RELATIONSHIPS BETWEEN INFERTILITY-RELATED STRESS, HAIR CORTISOL, COPING, AND QUALITY OF LIFE IN U.S. WOMEN UNDERGOING INFERTILITY TREATMENTS

by

Alison D. Swift

May, 2020

Director of Dissertation: Pamela Reis, PhD, CNM, NNP-BC, FACNM

Major Department: Nursing

Women with infertility, the inability to achieve or maintain a pregnancy after 12 months of unprotected sexual intercourse, are known to experience psychological distress. Little is known about infertility-related stress (IRS), coping strategies, and quality of life (QOL) in infertile women in the United States (U.S.). Hair cortisol, a measure of chronic stress, has not been compared to IRS, coping, or QOL. This study used a descriptive quantitative cross-sectional survey design to examine the relationships between IRS, hair cortisol, coping, and QOL in U.S. women undergoing infertility treatments, and these relationships to treatment type and pregnancy loss.

After conducting an integrative review, Facebook was found to be a viable option for recruiting participants in nursing research. In this study, 230 participants were recruited from infertility-related Facebook groups and pages. Infertility-related stress, coping, and QOL was measured using the Copenhagen Multi-centre Psychosocial Infertility Fertility Problem Scale Score (COMPI-FPSS), COMPI Coping Styles Scale (COMPI-CSS), and the Fertility Quality of Life (FertiQoL) tool, which was congruent with the study's theoretical framework of Lazarus & Folkman's transactional theory of stress and coping. Participants also completed demographic and infertility background information. Hair samples were collected from a subsample of 37

participants and analyzed by an independent laboratory. Pearson correlations and independent t-tests were conducted to compare IRS, coping, QOL, and in comparing these relationships to pregnancy loss and treatment groups (IVF vs. non-IVF). Findings concluded that high levels of IRS were associated with active-avoidance coping and lower QOL scores. There were no statistical differences in IRS among treatment groups, however women in the non-IVF group used more active-avoidance and had lower social QOL than women in the IVF group. Women with pregnancy loss were found to have higher levels of IRS, use more active-avoidance coping, and had lower QOL scores compared to women without pregnancy loss. Hypocortisolism was found in the subsample, with large and significant negative correlations found between hair cortisol levels and marital stress, and moderate and significant positive correlations found between hair cortisol and relational QOL and core QOL.

This study was significant in providing new knowledge of IRS, hair cortisol, coping, and QOL in U.S. women undergoing infertility treatments. Healthcare providers should provide psychological support to all women in infertility treatments, especially to support the quality of the partnered relationship and in women experiencing pregnancy loss. Future studies should further examine the impact of pregnancy loss within the infertility experience and investigate psychological interventions that reduce IRS, contribute to positive coping behaviors, and lead to positive pregnancy outcomes. In addition, the significance of hypocortisolism in women with infertility should be further explored.

RELATIONSHIPS BETWEEN INFERTILITY-RELATED STRESS, HAIR CORTISOL, COPING, AND QUALITY OF LIFE IN U.S. WOMEN UNDERGOING INFERTILITY TREATMENTS

A Dissertation

Presented to the Faculty of the Department of Nursing Science

East Carolina University

In Partial Fulfillment of the Requirements for the Degree

Doctor of Philosophy in Nursing

by

Alison D. Swift

May, 2020

RELATIONSHIPS BETWEEN INFERTILITY-RELATED STRESS, HAIR CORTISOL, COPING, AND QUALITY OF LIFE AMONG U.S. WOMEN IN INFERTILITY TREATMENTS

by

Alison D. Swift

APPROVED BY:

DIRECTOR OF DISSERTATION: _____

Pamela Reis, PhD, CNM, NNP-BC, FACNM

COMMITTEE MEMBER: _____

Melvin Swanson, PhD

COMMITTEE MEMBER: _____

Janice A. Neil, PhD, RN, CNE

COMMITTEE MEMBER: _____

Christyn Dolbier, PhD

CHAIR OF THE DEPARTMENT

OF NURSING SCIENCE: _____

Elaine Scott, PhD, RN, NE-BC

DEAN OF THE GRADUATE SCHOOL: _____

Paul J. Gemperline, PhD

DEDICATION

This dissertation is dedicated to my high-school sweetheart and husband, Brian, who has believed in me, supported me, and pushed me since we met many years ago. I cannot express my deep gratitude and appreciation for your endless love and support. I truly would not be here and could not have done this without you. I love you infinitely.

To my children, Matthew, Tanner, and Emily, who are the reasons for this dissertation. You are truly miracles and blessings from God. All things are possible with God, hard work, perseverance, and allowing flexibility. Thank you for your love and support on this journey with me. I love you all immensity.

ACKNOWLEDGEMENTS

This has been an incredible journey and there are many people to acknowledge with my gratitude. First, thank you God for walking beside me. Joshua 1:9. Thank you to my dissertation chair, Dr. Pamela Reis, for being my champion and mentor. I am forever appreciative of you pushing me to grow, your guidance and expertise, and the countless hours spent with me. I am so blessed you were with me on this journey and I look forward to our future collaborations.

Thank you to my dissertation committee members: Dr. Mel Swanson, Dr. Janice Neil, and Dr. Christyn Dolbier. I am grateful for your time spent with me, your patience in answering all my questions, and the lessons on how to be a scholar. I am so blessed you all were with me through this process to share your knowledge and guidance.

Thank you to my administrators and colleagues who supported and encouraged me to pursue and finish this journey. I could not have done this without your support. Many thanks to Beta Nu and the College of Nursing Research and Scholarship department for funding this study. Thank you to the PhD faculty: I learned so much from each of you. I am thankful for your direction and dedication to your students and nursing science.

Thank you to the best mother-in-law, Deborah, for helping with the children and support that made this journey possible. My loving parents and siblings: thank you for listening and reassuring me often. To the “2016 cohort PhD Rockstar’s”: I’m so glad we did this together and supported each through all the challenges. And of course, thank you to my husband and children. This dissertation is dedicated to you all and this would have not been possible without your love.

Lastly, I would like the acknowledge and thank the many women with infertility who took the time to share the survey or be a part of this study. I hope this is the start to building the knowledge and evidence needed to support all women with infertility and pregnancy loss.

TABLE OF CONTENTS

LIST OF TABLES x

LIST OF FIGURES xi

CHAPTER 1: INTRODUCTION 1

Background 1

Classification and Causes of Infertility 2

Infertility Therapies 3

Psychological and Physiological Stress 7

Significance 9

Prolonged Stress 9

Pregnancy Loss 11

Quality of Life 12

Coping Strategies 13

Purpose 15

Theoretical Framework 15

Specific Aims and Research Questions 20

Definitions 20

Assumptions 22

Descriptions of Manuscripts 22

Summary 23

CHAPTER 2: LITERATURE REVIEW 24

Theoretical Perspectives of Stress and Coping 24

Stress 24

Coping 25

Transactional Theory of Stress and Coping 26

Infertility-Related Stress in Women 27

Sources of Infertility-Related Stress 27

Primary Appraisals of Stress 29

Cortisol as a Measure of IRS 30
Personal and Situational Factors Association with IRS 32
Type of Infertility 33
Duration of Infertility 34
Pregnancy Loss 35
Demographic Factors 36
Infertility-Related Stress and Coping in Women 36
Infertility-Related Stress and Emotion-Focused Coping 37
Infertility-Related Stress and Problem- and Meaning-Focused Coping 38
Quality of Life in Women with Infertility 39
Infertility-Related Stress and QOL 40
Coping and QOL 40
Personal and Situational Factors and QOL 41
Limitations and Gaps 42
Summary 46
CHAPTER 3: METHODS 48
Introduction 48
Design 48
Setting 49
Sample 51
Human Subjects Protection 52
Instruments 53
Screening Questions 53
Copenhagen Multi-centre Psychosocial Infertility Fertility Problem Scale 54
Copenhagen Multi-centre Psychosocial Infertility Coping Styles Scale 54
Fertility Quality of Life 54
Demographics and Background Questionnaire 55
Hair Care Questionnaire 55

Procedures 55
Data Analysis 58
Limitations 60
Summary 61
CHAPTER 4: THE USE OF FACEBOOKS FOR RECRUITMENT IN NURSING RESEARCH: AN INTEGRATIVE REVIEW 63
Abstract 63
Introduction 64
Background 64
Methods 66
Design 66
Search Methods 66
Search Outcome 67
Data Evaluation 68
Data Extraction and Analysis 68
Results 69
Study and Sample Characteristics 69
Social Media Recruitment 69
Discussion 71
Limitations 76
Implications and Recommendations 76
Conclusion 77
CHAPTER 5: INFERTILITY-RELATED STRESS, HAIR CORTISOL, COPING, AND QUALITY OF LIFE IN U.S. WOMEN UNDERGOING INFERTILITY TREATMENTS 82
Abstract 82
Introduction 83
Theoretical Framework 86
Materials and Methods 87
Participants 87

Surveys 88
Hair Cortisol 91
Outcomes and Statistical Analysis 91
Results 93
Demographic Characteristics 93
Relationships between IRS, Coping, and QOL 95
Coping and QOL 98
Treatment type and Pregnancy loss and IRS, Coping, and QOL 98
Hair Cortisol, IRS, Coping, and QOL 100
Discussion 101
Limitations 106
Conclusions 108
REFERENCES 123
APPENDIX A: IRB APPROVAL LETTER 160
APPENDIX B: IRB AMENDMENT APPROVAL LETTER 161
APPENDIX C: PERMISSION TO USE TOOLS 162
APPENDIX D: SOCIAL MEDIA SCRIPT 163
APPENDIX E: CONSENT LETTER FOR SURVEY RESEARCH 164
APPENDIX F: INFORMED CONSENT FOR HAIR SAMPLE 165
APPENDIX G: SCREENING QUESTIONS 168
APPENDIX H: COPENHAGEN MULTI-CENTRE PSYCHOSOCIAL INFERTILITY FERTILITY PROBLEM SCALE SCORE (COMPI-FPSS) 169
APPENDIX I: COPENHAGEN MULTI-CENTRE PSYCHOSOCIAL INFERTILITY COPING STRATEGY SCALE (COMPI-CSS) 170
APPENDIX J: FERTILITY QUALITY OF LIFE SCALE (FERTIQOL) 171
APPENDIX K: BACKGROUND AND DEMOGRAPHIC DATA 175
APPENDIX L: HAIR CARE QUESTIONNAIRE 179
APPENDIX M: HAIR SAMPLE PROCEDURE FOR PARTICIPANTS 181
APPENDIX N: STUDIES INCLUDED IN REVIEW 183

LIST OF TABLES

1. Demographic Characteristics of Studies Reviewed 79

2. Social Media Recruitment Characteristics of Studies Reviewed 80

3. Recommendations for Recruiting on Facebook 81

4. Demographic Characteristics of Study Participants Total Group and Subsample 110

5. Means for COMPI Fertility Problem Stress Scales, Coping Strategy Scales, Fertility Quality of Life (QOL) Subscales and Core Total QOL 111

6. Percent of Respondents Reporting "Used Quite a Bit" or "Used a Great Deal" on the COMPI Coping Strategy Scale Items and Average Percent of Such Responses on the Four Coping Strategy Domains 112

7. Coping Strategy "Used Quite a Bit" or "Used a Great Deal" Between Low and High Stress Groups 113

8. Core Fertility Quality of Life in Total Group and Low and High Stress Groups 114

9. Correlations of COMPI Fertility Problem Stress Scale Scores with Coping Strategies Scales Scores, Fertility Quality of Life Subscales and Total Scale Scores 115

10. Percent of Respondents Reporting "Strongly Agree" on the COMPI Fertility Problem Stress Scale Items and Average Percent of Such Responses on the Three Stress Domains in Total Group and Low and High Stress Groups 116

11. COMPI Fertility Problem Stress Scales, Coping Scales, and Fertility Quality of Life Between Non-IVF and IVF Groups 117

12. Relationships Among Infertility-Related Stress Groups, Pregnancy Loss, and Treatment Type 118

13. Relationships of COMPI Fertility Problem Stress Scale, Coping Strategies Scale, and Fertility Quality of Life Among Pregnancy Loss and Treatment Type 119

14. IVF and Non-IVF Group Differences for Infertility-Related Stress and Infertility Coping Strategies Between Groups that Did or Did Not Have a Pregnancy Loss 120

15. Correlations of Hair Cortisol Concentrations, COMPI Fertility Problem Stress Scale Scores with Coping Strategies Scales Scores, Fertility Quality of Life Subscales and Total Scale Scores in Subsample 121

16. Means for Hair Cortisol Concentration (log), COMPI Fertility Problem Stress Scales, Coping Strategy Scales, Fertility Quality of Life (QOL) Subscales and Core Total QOL for Subsample 122

LIST OF FIGURES

1. Model of the Experience of Being Infertile 19

2. PRIMSA Flowchart 78

CHAPTER 1: INTRODUCTION

Background

Infertility is recognized by medical standards from the American Society of Reproductive Medicine (ASRM), American College of Obstetricians and Gynecologists (ACOG), and the World Health Organization (WHO), as the inability to conceive or carry a pregnancy to term after 12 months of unprotected sexual intercourse (ACOG, 2019; ASRM, 2019; WHO, 2019a). Currently, the Center for Disease Control and Prevention (CDC) estimates 1 in 8 couples in the United States (U.S.) are affected with infertility (CDC, 2018). On a global level, the WHO considers infertility a global health issue, as over 186 million women in developing countries, or 1 in 4 women, have difficulty conceiving (WHO, 2019b).

Globally, fertility rates have declined substantially, by almost half, since 1950 (Murray et al., 2018). In 2017, the U.S. had the lowest fertility rate in 30 years (Hamilton, Martin, Ostermann, Driscoll, & Rossen, 2018), and was 16% below the rate needed for population replacement (Matthews & Hamilton, 2019). Fertility rates continued to decline by another 2% in 2018, with Hamilton, Martin, Osterman, & Rossen (2019) reporting another record low. Declining fertility rates have been attributed to socio-economic causes, access to birth control, family planning, and lifestyle factors such as obesity and environmental hazards (Nargund, 2009). In the U.S., 33% of Americans report undergoing or knowing someone who has undergone infertility treatments (Livingston, 2018). The declining fertility rates and reported fertility problems among women in the U.S. warrants further examination of infertility and women's experiences of infertility. Particularly, women with infertility report the experience as being stressful, affecting social, marital, personal, and physical domains which may impact quality of life (Li, Zhang, Shi, Guo, & Wang, 2019; Martins et al., 2013).

Infertility treatments to assist women in achieving pregnancy are costly, especially in the U.S. Medication-only treatment can average around $1,500 per treatment cycle while in vitro fertilization cycles can average around $24,000 or more per treatment cycle (Katz et al., 2011). The costs of infertility treatments may be one reason why women opt to not continue treatments (Bunting & Boivin, 2007); however psychological distress is reported to be the most common reason for discontinuation of treatment (Pedro et al., 2017). Further, long-term mental health consequences have been found in women who do not achieve pregnancy after infertility evaluations. Kjaer et al. (2011) found that women who did not have a child after the initial infertility evaluation were 2.43 (95% CI: 1.38–3.71) times more likely to commit suicide than women who had at least one child post-evaluation. In women with secondary infertility, there was also an increased risk of suicide compared to women who had at least one child post-evaluation (HR 1.68; 95% CI, 0.82–3.41). Marital relationships are also impacted by unsuccessful infertility treatments, leading to a higher likelihood of spousal separation for childless couples (Martins, Vassard, Hougaard, & Schmidt, 2018). The financial burden of infertility treatments, long-term mental health consequences of infertility, and the impact on marital relationships further support the need to explore infertility-related stress, coping strategies, and quality of life among women with infertility. There are two classifications of infertility and multiple causes of infertility, which are described below.

Classification and Causes of Infertility

Infertility is classified as primary or secondary. Primary infertility describes women whom have not been able to become pregnant or have not carried a pregnancy to a live birth. Secondary infertility occurs when women have not been able to conceive or carry a pregnancy following a previous ability to carry a pregnancy to live birth (WHO, 2019a). The causes of primary or

secondary infertility can be female factor, male factor, male-female factor, or unknown. Female factor infertility causes 30% of infertility in couples and includes hormonal or structural abnormalities that affect the female reproductive system (RESOLVE, 2019a). Some examples of causes of female factor infertility are advanced age, premature ovarian failure, polycystic ovary syndrome, endometriosis, uterine lining abnormalities, uterus or fallopian tube defects, and hormonal or immunologic problems that affect the female reproductive system (RESOLVE, 2019a). Male factor infertility affects 30% of couples with infertility and encompasses male-related reasons for infertility such as low sperm count levels, or defects in the motility or structure of the sperm cell, ejaculatory disorders, or immunologic and endocrine problems (RESOLVE, 2019a). About 30% of couples have a combination of female and male factors, and 10% have unexplained infertility (RESOLVE, 2019a). Infertility is managed with different treatment modalities as described in the following section.

Infertility Therapies

For most individuals, infertility is treated with surgical or medical management. Structural defects of the reproductive system, such as fallopian tubal obstruction in women or testicular tube obstructions in men, may be repaired to restore fertility (Lindsay & Vitrikas, 2015). Women may take medications orally or subcutaneously to enhance ovarian stimulation or ova production, such as clomiphene citrate, letrozole, follicle-stimulating hormone, human menopausal gonadotropin, or gonadotropin-releasing hormone (Xia, Inagaki, Zhang, Wang, & Song, 2017). Other medications may be used to stimulate or "trigger" ovulation, such as human chorionic gonadotropin (hCG), or medications may be taken during the luteal phase of the menstrual cycle to sustain progesterone levels. Progesterone is an important hormone in sustaining early pregnancy and is a necessary hormone for women undergoing in vitro fertilization (IVF).

Normally after ovulation, progesterone is secreted by the corpus luteum to support embryonic implantation and growth and immune responses. The use of progesterone in post-embryonic transfer, post-intrauterine inseminations, and in women with recurrent miscarriages helps support the luteal phase and provides immunomodulary effects to sustain a pregnancy (Ciampaglia & Cognigni, 2015). Genetic testing for couples may also be considered for couples with recurrent miscarriages to assess for chromosomal abnormalities in the man or woman and assess for thrombolytic syndromes that impact fertility (Ciampaglia & Cognigni, 2015).

Advancements in technology have proved useful in treating infertility. Assisted reproductive technology (ART), such IVF, can be used to further help men and women achieve pregnancy. The use of ART cycles has increased by 39% between 2007-2016 (CDC, American Society for Reproductive Medicine [ASRM], & Society for Assistive Reproductive Technology [SART], 2018a). In 2016, 27% of ART cycles using fresh (non-frozen) embryos resulted in pregnancy, with 81% of these pregnancies resulting in a live birth (CDC, ASRM, & SART). The IVF procedure includes removing ova and sperm from the donors, combining the ova and sperm for fertilization outside of the body, monitoring the embryo formation, and then transferring an embryo into the woman's uterus for implantation (SART, 2019). There are also other forms of IVF, such as gamete and zygote intrafallopian transfers, however these are rarely used (CDC, ASRM, & SART, 2018b). Retrieved ova and embryos created from ART procedures can be frozen for future use. The number of ART cycles used for banking ova or embryos has increased from under 10,000 cycles to near 70,000 cycles between 2007-2016 (CDC, ASRM, & SART, 2018a). Chromosomal analysis during embryo formation is possible prior to transferring the embryo to the woman's uterus to ensure a viable embryo before embryonic transfer (SART, 2019). Women who undergo medical infertility treatment are four times more likely to receive

non-ART treatments rather than ART (Schieve, Devine, Boyle, Petrini, & Warner, 2009). Only 1-2% of women who undergo infertility treatments will receive ART (Katz et al., 2011).

Infertility treatments, especially ART treatments, are costly and are often the responsibility of the patient undergoing treatment since these therapies are often not covered by insurance. Only 16 states have laws mandating infertility insurance coverage (RESOLVE, 2019b). Most medical treatments involve close monitoring of the patient, which may include multiple laboratory tests, ultrasounds, or other procedures. These additional monitoring tests are necessary but contribute to the overall costs of infertility. In the U.S., the average estimated cost for a fresh IVF cycle (using non-frozen embryos) is between $12,500 (Chambers, Zhu, & Illingworth, 2012) and $24,000 (Katz, et al., 2011). Non-ART cycles, which are primarily medications with or without intrauterine seminations, are estimated to cost between $1,200-$8,600 per cycle (Katz et al., 2011). Additionally, women who are employed may suffer additional financial loss due to missed work for medical appointments related to their infertility treatments.

Alternative and complementary or integrative therapies may also be used as a treatment option for women with infertility. Acupuncture is the most well used and well-studied of integrative therapies but has mixed results for treatment outcomes, which could include psychological measures or achievement of pregnancy. Smith, Ussher, Perz, Carmady, & de Lacey (2011) conducted a randomized control trial and found acupuncture reduced infertility-related stress in women undergoing infertility treatments. Balk, Catov, Horn, Gecsi, & Wakim (2010) also found that acupuncture reduced perceived stress scores, and women that participated in acupuncture had higher rates of pregnancy. However, other studies have found no significant improvement in pregnancy rates for acupuncture during IVF cycles (El-Toukhy et al., 2008). In addition, other forms of alternative and integrative measures have been studied in women with

infertility with positive results in reducing stress such as yoga (Valerian et al. 2014), mindfulness-based stress reduction (Domar, Seibel, & Benson, 1990; Galhardo, Cunha, & Pinto-Gouveia, 2013; Psaros, Kagan, Auba, Alert, & Park, 2012), and traditional Chinese medicine (Ried & Alfred, 2003). Studies considering the use of integrative therapies in conjunction with allopathic infertility treatments to improve pregnancy rates still need further consideration given the lack of studies in the area and mixed results (Miner et al., 2018; Xi et al., 2018). In addition, receiving integrative therapies may result in additional costs and may not be a feasible option for women who have financial constraints.

Finally, patients may choose to forgo or discontinue treatment for a number of reasons. Women who are older and display depressive symptoms are more likely to withdrawal from infertility treatments (Pedro et al., 2017). The costs of infertility treatments further contribute to disparities in health care access. Those who cannot afford to initiate or continue infertility treatments may not seek treatment. There is little in the literature about the characteristics of those who do not seek treatment for infertility and the reasons for their decision not to pursue treatment. Bunting & Boivin (2007) found that women who have not sought treatment were fearful of infertility diagnosis, treatments, and the cost of infertility treatments.

Regardless of the cause of infertility, women are often met with the burden of undergoing some form of infertility treatment compared to men. For example, although sperm motility, morphology, and count may affect fertility, a couple with male factor infertility may still require that the female partner takes medications to enhance ovarian stimulation, in combination with intrauterine inseminations or IVF to improve pregnancy rates (Lindsay & Vitrikas, 2015). For women, treatment for infertility often involves planning and determining optimal timing of treatments, medications, monitoring, intercourse, or other procedures related to their menstrual

cycle. The cognitive appraisals and rumination in planning these activities related to infertility treatments combined with the potential for life disruptions in planning, and undergoing monitoring and treatments, in addition to suffering due to not being able to achieve pregnancy or have a child, may lead to negative psychological consequences in the woman with infertility.

Psychological and Physiological Stress

The psychological and physiological consequences of infertility are important to consider. Not only are infertility treatments stress-inducing (Greil, McQuillan, Lowry, & Shreffler, 2011; Pasch et al., 2012), but infertility-related stress (IRS) is its own construct and distinct from general stress (Casu, Zaia, Fernandes Martins, Parente Barbose, & Gremigni, 2019; Sexton, Byrd, & von Kluge, 2010). Sexton et al. (2010) first proposed IRS as distinct from general stress based on findings from their study in which IRS and general stress measures were correlated but not analogous. A recent study by Cesta et al. (2018) also found a correlation ($r = .461$) among perceived stress and IRS measures, but was not measuring the same construct. Casu et al. (2019) argues infertility affects multiple domains of a person, including social, personal, and marital aspects. Therefore, evaluating IRS should be done through infertility-specific measures rather than general stress measures to sufficiently capture women's experiences (Greil et al., 2011). The impact of IRS on multiple life domains can negatively affect a person's quality of life (Kim, Shin, & Yun, 2018). For example, women with higher levels of IRS had more depression, less marital satisfaction, and lower perceived quality of life (Kim et al., 2018).

Physiologic reactions to psychological distress can include activation of several biological systems, including the hypothalamic pituitary adrenal (HPA) axis. Psychological and physical stressors cause a release of corticotropin-releasing hormone (CRH) from the hypothalamus. The presence of CRH initiates the release of adrenocorticotropin hormone (ACTH) from the pituitary

gland. ACTH travels systemically into the adrenal gland, where it is synthesized, and cortisol is released from the adrenal gland (Miller, Chen, & Zhou, 2007). With the presence of psychological distress, the HPA axis is stimulated to achieve homeostasis through the production of cortisol, a glucocorticoid. Cortisol effects multiple systems and functions in the body including the neurologic, endocrine, cardiovascular, and immune systems, as well as metabolism and behavior (Nater, Skoluda, & Strahler, 2013; Ranabir & Reetu, 2011; Whitworth, Williamson, Mangos, & Kelly, 2005). Chronic stress conditions can increase allostatic load, or 'wear and tear' of the body from chronic stress (McEwen, 1998) and cause dysregulation of body systems (Schetter & Dolbier, 2011), including HPA axis dysregulation leading to hypercortisolemia. Chronic hypercortisolemia has been associated with insulin resistance, metabolic syndrome, obesity, and chronic low-grade inflammation state (Kyrou & Tsigos, 2009). Insulin resistance can be found in polycystic ovary syndrome, which is a known cause of infertility in women (Tanbo et al., 2018).

Psychological appraisals and reactions to distress can lead to physiologic activation of stress hormones, especially in unpredictable situations and temporal uncertainty (Lazarus & Folkman, 1984). The experience of infertility is met with uncertainty, as there is no predictability in response to infertility treatments, or when and if a woman conceives (Sandelowski & Pollock, 1986; Sandelowski, 1987; Sweeny, Andrews, Nelson, & Robbins, 2015). However, the exact chain of responses between psychological stress and physiologic reactions to general stress are not well understood (Pruessner & Ali, 2015).

The role of physiologic stress hormones and their association to infertility is unclear. Cortisol, as a biological marker of stress, has been studied within the infertility population. Cesta et al. (2018) studied morning and evening salivary cortisol levels in relation to perceived stress

and IRS scores in women undergoing IVF but did not find any correlation or statistical significance. Miller et al. (2019) also studied salivary cortisol patterns during IVF and found no relationships between salivary cortisol and anxiety, however cortisol was significantly higher in the treatment phase of IVF compared to before or after treatments. Massey et al. (2016) found that hair cortisol, rather than salivary cortisol, was associated with IVF treatment outcome. In their study, women undergoing IVF that had higher hair cortisol levels had lower pregnancy rates. Hair cortisol measures chronic cortisol concentrations, as opposed to salivary cortisol which measures acute concentrations (Massey, Campbell, Raine-Fenning, Pincott-Allen, 2014). To date, only one study was found that compared the relationships between hair cortisol and psychological measures in women with infertility. Santa-Cruz, Caparros-Gonzalez, & Garcia-Velasco (2019) found no relationships between hair cortisol and anxiety, however hair cortisol levels increased over a three-month treatment period ($p < 0.001$), and was higher in women who did not conceive compared to women that did conceive after 12 weeks ($p < 0.001$). In the U.S., there is insufficient research focusing on psychological health, well-being, and psychological support for women with infertility. The following section will provide further background and significance for this study.

Significance

Prolonged Stress

Prolonged stress related to infertility can have profound consequences on physical and mental well-being. Infertility not only affects reproductive organs, but it can have psychological effects on patients as well. Lazarus & Folkman (1984) define psychological stress as "a particular relationship between the person and the environment that is appraised by the person as taxing or exceeding his or her resources and endangering his or her well-being" (p. 19).

Psychological distress in the literature is often operationalized broadly by measures of depression, anxiety, stress, and low well-being (Greil, 1997; Yuit Yah Wong et al., 2012). Infertility is well known to be a stressful life event for women, and has paralleled similar stress levels of chronic conditions, such as cancer (Cousineau & Domar, 2007; Laubmeier, Zakowski, & Bair, 2004). Women have rated infertility as one of the most dramatic stressful life events, consistent with parental death or partner infidelity (Matsubayashi et al., 2004). Infertility causes economic hardship (Wiersema et al., 2006) and psychological health consequences such as stress, anxiety, and depression (Greil, 1997; Yuit Wah Wong et al., 2012). There is strong evidence supporting that women have higher amounts of infertility-related stress (IRS) than men (Abbey, Andrews, & Halman, 1991; Casu & Gremigni, 2016; El Kissi et al., 2013; Galhardo et al., 2013; Newton, Sherrard, & Glavac, 1999; Peterson, Newton, Rosen, & Skaggs, 2006; Peterson, Pirritano, Christensen, & Schmidt, 2008).

Appraisals of stress can affect psychologic and physiological responses. Cortisol is a biological hormone secreted by the adrenal glands and is associated with acute and chronic stress through the HPA pathway. The HPA axis stimulation is especially sensitive to acute and chronic psychological stress (Nater et al., 2013), which causes the release of cortisol into the bloodstream, saliva, and hair (Lynch, Sundaram, Maisog, Sweeney, & Buck Louis, 2014). There have been few studies linking IRS to physiologic markers, such as cortisol, in women with infertility. In studies that measured cortisol levels in women with infertility, the majority collected salivary cortisol and did not show a statistically significant relationship between salivary cortisol levels and stress (Cesta et al., 2018; Lynch et al., 2014; Miller et al., 2019). Salivary cortisol concentrations measure acute stress levels (Nater et al., 2013) and may account for the lack of significant results since IRS is most likely an ongoing and chronic phenomenon.

