

Efficacy of a midwife-coordinated, individualized, and specialized maternity care intervention (ChroPreg) in addition to standard care in pregnant women with chronic disease: protocol for a parallel randomized controlled trial

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Method Article

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Abstract

Background: The number of women of childbearing age with chronic diseases is rising. The risk of obstetric complications and poor psychological well-being is higher among these women, and research is needed to investigate how to meet the obstetric and psychological needs of this group during pregnancy and in the postpartum period. Previous research has shown that care coordination, continuity of care, woman-centered care and specialized maternity care interventions delivered to women with high-risk pregnancies can improve patient-reported outcomes, pregnancy outcomes, and be cost-effective. However, no previous trials have examined the efficacy and cost-effectiveness of such interventions among pregnant women with chronic diseases. This paper describes the protocol of a randomized controlled trial (RCT) of a midwife-coordinated, individualized and specialized maternity care intervention (ChroPreg) as an add-on to standard care for pregnant women with chronic diseases.

Methods: This two-arm parallel group RCT study will be conducted from October 2018 – June 2020 at the Department of Obstetrics, Copenhagen University Hospital, Rigshospitalet, Denmark. Pregnant women with chronic diseases are invited to participate; 274 women will be randomized and allocated 1:1 to the ChroPreg intervention plus standard care or standard care alone. The ChroPreg intervention consists of three main components: 1. Coordinated and individualized care, 2. Additional ante- and postpartum consultations, and 3. Specialized midwives. The primary outcome is length of hospital stay (LOS) during pregnancy and in the postpartum period and secondary outcomes are: psychological well-being (the five-item World Health Organization Well-being Index, Edinburgh Postnatal Depression Scale, Cambridge Worry Scale), health-related quality of life (the 12-Item Short Form Survey), patient satisfaction (The Pregnancy and Childbirth Questionnaire), and number of antenatal visits. Explorative outcomes will be pregnancy and delivery outcomes. Data is collected via patient-administered questionnaires and from medical records.

Discussion: This trial is anticipated to contribute to the field of knowledge on which planning of improved antenatal, intra- and postpartum care for women with chronic disease is founded.

Trial Registration: ClinicalTrials.gov: NCT03511508. Registered June 22, 2018

Keywords: Pregnancy, chronic disease, midwifery, maternity care, antenatal care, psychological well-being, complex intervention

Background

In Denmark and worldwide, the number of individuals living with chronic disease is rising (1, 2) and more than one in three Danish adults live with one or more chronic diseases (1). The management and prevention of chronic disease is worldwide a major public health problem and one of the issues most targeted by the World Health Organization (3).

The number of pregnant women affected by chronic diseases such as autoimmune disease, cardiovascular disease, and endocrine disease is also rising; and in 2015, the prevalence in Denmark was

16% among pregnant women (4) and international studies report a prevalence between 16 and 27% (5, 6). The observed rise in chronic disease among pregnant women reflects the rise in chronic disease in the general population (1). Factors also contributing to this rise include the increasing age of childbearing women, improvements in medical and surgical treatment options, increased usage of assisted reproductive technologies, and improvements in diagnostic challenges with better registration of correct diagnoses (4, 7).

Pregnant women with chronic diseases comprise a vulnerable group, and overall these women have a higher risk of preterm birth, pregnancy complications such as gestational diabetes and pre-eclampsia, operative deliveries and postpartum depression (6-9), while children of women with chronic diseases have a higher risk of low birth weight, low Apgar score, and birth defects (10-12). For some women the chronic disease can be worsened by pregnancy (13), though in some cases the women experience remission from symptoms during pregnancy (10, 14). Furthermore, for some chronic diseases there is an increased risk of postpartum flares such as multiple sclerosis and rheumatoid arthritis (14, 15). In qualitative studies, women with chronic diseases indicate that information given by caregivers can be uncoordinated and divergent (e.g. information about medication safety, mode of delivery and breastfeeding). Women also described inadequate care, expressed a general experience of “feeling abandoned” postpartum, and how support for and understanding of their needs was lacking (16, 17). The consequences of the increasing population of pregnant women with chronic diseases are numerous, including a higher demand on maternity care providers to skillfully manage pregnancies complicated by chronic diseases. Furthermore, this increase calls for all maternity care providers to provide coordinated care and consistent counselling (18-20) and to support the pregnant woman in her ability to manage her everyday life with a chronic disease both during pregnancy and postnatally as a new mother (17). It is therefore important that care providers apply highly specialized medical knowledge combined with an ability to provide psychosocial support in the care for this vulnerable group of pregnant women (21, 22). Previous RCT studies that evaluated the effect of maternity care interventions for women with high-risk pregnancies have found that the following components had a positive effect on patient-reported, obstetric, and health economic outcomes: implementation of specialized multidisciplinary teams (23-25), care-coordination (18, 26), continuity of care (27), antenatal and postpartum telephone-support (28), and maternity care with focus on care transitions (29). Also, a study showed that length of hospital stay was increased for pregnant women with chronic disease compared to other pregnant women (30). The introduction of nurse specialists in the care during pregnancy and the postpartum period for pregnant women with epilepsy had a positive effect on satisfaction with the care provided and a reduction in the length of hospital stay was seen in a review of RCT studies (22).

