0



CHAPTER 4

Early pregnancy care over time: should we promote an early pregnancy assessment unit?

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Reproductive BioMedicine Online 2015;31(2):192-198

Abstract

In this observational study, the effect of the introduction of the first Early Pregnancy Assessment Unit (EPAU) in a university hospital in The Netherlands in 2008 on early pregnancy care is analysed. Derivatives of quality of care were measured before and after the establishment of the EPAU, with the aim of reducing unnecessary care. Care within three time periods was measured: 2006, 2009 and 2012. In 2006, 14% of women who had experienced a miscarriage were admitted to the hospital, whereas in 2009 and 2012 no women were admitted. The surgical management rate for miscarriage decreased from 79% (2006) to 6% (2009) and 28% (2012). Karyotyping of couples who had experienced recurrent miscarriage decreased from 100% (2006) to 17% (2009) and 33% (2012). The surgical management rate for ectopic pregnancy decreased from 50% (2006) to 25% (2009) and 29% (2012). The mean total cost per woman treated in 2006 was €1111 (95% CI €808 to 1426), €436 (95% CI €307 to 590) in 2009 and €633 (95% CI €586 to 788) in 2012. We can therefore conclude that an EPAU results in higher quality and cost-effective care, and has a positive effect on early pregnancy care.

Introduction

Early pregnancy assessment units (EPAU) have been established to provide an accurate service for women with early pregnancy complications (Bigrigg and Read, 1991; Shillito and Walker, 1997; Turner et al., 1991). The most frequent complication in early pregnancy is miscarriage. Of all clinically recognized intrauterine pregnancies, 10–15% result in miscarriage (Rai and Regan, 2006). Up to 5% of all women of reproductive age will face recurrent miscarriage, with at least two or more miscarriages (Jaslow et al., 2010; Rajcan-Separovic et al., 2010). Another early pregnancy complication is ectopic pregnancy, with an incidence of about 1–2% of all pregnancies (Storeide et al., 1997; Crowhurst and Plaat, 1999; Centre for Disease Control and Prevention, 2012).

The UK was the first country to introduce EPAU in the early 1990s (Bigrigg and Read, 1991). To date over 200 EPAU have been established in England and Wales (Newbatt et al., 2012; Association of Early Pregnancy Units, 2007), but the concept of a dedicated multi-professional service for women with early pregnancy complications is now spreading even beyond Western countries (Iyoke et al., 2014).

An EPAU helps to streamline patient care by general practitioners, midwives and gynaecologists (Bigrigg and Read, 1991; Newbatt et al., 2012; O'Rourke and Wood, 2009). In dedicated EPAU, the discontinuity in care is minimized (Goddijn et al., 2009). Moreover, it has been reported that EPAU enable considerable savings in financial and hospital staff resources. For example, the prompt and easy access to transvaginal ultrasound with immediate reassurance in case of a viable intrauterine pregnancy has rendered hospital admission obsolete (Bigrigg and Read, 1991; Haider et al., 2006; Shillito and Walker, 1997; Wendt et al., 2014; Wren and Craven, 1997).

An EPAU enhances the implementation of evidence-based guidelines because of the centralization of early pregnancy care. Guidelines change over time based on new available evidence. It has been shown that expectant management and medical treatment are safe alternatives to a surgical intervention for miscarriage (Graziosi et al., 2004; Wieringa-de et al., 2002) and for selected women with ectopic pregnancy (van Mello et al., 2013). For women who have experienced recurrent miscarriage, it has been shown that karyotyping can be avoided in low-risk women (Franssen et al., 2005, 2007).

In The Netherlands, the first EPAU opened in the Academic Medical Centre (AMC) in Amsterdam in June 2008. In October 2005, an integral project plan had already been written to establish such an extensive logistic project as an EPAU in a university hospital. Staff members of the various subdivisions of the Department of Obstetrics and Gynaecology (Obstetrics, the Fetal Medicine Unit, Gynaecology, Gynaecologic Oncology and the Centre of Reproductive Medicine) consented on various topics, among which was service provision in the EPAU. The EPAU provides 24-h care 7 days a week (24/7) for women with clinical symptoms in early pregnancy, and non-emergency care for non-pregnant women with a history of recurrent miscarriage in a 'Recurrent Miscarriage' unit, as an annex of our EPAU in an outpatient daytime setting. Women are referred by their general practitioner or midwife, or by the hospital's emergency department. Occasionally, self-referrals are seen.

An improvement was expected in the quality of medical care and a decrease of costs after the establishment of the EPAU (Goddijn et al., 2009). To confirm or refute this hypothesis, various goals were defined for the EPAU, which were formulated after discussion with experts in the field of early pregnancy care and The Board of Directors and policy makers in the AMC who aimed for reduction of costs. The pre-set goals of the EPAU were as follows: (i) to decrease the percentage of emergency inpatient admissions for miscarriage; to decrease the percentage of surgical management for miscarriage; to decrease the number of repeat consultations for recurrent miscarriage; (ii) to decrease the number of karyotypings for recurrent miscarriage; and (iii) to decrease the percentage of surgical management for ectopic pregnancy; and to reduce costs. To explore if these goals as measurable derivates of quality of care were met, an observational study was conducted in which the care provided in the EPAU was compared with the care provided in the period before the introduction of the EPAU.

Material and methods

A baseline assessment for the provided care was carried out before the introduction of the EPAU in the AMC in June 2008. This baseline assessment comprised all women with early pregnancy complications presenting at the AMC between May and July 2006. At that time, these women were seen at various units within the obstetrics and gynaecolgoy department: the outpatient clinics Obstetrics, Fetal Medicine Unit, Gynaecology, Centre for Reproductive Medicine and Recurrent Miscarriage unit and the inpatient Gynaecology ward. Women with early pregnancy complications who presented at the hospital emergency department without referral to the obstetrics and gynaecology department were also included.

Early pregnancy complications were defined as follows: abdominal pain, vaginal bleeding during the first trimester, or both; an inconclusive first-trimester scan in the absence of clinical symptoms; and analysis of recurrent miscarriage (two or more not necessarily consecutive miscarriages in non-pregnant women) (Dutch Society of Obstetrics and Gynaecology (NVOG), 2007). During the 3-month period, all women who met one of these definitions were prospectively registered and data were collected using a case-record form, whereas women who presented at the hospital emergency department without referral to the obstetrics and gynaecology department were registered retrospectively.

After the establishment of the EPAU, two similar assessments were carried out in May to July 2009 and May to July 2012. For women with early pregnancy complications during the assessment periods in 2009 and 2012 who were seen in the obstetric and gynaecology department or hospital emergency department, consultations were checked by using the hospital financial registration system, which registers all diagnosis-treatment combinations by department.

At the same time that the EPAU was established, a private gynaecological clinic was set up in the referral area of the AMC. This ‘Zuidoost Clinic’ was founded by two gynaecologists who had the knowledge and skills to diagnose early pregnancy

complications and offer expectant management or medical treatment in case of miscarriage or ectopic pregnancy according to the guidelines of the Dutch Society of Obstetrics and Gynaecology and the academic hospital protocol (AMC). In case of diagnostic problems, complications, or if surgical treatment was indicated, the clinic referred women to the EPAU. No changes in management took place over time except for medical treatment with misoprostol for miscarriage when it became more available, leading to fewer consultations in the EPAU for this indication. One year later in 2009, a General Practitioners Emergency Department was set up adjacent to the hospital emergency department of the AMC. In this department, self-referred women, or women whose complaints were triaged in the hospital emergency department as primary care were seen, and therefore referred to the General Practitioners Emergency Department. In this department, urinary pregnancy tests were available to triage early pregnancy complications, but ultrasound facilities were not. A local multidisciplinary protocol of the AMC was used, which stated that every pregnant woman with vaginal bleeding, abdominal pain, or both, should be immediately referred to the EPAU for further evaluation. There were no changes in this policy over time. These two referral locations were also involved in the analysis in 2009 and 2012.

Data collected included women's characteristics, diagnostic management, treatment and follow-up. Furthermore, data on time of first contact (day, afternoon, night time), referral status (general practitioner, midwife, emergency department physician, other specialist or self-referral), waiting time, time of discharge, time to diagnosis, time to treatment and choice of treatment, number of consultations in the unit or by telephone were registered for every woman. The Statistical Package for Social Sciences (SPSS version12.0.2, SPSS Inc., USA) database was used for collection of data and analyses.

Three investigational periods (2006, 2009 and 2012) were compared for the percentage of hospital admissions in women diagnosed with miscarriage; the percentage of surgical management for miscarriage; the number of repeat consultations for recurrent miscarriage; the number of karyotypings for recurrent miscarriage; the percentage of surgical management for ectopic pregnancy; and associated direct medical costs. A descriptive analysis was used to detect differences and possible improvements during the three investigational periods.

Cost calculations

An economic analysis was carried out from a healthcare perspective and was based on direct medical costs. A standard price was used for the hospital visits, telephone consultations, surgical management and karyotyping, and this price reflected the unit of staff, materials, equipment, housing, depreciation and overheads. The overhead costs are direct medical costs covered by the healthcare system. Costs for medical treatment with misoprostol for miscarriage and systemic methotrexate for ectopic pregnancy were measured by multiplying the total dose used based on the corresponding unit prices (College voor Zorgverzekeringen (CVZ) [Health insurance Board], 2014). The costs for hospital admission, surgical treatment, repeat consultations and karyotyping

a couple were based on the hospital financial registration system (diagnosis–treatment combination). Total costs were expressed as means per woman with 95% confidence interval (CI)as estimated by bootstrapping for 10000 bootstrap samples.

Total costs per woman in 2009 and 2012 were anticipated to be lower than in 2006 before the establishment of the EPAU and, therefore, the primary cost analysis focused on the cost difference between these three periods. To account for any policy changes and to overcome overrating, another cost analysis was conducted. In this analysis, totalcosts per woman in 2009 and 2012 were calculated as if these women were treated according to the management standards of 2006 (baseline). The difference between these imputed cost-estimates and the real total costs provides a better reflection of the possible cost savings as acquired by the establishment of our EPAU.

Ethics statement

According to the Dutch 'Medical Research Involving Human Subjects Act', no formal ethical approval was needed for this study (article 1, paragraph b, 1998).

Results

In total, 433 women with early pregnancy complications were included in the analysis (Table 1). In 2006, 111 women were registered. Most women were seen at the Centre for Reproductive Medicine (26/111 [23%]) and at the hospital emergency department (27/111 [24%]). In 2009, 163 women were registered, of whom more than one-half were seen at the EPAU (92/163 [56%]). In 2012, 159 women were registered, of whom more than one-half were seen at the EPAU (84/159 [53%]).

All 14 women who were initially seen at the hospital emergency department in 2009 and 2012 were referred to the EPAU. In 2009, two of the 24 women (8%) presenting at the Zuidoost clinic were referred to the EPAU, one woman diagnosed with a suspected ectopic pregnancy and one woman with an incomplete miscarriage, necessitating surgical management. In 2012, six of the 31 women (19%) were referred to the EPAU, three women with a suspected ectopic pregnancy, two women with an incomplete miscarriage and one woman with a history of recurrent miscarriage. Of the 27 women initially seen at the General Practitioners Emergency Department in 2009 and 2012, only seven (26%) were referred to the EPAU. One woman was sent to the Zuidoost clinic for further follow up. The other 19 women were reassured and sent home without having an ultrasound scan done. No follow-up was available for these women.

Time of day of initial presentation at the EPAU, hospital emergency department and General Practitioners Emergency Department for all three time periods is shown in Table 2. In all time periods, most women were seen during working hours (174/283 [61%]), whereas only 11% (32/283) presented during night time (23.00–08.00 h).

The number of hospital admissions and various treatments for miscarriages, the number of repeat consultations and karyotypings for recurrent miscarriage and the number of hospital admissions and various treatments for ectopic pregnancy are summarized in Table 3.

Table 1. Location of initial presentation of all included women

Location	Baseline measurement before EPAU May – July 2006	First measurement after EPAU May – July 2009	Second measurement after EPAU May – July 2012
Early Pregnancy Assessment Unit	na	92 (56)	84 (53)
Outpatient clinic Gynaecology	16 (14)	0	0
Outpatient clinic Obstetrics	0	0	9 (6)
Fetal Medicine Unit	2 (2)	0	0
Centre for Reproductive Medicine	26 (23)	8 (5)	10 (6)
Recurrent Miscarriage unit	19 (17)	9 (6)	14 (9)
Inpatient Gynaecology ward	14 (13)	0	0
Inpatient delivery ward	7 (6)	0	0
Hospital Emergency department	27 (24)	10 (6)	4 (3)
Zuidoost clinic	na	24 (15)	31 (19)
General Practitioner Emergency department	na	20 (12)	7 (4)
Total	**111 (26)**	**163 (38)**	**159 (37)**

Percentages in parentheses
EPAU = early pregnancy assessment unit; NA = not applicable.

Table 2. Time frame of initial presentation in EPAU, Hospital Emergency department and General Practitioner Emergency department

hours	Baseline measurement before EPAU May – July 2006	First measurement after EPAU May – July 2009	Second measurement after EPAU May – July 2012	Total
08.00 – 17.00	40 (61)	63 (52)	71 (75)	**174 (61)**
17.00 – 23.00	18 (27)	40 (33)	19 (20)	**77 (27)**
23.00 – 08.00	8 (12)	19 (16)	5 (3)	**32 (11)**
Total	**66 (23)**	**122 (43)**	**95 (34)**	**283 (100)**

Percentages in parentheses.
EPAU = early pregnancy assessment unit.

Table 3. Results of the established goals of the EPAU

	Baseline measurement before EPAU May – July 2006	First measurement after EPAU May – July 2009	Second measurement after EPAU May – July 2012
Miscarriage	14	36	40
- hospital day admission[a]	9 (64)	2 (6)	1 (3)
- hospital clinical admission[a]	2 (14)	0	0
- surgical management[a]	11 (79)	2 (6)	11 (28)
- medical treatment	na	3 (8)	11 (28)
- expectant management	3 (21)	31 (86)	18 (45)
Recurrent miscarriage	19	23	36
- repeat consultations[a]	1 [0-3]	1 [0-3]	1.3 [0-4]
- repeat consultations by phone[a]	2 [0-4]	0.44 [0-1]	0.79 [0-2]
- karyotypes[a]	19 (100)	4 (17)	12 (33)
Ectopic pregnancy	20	12	14
- hospital admission	10 (50)	4 (33)	5 (36)
- surgical management[a]	10 (50)	3 (25)	4 (29)
laparoscopic salpingotomy	1 (10)	1 (33)	0 (0)
laparoscopic salpingectomy	9 (90)	2 (66)	4 (100)
- medical treatment (systemic MTX)	2 (10)	6 (50)	3 (21)
- expectant management	8 (40)	3 (25)	7 (50)

Data presented as number (%), number (range) or mean (range)
EPAU = early pregnancy assessment unit; NA = not applicable.
[a]Established goals as referred to in the text.

Cost calculations

The costs of the various treatments of miscarriage, karyotyping of a couple and various treatments of ectopic pregnancy are summarized in Table 4. To be able to compare costs over time, unit prices based on year 2012 were used for all three time periods.

The mean total costs per woman treated in the EPAU in 2009 (€436, 95% CI €307 to 590) and 2012 (€633, 95% CI €586 to 788) were lower than in 2006 (€1,111, 95% CI €808 to 1,426) (Table 5).

Estimated costs implementing the management standards in 2006 would have been €1035 (95% CI €858 to 1241) in 2009 and €1290 (95% CI €1110 to 1484) in 2012. The difference between these estimated costs and the real total costs better reflects the cost savings after the establishment of the EPAU. These cost savings per woman were estimated to be €599 in 2009 and €657 in 2012 per woman (Table 5).

Table 4. Unit prices

	Unit	Unit prices (€)	Valuation method (source)
Miscarriage			
- surgical treatment	Procedure	1858,55	DBC
- medical treatment	Procedure	500,69	DBC
- misoprostol	4 tablets 200 microgram	3,81	College voor Zorgverzekeringen (CVZ) (health insurance Board], 2014)
- expectant management	Procedure	500,69	DBC
Recurrent Miscarriage			
- Karyotyping (couple)	Procedure	1540,34	DBC
Ectopic pregnancy			
- surgical treatment	Procedure	5757,00	DBC
- medical treatment	Procedure	500,69	DBC
- systemic MTX	75 mg (25mg/mL, 1 mL)[a]	62,23	College voor Zorgverzekeringen (CVZ) (health insurance Board], 2014)
- expectant management	Procedure	500,69	DBC

[a]Based on an average weight of 75 kg
DBC = diagnosis-treatment combination (2012);

Table 5. Costs calculations

Mean total costs per woman (€)	Baseline measurement before EPAU May – July 2006	First measurement after EPAU May – July 2009	Second measurement after EPAU May – July 2012
Real costs	1111 (808 – 1426)	436 (307 – 590)	633 (586 – 788)
Fictitious costs based on the 2006 management standards	-	1035 (858 – 1241)	1290 (1110 – 1484)
Possible costs savings[a] (difference between real and fictitious costs)	-	599	657

[a] = established goal as referred to in the manuscript
95% Confidence interval in parentheses
EPAU = early pregnancy assessment unit;

Discussion

This is the first evaluation of clinical care of women with early pregnancy complications after the establishment of an EPAU. Our goals, set before the establishment of the EPAU, were all accomplished (i.e. a reduction in hospital admissions and surgical management for miscarriage, a reduction of repeat consultations [by telephone] and a reduced number

of karyotyping for recurrent miscarriage, a reduction of surgical management for ectopic pregnancy and a reduction in costs).

To date, evidence to support the improvement of care by the introduction of EPAU is still limited (Newbatt et al., 2012; NHS National Institute for Health and Clinical Excellence, 2012), whereas the change of practice in itself over time will affect the costs of early pregnancy care. The importance of a reduction of costs is obvious in view of the global economic crisis, which has confronted many with reduced budgets. Also, in general health care, we know the concept of 'not value-added care' or so-called waste of care (Berwick and Hackbarth, 2012). This concept also applies to early pregnancy care (e.g. in the management of recurrent miscarriage, where many diagnostic tests and ineffective therapeutic interventions are being carried out without clinical implications) (Franssen et al., 2007). Our observational study illustrates how the EPAU allowed us to save costs in early pregnancy care by reducing waste of care.

The strength of our study is that we focused on clear clinical outcomes to measure the effect of an EPAU on the quality of care. The measurement of three time periods over 6 years gives a clear overview of the changes in early pregnancy care over time in the university hospital (AMC). A limitation of our study is the relatively low number of included women. We only registered women with early pregnancy complications during a 3-month period in 2006, 2009 and 2012. The number of women attending the EPAU fluctuates during the year. By studying an identical 3-month period (May until July), we aimed to avoid seasonal fluctuations. The risk of missing women or data was minimized by using case record forms (prospective data) and the financial hospital system (retrospective data).

Good standard care requires 24/7 access to the EPAU (Newbatt et al., 2012), but may be halted by logistical barriers, such as financial or personnel scarcity (Bourne et al., 2013). In our study, only 11% of women attended the EPAU during the night (23.00–08.00 h). It may be possible that the knowledge of 24/7 access has a positive psychological effect on women, resulting in some sort of calmness, which results in fewer visits during night hours. Staffing an EPAU, especially during night-time and weekends, tends to increase costs. Therefore, we intentionally decided to locate our EPAU adjacent to the 24/7 obstetrical ward to facilitate staffing, weighed against the burden that women with early pregnancy complications and recurrent miscarriage might experience when exposed to seeing women with ongoing pregnancies. To date, all our non-emergency care for couples with recurrent miscarriage is provided in our 'Recurrent Miscarriage Clinic', an annex of the EPAU in an outpatient daytime setting.