Infertility can last for months and often years, leading to chronic IRS; therefore, considering the association of IRS and chronic physiologic markers is an important consideration. Hair cortisol levels indicate chronic cortisol levels (Hodes et al., 2017; Meyer, Novak, Hamel, & Rosenberg, 2014). Since hair grows one cm per month, a cumulative cortisol concentration over time can be derived from the length of hair taken at the root of the hair. In one study, women with infertility undergoing IVF with elevated hair cortisol levels had a reduced likelihood of pregnancy (Massey et al., 2016). While hair cortisol appears to be an important biomarker of chronic stress, the associations between hair cortisol levels and psychological measures such as IRS, coping, and quality of life are not known to be studied to date in women with infertility.

Pregnancy Loss

Pregnancy loss or miscarriage can also be a source of stress for women. It is estimated that 10-20% of recognized pregnancies (diagnosed by a urine pregnancy test) and 30-40% of all conceptions or unrecognized pregnancies (human chorionic gonadotropin elevation around embryo implantation prior to a diagnosis) result in pregnancy loss (Michels & Tiu, 2007). Pregnancy loss in the first trimester is more common than other trimester losses and was found in 43% of child-bearing age women (Cohain, Buxbaum, & Mankuta, 2017). Pregnancy loss rates of women experiencing infertility as a whole are largely unknown. However, the miscarriage rate for women who conceived after ART is reported as 16.2%, but increases significantly with age, with 58% of ART cycle pregnancies ending in miscarriage in women age 44 or older (CDC, ASRM, & SART, 2018a).

Pregnancy loss can have a significant psychological impact on women, including depression, anxiety, post-traumatic stress disorder, and suicide (Bhat & Byatt, 2016). Achievement of pregnancy after difficulty conceiving, and subsequent pregnancy loss can be

devastating emotionally for women with infertility. Cheung, Chan, & Ng (2013) compared psychological distress after pregnancy loss in women who conceived naturally and women who conceived through ART. The authors used the General Health Questionnaire to assess anxiety, depression, and mental well-being, and the Revised Impact of Event Scale to measure post-traumatic stress following miscarriage. There were significantly higher scores for both measures in women who conceived with ART at 4-and 12-weeks post-miscarriage compared to women who conceived naturally. Additionally, women who conceived after ART had higher hyperarousal symptoms on the Revised Impact of Event Scale at 4- and 12-weeks post-miscarriage compared to the women who naturally conceived ($p < 0.002$ and $p < 0.035$, respectively). This is significant as it emphasizes the highly traumatic nature of the miscarriage event for women who conceived with ART compared to those who conceived naturally (Cheung et al., 2013).

Quality of Life

Consequences of psychological distress and higher rates of IRS in the infertile woman have been associated with higher numbers of infertility treatment cycles (Boivin & Schmidt, 2005), lower pregnancy rates (Boivin & Schmidt, 2005; Hammerli, Znoj, & Barth, 2009), and decreased quality of life, impacting family ($p < .01$) and psychological/spiritual domains ($p < .05$) (van den Akker, 2005). The WHO defines quality of life (QOL) “as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns” (WHO, 2019b, para 2). Social and marital relationships impact QOL and are affected in women with infertility (Coëffin-Driol & Giami, 2004; Nelson, Shindel, Naughton, Ohebshalom, & Mulhall, 2008). Cultural and social influences in the context of infertility can lead to negative perceptions of womanhood (Hasanpoor-Azghdy,

Simbar, & Vedadhir, 2014) and contribute to social isolation (Wiersema et al., 2006). Further, social, relational, emotional, and mind/body components of a person contribute to psychological well-being and overall QOL (Boivin, Takefman, & Braverman, 2011). In those experiencing infertility, QOL impairment has been shown to affect women more than men (El-Messidi, Al-Fozan, Tan, Farag, & Tulandi, 2004; Rashidi et al., 2008).

Coping Strategies

To manage IRS, coping strategies are employed to adjust and control the emotions and challenges related to the experience of infertility. Coping strategies are particularly helpful to manage psychological distress. McQueeny, Stanton, & Sigmon (1997) conducted a longitudinal randomized control intervention comparing emotion and problem-focused coping strategies for women with infertility. The emotion-focused coping intervention group was encouraged to express emotions and engage in activities that reduced negative emotions, while the problem-focused coping intervention group focused on ways to increase perception of control, infertility information gathering, and infertility-related problem-solving strategies. Findings from the study suggested both emotion-focused and problem-focused coping strategies were effective in reducing psychological distress; however, at the 18-month follow up, the problem-focused coping intervention group had higher rates of pregnancy than the emotion-focused coping intervention group. Similarly, other studies found expressing emotions as a coping strategy was associated with lower pregnancy rates (Demyttenaere, Nijs, Evers-Kiebooms, & Koninckx, 1992; Demyttenaere et al., 1998; Panagopoulou, Vedhara, Gaintarzti, & Tarlatzis, 2006). However, “letting go” as an emotion-focused coping strategy was positively and significantly associated with higher pregnancy rates (Rapoport-Hubschman, Gidron, Reicher-Atir, Sapir, & Fisch, 2009). These findings suggest that emotion- and problem-focused coping strategies are

both effective for women with infertility, but the use of coping strategies at different points during the infertility experience may be important (McQueeny et al., 1997).

In summary, the focus of infertility research has primarily been treatment-focused, rather than focused on the experience of infertility from a holistic perspective. Holism considers the connection between the mind and body, which cannot be separated (Fontaine, 2015). Most infertility research to date does not focus on the mind-body connection or psychological aspects of a person. Recent infertility literature on stress between 2003 to 2019 is focused on couples, gender differences related to stress, and differences in coping strategies. The interlace between psychological and physiological IRS, coping, and QOL in women with infertility has not been examined to date. Further, there is a dearth of studies conducted in the U.S. that examine the psychological well-being of women with infertility. Furthermore, the multicultural implications of infertility impact our understanding of levels of stress, coping, and QOL in all women undergoing infertility treatments. This study examined relationships between IRS, coping, and QOL in women with infertility to further inform the development of appropriate nursing interventions related to coping, decreasing stress during the infertility experience, improving psychological health, and increasing QOL.

This study also contributed innovative approaches to measuring chronic stress in a sample of women with IRS through hair cortisol concentrations and using internet-based recruitment through Facebook. Recruiting population-based participants through online social media was an innovative strategy when compared to the clinic-based recruitment that dominates the literature and limits generalizability. Recruiting through an online strategy increased the reach of the study to a national level, which is important given the lack of studies considering IRS, coping, and

QOL in the U.S. Further discussion and exploration of the use of social media for recruitment in nursing research is presented in Chapter Two and in the first manuscript of this dissertation.

Purpose

The purpose of this study was to a) examine the relationships between infertility-related stress, coping, and quality of life in women undergoing infertility treatments, b) evaluate the relationships between chronic cortisol levels (hair cortisol) and infertility-related stress, coping, and quality of life in women undergoing infertility treatments, and c) determine the relationships between infertility characteristics (IVF, non-IVF, and pregnancy loss) and infertility-related stress, coping, and quality of life in women undergoing infertility treatments.

Theoretical Framework

The theoretical framework for this research study was the transactional theory of stress and coping (TTSC) by Lazarus & Folkman (1984), a well-known theory used in health and social sciences. Within nursing research, the TTSC has been used in a variety of patient populations including those with HIV, asthma, pain, chronic heart failure, psychiatric disabilities, military, new motherhood, and pregnancy loss (Rice, 2012). It has also been used in psychology and sociology in similar patient populations such as individuals with chronic pain (Banerjee, Bhattacharya, & Sanyal, 2014) and psychological adjustment to cancer (Laubmeier et al., 2004).

Stress and coping are terms that have been used in the physical world; stress is often associated with strain, exerting force, tension, or pressure upon an object or part (Oxford English Dictionary, 2017a) and coping could refer to a type of joint and saw, called a coping joint and a coping saw, or the angle of a wall or ceiling (Oxford English Dictionary, 2017b). However, it is within the biological and psychological worlds that stress and coping relate to the human experience. Assumptions within the TTSC imply that stress and coping are conceptual terms that

cannot be separated; therefore, a person cannot experience psychological stress without having a coping response as a result of the stress. Lazarus & Folkman (1984), defined stress as "a particular relationship between the person and the environment that is appraised by the person as taxing or exceeding his or her resources and endangering his or her well-being" (p. 19). Coping, therefore, is the "process through which the individual manages the demands of the person-environmental relationship that are appraised as stressful and the emotions they generate" (Lazarus & Folkman, 1984, p.19).

According to the TTSC, antecedents of the model include a person's values and beliefs, environmental factors, social networks, vulnerability, genetic factors, and other risk factors related to a potential stressor. These antecedents, or precursors to an appraisal of a stressor can influence how a person perceives the stressor, and later manages the stressor. A person can appraise a situation or event, known as a primary appraisal, as irrelevant (no implication for well-being), benign-positive (construed as positive, or enhances well-being), or stressful (threat, harm/loss, or challenge). Stress appraisals lead to a positive or negative view of the stressor, which determines if the person perceives the stressor as a challenge (positive), or threat or harm/loss (negative), which can occur together or separate. Personal and situational factors influence a person's appraisal of a stressor. Personal factors including beliefs, commitments, and vulnerability, and situational factors including uncertainty, predictability, and duration, can influence the primary appraisal (Lazarus & Folkman, 1984).

Once the primary appraisal of the stressor is complete, a secondary appraisal assessing the coping options, the likelihood of the effectiveness of those options, and the expectations of the coping options to control the stressor is made. Coping is accomplished through emotional-based or problem-based coping, to both lessen and regulate the emotional response, and/or to

alter the problem causing the distress. Coping strategies based on either emotion- or problem-based coping are then used. Emotion-focused coping includes emotion regulation strategies and problem-focused coping includes finding solutions and removing barriers (Lazarus & Folkman, 1984).

Perceived levels of threat can also influence a person's coping strategy. Often, primary appraisals of a threat or harm/loss are met with emotion-focused coping. Examples of emotion-focused coping include avoidance, distancing, minimizing negative feelings with positive values, using social support, meditating, or activities that can distract the person from the stress. Emotion-focused coping is used to maintain optimism and hope. Primary appraisals of a challenge can result in problem focused coping, which alter the environment or internal cognitive change. Examples of problem-focused coping strategies include delineating the problem, finding alternative solutions, overcoming barriers and finding new resources, and developing or learning new skills.

Coping effectiveness is appraised for outcomes, which are viewed as effective or ineffective based on management of negative feelings. Later work by Folkman (1997) and Park & Folkman (1997) included the addition of meaning-based coping as a further strategy to manage negative feelings from ineffective emotion- and problem-focused coping strategies. Meaning-based coping includes positive reappraisals, spiritual beliefs, and revised goals to manage feelings of distress (Park & Folkman, 1997).

Lastly, reappraisal of the coping strategies and the stressor causing the stress occurs. Immediate outcomes of coping, according to Lazarus & Folkman (1984), include physiologic changes, positive or negative feelings, acute illness, and social support or alienation. Long-term

effects or consequences include social failure or success, morale, quality of life, and recovery from illness or chronic illness (Lazarus & Folkman, 1984).

The TTSC can be applied within the context of infertility. Figure 1 describes the model of the experience of being infertile. In the context of infertility, antecedents, or factors or events that occur prior to the presence of a concept (Walker & Avant, 2011), are personal factors, including attitudes, expectations, past coping behaviors and beliefs, as well as situational factors, including the etiology of infertility, duration of infertility, and the financial burden of infertility. The stressors of infertility include the infertility diagnosis and subsequent infertility treatments. The stressor is appraised as a threat, harm/loss, or challenge. Personal, social, and cultural factors, a person's commitment to parenthood, and uncertainty of the experience of infertility will influence the secondary appraisal or options for coping with infertility. These factors also influence the subsequent coping strategies that are utilized by the person experiencing infertility. Coping can be emotion-focused, problem-focused, or meaning-based to regulate responses to infertility. Most typically, threat or harm/loss appraisals related to the use of emotion-focused coping, and challenge appraisals related to the use of problem-focused coping (Lazarus & Folkman, 1984). Coping is evaluated as effective or ineffective, and influences self-efficacy, resilience, or emotional fragility, within the model. Reappraisal of coping and stress occurs. Additionally, social and cultural factors influence the experience. Psychological consequences of the model in the context of infertility include increased or decreased IRS, anxiety, or depression. Empirical referents, or characteristics that demonstrate the concept occurred (Walker & Avant, 2011), include positive or negative relationship satisfaction, emotional stability in regulating emotions and behaviors, QOL, and pregnancy rates. The TTSC guided the research questions and the state of science for the research study.

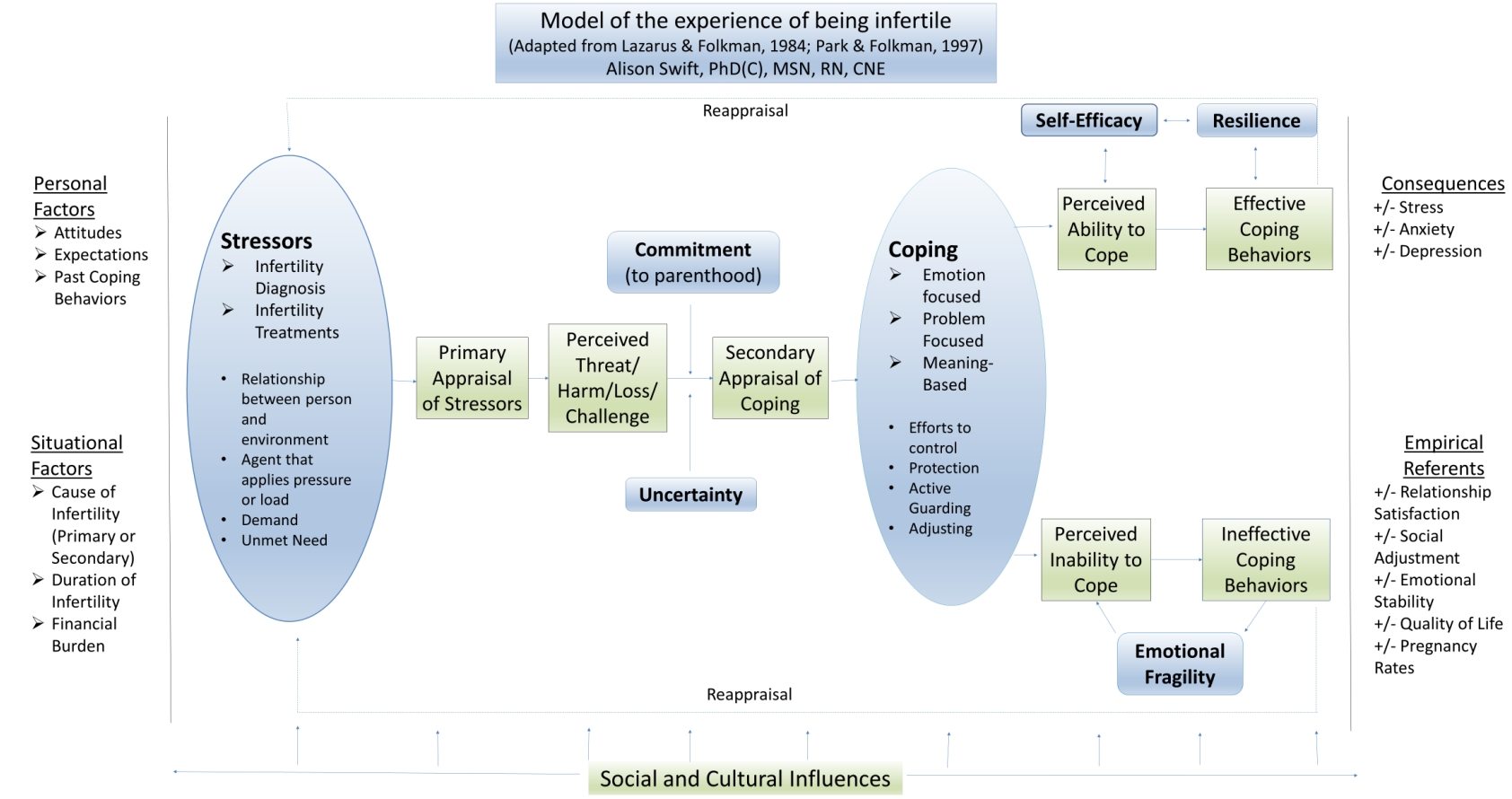


Figure 1. Model of the Experience of Being Infertile

Specific Aims and Research Questions

The aims of the study were to examine the relationships between IRS, coping, and QOL in women undergoing infertility treatments; evaluate the relationships between chronic stress as measured by hair cortisol levels and IRS, coping, and QOL in women undergoing infertility treatments; and determine the relationships between personal and situational factors and infertility characteristics and IRS, coping, and QOL in women undergoing infertility treatments. Therefore, the research questions are:

1. In women undergoing infertility treatments, what are the relationships between infertility-related stress, coping, and quality of life?
2. In women undergoing infertility treatments, what are the relationships between hair cortisol levels, infertility-related stress, coping, and quality of life?
3. What are the relationships between infertility characteristics (infertility treatment types [IVF vs. non-IVF] and pregnancy loss) and infertility-related stress, coping, and quality of life?

Definitions

The following terms are defined for this study:

Infertility: the inability to maintain or achieve a pregnancy after 12 months of unprotected sexual intercourse. This is operationalized by self-report in the study.

Primary infertility: "unable to ever bear a child, either due to the inability to become pregnant or the inability to carry a pregnancy to a live birth" (WHO, 2019a, para 7). This is operationalized by self-report.

Secondary infertility: "unable to bear a child, either due to the inability to become pregnant or the inability to carry a pregnancy to a live birth following either a previous pregnancy or a

previous ability to carry a pregnancy to a live birth" (WHO, 2019a, para 8). This is operationalized by self-report.

Infertility-related stress: a form of psychological distress that affects multiple life domains and results in the person's appraisal of the situation as taxing, exceeding resources, and endangering well-being. This is operationalized by the Copenhagen Multi-centre Psychosocial Infertility Fertility Problem Scale (Schmidt, 2006).

Hair cortisol: a physiologic biomarker that measures chronic stress. One centimeter of root hair measures the accumulation of 1 month of cortisol. This is measured through hair cortisol processing at an independent laboratory.

Coping: "constantly changing cognitive behavior efforts to manage specific external or internal demands that are appraised as taxing or exceeding the resources of the person" (Lazarus & Folkman, 1984, p. 141). Coping can be problem-focused (altering the problem causing the stress), emotion-focused (regulating emotions to manage stress) or meaning-based (placing meaning or value on the stress). This is operationalized by the Copenhagen Multi-centre Psychosocial Infertility Coping Styles Scale (Schmidt, 2006).

Quality of Life: "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (WHO, 2019, para 2). This is operationalized by the Fertility Quality of Life questionnaire (Boivin et al., 2011).

Personal Factors: individual characteristics that influence a person's appraisals of stress and coping options, which include commitments, beliefs, and vulnerability (Lazarus & Folkman, 1984).

Situational Factors: aspects and components of a situation that influence a person's appraisals of stress and coping options, which include new situations, predictability, uncertainty, imminence, and duration of the stressor (Lazarus & Folkman, 1984).

Assumptions

Underlying the study are several assumptions. First, primary appraisals of infertility are framed as a stress appraisal, which includes threat, harm/loss, or challenge. Second, because infertility and infertility treatments are appraised as stressful, there is a natural progression to a secondary appraisal to assess coping strategies. Third, quality of life is impacted by stress and coping responses as an empirical referent of stress and coping. Fourth, participants who answered the questions and completed questionnaires met the inclusion criteria for the study. Fifth, hair cortisol samples were taken from the individual who completed the survey. Lastly, hair cortisol samples were obtained according to the instructions given to participants on how to obtain the hair sample.

Descriptions of Manuscripts

The dissertation presented in this paper follows the Manuscript Option Dissertation. In lieu of Chapter 4 and 5 of the traditional dissertation, two manuscripts are presented.

Manuscript one is an integrative review using systematic methods to examine the use of Facebook for participant recruitment in nursing research. The research methodology of this dissertation study involved using Facebook for participant recruitment, and therefore the examination of recruitment strategies and best practices was warranted. The second manuscript answers the research questions proposed in this dissertation.

Manuscript two presents the findings of the study examining the relationships between IRS, hair cortisol concentrations, coping, and QOL among women undergoing infertility treatments,

and relationships between IRS, coping, QOL among treatment types (IVF and non-IVF), and pregnancy loss.

Summary

Infertility is defined as the inability to maintain or achieve pregnancy after 12 months of unprotected sexual intercourse. The TTSC provided a useful framework to examine IRS and coping because it is a well-accepted theory and applicable in the context of infertility. Infertility-related stress affects multiple domains of a person's life and well-being, such as personal, social, and marital domains. Personal and situational factors influence appraisals of infertility as a threat, harm/loss, or challenge. Appraisals of IRS lead to emotion-focused, problem-focused, or meaning-based coping, which manage the emotions and challenges of infertility and impact psychological well-being and QOL.

Physiologic stress, such as elevated cortisol levels has been studied as a measure of stress in women with infertility, most commonly using salivary cortisol, however results are mixed with most recent findings showing no statistically significant results between cortisol measures and stress. Hair cortisol concentrations to measure chronic cortisol levels with psychological stress symptomatology has not been examined in women with infertility. There are few studies conducted in the U.S. that consider the psychological health and well-being of women with infertility from a holistic perspective.

This study evaluated IRS, hair cortisol levels, coping, and QOL in women undergoing infertility treatments, and examined the relationships between IRS, coping, and QOL among treatment types (IVF and non-IVF) and pregnancy loss.

CHAPTER 2: LITERATURE REVIEW

The purpose of this study was to 1) examine the relationships between infertility-related stress (IRS), coping, and quality of life (QOL) in women undergoing infertility treatments, 2) evaluate the relationships between chronic cortisol levels (hair cortisol) and IRS, coping, and QOL in women undergoing infertility treatments, and 3) determine the relationships between infertility characteristics (IVF vs. non-IVF and pregnancy loss) and IRS, coping, and QOL in women undergoing infertility treatments. Consistent with the aims of this study, the review of the literature is as follows: (a) literature that describes the theoretical perspectives of stress and coping, (b) literature that describes IRS and physiologic (cortisol) stress in women with infertility, (c) literature that describes personal and situational factors associated with IRS, (d) literature that describes the relationship between IRS and coping, and (e) literature that describes QOL in women as it relates to IRS, coping, and personal and situational factors. Limitations and gaps of the literature are also examined.

Theoretical Perspectives of Stress and Coping

The theoretical framework that guided this study was the transactional theory of stress and coping (TTSC), as described by Lazarus & Folkman (1984). The TTSC is defined by the concepts of psychological stress and coping. A literature review to further clarify the concepts of stress and coping within the TTSC is presented in the following sections.

Stress

Biological stress was first described by Hans Selye, noted as the father of biological stress and adaptation, in his development of the General Adaptation Syndrome theory (Selye, 1954). Stress from a psychological standpoint was first considered after World War II, and then further developed by Lazarus throughout the 1950s. In the 1960s and 1970s, Lazarus connected the link between stress and adaptation in response to stress (Lazarus & Folkman, 1984).

Collaboration with Folkman led to the early beginnings of the TTSC in the late 1970s. Lazarus & Folkman (1984) define psychological stress resulting from an interaction between a person and environment that is appraised as taxing or exceeding resources that threatens well-being.

According to the TTSC, stressors are primarily appraised as threat, harm/loss, or challenge. Appraisals of threat result when a harm/loss has not yet occurred. Harm/loss appraisals occur when damage to well-being or commitments has transpired. Threat and harm/loss appraisals elicit negative emotions, such as anxiety, fear, and anger. Stress that has the potential for growth or gain is appraised as a challenge, and will have more positive emotions, such as eagerness (Biggs, Brough, & Drummond, 2017; Lazarus & Folkman 1984). A secondary cognitive appraisal for coping options occurs after the primary appraisal concludes (Lazarus & Folkman, 1984). The concept of coping within the TTSC is described in the following section.

Coping

In the 1960s and 1970s, Menninger, Haans, and Valliant each developed hierarchical ego processing adaptation models, which included coping with stressful situations as a top priority and described various coping styles. This effort in ego processes led to the cognitive styles of coping developed by Lazarus and Folkman and served as a basis for the theoretical underpinnings of the TTSC (Lazarus & Folkman, 1984). Adaptations to stress, or coping, is defined as "constantly changing cognitive and behavioral efforts to manage specific external and/or internal demands that are appraised as taxing or exceeding the resources of the person" (Lazarus & Folkman, 1984, p.141). Coping strategies are emotion-focused coping (strategies employed to manage the emotions of a stressor) or problem-focused coping (strategies employed to problem-solve or alter the stressor). Emotion-focused coping includes strategies such as avoidance and distancing, and is widely considered to be maladaptive. Problem-focused coping

includes planning and problem-solving within the context of the stressor and is considered to be adaptive (Biggs et al., 2017; Lazarus & Folkman 1984). However, emotion-focused coping may be particularly useful in the short-term to regulate negative emotions of a stressor so that problem-focused coping strategies may be appraised later (Biggs et al., 2017; Folkman & Moskowitz, 2004).

TTSC

The TTSC is one of the most widely used and supported theories for psychological stress and coping (Folkman, 2010). A notable revision to the TTSC is the inclusion of meaning-based coping. Meaning-based coping, or meaning-focused coping, modifies appraisals to assign meaning on the stressor based on values, beliefs, and goals (Folkman, 1997). The use of meaning-based coping creates positive emotions and is helpful with chronic stress and uncontrollable situations (Biggs et al., 2017; Folkman, 1997).

The TTSC has been used in a variety of disciplines, especially in psychology and sociology (Banerjee et al., 2014; Laubmeier et al., 2004). In the nursing profession, the TTSC has been used in studies of chronic health conditions such as HIV, pain, chronic heart failure, and psychiatric disabilities (Rice, 2012). Within the infertility experience, the TTSC is the most often used theoretical framework to describe IRS and coping (Gourounti et al., 2012; Lykeridou et al., 2011 Schmidt, 2006), and therefore was selected as a guiding theoretical framework for this study. The concept of stress from the TTSC perspective provides a framework for the concept of infertility-related stress (IRS) within the infertility experience. Literature describing IRS in women is discussed in the following sections.

Infertility-Related Stress in Women

The stress of infertility has often been studied qualitatively, with patients reporting feelings of stress, tension, and pressure, making statements such as, “It was really stressful, very stressful” (Benasutti, 2003). Temporal and spiritual stress was also found in women with infertility, describing rumination in the uncertainty of infertility duration (Sandelowski & Pollock, 1986). While at times authors of studies discussed stress as the variable of interest, stress was often assessed by a variety of measurements and with other related constructs, such as anxiety and depression. Anxiety (Demyttenaere,Nijs, Evers-Kiebooms, & Koninckx, 1991; Demyttenaere et al., 1992; Pasch et al., 2012) and depression (Hynes, Callan, Terry, & Gallois, 1992; Pasch et al., 2012) were used to measure infertility related stress, with high levels of anxiety and depressive symptoms found in women with infertility.

The findings of IRS research have conflicting results. Some studies suggested high levels of IRS in women (Donkor & Sandall, 2007; Miles, Keitel, Jackson, Harris, & Licciardi, 2009; Turner et al., 2013). However, other studies found women with infertility had low to moderate levels of IRS (Gourounti, Anagnostopoulos, & Vaslamatzis, 2011; Lykeridou, Gourounti, Deltsidou, Loutradis, & Vaslamatzis, 2009; Lykeridou et al., 2011) or similar stress levels compared to the general population (Greil,1997). Women with infertility may perceive high levels of stress that might not be clinically significant or much different than the overall stress levels of the general population (Greil, 1997).

Sources of Infertility-Related Stress

Newton et al. (1999) described IRS from various domains of a person’s experience, including social, relationship, sexual, the need for parenthood, and rejection of the childfree lifestyle. Other infertility-related stressors include personal, marital and social stress (Aflakseir & Zarei, 2013; Lykeridou et al., 2009; Lykeridou et al., 2011; Martins, Peterson, Almeida, &

Costa, 2012), occupational stress (Barzilai-Pesach et al., 2006), and the stress of infertility treatments (Chiba et al., 1997; Greil et al., 1997; Greil et al., 2011; Pasch et al., 2012; Sandelowski & Pollock, 1986).

The level of personal stress of the infertile woman can vary depending on the intensity of threat potential for childlessness and the need for parenthood. Personal stress is the disruption of personal life, including perceived strain on relationships with other women with children or who are pregnant, and includes stress related to physical and mental health perceptions (Schmidt, Holstein, Christensen, & Boivin, 2005a). In the studies examined, women with infertility had higher levels of personal stress compared to other dimensions of stress, such as marital stress (perceived crisis in marriage) or social stress (relationship strain with friends and family) (Aflakseir & Zarei, 2013; Lykeridou et al., 2011; Martins et al., 2012).

Infertility-related stress has also been found during the treatment cycles of infertility (Greil et al., 1997). Higher levels of psychological distress were found in women prior to the start of an in vitro fertilization (IVF) cycle and immediately after the cycle concluded (Pasch, et al., 2012). Patients have described infertility treatments and treatment outcomes as uncertain (Sandelowski & Pollock, 1986, p. 142), which can increase IRS in the infertile woman.

The multiple sources of stress for the infertile woman does not lend to defining a specific source of stress or stressor that affects treatment outcomes and the overall psychological health of the woman. Identifying a specific stressor that has the biggest impact on the experience of infertility may not be possible. The unique nature of the infertility experience encompasses the presence of multiple sources of stress and individual appraisals. Individual perception of personal and environmental factors can lead to appraisals or assessment of stress as a threat,

harm/loss, or challenge (Lazarus & Folkman, 1984), which is described more below in the context of the infertility experience.

Primary Appraisals of Stress

Primary appraisals are defined by Lazarus & Folkman (1984) as the cognitive process of an individual to categorize an encounter or event, with respect to its importance on well-being. Stressors that are perceived as stressful are primary appraised as a threat, harm/loss, or challenge (Lazarus & Folkman, 1984).