To our knowledge, no previous RCT has evaluated the effect of the implementation of a midwife-coordinated, individualized, and specialized maternity care intervention as an add-on intervention to standard care delivered to pregnant women with chronic diseases. In previous systematic reviews, the authors have addressed the need for trials that include patient-reported outcomes such as satisfaction with maternity care and psychological well-being during pregnancy and in the postpartum period with validated psychometric instruments (24, 31).

Aim

The aim of this RCT entitled the ChroPreg Trial, is to evaluate the efficacy of a midwife-coordinated, individualized and specialized maternity care intervention as an add-on to standard care for pregnant women with chronic diseases. The primary outcome is the length of hospital stay (LOS) measured in days of hospitalization during pregnancy and postpartum. Secondary outcomes are patient-reported psychological well-being, health-related quality of life, satisfaction with care and number of antenatal visits. Exploratory outcomes will be pregnancy and delivery outcomes.

Hypothesis

The trial was designed to evaluate the effect of a midwife-coordinated, individualized and specialized maternity care intervention provided to pregnant women with chronic diseases. We hypothesize that this complex intervention with all its components will have a positive impact on the self-reported psychological well-being of the participants, increase the health-related quality of life and the satisfaction with the care provided, and enhance the participants' ability to cope with everyday life during pregnancy and in the immediate postpartum period. We hypothesize that the sum of these components will reduce the total number of days of hospitalization.

Methods

Study design

The ChroPreg trial is a two-arm parallel-group investigator-initiated RCT. Participants will be randomized to either a midwife-coordinated, individualized, and specialized maternity care intervention (ChroPreg) as an add-on intervention to standard care or standard care alone with a 1:1 allocation. The trial is designed in accordance with the *Consolidated Standards of Reporting Trials* (CONSORT) guidelines for RCTs (32), extended in the *Better reporting of interventions: template for intervention description and replication* (TIDieR) checklist and guide (33), and in accordance with the *Standard Protocol Items: Recommendations for Interventional Trials* (SPIRIT) guidelines for reporting trial protocols (34).

Study setting

The study will take place at the Department of Obstetrics, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark. The department is highly specialized and in addition to serving as a birth facility for women living in the local area of the hospital in Copenhagen, it is a tertiary referral center for a large geographical area. In 2017, 5471 women gave birth at the hospital and 700 of these women had one or more chronic diseases. Participants will be recruited among the women attending antenatal care at Rigshospitalet. In Denmark, all women with normal pregnancies receive antenatal care primarily from midwives, whereas pregnant women with chronic disease and complicated pregnancies receive obstetrician-led antenatal care including consultations with midwives.

Inclusion and exclusion criteria

The Danish Health Authorities define chronic disease as a prolonged disease or a disease that continuously recurs (35). Eligible participants will be: pregnant women with one or more chronic diseases diagnosed before pregnancy and for which the pregnant woman is followed by an obstetrician during pregnancy, ≥ 18 years, able to understand spoken and written Danish, give informed consent, pregnant with a single live fetus, and be between week 12 and 19 of pregnancy at time of inclusion. Potential participants will be excluded from the study for the following reasons: multiple pregnancy, substance abuse, psychiatric disease as the only chronic disease, and pregnant women with diabetes and heart disease (these women already receive specialized care programs at Rigshospitalet).