The improvement in quality of care for early pregnancy complications cannot be contributed to the establishment of the EPAU alone. Other factors, such as the introduction of new or revised guidelines, practice changes or ongoing clinical trials might greatly influence aspects of quality care provision. For instance, selective parental karyotyping in recurrent miscarriage was introduced in our hospital from 2005 onwards (for women under the age of 34 years and for older women in whom family members were known to have experienced recurrent miscarriage) instead of routine karyotyping

(Franssen et al., 2005). Selective parental karyotyping was then incorporated in the European Society of Human Reproduction and Embryology guidelines and in the Dutch guideline on recurrent miscarriage (Jauniaux et al., 2006; Dutch Society of Obstetrics and Gynaecology (NVOG), 2007). Full implementation of these guidelines might in itself have led to a reduction in the numbers of karyotyping (van den Boogaard et al., 2011). Outpatient medical treatment with misoprostol was first used for (incomplete) miscarriage at the same time as the establishment of the EPAU in our hospital, and became standard care. Systemic methotrexate treatment and expectant management for ectopic pregnancy, already being standard care in eligible women, were enhanced during our study as a result of the METEX study (ISRCTN 48210491), an ongoing randomized controlled trial comparing these interventions (van Mello et al., 2013). These factors might also have influenced quality of care and decreased costs of hospital admission and surgical treatment.

There is no clear explanation why costs increased in 2012 compared with 2009. We cannot explain this by inflation only. In general, healthcare costs fluctuate over time. Our hypothesis is that, since the establishment of the EPAU, more women with serious early pregnancy complications are referred to the EPAU. This results in more consultations and an increase in costs but also reflects the success of the EPAU. It is important, however, that an overall decrease in costs has occurred since the establishment of our EPAU (2009 and 2012 compared with 2006).

The inherent higher number of repeat consultations and hCG monitoring had no effect on total costs. Over time, scanning facilities were not changed. The effect of the availability of the private gynaecological clinic 'Zuidoost Clinic' and General Practitioners Emergency Department on the referral status to the EPAU is still unknown. We found that only 26% of women presenting with early pregnancy complications at the General Practitioners Emergency department was referred to the EPAU. In 2009, a local protocol was published for general practitioners in the Amsterdam region stating that all women with early pregnancy complications should be referred to the EPAU for transvaginal ultrasound to rule out an ectopic pregnancy (HAG-desk AMC, 2009). Although the final diagnosis in the non-referred women is not known, we think that women may benefit and cost savings are gained by referral according to this local protocol.

Ideally, quality of care is expressed by adherence to developed quality indicators. These quality indicators are measurable elements of practice performance based on evidence, guidelines or consensus (Donabedian, 1988; van den Boogaard et al., 2010). Quality indicators for organizational aspects of an EPAU are still lacking and should be developed based on recent guidelines.

Our study focuses on the doctor's perspective on care for women with early pregnancy complications. Recent reports in subfertility care state that women prefer patient-centered care and not only effective treatment (Dancet et al., 2010; Schmidt et al., 2003; van Empel et al., 2010). To date, it is not known what preferences women facing early pregnancy complications have with regard to an EPAU. Future studies should

focus on patient-centered care and should elucidate what kind of early pregnancy care women prefer.

In conclusion, an EPAU has a positive effect on the quality of care provided to women with early pregnancy complications. The reduction in costs may be coincidental to changes in medical decision making over time. This study may motivate other clinicians in the field to establish an EPAU in their hospital. Further research can then be facilitated to compare early pregnancy care and costs and patient satisfaction between hospitals with and without an EPAU.

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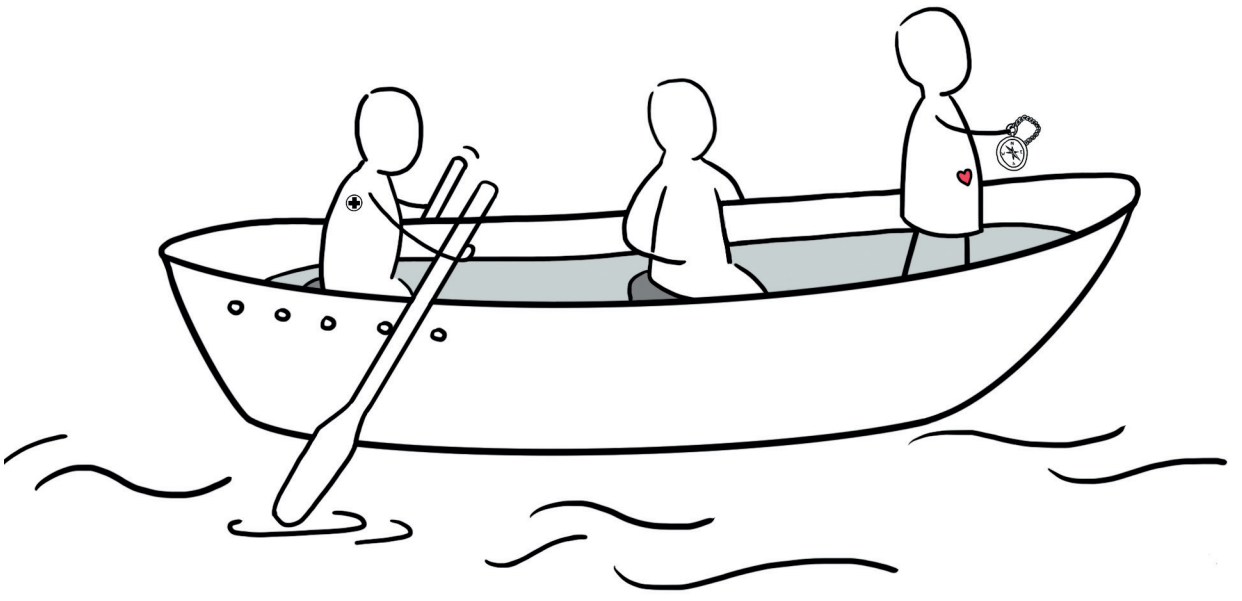

CHAPTER 5

Guideline-based quality indicators for early pregnancy assessment units

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Reproduction Biomedicine Online 2020;40(3):1475-1482

Abstract

Research question

What valid guideline-based quality indicators can measure quality of care in early pregnancy assessment units (EPAU)?

Design

The systematic RAND-modified Delphi method was used to develop an indicator set from four evidence-based guidelines. An international expert panel was assembled to extract recommendations from these guidelines to establish quality indicators.

Results

A total of 119 recommendations were extracted. Eleven recommendations received a high median score and top five score above the 75th percentile and were selected as key recommendations. The expert panel reassessed 15 high score recommendations and top five score between the 50th and 75th percentile as well as one high score recommendation without consensus. Eight of these 16 recommendations were selected in the second round as key recommendations. The key recommendations were formulated into a set of 19 quality indicators, summarized as follows: women referred to an EPAU could be seen within 24 h and receive a clear explanation on treatment options; designated senior staff members could be responsible for the unit and staff could have had ultrasound training; protocols could be available for daily practice covering all treatment options for miscarriage and ectopic pregnancy; and an EPAU could have access to urine pregnancy testing and serum HCG assays.

Conclusions

Nineteen quality indicators to measure early pregnancy care provided by EPAU were identified.

Introduction

Early pregnancy assessment units (EPAU) help to streamline service provision for early pregnancy complications (Goddijn et al., 2009; van den Berg et al., 2015). The most frequent early pregnancy complications are miscarriage and ectopic pregnancy (Rai and Regan, 2006; Hajenius et al., 2007). Early pregnancy assessment units were first established in the UK, and over 200 EPAU have now been established (Association of Early Pregnancy Units website, 2019). Other countries, such as Australia, Denmark, Belgium and the Netherlands, are working with the concept of an EPAU or have dedicated outpatient clinics focused on early pregnancy complications.

The Association of Early Pregnancy Units, the Royal College of Obstetricians and Gynaecologists (RCOG), the National Institute for Health and Clinical Excellence, UK, and the Ministry of Health in New South Wales, Australia, have developed guidelines for setting up and running an EPAU. Despite these guidelines, considerable variation still exists between them in access to services and quality of care provided (Association of Early Pregnancy Units, 2007; RCOG, 2008; Poddar et al., 2011; Ministry of Health New South Wales, 2012; NHS NICE, 2012). Quality indicators for the care delivered by EPAU to reduce this variation are still lacking (Grol et al., 2002; Campbell et al., 2003; Poddar et al., 2011). The aim of this study was to develop a set of valid guideline-based quality indicators for EPAU.

Material and Methods

Design and settings

The stepwise RAND-modified Delphi method was used to develop valid quality indicators based on four available guidelines on the organization of early pregnancy care; the Association of Early Pregnancy Units, the Royal College of Obstetricians and Gynaecologists guidelines, the National Institute for Health and Clinical Excellence guidelines and the Ministry of Health NSW Australia guidelines (Dalkey et al., 1969; Fitch et al., 2001; Campbell et al, 2003; Association of Early Pregnancy Units, 2007; RCOG, 2008; Ministry of Health NSW, 2012; NHS NICE, 2012).

An international expert panel was assembled to extract key recommendations from these guidelines to establish measurable and valid quality indicators. Eleven gynaecologists who specialized in early pregnancy care were invited to join the expert panel. These gynaecologists from the Netherlands, UK, Denmark and Australia were selected for the panel because they were involved in setting up or are working in an EPAU, were active in developing guidelines, were (board) members of the European Society of Human Reproduction and Embryology special interest group 'Early Pregnancy' at some time, or both.

Procedure for indicator development

The development of quality indicators involved four steps (Campbell et al., 2003). In step one, two authors (MvdB and EvdB) independent from each other extracted all recommendations from the guidelines. Subsequently, they categorized the

recommendations into four domains, e.g. recommendations concerning patient, doctor, process and organizational aspects of care. These domains are generally considered to represent all aspects of care (Mol et al., 2011; den Breejen et al., 2016). The extracted recommendations were presented with concomitant evidence levels in an electronic questionnaire in English for appraisal by the expert panel (Figure 1).

Figure 1. Example of an recommendation transformed in a digital questionnaire.

To which extent is the realisation of the following recommendation an important tool for the measurement of quality of care provided by an Early Pregnancy Assessment Unit in light of health gain and overall efficacy?		Evidence level
1. All maternity services must provide or be networked to a dedicated EPAU	**1 2 3 4 5 6 7 8 9** ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☒ ☐ **[----------]** very poor excellent ☐ *unknown*	C

In step two, the electronic questionnaire was presented to the members of the expert panel. All members of the expert panel individually scored each recommendation on a nine-point Likert scale, ranging from 1 = hardly relevant to 9 = extremely relevant. The expert panel was also allowed to add new recommendations with their underlying reasoning, e.g. from daily experience. In addition, the expert panel prioritized the recommendations per domain using a top-five ranking system. Recommendations were rated as valid according to the Campbell criteria, if an overall high median score was achieved (8 or 9) on the Likert scale and if 'agreement' between the ratings of the independent members of the expert panel was reached (Campbell et al., 2003). Agreement was reached when 75% or more ratings within the expert panel were in the highest (7, 8, 9) or the lowest (1, 2, 3) tertile. The percentage of the maximum top-five score was calculated. Recommendations were ranked as one in the top-five ranking 5 points, two in the top five ranking 4 points and so on. Recommendations with a high median score (8 or 9) and a top-five ranking above the 75th percentile of the maximum top five score were eligible for the set of potential key recommendations.

In step 3, a second electronic survey was presented in English, with the potential key recommendations as well as the recommendations with a high median score (8 or 9) and top five score between the 50th and 75th percentile to the expert panel. Each member was shown their individual scores in relation to those of the other members of the expert panel. Expert panel members were asked whether they agreed with the selected potential key recommendations. Also, the expert panel were asked whether recommendations with a top five score between the 50th and 75th percentile should also be included as a key recommendation. These recommendations were selected as a key recommendation if more than 75% of the expert panel members agreed. In this step, the expert panel was again allowed to add recommendations. After this step, a final consensus-based set of key recommendations was compiled. In case of disagreement of

the potential key recommendations, another consensus round with an electronic survey would have taken place.

In the last step, two authors (MvdB and EvdB) critically evaluated the final key recommendations and comments from the expert panel. The key recommendations were then formulated into quality indicators by defining numerators and denominators, i.e. the number of units in which a specific treatment option is available divided by the number of units in which a specific treatment option should be available (Figure 2).

Figure 2. Example of a quality indicator based on one of the key recommendations and corresponding adherence.

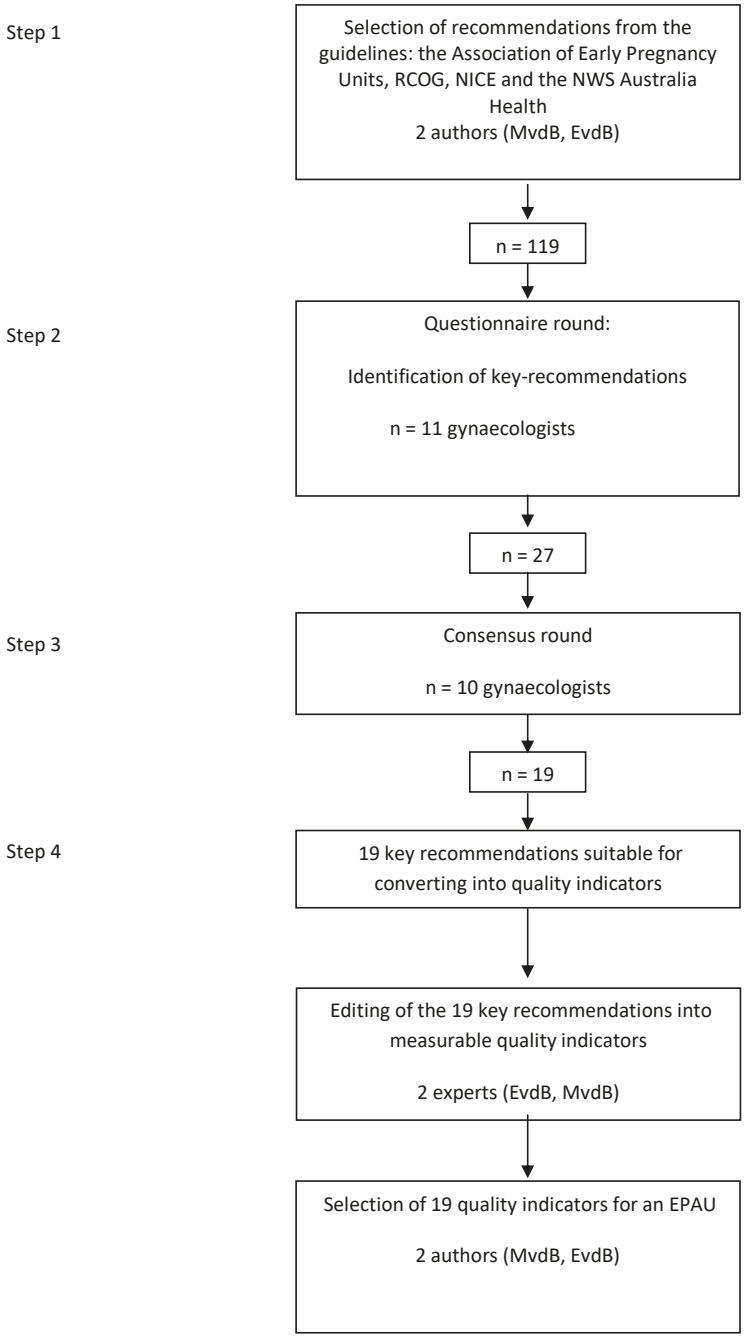
The number of early pregnancy units in which a 24/7 hCG option is available	* 100 =	% of adherence to the indicator
Total number of early pregnancy units in which a 24/7 hCG option should be available		

Results

The results of the procedure of the development of the quality indicators are presented in Figure 3. In step 1, 119 recommendations on patient (n = 13), doctor (n = 18), process (n = 37) and organizational (n = 51) aspects of care were extracted from the guidelines and presented to the 11 expert panel members.

In step 2, 10 out of 11 questionnaires (91%) were returned by the expert panel and were fully completed. One gynaecologist initially agreed to participate but withdrew from the study owing to lack of time. Eleven out of the 119 recommendations (9%) were proposed as directly eligible as key recommendations based on high median scores and top five rankings above the 75th percentile. The following recommendations received the highest score per domain from the expert panel: 'women who are referred to an EPAU should be seen promptly' (patient); 'a designated senior staff member should be responsible for the unit' (doctor); 'protocols should be available for daily practice' (process); and 'there should be good-quality ultrasound equipment' (organizational). Fifteen out of the 119 recommendations (13%) had a high median score and a top five score between the 50th and 75th percentile. One recommendation received a score above the 75th percentile, but without agreement between the individual members. The expert panel reassessed these 16 recommendations. The expert panel suggested no new recommendations.

Figure 3. Procedure of development of quality indicators for an Early Pregnancy Assessment Unit



In step 3, all members of the expert panel agreed on the initial set of 11 potential key recommendations. Eight of the 16 recommendations in the second round (50%) were also selected as key recommendations. Two of these were uniformly selected by all members of the expert panel, being 'women in the first trimester who have a positive pregnancy test and abdominal pain can be referred to an EPAU'; and 'women in the first trimester who have a positive pregnancy test and vaginal bleeding can be referred to an EPAU'.

Ultimately, of the initial 119 recommendations extracted from the guidelines, 19 (16%) were identified as potential key recommendations; two out of 13 (15%) were initial patient recommendations, two out of 18 (11%) were initial doctor recommendations, five out of 37 (14%) were initial process recommendations and 10 out of 51 (20%) were initial organizational recommendations (Table 1). As consensus was completely reached within the second questionnaire round, it was not necessary to convene a face-to-face consensus round.

Some of the 19 key recommendations were not applicable for translation into quality indicators. Therefore, it was decided that eight key recommendations would be adapted to make these more tangible and thereby measurable. The first key recommendation was adapted to 'women who are referred to an EPAU should be seen within 24 hours' instead of 'should be seen promptly'. The second key recommendation was also extended: 'women should receive a clear explanation on treatment options' with the sentence 'this means that they should have face-to-face explanation as well as written patient information'. The sixth recommendation was also adapted into 'a digital system should register the ultrasound findings' instead of 'standard system'. Finally, the tenth recommendation 'there should be good-quality ultrasound equipment' was extended to 'good quality is indicated as a proper endovaginal probe, regular maintenance and a visible write-off date'.

The recommendations were adapted according to the European Society of Human Reproduction and Embryology agreement on textual definitions used for recommendations (Vermeulen et al., 2018). This means the use of 'should' for level one or two evidence and the use of 'could' for recommendations based on level three and four evidence. The guidelines, on which our quality indicators are based, use low levels of evidence in their recommendations (evidence level C). Therefore, the word 'should' or 'can' was changed into 'could' for all recommendations.

In step 4, the 19 key recommendations were formulated into a final set of 19 quality indicators which, in summary, state that women referred to an EPAU could be seen within 24 h and receive a clear explanation on treatment options; that designated senior staff members could be responsible for the unit and staff could have had ultrasound training; that protocols could be available for daily practice covering all treatment options for miscarriage and ectopic pregnancy; and that an EPAU could have access to urine pregnancy testing and serum HCG assays (Table 2).

Table 1. Final set of key recommendations

Key recommendations (per domain)		AEPU[1]	RCOG[2]	NICE[3]	NSW[4]
Patient					
1	Women who are referred to an EPAU should be seen promptly.			X	
2	Women should receive a clear explanation on treatment options.	X	X		
Doctor					
3	A designated senior staff member should be responsible for the unit.		X		
4	Staff should have had recognized ultrasound training.	X	X		X
Process					
5	Protocols should be available for daily practice.		X		X
6	A standard system should register the ultrasound findings.				X
7	A system for the registration of serious untoward incidents and complications should be used.		X		
8	All treatment options for miscarriage should be available (expectant, medical or surgical).		X		
9	All treatment options for ectopic pregnancy should be available (expectant, medical or surgical).		X		
Organisational					
10	There should be good quality ultrasound equipment.	X		X	X
11	There should be access to urine pregnancy testing.	X			
12	There should be access to serum hCG assay.	X	X	X	X
13	There should be a designated examination room to provide privacy.		X		
14	There should be a designated interview room to allow discreet communication of sensitive information.		X		X
15	There should be a discrete waiting area.	X			X
16	Women with a history of ectopic pregnancy can refer themselves		X	X	
17	Women in the first trimester who have a positive pregnancy test and a previous ectopic pregnancy can be referred to an EPAU.	X	X		
18	Women in the first trimester who have a positive pregnancy test and abdominal pain can be referred to an EPAU.	X	X		
19	Women in the first trimester who have a positive pregnancy test and vaginal bleeding can be referred to an EPAU.	X	X		

[a]The Association of Early Pregnancy Units, 2007

[b]The Royal College of Obstetricians and Gynaecologists, 2008

[c]The National Institute for Health and Clinical Excellence in the United Kingdom, 2012

[d]The Ministry of Health, in NSW Australia, 2012.