Threat. Stressors appraised as a threat are harm or loss that has not happened yet and often leads to anxiety, fear, and anger (Lazarus & Folkman, 1984). Women undergoing infertility treatments were found to not use threat appraisals, but rather harm/loss or challenge appraisals (Hansell, Thorn, Prentice-Dunn, & Floyd, 1998). However, in the study by Hansell et al. (1998), it is not known if threat appraisals occurred, since appraisals were not measured prior to treatments initiation.

Harm/loss. Stressors that are primarily appraised as a harm/loss occur when damaging life events that have significant psychological implications have been sustained. Hansell et al. (1998) and Prattke & Gass-Sternas (1993) found primary appraisals of women with infertility were perceived as a harm/loss or challenge while undergoing infertility treatments. For a woman undergoing infertility treatments, a harm/loss appraisal could signify profound harm or loss of fertility and depressive symptoms. Women who appraise social expectations of motherhood or view the need for parenthood as important may appraise the situation as a threat or harm/loss. Studies have found women who appraise social expectations of motherhood and the need for parenthood as important had higher levels of IRS (Lansakara, Wickramasinghe, & Seneviratne, 2011; Miles et al, 2009). Additionally, cultural expectations, such as the expectation of women to

bear children, may also impact primary appraisals as a threat or harm/loss, particularly when violence may be inflicted on the woman by a husband for being infertile, and women who are infertile are socially excluded (Aflakseir & Zarei, 2013; Karaca & Unsal, 2015).

Challenge. Primary appraisals of challenge focus on the potential for growth and often include positive emotions, such as eagerness (Lazarus & Folkman, 1984). Perceiving infertility as a challenge was associated with decreased distress compared to the other appraisals of loss and threat (Hansell et al., 1998; Prattke & Gass-Sternas, 1993). Challenge appraisals prior to or during infertility treatment could signify optimism for the potential of successful treatment.

Cortisol as a Measure of IRS

Cortisol, a glucocorticoid hormone, is a well-documented stress hormone derived from complex hormonal pathways through the hypothalamus, pituitary, and adrenal glands (Kyrou & Tsigos, 2009). There are limited studies with mixed results considering the role of cortisol in the woman with infertility. Cortisol has been measured in women with infertility through salivary, serum, urine, and hair samples. Salivary cortisol measures are the most reported in the literature.

In women undergoing IVF, several studies found no association between salivary cortisol levels and pregnancy rates (Cesta et al., 2018; Massey et al., 2016; Miller et al., 2019; Nouri et al., 2011) or perceived stress (Cesta et al., 2018). Miller et al. (2019) measured salivary cortisol levels and perceived stress at various times during the IVF treatment cycle. Throughout the treatment cycle, perceived stress and salivary cortisol levels were shown to increase to a maximum level at oocyte retrieval day (39% increase for perceived stress, salivary cortisol 0.59 $\pm$ 0.29 μg/dl, $p < 0.029$), then decrease at embryo transfer day (12% decrease for perceived stress, salivary cortisol 0.42 $\pm$ 0.23 μg/dl, $p < 0.0162$). While these findings showed variations in the stress patterns of women with infertility during an IVF treatment cycle, the authors found no

significant correlations among salivary cortisol levels, perceived stress and pregnancy outcomes (Miller et al., 2019). Other studies of infertile women that measured serum or plasma cortisol levels did not find an association between cortisol and depression (Freeman et al., 2018) or ovarian reserve (Pal et al., 2010). Contrary, Demyttenaere et al. (1991) found that what they described as elevated anticipatory serum cortisol, measured before oocyte retrieval during IVF, predicted higher depression scores. Massey et al. (2014) conducted a systematic review and found 16 studies that considered salivary, serum, or urine cortisol and IVF outcomes. Half of the studies in Massey et al. (2014) systematic literature review found associations between cortisol and IVF outcomes, which included pregnancy rates, oocyte retrievals, fertilization rates, and pregnancy loss.

Salivary cortisol is an acute marker of stress as compared to hair cortisol, which is a chronic marker of stress (Massey et al., 2016). The timing of collection of salivary cortisol may influence the results related to circadian rhythms. Cortisol peaks in the morning and is lower in the evening. An inconsistency in the collection time of participants between the studies could have resulted in the inconsistency of results in studies of women with infertility in which salivary cortisol was measured. Further, adrenal exhaustion from chronic stress may lower cortisol levels temporarily (Vashist & Schneider, 2014). It may be that chronic dysregulation from stress may lead to hypoactive HPA axis stimulation, which could result in lower cortisol levels (Vives et al., 2015).

Hair cortisol is a newer technique in analyzing cortisol levels, but has been rarely used as a measure of stress in women with infertility. Cortisol may accumulate by diffusion in the medulla of the hair shaft and may represent systemic cortisol levels. With the hair growth rate of one cm per month, it is possible to measure cortisol from a chronic standpoint over a period

several months (Russell, Koren, Rieder, & Van Uum, 2012). Variations in hair cortisol levels have been shown among other study cohorts (Vives et al., 2015), and may be influenced by medications, hair characteristics, hair care, or analysis method (Binz et al., 2018; Meyer et al., 2014). Binz et al. (2018) established a reference range for hair cortisol levels in toddlers, adolescents, and adults. The adult reference range is 4-15 pg/mg.

In women with infertility, hair cortisol has shown to be associated with pregnancy rates. Massey et al. (2016) found hair cortisol was able to predict IVF pregnancy outcome ($p < .017$) and accounted for 26.7 % of the variance in lower pregnancy rates for women undergoing IVF. Nery et al. (2019) conducted a randomized control trial of an eight-week mind-body program intervention for IRS. There was a significant reduction in IRS and depression and increase in quality of life compared to a no intervention control group. Hair cortisol concentrations did not differ significantly pre- and post-intervention; however, it is important to note the small subsample size in the hair cortisol cohort and that the mind-body intervention was short (eight weeks) compared to other mind-body interventions in the literature that are at least 10 weeks (Domar et al., 2000; Galhardo et al., 2013; Psaros et al., 2012). Only one study was found that considered psychological distress and hair cortisol. Santa-Cruz et al. (2019) found no relationship between hair cortisol and anxiety, though higher hair cortisol was associated with more depressive symptoms and lower pregnancy rates. There were no other studies found that considered IRS relevant to hair cortisol in infertile women.

Personal and Situational Factors Associated with IRS

Situational and personal factors can impact primary appraisals of stress. Situational factors include new situations, predictability, uncertainty, imminence, and duration of the stress. Personal factors that may influence primary appraisals include vulnerability, beliefs, values, and

commitments (Lazarus & Folkman, 1984). When applying the TTSC to the infertility experience, situational factors may include the infertility diagnosis and infertility treatments, including duration and potential for pregnancy outcomes, which are unpredictable and uncertain. Personal factors may include commitment to parenthood, beliefs and values related to social and cultural influences, as well as demographic-related factors, such as age and socioeconomic status.

Several studies reviewed considered relationships between IRS and personal and situational factors within the infertility experience. Variables within the experience of infertility considered for this review are based on the specific aims and potential factors that affect IRS, coping, and QOL, such as the type of infertility (either primary or secondary), duration of infertility in years, presence of pregnancy loss, and other population demographics.

Type of Infertility

Several studies found no relationship between the type of infertility and IRS (Donkor & Sandall, 2007; Gibson & Myers, 2002; Gourounti et al., 2012); however, other studies reviewed did find a relationship between the type of infertility and IRS (Lansakara et al., 2011; Lykeridou et al., 2009).

Primary infertility, defined as the inability to ever conceive or carry a pregnancy to live birth (WHO, 2019a), was significantly associated with psychological distress ($p < 0.001$), with 61% of women with primary infertility reporting some form of psychological distress (Lansakara et al., 2011). Higher levels of state anxiety ($p < 0.007$) and social stress ($p < 0.007$) were found in women who were infertile due to male factor infertility compared to women with unexplained infertility or a combination of male and female factors (Lykeridou et al., 2009). Most findings

support no relationship in stress levels to the etiology of infertility, which supports that there is stress across the experience of infertility, regardless of the cause or diagnosis.

Duration of Infertility and Treatment Cycles

Duration of infertility, defined as the number of years with infertility, was not associated with IRS in several studies (Demyttenaere et al., 1991; Gourounti et al., 2012; Lansakara et al., 2011; Lykeridou et al., 2009; Pasch et al., 2012). Some studies found no relationship between the number of treatment cycles and IRS (Demyttenaere et al., 1991; Gourounti et al., 2012; Lykeridou et al., 2009), while others did find an association between the number of treatment cycles and IRS (Donkor & Sandall, 2007; Prattke & Gass-Sternas, 1993). For example, psychological distress increased as the treatment cycle progressed (Hynes et al, 1992; Lawson et al, 2014), especially in the waiting stage between ovulation or egg transfer and pregnancy test (Boivin & Lancastle, 2010). The studies by Hynes et al. (1992), Lawson et al. (2014), and Boivin & Lancastle (2010) suggest there is an association between IRS and the treatment cycle, but the association could vary based on when in the cycle the infertility related stress is measured. Reasons for the lack of association of stress related to duration of infertility are unknown. Perhaps overtime, the uncertainty of the experience of infertility treatment itself could lessen, especially related to the stress of treatment cycles, as the woman becomes more familiar with the treatment experience. Less uncertainty could have a protective effect for the woman who has experienced infertility treatment cycles compared to a newly diagnosed woman who would be unsure of the treatment experience. However, the uncertainty of the outcome of treatment, such as a positive pregnancy test or confirmed pregnancy remains.

Pregnancy Loss

Pregnancy loss in the first trimester can cause increased psychological distress for women with infertility, including increased levels of stress and depressive symptoms, and lower quality of life scores, compared to women who do not have a diagnosis of infertility (Cheung et al., 2013). Interestingly, only three studies were found that considered the relationship between stress and pregnancy loss in infertile women. Schwerdtfeger & Shreffler (2009) compared four groups of women in the United States (U.S.): mothers with no fertility problems, mothers with a history of pregnancy loss, women who were childless with pregnancy loss, and women who were childless and infertile. Childless women who experienced infertility and pregnancy loss had high amounts of distress, as measured by perceived levels of depression and self-esteem, and lower life satisfaction scores, especially compared to mothers who experienced pregnancy loss ($p < .001$ and $p < .05$, respectively). Schwerdtfeger & Shreffler (2009) did not report if the women in their study were seeking treatments, undergoing treatments, or foregoing treatments for infertility at the time of the study. This could be an important distinction of stress levels related to the active experience of infertility, which often includes treatments.

Concurrent treatment cycles with a recent experience of pregnancy loss could result in high levels of stress. Women with infertility who experience pregnancy loss reported feelings of starting from “square one”, struggling with hope, running out of time, anger and frustration, a lack of understanding by others, feeling guilty about causing the loss, feeling alone, and feeling numb with grief (Freda, 2003). While these themes do not directly define stress, many of these themes and statements by the women in the study indicate appraisals of threat or harm/loss, which are appraisals indicating stress.

Demographic factors

Demographic factors such as age, socioeconomic status, and educational attainment have been examined in the context of IRS in the literature. Infertile women older than 35 years were found to report more stress, anxiety, and depression than their younger counterparts (Demyttenaere et al., 1991; Gourounti et al., 2012; Lansakara et al., 2011). A woman's fertility lessens with age (Bensasutti, 2001), resulting in feelings of increased pressure related to time and childbearing potential (Sandelowski & Pollock, 1986). Lower income levels were associated with greater IRS (Boivin, Saunders, & Schmidt, 2006; Donkor & Sandall, 2007), especially personal stress (Lykeridou et al., 2011). Additionally, infertile women with less education had higher levels of IRS (Donkor & Sandall, 2007; Lansakara et al., 2011; Lykeridou et al., 2009), with the exception of two studies that found no relationship between IRS and education level (Gourounti et al., 2012; Pasch et al., 2012). In the U.S., income levels are often reported in studies with infertility participants, rather than socioeconomic status. Women undergoing infertility treatment in the U.S. often pay out-of-pocket for treatments since insurance typically does not cover the high costs of infertility-related treatment (RESOLVE, 2019b), placing a significant burden on women who are economically challenged.

Infertility-Related Stress and Coping in Women

The following section will discuss the relationship between stress and coping in women with infertility, using the framework developed by Lazarus and Folkman (1984). According the Lazarus & Folkman (1984), after the initial stress appraisal, a secondary appraisal to determine the appropriate coping option, such as emotion-focused or problem-focused coping, is considered by the individual. In the context of the infertility experience, emotion-focused and problem-focused coping would most likely be employed to manage IRS. The relationship

between IRS and emotion-focused coping, and the relationship between IRS and problem-focused coping are discussed below.

Infertility-Related Stress and Emotion-Focused Coping

According to Lazarus & Folkman (1984), emotion-focused coping is a coping function that regulates emotional response to a stressor. Emotion-focused coping is more likely to occur in situations where nothing can be done to change the situation or stressor (Lazarus & Folkman, 1984). Examples of emotion-focused coping strategies include avoidance/distancing, positive comparisons, minimizing the threat, wishful thinking, seeking social support, and blaming self. Often, concerns about physical health is appraised as a threat, and will lead to emotion-focused coping (Lazarus & Folkman, 1984).

High levels of IRS in women were found to be associated with emotion-focused coping (Gourounti et al., 2012; Karaca & Unsal, 2015), particularly the use of avoidance coping (Aflakseir & Zarei, 2013; Demyttenaere et al., 1991; Gourounti et al., 2012; Hynes et al., 1992; Lykeridou et al., 2011; Panagopoulou et al., 2006) and seeking social support (Demyttenaere et al., 1991; Hynes et al., 1992). Expression of emotion may occur after seeking social support, and has been found to be maladaptive if used long-term as opposed to short term (Carver, Scheier, & Weintraub, 1989; Hynes et al., 1992). However, emotion-focused coping was helpful in decreasing stress in infertile women (Gibson & Myers, 2002), especially when the strategy of expressing emotions was employed (Panagopoulou et al., 2006) or and seeking emotional or social support (Gibson & Myers, 2002; Qadir, Khalid, & Medhin, 2015).

When coping with uncertainty, emotion-focused coping strategies are usually employed, as the problem of the stressor may be difficult to identify or address (Schmidt et al., 2005). Lazarus & Folkman (1984) maintain that uncertainty and lack of control lead to emotion-focused

coping strategies when the situation is appraised as uncontrollable. There is strong support for uncertainty in the experience of being infertile (Sandelowski & Pollock, 1986; Sandelowski, 1987; Sweeny et al., 2015). Based on this review of literature, coping strategies most often reported to be used by women with infertility are aspects of emotion-focused coping, which could be related to the level of uncertainty in the experience of infertility. Use of emotion-focused coping in women with infertility would be supported based on the uncertainty model (Sweeny et al., 2015), including uncertainty about physical health (Lazarus & Folkman, 1984). However, it is not known if emotion-focused coping is considered more helpful for the patient with infertility compared to problem-focused (action-focused) coping that is associated with resilience (de Lacey, Smith, & Paterson, 2009; Sexton et al., 2010).

Infertility-Related Stress and Problem- and Meaning-Focused Coping

Problem-focused coping directly modifies or alters the problem causing the stress, as the stressor is appraised as modifiable to change. Problem-focused coping strategies include finding alternative solutions to a problem and is contextual in application. The situation will define the solution to a particular problem; therefore, solutions in one context may not be plausible in another context (Lazarus & Folkman, 1984). Examples of problem-focused coping strategies include gathering information to weigh options that may amend the stressor and planning and implementing the solution to modify the stressor. Additionally, problem-focused coping strategies are often used in situations where there is controllability of the stressor (Hynes et al., 1992). The uncertainty in infertility could be a contributing factor to the lack of literature about problem-focused coping in this context, as often infertility is appraised as unmodifiable to change.

Problem-focused coping in women with infertility was associated with high levels of well-being (Hynes et al., 1992) and increased psychological adjustment (Benyamini et al., 2008). Additionally, the use of problem-focused coping in women with infertility was associated with lower amounts of stress (Gourounti et al., 2012), especially when using active coping (such as self-care behaviors) to increase resilience was employed (Sexton et al., 2010).

Meaning-based coping (perceiving infertility in a positive light) is neither problem-focused nor emotion-focused, but rather appraisal-focused within the context of the situation (Folkman, 1997; Park & Folkman, 1997), and has been shown to lower IRS (Aflakseir & Zarei, 2013; Lykeridou et al., 2011). Examples of meaning-based coping include positive-reappraisals or resetting goals, in which meaning is applied. Often meaning is spiritual, religious, or existential (Lazarus & Folkman, 1984; Park & Folkman, 1997).

In general, problem-focused coping is thought to be more adaptive and a healthy form of coping when compared to emotion-focused (Lazarus & Folkman, 1984). Overall, the review of the literature supports the positive psychological benefit of problem-focused coping, with the potential benefit of increasing pregnancy rates (Gourounti et al., 2011) and resilience (Sexton et al., 2010).

Quality of Life in Women with Infertility

The World Health Organization (WHO) defines quality of life (QOL) as personal perceptions of one's life circumstances, from the context of culture and values, goals, expectations, and standards. Quality of life was not specifically defined by Lazarus & Folkman (1984); however, the authors describe a long-term adaptational outcome of stress and coping as morale, or life satisfaction, denoting how one feels about themselves and their situation in life. Quality of life has been measured in women with infertility, and most studies reported low QOL

scores overall, based on findings from a systematic review (Hubens, Arons & Krol, 2018). However, studies of associations between QOL, IRS, coping, and personal or situational factors in women with infertility are limited, especially in the United States. The following sections will describe the current state of knowledge about QOL as it relates to IRS, coping, and personal or situational factors (etiology, age, duration of infertility and treatment failure, pregnancy loss, and sociodemographic variables).

Infertility-Related Stress and QOL

While it is known that anxiety and depressive symptoms are negatively correlated with QOL in women with infertility (Aarts et al., 2011; Kahyaoglu Sut & Balkanli Kaplan, 2015; Kim et al., 2018; Maroufizahdeh, Ghaheri, Amini, & Samani, 2017; Namdar, Naghizadeh, Zamani, Yaghmaei, & Sameni, 2017; Pinar & Zeyneloglu, 2012), little is known about how IRS effects women's perceptions of QOL. In a study by Cheng et al. (2018), Taiwanese women with high amounts of IRS related to social concern, relationship concern, and need for parenthood had lower QOL scores. Li et al. (2019) found infertile Chinese women with higher IRS had lower QOL scores ($r = -.575$, $p < 0.01$). Kim et al. (2018) found higher IRS and lower QOL scores in South Korean women when compared to their husbands. These studies suggest that higher IRS is associated with lower QOL; however further investigation is needed, particularly in women residing in the U.S.

Coping and QOL

There is a dearth of knowledge about QOL and coping in the context of infertility. Meaning-based coping was found to be positively correlated ($r = .457$) with higher QOL in women with infertility, and active avoidance ($r = -.379$) and passive avoidance ($r = -.369$) coping were found to be negatively correlated with QOL (Madhavi, Alka, Ravindia, & Charles,

2013). Women undergoing assisted reproductive technologies had lower QOL scores and used more mental disengagement and denial coping strategies than women opting for adoption or surrogacy (van den Akker, 2005), which corresponds to avoidance strategies described in the Madhavi et al. (2013) study, highlighting the stress of infertility treatments. For this literature review, no studies were found that comprehensively examined the linkage between IRS, coping, and QOL in women with infertility.

Personal and Situational Factors and QOL

Type of Infertility. Lower QOL has been found in women with primary infertility versus secondary infertility (Karabulut, Ozkan, & Oguz, 2013; Madhavi et al., 2013). Women with female factor infertility reported lower QOL scores ($p = 0.007$) than women with other types of infertility such as male factor, mixed factors, or unexplained etiology (Li et al., 2019).

Age. Younger women with infertility tended to have lower QOL scores compared older women with infertility (Chachamovich et al., 2010), however, two studies did not find lower QOL scores in younger women (Karabulut et al., 2013; Maroufizahdeh et al., 2017).

Duration of infertility and treatment failure. Prolonged duration of infertility was found to be correlated with lower QOL (Kahyaoglu Sut & Balkanli Kaplan, 2015; Karabulut et al., 2013; van den Akker, 2005), as well as treatment failure or not conceiving after an infertility treatment (Chachamovich et al., 2010; Kahyaoglu Sut & Balkanli Kaplan, 2015; Maroufizahdeh et al., 2017).

Pregnancy loss. Only one study in the literature compared pregnancy loss and QOL in the infertile woman. Maroufizahdeh et al. (2017) did not find significant associations between pregnancy loss and core total QOL scores in infertile Iranian women. For a related construct to

QOL, women with pregnancy loss and infertility reported lower life satisfaction scores (Schwerdtfeger & Shreffler, 2009).

Sociodemographic variables. Infertile women who had lower income and were living in a rural area had lower QOL compared to those with higher income and living in an urban area (Maroufizahdeh et al., 2017; Namdar et al., 2017). Li et al. (2019) found lower QOL scores in infertile Chinese women with lower income levels, but there was no association between rural and urban living in this cohort.

Limitations and Gaps

Many studies found in the literature review were quantitative cross-sectional surveys, though several studies consider IRS over time (Boivin & Lancastle, 2010; Greil et al., 2011; Hynes et al., 1992; Verhaak, Smeenk, Van Minnen, Kremer, & Kraaimaat, 2005). There is concern about sample size, since samples were often small and obtained at a single infertility clinic rather than multiple sites. The literature is not clear about the timing of administration of the questionnaires within the treatment cycle, which could also lead to the variability in findings. For example, Boivin & Lancastle's (2010) findings show hopeful emotions during the stimulation phase (ovary stimulation with medications) and waiting phase (waiting for ovulation and pre-pregnancy test), with anxiety increasing as the cycle continues, and concluding with depressive symptoms when the cycle is unsuccessful in achieving pregnancy. Therefore, stress in a woman undergoing treatments could be influenced by the timing of the stress measurement.

From a conceptual point of view, IRS is not clearly defined in the literature. Stress was measured with other constructs and using a variety of tools such as depression and anxiety scales, psychological adjustment survey (Staton, 1991), Fertility Problem Stress Scale (Schmidt, 2006), and Fertility Problem Inventory (Newton et al., 1999). Coping was measured with several

tools, such as the COPE questionnaire (Carver et al., 1989), Ways of Coping Questionnaire (Folkman & Lazarus, 1988), Coping Resources Inventory (Hammer & Marting, 1988), and Coping with Infertility Questionnaire (Benyamini et al., 2008). While there seems to be good consensus that stress exists in the infertile woman, the inconsistency of tools used to measure stress or coping make findings difficult to compare across studies, resulting in uncertainty about if each tool is measuring similar or disparate constructs. Standardization of measuring stress and coping would be beneficial. Further research should be conducted to consider which stressor, or the summation of stressors, are most significant in affecting IRS and treatment outcomes.

There are limited and mixed results in studies considering physiologic stress in women with infertility. Most studies measured salivary or serum cortisol levels in women undergoing IVF. No studies were found that measured cortisol levels in women undergoing other types of infertility treatments, such as ovulation induction only or intrauterine insemination. Research using hair cortisol measures is extremely limited in the literature, with only two studies found that measured hair cortisol levels in women with infertility. Neither of these studies considered the association of hair cortisol levels to IRS, coping, or QOL.

The conflicting results in the effectiveness of problem-focused coping compared emotion-focused coping strategies may limit the development of evidence-based strategies to enhance positive coping strategies to reduce IRS. Alternatively, inconsistency in study findings could be due to the ability of individuals to use a combination of emotion- and problem-focused coping to manage the situation of infertility. According to Lazarus & Folkman (1984), a person can use problem-focused and emotion-focused coping forms concurrently to deal with a stressful situation. The current literature about IRS and coping does not clearly distinguish which type of coping is considered adaptive or maladaptive in reducing stress. This could be due partially to

study design when participants do not have the option to choose both emotion- or problem-focused coping during surveys, or if emotion- and problem-focused coping strategies are both utilized, but at different times during the experience of infertility. Further studies should explore both emotion- and problem-focused coping strategies used together to weather the infertility experience.

Most studies in the literature that focused on QOL in women with infertility primarily considered those with infertility who are undergoing assisted reproductive technologies (ART), such as IVF. Little is known about women who are in treatment for infertility who are not receiving ART treatments. This is significant because most women receiving infertility treatment are not receiving ART (Schieve et al., 2009). Only 1-2% of women who undergo infertility treatments will undergo ART (Katz et al., 2011). Only one study was found that considered differences in QOL among types of treatment and found no statistically significant differences in QOL scores among those undergoing ART treatments such as IVF, compared to women who were receiving non-ART treatments such as ovulation induction with timed intercourse, intrauterine inseminations, or surgical treatment (Aarts et al., 2011). The lack of statistical significance in QOL in women undergoing ART versus non-ART treatments could imply QOL for all women undergoing treatment is impaired, and more studies focusing on non-ART treatments are warranted.

The limited number of studies conducted in the U.S threatens generalizability. Many studies related to stress and coping in infertile women originate from Belgium, Greece, Iran, Israel, Netherlands, and the United Kingdom. Only one study of QOL in U.S. women with infertility was found (Boulet et al., 2017). The cultural and social differences between the U.S. and other countries may limit the generalizability of the findings. For example, Israel provides

infertility coverage to families until two children are achieved, with no cycle limits (Rapoport-Hubschman, et al., 2009), compared to the lack of coverage of infertility care that is present in the U.S. (RESOLVE, 2019b). The ability to receive unlimited treatments could be appraised as less stressful and lead to different appraisals of stress and coping strategies than are found in women from the U.S.

The U.S. is considered a multi-cultural nation, with 13.6% of the total U.S. population comprised of immigrants from various countries (Radford, 2019). Findings from other countries could clarify the impact of IRS, coping, and QOL in women who emigrate to the U.S. Further research is needed in examining the impact of IRS, coping, and QOL in U.S. women.

In almost all IRS studies, participants were recruited through traditional methods, such as flyers, brochures, and face-to-face recruitment at infertility clinics. To the authors knowledge, recruiting through online methods, such as social media, has not been previously considered in IRS research, and could provide an innovative strategy to recruit women with infertility. Nursing researchers have used social media to conduct interventions (Jones, Lacroix, & Nolte, 2015) and recruit vulnerable populations, such as those with health disparities, stigma, and racial or ethnic minority status (Mitchell, 2014; Staffileno, et al., 2017). Facebook is one of the most popular social media sites in the U.S., with 68% of adults reporting use of Facebook, and 74% of U.S. women reporting using Facebook (Smith & Anderson, 2018). Facebook sites, such as groups and pages, exist for women with infertility. With the popularity of social media use, particularly Facebook, there is an opportunity to recruit women with infertility and should be explored further. Using Facebook, this study helped to address the gap found in the literature related to limited use of social media for recruitment in IRS research. Further, this study addresses many of these limitations and gaps identified in the literature review.

The limited numbers of studies considering IRS, coping, and QOL in women with infertility, and conflicting findings, support the need for extending the science in this area. Further, the limited number of studies conducted in the U.S. confirm the need for further investigation to understand how these concepts impact the infertility experience for women in the U.S.

Summary

This review of the literature summarized the state of science about IRS, cortisol, coping, and QOL in the context of infertility, including personal and situation factors within the infertility experience. Theoretical perspectives of stress and coping was explored.

The transactional theory of stress and coping provided a well-developed and well-studied theory to frame the experience of infertility (Lazarus & Folkman, 1984). Infertility-related stress was found in the literature. Appraisals of IRS as a threat, harm/loss, or challenge occur, which can stem from multiple sources including personal, social, and marital domains as well as others (Greil et al., 1997; Newton et al., 1999; Schmidt, 2006;). However, there are limitations in conceptual definitions of IRS leading to operationalization concerns.

Cortisol has been examined as a measure of IRS, with most studies examining salivary cortisol. Hair cortisol, a measurement of chronic stress (Massey et al., 2016), has been studied in women with infertility on a very limited basis and has not been examined in the context of IRS, coping, and QOL. Factors associated with IRS, such as pregnancy loss and personal and situational factors, showed inconsistent findings in terms of relevance and impact. The relationships between IRS and coping strategies were inconclusive, though many findings support use of emotion-focused coping with higher levels of IRS (Gourounti et al., 2012; Karaca & Unsal, 2015).

Quality of life has been measured in women with infertility, but limited studies exist comparing QOL to IRS and coping. Most of the studies reviewed reported low QOL scores in women with infertility (Hubens et al., 2018; Kim et al., 2018; Li et al., 2019). The limited number of overall studies considering the relationships between IRS, coping, QOL, personal and situational factors, as well as the country of origin, sample size constraints, and the variety of measurement tools used may have led to the variation in the findings.

Future interventional studies related to IRS, hair cortisol, coping, and QOL will be important in moving the science forward resulting in holistic nursing care and improved patient outcomes. This review of the literature highlights the need to examine IRS, hair cortisol, coping, and QOL in U.S. women with infertility, and to examine situational factors, such as treatment type and pregnancy loss in women with infertility.

CHAPTER 3: METHODS

Introduction

The purpose of this study was to examine the relationships between IRS, cortisol, coping, and QOL in women undergoing infertility treatments, and determine the relationships between personal and situational factors and infertility characteristics and IRS, coping, and QOL in women undergoing infertility treatments to answer the following research questions:

1. In women undergoing infertility treatments, what are the relationships between infertility-related stress, coping, and quality of life?
2. In women undergoing infertility treatments, what are the relationships between hair cortisol levels, infertility-related stress, coping, and quality of life?
3. What are the relationships between demographic variables and infertility characteristics (infertility treatment types [IVF vs. non-IVF] and pregnancy loss) and infertility-related stress, coping, and quality of life?

The theoretical framework that guided the study was Lazarus & Folkman's (1984) transactional theory of stress and coping. The following sections will discuss the design, setting, sample, protection of human subjects, instruments, procedures, and data analysis of the research study. Lastly, the limitations of the study are discussed.