Recruitment procedure

As a part of the standard antenatal care, women who fulfill the study criteria will be invited to participate in the study by a midwife responsible for the coordination of specialized antenatal care. Eligible participants who verbally consent to receiving more information about the study will be given written information, and subsequently be contacted by telephone by one of the investigators. If the woman is still interested in receiving information about the study, preliminary questions will be answered. Thereafter, the woman is given the choice between a face-to-face meeting at the hospital or receiving additional information by telephone. At the face-to-face meeting or during the telephone conversation, more detailed verbal information about the study will be provided and the potential study candidate will have the opportunity to ask further questions about the study. If the woman decides to participate, informed consent will be obtained, and the baseline questionnaire will be completed. The randomization and allocation to one of the two RCT arms will be carried out by one of the investigators. The choice between mode of receiving information either by telephone or face-to-face is provided to accommodate women who do not live near the hospital or have other reasons to prefer receiving information by telephone. A Danish RCT study tested the effect of face-to-face versus telephone information when including study participants and found no differences in level of comprehension between the two groups (36).

Randomization and blinding

After verbal and written informed consent is obtained the participants are randomized by one of the investigators to either the ChroPreg intervention plus standard care or standard care alone in a ratio of 1:1. The allocation sequence is computer-generated with a varying block size concealed to the researchers. The allocation will be centrally conducted using the online clinical trial management and randomization system EasyTrial (easytrial.net, Aalborg, Denmark). After allocation the participants will be informed about the allocation and further plan of the trial.

The specialized midwives who will deliver the intervention will not be blinded to the allocation and neither will the participants. However, the research staff who will collect data from medical records and questionnaires will be blinded to treatment allocation, as will the chief investigator (HKH) and the trial statistician (SR).

Sample size calculation

A total of 274 women will be enrolled in the study. The sample size was determined using unpublished data on 426 pregnant women with chronic diseases hospitalized at Rigshospitalet during pregnancy and in the post-partum period in 2017. The average length of hospital stay (LOS) during pregnancy was 3.9 days; however, due to a right-skewed distribution, log-transformed LOS was used as the outcome for the sample size calculation. Therefore, the effect of the intervention is expressed as a ratio. We expect a reduction of 25% in LOS in the intervention group compared to the control group, corresponding to an improvement of $\log(1-0.25) = -0.29$ on log scale. The SD of number of days in hospital on log scale was 0.80. With a difference of 0.29, SD = 0.80, a power of 0.8 and a significance level of 0.05, an analysis by the two-sample t-test requires 123 women in each group. We expect 10% to be lost to follow-up, leading to a total of 137 women needing to be enrolled in each group.

The intervention

Standard care alone

Participants allocated to the control group will receive standard care alone. Pregnant women with chronic disease are considered to have high-risk pregnancies and are referred to the appropriate level of specialized maternity care. All pregnant women with chronic disease will be followed by an obstetrician and an individual care plan is designed considering the character and severity of the disease and the pregnancy associated risks. Routinely in Denmark, all pregnant women including pregnant women with chronic diseases are also followed by midwives during pregnancy. The standard care appointments for midwife consultation are timed approximately around weeks: 14–18, 28, 35, 38, and 40 and include physical examinations, discussion about lifestyle, symptoms of normal and complicated pregnancy, breastfeeding and preparation for delivery. At Rigshospitalet, all pregnant women are offered two auditorium prenatal classes delivered by a midwife. After childbirth, women can contact the department and request a conversation about the delivery with a midwife, and women who have experienced severe or unexpected complications may be offered a postnatal consultation with an obstetrician.

The Chropreg intervention plus standard care

The ChroPreg intervention is designed based on a review of the literature on complex interventions in maternity care (18-20) and aimed to fit the needs of women with chronic disease. Complex interventions (37) consist of a number of components that may work independently and interdependently, and it can be difficult to identify the “active ingredient” of the intervention, rendering it even more important to describe the different components, the hypothesized mechanism behind each component, and the interaction between the components (37). The three main components of the ChroPreg intervention are described in more detail below.

The ChroPreg intervention is provided by specialized midwives (SM). In addition to the standard care outlined above, women in the intervention group will receive additional antenatal consultations, postpartum follow-up and care coordination. Both standard care midwife consultations and the extra consultations will be provided by the same SM (content described below and Table 1).