Table 2. Final set of quality indicators per domain

Patient
Women who are referred to an EPAU could be seen within 24 hours.
The number of women who are referred to an EPAU and are seen within 24 hours
Total number of women referred to an EPAU
Women could receive a clear explanation on treatment options. This means that they could have face-to-face explanation as well as written patient information.
The number of women which received clear explanation on treatment options by the doctor.
Total number of women which received treatment
Doctor
A designated senior staff member could be responsible for the unit.
The number of units where a designated senior staff member is responsible for the unit
Total number of staff members working in the OB/GYN department
Staff could have had recognized ultrasound training.
Number of staff members working in an EPAU with a recognized ultrasound training
Total number of staff members working in an EPAU
Process Numerator is given and the denominator is the total number of EPAUs
Protocols could be available for daily practice.
The number of units where protocols are available for daily practice
A digital system could register the ultrasound findings.
The number of units where ultrasound findings are registered by a standard system
A system for the registration of serious untoward incidents and complications could be used.
The number of units where a system for the registration of serious untoward incidents and complications is used
All treatment options for miscarriage could be available (expectant, medical or surgical).
The number of units where all treatment options for miscarriage are available (expectant, medical or surgical)
All treatment options for ectopic pregnancy could be available (expectant, medical or surgical).
The number of units where all treatment options for ectopic pregnancy are available (expectant, medical or surgical)
Organisational Numerator is given and the denominator is the total number of EPAUs
There could be good quality ultrasound equipment (proper endovaginal probe, regular maintenance and visible write-off date).
The number of units where there is good quality ultrasound equipment available
There could be access to urine pregnancy testing.
The number of units where there is access to urine pregnancy testing
There could be access to serum hCG assay.
The number of units where there is access to serum hCG assay

There could be a designated examination room to provide privacy.	
	The number of units where there is a designated examination room to provide privacy
There could be a designated interview room to allow discreet communication of sensitive information.	
	The number of units where there is a designated interview room to allow discreet communication of sensitive information
There could be a discrete waiting area.	
	The number of units where there is a discrete waiting area
Women with a history of ectopic pregnancy could refer themselves to an EPAU.	
	The number of units where women with a history of ectopic pregnancy can refer themselves
Women in the first trimester with a positive pregnancy test and a previous ectopic pregnancy could be referred to an EPAU.	
	The number of units where women in the first trimester who have a positive pregnancy test and a previous ectopic pregnancy can be referred to an EPAU
Women in the first trimester with a positive pregnancy test and abdominal pain could be referred to an EPAU.	
	The number of units where women in the first trimester who have a positive pregnancy test and abdominal pain can be referred to an EPAU
Women in the first trimester with a positive pregnancy test and vaginal bleeding could be referred to an EPAU.	
	The number of units where women in the first trimester who have a positive pregnancy test and vaginal bleeding can be referred to an EPAU

Discussion

We developed a set of 19 quality indicators out of 119 initial recommendations derived from four international guidelines to measure early pregnancy care provided by EPAU. These 19 quality indicators state that women referred to an EPAU could be seen within 24 h and receive a clear explanation on treatment options; that designated senior staff members could be responsible for the unit and staff could have had ultrasound training; that protocols could be available for daily practice covering all treatment options for miscarriage and ectopic pregnancy; and that an EPAU could have access to urine pregnancy testing and serum HCG assays.

The strength of our study is that we used the Rand-modified Delphi technique, which has proved to be effective in previous indicator development strategies (Campbell et al., 2000; Hermens et al., 2006; van den Boogaard et al., 2010; Mol et al., 2011). As we only included recommendations with a high median score (≥8) and a high top five score based on the Campbell criteria, we can guarantee high internal face and content validity (Campbell et al., 2003). All recommendations could be formulated into measurable indicators by adapting less defined statements or multi interpretable sentences. For example, in the recommendation 'women who are referred to an EPAU should be seen promptly', promptly can be interpreted as within 24 h, the next day or the first

possibility available. Another strength is that the developed quality indicators are based on international guidelines and assessed by international experts in the field of early pregnancy, and therefore have external validity and can be used internationally. Clinicians in countries not working with the concept of an EPAU can use these guideline-based quality indicators to establish and run a high-quality evidence-based EPAU.

A limitation of our study is that the available guidelines, on which the quality indicators are based, use low levels of evidence in their recommendations (evidence level C). Nevertheless, to date, no evidence above level C is available. One may argue that a self-appointed expert panel is another limitation, especially as some members of the expert panel were also involved in the development of the guidelines. Furthermore, the process key recommendation 'protocols available for daily practice covering all treatment options for miscarriage and ectopic pregnancy' does not mean that these protocols will be followed. For the tenth recommendation, we state that good quality is indicated as a proper vaginal probe meaning using a 5MHz endovaginal probe. Also, the testing schedule and turnaround time are not included in the twelfth key recommendation: 'there could be access to serum HCG assay.' We advise having access to HCG screening 24 h a day, 7 days a week, including holidays with a turnaround time of at most 1 h. As for the urinary pregnancy testing, the sensitivity of the test should be high enough to avoid false negative results.

Most quality measurement programmes apply an upper limit of 10 indicators (McGory et al., 2005). Our set of 19 quality indicators represents the variation in which countries provide various types of care and support in early pregnancy care and points to the need for developing evidence-based quality indicators for EPAU less dependent of cultural and economic interests to reduce practice variation.

A tool to monitor the performance of EPAU covering items on workforce, clinical activities, clinical outcomes and risk management has recently been designed (Wahba et al., 2015). The authors did not describe how, and on which evidence it was based, in contrast to the present study design, and is therefore not applicable for all EPAU.

The present study is the first step in the process of guideline implementation in EPAU. The developed quality indicators need to be understood by all stakeholders and could be supported by standard operational procedures. Further research could focus on measuring actual care in, and between, various EPAU by using the quality indicators on identification of facilitators and barriers and, if necessary, on the development of an implementation strategy to improve guideline adherence.

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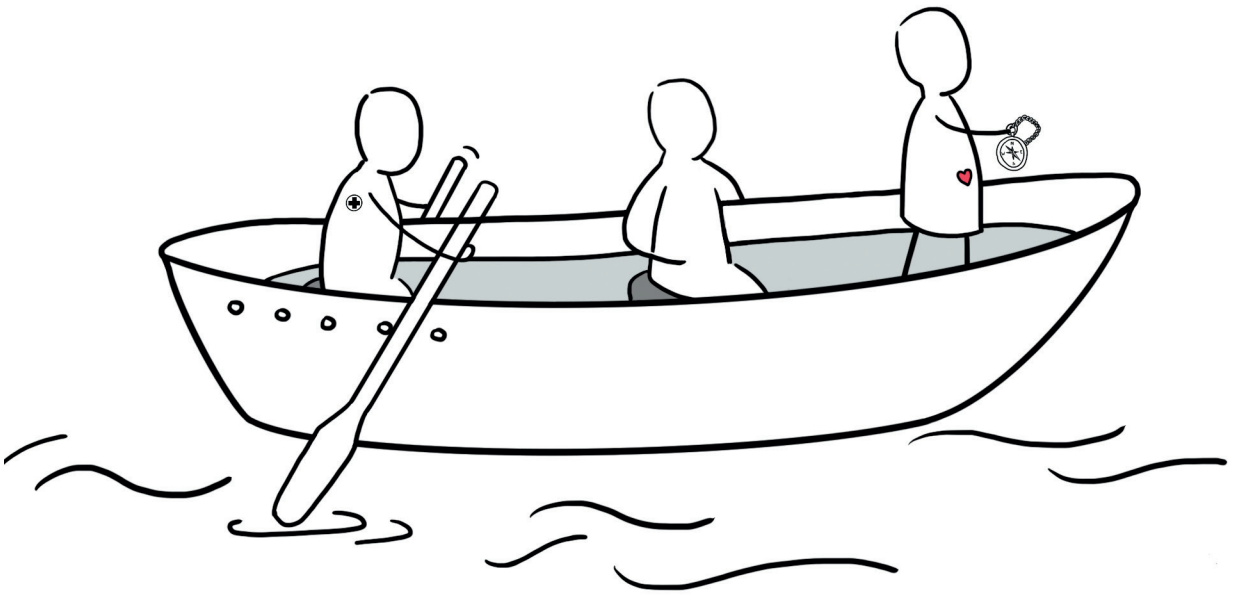

CHAPTER 6

Adherence to guideline-based quality indicators in early pregnancy care in hospitals with and without an early pregnancy assessment unit

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Reproductive BioMedicine Online 2022;45(3):583-588

Abstract

Research question

How do hospitals with and without an early pregnancy assessment unit (EPAU) adhere to guideline-based quality indicators for an EPAU relating to logistics, access to services and quality of early pregnancy care?

Design

A qualitative interview study assessing the adherence to 19 quality indicators in four hospitals with an EPAU and four hospitals without an EPAU in the Netherlands. For each quality indicator, a ratio for guideline adherence was calculated. Overall non-adherence per hospital was defined as less than 100% adherence to the 19 quality indicators.

Results

Non-adherence was seen in three indicators (3/19 [16%]) for hospitals with an EPAU and in five indicators (5/19 [26%]) for hospitals without an EPAU. A standard digital system for the registration of ultrasound findings and clear explanation of all treatment options was present in all hospitals with an EPAU and in three hospitals without an EPAU. Certified ultrasound training for working staff members was absent in all hospitals. A discrete waiting area was present in one hospital with an EPAU compared with none of the hospitals without an EPAU. Self-referrals from women with a previous ectopic pregnancy was accepted in one hospital with and in one hospital without an EPAU.

Conclusions

Non-adherence to guideline-based quality indicators for an EPAU was about the same for hospitals with and without an EPAU in the Netherlands.

Introduction

Early pregnancy assessment units (EPAUs) have been established to provide the best possible care for women experiencing complications in early pregnancy, most notably miscarriage and ectopic pregnancy (Association of Early Pregnancy Units, 2020). EPAUs vary with respect to logistics, access to services and quality of early pregnancy care (Poddar et al., 2011). Guidelines on setting up and running an EPAU have been developed to reduce practice variation and to improve quality of early pregnancy care, but are based upon low level evidence (level C) (Association of Early Pregnancy Units, 2013; Ministry of Health NSW, 2012; NICE, 2012, RCOG, 2008). In the Netherlands, these international guidelines were used to set up an EPAU in the Amsterdam University Medical Centre (UMC, location AMC), as no national guideline was available on this subject. Being a pioneer for some years, a few other hospitals in the Netherlands followed the example of Amsterdam UMC and also started an EPAU or created a dedicated outpatient clinic providing early pregnancy care but not situated in a designated unit.

After establishing the EPAU in Amsterdam UMC, financial costs savings were obtained due to a reduction in hospital admissions for miscarriage and a reduction of surgical management in favor of medical and expectant management for women with miscarriage or ectopic pregnancy (van den Berg et al., 2015). Evidenced-based quality indicators to measure the quality of early pregnancy care correctly were lacking at the time of that publication. Recently, we developed quality indicators for EPAUs from the international guidelines which makes it possible to measure the adherence to the guidelines and thus to compare the quality of early pregnancy care provided by hospitals with and without an EPAU (van den Berg et al., 2020). These guideline based quality indicators are predominantly structure indicators focusing on logistics and access to services more than procedural or outcome indicators for clinical diagnostic and therapeutic purposes.

The aim of this qualitative study was to assess to what extent hospitals with and without an EPAU adhere to the guideline based quality indicators for setting up and running an EPAU as a proxy for quality of early pregnancy care.

Material and methods

A set of four hospitals with an EPAU or a dedicated early pregnancy outpatient clinic (hospital 1 to 4), and a set of four hospitals without an EPAU (hospital 5 to 8), were assembled out of the 70 hospitals in the Netherlands. Both sets comprised two university hospitals and two non-teaching hospitals.

Study design

Interviews were conducted with the heads of the EPAU or heads of the obstetrics and gynaecology departments. All department heads were gynaecologists who were involved in daily clinical care, supervised residents and frequently treated women with complications in early pregnancy themselves.

All interviews were held between January 2019 and April 2019 by one researcher (MvdB). No formal ethical approval was needed for this study according to the Dutch 'Medical Research Involving Human Subjects Act' (article 1, paragraph b, 1998).

Data collection

A set of 19 valid guideline-based quality indicators developed for logistical aspects, access to services and quality of early pregnancy care was used (Table 1). These indicators are based on four international guidelines (level C evidence) and were developed with the help of an international expert panel by using the systematic RAND-modified Delphi method. With this method, the first step was the extraction of 119 recommendations from the four available guidelines at that time (RCOG, 2008; NICE, 2012; Ministry of Health NSW, 2012; Association of Early Pregnancy Units, 2020). The second step was the presentation of a digital questionnaire to the members of the expert panel to individually score each of these 119 recommendations on a nine-point Likert scale and to add new recommendations if required. The recommendations were prioritized using a top-five ranking system. Eleven recommendations with a high median score (8 or 9) and a top-five ranking above the 75th percentile of the maximum top five score were selected as key recommendations. The third step was the presentation of a second survey to the expert panel to reassess 15 recommendations with a high score (8 or 9) and a top 5 score between the 50th and 75th percentile and one high score recommendation without consensus. Eight of these 16 recommendations were selected in the second round as key recommendations. The fourth and last step was to evaluate the 19 final key recommendations and comments from the expert panel and transcribe these recommendations into measurable quality indicators by defining numerators and denominators. To do so, some of the key recommendations were adjusted. The first key recommendation' women who are referred to an EPAU should be seen promptly' was adapted to 'should be seen within 24 h'. The second key recommendation 'women should receive a clear explanation on treatment options' was extended with the sentence 'this means that they should have face-to-face explanation as well as written patient information leaflets'. The sixth and tenth recommendations, respectively, were made more tangible: 'a standard digital system should register the ultrasound findings' and 'there should be good quality ultrasound equipment' supplemented with 'good quality is indicated as a proper endo-vaginal probe, regular maintenance and a visible write-off date' (van den Berg et al., 2020).

A checklist was developed as a guidance tool during the interview sessions to address all 19 quality indicators (Supplementary Table). The researcher (MvdB) visited the hospitals to interview the heads of the departments and to see for herself whether an indicator was present or not. To measure actual given care in the domain 'Patient' (Supplementary Table, question 1a and 2a), the heads of the departments were asked to present data on women with complications in early pregnancy, defined as vaginal bleeding, abdominal pain or abnormal ultrasound findings on the first trimester scan, or both, who were seen in a 12-month period between 1 January 2018 to 31 December

2018. To do so, the heads of the departments identified these women by the hospital financial registries and reported on the written data in their medical chart.

Table 1. Guideline based quality indicators in early pregnancy care and measurement of actual care

Dimension	Type of indicator	Description	Formula
Patient	Patient	Women who are referred to an EPAU could be seen within 24 hours	Numerator: The number of women who are referred to an EPAU and are seen within 24 hours between January 1st, 2018 to December 31st, 2018
			Denominator: Total number of women referred to an EPAU between January 1st, 2018 to December 31st, 2018
		Women could receive clear explanation on treatment options. This means that they could have face-to-face explanation as well as written patient information.	Numerator: The number of women who received clear explanation on treatment options by the doctor. This means face-to-face explanation as well as written patient information between January 1st, 2018 to December 31st, 2018
			Denominator: Total number of women who received treatment between January 1st, 2018 to December 31st, 2018
Doctor	Structure	A designated senior staff member could be responsible for the clinical area	Numerator: The number of units with a designated senior staff member responsible for the unit
			Denominator: Total number of EPAUs
		Working staff could have had recognised ultrasound training	Numerator: Number of working staff members with a recognised ultrasound training
			Denominator: Total number of staff members working in an EPAU

Table 1. Continued.

Dimension	Type of indicator	Description	Formula
General	Structure	Protocols could be available for daily practice	Numerator: The number of units with protocols available for daily practice
			Denominator: Total number of EPAUs
		A standard digital system could register the ultrasound findings	Numerator: The number of units with ultrasound findings registered in a standard digital system
			Denominator: Total number of EPAUs
		A system for the registration of serious untoward incidents and complications could be used	Numerator: The number of units which use a system for the registration of serious untoward incidents and complications
			Denominator: Total number of EPAUs
		All treatment options for miscarriage could be available (expectant management, medical or surgical treatment)	Numerator: The number of units with all treatment options available for miscarriage (expectant management, medical or surgical treatment)
			Denominator: Total number of EPAUs
		All treatment options for ectopic pregnancy could be available (expectant management, medical or surgical treatment)	Numerator: The number of units with all treatment options available for ectopic pregnancy (expectant management, medical or surgical treatment)
			Denominator: Total number of EPAUs

Table 1. Continued.

Dimension	Type of indicator	Description	Formula
Logistic	Structure	There could be good quality ultrasound equipment (proper endo-vaginal probe, regular maintenance and visible write-off date)	Numerator: The number of units with good quality ultrasound equipment available (proper endo-vaginal probe, regular maintenance and visible write-off date)
			Denominator: Total number of EPAUs
		There could be access to urine pregnancy testing	Numerator: The number of units with access to urine pregnancy testing
			Denominator: Total number of EPAUs
		There could be access to serum hCG assay	Numerator: The number of units with access to serum hCG assay
			Denominator: Total number of EPAUs
		There could be a designated examination room to provide privacy	Numerator: The number of units with a designated examination room to provide privacy
			Denominator: Total number of EPAUs
		There could be a designated interview room to allow discreet communication of sensitive information	Numerator: The number of units with a designated interview room to allow discreet communication of sensitive information
			Denominator: Total number of EPAUs
		There could be a discrete waiting area	Numerator: The number of units with a discrete waiting area
			Denominator: Total number of EPAUs
		Women with previous ectopic pregnancy could refer themselves to an EPAU	Numerator: The number of units where women with a previous ectopic pregnancy can refer themselves
			Denominator: Total number of EPAUs
		Women in the first trimester who have a positive pregnancy test and a previous ectopic pregnancy could be referred to an EPAU	Numerator: The number of units where women in the first trimester who have a positive pregnancy test and a previous ectopic pregnancy can be referred to an EPAU
			Denominator: Total number of EPAUs
		Women in the first trimester who have a positive pregnancy test and abdominal pain could be referred to an EPAU	Numerator: The number of units where women in the first trimester who have a positive pregnancy test and abdominal pain can be referred to an EPAU
			Denominator: Total number of EPAUs
		Women in the first trimester who have a positive pregnancy test and vaginal bleeding could be referred to an EPAU	Numerator: The number of units where women in the first trimester who have a positive pregnancy test and vaginal bleeding can be referred to an EPAU
			Denominator: Total number of EPAUs

Analysis

The percentage of adherence to an indicator within the actual care provided was expressed, i.e. the number of hospitals in which a specific diagnostic test or treatment option was available (numerator), divided by the number of hospitals in which a specific diagnostic test or treatment option should be available under ideal circumstances according to the 19 quality indicators (denominator) (Table 1). With all quality indicators being structure indicators, overall non-adherence per hospital was defined as less than 100% adherence to the 19 quality indicators. Structural aspects of care should be 100% guaranteed within an EPAU.

