PROTOCOL TITLE:
Promoting ReprOductive WellbEing through Shared medical appointments and health coaching Sessions (PROWESS)

PRINCIPAL INVESTIGATOR:

Christine Kaiser, DACM, LAc, FABORM
UH Connor Whole Health
(216)285-4070
CHRISTINE.KAISER@UHhospitals.org

UH FACULTY ADVISOR:
If the principal investigator's primary role at UH is resident, fellow or student, identify a faculty advisor.

☒ N/A

OTHER DEPARTMENTS INVOLVED IN THIS STUDY (IF APPLICABLE):
☒ N/A

DATE:
12/20/2023

1. Objectives

1) To examine the feasibility and acceptability of the Whole Health Lifestyle Care for Reproductive Well-being Pilot Program ("Lifestyle Care for Fertility" or LCF) and collection of health behavior and patient-reported outcomes
2) To examine the longitudinal changes in health behaviors, and patient reported outcomes of participants in the Lifestyle Care for Fertility program

2. Background

Approximately 10 to 15% of couples are impacted by infertility (1). Struggles with fertility can have a wide range of effects on an individual's and couple's life including physical, emotional, sexual, spiritual, and financial aspects. Studies have shown that infertile couples experience significant emotional distress including anxiety, grief, loss, and depression (2). Fertility treatments can be physically demanding and uncomfortable, with side effects including pain, mood changes, headaches, bloating, hot flashes, and sleep disturbance. Recently, research is starting to focus more on diet and lifestyle factors as a way to improve time to pregnancy and therefore lessen the burden of infertility felt by couples (3, 4, 5). Lifestyle factors are the modifiable habits and ways of life that can greatly influence overall health and well-being, including fertility. Many lifestyle factors such as nutrition, weight, exercise, psychological stress, environmental toxins, and others can have substantial effects on fertility.

A combination lifestyle approach is an evidence-based practice in which nutrition, exercise, and integrative therapies such as mindfulness training and stress management have been shown to improve health and well-being, as well as positively impact chronic disease management (6). Evidence shows that patient-centered coaching yields positive results related to lifestyle behaviors (7). Health and wellness coaching (HWC) can provide significant value to patients' healthcare in the combination lifestyle approach (7). Applying the concept of HWC to fertility patients has the potential to yield improved fertility outcomes, decreased time to pregnancy, and enhanced well-being during the fertility journey, healthier pregnancy as pre-conception is an ideal time to optimize diet and lifestyle habits, and impact future generations with better health and better health habits. This combination lifestyle approach is particularly important for women with polycystic ovarian syndrome (PCOS) which is one of the most common causes of female infertility. International evidence-based guidelines for the management of PCOS include the recommendation of healthy lifestyle behaviors encompassing healthy eating, weight loss, and regular exercise, which are all supported through HWC (8).

3. Inclusion and Exclusion Criteria

	Inclusion Criteria
1.	Adult with a uterus aged from 18 to 50 years
2.	Participating in the Lifestyle Care for Fertility program
3.	Able to speak and understand English.

4.	Has email address and access to mobile device with a functioning data plan.
5.	Infertility-related diagnosis

	Exclusion Criteria
1.	Age < 18 or > 50 years
2.	Having a significant and uncorrected visual, hearing, or cognitive impairment
3.	Inability to provide consent
4.	Current pregnancy

4. Study Design

This is an observational outcome evaluation of the Lifestyle Care for Fertility program.

5. Study Procedures

Setting

Consent will take place either virtually via telehealth or in a private room at the UH Connor Whole Health (CWH) Beachwood office. The shared medical appointments (SMA) occur at the CWH Beachwood office and the individual Health and Wellness Coaching (HWC) sessions are virtual. Data will be collected via a link to REDCap sent to participants' mobile device.

Participants and Recruitment:

Study participants will be patients of UH CWH who have a fertility-related diagnosis and who are participating in LCF. Patients are referred to the program by their Integrative Medicine provider. The HWC, who is also IRB approved research staff, will then screen program participants for research eligibility and send a recruitment email about the research to those who meet eligibility criteria. Seven days later, the program's HWC will call the patient to tell them about the research study and ask if they are interested to particpate. The HWC will make it clear that the patient can participate in the program without participating in the research. If the patient is interested in participating in the research, the HWC will verify that the patient has access to a mobile device with a data plan to complete the study surveys. The coach will then schedule the informed consent with those who have appropriate access.

Consent Process

The consent process begins when the HWC first calls the potential participant and explains the study to them. Interested individuals will schedule a time to meet with the coach or other research staff via telehealth or in person, depending on patient preference and availability, for consent. Potential participants will receive a copy of the informed consent form ahead of time by mail or email and be asked to read it carefully. At the scheduled time via telehealth, the research staff will present the consent form in detail, making sure the participant understands the research by encouraging them to ask any questions they may have, and asking them to explain what the study will involve in their own words. The participant a will be given sufficient time to read the informed consent form and the opportunity to ask questions. The patient will be informed that acceptance or refusal to participate in the research will not influence their

ability to receive clinical care, or to participate in the program, and that they are free to withdraw from study participation at any time. Once all of the patient's questions are answered, they will sign an electronic version of the consent form in REDCap, either on their own device or on a study iPad.