1. Midwife-coordinated and individualized care

The participant will be seen by the same SM throughout pregnancy, and in the postpartum period. During the study period, the SM will identify the special needs and wishes of each woman and will discuss the optimal care of the woman with the obstetrician responsible for her medical care. The SM will be assisting the participants in coordinating antenatal visits to fit their everyday life and to avoid unnecessary hospital visits and in communicating with other care providers, who are part of the standard Danish healthcare system (e.g. general practitioner and health visitor) as well as other health care professionals from other departments at the hospital. The participants can contact the SM by e-mail and during weekly phone hours. If the participant is hospitalized during pregnancy the SM will contact the woman by phone and arrange an appointment. Assisting the participants when in labor is not a part of the intervention.

2. Additional ante and postpartum consultations

In addition to the standard care, two additional antenatal consultations will be scheduled with the SM at 20–24 and 30–33 weeks of pregnancy to discuss psychological well-being in pregnancy, breastfeeding and individualized preparation for childbirth, and postpartum care. The purpose is to support the woman's own capacity to handle her pregnancy, childbirth and everyday life as a new mother with a chronic disease. If the need arises, the SM can refer the woman to a psychologist at the hospital for additional consultation. After birth, the SM follows up on the psychological well-being during the planned telephone support postpartum, and 4–6 weeks after birth, a consultation is planned with the SM to discuss the woman's overall experience and issues important to the woman regarding her pregnancy and delivery.

3. Specialized midwives (SM)

The SMs have attended a 3-day training in chronic disease and pregnancy. The training includes basic medical knowledge on lupus erythematosus, rheumatoid arthritis, lung disease, kidney disease, hypertension, multiple sclerosis, epilepsy and other neurological diseases, inflammatory bowel disease, hematological diseases, and thyroid disease. Additional topics in the training program are: pre-pregnancy counseling, pathophysiology, pregnancy complications, obstetric treatment, medication, lactation, and interdisciplinary collaboration. The training also includes psychological aspects of pregnancy complicated by chronic disease. Topics covered in the program are: psychological development during pregnancy, signs and symptoms of depression and anxiety during pregnancy and postpartum, prenatal attachment, and facilitating conversations about the woman's experience of childbirth. Furthermore, the SMs will receive training in how to best support pregnant women in coping with the everyday challenges of pregnancy and their new role as a mother when living with a chronic disease. A manual for all activities in the intervention will be developed and used as a tool by the SMs.

Table 1. Description of planned midwife-activities in the ChroPreg intervention group and standard

Table 1. should be placed here (located at the end of this document)

Outcome measures

Data will be collected from medical records and using electronic self-administered questionnaires. Data will be obtained at baseline (*t1*) and three times during the study period: at 33–37 weeks of gestation (*t3*), at two weeks after delivery (*t4*), and at two months after delivery (*t5*). The participants will complete the

first electronic questionnaire after signing the informed consent to participate and before randomization. The subsequent questionnaires will be sent as a link in an e-mail.

Primary outcome

The primary outcome is *Length of Hospital Stay* (LOS) measured as the number of days (mean and standard deviation (SD)) spent in hospital during pregnancy and until two weeks after delivery. Data will be collected from patient records two weeks after delivery.

Secondary outcomes

1. Psychological well-being

a. *WHO (Five) Well-Being Index (WHO-5)* (38) measures current (e.g. preceding two weeks) psychological well-being and consists of 5 positively phrased items, each scored on a Likert scale (0 = none of the time, 5 = all the time). The raw score ranges from 0, indicating the lowest possible well-being, to 25, indicating the highest possible well-being. This score is multiplied by a factor of 4, creating a score ranging from 0–100 with 100 being the highest possible well-being. WHO-5 has high psychometric validity and it can be used as an outcome measure in clinical trials (38).

b. *Edinburgh Postnatal Depression Scale (EPDS)* (39) is a self-reported scale consisting of 10 items scored on a 4-point Likert scale (0–3) concerning intensity of depressive mood and symptoms during the last seven days (0 indicates absence of depressive mood and/or symptoms and 3 indicates the worst mood and/or symptoms on a given item). The lowest overall score is 0 and the highest overall score is 30. Cut-off scores for likelihood of clinical depression have been suggested to be at ≥ 10 and ≥ 13 (39, 40) and therefore we include both cut-offs scores in our statistical analysis to avoid the risk of failed detection of cases. The EPDS has been validated for use as a detection tool for antenatal and postnatal depression (40, 41) and it has been translated and used in Danish research (42)

c. *Cambridge Worry Scale (CWS)* (43) measures pregnant women's degree of worry during pregnancy. The questionnaire consists of 16 items concerning different areas of possible worry on a 6-point Likert scale (0 = no worry, 5 = highest degree of worry). The scale ranges from 0 to 60 with 60 indicating the highest possible level of worry. CWS has a high internal validity and reliability and has been utilized in clinical studies including populations of women with high-risk pregnancies (44, 45) .