Results

An overview of the adherence to the guideline-based quality indicators in early pregnancy care for hospitals with and without an EPAU is presented in Table 2. All four hospitals with an EPAU showed overall non-adherence on up to three (3/19 [16%]) quality indicators. Only one hospital had a discrete waiting area and one accepted self-referrals in case of a previous ectopic pregnancy. None of the hospitals offered certified ultrasound training for their working staff.

The four hospitals without an EPAU showed non-adherence on at least one out of five (5/19 [26%]) quality indicators. None of the hospitals had a discrete waiting area. Three hospitals gave explanation on treatment options, including a written patient information leaflet, whereas one hospital only gave face-to-face explanation. Three hospitals used a standard digital registry system for ultrasound findings. Only one hospital accepted self-referrals in case of a previous ectopic pregnancy. None of the hospitals offered certified ultrasound training for their staff members.

None of the hospitals documented referral time to the hospital, nor did the clinicians document whether they had given the women a written patient information leaflet (Table 3, sub-questions 1a and 2a).

Table 2. Adherence to guideline based on quality indicators for early pregnancy care

Domain	Quality indicator	Hospitals with an EPAU	Hospitals without an EPAU
		n/N_{total}	n/N_{total}
Patient	1. Referred women seen within 24 hours	4/4	4/4
	2. Clear explanation on treatment options?	4/4	3/4
Doctor	3. Designated senior staff	4/4	4/4
	4. Recognised ultrasound training	0/0	0/0
General	5. Protocols for daily practice	4/4	4/4
	6. Standard digital system for ultrasound findings	4/4	3/4
	7. System for serious untoward incidents and complications	4/4	4/4
	8. All treatment options available for miscarriage	4/4	4/4
	9. All treatment options available for ectopic pregnancy	4/4	4/4
Logistic	10. Good quality ultrasound equipment	4/4	4/4
	11. Urine pregnancy testing	4/4	4/4
	12. Serum HCG assay	4/4	4/4
	13. Designated examination room	4/4	4/4
	14. Designated interview room	4/4	4/4
	15. Discrete waiting area	1/4	0/0
	16. Self-referral for women with previous ectopic pregnancy	1/4	1/4
	17. Women with positive pregnancy test and previous ectopic pregnancy can be seen instantly	4/4	4/4
	18. Women with positive pregnancy test and abdominal pain can be seen instantly	4/4	4/4
	19. Women with positive pregnancy test and vaginal bleeding can be seen instantly	4/4	4/4

Guideline: van den Berg et al., 2020

Table 3. Sub questions on quality indicators for early pregnancy care

Domain	Quality indicator	Hospitals with an EPAU	Hospitals without an EPAU
Patient	1a. Data for eligible women seen within 24 hours of referral in 2018?	Not available for all hospitals	Not available for all hospitals
	2a. Data foreligible women receiving clear information on treatment options in 2018?	Not available for all hospitals	Not available for all hospitals
Doctor	4a. Number of staff members with ultrasound training?	1. none (0%)	5. 12 / 17 (71%)
		2. 10 / 25 (40%)	6. none (0%)
		3. none (0%)	7. none (0%)
		4. none (0%)	8. 9 / 14 (64%)
General	5a. When was the last update of the protocols, i.e. how often are the protocols updated?	1. every 2 years	5. every 2,5 years
		2. every 2 years	6. every 2 years
		3. every 2 years	7. every 5 years
		4. every 2 years	8. every 2 years
	6a. Which digital registry system is used to register the ultrasound findings?	1. Astraia	5. HiX
		2. Astraia	6. Not applicable
		3. EPIC	7. HiX
		4. Astraia	8. Not applicable
	7a. Which digital patient system is used to register serious untoward incidents and complications?	1. EPIC	5. HiX
		2. HiX	6. EPIC
		3. EPIC	7. HiX
		4. EPIC	8. HiX
	8a. What is the waiting time for surgical management for women diagnosed with a miscarriage?	1. < 2 weeks	5. 1-2 weeks
		2. 1-2 weeks	6. < 2 weeks
		3. < 2 weeks	7. < 1 week
		4. 1-2 weeks	8. < 1 week
	9a. What is the waiting time for surgical management for women diagnosed with an ectopic pregnancy?	1. none	5. none
		2. none	6. none
		3. none	7. none
		4. none	8. none
Logistic	10a. When was the last maintenance of the ultrasound equipment, i.e. how often is the maintenance of the ultrasound equipment?	1. every year	5. every year
		2. every year	6. every year
		3. every year	7. every year
		4. every year	8. every year

For checklist see Supplementary Table.

Discussion

Adherence to the 19 guideline based quality indicators for early pregnancy care could be improved on three indicators for hospitals with an EPAU compared to five indicators in hospitals without an EPAU. In hospitals with and without an EPAU improvements can be made on creating a discrete waiting area, accepting self-referrals for women with a previous ectopic pregnancy and offering certified ultrasound training for working staff members. In addition, in hospitals without an EPAU improvements can be made on better patient information tools covering all treatment options and on using a standard digital registry system for ultrasound findings. In our opinion, these improvements are easy to implement and should be no barrier to further improve quality of patient centered care in early pregnancy both in hospitals with and without an EPAU.

We consider the method used to measure the adherence to the quality indicators for early pregnancy care precise and widely applicable because of the standardised development procedure of the guideline based quality indicators (van den Berg et al., 2020). Another strength of our study is that we minimised the chances of inter-observer bias by having one interviewer for all interviews. Although the heads of the departments might have a vested interest in the outcomes of this study, it is unlikely that this biased the results by giving socially desirable answers to the questions, since the structured checklist was based on valid quality indicators. Only two (Table 1, question 1a and 2a), of the 19 quality indicators could potentially be answered subjectively, the other 17 are structure indicators that are either present or not.

A limitation of our study is that our sample size was confined to only eight hospitals, of which four had an EPAU. Another limitation is that none of the clinicians documented the referral time to the hospital or whether they had given the women a written patient information leaflet. Therefore, we were not able to calculate the adherence to those two quality indicators (Supplementary Table, question 1a and 2a).

Although none of the hospitals offered a certified ultrasound training for their staff members, in the Netherlands, obstetrics and gynaecology residents must follow required certified ultrasound courses in their internship as specified by the Dutch Society of Obstetrics and Gynaecology (Dutch Society for Obstetrics and Gynaecology 2022). Therefore, consultants supervising residents, or who treat women with complications in early pregnancy themselves, are adequately trained and appropriately skilled in transvaginal sonography.

Adherence to clinical guidelines for the management of early pregnancy complications have been published previously (Mol et al., 2011; van den Boogaard et al., 2013). The present study, however, focuses on adherence to guidelines on the organization of early pregnancy care relating to logistics, access to services and quality of early pregnancy care. Furthermore, this study focuses on doctors' perspectives on early pregnancy care. We previously assessed patients' perspectives in a systematic review of quantitative and qualitative studies (van den Berg et al., 2018).

This systematic review shows that the most important potential targets for improvement in the patient-centeredness in miscarriage care were 'understandable

information provision about the etiology of pregnancy', 'staff discussing patients' distress', 'informing women on pregnancy loss in the presence of a friend or partner' and 'staff performing follow-up phone calls to support their patients after a miscarriage'. Other potential targets for improvement were 'women found it important to not be seated in a waiting room together with pregnant women awaiting a routine ultrasound scan' and 'women value information provision by their doctor at the time of the miscarriage'. In our study, all four hospitals with an EPAU had an adherence for giving clear explanation on treatment options and one hospital had a discrete waiting area compared with three and none, respectively, for hospitals without an EPAU. An EPAU, therefore, meets the perspectives of women and their partners and thereby enforces patient-centered early pregnancy care. Furthermore, one should not overlook the existing evidence that EPAU have rendered hospital admission obsolete and produce considerable savings in financial and staff recourses (Shillito and Walker, 1997; Wren et al., 1997; Haider et al., 2006; Wendt et al., 2014; van den Berg et al. 2015).

In conclusion, the non-adherence to 19 guideline-based quality indicators for an EPAU was around the same for hospitals with and without an EPAU in the Netherlands. Follow-up studies are needed to assess how the adherence to clinical guidelines for miscarriage and ectopic pregnancy care develop over time in hospitals with and without an EPAU, and to assess patients' perspectives on ectopic pregnancy care.

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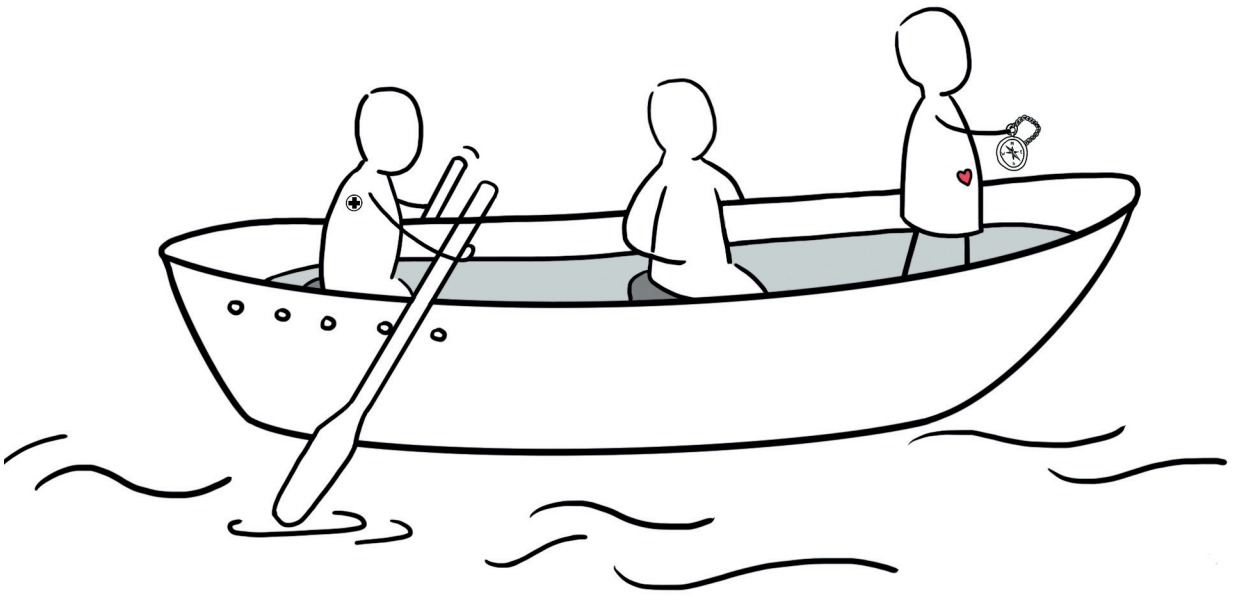
Supplementary table 1. Checklist developed for the interview covering the 19 guideline based quality indicators

Patient	
1	Are women who are referred to an EPAU seen within 24 hours?
1a	Data of eligible women between January 1st 2018 – December 31st 2018
2	Do women receive clear explanation on treatment options? This means face-to-face explanation as well as a written patient information leaflet
2a	Data of eligible women between January 1st 2018 – December 31st 2018
Doctor	
3	Is there a designated senior staff member responsible for the clinical area?
4	Has the staff had recognized ultrasound training?
4a	Number of staff members with a recognized ultrasound training
General	
5	Are there protocols available for daily practice?
5a	When was the last update of the protocol?
6	Is there a standard system that registers the ultrasound findings?
6a	Which system?
7	Is there a system for the registration of serious untoward incidents and complications?
7a	Which system? Is there a standard operating procedure available?
8	Are all treatment options available for women with a miscarriage (expectant management, medical or surgical treatment)?
8a	What is the waiting time for surgical management?
9	Are all treatment options available for women with an ectopic pregnancy (expectant management, medical or surgical treatment)?
9a	What is the waiting time for surgical management?
Logistic	
10	Is there good quality ultrasound equipment available?
10a	When was the last maintenance of the ultrasound equipment?
11	Is there access to urine pregnancy testing?
12	Is there access to serum hCG assay?
13	Is there a designated examination room available to provide privacy?
14	Is there a designated interview room available to allow discreet communication of sensitive information?
15	Is there a discrete waiting area?
16	Can women with a history of ectopic pregnancy refer themselves to an EPAU?
17	Can women with high risk of ectopic pregnancy (defined as a positive pregnancy test and a previous ectopic pregnancy) be referred instantly?
18	Can women with high risk of ectopic pregnancy (defined as a positive pregnancy test and abdominal pain in the first trimester) be referred instantly?
19	Can women with high risk of ectopic pregnancy (defined as a positive pregnancy test and vaginal bleeding in the first trimester) be referred instantly?



CHAPTER 7

Recurrent Miscarriage Clinics

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Obstetrics and Gynecology Clinics of North Ameria 2014; 41(1): 145-155

Abstract

A recurrent miscarriage clinic offers specialist investigation and treatment of women with recurrent first- and second-trimester miscarriages. Consultant-led clinics provide a dedicated and focused service to couples who have experienced at least two prior miscarriages. The best treatment strategy for couples with recurrent miscarriage is to discuss a treatment plan for a future pregnancy. Evidence-based up-to-date guidelines are required to reduce ineffective management of recurrent miscarriage couples, including over diagnostics and under diagnostics. Scientific research is necessary to study the effectiveness of new interventions, to study patient preferences, and to evaluate health care and costs or other outcomes.

Introduction

A miscarriage is the spontaneous loss of a clinically established intrauterine pregnancy before the fetus has reached viability. It includes pregnancy losses until the maximum of 24 weeks of gestation.[1] Between 10% and 15% of all clinically recognized pregnancies result in a spontaneous miscarriage. However, the overall prevalence of pregnancy losses, including biochemical pregnancies, is generally assumed 4 to 5 times higher (Rai and Regan, 2006). Approximately one-quarter of all women experience at least one miscarriage during their lives (Stephenson et al., 2007; Stern et al., 1996) In conclusion, a miscarriage is a frequent event and it is known that a miscarriage has a huge impact on a patient's life.

Up to 5% of all couples face recurrent miscarriage (RM). The definition may vary but starts when at least two or more miscarriages have occurred (Jaslow et al., 2010; Raijcan-Separovic et al., 2010). The sequence of the miscarriages is not necessarily consecutive (Jaslow et al., 2010; van den Boogaard et al., 2010)

A RM clinic offers specialist investigation and treatment of women with recurrent first- and second-trimester miscarriages. It is an outpatient clinic with reproductive gynecologists specialized in evidence-based RM care. This consultant-led clinic provides a dedicated and focused service to couples who have experienced at least two prior miscarriages.

Guidelines

Guideline Adherence

To improve the quality of care for RM, guidelines have been developed. These guidelines address the facilitation of evidence-based practice and reduce practice variation between professionals (Jauniaux et al., 2006). Couples with RM are often not treated according to the most up-to-date clinical evidence, as summarized in recent guidelines (Franssen et al., 2007; van den Boogaard et al., 2011) Ineffective management of couples with RM is caused by under diagnostics as well as over diagnostics, resulting in unnecessary tests and costs (Berwick et al., 2012) This barrier and other barriers to RM management are shown in Box 1. The introduction of new guidelines alone is not enough to prevent this ineffective management. Guideline implementation research shows that to achieve a high level of guideline adherence, implementation efforts are necessary (Bero et al., 1998; Grol et al., 1997). So far, it is not obvious which implementation strategy to apply to improve guideline adherence and, meanwhile, quality of care in couples with RM.

Guideline adherence could be improved with a multifaceted implementation strategy. In total, 23 quality indicators for care in couples with RM have been identified (van den Boogaard et al., 2010). These can be used to measure and monitor care for RM patients. These guidelines improved remarkably after introduction of the developed implementation strategy (van den Boogaard et al., 2010).

Another essential step in the implementation process of guidelines is qualitative research to identify barriers to and facilitators for guideline adherence (Jauniaux et al, 2006; Bero et al., 1998). One study identified barriers in management of RM in four domains: the guidelines, professionals, patients, and organization by semistructured

interview among professionals and patients (van den Boogaard et al., 2011). The most important identified barriers for guideline adherence were the guidelines being too complicated, lack of up-to-date patient information, and lack of detailed knowledge about family history (van den Boogaard et al., 2011) Based on the detected determinants for non-adherence and the barriers experienced by professionals and patients, an implementation strategy for improvement could be developed.

Guidelines state that all couples who suffer from RM should be offered advice and referred to a specialist clinic with appropriately trained health care professionals (RCOG, 2008). Couples with unexplained RM should be informed about their individual chances of success in a next pregnancy (Brihjam et al., 1999). Tender loving care (TLC) and health advice are the two established treatments of RM (discussed later) (Jauniaux et al., 2006). Health advice includes intake of folic acid, restriction of the intake of coffee, stopping smoking and drinking alcohol, and lifestyle advice and/or dietary measures in cases of overweight (Jauniaux et al., 2006). For women with RM and a subsequent confirmed pregnancy test, arrangements should be in place for an ultrasound scan and for receiving shared antenatal care in a high-risk obstetric clinic (RCOG, 2008). It is extremely important that all staff dealing with RM couples are trained in emotional aspects of pregnancy loss. In this way, immediate support can be provided and patients have direct access to specialist counseling (RCOG, 2008). The aim is to make all health professionals providing early pregnancy care aware of the current approach to this problem (Rai and Regan, 2006).

Box 1. Barriers to RM Management

Guidelines
- The definition of RM differs: two versus three miscarriages and consecutive versus non – consecutive miscarriage
- Few good RCT's have been performed to investigate diagnostic and treatment options

Organization
- Not every hospital has a recurrent miscarriage clinic / early pregnancy unit
- Not every hospital works with a RM expert
- Not every hospital offers the participation of RCT's

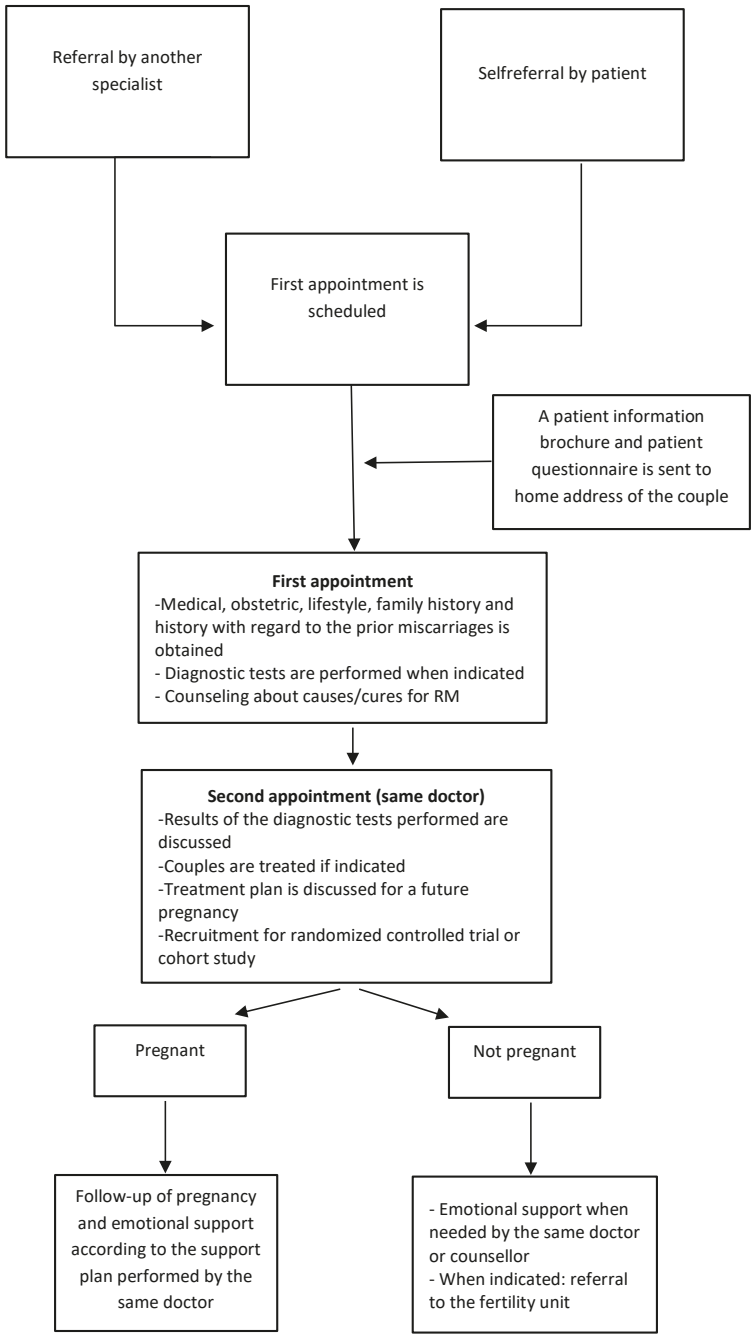
Professionals
- Doctor wants to offer their help despite the lack of evidence

Patients
- Patients have a strong will to perform diagnostic tests despite the lack of evidence
- Patients have a strong will to start treatment despite the lack of evidence

Logistical requirements

Couples who have suffered two or more miscarriages should be referred to a RM clinic. Fig. 1 provides a flowchart for the entry in a RM clinic. Preferably a patient information brochure has been sent to couples before their first visit to the clinic. This way, a couple's expectations can be met. Box 2 and Fig. 2 give an overview of the tools provided by RM clinics.