Design

A quantitative descriptive and correlational cross-sectional study design was used to study a national sample in the United States (U.S.). The cross-sectional method was consistent with other approaches used in the literature to study psychological distress in women with infertility; however, this study differed and added to the body of knowledge in several ways. First, there is minimal research examining the relationships between IRS, coping, and QOL in

women with infertility. There are many instrumentation concerns in studies with each of the concepts of IRS, coping, and QOL in the literature, such as measurements of anxiety and depression rather than IRS, and inconsistent tools to measure IRS, coping, and QOL. This study added clarity to the relationships between IRS, coping, and QOL by clearly defining the constructs and using tools developed to assess these constructs that were validated specifically for women with infertility. Second, the study included collection of hair cortisol, a biological marker for chronic stress, from a small sub-group of women. Measuring a biological marker and comparing the levels to psychological measures of IRS, coping, and QOL had not been considered in previous studies. Third, recruiting population-based participants through online social media was an innovative strategy when compared to the clinic-based recruitment design that dominates the literature and limits generalizability. Recruiting through an online strategy increased the reach of the study to a national level, which was important given the lack of studies considering IRS, coping, and QOL in the U.S. Increasing sample size and sample diversity through a national recruitment strategy helped to ensure a diverse sample to answer the proposed research questions. Lastly, increasing sample diversity may aid in cultural considerations of the diverse background of women with infertility in the U.S.

Setting

The setting for the study was an online social media environment via Facebook. A specific East Carolina University (ECU) study email was created to develop a public Facebook page that contained study information and an imbedded link to the secure online survey.

Facebook was chosen as a social media recruitment strategy for several reasons. Facebook is the most widely used social media platform in the U.S. (Pew Research Center, 2018). Facebook user frequency ranges from accessing the site multiple times per day, to once

per day, to less often. Seventy-four percent of Facebook users log-in at least once a day. In the U.S., 74% of women consider themselves "users" of Facebook and 80% of U.S. adults between the ages of 18-49 years consider themselves users (Pew Research Center, 2018). Additionally, the presence of infertility groups and pages related to infertility in the private and public domains of Facebook are extensive.

Participants were recruited through convenience and snowball sampling by sharing of the Facebook study page. Current best practice for online recruitment suggests obtaining permission from group administrators (Eysenbach & Wyatt, 2002), which followed ECU policies and procedures for human recruitment (ECU, 2016). Recruitment involved contacting infertility-related Facebook page or group administrators through Facebook messenger, email, or by phone call. Facebook pages or groups were evaluated for selection using the following criteria: a U.S. infertility-related group or page (such as an infertility support group, infertility information page, or infertility-related organization), a U.S. infertility clinic that provided infertility treatments, or a U.S. obstetrics and gynecology (OB/GYN) clinic that states they treat infertility on their Facebook page or business website. The administrators from the selected Facebook pages or groups were sent a script describing the study, a link to the Facebook study page or survey, and were asked to share the study page on their respective page or within their group. Facebook users could also share the Facebook study page or the Facebook post that contained the script and a link to the survey. Where public infertility pages allowed access, the Facebook study page was posted by the PI. Lack of access to support groups by the PI helped to ensure the privacy and anonymity of the group members. Recruiting from U.S. selected groups and pages related to infertility helped to increase the validity of the sample by targeting those that were likely to meet the inclusion criteria (Kramer et al., 2014). The script used in recruitment is in Appendix D.

Sample

Participants included women with infertility. Infertility is defined as the inability to conceive or carry a pregnancy to term after 12 months of unprotected sexual intercourse (CDC, 2018). Inclusion criteria consisted of women between the ages of 18-55 who live in the U.S., had an infertility diagnosis, were currently undergoing infertility treatments or had undergone treatments within the past six months, and were able to speak and read English. Including women who were in treatment within the past six months captured women who had undergone treatments recently, but who may have been in a treatment pause to have medical testing or procedures (such as blood work, surgery, or radiology procedures) related to continuing infertility treatments. Women with various types of infertility diagnoses, including male factor infertility, were included. Exclusion criteria included men, women who did not read or speak English, women who did not live in the U.S., women who were trying to conceive but did not have an infertility diagnosis, and women who had an infertility diagnosis but were not actively trying to conceive with treatments within the past six months. Using a power analysis for correlations, assuming a power = .80, $\alpha = .05$, and an average population correlation (effect size) of .20 in nursing studies (Polit & Beck, 2017), the sample size would need to be N = 194. A sample size of N = 171 was targeted to combine with pilot data previously recorded using the same measures for a total sample size of N = 200. For the hair cortisol subsample, the participants from who agreed to submit a hair sample were selected through consecutive sampling. The target subgroup sample for hair cortisol collection was n = 27. The hair cortisol collection sample was combined with pilot data previously recorded to obtain a targeted total hair cortisol sample size of n = 30.

Human Subjects Protection

The University and Medical Center Institutional Review Board at ECU reviewed and approved the study (Appendix A and Appendix B). A letter of consent to participate in the study was presented to participants prior to the start of the survey (Appendix E). If the participant agreed to participate by clicking the AGREE button in the online survey, the questions were displayed. Written informed consent was obtained from participants (Appendix F) who agreed to submit a hair sample for cortisol level testing by mailing the consent document with the collection kit, instructions, and hair care questionnaire. The PI provided contact information should the participant have questions related to consent.

The direct benefit to the participant may have been none or may have been the satisfaction of potentially helping researchers understand the relationships under study to help other women in similar situations. There was minimal harm to answering survey questions. The survey did include intimate questions related to perceptions of IRS, coping, and QOL in personal, social, and relationships. Answering the questions could have caused the participant to feel uncomfortable; however, the participant could stop the survey at any point. Those who participated in the survey remained anonymous to the PI and research team. Participants had the option of including an email address if they were willing to potentially submit a hair sample for cortisol analysis. Potential breech in privacy and confidentiality related to participant email addresses was a minimal risk, but safeguards were in place to protect the data. Data were obtained and stored in REDCap, which is secured and HIPAA compliant. Additionally, any data extracted from REDCap was stored on the secured and HIPAA compliant ECU Piratedrive. Those who consented to the hair cortisol sample were given an ID number with their associated

email address. The master list of participant ID data was stored electronically on the ECU Piratedrive, and a paper copy was kept in a locked filing cabinet in the PI's locked office.

Hair samples were obtained by the participant, minimizing the risk of harm to the participant by the researchers. This reduced the risk of accidental scrape of the scalp by the researcher and allowed participants to select an inconspicuous place on the crown head to minimize image disturbance.

Instruments

Instruments used in the data collection for this study were: a) screening questions (see Appendix G), b) Copenhagen Multi-centre Psychosocial Infertility Fertility Problem Scale Score (see Appendix H, c) Copenhagen Multi-centre Psychosocial Infertility Coping Styles Scale (see Appendix I), d) Fertility Quality of Life (see Appendix J), e) demographics/background questionnaire (see Appendix K), and f) a hair care questionnaire as required by the independent laboratory for cortisol testing (see Appendix L). Hair cortisol concentrations were measured by an independent laboratory at the University of Massachusetts at Amherst using their prescribed procedures and methods for hair sample collection (Meyer et al., 2014).

Screening Questions

Inclusion criteria screening questions were initially presented to the participant after survey consent. Screening questions included the presence of an infertility diagnosis and if participants were currently undergoing infertility treatments within the past 6 months, which may include medical consultation, surgery, medications, or other procedures to help achieve pregnancy. Other screening questions included biological sex, age at last birthday, and if the participant lived in the United States.

Copenhagen Multi-centre Psychosocial Infertility Fertility Problem Scale

Infertility-related stress was measured using hair cortisol concentrations and the Copenhagen Multi-centre Psychosocial Infertility Fertility Problem Scale Score (COMPI-FPSS). The COMPI-FPSS is a 9-item Likert scale tool that measures three dimensions of IRS including personal, marital, and social, which is consistent with the transactional theory of stress and coping (TTSC) by Lazarus & Folkman (1984). Reliability and validity estimates are strong with internal consistency reliability estimates between .73 to .81 for each domain (Schmidt, 2006; Sobral et al., 2017). The tool was developed and validated with persons experiencing infertility.

Copenhagen Multi-centre Psychosocial Infertility Coping Styles Scale

Coping was measured using the Copenhagen Multi-centre Psychosocial Infertility Coping Styles Scale (COMPI-CSS). The COMPI-CSS is a 19-item Likert scale tool developed from the TTSC, and has 4 domains, including active-avoidance, active-confronting, passive-avoidance, and meaning-based coping (Schmidt, 2006). These domains were congruent with the theoretical framework for this study. Reliability and validity estimates range from 0.80–0.85 per domain (Lykeridou et al., 2011). The tool was created by the same researchers who developed the COMPI-FPSS for persons with infertility and has also been validated in the infertility population.

Fertility Quality of Life

Quality of life was measured using the Fertility Quality of Life tool (FertiQoL). FertiQoL is a 36-item Likert scale tool specifically developed and validated in the infertility population, and measures overall quality of life and four domains of QOL including emotional, mind/body, relational, social, and a QOL treatment module. The FertiQoL has a high internal consistency reliably estimates ranging from .72-.92 for each domain and overall score (Boivin et al., 2011). This instrument was chosen for this study due to the well-described psychometric development,

which included participants with infertility; the specificity to the infertility experience; and inclusion of the four domains, which are consistent with the TTSC.

Demographics/Background Questionnaire

Demographic/background data were obtained through participant self-report. The questions included in the demographic questionnaire include were the duration, type, and cause of infertility, current infertility treatment and point in treatment cycle, pregnancy loss, coping strategies, race, ethnicity, marital status, education, employment status, average household income, infertility insurance coverage, state, and geographic community living area (rural, suburban, urban). Information was gathered on how the participant found the study on Facebook, and the opportunity to provide an email address was given if the participant was interested in being contacted by the PI to provide a hair sample for cortisol analysis.

Hair Care Questionnaire

The hair care questionnaire was developed and required by the independent laboratory at the University of Massachusetts at Amherst. The questions on the survey included disclosure of a treated medical condition, steroid-containing medication use, and hair care practices, such as washing or hair coloring. Other lifestyle behaviors, such as swimming and frequent exercise were also included in the questionnaire.

Procedures

The PI obtained an ECU study email for purposes of the study. An email provided through ECU is secured and encrypted, and this allowed the PI to build the study page through Facebook without linking to the PI's private account. The ECU study email was included in the Facebook page information as contact information for the study and the PI. Data were collected through an online survey design, using the ECU-approved REDCap survey application to build

and manage the online survey, since it is secured and HIPAA-compliant (ECU ITCS, 2018). The survey presented an introduction containing the research consent, followed by the initial screening questions, study questionnaires, and demographic and background data. The screening questions included age at last birthday, biological sex, the presence of an infertility diagnosis, treatment status, and if the participant was currently living in the U.S. Those who did not identify as female, having infertility, currently being in treatment or treatment within the past six months, not between the age of 18-55 years, and not currently living in the U.S. were excluded from data analysis. Questionnaires included in the survey were the Copenhagen Multi-centre Psychosocial Infertility Fertility Problem Scale Score (COMPI-FPSS), Copenhagen Multi-centre Psychosocial Infertility Coping Styles Scale (COMPI-CSS), and the Fertility Quality of Life (FertiQoL) tool. Background and demographic data included information about the participant's infertility experience such as the cause of infertility (female factor, male factor, combination of female and male factors, or unknown), the type of infertility (primary or secondary), duration of infertility and treatment, type of treatments (non-IVF, IVF, surgical, other procedures, no treatment, or other), current state or point in the treatment cycle, presence of pregnancy loss and number of pregnancy losses, coping strategies, current mental health diagnoses, as well as other demographics such as the resident state and type of geographic community in the U.S., marital status, race, ethnicity, income, number of individuals in the household, education level, employment status, type of insurance coverage, how participants became aware of the study, and an option to leave an email address indicating a willingness for further contact to provide a hair sample for cortisol analysis.

The study questions, including questionnaires and demographic and background data questions are presented in Appendices G-K. Permissions to use the measurement tools were

obtained from the researchers who developed the tools or tools were obtained from a public domain source. Participants who completed the survey and provided an email address in the survey were contacted by the PI to ask if they would provide a hair sample, and for their mailing address. After three failed attempts for a response, the PI halted contact for hair sample participation. Within two weeks of completing the online survey, participants who agreed to hair sampling were mailed a written consent to collect the hair sample, written instructions including links to videos about how to collect the hair sample (See Appendix M), a hair care questionnaire (See Appendix L), an aluminum foil pouch for storing the hair sample, and a postage-paid envelope. The PI provided contact information should the participant have questions about hair sample collection. The PI followed-up with participants who were mailed the documents and foil pouch weekly as a reminder to collect the hair sample and to address questions or concerns from the participant. After 3 failed attempts to invoke a response from the participant, the PI stopped contact. The hair sample was collected using the University of Massachusetts at Amherst directions and procedures (See Appendix M). The participants returned the signed written consent, the hair care questionnaire, and the hair sample placed in the foil pouch back to the PI in a postage-paid envelope. The PI stored the hair samples and consent documents in a secure locked location in the PIs locked office. When all samples were obtained, the PI sent them to the University of Massachusetts at Amherst laboratory for analysis. Participants who provided a hair sample for cortisol analysis were given the result of their personal hair cortisol level as appreciation for providing a hair sample. No interpretation of the results was given. If a participant had a concern or question regarding their result, the participant was advised to discuss the result with their health care provider.

Data Analysis

Data was analyzed using SPSS 24 (version 24; IBM Corp., Armonk, New York). Respondents who identified as male, not having infertility, not currently in treatment within the past 6 months, not between the age of 18-55 years, and not currently living in the U.S. were excluded from data analysis. Descriptive statistics to describe the sample were conducted through means and standard deviations for continuous data, and frequencies and percentages for categorical data. Reliability of the COMPI-FPSS, COMPI-CSS, and FertiQoL subscales and total scales were analyzed using Cronbach's alpha for this study sample (Pallant, 2016). No items needed to be reverse coded on the COMPI scales. Seven items (questions 4, 11, 14, 15, 21, and treatment questions 2 and 5) needed to be reverse coded on the FertiQoL tool prior to scoring. Data analysis for each research question using the following statistical methods was conducted as follows:

RQ1: In women undergoing infertility treatments, what are the relationships between infertility-related stress, coping, and quality of life?

Pearson correlations coefficient (r) was conducted to examine relationships between the four infertility-related stress subscales, four coping subscales, and the five quality of life subscales. A Two-Step procedure was conducted using the nine items of the COMPI-FPSS to examine naturally occurring subgroups who varied in their IRS scores. The Two-Step procedure does not identify a numerical cut-score, but rather separates the groups based on the COMPI-FPSS items identified as important in forming the subgroups. Two subgroups were identified. Individuals with high scores on the "importance items" were categorized in the "high stress" group, and those with low scores on the "importance items" were categorized in the "low stress" group. Items in the COMPI-FPSS were also categorized into a binary score, where participants

who answered “strongly agree” were coded as 1, and other responses coded as 0. Similarly, items in the COMPI-CSS were categorized into binary scores as “used a great deal” and “used quite a bit” as 1, and “not used” or “used somewhat as 0. Independent samples t-test was conducted to compare the mean scores for the COMPI-FPSS, COMPI-CSS, and FertiQoL scales.

RQ2: In women undergoing infertility treatments, what are the relationships between hair cortisol levels, infertility-related stress, coping, and quality of life?

Pearson correlation coefficient (r) was used to examine the relationship between hair cortisol levels, infertility-related stress, coping, and quality of life. Hair cortisol samples were analyzed at an independent laboratory at the University of Massachusetts at Amherst. The hair preparation procedure conducted by the independent laboratory is as follows: Hair samples were washed twice in 5 ml of isopropanol and placed on an inversion rotator for 3 minutes each wash, dried for 2-3 days, and crushed into a fine powder using a stainless-steel grinding ball and a bead beater for 1-2 minutes. The powdered hair was placed in 1.5 ml of methanol and continuously inverted for 18-24 hours at room temperature. The sample was then placed in a centrifuge for 5 minutes. The hair powder was dried in a vacuum evaporator, then an enzyme immunoassay buffer was added to the cortisol extract and analyzed using an enzyme immunoassay kit (Hodes et al., 2017; Meyer et al., 2014).

RQ3: What are the relationships between infertility characteristics (infertility treatment types [IVF vs. non-IVF] and pregnancy loss) and infertility-related stress, coping, and quality of life?

Independent-samples t-test was used to compare infertility-related stress, coping, quality of life, and mean differences between independent subgroups based on type of infertility treatments and pregnancy loss. Chi-square for independence was conducted to compare

differences between high and low stress groups in coping and QOL scores in participants with pregnancy loss (yes or no) and type of infertility treatment (IVF and non-IVF).

Limitations

There were several limitations of this study. Cross-sectional designs collect data at a single point in time. Data were self-reported, and participants could choose to answer or defer a question, which resulted in incomplete data. The options in the survey may not have captured all the variances in participants' perceptions of their infertility experience or demographic and background data. Most demographic questions included "other" as an option, however participants could choose to defer submitting an answer. While the anonymous survey design protected the privacy of participants, there was no option to contact participants for clarification about questionable or incomplete survey answers.

Online recruitment has several advantages including low-cost, faster recruitment, larger samples, and potential to reach subjects who are geographically dispersed (Holmes, 2009). However, there are limitations to online recruitment, including access to the internet leading to selection bias (Eysenbach & Wyatt, 2002), potential duplicate responses, misrepresentation (Holmes, 2009), and technical issues (Ahern, 2005). Though limitations to online recruitment exist, they can for the most part be overcome or accounted for, as misrepresentation is low (Whitehead, 2007), and lack of financial incentive in the proposed study may have reduced misrepresentation (Eysenbach & Wyatt, 2002; Wright, 2005). Technical issues through REDCap were unlikely. The REDCap survey application is approved by ECU to build and manage online surveys, as it is secured and HIPAA-compliant (ECU ITCS, 2018).

Because of the high cost of infertility treatments in the U.S. (RESOLVE, 2019b), it can be inferred that women who were undergoing treatments were financially able to have access to

the internet. In addition, access to the internet is wider now than in previous years, which may improve the racial and ethnic diversity of the sample (Whitehead, 2007).

Other limitations include the previously discussed recruitment and sample validity concerns. Some Facebook pages or groups did not have a way to message the administrator to obtain permission to post or share the survey or study page. In this case, other ways to contact the page or group administrator were needed, such as a phone number or email address. Some administrators may not have felt comfortable sharing the study information on their public page or group. Further, tracking snowball sharing of the study page or survey link was difficult. Although some analytic information about how the study page or survey link was shared could be obtained, it was difficult to specifically track when the page and link to the survey was shared and who shared the link. Obtaining information about the resident state from participants helped track the reach of the survey within the U.S.

The PI provided written education and links to instructional videos to participants on hair sample collection procedures and followed up with participants who received a hair sample collection kit weekly for three weeks. However, limitations to collecting hair samples for cortisol levels included inappropriate hair sample submission (such as failure to collect hair from the correct sample site hair location and/or to provide an adequate sample weight of hair), and failure of participants to mail the hair samples back to the PI. Participants who did not return the hair collection kit after four weeks were not contacted further and were assumed to have opted out of participating.

Summary

This chapter described the methodological approach to examine the relationships between IRS, hair cortisol, coping, and QOL in women undergoing infertility treatments. This study used

a cross-sectional descriptive correlational design and was approved by the University Medical Center Institution Review Board at ECU. Lazarus & Folkman's (1984) transactional theory of stress and coping guided the study. To increase the number and diversity of participants, Facebook was used as a recruitment tool, which was innovative in the context of infertility research. Additional innovation in the study design included the collection of hair cortisol samples as a measure of chronic IRS in a subsample of participants. Limitations of the research design exist, however the methodological approach used in this study adds innovation and a creative approach in the exploration of IRS, coping, and QOL in women undergoing infertility treatments.

CHAPTER 4: THE USE OF FACEBOOK FOR RECRUITMENT IN NURSING RESEARCH: AN INTEGRATIVE REVIEW

This chapter contains manuscript one to be submitted for publication regarding an integrative review examining the use of Facebook for recruiting participants in nursing research. Background is presented about the use of social media for recruitment in nursing research, followed by the methodology of the integrative review, results, recommendations, and conclusions.

Abstract

The development of social media has increased the social interaction of people online. Innovative strategies using social media to recruit patient populations in research studies has been used in other disciplines, but little is known about how nursing researchers have used social media for recruitment. The purpose of this integrative review is to explore how nursing researchers have used Facebook in recruitment efforts and to identify best strategies for recruiting through Facebook. The integrative review followed Whittemore and Knafl's framework and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Method. PsycINFO, CINHAL, and PubMed databases were searched using key terms and limiters. Inclusion and exclusion criteria were applied that yielded 31 articles for review. Articles were reviewed for quality using the Mixed Methods Appraisal Tool (MMAT). Data were extracted and analyzed using a matrix and data display graphs. Most of the studies in the review were from the United States and were of quantitative cross-sectional design. Recruitment through Facebook strategies was prominent in half the studies, with other studies combining Facebook and traditional recruitment strategies. Banner advertisements, graphic displays on the top or sides of a webpage, were most commonly used and were also cost-effective compared to

traditional recruitment strategies. Ethical considerations, rationale for using social media, and transparency in methods could be addressed in future nursing research.

Introduction

Social media platforms exploded in popularity among internet users following the founding of Facebook in 2004 (Facebook, 2019; Pew Research Center, 2018). With millions of daily users on social media networks, the potential for using social media in nursing research is significant. Some nursing researchers have used social media to conduct interventions (Haines-Saah et al., 2015; Jones et al., 2015) and share educational resources (Drake et al., 2017).

Participant recruitment in nursing research is most often conducted through traditional methods. These methods often include face-to-face interactions, telephone, flyers, and brochures to recruit research participants into a study. Non-traditional methods of recruitment, for example, the use of recruiting through social media, have been used in other disciplines such as medicine, anthropology, and sociology (Das, Machalek, Molesworth, & Garland, 2017; Reyes-Foster et al., 2015). However, little is known about the use of social media for participant recruitment for nursing research.

The purpose of this integrative review is to investigate the use and best practices for the use of social media, specifically Facebook, for recruitment of participants in nursing research. This review contributes to the body of nursing science by synthesizing the use and best practices of social media for participant recruitment in select primary research articles, quantitative, qualitative, and mixed methods studies.

Background

The birth of the internet in the mid-1990s led quickly to online interaction among internet users worldwide. Early social media platforms, such as “SixDegrees”, “MySpace”, and instant

messaging were wildly popular with internet users as the idea of global connections became reality (Boyd & Ellison, 2007). Shortly after the creation of Facebook, the establishment of other social networking sites, such as Twitter and YouTube followed in the mid-2000s (Boyd & Ellison, 2007), and Instagram and Pinterest launched in 2010 (Instagram, 2019; Sharp, 2017). Currently, Facebook is one of the most widely used social media networks in the United States (U.S.), with about 68% of U.S. adults using it. Seventy-four percent of Facebook users visit the site at least once a day, and 51% of users visit the site several times a day (Smith & Anderson, 2018). In addition, women use social media more than men. Seventy-four percent of women in the U.S. report using Facebook, 72% YouTube, 41% Pinterest, 39% Instagram, and 24% Twitter (Smith & Anderson, 2018).

With the abundance of social media users worldwide, researchers have a unique opportunity to recruit participants from social media platforms. Other disciplines have used social media for recruitment and have been successful. For example, a study conducted by anthropology and sociology researchers, Reyes-Foster et al. (2015) recruited participants through Facebook by distributing the survey link to multiple groups and pages related to breastfeeding and mothers. The survey link was shared by group or page members. The recruitment strategy was successful as the survey was completed by 392 participants with non-random purposeful sampling located to a single region of the U.S. Medicine has also used social media for recruitment in research. Das et al. (2017) used Facebook advertising to recruit males for a human papilloma virus prevalence study in Australia. Recruiting using Facebook advertisements in the study was successful, with 1,072 men expressing interest and 535 men completing the survey.

Nursing can utilize social media for participant recruitment; however, it is unknown how nursing researchers have used social media for recruitment. Additionally, researchers in

women's health could potentially have a larger recruitment base because of the large percentage of women who use social media platforms. Therefore, this integrative review will explore how nursing scientists have used social media for participant recruitment, the best strategies to recruit through social media, and the implications for nursing researchers.

Methods

Design

The integrative review framework of Whittemore & Knafl (2005) was used to guide the methods of the literature search, data extraction, and data analysis. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Method (Moher, Liberati, Tetzlaff, & Altman, 2009) is supported by Whittemore & Knafl (2005) for use in integrative reviews. Thus, the PRISMA method was used to conduct the literature search and review. The PRISMA method and flowchart guides researchers conducting systematic or meta-analysis reviews to be transparent in documenting and reporting the methods undertaken during literature reviews (Liberati et al., 2009). The integrative framework presented by Whittemore & Knafl (2005) allowed the inclusion of all methods of nursing research. The inclusion of quantitative, qualitative, and mixed method studies supports the range of research methods that nursing researchers utilize and is important to help answer the research questions:

1. How has social media been used for participant recruitment in nursing research?
2. What are the best practices for using social media to recruit participants in nursing research?

Search Methods

The concept of using social media as a recruitment strategy was searched in the literature using the PsycINFO, CINHAL, and PubMed databases. The search included literature from

1994-2019 to exclude articles prior to 1994, as these would be unrelated to internet social media use. Additional limiters were applied to include English language and peer-reviewed articles. Search terms included social media OR social network OR Facebook OR Twitter OR Instagram OR YouTube OR Pinterest AND nursing AND research.

Search Outcome

The initial search using the search methods described yielded 438 articles. Bibliographies were reviewed to identify thirteen other sources not yielded in the search. Four duplicates were removed, and the titles, keywords, and abstracts of the articles were reviewed for inclusion and exclusion criteria. Inclusion criteria included peer-reviewed qualitative, quantitative, or mixed methods nursing research articles, or articles in which a nurse was an author, that used social media as a recruitment strategy. The articles that were excluded included those from a discipline or profession other than nursing, research that did not use social media for recruitment, and articles that were not research, such as editorials, commentaries, or reviews. If the title, keywords, or abstract of the article were not clear if social media was used as a recruitment strategy, the article was located and reviewed based on the inclusion or exclusion criteria. A total of 87 articles were retained for a secondary review. This review lead to further exclusion of 29 articles based on the inclusion or exclusion criteria. The reasons for exclusion included abstracts from conferences or presentations, discussion board forums or blogs not on a social media site, recruitment not conducted on social media, or articles in which a nurse was not an author. This yielded 58 articles retained for the review. Subsequently a decision to include only studies using Facebook for participant recruitment was made. Facebook was used for participant recruitment in most of the studies found and therefore deeper exploration was warranted. In addition, Facebook offers the potential for more social support and connection in comparison to other

social media platforms, such as Twitter (Alhabash & Ma, 2017). Therefore, articles containing Twitter, MySpace, or Youtube were excluded to yield 31 articles retained for the integrative review that are presented in Appendix N. The PRISMA flowchart for the search can be found in Figure 1.

Data Evaluation

The quality of the 31 articles retained for review were reviewed using the Hong et al. (2018) Mixed Methods Appraisal Tool (MMAT). This tool was designed to be used in the quality appraisal of research for systematic and integrative reviews for qualitative, qualitative, and mixed method study designs. Using the same tool to evaluate studies regardless of methodology allows ease of comparisons across the variety of research methods. No articles were excluded based on the quality analysis; however, quality was taken into consideration when analyzing the results.

Data Extraction and Analysis

A systematic analytic method was planned prior to the literature search, which included data reduction and comparison strategies**.** Data was extracted from the primary research articles and reduced into subgroups and categories using a pre-planned matrix. Some of these categories and subgroups included study characteristics of methodology, country of origin, study sample, as well as variables of interest for participant recruitment such as consent and descriptions of the recruitment strategy. Organizing the primary articles into a matrix with subgroups and categories facilitated the comparisons and analysis of variables and characteristics. Graphs and charts to compare and analyze the data extracted were created. The visual data included percentages of primary research articles that contained a characteristic or variable under consideration for the review.

Results

Study and Sample Characteristics

A table containing study characteristics are presented in Table 1. Of the 31 studies reviewed, most studies were conducted in the U.S. (58%) followed by Australia (16%). Eight other countries or regions also had representation, including Canada, Jordan, Malaysia, South Africa, Taiwan, Brazil, Thailand, and the Caribbean Islands. Sixty-one percent of the articles were quantitative methods, 26% qualitative, and 13% mixed methods. Of the quantitative study methods, most were cross-sectional designs (74%), 21% were intervention designs, and only 1 study (5%) was a quasi-experimental design. Qualitative methodology included content analysis (62.5%), and descriptive, interpretive, and phenomenological at 12.5% each. Three of the four mixed method studies were designed as a cross-sectional study with content analysis (75%), and one study was tool development.

There were many areas of research represented in the 31 articles reviewed. Ten categories were identified. Studies considering nurses (19%) and persons with sexually-transmitted diseases, including HIV (19%), represented most of the studies reviewed. Other areas of research included women's health (16%), parents of children (13%), pediatrics (7%), mental health (7%), chronic diseases (7%), cancer (7%), nursing education (3%), and traumatic brain injuries (3%).

Social Media Recruitment

Social media recruitment results are presented in Table 2. Recruitment strategies were considered and analyzed among the 31 studies reviewed. More than half of the studies reviewed used only Facebook for recruitment (55%) and 45% used Facebook combined with other strategies for recruitment. Facebook banner advertisement was the most popular strategy used for participant recruitment, with 42% of the studies reviewed using Facebook advertisement. Banner advertisements are graphic displays on the top or sides of a webpage often targeting Facebook

users based on user characteristics (Namin, Hamilton, & Rohm, 2017). Of these articles that used Facebook banner advertisement, half of the studies recruited using only advertisements and half combined the use of Facebook advertisements with other recruitment strategies. Recruiting through public pages and public groups (23%), as well as creating a public Facebook page or group with the study information embedded into the page (19%) were also popular strategies. Other strategies included recruiting through a closed group (10%), "snowball sharing" of the study information (10%), and sending messages through Facebook Messenger about the study (6%). Some studies combined multiple strategies of using Facebook for recruitment. For example, Benham-Hutchins et al. (2017) created a study Facebook page and shared the page with online support groups. Berry & Rutledge (2016) also created a Facebook study page and encouraged Facebook users to share the page and posted the page on public groups and pages.