2. Health-Related Quality of life (HRQoL) and self-rated health

SF-12 (46) is an abridged version of the 36-Item Short Form Survey questionnaire developed to measure health-related quality of life and thereby self-rated health in a single item. The instrument is well-validated and reliable and widely used including during pregnancy and in the postpartum period (46, 47) . The SF-12 questionnaire consists of 12 items that measure physical and mental health, divided into eight subscales: physical and social functioning, role limitation due to physical and mental health, bodily pain, general health perceptions (self-rated health), vitality, and mental health. The scores from the subscales can be calculated in two overall scores: Physical Component Summary (PCS) and Mental Component Summary (MCS) with higher scores indicating better health-related quality of life (46).

3. Patient satisfaction

The Pregnancy and Childbirth Questionnaire (PCQ) (48) contains two subscales: 1) pregnancy-related items (18 items) covering two domains, personal treatment and patient education/information, and 2) birth-related items (7 items). The PCQ consists of 25 items rated on a 5-point Likert scale (1 = totally agree, 5 = totally disagree). Higher scores indicate higher patient satisfaction with quality of care. The questionnaire has been rated to have good internal consistency and reliability (49).

4. Health-economic outcomes

a. *Antenatal contacts* (measured as number of scheduled and unscheduled visits with obstetric doctors and midwives and telephone consultations).

Exploratory outcomes

1. Pregnancy and delivery outcomes

Pregnancy and delivery outcomes will be tracked for the purposes of this study. Exploratory outcomes are considered to be hypothesis generating.

Pregnancy complications (gestational diabetes, pregnancy-induced hypertension, preeclampsia) (yes/no); *labor onset* (spontaneous or induced); *preterm delivery* (yes/no); *mode of delivery* (percentage of participants with spontaneous vaginal delivery, or caesarean section (planned or emergency)); *use of labor analgesia* (no analgesia/any analgesia, epidural analgesia (yes/no)); *outpatient telemonitoring for pregnancy complications* (yes/no and duration (days)); *newborn's well-being at time of delivery* (Apgar score ≤ 7 at 5 minutes postpartum (yes/no)) ; *newborn's birth weight* (measured in kilograms); *breastfeeding* (intention to breastfeed (yes/no); breastfeeding two months after delivery (yes/no); and intended duration (months) of breastfeeding).

Data analysis

Analyses are to be performed based on the intention-to-treat principle. Unadjusted and adjusted comparisons of log-transformed number of days in hospital in the two groups will be performed using the general linear model; however, optionally, a generalized linear model (e.g. Poisson or negative binomial) will be used if we find such a model to fit better to the distribution of the number of days in hospital. Furthermore, the two groups will be compared with respect to the proportion of women with three or fewer days in hospital. Comparison of secondary and exploratory outcomes will similarly be performed using the general or generalized linear models as appropriate. In case of an uneven allocation of pregnancies with congenital malformations or chromosomal abnormalities to the two groups, analyses will be performed in the sub group of women without pregnancies with congenital malformations or chromosomal abnormalities. Missing data techniques (e.g. multiple imputation) will be employed if a substantial amount of the data is missing.

Discussion

The WHO estimates that chronic disease is the cause of the majority of premature deaths in the world and that most of these could be prevented by giving people better access to appropriate health care and treatment and by reducing modifiable risk factors such as diet, exercise and smoking (2). Worldwide, the

proportion of women of childbearing age living with one or more chronic diseases is growing (4, 6), and pregnancies affected by chronic disease are associated with a higher risk of complications (7, 10) and poor psychological health (9).

The perinatal period is a theoretically favorable time in a woman's life to implement effective preventive and health promoting interventions to women (50). Interventions delivered in the perinatal period can therefore hypothetically reduce the potentially negative health impact in pregnancy caused by chronic disease and possibly also empower and strengthen the women's long-term self-care ability with their chronic disease.

The ChroPreg trial is highly relevant, and to the best of our knowledge, the largest scale RCT designed to investigate the effect of a midwife-coordinated, individualized and specialized maternity care add-on intervention for pregnant women with chronic diseases on patient-reported, obstetric, and health economic outcomes.