Figure 1. Flowchart for entry into a RM clinic



Location

The service is often situated in a gynecology outpatient clinic or near an early pregnancy unit. Avoid, whenever possible, locating a clinic near an antenatal clinic to reduce any distress experienced by women seeing ongoing pregnancies while waiting (Bourne and Condous, 2007).

Rooms

A room is necessary for taking history and examination. It is important that the room can be locked to guarantee privacy while women are changing and being examined (Bourne and Condous, 2007). In certain units, a separate room is used to perform the transvaginal sonography . These rooms should be warm and have good lighting for vaginal examinations. Another separate room for breaking bad news may be valuable. In this way, women are allowed to have some time to reflect and compose themselves before proceeding with further management. It is preferable that this room has telephone access to allow calls to relatives or friends (Bourne and Condous, 2007).

Staffing

All RM clinics should have a consultant with a special interest in RM. RM care should be provided by only one doctor per couple. Multidisciplinary support should be provided by other departments, such as clinical genetics, an early pregnancy assessment unit, pathology, radiology, internal medicine, endocrinology, and/or hematology departments. It is important that all staff dealing with RM couples are trained in emotional aspects of pregnancy loss. In this way, immediate support can be provided and every couple has direct access to specialist counseling (RCOG, 2008). The aim is to make all health professionals providing early pregnancy care aware of the current approach to manage RM (Association of early pregnancy units, 2007).

Equipment

For follow-up of a future pregnancy to confirm a miscarriage, the ability to perform transvaginal and/or transabdominal scan is necessary. It is preferable that the ultrasound has the ability to store copies of all images to be given to the women if requested (Bourne and Condous, 2007). Also an electronic database is advisable for documentation of all images. This gives an opportunity to exchange images with an early pregnancy unit.

Record Keeping

History, examination, and scan findings need to be documented and archived in the women's patient notes or in a database that is secured with a password-based access (Bourne and Condous, 2007). A standardized protocol should be used for the documentation of history and examination. This way, all patients are asked the same questions and the chance of forgetting something is low.

Laboratory Services

A basic requirement is access to hematology and biochemistry to facilitate RM diagnostic work-up (Bourne and Condous, 2007).

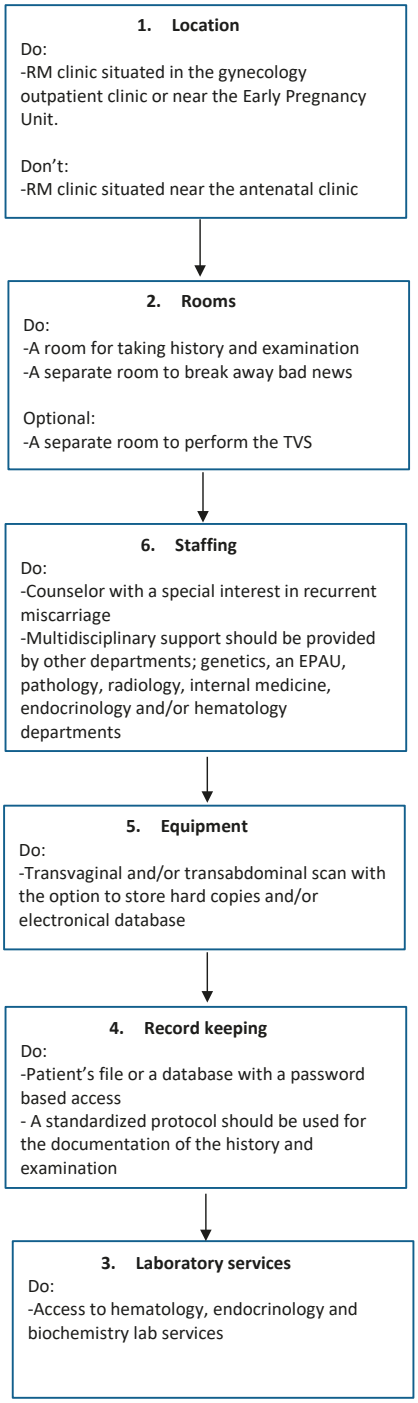
One-Stop Recurrent Miscarriage Clinics

Some clinics are organized as an one-stop RM clinic (Habayeb et al., 2004). When a couple is referred to a RM clinic, they receive a letter with a set of investigation forms and are advised to take blood tests. This way, the results of the blood tests are known and can be discussed when the couple attends the clinic for the first time. During the same consultation, history and physical examination are documented, which leads to a management plan. Couples only attend the RM clinic once and do not need any unnecessary repeat consultations. Before leaving the clinic, each couple is seen by a nurse counselor. They are given a direct telephone number to the antenatal assessment area (AAA), where all pregnancies are followed-up by the counselor. When a couple is pregnant, they call the AAA to receive follow-up scans and antenatal care. This one-stop clinic reduced the interval of visits by 36% (206.6–130.4 days; P<.001) and reduced the number of visits by 60% (2.5–1; P<.002) (Habayeb et al., 2004). This approach provides no patient-centered care, however. There is no explanation as to which diagnostic test is performed. Also, not all couples need to go through all diagnostic tests. Preferably, diagnostic work-up is based on proper history taking and individually tailored. Most diagnostic tests should only be performed on indication.

Box 2. Tools for recurrent miscarriage clinics

- A RM specific protocol for diagnosis & treatment should be available so that all couples receive the same standard care which is in line with the information on the patient information brochure.
- Proper work-up for diagnosis and treatment is indicated.
- Unproven therapies should be used only in the setting of a properly conducted randomized trial.
- Couples with unexplained RM should be informed about their individual chances of success in a next pregnancy.
- A plan should be made how to offer good support during the first trimester in the next pregnancy.
- Because the chance of successful pregnancy still promising, treatment should focus on supportive care, where possible.
- Involve the male partner.
- Couple-based psychological care should be offered to couples with RM
- A RM clinic should preferably be organized in a way that couples will receive individual care from one doctor per couple.
- A patient information brochure must be available and preferably send to the couple before the first visit, so they know what to expect from the RM clinic.

Figure 2. Flowchart of logistical requirements for a RM clinic.



Doctor preferences

Diagnostic Tests

When a couple is seen at first consultation for RM, a detailed history is taken with regard to prior miscarriages and medical, obstetric, lifestyle, and family history. The decision to perform diagnostic investigations depends on the medical history. Diagnostic tests should only be carried out if the test can either give insight in the prognosis of an individual patient or if the established cause can be treated effectively. Diagnostic tests are performed and treatments are described despite a lack of evidence. Before introducing new diagnostic investigations in clinical practice, these tests should be evaluated thoroughly. The increasing costs of health care have been calling for elimination of ineffective medical testing (Berwick et al., 2012). Women with RM are often desperate and can be demanding. In clinical practice, it has been shown that too many diagnostic investigations and unproved treatments are performed in women with RM. This is a result of doctors who find it difficult to resist insistent women (Franssen et al., 2007).

Many of the diagnostic tests available for couples with RM give no information with regard to the prognosis in a future pregnancy. There is also a lack of evidence of potential treatment options in cases of a positive test result. Therefore, there is a need for evidenced-based guidelines, based on prospective cohort studies for prognostic purposes and randomized controlled trials (RCTs) to investigate the usefulness of the treatment options available for RM couples.

Work-Up

The guidelines of the Association of Early Pregnancy Units suggest that patients should not be subjected to tests without a proper plan of further follow-up and management (www.earlypregnancy.org.uk). It is important that both partners are aware of what is going to happen. The couple should be prepared for the fact that in a majority of cases no cause is found for the RM. Encourage the partner's participation and encourage the couple to talk about their fears and anxieties. Diagnostic testing should not be done only to reassure patients that something is being done. If diagnostic tests are performed, make sure that an explanation is given of all tests before taking blood samples. Reassure the couple that all known risk factors for RM will be explored. Discuss lifestyle end preconceptual care with the couple as available treatment plans. This prepares the couple for their future consultation. If a couple achieves a pregnancy, a doctor should arrange ultrasound scanning at 6 weeks' gestation and thereafter every week or 2 weeks, after discussing with the couple, for maternal assurance until seen in the antenatal booking clinic (www.earlypregnancy.org.uk). It is important to discuss a treatment plan for a future pregnancy with the couple. Not all couples want to have an ultrasound scan every other week. It is important that the doctor listens to the patient (Musters et al., 2011, Musters et al., 2013). Management of women with RM based on emotional support supplemurrent approach to this pro-ented by ultrasound scan in early pregnancy has success rates of between 70% and 80%. Individual changes depend on the number of

prior miscarriages and, more importantly, female age (Clifford et al., 1997; Liddell et al., 1991).

Scientific Research Programs

For more than 50% of women with RM, no underlying cause is found. This is frustrating for couples but also for clinicians and, therefore, it is tempting to start empiric treatment. Treatments of the RM population are often introduced without evaluating effectiveness. The only way to improve quality of care, however, is to apply an evidence-based approach.

Scientific research is necessary to study the effectiveness of new interventions, to study patient preferences, and to evaluate health care and costs or other outcomes. Cooperation between multiple centers, nationally and internationally, will facilitate research projects. Research networks will improve the infrastructure for scientific studies. This leads to a faster recruitment of patients in trials and better and faster implementation of study results but also standardization of care.

Patient data of women visiting the RM clinics should be recorded in databases to obtain large cohorts of RM patients. These anonymous data can be used for both scientific research projects and evaluation of health care.

Patient preferences

Psychological and Relational Consequences of Recurrent Miscarriage

Experiencing RM can be a traumatic event and is often accompanied by negative emotional distress (Lee et al., 1996). Different psychological and psychiatric effects can be induced. Feelings of grief, lowered self-esteem, guilt, anger, and depression and anxiety disorders are common after miscarriage but also during the subsequent pregnancy (Geller et al., 2004; Serrano et al., 2006). Anxiety is the predominant response to RM (Geller et al., Klock et al., 1997 Mevorach-Zussman et al., 2012). Different prevalence rates have been described for depressive symptoms, varying from 10% to 30% (Craig et al., 2002; Klock et al., 1997; Neugebauer et al., 1997; Thapar et al., 1992). Symptoms of anxiety and depression can be present for 6 months after a pregnancy loss (Conway et al., 2000; Geller et al., 2004; Neugebauer et al., 1997).

Psychological reactions and grief reactions after RM are different in women than in men. Women are more distressed than men after RM and men have lower anxiety levels (Beutel et al., 1996; Kagami et al., 2012; Serrano et al., 2006). Unlike women, men do not react with an increased depressive reaction. Men grieve but less intensely and enduringly than their partners (Serrano et al., 2006). Some men feel burdened by their wives' grief or depressive reactions (Conway et al., 2000). These gender differences may worsen or have a negative impact on the psychological adjustment and marital relationships in RM couples. Conflicting reactions may affect couples' interactions and promote depressive reactions in the women. Low marital adjustment and sexual changes after RM have been reported (Klock et al., 1997; Serrano et al., 2006). Data on whether a couple's relationship is adversely affected by RM are conflicting. One study does not describe a negative

impact on the relationship (Serrano et al., 2006). But there is also evidence that women with a history of RM were at a higher risk of their relationships ending compared with women without a history of miscarriage (Sugiura-Ogasawara et al., 2013).

Supportive Care

A majority of women with RM are classified as having unexplained RM. For these patients, no effective treatment intervention exists. Current guidelines advise supportive care for women with (unexplained) RM during the next pregnancy (Jauniaux et al., 2006). The guidelines of the Association of Early Pregnancy Units suggest that all staff members should be trained in emotional aspects of early pregnancy loss and offer bereavement counseling (www.earlypregnancy.org.uk). Offering so-called TLC, which consists of reassurance and psychological support, has led to an improvement in pregnancy outcome after unexplained RM in controlled studies (Brigham et al., 1999; Clifford et al., 1997; Liddel et al., 1991; Stray-Pedersen et al., 1984). Live birth rates up to 85% have been reported after supportive care. These studies were of low quality, however, because a clear definition of TLC is lacking and the study populations were too small. The supportive care offered in earlier studies varied widely and no clear definition of supportive care exists. How supportive care is defined and experienced depends on the perception of clinicians and patients and, therefore, is difficult to analyze as a clear outcome measure.

Because pregnancy-related fear may have a negative impact on the course of pregnancy and delivery, interventions to reduce anxiety are highly recommended (Fertl et al., 2009). It is not clear from the literature whether anxiety might be reduced due to supportive care or treatment in an RM clinic. One study showed that offering supportive care in a RM clinic does not significantly change anxiety levels (Mevorach-Zussman et al., 2012). This was only investigated in one study and the study population was too small to draw final conclusions about reduction of anxiety levels by supportive care.

There is limited evidence on the effect of RM clinics on psychological outcomes. Possible explanations for this are that supportive care should be more accurately defined and that analyzing supportive care as an outcome remains difficult.

Patient Preferences and Perspectives

Women's perceptions and preferences for supportive care options have been studied in qualitative and quantitative research (Musters et al., 2011; Musters et al., 2013). Women with RM prefer the following supportive care option for their next pregnancy: a plan with one doctor, who shows understanding, takes them seriously, has knowledge of their obstetric history, listens to them, gives information about RM, shows empathy, informs on progress, and enquires about emotional needs. Also, there is a need for ultrasound examination during symptoms, directly after a positive pregnancy test, and every 2 weeks. If a miscarriage occurs, most women prefer to talk to a medical or psychological professional afterward. A majority of women have a low preference for admission to a hospital (Musters et al., 2013).

Couples do not always experience the supportive care of health professionals as optimal (Conway et al., 2000). An important task for clinicians is to discuss with couples what their preferences are for supportive care and to make a plan for the next pregnancy. This improves patient-centered care.

Recommendations

RM patients are vulnerable and should receive good clinical supportive care. A RM clinic is necessary to provide this care. Couples can be guided by one doctor and a plan can be made together with the couples for a future pregnancy. Also, by working with a specific protocol, all patients receive the same standard care.

All women who present with RM should have access to a specialized RM clinic with appropriately trained health care professionals (RCOG, 2008).

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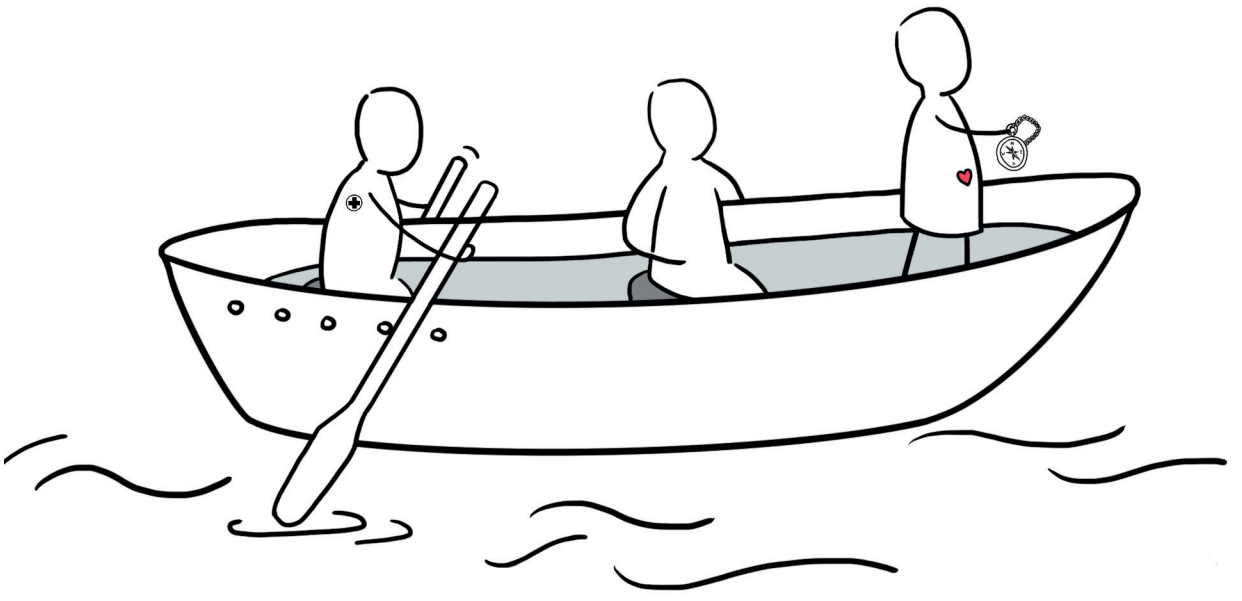

CHAPTER 8

Summary and implications for the future

In this thesis, 'How to organise patient-centered care in early pregnancy', we address patient-centered care for women and / or couples with complications in early pregnancy. Complications in early pregnancy include miscarriage, recurrent miscarriage and ectopic pregnancy. It is known that the loss of a desired pregnancy is a major life-event for women and/or couples which may lead to isolation, stress, anxiety, depression, grief and self-blame, post-traumatic stress disorder and even suicide for couples diagnosed with miscarriage (Coomarasamy et al., 2021). It has been generally acknowledged that patient-centered care in these specific women and / or couples implies the best possible medical care and psychological guidance for the loss of their desired pregnancy (Association of Early Pregnancy Units, 2007; Ministry of Health NSW, 2012; NHS NICE, 2012; RCOG, 2008). EPAUs are specialized units staffed by healthcare professionals competent to diagnose, treat and care for women with complications in early pregnancy. These professionals are trained in sensitive communication and breaking bad news (Association of Early Pregnancy Units, 2020).

The hypothesis underlying this thesis is that an early pregnancy assessment unit (EPAU) is the best organisational structure in providing patient-centered early pregnancy care. To confirm or refute this hypothesis, we investigated the actual patients' and doctors' perspectives on early pregnancy care. We did so by first focusing on how early pregnancy care was valued by women and/or their partners by means of a systematic review. This review identified which aspects of care were valued by women and/or their partners faced with miscarriage or recurrent miscarriage, and their perspectives on actual given care. This way, we identified potential improvement targets for miscarriage and recurrent miscarriage care. However, this review also revealed that there were no data available on care aspects important to and perspectives on actual care in women diagnosed with ectopic pregnancy. Therefore, the next topic of our research was to assess how women and their partners experienced the trajectory of diagnosis and treatment.

Thereafter, we looked at the doctors' perspectives on early pregnancy care. We examined whether the establishment of the EPAU in the Academic Medical Centre (AMC) Amsterdam (currently named Amsterdam UMC), the Netherlands in 2008 had improved the quality of early pregnancy care by assessing whether the pre-set goals, defined by clinicians, were reached in the period after the establishment. This proved to be the case, but since a before/after design study is open to bias -for instance coincidental changes in medical decision making over time- we realised that a better tool to measure quality of early pregnancy care would be to use evidence-based quality indicators. We thus developed a set of evidence-based quality indicators valued by international experts in the field of early pregnancy to measure care provided by EPAUs more accurately. We then used these indicators to compare early pregnancy care provided by hospitals with EPAU and by hospitals without an EPAU.