Traditional approaches to recruitment were combined with Facebook recruitment in many studies. These included email invites to the study link or webpage, advertising in online support groups or webpages, posting flyers and brochures, sending letters, newspaper advertisements, and face-to-face recruitment. Ladores & Aroian (2015) used traditional recruitment methods of posting flyers and brochures at clinics and posted flyers on Facebook.

In quantitative study designs, sample sizes ranged from 35 to 1,037 participants. While it is difficult to compare the sample size across the studies reviewed due to the variety in research design and participant population, there was little difference in the number of participants noted between quantitative studies that used Facebook-only recruitment versus combining Facebook and another method of recruitment. Of the studies that used Facebook-only for recruitment, the 11 studies yielded 2,501 participants, for an average of 227 participants per study. Combining Facebook recruitment with other strategies did not yield more participants. There were a total of

1,907 participants recruited from the 8 studies that used multiple means of recruitment, for an average of 238 participants per study. Of the qualitative and mixed method studies that did report sample sizes (77%), sample sizes ranged from 10 to 374.

Rationale for using social media for recruitment was described in about half of the studies reviewed (48%). Access to participants who are vulnerable or difficult to find and protection of privacy was cited as rationale for using social media recruitment (Berry & Rutledge, 2016; Ko et al., 2013). The popularity of the use of Facebook or social media platforms was also described as rationale for the recruitment strategy (Moreno et al., 2012; Rogers et al., 2009). Two studies used Facebook for recruitment after traditional recruitment strategies failed (Close at el., 2013; Wahlberg et al., 2016). It is unknown why 52% of authors did not disclose a rationale for using social media for recruitment.

Ethical protection of participants was also considered through the presence of consent. Consent was clearly obtained in 68% of the studies in the review. Most studies that obtained consent used a consent form (80%), and 4 studies used implied consent by completion of the survey (20%). Two studies in the review were considered exempt and did not obtain consent; the data obtained and analyzed in the study was considered "public data" (Gage-Bouchard et al., 2017; Kim, Wyatt, Li, & Gaylord, 2016). Obtaining consent is unknown for eight studies (26%) as either it was not clearly written or there was no mention of consent or obtaining consent.

Discussion

Assessing the use of social media, notably Facebook, in nursing research through this integrative review was an important step to synthesize how nursing researchers have used the social media platform for nursing recruitment. Additionally, the review led to new findings. Much of the research conducted in the articles reviewed was in the U.S. or Australia. Developed

countries have plentiful technology access where online recruitment may be more feasible. However, research articles in this review also were from developing countries and were successful in recruitment. The heighted availability of technology globally and the popularity of social media, especially Facebook, may overcome the challenges of recruiting online.

Most of the research articles reviewed used a quantitative cross-sectional study design, with fewer studies using qualitative and intervention designs. Cross-sectional designs can protect the privacy and provide anonymity of participants. The qualitative articles found in this review often used public data or content analysis from written language. Nursing researchers have the unique opportunity to extend beyond the boundaries of traditional research design and explore innovative strategies for recruiting and conducting research. There are many web-conference platforms available that could be used to recruit or obtain participant consent. In addition, interviews could be conducted virtually, which would gather spoken language, non-verbal expressions, and potentially environmental factors that could increase the richness of data in online qualitative research. Similar web-conferencing platforms could be used in conducting interventions for a participant or group of participants.

While there were a variety of research areas found in the review, there are many other research focus areas that were not represented. Many of the research articles reviewed focused on health behaviors of various patient populations. Only a few studies focused on psychological or psychosocial factors (Close et al., 2013; Moreno et al., 2012; Wahlberg et al., 2016). The prospect for nursing scientists to use social media for participant recruitment across research foci are vast, especially for populations who may be hard to recruit. Finding research participants is a challenge for most researchers. The use of social media can assist researchers in the recruitment effort. The articles retrieved for this review contained no studies in which participant recruitment

was minimal. Notably, two articles described the addition of recruiting on Facebook after a low recruitment response using traditional recruitment methods (Close at el., 2013; Wahlberg et al., 2016). Several of the articles reviewed recruited vulnerable populations and were effective in the recruitment through Facebook. Close et al. (2013) recruited boys between the ages of 8-18 using Facebook combined with traditional recruitment strategies. Vulnerable populations in healthcare research can include participants where stigma, disparities in resources, marginalization, or psychological considerations are necessary (Flaskerud & Winslow, 1998). Several studies found in this review recruited men who have sex with men, which would be considered a vulnerable population (Khumsaen & Stephenson, 2017; Ko et al., 2013; Mitchell, 2014).

An important finding of this integrative review was the need for refinement of the concept of recruitment and research participation. Ethical considerations of what constitutes participation and consent in research is important to protect research participants. Researchers should clearly state the method of consent. Nursing researchers using social media may consider recruitment through people, comments, or posts which highlights the need for a clear informed consent process. Qualitative researchers may be more likely to use public data; studies found in this review that used public data were qualitative designs. Two studies in the review were found to use public domains or public information with the rationale of exclusion of consent (Gage-Bouchard et al., 2017; Kim et al., 2016). Eight studies in this integrative review lacked clear documentation as to how consent was obtained. Recently, Kamp et al. (2019) discussed important ethical considerations in using Facebook for participant recruitment on Facebook. Researchers should consider Facebook's policies on Banner advertisements and group policies for postings in groups. Administrator approval of Facebook groups may need to be obtained prior to posting. Kamp et al. (2019) also discusses the need for participant consent and honesty

of recruitment for research. Participants should be informed when their data is being used for research and informed consent should provide this transparency. The researcher also should be concerned for their own privacy and be aware of Facebook privacy settings when posting to groups or pages (Kamp et al., 2019). An option to protect the researcher is the creation of a Facebook account not associated with the personal Facebook account of the researcher.

Cost of recruitment is another issue. Traditional methods of recruitment in which the researcher approaches potential participants face-to-face are effective but can be time consuming and costly in time, materials, and effort. Facebook recruitment was an effective strategy in cost containment and enrolling participants when compared to traditional methods, especially Banner advertisements. A study by Akard et al. (2015) had an average cost per "click" on the banner advertisements of $1.08. Feasibility studies of recruiting on Facebook reported lower costs per participant when compared to traditional methods (Perry et al., 2017). Carter-Harris et al. (2016) reported Facebook recruitment costs of $1.51 per completed survey compared to $40.80 per completed survey through a newspaper advertisement. Similarly, Staffileno et al. (2017) reported Facebook recruitment costs of $1,034 compared to traditional recruitment methods costing $13,984 in their study. Nurse researchers may find Facebook recruitment a more budget-friendly method to yield a large number of participants.

When funding advertisements is a concern, a cost-effective strategy to recruit using Facebook is through using their pages or groups. Extracting public data, sharing information to groups or pages, or creation of a Facebook page or group was found to be effective among the articles reviewed and cost-free (Al Qadire, 2019; Atarhim, Lee, & Copnell, 2019; Gage-Bouchard et al., 2017). However, the ethical consideration of extracting public data needs special considerations, as discussed. Recruitment through a snowball sampling or sharing of information

related to the study is effective on Facebook, where users can share information with other users quickly and easily (Siegmund, 2018). “Snowball sharing” of study information has benefits and limitations. Snowball sharing or snowball sampling is cost effective and can reach many people. However, it is difficult and often impossible to track who shares the information and how the information is shared.

Combining other recruitment strategies with Facebook recruitment efforts did not yield higher enrollment when compared to Facebook-only recruitment. There was no difference found in the number of participants in quantitative studies that used only Facebook for recruitment compared to studies that combined Facebook and other strategies. Only one study was found in which a large number of participants were recruited using combined strategies. Ko et al. (2013) used Facebook recruitment combined with other recruitment strategies to yield 1,037 participants. This study may be an outlier of the studies reviewed. Some of the qualitative and mixed method studies contained missing information related to the number of participants or did not report the number of participants in the study. Studies that contained public data or used content analysis for comments or posts did not report the number of participants from which the content was derived. The use of Facebook for recruitment when compared to traditional only recruitment seems effective. Close et al. (2013) and Wahlberg et al. (2016) expanded recruitment efforts to Facebook after traditional methods were unsuccessful in recruiting participants. Other feasibility studies also found Facebook recruitment was successful over traditional strategies in recruiting higher numbers of inquiries and participants (Carter-Harris et al., 2016; Jones, Lacroix, & Porcher, 2017; Staffileno et al., 2017).

Limitations

There are limitations in this integrative review. While care was taken to find all nursing research articles that used social media and Facebook for nursing research recruitment, there could have been studies inadvertently not included in the review. Keywords used in the search may not have identified articles that may have used social media or Facebook for nursing research recruitment. In addition, there could have been studies that did use social media or Facebook for recruitment, but the authors may not have described the methods clearly or included using social media as a part of the recruitment strategy.

Implications and Recommendations

Recommendations for researchers who are considering using social media and/or Facebook for recruitment include the consideration of Facebook ads to heighten recruitment efforts. Facebook ads for recruitment are more cost effective than traditional methods, however cost remains associated with the strategy. Recruiting participants through public or private groups or pages and creating a Facebook page or group about the study are cost-free strategies that are effective in recruitment.

Researchers using social media and Facebook for recruitment should be transparent in the methods used to recruit participants on social media platforms. Many of the articles in this review did not have detailed description of the methods used for recruitment, making studies and strategies difficult to reproduce. Lack of description of methods can lead to untrustworthiness and question the validity of the study results. Clarity of methods used in studies using social media is important for nursing researchers to employ when designing research studies and when disseminating the research results. In addition, nursing scientists should provide informed consent to participants prior to collecting any data, regardless of the public availability of data

being collected. Future studies should consider using social media, or Facebook, as a recruitment strategy. Recommendations for how to use Facebook for recruitment is presented in Table 3.

Conclusion

Exploring the ways in which Facebook has been used for participant recruitment by nursing researchers helped identify limitations and best practices for recruiting participants for research. The discoveries found through this integrative review should guide other nursing researchers in understanding the current state of nursing science for Facebook as a recruitment tool and best practices in using Facebook for participant recruitment. Refinement of recruitment as a concept must be considered. Most studies in this review were a quantitative cross-sectional design from a variety of nursing research areas and patient populations. Just over half of the studies reviewed used a Facebook only recruitment method, while the other half used a combined strategy recruiting effort. Facebook ads were the most commonly used recruitment method. Other strategies that were combined with Facebook used other online modalities, such as email or websites, or more traditional methods such as flyers and face to face recruitment.

Nursing researchers are encouraged to provide rationale for recruiting using social media and to provide informed consent. In addition, nursing scientists should be clear in reporting the methods used to recruit participants into a study. Providing rationale, consent, and transparency of methods will help to increase the rigor and ethical standards that are needed in research. This integrative review supports the many opportunities for the use of social media, especially Facebook, in participant recruitment and study design. Facebook can be used as a valuable tool for participant recruitment in nursing research.

Figure 1.

PRISMA Flow Diagram

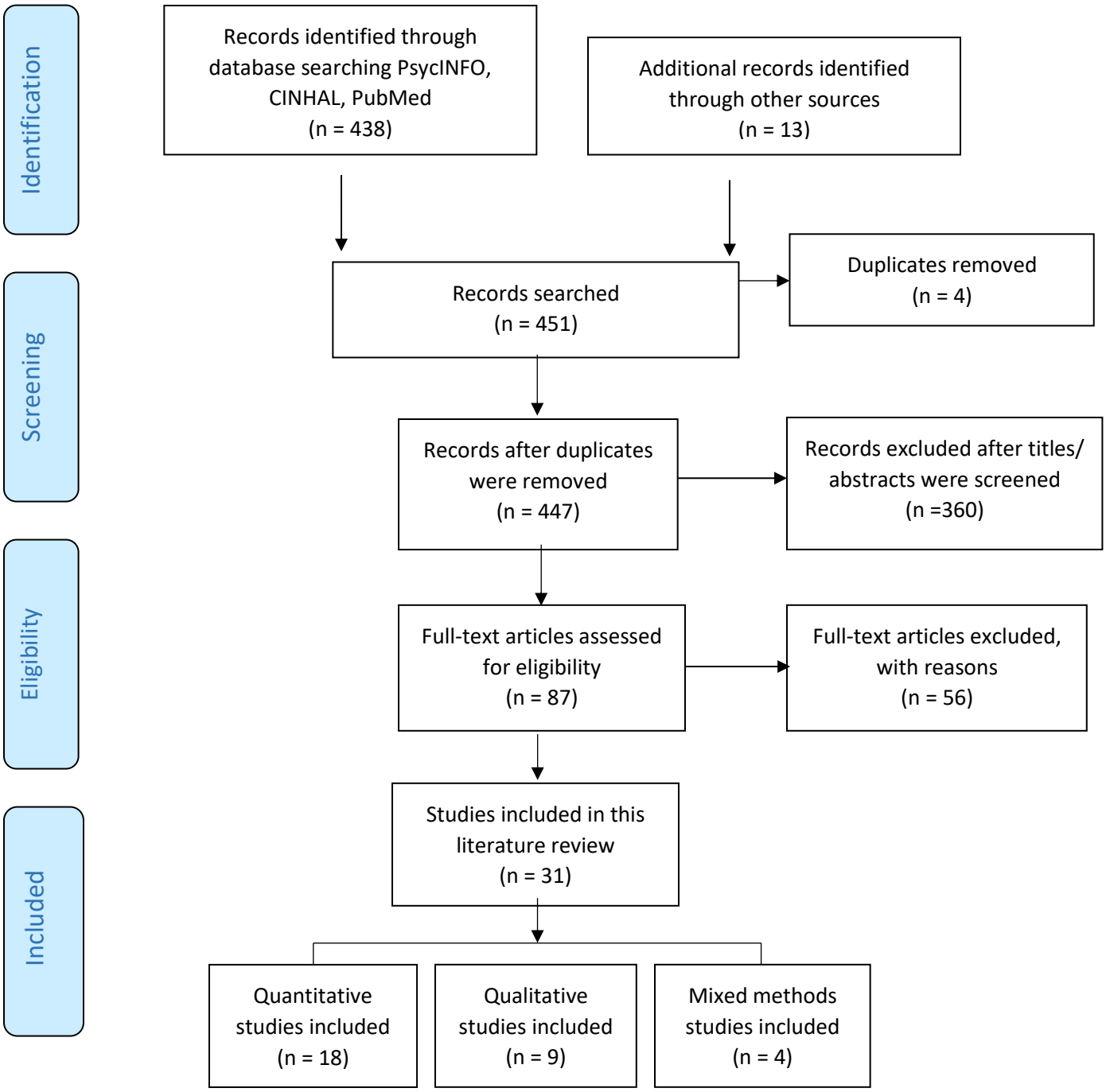


Table 1.

Demographic Characteristics of Studies Reviewed (N = 31)

Characteristic	*n*	%
Country of origin		
USA	18	58
Australia	5	16
Brazil	1	3
Canada	1	3
Caribbean	1	3
Jordan	1	3
Malaysia	1	3
South Africa	1	3
Taiwan	1	3
Thailand	1	3
Study Design		
Quantitative	19	61
Cross-Sectional	14	74
Intervention	4	22
Quasi-Experimental	1	5
Qualitative	8	26
Content Analysis	5	62.5
Descriptive	1	12.5
Interpretive	1	12.5
Phenomenological	1	12.5
Mixed Methods	4	13
Cross-sectional with Content Analysis	3	75
Tool Development	1	25
Research Areas		
Nurses	6	19
Sexual Health/HIV	6	19
Women's Health	5	16
Parents of Children	4	13
Cancer	2	7
Chronic Diseases	2	7
Mental Health	2	7
Pediatrics	2	7
Nursing Education	1	3
Traumatic Brain Injury	1	3

Table 2.

Social Media Recruitment Characteristics of Studies Reviewed (N = 31)

Characteristic	*n*	%
Consent		
Yes	21	68
No	2	6
Unknown	8	26
Rationale		
Yes	15	48
No	16	52
Ways of Recruitment		
Facebook Only	17	55
Facebook with Other	14	45
Facebook Only Recruitment		
Advertisements	13	76
Public pages/groups	7	41
Facebook study page/group	6	35
Closed group/page	3	18
Snowball sharing	3	18
Facebook Messenger	2	12
Facebook with Other		
Email Invites	5	36
Flyers/Brochures	4	29
Face to Face	4	29
Websites	4	29
Online Support Groups (not Facebook)	4	29
Newspaper	2	14
Letters	1	7

Table 3.

Recommendations for Recruiting on Facebook

Recommendations
1. Align research design with recruitment strategy.
2. Assure presence of population on Facebook and consider vulnerability.
3. State rationale for recruiting on Facebook versus other strategies.
4. Explore options for recruiting target population (ex. Banner ads, snowball sharing, etc.).
5. Review Facebook policies.
6. Consider Facebook group/page administrator approval if applicable.
7. Provide consent for participants.
8. Protect privacy of data collected.
9. Use transparency when disseminating rationale and research methods of using Facebook for recruitment.

CHAPTER 5: INFERTILITY-RELATED STRESS, HAIR CORTISOL, COPING, AND QUALITY OF LIFE IN U.S. WOMEN UNDERGOING INFERTILITY TREATMENTS

This chapter contains manuscript two regarding research on infertility-related stress, cortisol, coping, and quality of life in U.S. women undergoing infertility treatments. The background and significance are presented in the introduction, followed by the methodology and results. The article ends with the discussion and conclusions.

Abstract

Background: Infertility-related stress (IRS) is prevalent among women with infertility, however little is known about the perceptions of IRS, coping strategies, and quality of life (QOL) of women in the United States (U.S.). Hair cortisol measures chronic stress, but has not been studied in the context of IRS, coping, or QOL in women with infertility. The research on relationships between IRS, coping, and QOL in women undergoing different treatment types has conflicting findings, and there is limited research focusing on women with infertility and pregnancy loss.

Purpose: The purpose of study is to determine the relationships between IRS, hair cortisol, coping, and QOL in U.S. women undergoing infertility treatments and to examine relationships between infertility treatment type (IVF and non-IVF) and pregnancy loss and IRS, coping, and QOL.

Methods: A descriptive correlational cross-sectional design was used. Two-hundred and thirty U.S. women between 18-55 years old undergoing infertility treatments were recruited from infertility-related Facebook groups and pages through convenience sampling. Participants completed the Copenhagen Multi-centre Psychosocial Infertility Fertility Problem Scale Score, Copenhagen Multi-centre Psychosocial Infertility Coping Styles Scale, Fertility Quality of Life

survey, and demographic and background data. Root hair samples for cortisol analysis were collected from a subsample of 37 participants.

Results: Higher IRS was associated with more active-avoidance coping ($p < .05$), and lower QOL in all domains ($p < .05$). There were no differences in IRS among treatment types, however the non-IVF group used more active-avoidance coping, less meaning-based coping, and had lower social QOL than the IVF group ($p < .05$). Women with pregnancy loss had more IRS ($p < .05$), used more active-avoidance coping ($p < .05$) and had lower QOL scores ($p < .01$) compared to women with no pregnancy loss. Low cortisol levels were found in the subsample ($M = 1.01$, $SD = .90$), with low cortisol levels associated with higher IRS, especially marital stress ($p < .001$). Higher QOL scores were associated with higher cortisol levels, especially relational QOL ($p < .01$) and core QOL ($p < .05$).

Conclusions: Women with infertility and women with infertility and pregnancy loss have higher IRS, use more active-avoidance coping, and have lower QOL, though the quality of the partnered relationship may offer protection against IRS. Hypocortisolism was prevalent in the subsample and warrants further exploration.

Introduction

Fertility rates in the United States (U.S.) have declined to a 30-year low (Hamilton et al., 2018), and 33% of Americans report undergoing or knowing someone who has undergone infertility treatments (Livingston, 2018). Infertility, the inability to maintain or achieve a pregnancy to term after 12 months of unprotected sexual intercourse (WHO, 2019a), affects 1 in 8 couples in the U.S (CDC, 2018), and is well-known to be a stressful situation. Prolonged infertility-related stress (IRS) has been compared to similar levels of cancer-related stress (Cousineau & Domar, 2007; Laubmeier et al., 2004). Further, women experience IRS and other

psychological distress more often than men with infertility (Casu & Gremigni, 2016; El Kissi et al., 2013) and perceive lower QOL (El-Messidi et al., 2004). Women are 2.43 times more likely to commit suicide post-infertility evaluation if no child was conceived compared to women who had 1 child post-infertility evaluation (Kjaer et al., 2011).

Physiologic manifestations may result from psychological distress. Cortisol, a hormone secreted from the adrenal glands as a result of the hypothalamic-pituitary-adrenal (HPA) pathway, maintains homeostasis from acute and chronic stress (Nater et al., 2013). Chronic stress may damage the HPA axis and lead to hypo- or hypercortisolism (Guilliams & Edwards, 2010). Chronic hypercortisolemia can negatively affect body systems (Kyrou & Tsigos, 2009) and may alter menstrual cycle patterns (Prokai & Berga, 2016). Chronic hypocortisolism is associated with systemic inflammation disorders and psychological disorders such as post-traumatic stress disorder (Guilliams & Edwards, 2010). Hair cortisol is a newer technique to measure chronic stress, as each centimeter of hair growth represents one month of cortisol secretion (Russell et al., 2012). According to Binz et al. (2018), the reference range for hair cortisol levels in adults is 4 to 15 pg/mg. Studies measuring hair cortisol in women with infertility are limited, and only one study was found that compared hair cortisol to anxiety and depression in women with infertility (Santa-Cruz et al., 2019). The associations between hair cortisol, IRS, coping, and QOL are not known to have been considered to date.

There are many sources of stressors that can contribute to IRS, such as social, martial, and personal stress (Schmidt, 2006). Cultural and social differences in expectations of womanhood can influence perceived stress levels (Aflakseir & Zarei, 2013; Lee et al., 2010). Little is known about how women in the U.S. manifest IRS, coping, or QOL in the context of infertility due to few studies conducted in the U.S. considering these variables. In the U.S., the

financial burden of infertility treatments is high, since infertility treatments are not often covered by insurance (Chambers et al., 2012). Studies of other factors, such as the types or origins of infertility have resulted in inconsistent findings in determining if these factors are associated with IRS (Donkor & Sandall, 2007; Gourounti et al., 2012; Lansakara et al., 2011).

Infertility treatments are stress inducing (Pasch et al., 2012); however, most studies considering IRS focus on assisted reproductive technology (ART), such as in-vitro fertilization (IVF) treatments, and do not include women undergoing non-assisted reproductive therapy treatments, such as medication-only cycles or intrauterine inseminations. Moreover, women with pregnancy loss who underwent infertility treatments have been found to have more post-traumatic stress symptoms than women with pregnancy loss who later conceived naturally (Cheung et al., 2013).

To manage IRS, coping strategies are used to control the emotions resulting from the infertility experience. Coping strategies to manage the stress of infertility may be meaning-based coping (appraisal to provide positive meaning of the stress), emotion-focused coping (emotional regulation of the stress) or problem-focused coping (finding solutions to manage the stress) (Lazarus & Folkman, 1984; Park & Folkman, 1997), but there are inconsistencies in the literature about the coping strategies that may be useful in decreasing IRS (Gourounti et al., 2012; Lykeridou et al., 2011; Sexton et al., 2010).

The accumulation of these various sources of stress and coping strategies used to manage stress can impact QOL in infertile women (van den Akker, 2005). Li et al. (2019) and Cheng et al. (2018) found IRS was associated with lower QOL scores in Chinese and Taiwanese women. Meaning-based coping was associated with higher QOL scores in Indian women with infertility, while avoidance-coping strategies was correlated with lower QOL scores (Madhavi et al., 2013).

The lack of studies about QOL in the context of infertility, especially in U.S. women, justifies further consideration.

The aims of this study were to determine the relationships between IRS, hair cortisol, coping, and QOL in U.S. women undergoing infertility treatments, and to examine relationships between infertility treatment type (IVF and non-IVF) and pregnancy loss and IRS, coping, and QOL.

Theoretical Framework

The transactional theory of stress and coping (TTSC) by Lazarus & Folkman (1984) guided the study. According to the TTSC, personal factors such as beliefs, values, social networks, and situational factors such as uncertainty can influence primary appraisals of a stressor. Stressors can be appraised as irrelevant, benign-positive, threat, harm/loss, or challenge; however, it is appraisals of threat, harm/loss, or challenge that lead to coping appraisals. Coping options may be emotion-focused coping, which seeks to control the negative emotions of the stress, or problem-focused coping, which focuses on problem solving solutions. Later work by Park & Folkman (1997) described meaning-based coping, which seeks to modify primary appraisals and adjust beliefs and goals to accommodate the stressor. Lastly, reappraisals of the effectiveness of the coping strategies and appraisals of the stressor occur.

In applying the TTSC to the experience of infertility, infertility and infertility treatments are appraised as a threat, harm/loss, or challenge. Emotion-focused, problem-focused, and meaning-based coping strategies are used, which may be effective or ineffective. Social and cultural factors, commitment to parenthood, and uncertainty of the situation can influence coping strategies, appraisals, and reappraisals, and impact QOL as a downstream consequence.

Materials and Methods

Participants

Infertility-related Facebook groups and pages were targeted to recruit women with infertility. Inclusion criteria were: females between the ages of 18-55 years, living in the U.S., had an infertility diagnosis, were currently undergoing infertility treatments or had undergone treatments within the past six months, and were able to speak and read English. Facebook was used for this study since it is one of the most widely used social media platforms among women in the U.S. (Pew Research Center, 2018), digresses from clinic-based recruitment which dominates the literature in infertility research, and provides the ability to reach women across the U.S. A Facebook study page was developed with the study information and a link to an online survey. Administrators from infertility-related Facebook pages and groups were contacted through Facebook Messenger and were provided a description of the study and a link to the Facebook study page or survey. Current best practice for online recruitment suggests obtaining permission from group administrators (Eysenbach & Wyatt, 2002). Administrators were asked to share the Facebook study page or survey to their respective group or pages, or to allow permission for the primary investigator (PI) to share the study page on the page or group. Further recruitment involved snowball sampling, or snowball sharing of the Facebook study page or survey link by Facebook users. Using a power analysis for correlations, assuming a power = .80, $\alpha = .05$, and an average population correlation (effect size) of .20 in nursing studies (Polit & Beck, 2017), the targeted sample size for this study was N = 194.

A subsample was recruited for hair cortisol sampling through consecutive sampling technique. Participants who were interested in providing a hair sample provided their email address at the end of the survey and were contacted within 2 weeks to provide a mailing address.

Contact was halted for participants who did not respond after three contact attempts. Women who provided a mailing address were mailed a stamped envelope, aluminum foil pouch, consent form, hair care questionnaire, and instructions with video links on how to provide the hair sample. Participants were instructed to cut a "pencil-width" amount of hair from the crown of their head, as close to the scalp as possible without cutting the scalp. A three-centimeter ruler was printed on the instructions, so participants could measure 3 cm of hair from the root and discard any excess hair. Participants returned the consent form, hair care questionnaire, and the hair sample stored in the aluminum foil pouch in the postage-paid envelope. A follow-up email was sent to participants who received the hair collection information weekly until samples were returned. After three failed attempts for response, contact was halted. The target subgroup for hair cortisol collection was n = 30. The number of participants in the subset was determined based on available funding, and represented a feasibility study for hair cortisol sampling in women with infertility.

Surveys

Instruments and questionnaires used in the this study were screening questions, the Copenhagen Multi-centre Psychosocial Infertility Fertility Problem Scale Score (COMPI-FPSS), the Copenhagen Multi-centre Psychosocial Infertility Coping Styles Scale (COMPI-CSS), the Fertility Quality of Life (FertiQoL) tool, a demographics and background questionnaire, and a hair care questionnaire. Initially, participants were screened to ensure they met the inclusion criteria, however participants could choose to participate regardless of their responses to the screening questions.

Screening questions. Inclusion criteria screening questions included self-report of an infertility diagnosis, infertility treatment within the past 6 months, biological sex, age, and if the participant currently resided in the U.S.

COMPI-FPSS. The COMPI-FPSS is a 9-item tool that measures three dimensions of IRS including personal, marital, and social stress. The personal domain considers the physical and mental health of the person, the marital domain asks questions related to the partnered relationship, and the social domain considers the relationship of the person to family and friends. The tool was constructed using the TTSC and was developed and validated with persons experiencing infertility as a 14-item tool (Schmidt, 2006), and underwent further validation by Sobral et al. (2017) after being reduced to a 9-item tool due to several items with low-factor or cross-factor loadings. The 9-item tool was selected for this study. Reliability and validity estimates for the COMPI-FPSS are strong with internal consistency reliability estimates between .73 to .81 for each domain (Schmidt, 2006). In this study, coefficient alphas were .66 for the personal domain, .74 for the martial domain, and .72 for the social domain.

COMPI-CSS. The COMPI-CSS is a 19-item tool that assesses coping styles and was developed from the TTSC. The COMPI-CSS has 4 domains: active-avoidance, active-confronting, passive-avoidance, and meaning-based coping (Schmidt, 2006). These domains are congruent with the theoretical framework for this study. Reliability and validity estimates range from 0.80–0.85 per domain (Lykeridou et al., 2011). The tool was created by the same researchers who developed the COMPI-FPSS for persons with infertility and has been validated in women with infertility. In this study coefficient alphas were .66 for active avoidance, .76 for active-confronting, .71 for passive-avoidance, and .74 for meaning-based coping.

FertiQoL. FertiQoL is a 36-item tool specifically developed and validated for men and women with infertility, and measures four core domains of QOL: emotional, mind/body, relational, social. The four core domains are combined for a core total QOL. The FertiQoL also contains a treatment module to measure treatment-related QOL and may be used with the core domains or as a separate module. The FertiQOL treatment module includes environment and tolerability domains and can be combined with the core domains to give an overall QOL score. This study included only the four core domains of QOL and the core total QOL, as these are the major aspects of QOL considered in this study.