Systematic reviews of RCTs have found previous complex maternity care interventions to be cost-effective compared to standard care (26, 27). However, in these reviews, the authors have called for trials that evaluate psychological well-being and patient satisfaction with maternity care with validated psychometric instruments (18, 31). Therefore, in this RCT we utilize validated patient-reported questionnaires to estimate psychological well-being during pregnancy and postpartum (38, 39, 43), health-related quality of life (46), and patient satisfaction with maternity care (48).

In this trial we will also combine face-to-face consultations with add-on telephone support and e-mail correspondence delivered by the SM who follow the participants throughout pregnancy and postpartum. Telephone support during pregnancy and after birth has been suggested to be of benefit to women at risk of depression, reducing signs of depression and facilitating breastfeeding initiation and continuation (28). However, these interventions have not yet been tested among pregnant women with chronic diseases, and therefore the results from this trial may inform us on how to design future woman-centered and cost-effective interventions for women with chronic disease.

As this is a low-risk intervention adding to standard care and not involving any known side effects, we anticipate that most eligible women with chronic disease will be interested in participating in the trial, and we do not expect a high level of drop-outs. Measures to monitor and enhance adherence to the intervention will be taken. The two self-reported questionnaires, one at 33–37 weeks of pregnancy and one at two months postpartum will be followed up with reminders if not completed within the time frame, and text message reminders will be sent in advance; adherence to all planned activities of the interventions will be monitored and recorded. The primary outcome (LOS) data is collected from medical records and does not rely on patient reporting. To avoid risk of selection bias, eligible women will be offered the choice between a face-to-face meeting or a telephone conversation for information about the study, informed consent, and randomization, accommodating women living farther from the hospital. The ChroPreg trial will provide an extensive evaluation of a coordinated, individualized and specialized maternity care intervention for pregnant women with chronic diseases. The results from this trial will be among the first of its kind and will help clinicians and policy makers to make evidence-based decisions

when developing and implementing efficient, woman-centered and cost-effective maternity care interventions for women with chronic disease.

To conclude, this paper outlines the background, aim, and methods of a RCT in which the ChroPreg intervention plus standard care is compared with standard care alone in a population of pregnant women with chronic disease. We hypothesize that the sum of active components in the ChroPreg intervention will reduce the overall need for hospitalization and enhance the psychological well-being and satisfaction with care for the participants.

Abbreviations

CONSORT: Consolidated Standards of Reporting Trials

LOS: Length of Hospital Stay

SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)

TIDieR: Better reporting of interventions: template for intervention description and replication

SM: Specialized midwives

RM: Regular midwife

GP: General practitioner

SD: Standard deviation

WHO-5:WHO (Five) Well-Being Index

EPDS: Edinburgh Postnatal Depression Scale

CWS: Cambridge Worry Scale

HRQoL: Health-Related Quality of life

PCS: Physical Component Summary

MCS: Mental Component Summary

PCQ: The Pregnancy and Childbirth Questionnaire

Declarations

Trial status

Recruitment of participants was initiated October 1, 2018 and the current number of enrolled participants

is in line with what was expected from our calculations. Recruitment is anticipated to continue until January 31, 2020, and data collection will be concluded by June 1, 2020. No interim analyses will be performed.

Ethics approval and consent to participate

The trial protocol has been reviewed by the Regional Committee on Health Research Ethics (Jr. no. H-18015521). The intervention was assessed to be a low-risk add-on intervention to the standard care offered to pregnant women with chronic disease, and the board has judged that no known risk is involved with participating in the trial. The Regional Committee on Health Research Ethics have therefore concluded that the study can be initiated without further ethical approval. The trial will be carried out in accordance with the principles of the National Committee on Health Research Ethics in Denmark (51) and the principles of the Helsinki Declaration (52). Written informed consent will be obtained, and all participants will be informed about the voluntary nature of their participation and their right to withdraw from the study. No side-effects or harms to the participants are anticipated. However, if participants wish to withdraw from the trial, their data will not be included in the final analysis, but they will continue to receive standard care. All data from participants will be handled anonymously and secured in a logged database. The trial has been approved by the Danish Data Protection Agency (Jr. no.: RH_2017-346. I-suite no.: 06055). If any important protocol modifications are made, these will be reported in the trial registry (ClinicalTrials.org).