Lastly, we describe the organisation of patient-centered care in a recurrent miscarriage clinic, which serves a different purpose from EPAUs, as non-acute non-pregnant women are seen and only during office hours.

In **chapter 2** we present a systematic review which provided an overview of aspects of care valued by women and/or their partners faced with complications in early pregnancy. In July 2017 we searched five electronic databases for empirical quantitative or qualitative studies on patients' perspectives of early pregnancy care. We selected 27 studies -all focusing on miscarriage or recurrent miscarriage care- for inclusion in this review. In total, we identified 24 valued aspects of care, which all covered the eight dimensions for patient-centered care.

For 13 out of these 24 aspects of early pregnancy care the perspectives of women and / or their partners on actual care given by clinicians (service quality assessment) was available. The quantitative studies all documented problematic service quality for these 13 aspects of early pregnancy care, in other words the perspectives on actual care were 'negative' concerning these 13 aspects. We therefore considered these 13 aspects as potential targets for improvement in the patient-centeredness of miscarriage and recurrent miscarriage care.

Since quality assessment was not available for the remaining 11 valued aspects of care, we identified these as unclassified potential improvement targets. Targets under concern were the following: staff should acknowledge the human nature of the fetus rather than using distant medical terms; perform an ultrasound scan confirming the viability of the pregnancy during each acute visit to the clinic; appraise the patient as urgent rather than adding the patient to the queue; give understandable information; give information about care aspects to be expected after pregnancy loss; provide written information; recognise patient's physical pain; provide a waiting room separate from women scheduled for a routine pregnancy scan or antenatal visit; allocate patients to a bed in a quiet room during acute visits to the clinic; provide sufficient analgesia during curettage; and -most importantly- discuss patients' grief.

We divided the 13 potential targets for improvement into four groups. The first group, the so called very likely target of improvement, was classified if 75 - 100% of the women and / or their partners reported a problematic quality assessment on one of the 24 identified aspects of early pregnancy care. None of the potential targets were classified as a very likely target for improvement.

The second group, the so called likely target for improvement, was classified if 50 - 75% of the women and / or their partners reported a problematic quality assessment. We identified four likely targets for improvement. These targets for improvement were: provision of understandable information about the etiology of early pregnancy loss; staff discussing patients' distress; informing patients on pregnancy loss in the presence of their partner or friend (a significant other); and staff performing follow-up phone calls to support their patients after a miscarriage.

The third group, the so called unlikely target for improvement, was classified if 25 - 50% of the women and / or their partners reported a problematic quality assessment. We identified six unlikely targets for improvement. These targets for improvement were: treating patients as an individual person experiencing a significant live event rather than a common condition; provision of information about the expected degree of pain

and bleeding while awaiting spontaneous miscarriage; provision of information about planning future pregnancies; provision of information about support groups; give women and / or couples time in a private room to cope with the diagnosis of pregnancy loss; and staff showing empathy for patients' emotional pain.

The fourth group, the so called very unlikely targets for improvement, was classified if 0 - 25% of the women and / or their partners reported a problematic quality assessment. We identified three very unlikely targets for improvement. These targets were: appraise the patient as exceptional rather than one of many by the clinicians; offer of a follow-up medical consult after pregnancy loss; and limit the duration of waiting times in waiting rooms.

It is important for clinicians to realise that women and their partners undergoing a miscarriage experience a significant live event and appreciate an individual approach. We feel that staff members working in the field of early pregnancy may benefit from this literature review since it describes in detail what aspects of early pregnancy care are relevant in a patient-centered approach.

In **chapter 3** we assessed how women and their partners experience diagnosis, treatment and follow-up of an ectopic pregnancy. We interviewed eight women who had been diagnosed with and treated for an ectopic pregnancy in the Amsterdam UMC between April and November 2021. To explore which aspects of care they valued we asked women to share their experiences of the diagnosis, treatment and follow-up of their ectopic pregnancy.

Women valued specific information on the diagnosis and treatment of ectopic pregnancy and on implications for their fertility in both an oral and written format. Women also appreciated sharing decisions with an empathic clinician who provided clear information. Women shared negative experiences with the waiting time after referral for a pregnancy test and/or an ultrasound scan and would have preferred to be seen directly by a gynaecologist instead of a general practitioner or staff from the emergency room. All women shared that adequate communication would have lowered their level of frustration around waiting times.

We conclude that patient-centeredness of ectopic pregnancy care can be improved in particular by direct referral to an EPAU. In the EPAU, staff should adhere to recent evidence-based guidelines, and should be trained in communication skills to address the issues mentioned by women in this study.

Chapter 4 analyses the effect of the introduction of the first EPAU in the university hospital Amsterdam UMC in 2008. The aims were to decrease the percentage of emergency inpatient admissions, to decrease the percentage of surgical management for miscarriage and ectopic pregnancy, to decrease the number of repeat consultations and to decrease the number of karyotyping of couples with recurrent miscarriage and to reduce costs. To explore whether these goals as measurable derivates were met, we

conducted an observational study. We measured early pregnancy care within three time periods; 2006, 2009 and 2012.

Hospital admission was necessary for 14% of women who had experienced a miscarriage in 2006, whereas in 2009 and 2012 no women were admitted. Surgical management rate for miscarriage decreased from 79% (2006) to 6% (2009) and 28% (2012). Surgical management rate for ectopic pregnancy decreased from 50% (2006) to 25% (2009) and 29% (2012). Karyotyping of couples who had experienced recurrent miscarriage decreased from 100% (2006) to 17% (2009) and 33% (2012). The mean total cost per woman treated in 2006 was €1111 (95% CI €808 to 1426), €436 (95% CI €307 to 590) in 2009 and €633 (95% CI €586 to 788) in 2012.

We conclude that the aimed targets were met and that an EPAU has a positive effect on the quality of care provided to women with complications in early pregnancy.

In **chapter 5** our aim was to develop a set of valid guideline based quality indicators for EPAUs, since there is still considerable variation with respect to access to services and quality of early pregnancy care between EPAUs. Quality indicators can measure and compare quality of early pregnancy care between EPAUs. We used the stepwise RAND-modified Delphi method to develop valid quality indicators based on four available guidelines on the organisation of early pregnancy care. This method entails four steps; in step 1, two authors extracted 119 recommendations from the guidelines, independent from each other. Subsequently, they categorised the recommendations into four domains, e.g. recommendations concerning patient (n=13), doctor (n=18), process (n=37) and organisational (n=51) aspects of care. We presented the extracted recommendations in a digital questionnaire. In step 2, we presented this digital questionnaire to 11 international experts in the field of early pregnancy. All members of the expert panel individually scored each recommendation on a nine-point Likert scale, ranging from 1, being hardly relevant, to 9, being extremely relevant. The expert panel members were also allowed to add new recommendations with their underlying reasoning. In addition, the expert panel prioritised the recommendations per domain using a top-five ranking system.

In total, 10 out of 11 questionnaires (91%) were returned by the expert panel and were fully completed. One gynaecologist initially agreed to participate, but withdrew from the study due to lack of time. Eleven recommendations received a high median score and top 5 score above the 75th percentile and were selected as key recommendations. The expert panel reassessed 15 high score recommendations and top 5 score between the 50th and 75th percentile as well as one high score recommendation without consensus. Eight of these 16 recommendations were selected in the second round as key recommendations. In step 3, we presented a second digital survey with the potential key recommendations as well as the recommendations with a high median score (8 or 9) and top 5 score between the 50th and 75th percentile to the expert panel. We asked the expert panel members whether they agreed with the selected potential key recommendations. Also, we asked the expert panel if the recommendations with a top 5 score between the 50th and 75th percentile should also be included as a key recommendation or not. We

selected the 19 recommendations as a key recommendation which we transcribed into a set of 19 quality indicators. These 19 quality indicators state that women referred to an EPAU could be seen within 24 hours and receive a clear explanation on treatment options, that designated senior staff members could be responsible for the unit and working staff members could have had ultrasound training, that protocols could be available for daily practice covering all treatment options for miscarriage and ectopic pregnancy and that an EPAU could have access to urine pregnancy testing and serum hCG assays.

We feel that our developed set of 19 evidence-based quality indicators derived from four international guidelines can be used as the foundation for setting up and running an EPAU.

In **chapter 6** we assessed how hospitals with an EPAU and hospitals without an EPAU in the Netherlands adhere to the developed guideline based quality indicators. We performed a qualitative interview study with the heads of the EPAU's or the OBGYN departments and assessed the adherence to 19 indicators in four hospitals with and four hospitals without an EPAU in the Netherlands. We developed a checklist to address all 19 quality indicators and used this as a guidance during the interview sessions. Concerning two sub-questions, i.e. 'Are women who are referred to an EPAU seen within the next 24 hours?' and 'Do women receive clear explanation on treatment options, which means face-to-face explanation as well as a written patient information leaflet' we wanted to collect data on women with complications in early pregnancy (defined as vaginal bleeding and/or abdominal pain or abnormal ultrasound findings on the first trimester scan) who were seen in a 12 month period between January 1st, 2018 to December 31st, 2018 to check for actual given care. For each quality indicator, a ratio for guideline adherence was calculated for hospitals with and without an EPAU. We defined non-adherence as less than 100% adherence. Non-adherence was seen on three indicators (16%, 3/19) for hospitals with an EPAU and on five indicators (26%, 5/19) for hospitals without an EPAU. A standard digital system for the registration of ultrasound findings and clear explanation on all treatment options was present in all hospitals with an EPAU (100%) against in three hospitals without an EPAU (75%). A certified ultrasound training for working staff members was not offered in all hospitals (0%). A discrete waiting area was present in one hospital with an EPAU (25%) against in none of the hospitals without an EPAU (0%). Self-referrals from women with a previous ectopic pregnancy was accepted in one hospital with and in one hospital without an EPAU (both 25%).

We conclude that early pregnancy care in the Netherlands is relatively well organised. Nevertheless, EPAUs do have an added value in early pregnancy care by better adherence to the guideline based quality indicators.

In **chapter 7** we present an explorative search of the literature to provide an overview of logistical requirements, doctors' preferences and patients' preferences for a recurrent miscarriage clinic. A recurrent miscarriage clinic offers specialised investigation and treatment for women with a history of recurrent first- and second-trimester miscarriages

on a non-acute outpatient basis. A recurrent miscarriage clinic differs from an EPAU due to this non-acute day-time setting for non-pregnant women.

The data obtained from the literature led to the following recommendations: for the logistical requirements, whenever possible, avoid locating a recurrent miscarriage clinic near an antenatal clinic. There should always be a consultant present with a special interest and trained in emotional aspects of pregnancy loss and recurrent miscarriage. Treatment strategies should be designed together with the couple, preferably provided by the same doctor. The goal is that all women and / or couples receive the same standardised care by working with a specific protocol.

We conclude that all women with recurrent miscarriage should have access to a specialised recurrent miscarriage clinic.

Implications for clinical practice

Our overall conclusion on the role of EPAUs in early pregnancy care is that these units do have an added value especially from the patients' perspective point of view. This leads to the following recommendations:

First, we recommend all clinicians working in the field of early pregnancy to embrace the concept of an EPAU and a recurrent miscarriage clinic. All women and / or couples should receive evidence-based patient-centered care from appropriately trained clinicians. Clinicians should realise that women and their partners undergoing a miscarriage or ectopic pregnancy experience a significant life event and appreciate an individual approach. Clinicians should be open for shared decision making and pay attention especially to understandable information provision about the etiology of pregnancy loss and the inevitable waiting time for reaching diagnosis and/or treatment; discuss patients' distress; inform patients on pregnancy loss in the presence of their partner or friend (significant other); to perform follow-up phone calls to support women and/or couples after miscarriage; and to perform follow-up phone calls to address the loss of a desired pregnancy for women and/or couples after a miscarriage or ectopic pregnancy. On an organisational level, clinicians should use a separate blue room when available for women or couples to cope with the bad news.

Second, we recommend clinicians to use our guideline-based quality indicators to set up an EPAU in their clinic or to improve the quality of their EPAU. From a doctors' perspective, the most important recommendations for early pregnancy care are that women who are referred to an EPAU are seen within 24 hours and receive a clear explanation on all treatment options, that designated senior staff members are responsible for the unit, that working staff members have had certified ultrasound training, that protocols are available for daily practice covering all treatment options for miscarriage and ectopic pregnancy and that an EPAU has access to urine pregnancy testing and serum hCG assays.

Implications for future research

In this thesis we studied both patients' and doctors' perspectives on early pregnancy care separately. Future studies could focus on the development of quality indicators with both patients and clinicians together in an expert panel. These indicators could provide clinicians a way to further improve patient-centered early pregnancy care in their clinic.

The next step following our qualitative research on the experiences of women on diagnosis, treatment and follow-up of ectopic pregnancy would be to quantify this data by developing a questionnaire based on the results and to apply this questionnaire to a larger cohort of women and couples diagnosed with ectopic pregnancy.

With our studies on the development of quideline-based quality indicators and the measurement of actual early pregnancy care we took the first two steps for the measurement of quality of care. A next step would be to identify barriers and facilitators, and to develop a strategy for the implementation of guidelines in clinical practice.

We compared actual early pregnancy care between hospitals with and without an EPAU in the Netherlands. Future research could especially focus on the comparison of early pregnancy care between hospitals with and without an EPAU in a more extensive setting of international collaboration, also taking into account financial costs and patient satisfaction.

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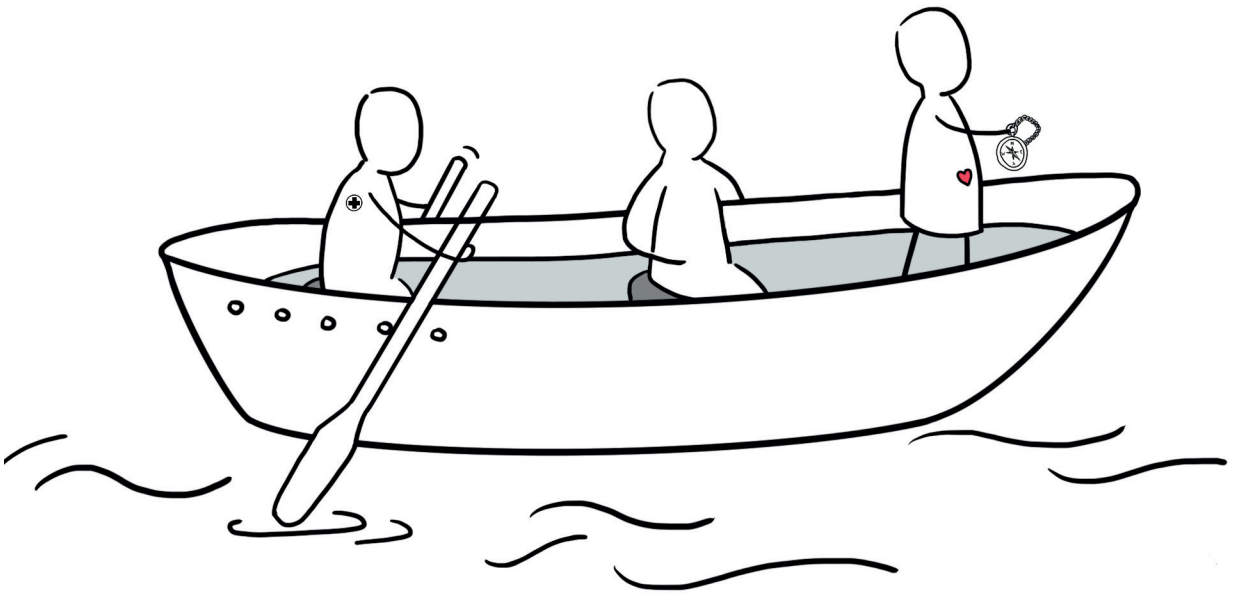

CHAPTER 9

Nederlandse samenvatting

In dit proefschrift, 'How to organise patient-centered care in early pregnancy', bespreken we patiëntgerichte zorg voor vrouwen en/of paren met complicaties in de jonge zwangerschap. Deze complicaties in de jonge zwangerschap zijn miskraam, herhaalde miskraam of een buitenbaarmoederlijke zwangerschap. Het verlies van een zwangerschap is een belangrijke levensgebeurtenis voor vrouwen en/of paren wat soms kan leiden tot isolatie, stress, angst, depressie, rouw, post-traumatische stressstoornis en zelfs zelfmoord bij koppels die een miskraam doormaken (Coomarasamy et al., 2021). Het wordt algemeen erkend dat voor deze groep vrouwen en/of paren patiëntgerichte zorg de best mogelijke medische zorg en psychologische begeleiding biedt voor het verlies van een gewenste zwangerschap (Association of Early Pregnancy Units, 2007; Ministry of Health NSW, 2012; NHS NICE, 2012; RCOG, 2008). Een jonge zwangerschapsunit (JZU) is een gespecialiseerde unit waar clinici werken die ervaring hebben met het diagnosticeren, behandelen en zorgen voor vrouwen met complicaties in de jonge zwangerschap.

De hypothese van dit proefschrift is dat een JZU de best mogelijke afdeling is om deze patiëntgerichte zorg te kunnen bieden. Om deze hypothese te bevestigen of te verwerpen, hebben we het perspectief van patiënten en van artsen op jonge zwangerschapszorg onderzocht.

We hebben eerst gekeken naar het perspectief van de vrouwen en waar mogelijk hun partners op jonge zwangerschapszorg. Dit systematische review geeft een overzicht van aspecten van kwaliteit van zorg die belangrijk zijn voor vrouwen en/of hun partners die gediagnosticeerd zijn met een miskraam of herhaalde miskramen en geeft aan hoe zij de geleverde zorg ervaren hebben. Op deze manier hebben we potentiele verbeterpunten geïdentificeerd. Ook kwam naar voren dat dergelijke gegevens niet beschikbaar zijn van vrouwen die gediagnosticeerd zijn met een buitenbaarmoederlijke zwangerschap. Het perspectief van deze vrouwen hebben we met een kwalitatieve studie onderzocht. De volgende stap was om te kijken naar het perspectief van de dokter op jonge zwangerschapszorg. We hebben onderzocht of de oprichting van een JZU in het Academisch Medisch Centrum (AMC) Amsterdam (nu Amsterdam UMC) in 2008 de kwaliteit van de jonge zwangerschapszorg heeft verbeterd. Dit hebben we gedaan door te onderzoeken of door artsen gedefinieerde vooropgestelde doelen zijn behaald in de periode na de oprichting van de unit. Dit bleek het geval te zijn. Echter, deze voor / na onderzoeksopzet kan beïnvloed worden door externe factoren, zoals het implementeren van nieuwe richtlijnen en protocollen. We realiseerden ons dat we vervolgens op wetenschappelijk bewijs gebaseerde kwaliteitsindicatoren konden gebruiken om de kwaliteit van jonge zwangerschapszorg te meten. Daarom hebben we, in samenwerking met internationale experts, kwaliteitsindicatoren ontwikkeld op het gebied van jonge zwangerschapszorg om de geleverde zorg in JZUs te kunnen onderzoeken. Daarna hebben we deze indicatoren gebruikt om de geleverde jonge zwangerschapszorg te vergelijken tussen ziekenhuizen met en zonder een JZU.

Tot slot beschrijven we de organisatie van patiëntgerichte zorg in een herhaalde miskraam kliniek. Deze kliniek heeft een ander doel dan de JZU, omdat daar in een niet

acute setting evaluatie en begeleiding plaatsvindt van niet zwangere vrouwen tijdens kantoortijden.

In **hoofdstuk 2** tonen we de resultaten van een systematische review, dat een overzicht geeft van zorgaspecten die belangrijk zijn voor vrouwen en/of hun partners die geconfronteerd worden met complicaties in de jonge zwangerschap. In juli 2017 hebben we vijf literatuur databases doorzocht naar gepubliceerde kwantitatieve en kwalitatieve studies over het perspectief van de patiënt op jonge zwangerschapszorg. We hebben 27 studies geïncludeerd voor ons review, die allemaal betrekking hebben op de zorg bij miskraam of herhaalde miskraam. In totaal hebben we 24 zorgaspecten geïdentificeerd, die allemaal vallen onder de acht dimensies van patiëntgerichte zorg.