The emotional QOL domain measures the impact of emotions on QOL, such as resentment, grief, despair, depression, and anger. The mind/body domain focuses on concentration, pain, fatigue, and daily life activities. The relational domain considers the impact of the partnered relationship on the sexual relationship, affection, commitment, communication, and contentment. The social domain considers social relationships, such as friends and family, social situations, and social pressure. The FertiQoL has high internal consistency reliability estimates ranging from .72-.92 for each domain and overall score (Boivin et al., 2011). In this study, the coefficient alphas for the core domains were .83 for emotional, .80 for mind/body, .82 for relational, .71 for social, and .89 for the core total QOL.

Demographics and background questionnaire. In addition to demographic information such as race, ethnicity, marital status, education, employment achievement, average household income, the number of individuals in the household, infertility insurance coverage, and state and community living area (rural, suburban, urban), questions in this survey included the duration, type, and cause of infertility, current infertility treatment and point in treatment cycle, history of pregnancy loss, number of pregnancy losses if applicable, and coping strategies. Information was

obtained about how the participant found the study on Facebook, and the opportunity to provide an email address was given if the participant was interested in being contacted by the PI to provide a hair sample for cortisol analysis.

A hair care questionnaire as required by the independent laboratory for cortisol testing was mailed to participants who agreed to provide a hair sample for cortisol analysis. The questions on the survey included disclosure of a treated medical condition, steroid-containing medication use, and hair care practices, such as washing or hair coloring. Other lifestyle behaviors, such as swimming and frequent exercise were also included in the questionnaire.

Hair Cortisol

The hair sample was collected by the participant using the independent laboratory directions and procedures. The hair sample included three centimeters of root hair cut from the crown of the head that was placed in a foil pouch and mailed to the PI. Hair samples and hair care questionnaires were coded with identification numbers to protect participants' privacy and mailed to the independent laboratory. Participants who provided a hair sample were given the result of their personal hair cortisol level as appreciation for providing the sample. No interpretation of the results was given, and participants were advised to consult their health care provider if they had questions about their results.

Outcomes and Statistical Analysis

Data were collected through an online survey design, using the university-approved REDCap survey application to build and manage the survey, since REDCap is secured and HIPAA-compliant (ECU ITCS, 2018). The University and Medical Center Institutional Review Board at East Carolina University reviewed and approved the study. A letter of consent to participate in the study was presented to the participant prior to the start of the survey. Written

informed consent was obtained from participants that provided a hair sample for cortisol analysis.

IBM SPSS (version 24; IBM Corp., Armonk, New York) was used to conduct all analyses. Descriptive statistics including means and frequencies were used for demographic and background data. Pearson correlations were conducted to examine relationships between the three IRS subscales, four coping subscales, five quality of life subscales, and infertility characteristics (treatment type and pregnancy loss). Independent-samples t-tests were used to compare IRS, coping, QOL, and mean differences between independent subgroups based on type of infertility treatments (IVF vs. non-IVF) and pregnancy loss.

The SPSS Two-Step Cluster procedure was conducted using the nine items of the IRS scale (COMPI-FPSS) to explore the presence of naturally occurring subgroups in the study sample who varied in their IRS scores. Two subgroups were identified and were categorized as a "high IRS" group, and a "low IRS" group for further analysis. Each item was categorized into a binary score, where 1 = strongly agree and 0 = strongly disagree to somewhat agree to examine those who strongly agreed with the item compared to those who did not strongly agree. Similarly, for the coping strategies scale (COMPI-CSS), each of 19 items were categorized into a binary score, where 1 = "used quite a bit" or "used a great deal" and 0 = "not used" or "used somewhat". An independent-samples t-test was used to (1) compare the mean IRS scores on the individual items and subscale average scores between low and high IRS groups, (2) to compare mean coping strategy scores on individual items and subscale average scores between low and high IRS groups, and (3) to compare mean QOL core subscales and total core quality of life between low and high IRS groups. The chi-square test for independence was used to compare the proportion of low and high IRS participants with pregnancy loss (yes or no) and type of

infertility treatment (IVF or non-IVF). The η^2 statistic was used to describe the strength of the statistical test of mean differences, and the phi statistic was used to describe the strength of the chi-square test for independence.

Hair Cortisol Analysis. Hair cortisol concentrations were analyzed at an independent laboratory. Three-centimeter hair samples were washed twice in 5 ml of isopropanol and placed on an inversion rotator for 3 minutes each wash, dried for 2-3 days, and crushed into a fine powder using a stainless-steel grinding ball and a bead beater for 1-2 minutes. The powdered hair was placed in 1.5 ml of methanol and continuously inverted for 18-24 hours at room temperature. The sample was then placed in a centrifuge for 5 minutes. The hair powder was dried in a vacuum evaporator, then an enzyme immunoassay buffer was added to the cortisol extract and analyzed using an enzyme immunoassay for saliva samples (Hodes et al., 2017; Meyer et al., 2014). Hair cortisol concentrations reported in research are well known to fall outside of a normal distribution curve (Abell et al., 2016), which was also found in this study, therefore a log transformation was conducted to normalize the results prior to data analysis. Pearson correlations were conducted to examine the relationship between hair cortisol levels, IRS, coping, and QOL.

Results

Demographic Characteristics

A total of 49 infertility-related Facebook support groups and 28 infertility-related Facebook pages were contacted between March and May 2019 and then again between July and September 2019. Seventeen support groups and three infertility-related pages shared the study Facebook study page or survey link with their respective members. A total of 500 survey

responses were obtained, with 230 completed surveys whose respondents met the study inclusion criteria.

Demographic data for the total sample and subsample are presented in Table 1. In the total sample, participants were from 36 states. The mean age of participants was 32 years (SD = 4.18), and the mean duration of infertility was 4 years (SD = 3.09). Most participants were non-Hispanic or Latino (83%), Caucasian or white (90%), and educated with some college or higher (96%). Most participants had a yearly household income range between $51,000-$100,000 (43%) and most had partial fertility insurance coverage (49%) or no fertility insurance coverage (45%). Infertility-related characteristics included 65% primary infertility, and 32% secondary infertility. Most participants were undergoing non-IVF treatment (52%) and 44% were undergoing IVF treatment with both groups in all stages of the infertility treatment cycle (beginning of cycle, ovulation induction, ovulation, two-week wait, failed cycle). Forty-eight percent of participants had pregnancy loss and 47% did not report pregnancy loss.

Thirty-seven hair samples were obtained from a subsample to examine cortisol levels. Participants were from 18 states. The raw hair cortisol mean was 4.0 pg/mg (SD = 3.86). After log transformation, the mean hair cortisol concentration was 1.01 pg/mg (SD = .90). One hair cortisol sample was deemed an outlier and was excluded from data analysis. The subsample group had similar demographics to the total sample. Participants in the subsample had a mean age of 33.6 years (SD = 4.19) and a mean duration of infertility of 4.4 years (SD = 3.69). Subsample participants were mostly non-Hispanic or Latino (86.1%), Caucasian or white (94.8%), and 83.3% were educated with some college or higher. Most subsample participants had a yearly income between $51,000-$100,000 (52.8%) and either had partial fertility insurance coverage (52.8%) or no fertility insurance coverage (41.7%). Most participants had primary

infertility (63.9%) and 58.3% reported having a pregnancy loss. Sixty-six of the subsample participants were receiving non-IVF treatment and represented all stages of the treatment cycle.

Relationships between IRS, Coping, and QOL

Overall, the participants in the study had high levels of IRS**,** especially in the personal domain (M = 11.10; SD = 1.65). Seventy-two percent of participants (n = 166) were in the high IRS group, compared to only 28% (n = 64) in the low IRS group. Theoretical scores with the total mean scores for the IRS scales, coping, and QOL scales are presented in Table 2.

The two coping domains with the highest response average of "used quite a bit" or "used a great deal" were passive-avoidance (M = 74%) and active-avoidance (M = 53%), while the two lowest coping usage responses were meaning-based (M = 36%) and active-confronting (M = 32%). The coping strategies with highest usage included passive-avoidance item 3 (78%), "have fantasies and wishes", item 1 (77%), "hope a miracle will happen", and item 2 (69%) "feel that the only thing I can do is to wait", and active-avoidance item 3 (60%), "try to keep my feelings to myself" and item 4 (61%), "turn to work or substitute activity to take my mind off things." The coping strategies used least often included meaning-based item 2 (11%), "think about the infertility in a positive light" and active-confronting items 4 (22%), "ask a relative or friend for advice" and 5 (23%), "read or watch television about childlessness." Coping strategies that participants reporting "used quite a bit" or "used a great deal" are presented in Table 3.

Table 4 presents the mean differences in coping strategies between participants with low and high IRS. When considering the differences between participants with low and high IRS, only active-avoidance coping mean usage was significantly different (34% versus 60%; $p < .001$). The two active-avoidance coping subscale items with the strongest mean difference included item 1 (17% versus 60%; $p < .001$), "avoid being with pregnant women or children"

and item 2 (25% versus 54%; $p < .001$), "leave when people are talking about pregnancies and children." Participants with low IRS used meaning-based coping subscale item 15 (64% versus 41%; $p < .01$), "have grown as a person in a good way" and item 16 (20% versus 7%; $p < .01$), "think about the infertility in a positive light" more frequently than participants with high IRS.

Table 5 presents the core QOL scores for the total group and low and high stress groups. Participants who did not complete all items in the QOL scales were excluded from QOL analysis to yield n = 222. Overall, participants had low QOL scores in all four core QOL domains and total core QOL, with the highest QOL score in the relational domain (M = 65.33; SD = 20.38). Participants with low IRS had significantly higher QOL scores on all core QOL subscales and total core scores compared to the high stress participants ($p < .001$), especially between emotional QOL (47.6 versus 26.6; $p < .001$) and mind/body QOL (59.6 versus 38.6; $p < .001$).

Personal Stress. Higher levels of personal stress were moderately correlated with active-avoidance coping ($r = .39$) and strongly associated with lower levels of emotional QOL ($r = -.64$), mind/body QOL ($r = -.57$), and core total QOL ($r = -.59$). Moderate negative associations were found between personal stress and social QOL ($r = -.41$). All correlations equal or greater to .15 were statistically significant to at least $p < .05$. Correlations between IRS, coping, and QOL are presented in Table 6.

When comparing "strongly agree" mean responses between low and high IRS groups, there were statistically significant differences on all items in the personal domain ($p < .001$). The strongest mean differences between low and high IRS groups were observed for the personal domain average (17% versus 67%; $p < .001$), personal domain item 1 "it is very stressful for me to deal with this infertility problem" (27% versus 84%; $p < .001$), and personal domain item 3 "stress related to your mental health" (22% versus 83%; $p < .001$). See Table 7 for percent of

respondents who reported “strongly agree” on the COMPI-FPSS in the total group and the low and high IRS groups.

Marital Stress. Higher levels of martial stress were negatively associated with meaning-based coping (r = - .30). Martial stress was found to have strong negative relationships with relational QOL (r = - .62), and moderate negative associations to core total QOL (r = - .47) and emotional QOL (r = - .39). All correlations equal or greater than .15 were statistically significant to at least $p < .05$. Correlations are presented in Table 6.

When comparing “strongly agree” mean responses between low and high IRS groups, there were statistically significant differences on the total marital domain score and items ($p < .001$), except for marital domain item 1, “the childlessness has caused a crisis in our relationship”. The strongest mean differences between low and high IRS groups were observed for the marital domain item 3, “stress related to your sex life” (8% versus 61%; $p < .001$). See Table 7 for percent of respondents who reported “strongly agree” on the COMPI-FPSS in the total group and the low and high IRS groups.

Social Stress. Table 6 presents the correlations between IRS domains, coping, and QOL domains. Higher levels of social stress were moderately associated with active-avoidance coping (r = .34). There were no relationships found between social stress and active-confronting or passive-avoidance coping. Social QOL was strongly negatively associated with social stress (r = - .54). Higher levels of social stress were moderately associated with lower emotional QOL (r = - .43), mind/body QOL (r = - .41), core total QOL (r = - .48). All other domains of QOL had small negative associations to social stress. All correlations equal or greater than .15 were statistically significant to at least $p < .05$.

Table 7 presents the percent of respondents who reported “strongly agree” on the COMPI-FPSS in the total group and the low and high IRS groups. When comparing “strongly agree” mean responses between low and high IRS groups, there were statistically significant differences on the total social domain score and items, except for social domain item 1, “stress related to family-in-law relationships”. The strongest mean differences between low and high IRS groups were observed for the social domain item 3, “stress related to friend relationships” (3% versus 28%; $p < .001$).

Coping and QOL

There was a large negative association between active-avoidance coping and emotional QOL ($r = -.50$), social QOL ($r = -.58$), core total QOL ($r = -.53$). Moderate negative relationships were found between active-avoidance coping and mind/body QOL ($r = -.47$). Meaning-based coping was moderately correlated to relational QOL ($r = .44$) and core total QOL ($r = .35$). Active-confronting coping and passive-avoidance coping were found to have small or no relationships to core QOL. All correlations equal or greater than .15 were statistically significant to at least $p < .05$ and are presented in Table 6.

Treatment type and Pregnancy loss and IRS, Coping, and QOL

Treatment type, IRS, coping, and QOL. Table 8 presents the data related to treatment type and IRS, coping, and QOL. There were no significant differences in IRS domains between participants in non-IVF and IVF treatment types. Women receiving non-IVF treatments used active avoidance coping significantly more than women undergoing IVF treatment ($p < .023$), but with a small effect size (eta squared = .024). There was a significant difference in use of meaning-based coping, with women in IVF treatments using more meaning-based coping ($p < .035$), but also with a small effect size (eta squared = .021). There were no significant differences

in QOL domains or core total QOL, except in the social QOL domain. Women receiving non-IVF treatments had lower social QOL scores compared to women undergoing IVF treatments ($p < .018$) with a small effect size (eta squared = .026).

Pregnancy loss, treatment type, coping, and IRS. Table 9 shows the relationship between pregnancy loss, treatment type, and IRS. Participants could choose not to answer the questions related to pregnancy loss, which yielded 205 records for this analysis of pregnancy loss. Of the 104 respondents who reported a pregnancy loss, 82 (79%) were in the high IRS group, compared to 62 (61%) of the 101 respondents who had high IRS but did not have a pregnancy loss ($p < .006$). Women undergoing infertility treatments with pregnancy loss were found to have more personal stress ($p < .026$) and more social stress ($p < .017$) than women in infertility treatments without pregnancy loss (see Table 10).

Women with pregnancy loss used active avoidance coping more ($p < .028$) and used meaning-based coping less ($p < .044$) than women with no pregnancy loss. Compared to women without pregnancy loss, women with pregnancy loss had lower emotional QOL ($p < .007$), mind/body QOL ($p < .045$) and core total QOL ($p < .008$). Effect sizes for all statistically significant differences were small, ranging from 0.02-0.03. The results are presented in Table 10.

In women undergoing non-IVF treatments, there were more women with pregnancy loss (85%) in the high stress group compared to women with no pregnancy loss (66%; $p = .024$) (Table 9). Women undergoing non-IVF treatments with pregnancy loss had significantly higher personal stress ($p = .047$), social stress ($p < .001$), and lower emotional QOL ($p = .024$) compared to those undergoing non-IVF treatments with no pregnancy loss (Table 11). In women receiving IVF, 32 (71%) of the 45 with a pregnancy loss were in the high stress group compared to 31 (57%) of the 54 undergoing IVF without a pregnancy loss ($p = .158$) as presented in Table

9. There were no statistically significant differences in IRS domain levels between women receiving IVF treatments with and without pregnancy loss; however there were significant differences in QOL, with women undergoing IVF treatments with pregnancy loss having lower emotional QOL ($p < .034$), mind/body QOL ($p < .038$), and core total QOL ($p < .019$), as presented in Table 11.

Hair Cortisol, IRS, Coping, and QoL

Table 12 presents the relationships between hair cortisol concentrations, IRS, coping, and QOL in the subsample. There was a large significant negative correlation between hair cortisol and marital stress ($r = - .54$; $p < .001$), and a non-significant small negative correlation between hair cortisol and personal stress ($r = - .21$). Hair cortisol had a small positive correlation with meaning-based coping ($r = .29$), though it was not statistically significant. Relational QOL was largely and significantly correlated with hair cortisol ($r = .45$; $p < .007$). Hair cortisol was moderately correlated with QOL core ($r = .39$; $p < .02$) and emotional QOL ($r = .31$).

Overall, the subsample had slightly more personal and marital stress and lower social stress than the total group. The subsample also used more active-avoidance coping and had lower QOL scores in all domains compared to the total group. Mean scores for hair cortisol, IRS, coping, and QOL scales are presented in Table 13. Correlations between IRS, coping, and QOL were similar in the subsample compared to the total group, though there were some differences. Social stress had a large and significant correlation to personal stress ($r = .52$; $p < .001$). Martial stress had the most impact on QOL domains overall, with a moderate negative correlation to core QOL ($r = - .41$; $p < .01$). Similar to the total group, active-avoidance coping had the strongest negative correlation to QOL, with significant correlations to emotional QOL ($r = - .37$; $p < .03$),

social QOL ($r = -.48$; $p < .003$), and QOL core ($r = -.36$; $p < .04$). Meaning-based coping was strongly correlated to relational QOL ($r = .427$, $p < .01$).

Discussion

This current study sheds light on comprehensive aspects of IRS in women residing in the U.S. from the woman's point, rather than focusing only on downstream effects of IRS such as anxiety or depression. Hair cortisol concentrations, coping, QOL, infertility treatment types, and pregnancy loss were explored in the context of IRS. Infertility-related stress and low QOL is significant and prevalent among U.S. women undergoing infertility treatments. Personal, marital, and social domains of IRS all contributed to a woman's perceived QOL, which is consistent with other studies (Cheng et al., 2018; Li et al., 2019). However, personal stress was most strongly associated with more active-avoidance coping, lower emotional and mind/body QOL, and lower core total QOL. The perceived personal stress of women in the study was profound and seemed to have the most impact on the use of negative (avoidance) coping strategies and lower QOL scores.

Both types of emotion-focused coping strategies (active-avoidance and passive-avoidance) were most used among the participants. Active-avoidance coping, considered a type of emotion-focused coping, was strongly and significantly related to higher levels of IRS and lower QOL scores. Higher levels of IRS with use of avoidance-coping as was found in this study was consistent with other studies (Aflakseir & Zarei, 2013; Gourounti et al., 2012; Lykeridou et al., 2011; Schmidt et al., 2005a). With uncertain and uncontrollable situations, emotion-focused coping strategies are more likely to be used (Lazarus & Folkman, 1984), which is consistent with the infertility experience. Women with higher levels of IRS reported avoiding pregnant women and children as a coping strategy. Offering a separate waiting area for women undergoing

infertility treatments in obstetrics and gynecology practices may be beneficial to women who are emotionally challenged by being around pregnant women.

This study did not find associations between problem-focused coping strategies (active-confronting) and IRS and QOL scores. In women with infertility, problem-focused coping has been reported to lower IRS (Gourounti et al., 2012), increase well-being (Hynes et al., 1992) and promote resilience (Sexton et al., 2010); however, the use of problem-focused coping is unlikely in uncertain or uncontrollable situations (Lazarus & Folkman, 1984), and uncertainty within the infertility experience has been documented (Sandelowski & Pollock, 1986; Sandelowski, 1987; Sweeny et al., 2015). Integrative health therapies, such as acupuncture and mind-body therapies, could enhance problem-focused coping strategies, but further research is needed to provide consistent evidence that the use of complementary therapies increases pregnancy rates.

In this study, meaning-based coping, or altering appraisals or beliefs to manage IRS, was found to be an important coping strategy, and was associated with lower marital stress, lower overall IRS, and higher QOL scores, which is consistent with findings from other countries (Aflakseir & Zarei, 2013; Lykeridou et al., 2011). Folkman (2010) supported meaning-based coping as important in chronic stress, after emotion- and problem-focused coping failed to manage the stressor effectively. Under chronic stress, meaning-based coping would provide connection to positive beliefs, values, and goals to help maintain coping efforts (Folkman, 2010). Offering psychological support and interventions aimed at increasing meaning-based coping, such as mindfulness (Garland, Gaylord, & Park, 2009), religiosity, and counseling to promote positive reframing of the stress, and revising beliefs or goals (Park & Folkman, 1997) may be helpful in reducing IRS and increasing QOL.

This study contributes significant findings to the body of knowledge about the physiology of chronic stress and the infertility experience. Both hypercortisolemia and hypocortisolemia can be found in those individuals with chronic stress. Over time allostatic load, or the 'wear and tear' on the body from stress accumulates (McEwen, 1998) and the repeated or prolonged stress state produces HPA axis dysfunction. Chronic hypercortisolism as a result of chronic stress can create adaptational changes in the HPA axis which results in hypoactivity of the HPA axis leading to chronic hypocortisolism (Guilliams & Edwards, 2010). Hypocortisolism may increase vulnerability for the development of autoimmune disorders, and has been found in those with systemic inflammatory conditions, such as chronic pain, chronic fatigue syndrome, and rheumatoid arthritis (Heim, Ehlert, & Hellhammer, 2000; Roerink et al., 2018). Hypocortisolism is also associated with psychological symptoms and disorders, such as depression, PTSD, and trauma exposure (Hinkelmann et al., 2013; Pochigaeva et al., 2017; Steudte et al., 2013).

The findings of hypocortisolism in women with infertility in this study is significant. The results support the overall theory that chronic stress can cause disruption in the HPA axis leading to hypocortisolism. The marital or partnered relationship may be an important factor in increasing or decreasing IRS. In this study, lower levels of hair cortisol, indicating HPA axis dysfunction, were associated with higher levels of marital stress.

The presence of hypocortisolism in women with infertility warrants further exploration for many reasons. Low levels of cortisol may lead to infertility and inhibit the continuation of a pregnancy (Anand & Beuschlein, 2018; Schonblum et al., 2018). Further research should consider the presence of hypocortisolism prior to an infertility diagnosis and the associations with pregnancy loss. In addition, since there are systemic inflammatory effects from hypocortisolism, future studies should also consider assessing inflammation-related biomarkers

and interventions to reduce systemic inflammation in women with infertility. Trauma exposure, especially childhood trauma, and PTSD are associated with low hair cortisol (Hinkelmann et al., 2013; Steudte et al., 2013) and should also be considered in the management of women with infertility. Women with adverse childhood events (ACEs) have been found have decreased fertility and amenorrhea compared to women with no traumatic childhood events (Jacobs, Boynton-Jarrett, & Harville, 2015). Future studies should consider the connection between hair cortisol, infertility, adverse childhood events, trauma exposure, and PTSD to improve outcomes for women with these experiences.

Studies of women with infertility are saturated with women undergoing IVF treatments, which is surprising given that most women undergoing infertility treatments are not receiving IVF (Katz et al., 2011; Schieve et al., 2009). This study is one of few that considered the psychological health of women undergoing non-IVF treatments and found that women in non-IVF treatments did not differ statistically in IRS. However, women receiving non-IVF treatments did differ in the use of more active-avoidance coping, less meaning-based coping, and had lower social QOL than women undergoing IVF treatments. The experience of infertility is stressful, regardless of the treatment type; therefore, these findings support the need for future studies that include women undergoing non-IVF treatments. Additionally, healthcare providers should offer psychological support for women undergoing all types of infertility treatments.

In this study, nearly half of the participants (48%) experienced pregnancy loss, which is much higher than the 19.7% incidence of pregnancy loss in the general population of U.S. women (Rossen, Aherens, & Branum, 2018). There are limited studies of pregnancy loss in women with infertility and the results are conflicting, with some studies reporting pregnancy loss rates similar to the general population (Pezeshki, Feldman, Stein, Lobel, & Grazi, 2000; Schieve,

Tatham, Peterson, Toner, & Jeng, 2003), and others reporting an increased incidence of pregnancy loss after infertility treatments (Wang, Norman, & Wilcox, 2004). Schwerdtfeger & Shreffler (2009) found that women who were involuntarily childless and had pregnancy loss experienced more psychological distress, including depressive symptoms, sleep problems, loneliness, and fertility-related distress compared to women with infertility alone, women with pregnancy loss, or women with no loss and no fertility problems. Likewise, Cheung et al., (2013) found higher post-traumatic stress syndrome symptoms in women with pregnancy loss who had conceived with assisted reproductive therapies than women with pregnancy loss who conceived naturally. In this study, pregnancy loss was a significant contributing factor for IRS, maladaptive coping, and decreased QOL. These are noteworthy findings that supports the devastating experience of pregnancy loss on women with infertility.

In this study, the lack of differences in marital stress and relational QOL between treatment types and pregnancy loss suggest the quality of the partnered relationship may be a protective factor against IRS, reduced QOL, and stress related to pregnancy loss. Further, hair cortisol results in this study indicated an association between higher marital stress, lower relational QOL, and lower hair cortisol concentrations, presumably as a result of HPA axis dysfunction, thus supporting the influence of marital stress in the partnered relationship. Marital benefit, the strengthening of the relationship in those in infertility treatments, has been described by Schmidt, Holstein, Christensen, & Boivin (2005b) and Peterson, Pirritano, Block, & Schmidt (2011) with mixed results for women. However, congruence in IRS levels between partners has been shown to support higher levels of marital adjustment (Peterson, Newton, & Rosen, 2003). Casu et al. (2019) also found greater perceived spousal support was associated with lower IRS, which also supports a potential protective factor of the quality of the partnered relationship

against IRS. Further research is needed to examine if the partnered relationship acts as a protective factor against IRS and stress related to pregnancy loss.

Participants in this study had similar demographics to other studies conducted in the U.S., with most of the participants having primary infertility, around age 30, white, and well-educated. Most participants were demographically similar participants described in other studies and women who seek infertility treatments (Kessler et al., 2013). In addition, this study was able to capture women from 36 of the 50 U.S. States and greater numbers of women undergoing non-IVF treatments compared to other studies conducted in the U.S. (Gibson & Myers, 2002; Sexton et al., 2010). In this study, Facebook was a viable option for recruiting women undergoing infertility treatments who were demographically similar to clinic-based studies, while capturing a diverse sample in treatment types and stages of the infertility treatment cycle. Overall, the relative consistency in the results of this study and other studies suggests that the experience of infertility is similar regardless of cultural variations of the experience, an important finding considering the racial and ethnic diversity of U.S. residents.

Limitations

There are several limitations of this study. This study employed a cross-sectional design with self-report and does not examine IRS or pregnancy outcomes longitudinally, which could give further insight into the infertility experience. Online recruitment offers challenges such as selection bias and duplicate responses (Eysenbach & Wyatt, 2002; Holmes, 2009). However, misrepresentation is low and access to the internet is widely available thereby enhancing ethnically diverse sampling (Whitehead, 2007). Though this study specifically targeted infertility-related groups or pages on Facebook, tracking snowball sharing outside of these

groups or pages was not always possible. Demographic information, such state of residence, was obtained to help track survey sharing and to ensure a national sample.

This study considered only women undergoing infertility treatments and did not account for women with infertility who are not currently undergoing treatment within the past six months. Women with a previous history of infertility or who remain childless should also be included in future studies to examine their perceptions of IRS, coping, and long-term impact of infertility on QOL and psychosocial well-being. Future analysis to determine the relationship between demographic characteristics and/or infertility characteristics to IRS, coping, or QOL should be considered. T

This study did not consider resilience or other "protective factors", so it is unclear how resilience influences IRS and coping strategies, though Sexton et al. (2010) did not find relationships between IRS and emotion-focused coping, a hallmark of resiliency. In another study however, resilience was found to be protective against IRS and impaired QOL (Herrmann et al., 2011). Resilience and "resilience resources" (Schetter & Dolbier, 2011) as moderators of IRS, coping, and QOL should be considered further to identify characteristics that influence resilience in women with infertility and to foster positive coping behaviors and increased QOL.

A limitation of using the COMPI-FPSS tool in the United States is there is no item related to financial stress. With most participants in this study having partial or no infertility insurance coverage, the financial burden on participants having to pay out of pocket infertility treatment expenses would likely add to IRS. A revision of the tool may be needed for use in countries where infertility insurance coverage is limited.

Hair cortisol was collected by the participants, introducing possible collection errors, which may have affected the findings of the study, even though written instructions with a ruler,

videos, and contact information for the PI for questions and concerns were provided. Several participants declined to participate in hair cortisol sampling due to concerns about amount of hair needed for analysis. Further research is needed to examine the connections between hair cortisol and IRS, especially with larger samples.

Conclusions

Women in the U.S. in infertility treatments have high levels of IRS, often use negative coping strategies such as avoidance-coping, and have low QOL scores. There were no differences in IRS levels in IVF compared to non-IVF treatment groups, however women undergoing non-IVF treatment used more active-avoidance coping and had lower social QOL, whereas women receiving IVF treatment used meaning-based coping more often. This suggests similar levels of IRS among women undergoing non-IVF and IVF treatments, which is an important finding given the lack of studies that include women receiving non-IVF treatments. Further, this study also supports that pregnancy loss during the infertility experience is a significant contributing factor to higher levels of IRS, use of less adaptive coping strategies, and lower QOL compared to women with infertility without pregnancy loss. Marital or partnered relationships may have a protective effect on IRS and QOL, but further studies are needed.

This study also provides evidence of hypocortisolism in women with infertility, which is seen in other chronic diseases, autoimmune disorders, and traumatic experiences, and may signify HPA axis dysfunction. Higher marital stress and lower relational QOL was strongly associated with hypocortisolism, further supporting the need to examine the partnered relationship, as well as associations of infertility to autoimmune disorders and traumatic events in future research.

Healthcare providers in the U.S. should offer and emphasize the importance of psychological support to all women undergoing infertility treatments, especially women in infertility treatments experiencing pregnancy loss. Additionally, studies that investigate the effectiveness of specific psychological interventions on IRS, coping, and QOL are warranted.

Acknowledgements

The authors acknowledge Beta Nu Chapter of Sigma Theta Tau International and the East Carolina University College of Nursing Office of Research and Scholarship for grant support for this study, Dr. Lee Ann Jarrett Johnson for Facebook page recruitment assistance, and the administrators and members of the Facebook groups and pages who participated in and supported this study.

Table 1.

Demographic Characteristics of Study Participants Total Group (N = 230) *and Subsample* (n = 36).