Consent for publication

N/A

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

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Authors' contributions

HKH is the chief investigator of the trial. HKH and MW designed the trial and coordinated the main preparation of study documents and the funding application. MW, MJ, ASE, AB, JM, AT, SR, and HKH contributed to the funding application and the study design. MW drafted the first version of the manuscript. All authors have been involved in revising the manuscript critically for important intellectual content and have given final approval of the version to be published.

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Tables

Table 1. Description of planned midwife-activities in the ChroPreg intervention group and standard care group.

ChroPreg intervention + standard care	Objective of activity	Standard care alone	Objective of activity
During pregnancy			
Week 14-18 Midwife appointment 30 Minutes Specialized midwife (SM) At the hospital	Medical history taking, follow up on information from general practitioner	Week 14-18 Midwife appointment 30 Minutes Regular midwife (RM) At the hospital	Medical history taking, follow up on information from general practitioner
Week 20-24 Midwife appointment 60 minutes Specialized midwife (SM) At the hospital	Focus on psychological well-being during pregnancy and preparation for breastfeeding. The consultation will be centered around the woman's experience of pregnancy, physical development, prenatal attachment, the interaction between pregnancy and chronic disease, normal pregnancy signs and symptoms and thoughts about breastfeeding.		
Week 28-30* Midwife appointment 30 Minutes SM At the hospital	Conversation about breastfeeding, rhesus prophylaxis, well-being and symptoms of pregnancy and chronic disease.	Week 28-30 Midwife appointment 30 minutes RM At the hospital	Conversation about breastfeeding, rhesus prophylaxis, well-being and symptoms of pregnancy
Week 30-33 Midwife appointment 60 minutes SM At the hospital	Focus on individual childbirth preparation and postpartum care. Information about birthing options and pain relief and management. The individual needs and wishes of the woman will be discussed and an individual birth plan will be made.		
Week 35-36 Midwife appointment 30 minutes SM At the hospital	Consultation about pregnancy, well-being, symptoms of chronic disease and the coming birth.	Week 35-36 Midwife appointment 30 minutes RM At the hospital	Consultation about pregnancy and the coming birth, and well-being.
Week 38-39 Midwife appointment 30 minutes	Consultation about pregnancy, well-being, symptoms of chronic disease, the coming birth and postpartum care and follow-up.	Week 38-39 Midwife appointment 30 minutes	Consultation about pregnancy, coming birth and postpartum care

SM		RM	
At the hospital		At the hospital	
Week 40	Consultation about coming birth, pregnancy and signs of labor, discussion about induced labor	Week 40	Consultation about coming birth,
Midwife appointment	Internal vaginal examination if woman wishes to	Midwife appointment	pregnancy and signs of labor,
30 minutes		30 minutes	discussion
SM		RM	about induced labor
At the hospital		At the hospital	Internal vaginal examination if woman wishes to
			to
Postpartum follow-up			
1st and 2nd week after discharge from hospital	Postpartum follow-up on breastfeeding, chronic disease management, medication, and psychological well-being. Coordination with primary health care workers if needed (GP/health visitor/medical specialists).	1st week after discharge from hospital	The woman can contact the hospital with questions and need for postpartum check-up.
30-60 minutes			
SM			
Telephone			
4-6 weeks postpartum	This visit is arranged for the woman to have the opportunity to discuss her experiences of pregnancy and childbirth with the SM. The midwife will have the medical records available, but the focus is to allow the woman to talk and elaborate on her experience. If the midwife and the woman identify a need for further counseling, referral can be made to a psychologist.	After discharge from hospital	The women can contact the department for an appointment to discuss experiences of pregnancy and childbirth.
60 minutes			
Midwife appointment			
SM			
At the hospital/ telephone (woman's choice)			
Activities throughout the study period			
E-mail correspondence	The woman can contact the specialized midwife by e-mail. This contact may concern all relevant issues during pregnancy and postpartum.	E-mail correspondence	No e-mail correspondence included. Women can contact the coordinating midwife department with questions and concerns
From inclusion to end of study period			
SM			
Weekly telephone hours	One day each week the specialized midwife will be available for telephone consultation as a supplement to the planned face-to-face consultations. Participants can call the midwife	Telephone correspondence	Women can contact the coordinating

**From inclusion
to end of study
period
SM**

with questions or concerns. The midwife will evaluate if further visits will be needed in addition to the telephone contacts.

midwife
department
with questions
and concerns.