Voor 13 van deze 24 zorgaspecten was bekend hoe de vrouwen en/of hun partners die specifieke zorg hebben ervaren (beoordeling van de service kwaliteit). De kwantitatieve studies toonden voor deze 13 zorgaspecten van jonge zwangerschapszorg allemaal een problematische beoordeling van de geleverde zorg. Met andere woorden, het perspectief op de geboden zorg was 'negatief'. Daarom hebben we deze 13 zorgaspecten allemaal aangemerkt als potentiële verbeterpunten in de patiëntgerichte miskraam en herhaalde miskraam zorg.

Omdat de beoordeling van de kwaliteit van de andere 11 zorgaspecten niet beschikbaar was, hebben we deze aangemerkt als niet geclassificeerde potentiële verbeterpunten. Dit betrof de volgende zorgaspecten: gebruik geen afstandelijke medische termen voor de foetus; maak een echo bij elke bezoek aan het ziekenhuis om de vitaliteit van de zwangerschap te beoordelen; behandel de patiënt als een spoed patiënt in plaats van haar te laten wachten; geef informatie in begrijpelijke taal; geef informatie over wat de patiënt kan verwachten na het verlies van een zwangerschap; zorg voor schriftelijke informatie; erken de fysieke pijn van patiënten; zorg voor een aparte wachtruimte, zodat vrouwen met een miskraam niet tussen vrouwen hoeven te zitten die komen voor een reguliere echo of zwangerschapscontrole; zorg bij opname van een patiënt voor een bed in een rustige ruimte; zorg voor voldoende pijnstilling tijdens een vacuümcurettage; en, erg belangrijk, maak het rouwproces van de patiënt bespreekbaar.

We verdeelden de 13 potentiële verbeteraspecten in vier groepen. De eerste groep, de zeer waarschijnlijke verbeteraspecten, werd als zodanig geclassificeerd indien 75 – 100% van de vrouwen en/of hun partners een problematische kwaliteit van de geleverde zorgrapporteerden op een van de 13 jonge zwangerschapszorg aspecten. Geen van deze aspecten werd geïdentificeerd als een zeer waarschijnlijk verbeteraspect.

De tweede groep, de waarschijnlijke verbeteraspecten, werd geclassificeerd indien 50 – 75% van de vrouwen en/of hun partners een problematische kwaliteit van de geleverde zorg rapporteerden. Er werden vier waarschijnlijke verbeterpunten geïdentificeerd. Deze verbeterpunten waren: het geven van begrijpelijke informatie over de etiologie van het verlies van een jonge zwangerschap; het bespreekbaar maken door de artsen van stress bij de patiënten; uitleg geven over de diagnose in het bijzijn van de partner of een vriend

(*significant other*); en het plannen van een telefonische follow-up afspraak met de arts ter ondersteuning van de patiënt na een miskraam.

De derde groep, genaamd de onwaarschijnlijke verbeteraspecten, werd geclassificeerd indien 25 – 50% van de vrouwen en/of hun partners een problematische kwaliteit van de geleverde zorg rapporteerden. We identificeerden zes onwaarschijnlijke verbeteraspecten: behandel de patiënt als een individu die een significante levensgebeurtenis doormaakt in plaats van een reguliere aandoening; informeer wat zij kan verwachten ten aanzien van buikpijn en vaginaal bloedverlies tijdens het doormaken van een miskraam; informeer over het nastreven van een toekomstige zwangerschap; informeer over het bestaan van supportgroepen; geef vrouwen en/of paren tijd in een aparte kamer om het nieuws van de diagnose te laten bezinken; en toon empathie naar de patiënt.

De vierde groep, genaamd de zeer onwaarschijnlijke verbeteraspecten, werd geclassificeerd indien 0 – 25% van de vrouwen en/of partners een problematische kwaliteit van de geleverde zorg rapporteerden. We identificeerden drie zeer onwaarschijnlijke verbeteraspecten: beschouw de patiënt als uitzonderlijk in plaats van één van velen; bied een fysiek follow-up consult aan na het verlies van een zwangerschap; en houd de wachttijd in de wachtkamer zo kort mogelijk.

Het is belangrijk dat artsen zich realiseren dat vrouwen en hun partners die een miskraam meemaken dit ervaren als een zeer belangrijke levensgebeurtenis en dat ze een individuele aanpak waarderen. We denken dat met behulp van deze studie artsen die werken in het gebied van jonge zwangerschap de patiëntgerichte zorg kunnen optimaliseren omdat de aspecten die daarvoor van belang zijn worden beschreven.

In **hoofdstuk 3** hebben we geëxploreerd hoe vrouwen en hun partners de diagnose, behandeling en poliklinische nacontrole van een buitenbaarmoederlijke zwangerschap hebben ervaren. We hebben acht vrouwen geïnterviewd die gediagnosticeerd en behandeld waren voor een buitenbaarmoederlijke zwangerschap in het Amsterdam UMC tussen April en November 2021. Om te onderzoeken welke zorgaspecten deze groep vrouwen belangrijk vindt, hebben we de vrouwen gevraagd om hun ervaringen te delen ten aanzien van de diagnose, behandeling en nacontrole van hun buitenbaarmoederlijke zwangerschap.

Vrouwen waardeerden specifieke mondelinge en geschreven informatie over de diagnose en behandeling van een buitenbaarmoederlijke zwangerschap en over de gevolgen voor hun toekomstige fertiliteit. De vrouwen waardeerden ook een empathische arts die duidelijke informatie geeft en die open staat voor de mening van de patiënt. De vrouwen hadden negatieve ervaringen met de wachttijden voor een zwangerschapstest in het bloed en/of een echo en zouden bij voorkeur direct door een gynaecoloog gezien willen worden in plaats van een eerste evaluatie door een huisarts of een arts werkzaam op de eerste hulp. Alle vrouwen gaven aan dat adequate communicatie hun frustratie rondom de wachttijden zou hebben verminderd.

We concluderen dat de patiëntgerichte buitenbaarmoederlijke zwangerschapszorg verbeterd zou moeten worden in het bijzonder door directe verwijzing naar een JZU. Clinici die werkzaam zijn op de JZU zouden zich moeten houden aan de meest recente richtlijnen en zouden getraind moeten worden in hun communicatie vaardigheden om regelmatig de reden en de duur van de wachttijd te bespreken.

In **hoofdstuk 4** beschrijven we het effect van de oprichting van de eerste JZU in een universitair ziekenhuis (AMC) in Nederland in 2008. De vooropgestelde doelen waren het verminderen van het aantal ziekenhuisopnames, het verminderen van het aantal chirurgische behandelingen voor miskramen en buitenbaarmoederlijke zwangerschappen, het verminderen van het aantal herhaalconsulten, het verminderen van het aantal karyotyperingen voor paren met herhaalde miskramen en het reduceren van de kosten. We zijn gestart met een observationele studie om te onderzoeken of deze doelen ook daadwerkelijk zijn behaald. We hebben op drie verschillende momenten gekeken: 2006, 2009 en 2012.

In 2006 was opname in het ziekenhuis noodzakelijk voor 14% van de vrouwen die gediagnosticeerd waren met een miskraam, terwijl in 2009 en 2012 niemand was opgenomen. Het aandeel van de chirurgische behandelingen voor een miskraam daalde van 79% (2006) naar 6% (2009) en 28% (2012). Het aandeel van de chirurgische behandelingen voor een buitenbaarmoederlijke zwangerschap daalde van 50% (2006) naar 25% (2009) en 29% (2012). Het aantal karyotyperingen voor paren met herhaalde miskramen daalde van 100% (2006) naar 17% (2009) en 33% (2012). De gemiddelde kosten per behandelde vrouw bedroeg in 2006 €1.111 (95% BI €808 - 1.426), €436 (95% BI €307 - 590) in 2009 en €633 (95% BI €586 - 788) in 2012.

We kunnen concluderen dat de vooropgestelde doelen behaald zijn en dat een JZU een positief effect heeft op de kwaliteit van zorg voor vrouwen met complicaties in de jonge zwangerschap.

In **hoofdstuk 5** hebben we op wetenschappelijk bewijs gebaseerde kwaliteitsindicatoren ontwikkeld voor het meten van de zorg die geleverd wordt door JZUs, omdat er verschil zit in de toegankelijkheid en kwaliteit van zorg tussen de verschillende units. Deze kwaliteitsindicatoren kunnen de kwaliteit van zorg meten en vergelijken. We hebben de stapsgewijze door RAND opgestelde Delphi methode gebruikt om valide kwaliteitsindicatoren te ontwikkelen, gebaseerd op vier beschikbare richtlijnen voor de organisatie van jonge zwangerschapszorg. Deze methode bevat vier stappen. In stap 1 hebben twee auteurs, onafhankelijk van elkaar, 119 aanbevelingen uit de richtlijnen geselecteerd. Daarna zijn deze aanbevelingen onderverdeeld in vier domeinen, te weten aanbevelingen voor de zorg die betrekking hebben op de patiënten (n=13), op de dokter (n=18), op het proces (n=37) en op de organisatie (n=51). Deze aanbevelingen werden omgezet in een digitale vragenlijst en deze werd in stap 2 gepresenteerd aan 11 internationale experts op het gebied van jonge zwangerschap. Alle leden van het expert panel scoorden individueel elke aanbeveling op een negen-punten Likert schaal, lopend

van 1, niet relevant, tot 9, extreem relevant. De leden van het expert panel konden ook nieuwe onderbouwde aanbevelingen toevoegen. Daarnaast werd van elke expert gevraagd om de aanbevelingen per domein te prioriteren in een top vijf.

In totaal werden 10 van de 11 vragenlijsten (91%) compleet teruggestuurd. Eén gynaecoloog had in eerste instantie toegezegd om te participeren in deze studie, maar trok zich later toch terug in verband met tijdsgebrek. Elf aanbevelingen kregen een hoge gemiddelde score en een top 5 score boven het 75ste percentiel en werden daarom geselecteerd als belangrijkste aanbevelingen. Het expert panel werd gevraagd om 15 hoog scorende aanbevelingen en met een top 5 score tussen het 50ste en 75ste percentiel, evenals een hoge scorende aanbeveling zonder consensus nogmaals te evalueren. In deze tweede ronde werden acht van deze in totaal 16 aanbevelingen geselecteerd als belangrijkste aanbevelingen. In stap 3 presenteerden we een tweede digitale vragenlijst met de potentieel belangrijkste aanbevelingen en de aanbevelingen met een hoge gemiddelde score (8 of 9) en een top 5 score tussen het 50ste en 75ste percentiel. Er werd gevraagd aan de leden van het expert panel of zij akkoord gingen met de geselecteerde potentieel belangrijkste aanbevelingen. Er werden uiteindelijk 19 aanbevelingen geselecteerd die werden omgezet in 19 kwaliteitsindicatoren. Deze 19 kwaliteitsindicatoren zeggen dat vrouwen die verwezen worden naar een JZU bij voorkeur binnen 24 uur gezien zouden moeten worden en duidelijke uitleg zouden moeten krijgen over de verschillende beschikbare behandelopties. Een senior medewerker zou verantwoordelijk moeten zijn voor de unit en artsen die werken bij deze unit zouden een echo training moeten hebben gehad, protocollen voor de dagelijkse praktijk zouden beschikbaar moeten zijn met daarin alle behandelopties voor miskraam en een buitenbaarmoederlijke zwangerschap en een JZU zou toegang moeten kunnen geven voor het testen op een zwangerschap in de urine en in het bloed.

We denken dat de 19 ontwikkelde kwaliteitsindicatoren gebaseerd op vier internationale richtlijnen gebruikt kunnen worden als een basis voor het opzetten van en het runnen van een JZU.

In **hoofdstuk 6** beschrijven we een kwalitatieve studie en kijken we hoe ziekenhuizen met een JZU en ziekenhuizen zonder een JZU zich houden aan de ontwikkelde, op richtlijnen gebaseerde, kwaliteitsindicatoren. We hebben een kwalitatieve interview studie opgezet met eindverantwoordelijken van de JZUs of gynaecologie afdelingen van ziekenhuizen met en zonder een JZU, om te meten hoe goed zij zich houden aan de 19 kwaliteitsindicatoren. We ontwikkelden een vragenlijst om alle 19 kwaliteitsindicatoren aan bod te laten komen en hebben deze gebruikt als basis van ons interview. Voor de twee sub-vragen; 'Worden de vrouwen die verwezen worden naar een JZU gezien binnen de volgende 24 uur?' en 'Krijgen de vrouwen heldere uitleg ten aanzien van de beschikbare behandelopties, zowel face-to-face als een schriftelijk in de vorm van een patiënt informatie folder?' wilden we data verzamelen van vrouwen met problemen in de vroege zwangerschap (gedefinieerd als vaginale bloeding en/of pijn in het abdomen of een afwijkende echobevinding bij de eerste echo) die gezien werden in de periode

van 1 Januari 2018 tot en met 31 December 2018. Voor elke kwaliteitsindicator werd een ratio berekend voor ziekenhuizen met en zonder een JZU. We definieerden het niet naleven van een indicator als een naleving van minder dan 100%. Het niet naleven werd gezien bij drie indicatoren (16%, 3/19) voor ziekenhuizen met een JZU en vijf indicatoren (26%, 5/19) voor ziekenhuizen zonder een JZU. Een gestandaardiseerd digitaal systeem voor het registreren van echobevindingen en heldere uitleg voor alle behandelopties was aanwezig in alle ziekenhuizen met een JZU (100%), tegen drie ziekenhuizen zonder een JZU (75%). Geen van de geïncludeerde ziekenhuizen bood een gecertificeerde echotraining voor artsen werkzaam op de afdeling (0%). Een discrete wachtruimte was aanwezig in één ziekenhuis met een JZU (25%) tegen geen ziekenhuis zonder een JZU (0%). Vrouwen met in de voorgeschiedenis een buitenbaarmoederlijke zwangerschap konden zichzelf verwijzen naar een ziekenhuis met een JZU en een ziekenhuis zonder een JZU (beiden 25%).

We concluderen dat jonge zwangerschapszorg in Nederland relatief goed is georganiseerd. Daarentegen hebben JZUs een toegevoegde waarde voor de jonge zwangerschapszorg, doordat ze zich beter aan de ontwikkelde kwaliteitsindicatoren houden.

In **hoofdstuk 7** presenteren we een exploratieve zoektocht in de literatuur om een overzicht te geven van de logistieke aanbevelingen, voorkeuren van patiënten en van artsen voor een herhaalde miskraam kliniek. Een herhaalde miskraam kliniek biedt niet acute, gespecialiseerde onderzoeks- en behandelmogelijkheden voor vrouwen met herhaalde eerste- en tweede trimester miskramen. Een herhaalde miskraam kliniek verschilt van een JZU door de niet acute setting voor niet zwangere vrouwen tijdens kantoortijden.

De volgende aanbevelingen kwamen naar voren uit de literatuur: probeer, indien mogelijk, een herhaalde miskraam kliniek niet naast een verloskunde polikliniek te plaatsen. Er dient elke dag een gynaecoloog aanwezig te zijn, die gespecialiseerd is en getraind is in de emotionele aspecten van het verlies van een zwangerschap en herhaalde miskramen. Een behandelplan zou moeten worden opgesteld in samenspraak met het koppel, bij voorkeur door dezelfde dokter. Het doel is om alle vrouwen en/of paren dezelfde gestandaardiseerde zorg te leveren door met een specifiek protocol te werken.

We concluderen dat alle vrouwen met herhaalde miskramen toegang zouden moeten hebben tot een gespecialiseerde herhaalde miskraam kliniek.

Implicaties voor de klinische praktijk

De uiteindelijke conclusie van ons onderzoek naar de rol van JZUs in jonge zwangerschapszorg is dat deze units, vooral vanuit het perspectief van de patiënt, een toegevoegde waarde hebben. Dit leidt ons tot de volgende aanbevelingen:

Ten eerste raden we alle artsen die werken op het gebied van de jonge zwangerschap aan om het concept van een JZU alsmede een herhaalde miskraam kliniek te gebruiken.

Alle vrouwen en/of paren zouden op wetenschappelijk bewijs gebaseerde patiëntgerichte zorg moeten ontvangen van goed getrainde artsen. Artsen zouden zich moeten realiseren dat vrouwen en hun partners die gediagnosticeerd zijn met een miskraam of buitenbaarmoederlijke zwangerschap een zeer belangrijke levensgebeurtenis doormaken en een individueel opgesteld plan voor in een volgende zwangerschap waarderen. Daarnaast zouden artsen open moeten staan voor de mening van de patiënt en extra aandacht moeten besteden aan het geven van begrijpelijke informatie over de etiologie van het zwangerschapsverlies en de onvermijdelijke wachttijden tot het stellen van een diagnose of het starten van een behandeling, het bespreken van stress bij patiënten, het informeren van de patiënten over het verlies van hun zwangerschap in het bijzijn van de partner of een vriend (significant other) en het inplannen van een telefonische vervolg afspraak om vrouwen en/of paren te steunen na de miskraam en om het verlies van een gewenste zwangerschap te bespreken. Op het gebied van organisatie zouden artsen een aparte ruimte, indien beschikbaar, moeten gebruiken om daar vrouwen of koppels het slechte nieuws te laten bezinken en verwerken.

Ten tweede raden we artsen aan om de ontwikkelde kwaliteitsindicatoren, die gebaseerd zijn op bestaande richtlijnen, te gebruiken voor het opzetten van een JZU in hun kliniek, of om de kwaliteit van hun JZU te bevorderen. De meest belangrijke aanbevelingen vanuit het perspectief van de dokter voor de zorg rondom de jonge zwangerschap zijn dat vrouwen die verwezen worden naar een JZU gezien zouden moeten worden binnen 24 uur en heldere uitleg zouden moeten krijgen ten aanzien van alle behandelopties, een senior staflid zou verantwoordelijk moeten zijn voor de unit, artsen die werken op de unit zouden een gecertificeerde echotraining moeten hebben gehad, protocollen moeten beschikbaar zijn voor de dagelijkse praktijk die alle opties voor miskraam en buitenbaarmoederlijke zwangerschap bieden en dat een JZU toegang biedt voor het testen op een zwangerschap in zowel de urine als in het serum.

Implicaties voor toekomstig onderzoek

In dit onderzoek hebben we zowel het perspectief op de jonge zwangerschapszorg van de patiënt als dat van de dokter onderzocht. Toekomstige studies kunnen focussen op het ontwikkelen van kwaliteitsindicatoren met patiënten en artsen samen in een expert panel. Deze indicatoren geven artsen de mogelijkheid om de patiëntgerichte jonge zwangerschapszorg te verbeteren in hun kliniek.

Een volgende stap naar aanleiding van ons kwalitatieve onderzoek naar de ervaringen van vrouwen die gediagnosticeerd en behandeld zijn voor een buitenbaarmoederlijke zwangerschap zou zijn om deze data te kwantificeren om een vragenlijst op te stellen en zo een grotere groep vrouwen te onderzoeken die gediagnosticeerd zijn met een buitenbaarmoederlijke zwangerschap.

Onze studies richtten zich op het ontwikkelen van de kwaliteitsindicatoren en het meten van de jonge zwangerschapszorg in Nederland en verschaften daarmee de eerste twee stappen voor het meten van de kwaliteit van zorg. De volgende stap zou

zijn om barrières te identificeren en om een strategie te ontwikkelen om richtlijnen te implementeren in de klinische praktijk.

We vergeleken bestaande jonge zwangerschapszorg tussen ziekenhuizen mét en ziekenhuizen zonder een JZU in Nederland. Toekomstige studies kunnen focussen op het vergelijken van jonge zwangerschapszorg tussen ziekenhuizen met en zonder een JZU in een internationale setting, daarbij ook rekening houdend met patiënt tevredenheid en financiële aspecten.