For consents conducted via telehealth, research staff will confirm the identity of the patient before signing the consent. Potential participants will confirm their identity by showing his/her driver's license or, if not available, any state or government-issued picture identification card. If they do not have picture identification available, they will be asked to provide the last four digits of the social security number, their date of birth and one of the following: account number, street address, insurance carrier name, insurance policy number, medical record number, birth certificate or insurance card.

Immediately following the consent, the research staff will send participants a REDCap link to complete the demographics form to be completed on the participant's own device or on the study iPad. The remaining baseline surveys will also be sent at this time if the first session is scheduled for within two weeks of the consent appointment. Otherwise the link to the remaining baseline surveys will be sent when it is within two weeks of Session 1.

Intervention Delivery
The program consists of an individual Integrative Health and Medicine (IHM) consultation with a CWH IHM provider, 4 Shared Medical Appointments (SMA) and 4 individual Health and Wellness Coaching (HWC) sessions. The SMA sessions take place at the UH CWH Beachwood office conference and movement rooms. The HWC sessions are virtual. The consultations are either virtual or in person at UH CWH Beachwood.

The following are the topics for each of the 8 weekly sessions:

Week	Type of Session	Topic
1	Shared Medical Appointment (SMA)	"NOURISH" with Nutrition experiential and cooking demo.
2	Health and Wellness Coaching (HWC)	Implement "NOURISH" education into patient's personal life.
3	SMA	"MOVE" with Yoga experiential and exercise discussion.
4	HWC	Implement "MOVE" education into patient's personal life.
5	SMA	"REST" with Meditation experiential and sleep discussion.
6	HWC	Implement "REST" education into patient's personal life.
7	SMA	"INTEGRATE" with Acupuncture experiential and supplement discussion.

8	HWC	Implement "INTEGRATE" education into patient's personal life.

Participation in the program is not contingent participation in the outcome evaluation. Patients with a uterus aged 18-50 who have a fertility related diagnosis are eligible to participate in the program. Participants in the outcome evaluation will be a subset of the participants in the program who give their consent to researchers to collect survey and EHR data.

Data Collection

Data will be collected at baseline, at 4 weeks, 8 weeks, and before, after, and in between each of the 8 weekly sessions. Data collected at baseline include demographics, PROMIS Sleep Disturbance 8a, Perceived Stress Scale 4 (PSS-4), Infertility Self Efficacy Scale (ISE), and current Health Behaviors (HB). The HB survey will be administered between Sessions 1-8, as well as after Session 8, to observe any longitudinal changes. Patients will complete the PROMIS Sleep Disturbance 8a, PSS-4, and ISE at 4 weeks and 8 weeks. Pre- and post- session data includes 0-10 NRS ratings of stress, energy, focus, wellbeing, perceived support (post-only), and satisfaction (post-only). Additionally, participants will complete a satisfaction survey post Session 8. All data will be collected in REDCap via a text message or email link sent to the participant. Research staff will conduct a review of the participant's medical record to collect data on the participant's demographics and clinical characteristics at baseline, and to collect chemical pregnancy data at six months after the 8 sessions have been completed. This data will be entered into REDCap.

6. Study Timeline

	Consent	Demographics	Baseline	4 Week	Pre- & Post sessions	Between Sessions/After Session 8	8 Week
Estimated time requirement of visit	30-45 min	2-3 min	10-15 min	8-10 min	Pre: 1 min x 8 Post: 2 min x 7, 6-8 min x 1	4-6 min x 8	8-10 min
Data Collection		X	X	X	X	X	X

7. Data to be Collected for Your Study (AFTER consent and HIPAA Authorization have been obtained)

We will collect pre-post outcome measures and satisfaction survey data. Please see attached surveys to be administered. We will also collect the following from the EHR:

- Age
- Sex

- History of mental health dx
- History of use Integrative Health and Medicine services
- Fertility diagnosis
- BMI
- Common comorbidities, including:
    - Hypertension
    - Diabetes
    - Obesity
    - Ischemic heart disease
- Pregnancy as confirmed by presence of human chorionic gonadotropin (hCG) within 6 months of program completion

Attendance data about participants will also be collected.

8. Data Analysis Plan

Acceptability
Patients' responses on the satisfaction survey will be assessed using descriptive statistics.

Feasibility of Study Recruitment and Retention
We will use counts and percentages to summarize recruitment rates (#enrolled/#approached) and pace of accrual for the study, as well as retention rates of study participants (#attended/#enrolled) at each program session.

Demographics and clinical characteristics
We will use descriptive statistics (e.g. means, standard deviations, counts, and percentages) to summarize demographics (e.g., education level, age, income) and clinical characteristics (e.g., fertility-related diagnoses and duration of fertility treatment).