*All standard midwife appointments from week 28 and on include urine testing for glucose and protein and measuring of blood pressure (screening for indicators for gestational diabetes and pre-eclampsia) and physical examinations (measuring the size, heart beat and position of the fetus).

Figures

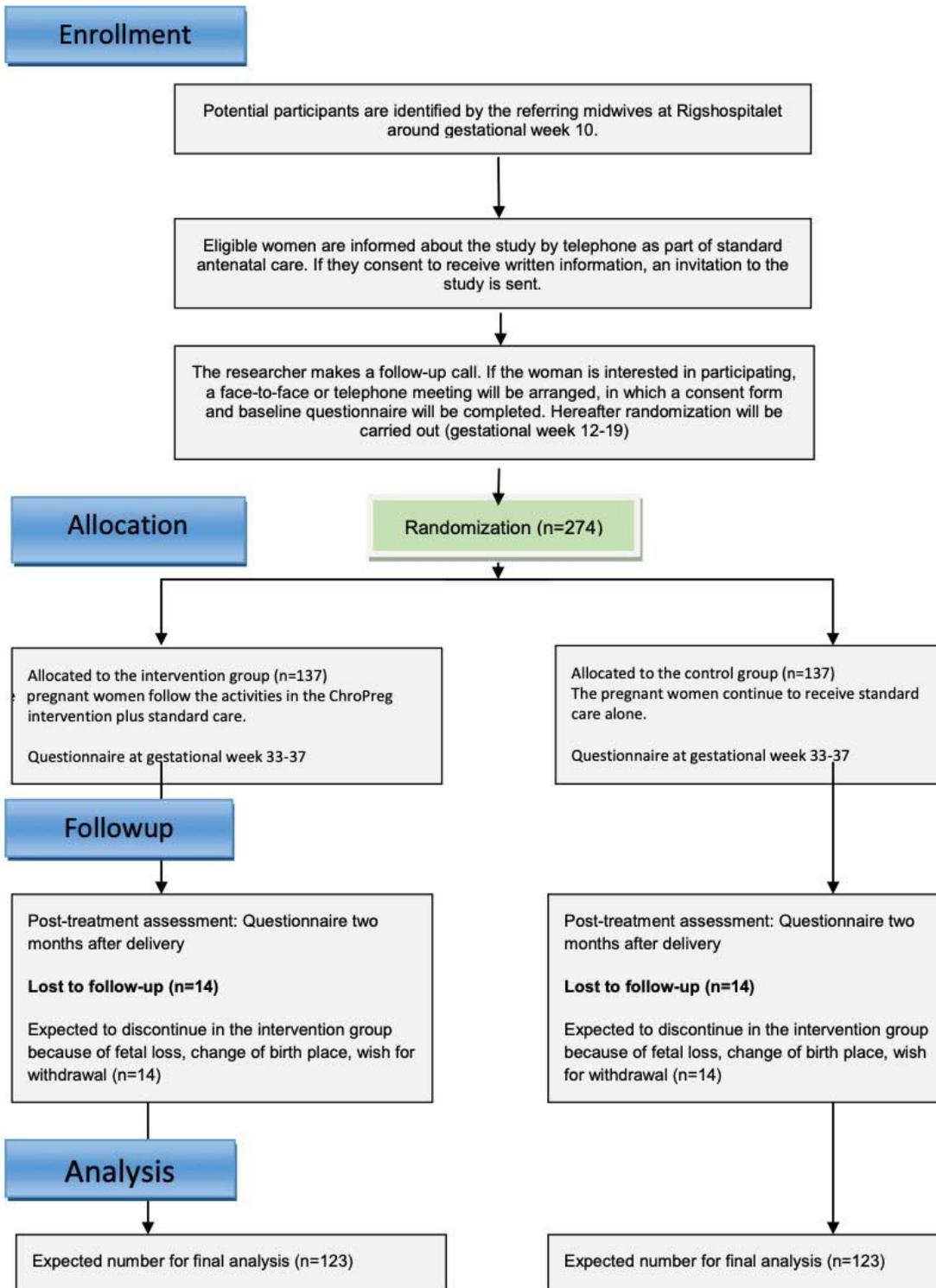


Figure 1

Figure 1. The expected flow diagram of progress through the ChroPreg trial.