Characteristic	Total	%	Subsample	%
Ethnicity				
Non-Hispanic or Latino	190	83	31	86
Hispanic or Latino	16	7	2	6
Other	24	10	3	8
Race				
African American/Black	3	1	0	0
Asian	5	2	1	3
Caucasian/White	207	90	34	95
Native Hawaiian or Pacific Islander	2	1	0	0
Multi or Mixed Race	5	2	0	0
Other	5	2	0	0
Education				
High School or less	10	4	0	0
Some College or degree obtained	121	53	9	25
Some Graduate School or higher	99	43	21	75
Marital Status				
Married	220	96	35	97
Committed Relationship	8	3	1	3
Divorced/Separated	2	1	0	0
Geographic Community Region				
Rural	56	24	7	19
Urban	54	24	5	14
Sub-urban	115	50	23	64
Household yearly income (U.S. dollars)				
<50,000	23	10	1	3
51,000-100,000	103	45	19	53
101,000-150,000	57	25	9	25
>151,000+	45	20	7	19
Fertility Insurance Coverage				
Full Coverage	12	5	2	5
Partial Coverage	13	49	19	53
No Coverage	104	45	15	42
Primary Infertility	150	65	23	64
Secondary Infertility	73	32	13	36
Unknown/Unsure	7	3	0	0
Current Treatment				
In Vitro Fertilization (IVF)	102	44	12	33
Non-In Vitro Fertilization (Non-IVF)	118	52	24	67
None	10	4	0	0
Pregnancy Loss				
Yes	110	48	21	58
No	107	47	14	39
Unsure	12	5	1	3
Age (years) (*M* and *SD*)	32	4.18		
Duration of Infertility (years) (*M* and *SD*)	4	3.09		

Table 2

Means for COMPI Fertility Problem Stress Scales, Coping Strategy Scales, Fertility Quality of Life (QOL) Subscales and Core Total QOL (N = 230)

COMPI Scales	Theoretical Score Range	M	SD
Infertility Stress Scales			
Personal domain total scale score	3-13	11.10	1.65
Marital domain total scale score	3-13	8.54	2.50
Social domain total scale score	3-12	7.00	2.34
Coping Strategy Scales			
Active-Avoidance	4-16	10.63	2.87
Active-Confronting	7-28	14.91	4.30
Passive-Avoidance	3-12	9.45	2.28
Meaning-Based	5-20	11.02	3.48
QOL Measures			
Core QOL			
Emotional	0-100	32.50	18.55
Mind/Body	0-100	44.60	19.75
Relational	0-100	65.30	20.38
Social	0-100	47.20	19.47
Core Total	0-100	47.20	14.81

Table 3

Percent of Respondents Reporting "Used Quite a Bit" or "Used a Great Deal" on the COMPI Coping Strategy Scale Items and Average Percent of Such Responses on the Four Coping Strategy Domains (N = 230)

COMPI Coping Strategy Scale	%
Active-Avoidance Coping Average	53
1. Avoid being with pregnant women or children	47
2. Leave when people are talking about pregnancies and children	46
3. Try to keep my feelings to myself	60
4. Turn to work or substitute activity to take my mind off things	61
Active-Confronting Coping Average	32
1. Let my feelings out somehow	41
2. Accept sympathy and understanding from someone	39
3. Ask other childless people for advice	30
4. Ask a relative or friend for advice	22
5. Read or watch television about childlessness	23
6. Talk to someone about my emotions as childless	30
7. Talk to someone about how tests and treatments affect me emotionally	38
Passive-Avoidance Coping Average	74
1. Hope a miracle will happen	77
2. Feel that the only thing I can do is to wait	69
3. Have fantasies and wishes	78
Meaning-Based Coping Average	36
1. Have grown as a person in a good way	47
2. Think about the infertility in a positive light	11
3. Find my marriage/partnership even more valuable now	55
4. Find other life goals	33
5. Believe there is a meaning in our difficulties in having children	36

Table 4

Coping Strategy "Used Quite a Bit" or "Used a Great Deal" Between Low and High Stress Groups

Coping Strategy	Low Stress (n = 64) M	SD	High Stress (n = 166) M	SD	t	η^2
Active-Avoidance Coping Average	34	30.0	60	30.5	5.81***	.129
1. Avoid being with pregnant women or children	17	38.0	58	49.5	5.92***	.133
2. Leave when people are talking about pregnancies and children	25	43.6	54	50.0	4.02***	.061
3. Try to keep my feelings to myself	48	50.4	64	48.2	2.15*	.020
4. Turn to work or substitute activity to take my mind off things	47	50.3	66	47.4	2.73**	.032
Active-Confronting Coping Average	28	25.5	34	29.0	1.39	.001
1. Let my feelings out somehow	31	46.7	45	49.9	1.93	.016
2. Accept sympathy and understanding from someone	42	49.8	38	48.7	0.59	.002
3. Ask other childless people for advice	28	45.3	30	46.0	0.30	<.001
4. Ask a relative or friend for advice	23	42.7	22	41.3	0.28	<.001
5. Read or watch television about childlessness	22	41.7	24	42.9	0.35	.001
6. Talk to someone about my emotions as childless	19	39.3	35	47.8	2.41*	.025
7. Talk to someone about how tests and treatments affect me emotionally	30	46.0	42	49.4	1.66	.012
Passive-Avoidance Coping Average	74	32.2	74	31.8	0.00	<.001
1. Hope a miracle will happen	77	42.7	77	42.5	0.00	<.001
2. Feel that the only thing I can do is to wait	69	46.7	69	46.5	0.00	<.001
3. Have fantasies and wishes	77	42.7	78	41.3	0.28	<.001
Meaning-Based Coping Average	44	31.6	32	28.0	2.65	.030
1. Have grown as a person in a good way	64	48.4	41	49.3	3.20**	.043
2. Think about the infertility in a positive way	20	40.6	7	26.0	2.90**	.035
3. Find my marriage/partnership even more valuable now	59	49.5	54	50.0	0.78	.003
4. Find other life goals	36	48.4	33	47.0	0.49	.001
5. Believe there is a meaning in our difficulties in having children	39	49.2	28	49.9	1.67	.012

* $p < .05$. ** $p < .01$. ***$p < .001$.

Table 5

Core Fertility Quality of Life in Total Group and Low and High Stress Groups

	Total (n = 222)		Low Stress (n = 61)		High Stress (n = 161)			
Core QOL	M	SD	M	SD	M	SD	t	η^2
Core QOL								
Emotional	32.3	18.56	47.6	19.21	26.6	14.66	8.74***	.258
Mind/Body	44.4	19.63	59.6	18.28	38.6	16.89	8.08***	.229
Relational	65.1	20.39	75.1	16.04	61.3	20.63	4.70***	.091
Social	47.1	19.37	60.7	17.75	42.0	17.44	7.08***	.186
Total Core	47.2	14.81	60.7	13.04	42.1	11.97	10.09***	.316

*** $p < .001$.

Table 6

Correlations of COMPI Fertility Problem Stress Scale Scores with Coping Strategies Scales Scores, Fertility Quality of Life Subscales and Total Scale Scores

Measure	1	2	3	4	5	6	7	8	9	10	11	12
1. Personal Stress	__											
2. Marital Stress	.38	__										
3. Social Stress	.39	.31	__									
4. Active-Avoidance Coping	.39	.16	.34	__								
5. Active-Confronting Coping	.11	.09	.06	-.09	__							
6. Passive-Avoidance Coping	.15	.06	.00	.15	.15	__						
7. Meaning-Based Coping	-.15	-.30	-.10	-.08	.29	.23	__					
8. QOL Core Emotional	-.64	-.39	-.43	-.50	-.02	-.21	.25	__				
9. QOL Core Mind/Body	-.57	-.27	-.41	-.47	-.04	-.11	.12	.71	__			
10. QOL Core Relational	-.21	-.62	-.11	-.06	.07	.08	.44	.22	.18	__		
11. QOL Core Social	-.41	-.26	-.54	-.58	.10	-.13	.21	.69	.64	.19	__	
12. QOL Core Total	-.59	-.50	-.48	-.53	.05	-.11	.35	.85	.83	.54	.83	__

Note. All coefficients ≥ .15 are significant at $p < .05$.

Table 7

Percent of Respondents Reporting "Strongly Agree" on the COMPI Fertility Problem Stress Scale Items and Average Percent of Such Responses on the Three Stress Domains in Total Group and Low and High Stress Groups

	Total (N = 230)	Low Stress (n = 64)		High Stress (n = 166)			
COMPI-FSS Stress Scale	M	M	SD	M	SD	t	η^2
Personal Domain Stress	53	17	22.2	67	27.8	12.92***	.423
1. It is very stressful for me to deal with this infertility problem.	68	27	44.5	84	36.5	10.11***	.309
2. Stress related to your physical health	25	2	12.5	34	47.4	5.35***	.112
3. Stress related to your mental health	66	22	41.7	83	38.1	10.54***	.338
Marital Domain Stress	22	4	10.5	30	27.5	7.38***	.193
1. The childlessness has caused a crisis in our relationship.	3	0	0.0	5	21.5	1.79	.014
2. Stress related to your marriage/ partnership	18	3	17.5	23	42.5	3.71***	.057
3. Stress related to your sex life	46	8	27.0	61	49.0	8.19***	.227
Social Domain Stress	13	2	10.1	17	25.6	4.66***	.087
1. Stress related to family relationships	9	3	17.5	11	31.2	1.87	.015
2. Stress related to family-in-law relationships	10	0	0.0	13	34.0	3.11**	.041
3. Stress related to friends relationships	21	3	17.5	28	45.2	4.33***	.076

**p < .01. ***p< .001.

Table 8

COMPI Fertility Problem Stress Scales, Coping Scales, and Fertility Quality of Life Between Non-IVF and IVF Groups

	Non-IVF (n = 114)		IVF (n = 102)			
COMPI-FPSS	M	SD	M	SD	t	η^2
Personal Domain	11.3	1.5	10.9	1.8	1.56	.011
Martial Domain	8.7	2.5	8.3	2.5	1.30	.008
Social Domain	7.0	2.3	7.0	2.2	.14	.000
COMPI-CSS						
Active-Avoidance Coping	11.0	2.8	10.1	2.9	2.30*	.024
Active-Confronting Coping	14.7	4.6	15.1	4.1	.58	.002
Passive-Avoidance Coping	9.5	2.3	9.3	2.2	.75	.003
Meaning-Based Coping	10.5	3.6	11.5	3.2	2.12*	.021
Fertility Quality of life Scale						
Emotional	30.5	18.2	35.0	19.3	1.74	.014
Mind/Body	44.7	18.0	44.2	21.4	.17	.000
Relational	64.4	20.6	66.3	20.2	.67	.002
Social	44.2	19.0	50.5	19.6	2.40*	.026
Core Total	45.7	14.1	49.0	15.5	1.61	.012

*$p < .05$

Table 9

Relationships Among Infertility-Related Stress Groups, Pregnancy Loss, and Treatment Type (N = 205)

	Pregnancy Loss						
	Yes		No				
Stress/Treatment Type	n	%	n	%	χ^2	p	Phi
Total Group							
Low Stress	22	21	39	39			
High Stress	82	79	62	61	7.47	.006	.191
Non-IVF							
Low Stress	9	15	16	34			
High Stress	50	85	31	66	5.12	.024	.220
IVF							
Low Stress	13	29	23	43			
High Stress	32	71	31	57	1.99	.158	.142

Table 10

Relationships of COMPI Fertility Problem Stress Scale, Coping Strategies Scale, and Fertility Quality of Life Among Pregnancy Loss and Treatment Type (N = 205)

	Pregnancy Loss						
	Yes		No				
Scales	M	SD	M	SD	t	p	η^2
COMPI-FPSS							
Personal Domain	11.3	1.48	10.8	1.83	2.24	.026*	.023
Marital Domain	8.8	2.42	8.2	2.53	1.80	.073	.015
Social Domain	7.4	2.25	6.6	2.44	2.40	.017*	.026
COMPI-CSS							
Active-Avoidance	11.0	2.72	10.2	3.00	2.21	.028*	.022
Active-Confronting	14.8	4.53	14.9	4.13	0.14	.892	<.001
Passive-Avoidance	9.4	2.34	9.5	2.20	0.37	.713	.001
Meaning-Based	10.5	3.22	11.5	3.68	2.03	.044*	.019
Fertility Quality of Life							
Emotional	29.5	15.64	36.3	20.85	2.73	.007**	.033
Mind/Body	42.6	18.89	48.1	20.69	2.02	.045*	.019
Relational	63.2	20.79	68.0	19.77	1.75	.082	.014
Social	45.7	18.40	49.8	20.20	1.55	.123	.011
Core Total	45.0	13.45	50.5	15.92	2.68	.008**	.034

* $p < .05$ ** $p < .01$

Table 11

IVF and Non-IVF Group Differences for Infertility-Related Stress and Infertility-Related Coping Strategies Between Groups that Did or Did Not Have a Pregnancy Loss

	IVF							Non-IVF						
	No Pregnancy Loss		Pregnancy Loss					No Pregnancy Loss		Pregnancy Loss				
	M	SD	M	SD	t	p	η^2	M	SD	M	SD	t	p	η^2
Infertility Stress														
Personal	10.7	1.97	11.1	1.64	1.05	.298	.011	10.9	1.77	11.5	1.36	2.01	.047*	.037
Marital	7.9	2.60	8.5	2.33	1.28	.202	.017	8.2	2.48	9.0	2.54	1.57	.120	.023
Social	6.6	2.40	7.4	2.06	1.55	.123	.024	6.0	2.16	7.7	2.25	3.79	<.001***	.121
Coping														
Active-Avoidance	9.7	2.93	10.5	2.84	1.37	.174	.019	10.6	3.14	11.5	2.60	1.56	.121	.023
Active-Confronting	15.0	3.90	15.3	4.25	0.36	.722	.001	14.7	4.38	14.6	4.82	0.16	.875	<.001
Passive-Avoidance	9.3	2.26	9.2	2.22	0.43	.666	.002	9.8	2.02	9.4	2.44	0.81	.420	.006
Meaning-Based	11.9	3.42	11.0	2.88	1.44	.153	.021	10.8	3.86	9.9	3.20	1.34	.184	.017
Fertility Quality of Life														
Emotional	39	21.6	32	15.0	1.85	.034*	.034	35	20.6	27	16.0	2.29	.024*	.048
Mind/Body	49	22.9	40	18.7	2.11	.038*	.045	48	19.1	43	17.5	1.32	.190	.017
Relational	70	19.4	62	21.2	1.89	.062	.035	66	20.0	63	21.1	0.68	.500	.004
Social	53	20.4	49	17.0	1.03	.304	.011	47	19.7	41	18.2	1.61	.111	.025
Core Total	53	16.1	46	13.4	2.38	.019*	.057	48	15.6	44	13.2	1.71	.091	.028

* $p < .05$ ** $p < .01$ *** $p < .001$

Table 12

Correlations of Hair Cortisol Concentrations, COMPI Fertility Problem Stress Scale Scores with Coping Strategies Scales Scores, Fertility Quality of Life Subscales and Total Scale Scores in Subsample (n=36)

Measure	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Hair Cortisol	__												
2. Personal Stress	-.21	__											
3. Marital Stress	-.54***	.28	__										
4. Social Stress	-.19	.52***	.09	__									
5. Active-Avoidance Coping	-.06	-.01	-.01	-.03	__								
6. Active-Confronting Coping	.10	.09	-.07	-.01	-.08	__							
7. Passive-Avoidance Coping	-.02	.03	-.06	-.06	.11	.08	__						
8. Meaning-Based Coping	.29	-.10	-.38*	.09	.06	-.04	.32	__					
9. QOL Core Emotional	.31	-.11	-.28	-.15	-.37*	-.32	-.01	.30	__				
10. QOL Core Mind/Body	.14	.02	-.01	.02	-.13	-.12	-.07	-.20	.52***	__			
11. QOL Core Relational	.45**	-.20	-.69***	.01	-.00	-.14	.03	.43**	.23	-.05	__		
12. QOL Core Social	.09	.13	-.09	-.08	-.48**	.02	.01	-.08	.57***	.35*	.10	__	
13. QOL Core Total	.39*	-.06	-.41**	-.07	-.36*	-.20	-.01	.17	.83***	.66***	.51**	.76***	__

***p < .001 **p < .01 *p<.05

Table 13

Means for Hair Cortisol Concentration (log), COMPI Fertility Problem Stress Scales, Coping Strategy Scales, Fertility Quality of Life Subscales and Core Total QOL for Subsample (N = 36)

	Theoretical Score	M	SD
Hair Cortisol Concentrations (pg/mg)	4-15	1.01	.90
COMPI Scales			
Infertility Stress Scales			
Personal domain total scale score	3-13	11.5	1.40
Marital domain total scale score	3-13	8.61	2.42
Social domain total scale score	3-12	6.47	2.02
Coping Strategy Scales			
Active-Avoidance	4-16	11.61	2.27
Active-Confronting	7-28	14.61	3.74
Passive-Avoidance	3-12	9.69	2.29
Meaning-Based	5-20	10.39	3.19
QOL Measures			
Core QOL			
Emotional	0-100	27.55	13.52
Mind/Body	0-100	43.52	14.21
Relational	0-100	64.12	16.83
Social	0-100	44.68	15.89
Core Total	0-100	44.97	10.29

REFERENCES

Aarts, J. W. M., Van Empel, I. W. H., Boivin, J., Nelen, W. L., Kremer, J. A. M., & Verhaak, C. M. (2011). Relationship between quality of life and distress in infertility: A validation study of the Dutch FertiQoL. *Human Reproduction, 26*(5), 1112-1118. https://doi.org/10.1093/humrep/der051

Abbey, A., Andrews, F. M., & Halman, L. J. (1991). Gender's role in responses to infertility. *Psychology of Women Quarterly*, *15*(2), 295-316. https://doi.org/10.1111/j.1471-6402.1991.tb00798.x

Abell, J. G., Stalder, T., Ferrie, J. E., Shipley, M. J., Kirschbaum, C., Kivimäki, M., & Kumari, M. (2016). Assessing cortisol from hair samples in a large observational cohort: The Whitehall II study. *Psychoneuroendocrinology, 73*, 148-156. https://doi.org/10.1016/j.psyneuen.2016.07.214

Aflakseir, A., & Zarei, M. (2013). Association between coping strategies and infertility stress among a group of women with fertility problem in Shiraz, Iran. *Journal of Reproduction & Infertility, 14*(4), 202-206. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3911816/

Ahern, N. R. (2005). Using the internet to conduct research. *Nurse Researcher, 13*(2), 55-70. doi:10.7748/nr.13.2.55.s7

Akard, T. F., Wray, S., & Gilmer, M. J. (2015). Facebook advertisements recruit parents of children with cancer for an online survey of web-based research preferences. *Cancer Nursing*, *38*(2), 155-161. doi:10.1097/NCC.0000000000000146

Alhabash, S., & Ma, M. (2017). A tale of four platforms: Motivations and uses of Facebook, Twitter, Instagram, and Snapchat among college students? *Social Media + Society*, *Jan-March*, 1-13, https://doi.org/10.1177/2056305117691544

Al Qadire, M. (2019). Undergraduate student nurses' knowledge of evidence-based practice: A short online survey. *Nurse Education Today, 72,* 1-5. doi:10.1016/j.nedt.2018.10.004

American College of Obstetricians and Gynecologists. (2019). FAQ. Treating infertility. Retrieved on May 21, 2019 from https://www.acog.org/Patients/FAQs/Treating-Infertility?IsMobileSet=false#what

American Society of Reproductive Medicine. (2019). Infertility. Retrieved on May 21, 2019 from https://www.asrm.org/topics/topics-index/infertility/

Anand, G., & Beuschlein, F. (2018). Management of endocrine disease: Fertility, pregnancy and lactation in women with adrenal insufficiency. *European Journal of Endocrinology, 178*(2), R45-R53. https://doi.org/10.1530/EJE-17-0975

Atarhim, M. A., Lee, S., & Copnell, B. (2019). An exploratory study of spirituality and spiritual care among Malaysian nurses. *Journal of Religion & Health, 58*(1), 180-194. doi:10.1007/s10943-018-0624-0

Balk, J., Catov, J., Horn, B., Gecsi, K., & Wakim, A. (2010). The relationship between perceived stress, acupuncture, and pregnancy rates among IVF patients: A pilot study. *Complementary Therapies in Clinical Practice, 16*(3), 154-157. https://doi.org/10.1016/j.ctcp.2009.11.004

Banerjee, U., Bhattacharya, N., & Sanyal, N. (2014). Stress, coping and emotional processing in chronic pain: A comparative analysis. *Somatic Inkblot Society Journal of Projective Psychology & Mental Health, 21*(2), 104-112.

Barzilai-Pesach, V., Sheiner, E. K., Sheiner, E., Potashnik, G., & Shoham-Vardi, I. (2006). The effect of women's occupational psychologic stress on outcome of fertility treatments. *Journal of Occupational and Environmental Medicine, 48*(1), 56-62. doi:10.1097/01.jom.0000183099.47127.e9

Benasutti, R. D. (2003). Infertility: Experiences and meanings. *Journal of Couple & Relationship Therapy, 2*(4), 51-71. https://doi.org/10.1300/J398v02n04_04

Benham-Hutchins, M., Staggers, N., Mackert, M., Johnson, A. H., & deBronkart, D. (2017). "I want to know everything": A qualitative study of perspectives from patients with chronic diseases on sharing health information during hospitalization. *BMC Health Services Research, 17*, 529. doi:10.1186/s12913-017-2487-6

Benyamini, Y., Gefen-Bardarian, Y., Gozlan, M., Tabiv, G., Shiloh, S., & Kokia, E. (2008). Coping specificity: The case of women coping with infertility treatments. *Psychology and Health*, *23*(2), 221-241. https://doi.org/10.1080/14768320601154706

Berry, K. M., & Rutledge, C. M. (2016). Factors that influence women to disclose sexual assault history to health care providers. *Journal of Obstetric, Gynecologic, & Neonatal Nursing: Clinical Scholarship for the Care of Women, Childbearing Families, & Newborns, 45*(4), 553-564. doi:10.1016/j.jogn.2016.04.002

Bhat, A., & Byatt, N. (2016). Infertility and perinatal loss: When the bough breaks. *Current Psychiatry Reports*, *18*(3), 31. https://doi.org/10.1007/s11920-016-0663-8

Biggs, A., Brough, P., & Drummond, S. (2017). Lazarus and Folkman's psychological stress and coping theory. In C. Cooper & J. Quick (Eds.), The handbook of stress and health (349-364). Wiley Blackwell.

Binz, T. M., Rietschel, L., Streit, F., Hofmann, M., Gehrke, J., Herdener, M., ... & Baumgartner, M. R. (2018). Endogenous cortisol in keratinized matrices: Systematic determination of baseline cortisol levels in hair and the influence of sex, age and hair color. *Forensic science international*, *284*, 33-38. https://doi.org/10.1016/j.forsciint.2017.12.032

Boivin J, & Lancastle D. (2010). Medical waiting periods: Imminence, emotions and coping. *Women's Health, 6*(*1*), 59-69. doi:10.2217/whe.09.79.

Boivin, J., Sanders, K., & Schmidt, L. (2006). Age and social position moderate the effect of stress on fertility. *Evolution and Human Behavior*, *27*(5), 345-356. https://doi.org/10.1016/j.evolhumbehav.2006.03.004

Boivin, J., & Schmidt, L. (2005). Infertility-related stress in men and women predicts treatment outcome 1 year later. *Fertility & Sterility. 83*(6). 1745-1752. https://doi.org/10.1016/j.fertnstert.2004.12.039

Boivin, J., Takefman, J., & Braverman, A. (2011). The Fertility Quality of Life (FertiQoL) tool: Development and general psychometric properties. *Human Reproduction, 26*(8), 2084-2091. https://doi.org/10.1093/humrep/der171

Books, C., Coody, L. C., Kauffman, R., & Abraham, S. (2017). Night shift work and its health effects on nurses. *The Health Care Manager, 36*(4), 347-353. doi:10.1097/HCM.0000000000000177

Boulet, S. L., Smith, R. A., Crawford, S., Kissin, D. M., & Warner, L. (2017). Health-related quality of life for women ever experiencing infertility or difficulty staying pregnant. *Maternal and Child Health Journal, 21*(10), 1918-1926. https://doi.org/10.1007/s10995-017-2307-y

Boyd, D. M, & Ellison, N. B. (2007). Social network sites: Definition, history, and scholarship. *Journal of Computer-Mediated Communication, 13*(1), 210-230. doi:10.1111/j.1083-6101.2007.00393.x

Bunting, L., & Boivin, J. (2007). Decision-making about seeking medical advice in an internet sample of women trying to get pregnant. *Human Reproduction*, *22*(6), 1662-1668. https://doi.org/10.1093/humrep/dem057

Carter-Harris, L., Ellis, R. B., Warrick, A., & Rawl, S. (2016). Beyond traditional newspaper advertisement: Leveraging Facebook-targeted advertisement to recruit long-term smokers for research. *Journal of Medical Internet Research, 18*(6), 1-12. doi:10.2196/jmir.5502

Carver, C. S., Scheier, M. F., & Weintraub, J. K. (1989). Assessing coping strategies: A theoretically based approach. *Journal of Personality and Social Psychology*, *56*(2), 267-283. https://doi.org/10.1037/0022-3514.56.2.267

Casu, G., & Gremgini, P. (2016). Screening for infertility-related stress at the time of initial infertility consultation: Psychometric properties of a brief measure. *Journal of Advanced Nursing 72*(3), 693–706. doi: 10.1111/jan.12830

Casu, G., Zaia, V., Fernandes Martins, M. d. C., Parente Barbosa, C., & Gremigni, P. (2019). A dyadic mediation study on social support, coping, and stress among couples starting fertility treatment. *Journal of Family Psychology*. *33*(3). 315-326. https://doi.org/10.1037/fam0000502.supp (Supplemental)

Center for Disease Control and Prevention. (2018). Infertility. Reproductive Health. Retrieved from http://www.cdc.gov/reproductivehealth/infertility/

Center for Disease Control and Prevention, American Society for Reproductive Medicine, & Society for Assistive Reproductive Technology. (2018a). 2016 Assisted reproductive technology national summary report. Atlanta (GA): US Dept of Health and Human Services. Retrieved from https://www.cdc.gov/art/pdf/2016-report/ART-2016-National-Summary-Report.pdf

Center for Disease Control and Prevention, American Society for Reproductive Medicine, & Society for Assistive Reproductive Technology. (2018b). 2016 Assisted reproductive technology fertility clinic success rates report. Atlanta (GA): US Dept of Health and Human Services. Retrieved from https://www.cdc.gov/art/reports/2016/fertility-clinic.html

Cesta, C. E., Johansson, A. L., Hreinsson, J., Rodriguez-Wallberg, K. A., Olofsson, J. I., Holte, J., ... & Nyman Iliadou, A. (2018). A prospective investigation of perceived stress, infertility-related stress, and cortisol levels in women undergoing in vitro fertilization: Influence on embryo quality and clinical pregnancy rate. *Acta Obstetricia et Gynecologica Scandinavica*, *97*(3), 258-268. https://doi.org/10.1111/aogs.13280

Chachamovich, J. R., Chachamovich, E., Ezer, H., Fleck, M. P., Knauth, D., & Passos, E. P. (2010). Investigating quality of life and health-related quality of life in infertility: A systematic review. *Journal of Psychosomatic Obstetrics & Gynecology*, *31*(2), 101-110. https://doi.org/10.3109/0167482X.2010.481337

Chambers, G. M., Zhu, R., & Illingworth, P. J. (2012). A reduction in public funding for fertility treatment-an econometric analysis of access to treatment and savings to government. *BioMed Central Health Services Research*, *12*(1), 142. https://doi.org/10.1186/1472-6963-12-142

Cheng, C. Y., Stevenson, E. L., Yang, C. T., & Liou, S. R. (2018). Stress and quality of life for Taiwanese women who underwent infertility treatment. *Journal of Obstetric, Gynecologic & Neonatal Nursing. 47*(4), 498–508. https://doi.org/10.1016/j.jogn.2018.03.005

Cheung, C. S., Chan, C. H., & Ng, E. H. (2013). Stress and anxiety-depression levels following first-trimester miscarriage: A comparison between women who conceived naturally and women who conceived with assisted reproduction. *British Journal of Obstetrics and Gynaecology: An International Journal of Obstetrics & Gynaecology, 120*(9), 1090-1097. https://doi.org/10.1111/1471-0528.12251

Chiba, H., Mori, E., Morioka, Y., Kashiwakura, M., Nadaoka, T., Saito, H., & Hiroi, M. (1997). Stress of female infertility: Relation to length of treatment. *Gynecologic and Obstetric Investigation, 43*(3), 171-177. https://doi.org/10.1159/000291848

Ciampaglia, W., & Cognigni, G. E. (2015). Clinical use of progesterone in infertility and assisted reproduction. *Acta Obstetricia et Gynecologica Scandinavica*, *94*(S161), 17-27. https://doi.org/10.1111/aogs.12770

Close, S., Smaldone, A., Fennoy, I., Reame, N., & Grey, M. (2013). Using information technology and social networking for recruitment of research participants: Experience from an exploratory study of pediatric Klinefelter syndrome. *Journal of Medical Internet Research, 15*(3), 171-181. doi:10.2196/jmir.2286

Coëffin-Driol, C., & Giami, A. (2004). The impact of infertility and its treatment on sexual life and marital relationships: Review of the literature. *Gynécologie, Obstétrique & Fertilité*, *32*(7-8), 624-637. doi:10.1016/j.gyobfe.2004.06.004

Cohain, J. S., Buxbaum, R. E., & Mankuta, D. (2017). Spontaneous first trimester miscarriage rates per woman among parous women with 1 or more pregnancies of 24 weeks or more. *BioMed Central Pregnancy and Childbirth, 17*(1), 437. https://doi.org/10.1186/s12884-017-1620-1

Cousineau, T.M. & Domar, A.D. (2007). Psychological impact of infertility. *Best Practice & Research: Clinical Obstetrics & Gynaecology, 21*(2), 293-308. https://doi.org/10.1016/j.bpobgyn.2006.12.003

Das, R., Machalek, D. A., Molesworth, E. G., & Garland, S. M. (2017). Using Facebook to recruit young Australian men into a cross-sectional human papillomavirus study. *Journal of Medical Internet Research, 19*(11). https://doi.org/10.2196/jmir.8739

de Lacey, S., Smith, C. A., & Paterson, C. (2009). Building resilience: A preliminary exploration of women's perceptions of the use of acupuncture as an adjunct to in vitro fertilization. *BioMed Central Complementary and Alternative Medicine, 9*(1), 50.