Effects on patient-reported outcomes
Descriptive statistics (e.g. means, standard deviations, counts, and percentages) will be generated for (1) patient-reported outcomes (PRO) collected at baseline, 4 weeks and 8 weeks (2) pre-and post-session NRS measures; and (3) responses to the health behavior survey. We will use linear mixed effects models to assess changes in quantitative measures of perceived stress, sleep disturbance, and self-efficacy over the course of the program. Means and bootstrapped 95% CI will be used to assess single-session effects on numeric rating scale measures of stress, energy, focus, and wellbeing. All statistical analyses will be conducted using R and RStudio.

Data Completeness
Data collected via REDCap at each time point will be evaluated for quality and completeness using reporting functions within REDCap.

9. Risks to Research Participants

Some of the questions might make participants feel uncomfortable. They may skip any questions that they may find upsetting.

There is a slight risk to losing privacy and confidentiality. All paper records will be kept in locked file cabinets and all electronic data will be stored in a password protected database to which only study staff will have access.

10. Provisions to Protect the Privacy Interests of Research Participants

Privacy will be ensured by conducting all study related interactions, including the consent process, within the private spaces, whether that is in person at the UH CWH clinic or remotely.

Confidentiality of the research data will be protected in several ways. Any paper study documents will be stored in locked cabinets within the locked research offices of the PI and/or study staff. Participants will be identified by a separate study ID number on all study records. The lists that link study ID codes with participant names, and all electronic study records will be stored on password-protected, encrypted computers or secure servers. Only aggregate data will be presented or published, and will be presented such that individuals cannot be identified. Only IRB approved study personnel will have access to participant data. All study personnel will be required to be certified in the protection of human subjects throughout the study.

Identifiable information will not be reused or disclosed to any person or entity outside of University Hospitals other than those identified in the protocol, except as required by law, for authorized oversight of the research study, or as specifically approved for use in another study by the IRB.

11. Potential Benefit to Research Participants

There is no guarantee of benefits to any participant in the outcome evaluation, but the knowledge gained may be of benefit to future fertility patients who participate in the program.

12.Withdrawal of Research Participants

The study PI can withdraw participation of research participants at any time without their consent for the following reasons:

- If the subject fails to follow directions for participating in the study;
- If it is discovered that the subject does not meet the study requirements;
- If the study is canceled; or
- For administrative reasons, including competitive enrollment - the target number of subjects has entered the study.

13. Alternatives to Participation

The only alternative to participation in the research is to not participate. Patients can participate in the Lifestyle Care for Fertility program regardless of participation in the research.

14. Drugs or Devices

NA

15. Additional Information

NA

16. Community-Based Participatory Research

NA

17. International information

NA

18. References

1. Sharma R, Biedenharn KR, Fedor JM, Agarwal A. Lifestyle factors and reproductive health: taking control of your fertility. Reprod Biol Endocrinol. 2013 Jul 16;11:66. doi: 10.1186/1477-7827-11-66. PMID: 23870423; PMCID: PMC3717046.
2. Hasanpoor-Azghdy SB, Simbar M, Vedadhir A. The emotional-psychological consequences of infertility among infertile women seeking treatment: Results of a qualitative study. Iran J Reprod Med. 2014 Feb;12(2):131-8. PMID: 24799871; PMCID: PMC4009564.
3. Emokpae MA, Brown SI. Effects of lifestyle factors on fertility: practical recommendations for modification. Reprod Fertil. 2021 Jan 8;2(1):R13-R26. doi: 10.1530/RAF-20-0046. PMID: 35128442; PMCID: PMC8812443.
4. Fabozzi G, Verdone G, Allori M, Cimadomo D, Tatone C, Stuppia L, Franzago M, Ubaldi N, Vaiarelli A, Ubaldi FM, Rienzi L, Gennarelli G. Personalized Nutrition in the Management of Female Infertility: New Insights on Chronic Low-Grade Inflammation. Nutrients. 2022 May 3;14(9):1918. doi: 10.3390/nu14091918. PMID: 35565885; PMCID: PMC9105997.
5. Sharma R, Biedenharn KR, Fedor JM, Agarwal A. Lifestyle factors and reproductive health: taking control of your fertility. Reprod Biol Endocrinol. 2013 Jul 16;11:66. doi: 10.1186/1477-7827-11-66. PMID: 23870423; PMCID: PMC3717046.
6. Rippe JM. Lifestyle Medicine: The Health Promoting Power of Daily Habits and Practices. Am J Lifestyle Med. 2018 Jul 20;12(6):499-512. doi: 10.1177/1559827618785554. PMID: 30783405; PMCID: PMC6367881.
7. Sforzo GA, Kaye MP, Harenberg S, Costello K, Cobus-Kuo L, Rauff E, Edman JS, Frates E, Moore M. Compendium of Health and Wellness Coaching: 2019 Addendum. Am J Lifestyle Med. 2019 May 26;14(2):155-168. doi: 10.1177/1559827619850489. PMID: 32231482; PMCID: PMC7092405.
8. Helena J Teede, Marie L Misso, Michael F Costello, Anuja Dokras, Joop Laven, Lisa Moran, Terhi Piltonen, Robert J Norman, International PCOS Network , Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary

syndrome, *Human Reproduction*, Volume 33, Issue 9, September 2018, Pages 1602-1618, https://doi.org/10.1093/humrep/dey256