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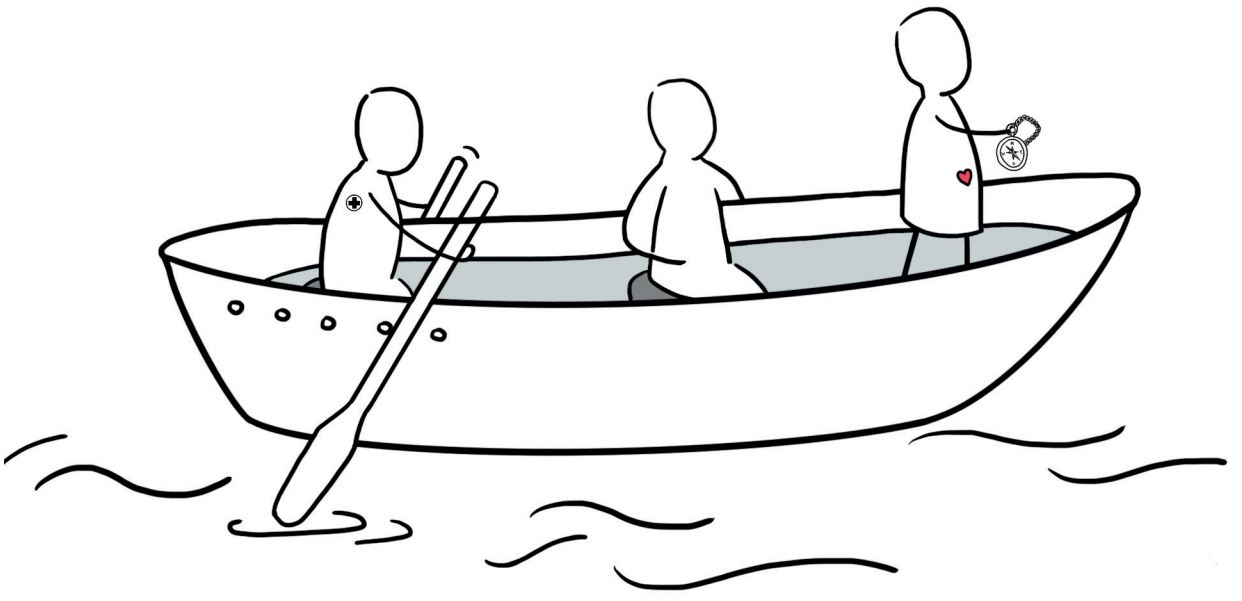

APPENDICES

List of co-authors and affiliations
Author contributions
PhD Portfolio
List of publications
Dankwoord
Curriculum Vitae

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M. van Wely	Center for Reproductive Medicine, Amsterdam University Medical Center, Amsterdam, The Netherlands
E.E. van Woerden	Zuidoost Clinic, Out-patient clinic for Gynaecological Care, Amsterdam, The Netherlands

Author contributions

Chapter 2

MMJvdB was responsible for the literature search and the study selection and drafted the paper. TE helped during the study selection process and the writing of the first draft manuscript. EAFD, FvdV, MG and PJH commented on the draft paper. PJH had overall responsibility of the study. All the authors read and approved the final paper.

Chapter 3

MMJvdB, PJH and MG invented this study. MMJvdB was responsible for the interviews and drafted the paper. MR transcribed the interviews. MG, FvdV PJH, and EAFD commented on drafts of the paper. EAFD had overall responsibility of the study. All the authors read and approved the final paper.

Chapter 4

PJH and MG designed the study. MMJvdB was responsible for the data collection and wrote the manuscript. MG, WMA, EEvW, FvdV, MvW and PJH commented on the draft paper. PJH had overall responsibility of the study. All the authors read and approved the final paper.

Chapter 5

MMJvdB was responsible for the data collection and drafted the paper. EvdB helped during the data collection process and writing the manuscript and had overall responsibility of the study. PJH, FM, RPMGH, FvdV and MG commented on the draft paper. All authors read and approved the final paper.

Chapter 6

MMJvdB interviewed the head of the departments and drafted the paper. EvdB helped to interpret the data. PJH, RPMGH, FvdV and MG commented on the draft paper. PJH had overall responsibility of the study. All authors read and approved the final paper.

Chapter 7

MMJvdB and RV collected the data and drafted the manuscript. MG had overall responsibility of the study. All authors read and approved the final paper.

Portfolio

Name PhD student Merel van den Berg
PhD period: November 2014 – November 2022

PhD training

General courses	**Year**	**ECTS**
Herregistratie BROK	2018	0.5
BROK: legislation and organization for clinical researchers	2014	0.9
Early pregnancy and emergency gynaecology, RCOG, London	2013	1.0
Qualitative Health Research, Graduate School UVA/AMC	2013	1.9
Seminars, workshops and master classes		
'Reproductive Immunology' ESHRE, Campus course, Austria, Innsbruck	2018	0.5
'Effects of ART and endometriosis on pregnancy outcome' ESHRE, Campus Course, Bulgaria, Sofia	2017	0.5
'When is surgery the answer to early pregnancy complications' ESHRE, Campus course, United Kingdom, Warwick	2015	0.5
'Early pregnancy' ESHRE, Campus course, Belgium, Brussels	2013	0.5
Jonge zwangerschap Symposium, The Netherlands, Rotterdam	2013	0.5
Weekly department seminars and journal club	2012-2015	1.5
Weekly department lunch meetings	2012-2015	1.5
Oral presentations		
'Medical versus surgical management of failed early pregnancy' ESHRE, 37th Annual Meeting, Virtual	2021	0.5
'Hebben we een Jonge Zwangerschapsunit nodig?' Doelencongres, The Netherlands, Rotterdam	2019	0.5
'ESHRE and the German/Austrian/Swiss guideline on RPL.' ESHRE, Campus course, Austria, Innsbruck	2018	0.5
'Quality indicators in early pregnancy.' ESHRE, 34th Annual Meeting, Spain, Barcelona	2018	0.5
'An early pregnancy assessment unit improves quality of care and reduces health care costs.' ESHRE, 30th Annual Meeting, Germany, Munich	2014	0.5
'Tools and logistical advices for setting up a Recurrent Miscarriage Clinic' ESHRE, Campus course, Belgium, Brussels	2013	0.5
'An early pregnancy unit: does it improve care?' Jonge zwangerschap Symposium, The Netherlands, Rotterdam	2013	0.5
Poster presentations		
'Guideline-based quality indicators for an early pregnancy assessment unit.' ESHRE, 32st Annual Meeting, Finland, Helsinki	2016	0.5

'Patient-centered care for couples faced with early pregnancy complications: a systematic review of the literature.' ESHRE, 31st Annual Meeting, Portugal, Lisboa	2015	0.5
'Patient-centered care for couples faced with early pregnancy complications: a systematic review of the literature.' ESHRE, Campus course, United Kingdom, Warwick	2015	0.5
'Genetics of early miscarriage' ESHRE, 28th Annual Meeting, Turkey, Istanbul	2012	0.5
'Genetics of early miscarriage' ESHRE, Campus course, The Netherlands, Amsterdam	2012	0.5
(Inter-)national conferences		
ESHRE, 37th Annual Meeting, Virtual	2021	0.5
ESHRE, 36th Annual Meeting, Virtual	2020	0.5
ESHRE, 34th Annual Meeting, Spain, Barcelona	2018	0.5
ESHRE, 33th Annual Meeting, Switserland, Geneve	2017	0.5
ESHRE, 32st Annual Meeting, Finland, Helsinki	2016	0.5
ESHRE, 30th Annual Meeting, Germany, Munich	2014	0.5
Other		
Chairing sessions		
Implantation and early pregnancy poster discussions ESHRE, 37th Annual Meeting, Virtual	2021	0.5
The endometrium in implantation early pregnancy ESHRE, 37th Annual Meeting, Virtual	2021	0.5
Pre-congress course: Old topics, new aspects: endometrium, implantation and early pregnancy ESHRE, 37th Annual Meeting, Virtual	2021	0.5
RM: new diagnostic and therapeutic aspects ESHRE, 36th Annual Meeting, Virtual	2020	0.5
Pre-congress course: Beyond IVF: Management of high risk pregnancies ESHRE, 36th Annual Meeting, Virtual	2020	0.5
Implantation and early pregnancy poster discussions ESHRE, 34th Annual Meeting, Spain, Barcelona	2018	0.5
Pre-congress course: Provision of an effective early pregnancy assessment and support service ESHRE, 34th Annual Meeting, Spain, Barcelona	2018	0.5
Pre-congress course: The role of ultrasound in early pregnancy ESHRE, 33th Annual Meeting, Switserland, Geneve	2017	0.5
Membership		
ESHRE membership	2017-2022	-
NVOG Special Interest Group 'Jonge zwangerschap'	2015-2022	-
ESHRE (junior) deputy of Special Interest Group 'Implantation and Early Pregnancy'	2017-2022	5.0

ESHRE member of 'Communications Committee'	2017-2019	2.0
NVOG member of the board of Special Interest Group 'Jonge zwangerschap'	2015-2020	2.0
AMC graduate school membership	2012-2022	-

Teaching

Verloskunde academie, onderwijs fertiliteit 2e jaars studenten	2015, 2016, 2018	0.5

Supervising

Tatiana Erlikh, Bachelor thesis, University of Amsterdam TOPIC: Patient-centered early pregnancy care: a systematic review of quantitative and qualitative studies on the perspectives of women and their partners	2016	1.0

ECTS system: workload of 28 hours=1 ECTS

List of Publications

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Richtlijn Miskraam vanuit NVOG, 2020. Mede-auteur hoofdstuk 'organisatie miskraamzorg' en 'emotionele ondersteuning & informatievoorziening'

Dankwoord

Mijn proefschrift is eindelijk af! Dit heb ik natuurlijk niet alleen gedaan. Jarenlang heb ik er samen met anderen, meestal met plezier, aan gewerkt. In dit dankwoord richt ik mij graag tot een aantal personen in het bijzonder.

Allereerst wil ik de vrouwen en partners bedanken die mee hebben gedaan aan ons onderzoek en hun ervaring hebben willen delen met de zorg rondom een buitenbaarmoederlijke zwangerschap. Daarnaast wil ik alle experts bedanken die hebben bijgedragen aan het ontwikkelen van de kwaliteitsindicatoren voor het meten van de jonge zwangerschapszorg. Ook wil ik de gynaecologen bedanken die deel hebben genomen aan onze kwalitatieve studie om te kijken hoe de jonge zwangerschapszorg geregeld is in Nederland.

Mijn promotieteam; voor mij de perfecte combinatie die er toe heeft geleid dat dit boekje er toch echt is gekomen. Ik wil jullie alle drie heel erg bedanken voor jullie samenwerking. Zonder jullie had ik dit niet gekund.

Beste Mariëtte, wat was ik blij dat ik onder jouw leiding mijn eerste artikel mocht schrijven, een vervolg op jouw eigen artikel. Het begin was moeilijk, maar dankzij je begeleiding is dat stuk er gekomen. De volgende stap, een promotie-traject, werd genomen. In dezelfde tijd ben jij gegroeid van co-promotor naar promotor tot hoofd van de afdeling VPG. Ondanks je drukke agenda heb je altijd de tijd genomen om mijn vragen te beantwoorden en me te helpen als ik het even niet meer zag zitten. Dit betekende veel voor mij, bedankt daarvoor. Gelukkig werken we in de kliniek nog samen!

Beste Fulco, wat ben ik blij dat deze dag is gekomen. Mijn proefschrift is af met jou als promotor. Elke keer als jij commentaar had, bleek je toch weer gelijk te hebben. De motorclub heb ik gelukkig niet zien langskomen, maar er waren momenten dat die erg dichtbij was. Ik heb veel geleerd van onze samenwerking en ik ben erg blij dat we de afgelopen tijd elkaar nog vaker hebben kunnen spreken. De lessen die ik van jou heb geleerd neem ik mee tijdens de rest van mijn carrière.

Beste Petra, in het begin van mijn traject hebben we vele uren samen achter de computer doorgebracht om de manuscripten te perfectioneren. Je aandacht voor detail heeft er toe geleid dat alles klopt. Je enthousiasme werkt aanstekelijk en tijdens mijn praatjes ben jij dan ook mijn persoonlijke cheerleader. Daarnaast heb je ook aandacht voor mij als persoon. Heel erg bedankt hiervoor.

Geachte leden van de promotiecommissie: Dr. W.M. Ankum, Prof. Dr. A. Coomarasamy, Prof. dr. A. Hoek, Prof. dr. J.S.E. Laven, Prof. dr. E. Pajkrt en Prof. dr. J.A. van der Post. Graag wil ik u bedanken voor de bereidheid om zitting te nemen in mijn promotiecommissie.

Alle medeauteurs wil ik bedanken voor hun bijdrage aan dit proefschrift. Beste Emmy, wat een geluk dat ik samen met jou aan de stukken kon werken met betrekking tot de kwaliteitsindicatoren. Het was erg fijn om te kunnen sparren en ervaringen te delen. Beste Eline, heel erg bedankt voor het delen van je kennis van het kwalitatieve onderzoek. Heel wat uren hebben we naast elkaar gezeten en het was niet altijd makkelijk, maar ik ben erg trots op onze review. Het interview stuk gaat er ook zeker komen! Rosella Hermens en Madelon van Wely bedankt voor jullie specifieke kennis en bijdrage aan de verschillende hoofdstukken. Maxime Rooijers heel erg bedankt voor het uitschrijven van alle interviews en het aanhoren van alle 'uhms'.

Lieve collega's van het CVV, lieve gynaecologen, fertiliteitsartsen, verpleegkundigen, dokterassistenten, iedereen van de back-office, de counsellors, de embryologen en de analisten. Toen ik in 2011 begon als fertiliteitsarts in het AMC had ik nooit verwacht dat ik hier zo lang zou blijven werken. Twee keer heb ik geprobeerd om elders te gaan werken, maar elke keer kwam ik weer terug. Bedankt voor alles wat ik geleerd heb tot nu toe en voor alle gezelligheid en interesse in mijn persoonlijke leven. Samen kunnen we elke uitdaging aan! Bedankt dat ik ook bij de CVV-familie mag horen.

Lieve roze muisjes, lieve Miriam, Odine, Judith en Noor, zo bijzonder om dagelijks te mogen samenwerken met vriendinnen. Deze tijd vergeet ik nooit meer.

Lieve PGT-collega's, lieve Carlijn en Tjitske, wat is het fijn om samen met jullie voor deze groep patiënten te mogen zorgen.

Gynaecologen van het MUMC; Prof. dr. J.L.H. Evers, dr. R.J.T. van Golde en dr. J.W.M. Maas, bedankt dat jullie mij als coassistent kennis hebben laten maken met de voortplantingsgeneeskunde. Mijn liefde voor het vak is hier begonnen.

Gynaecologen en collega's van het OLVG oost, bedankt voor de leerzame en gezellige tijd. In het bijzonder bedankt voor het fertiliteitsteam; Harold Verhoeve, Paul Flierman, Eugenie Kaaijk en alle doktersassistenten. Beste Eugenie, dankzij ons fijne en open gesprek heb ik uiteindelijk de keuze gemaakt om mijn gevoel te volgen en als fertiliteitsarts te blijven werken. Dit zal ik nooit vergeten, bedankt daarvoor.

Lieve vrienden en vriendinnen, lieve oudste vriendinnen; Anna en Roos, lieve luckies, lieve roze muisjes, lieve irenes, lieve bootcampgroep, lieve wintersportgroep, inclusief alle aanhang en kids, wat is het fijn dat jullie in mijn leven zijn. Dank voor alle gezelligheid, liefde en het feit dat jullie er altijd voor mij zijn!

Lieve Mandy, heel erg bedankt voor het maken van een ontwerp voor dit boekje. Het is echt heel erg mooi geworden!

Lieve schoonfamilie, bedankt voor alle mooie momenten, jullie interesse en het feit dat jullie er altijd voor mij en mijn gezin zijn.

Lieve paranimfen, wat ben ik blij dat jullie vandaag (in gedachten) naast mij staan.

Lieve Mir, vanaf het moment dat jij bij ons kwam werken op de CVV en we buddy's werden klikte het tussen ons. Wat was het heerlijk om je elke dag te zien en te spreken. Samen zijn we het perfecte team! Al snel zagen we elkaar ook buiten werk en hebben we al veel mooie momenten samen meegemaakt, zoals onze beiden huwelijken. Ik ben super trots op jou. Jullie tijd in New York gaat geweldig worden!

Lieve Odje, wat ben jij een heerlijk mens. Al snel werd duidelijk dat jij geen doorsnee arts bent en volledig je eigen plan trekt. Je liefde voor administratie en confetti heeft mij al meerdere malen verrast. Met jou erbij is alles een groot feest. De afgelopen jaren heb je laten zien dat je de wereld aankan. Ik ben super blij dat ik jou heb leren kennen. Ik hoop echt in de toekomst weer samen te kunnen werken.

Lieve Juud, elke keer als we elkaar spreken kom ik er weer achter hoeveel we op elkaar lijken. We denken over veel zaken hetzelfde wat onze gesprekken heel speciaal maakt voor mij. Met dit boekje sluit ik ook een periode af waarin we samen naar congressen gingen om praatjes te houden. Dit zal ik missen, maar gelukkig zien we elkaar nog! Ik vind het 'heel goed' hoe je alles doet en weet zeker dat jouw boekje er ook gaat komen.

Lieve zussen, lieve Malou, Jasmijn en Fleur, zo ontzettend verschillend maar wat horen wij bij elkaar. Ik ben echt heel erg blij dat jullie in mijn leven zijn. Ieder volgt zijn eigen pad, maar zodra er iets is zijn we er voor elkaar. De avonden dat wij samen zijn en herinneringen ophalen of dansen door de kamer zijn de leukste. Dank dat jullie mij laten inzien dat ik elke mijlpaal moet vieren. Ik zal er altijd voor jullie zijn.

Lieve Papa en mama, zonder jullie was ik nooit gekomen waar ik nu sta. Dankzij jullie stabiele basis, onvoorwaardelijke liefde en support probeer ik elke dag het beste uit mezelf te halen. Jullie geven ons de vrijheid en jullie vertrouwen om onze eigen keuzes te maken, ook als dat niet altijd goed uitpakt. Dit is het beste cadeau wat jullie ons hebben kunnen geven.

Lieve Bart, alles is leuker met jou erbij. Jij steunt me in alles en je bent altijd geïnteresseerd geweest in mijn onderzoek, hoewel ik er niet altijd over wilde praten. Nu is het dan eindelijk zo ver. Ik ben trots op ons en onze jongens en ik kan niet wachten om de rest van ons leven samen te vieren. Jij betekent alles voor mij.

Liefste Daan, Tijn en Mees, jullie zijn het aller-, aller- mooiste wat mij is overkomen.

About the author

Merel Marieke Johanna van den Berg was born in Eindhoven, the Netherlands on the 1st of October in 1986. After graduating in 2004 at the van Maerlant Pleincollege in Eindhoven, she started medical school at the University of Maastricht. During her studies, she was interested in reproductive medicine and chose this specialism for her final internship at the Maastricht University Medical Centre.

After her graduation she started working as a fertility doctor at the Centre for Reproductive Medicine of the Amsterdam University Medical Centre, location AMC in Amsterdam. One year later, in 2012, she was introduced to scientific research and started her PhD trajectory in 2014 under supervision of professor dr. M. Goddijn, professor dr. F. van der Veen and dr. P.J. Hajenius. She combined this with her work as a fertility doctor. In 2014, she interrupted her work as a fertility doctor at the AMC for one year to work as a resident at the department Obstetrics and Gynaecology of the OLVG in Amsterdam. This made her realise that she did not want to pursue a specialization in Obstetrics and Gynaecology. She still works as a fertility doctor at the AMC today.

Merel lives in Vught, together with her husband Bart and their three sons Daan (2017), Tijn (2019) and Mees (2022).