Demyttenaere, K., Bonte, L., Gheldof, M., Vervaeke, M., Meuleman, C., Vanderschuerem, D., & D'Hooghe, T. (1998). Coping style and depression level influence outcome in in vitro fertilization. *Fertility and Sterility, 69*(6), 1026-1033.

Demyttenaere K., Nijs P., Evers-Kiebooms G., & Koninckx, P. R. (1991). Coping, ineffectiveness of coping and the psychoendocrinological stress responses during in-vitro fertilization. *Journal of Psychosomatic Research, 35*(2/3), 231-243.

Demyttenaere, K., Nijs, P., Evers-Kiebooms, G., & Koninckx, P. R. (1992). Coping and the ineffectiveness of coping influence the outcome of in vitro fertilization through stress responses. *Psychoneuroendocrinology, 17*(6), 655-665.

Domar, A.D., Clapp, D., Slawsby, E., Kessel, B., Orav, J., & Freizinger, M. (2000). The impact of group psychological interventions on distress in infertile women. *Health Psychology, 19*(6), 568-575. doi:10.1037/0278-6133.19.6.568

Domar, A. D., Seibel, M. M., & Benson, H. (1990). The mind/body program for infertility: A new behavioral treatment approach for women with infertility. *Fertility and sterility, 53*(2), 246-249.

Donkor, E. S., & Sandall, J. (2007). The impact of perceived stigma and mediating social factors on infertility-related stress among women seeking infertility treatment in Southern Ghana. *Social Science & Medicine, 65*(8), 1683-1694. doi:10.1016/j.socscimed.2007.06.003

Drake, S. A., Zhang, N., Applewhite, C., Fowler, K., & Holcomb, J. B. (2017). A social media program to increase adolescent seat belt use. *Public Health Nursing, 34*(5), 500-504. doi:10.1111/phn.12342

du Plessis, E. (2016). Caring presence in practice: Facilitating an appreciative discourse in nursing. *International Nursing Review, 63*(3), 377-380. doi:10.1111/inr.12303

ECU. (2016). University & Medical Center Institutional Review Board. Recruiting for human research. Retrieved from https://author.ecu.edu/cs-acad/ORIC/irb/upload/SOP-Recruiting-for-Human-Research.pdf

ECU ITCS. (2018). REDCap online research surveys. Retrieved April 21, 2018 from http://www.ecu.edu/itcs/help/redcap

El Kissi, Y., Romdhane, A., Hidar, S., Bannour, S., Idrissi, K., Khairi, H., & Ali, B. (2013). General psychopathology, anxiety, depression and self-esteem in couples undergoing infertility treatment: A comparative study between men and women. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, *167*(2), 185–189. https://doi.org/10.1016/j.ejogrb.2012.12.014

El-Messidi, A., Al-Fozan, H., Tan, S. L., Farag, R., & Tulandi, R. (2004). Effects of repeated treatment failure on the quality of life of couples with infertility. *Journal of Obstetrics and Gynaecology Canada*, *26*(4), 333-337. https://doi.org/10.1016/S1701-2163(16)30361-9

El-Toukhy, T., Sunkara, S. K., Khairy, M., Dyer, R., Khalaf, Y., & Coomarasamy, A. (2008). A systematic review and meta-analysis of acupuncture in in vitro fertilisation. *British Journal of Obstetrics and Gynaecology: An International Journal of Obstetrics & Gynaecology*, *115*(10), 1203-1213. https://doi.org/10.1111/j.1471-0528.2008.01838.x

Eysenbach, G., & Wyatt, J. (2002). Using the internet for surveys and health research. *Journal of Medical Internet Research*, *4*(2), e13. http://doi.org/10.2196/jmir.4.2.e13

Facebook. (2019). Facebook. About. https://www.facebook.com/pg/FacebookIndia/about/

Flaskerud, J. H. & Winslow, B. J. (1998). Conceptualizing vulnerable populations health-related research. *Nursing Research*, *47*(2), 69-78. doi:10.1097/00006199-199803000-00005

Freeman, M. P., Savella, G. M., Sosinsky, A. Z., Marfurt, S. P., Murphy, S. K., Cohen, L. S., & Lee, H. (2018). Predictors of depressive relapse in women undergoing infertility treatment. *Journal of Women's Health, 27*(11), 1408–1414. https://doi.org/10.1089/jwh.2017.6878

Freda, M.C. (2003). The lived experience of miscarriage after infertility. *The American Journal of Maternal/Child Nursing, 28(*1), 16-23. doi:10.1097/00005721-200301000-00005

Folkman, S. (1997). Positive psychological states and coping with severe stress. *Social Science & Medicine, 45*(8), 1207-1221. https://doi.org/10.1016/S0277-9536(97)00040-3

Folkman, S. (2010). Stress, health, and coping: Synthesis, commentary, and future directions. In S. Folkman (Ed.), *The Oxford handbook of stress, health, and coping* (453-462). Oxford University Press. doi:10.1093/oxfordhb/9780195375343.013.0022

Folkman, S., & Lazarus, R. (1988). Coping as a mediator of emotion. *Journal of Personality and Social Psychology, 54*(3), 466-475. https://doi.org/10.1037/0022-3514.54.3.466

Folkman, S., & Moskowitz, J. T. (2004). Coping: Pitfalls and promise. *Annual Review of Psychology, 55*, 745-774. https://doi.org/10.1146/annurev.psych.55.090902.141456

Fontaine, K. (2015). *Complementary & alternative therapies for nursing practice*. (4th ed). Boston, Massachusetts: Pearson.

Fowler, C., Green, J., Elliott, D., Petty, J., & Whiting, L. (2019). The forgotten mothers of extremely preterm babies: A qualitative study. *Journal of Clinical Nursing, 28,* 2124-2134. doi:10.1111/jocn.14820

Gage-Bouchard, E., LaValley, S., Mollica, M., & Beaupin, L. K. (2017). Cancer communication on social media: Examining how cancer caregivers use Facebook for cancer-related communication. *Cancer Nursing, 40*(4), 332-338. doi:10.1097/NCC.0000000000000418

Galhardo, A., Cunha, M., & Pinto-Gouveia, J. (2013). Mindfulness-based program for infertility: Efficacy study. *Fertility and Sterility*, *100*(4), 1059-1067. http://dx.doi.org/10.1016/j.fertnstert.2013.05.036

Garland, E., Gaylord, S., & Park, J. (2009). The role of mindfulness in positive reappraisal. *Explore*, *5*(1), 37-44. https://doi.org/10.1016/j.explore.2008.10.001

Gibson, D. M., & Myers, J. E. (2002). The effect of social coping resources and growth-fostering relationships on infertility stress in women. *Journal of Mental Health Counseling*, *24*(1), 68-80. Retrieved from https://search.proquest.com/docview/198794403?accountid=10639

Gribble, K. D. (2013). Peer-to-peer milk donors' and recipients' experiences and perceptions of donor milk banks. *Journal of Obstetric, Gynecologic, & Neonatal Nursing: Clinical Scholarship for the Care of Women, Childbearing Families, & Newborns, 42*(4), 451-461. doi:10.1111/1552-6909.12220

Gribble, K. D. (2014). Perception and management of risk in internet-based peer-to-peer milk-sharing. *Early Child Development and Care*, *184*(1), 84-98. doi:10.1080/03004430.2013.772994

Gourounti, K., Anagnostopoulos, F., Potamianos, G., Lykeridou, K., Schmidt, L., & Vaslamatzis, G. (2012). Perception of control, coping and psychological stress of infertile women undergoing IVF. *Reproductive BioMedicine Online*, *24*(6), 670-679. https://doi.org/10.1016/j.rbmo.2012.03.002

Gourounti, K., Anagnostopoulos, F., & Vaslamatzis, G. (2011). The relation of psychological stress to pregnancy outcome among women undergoing in-vitro fertilization and intracytoplasmic sperm injection. *Women & Health, 51*(4), 321-339. doi:10.1080/03630242.2011.574791

Greil, A. L. (1997). Infertility and psychological distress: A critical review of the literature. *Social Science & Medicine*, *45*(11), 1679-1704. https://doi.org/10.1016/S0277-9536(97)00102-0

Greil, A. L., McQuillan, J., Lowry, M., & Shreffler, K. M. (2011). Infertility treatment and fertility-specific distress: A longitudinal analysis of a population-based sample of U.S. women. *Social Science & Medicine, 73*(1), 87-94. doi:10.1016/j.socscimed.2011.04.023

Guilliams, T. G., & Edwards, L. (2010). Chronic stress and the HPA axis. *The Standard, 9*(2), 1-12. Retrieved from http://www.pointinstitute.org/wp-content/uploads/2012/10/standard_v_9.2_hpa_axis.pdf

Haines-Saah, R. J., Kelly, M. T., Oliffe, J. L., & Bottorff, J. L. (2015). Picture me smokefree: A qualitative study using social media and digital photography to engage young adults in tobacco reduction and cessation. *Journal of Medical Internet Research, 17*(1). e27. https://doi.org/10.2196/jmir.4061

Hamilton, B., Martin, J., Ostermann, M., Driscoll, A., & Rossen, L. (2018). Vital statistics surveillance report. Vital statistics rapid release. Births: Provisional data for 2017. Retrieved from https://www.cdc.gov/nchs/data/vsrr/report004.pdf.

Hamilton, B., Martin, J., Ostermann, M., & Rossen, L. (2019). Vital statistics surveillance report. Vital statistics rapid release. Births: Provisional data for 2018. Retrieved from https://www.cdc.gov/nchs/data/vsrr/vsrr-007-508.pdf

Hammer, A., & Marting, M. (1988). Coping resources inventory manual. Palo Alto, CA: Consulting Psychologists.

Hammerli, K., Znoj, H., & Barth, J. (2009). The efficacy of psychological interventions for infertile patients: A meta-analysis examining mental health and pregnancy rate. *Human Reproduction Update, 15*(3), 279–295. http://doi.org/10.1093/humupd/dmp002

Hansell, P. L., Thorn, B. E., Prentice-Dunn, S., & Floyd, D. L. (1998). The relationship of primary appraisals of infertility and other gynecological stressors to coping. *Journal of Clinical Psychology in Medical Settings, 5*(2), 133-145. doi:10.1023/A:1026238530050

Hasanpoor-Azghdy, S. B., Simbar, M., & Vedadhir, A. (2014). The emotional-psychological consequences of infertility among infertile women seeking treatment: Results of a qualitative study. *Iranian Journal of Reproductive Medicine, 12*(2), 131-138. https://www.ncbi.nlm.nih.gov/pubmed/24799871

Heim, C., Ehlert, U., & Hellhammer, D. H. (2000). The potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders. *Psychoneuroendocrinology, 25*(1), 1-35. https://doi.org/10.1016/S0306-4530(99)00035-9

Helbing, E, Teems, M., & Moultrie, D. (2017). An investigation of job satisfaction among nurses in the emergency department. *Association of Black Nursing Faculty Journal, 28*(4), 103-108. Retrieved from https://search.proquest.com/docview/2039835878?accountid=10639

Herrmann, D., Scherg, H., Verres, R., von Hagens, C., Strowitzki, T., & Wischmann, T. (2011). Resilience in infertile couples acts as a protective factor against infertility-specific distress and impaired quality of life. *Journal of Assisted Reproduction and Genetics, 28*(11), 1111-1117. https://doi.org/10.1007/s10815-011-9637-2

Hetland, B., McAndrew, N., Perazzo, J., & Hickman, R. (2018). A qualitative study of factors that influence active family involvement with patient care in the ICU: Survey of critical care nurses. *Intensive and Critical Care Nursing, 44*, 67-75. doi:10.1016/j.iccn.2017.08.008

Hinkelmann, K., Muhtz, C., Dettenborn, L., Agorastos, A., Wingenfeld, K., Spitzer, C., ... & Otte, C. (2013). Association between childhood trauma and low hair cortisol in depressed patients and healthy control subjects. *Biological psychiatry*, *74*(9), e15-e17. https://doi.org/10.1016/j.biopsych.2013.04.021

Hodes, A., Lodish, M.B., Tirosh, A., Meyer, J., Belyavskaya, E., Lysssikatos, C.,…& Zilbermint, M. (2017). Hair cortisol in the evaluation of Cushing's syndrome. *Endocrine, 56*(1). 164-174. https://doi.org/10.1007/s12020-017-1231-7

Holmes, S. (2009). Methodological and ethical considerations in designing an internet study of quality of life: A discussion paper. *International Journal of Nursing Studies, 46*(3). 394-405. https://doi.org/10.1016/j.ijnurstu.2008.08.004

Hong, Q. N., Fàbregues, S., Bartlett, G., Boardman, F., Cargo, M., Dagenais, P., ... & Rousseau, M. C. (2018). The Mixed Methods Appraisal Tool (MMAT) version 2018 for information professionals and researchers. *Education for Information*, *34*(4), 285-291. doi: 10.3233/EFI-180221

Hubens, K., Arons, A. M., & Krol, M. (2018). Measurement and evaluation of quality of life and well-being in individuals having or having had fertility problems: A systematic review. *The European Journal of Contraception & Reproductive Health Care*, *23*(6), 441-450. https://doi.org/10.1080/13625187.2018.1539161

Hynes, G. J., Callan, V. J., Terry, D. J., & Gallois, C. (1992). The psychological well-being of infertile women after a failed IVF attempt: The effects of coping. *Psychology and Psychotherapy: Theory, Research and Practice*, *65*(3), 269-278. https://doi.org/10.1111/j.2044-8341.1992.tb01707.x

IBM Corp. (2016). IBM SPSS statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.

Instagram. (2019). Info center. Our story. Retrieved on March 13, 2019 from https://instagram-press.com/our-story/

Jacobs, M. B., Boynton-Jarrett, R. D., & Harville, E. W. (2015). Adverse childhood event experiences, fertility difficulties and menstrual cycle characteristics. *Journal of Psychosomatic Obstetrics & Gynecology*, *36*(2), 46-57. https://doi.org/10.3109/0167482X.2015.1026892

Jones, K., Baldwin, K. A., & Lewis, P. R. (2012). The potential influence of a social media intervention on risky sexual behavior and chlamydia incidence. *Journal of Community Health Nursing*, *29*(2), 106-120. doi:10.1080/07370016.2012.670579

Jones, R., Lacroix, L. J., & Nolte, K. (2015). "Is your man stepping out?" An online pilot study to evaluate acceptability of a guide-enhanced HIV prevention soap opera video series and feasibility of recruitment by Facebook advertising. *Journal of the Association of Nurses in AIDS Care. 24*(4). 368-386. https://doi.org/10.1016/j.jana.2015.01.004

Jones, R., Lacroix, L. J., & Porcher, E. (2017). Facebook advertising to recruit young, urban women into an HIV prevention clinical trial. *AIDS and Behavior, 21*(11), 3141-3153. doi:10.1007/s10461-017-1797-3

Kahyaoglu Sut, H., & Balkanli Kaplan, P. (2015). Quality of life in women with infertility via the FertiQoL and the Hospital Anxiety and Depression Scales. *Nursing & Health Sciences*, *17*(1), 84-89. https://doi.org/10.1111/nhs.12167

Kamp, K., Herbell, K., Magginis, W. H., Berry, D., & Given, B. (2019). Facebook recruitment and the protection of human subjects. *Western Journal of Nursing Research*. *41*(9). 1270-1281. https://doi.org/10.1177/0193945919828108

Karabulut, A., Özkan, S., & Oğuz, N. (2013). Predictors of fertility quality of life (FertiQoL) in infertile women: Analysis of confounding factors. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 170*(1), 193-197. https://doi.org/10.1016/j.ejogrb.2013.06.029

Karaca, A., & Unsal, G. (2015). Psychosocial problems and coping strategies among Turkish women with infertility. *Asian Nursing Research, 9*(3), 243-250. https://doi.org/10.1016/j.anr.2015.04.007

Katz, P., Showstack, J., Smith, J. F., Nachtigall, R. D., Millstein, S. G., Wing, H.,… Adler, N. (2011). Costs of infertility treatment: Results from an 18-month prospective cohort study. *Fertility and Sterility, 95*(3), 915-921. https://doi.org/10.1016/j.fertnstert.2010.11.026

Kessler, L. M., Craig, B. M., Plosker, S. M., Reed, D. R., & Quinn, G. P. (2013). Infertility evaluation and treatment among women in the United States. *Fertility and Sterility, 100*(4), 1025-1032. doi: 10.1016/j.fertnstert.2013.05.040

Khumsaen, N., & Stephenson, R. (2017). Beliefs and perception about HIV/AIDS, self-efficacy, and HIV sexual risk behaviors among young Thai men who have sex with men. *AIDS Education and Prevention, 29*(2), 175-190. doi:10.1521/aeap.2017.29.2.175

Kim, H. N., Wyatt, T. H., Li, X., & Gaylord, M. (2016). Use of social media by fathers of premature infants. *The Journal of Perinatal & Neonatal Nursing, 30*(4), 359-366. doi:10.1097/JPN.0000000000000214

Kim, J. H., Shin, H. S., & Yun, E. K. (2018). A dyadic approach to infertility stress, marital adjustment, and depression on quality of life in infertile couples. *Journal of Holistic Nursing, 36*(1), 6–14. https://doi.org/10.1177/0898010116675987

Kjaer, T. K., Jensen, A., Dalton, S. O., Johansen, C., Schmiedel, S., & Kjaer, S. K. (2011). Suicide in Danish women evaluated for fertility problems. *Human Reproduction, 26*(9), 2401-2407. https://doi.org/10.1093/humrep/der188

Ko, N., Hsieh, C., Wang, M., Lee, C., Chen, C., Chung, A., & Hsu, S. (2013). Effects of internet popular opinion leaders (iPOL) among internet-using men who have sex with men. *Journal of Medical Internet Research, 15*(2), 112-120. doi:10.2196/jmir.2264

Kramer, J., Rubin, A., Coster, W., Helmuth, E., Hermos, J., Rosenblood, D.,…& Lachowicz, M. (2014). Strategies to address participant misrepresentation for eligibility in web-based research. *International Journal of Methods in Psychiatric Research. 23*(1). 120-129. doi:10.1002/mpr.1415

Kyrou, I., & Tsigos, C. (2009). Stress hormones: Physiological stress and regulation of metabolism. *Current Opinion in Pharmacology, 9*(6), 787-793. doi:10.1016/j.coph.2009.08.007

Ladores, S., & Aroian, K. (2015). First-time mothers with a history of infertility: Their internalized pressures to breastfeed. *Journal of Human Lactation, 31*(3), 504-510. doi:10.1177/0890334415585511

Lansakara, N., Wickramasinghe, A. R., & Seneviratne, H. R. (2011). Feeling the blues of infertility in a south Asian context: Psychological well-being and associated factors among Sri Lankan women with primary infertility. *Women & Health, 51*(4), 383-399. doi:10.1080/03630242.2011.574790

Lawson, A. K., Klock, S. C., Pavone, M. E., Hirshfeld-Cytron, J., Smith, K. N., & Kazer, R. R. (2014). Prospective study of depression and anxiety in female fertility preservation and infertility patients. *Fertility and Sterility*, *102*(5), 1377-1384. https://doi.org/10.1016/j.fertnstert.2014.07.765

Laubmeier, K. K., Zakowski, S. G., & Bair, J. P. (2004). The role of spirituality in the psychological adjustment to cancer: A test of the transactional model of stress and coping. *International Journal of Behavioral Medicine*, *11*(1), 48-55. https://doi.org/10.1207/s15327558ijbm1101_6

Lazarus, R. S., & Folkman, S. (1984). *Stress, Appraisal, and Coping*. New York, New York: Springer Publishing Company.

Lee, S. H., Wang, S. C., Kuo, C. P., Kuo, P. C., Lee, M. S., & Lee, M. C. (2010). Grief responses and coping strategies among infertile women after failed in vitro fertilization treatment. *Scandinavian Journal of Caring Sciences*, *24*(3), 507-513. https://doi.org/10.1111/j.1471-6712.2009.00742.x

Li, Y., Zhang, X., Shi, M., Guo, S., & Wang, L. (2019). Resilience acts as a moderator in the relationship between infertility-related stress and fertility quality of life among women with infertility: A cross-sectional study. *Health and Quality of Life Outcomes*, *17*(1), 38. doi: 10.1186/s12955-019-1099-8

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P., ... & Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. *PLoS medicine*, *6*(7), e1000100. doi: 10.1371/journal.pmed.1000100

Lindsay, T. J., & Vitrikas, K. R. (2015). Evaluation and treatment of infertility. *American Family Physician*, *91*(5), 308-314. https://www.ncbi.nlm.nih.gov/pubmed/25822387

Livingston, G. (2018). A third of U.S. adults say they have used fertility treatments or know someone who has. Pew Research Center. Retrieved on March 27, 2019 from https://www.pewresearch.org/fact-tank/2018/07/17/a-third-of-u-s-adults-say-they-have-used-fertility-treatments-or-know-someone-who-has/

Lykeridou K, Gourounti K, Deltsidou A, Loutradis D, & Vaslamatzis G. (2009). The impact of infertility diagnosis on psychological status of women undergoing fertility treatment. *Journal of Reproductive & Infant Psychology*, *27*(3), 223–237. https://doi.org/10.1080/02646830802350864

Lykeridou, K., Gourounti, K., Sarantaki, A., Loutradis, D., Vaslamatzis, G., & Deltsidou, A. (2011). Occupational social class, coping responses and infertility-related stress of women undergoing infertility treatment. *Journal of Clinical Nursing*, *20*(13-14), 1971-1980. 10.1111/j.1365-2702.2011.03696.x

Lynch, C.D., Sundaram, R., Maisog, J.M., Sweeney, A.M., & Buck Louis, G.M. (2014). Preconception stress increases the risk of infertility: Results from a couple-based prospective cohort study—the LIFE study, *Human Reproduction*, *29*(5), 1067–1075, https://doi.org/10.1093/humrep/deu032

Madhavi, K., Alka, S., Ravindra, K., & Charles, P. (2013). Study of quality of life, coping, martial adjustment and psychopathology in women with infertility. *Indian Journal of Private Psychiatry*, *7*(1) 10-15.

Malik, S. H., & Coulson, N. S. (2010). Coping with infertility online: An examination of self-help mechanisms in an online infertility support group. *Patient Education and Counseling, 81*(2), 315-318. https://doi.org/10.1016/j.pec.2010.01.007

Marks, A., Wilson, V., & Crisp, J. (2014). The management of type 1 diabetes in Australian primary schools. *Issues in Comprehensive Pediatric Nursing, 37*(3), 168-182. doi:10.3109/01460862.2014.932860

Maroufizadeh, S., Ghaheri, A., Amini, P., & Samani, R. O. (2017). Psychometric properties of the fertility quality of life instrument in infertile Iranian women. *International Journal of Fertility & Sterility, 10*(4), 371-379. doi: 10.22074/ijfs.2016.4696

Martins, M. V., Peterson, B. D., Almeida, V. M., & Costa, M. E. (2012). Measuring perceived social support in Portuguese adults trying to conceive: Adaptation and psychometric evaluation of the Multidimensional Scale of Perceived Social Support. *Peritia*, *13*, 5-14.

Martins, M. V., Peterson, B. D., Costa, P., Costa, M. E., Lund, R., & Schmidt, L. (2013). Interactive effects of social support and disclosure on fertility-related stress. *Journal of Social and Personal Relationships*, *30*(4), 371-388. https://doi.org/10.1177/0265407512456672

Martins, M. V., Vassard, D., Hougaard, C. Ø., & Schmidt, L. (2018). The impact of ART on union dissolution: A register-based study in Denmark 1994–2010. *Human Reproduction, 33*(3), 434-440. https://doi.org/10.1093/humrep/dey002

Massey, A. J., Campbell, B., Raine-Fenning, N., Aujla, N., & Vedhara, K. (2014). The association of physiological cortisol and IVF treatment outcomes: A systematic review. *Reproductive Medicine and Biology, 13*(4), 161-176. doi: 10.1007/s12522-014-0179-z

Massey, A.J., Campbell, B.K., Raine-Fenning, N., Pincott-Allen, C., Perry, J., & Vedhara, K. (2016). Relationship between hair and salivary cortisol and pregnancy in women undergoing IVF. *Psychoneuroendocrinology, 74*, 397-405. doi:10.1016/j.psyneuen.2016.08.027

Matsubayashi, H., Hosaka, T., Izumi, S. I., Suzuki, T., Kondo, A., & Makino, T. (2004). Increased depression and anxiety in infertile Japanese women resulting from lack of husband's support and feelings of stress. *General Hospital Psychiatry*, *26*(5), 398-404. https://doi.org/10.1016/j.genhosppsych.2004.05.002

Matthews, T., & Hamilton, B. (2019). Total fertility rates by state and race and Hispanic origin: United States, 2017. *National Vital Statistics Reports. 68*(1). 1-11. https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_01-508.pdf

McEwen, B. S. (1998). Protective and damaging effects of stress mediators. *New England Journal of Medicine*, *338*(3), 171-179. doi:10.1056/NEJM199801153380307

McQueeney, D. A., Stanton, A. L., & Sigmon, S. (1997). Efficacy of emotion-focused and problem-focused group therapies for women with fertility problems. *Journal of Behavioral Medicine, 20*(4), 313-331. doi:10.1023/A:1025560912766

Meerwijk, E. L., & Weiss, S. J. (2018). Tolerance for psychological pain and capability for suicide: Contributions to suicidal ideation and behavior. *Psychiatry Research, 262*, 203-208. doi:10.1016/j.psychres.2018.02.005

Meyer, J., Novak, M., Hamel, A., Rosenberg, K. (2014). Extraction and analysis of cortisol from human and monkey hair. *Journal of Visualized Experiments, 83*, e50882, doi:10.3791/50882.

Michels, T. C., & Tiu, A. Y. (2007). Second trimester pregnancy loss. *American Family Physician, 76*(9). 1341-1346. https://www.ncbi.nlm.nih.gov/pubmed/18019878

Miles, L. M., Keitel, M., Jackson, M., Harris, A., & Licciardi, F. (2009). Predictors of distress in women being treated for infertility. *Journal of Reproductive & Infant Psychology, 27*(3), 238-257. https://doi.org/10.1080/02646830802350880

Miller, G. E., Chen, E., & Zhou, E. S. (2007). If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans. *Psychological Bulletin, 133*(1), 25–45. https://doi.org/10.1037/0033-2909.133.1.25

Miller, N., Herzberger, E. H., Pasternak, Y., Klement, A. H., Shavit, T., Yaniv, R. T., ... & Shulman, A. (2019). Does stress affect IVF outcomes? A prospective study assessing cortisol levels and stress questionnaires for women undergoing through IVF treatments. *Reproductive BioMedicine Online*. *39*(1). 93-101. doi: 10.1016/j.rbmo.2019.01.012

Miner, S. A., Robins, S., Zhu, Y. J., Keeren, K., Gu, V., Read, S. C., & Zelkowitz, P. (2018). Evidence for the use of complementary and alternative medicines during fertility treatment: A scoping review. *BioMed Central Complementary and Alternative Medicine, 18*(1), 158. https://doi.org/10.1186/s12906-018-2224-7

Mitchell, J. W. (2014). Characteristics and allowed behaviors of gay male couples' sexual agreements. *Journal of Sex Research, 51*(3), 316-328. doi:10.1080/00224499.2012.727915

Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G. & The PRISMA Group (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Medicine, 6*(7), e1000097. doi:10.1371/journal.pmed1000097

Moreno, M. A., Christakis, D. A., Egan, K. G., Jelenchick, L. A., Cox, E., Young, H., . . . Becker, T. (2012). A pilot evaluation of associations between displayed depression references on Facebook and self-reported depression using a clinical scale. *The Journal of Behavioral Health Services & Research, 39*(3), 295-304. doi:10.1007/s11414-011-9258-7

Murray, C., Callender, C., Kulikoff, R., Srinivasan, V., Abate, D., Abate, K.,…& Lim, S. (2018). Population and fertility by age and sex for 195 countries and territories, 1950–2017: A systematic analysis for the Global Burden of Disease Study 2017. *The Lancet, 392*(10159), 1995-2051. https://doi.org/10.1016/s0140-6736(18)32278-5

Namdar, A., Naghizadeh, M. M., Zamani, M., Yaghmaei, F., & Sameni, M. H. (2017). Quality of life and general health of infertile women. *Health and Quality of Life Outcomes, 15*(1), 139. https://doi.org/10.1186/s12955-017-0712-y

Namin, A., Hamilton, M. L., & Rohm, A. J. (2017). Impact of message design on banner advertising involvement and effectiveness: An empirical investigation. *Journal of Marketing Communications*, *26*(2), 115-129. doi.10.1080/13527266.2017.1393767

Nargund G. (2009). Declining birth rate in Developed Countries: A radical policy re-think is required. *Facts, Views & Vision in ObGyn*, *1*(3), 191-193. https://www.ncbi.nlm.nih.gov/pubmed/25489464

Nater U.M., Skoluda, N., Strahler, J. (2013). Biomarkers of stress in behavioural medicine. *Current Opinion in Psychiatry, 26*(5), 440-445. doi:10.1097/YCO.0b013e328363b4ed

Nelson, C. J., Shindel, A. W., Naughton, C. K., Ohebshalom, M., & Mulhall, J. P. (2008). Prevalence and predictors of sexual problems, relationship stress, and depression in female partners of infertile couples. *Journal of Sexual Medicine*, *5*(8), 1907-1914. https://doi.org/10.1111/j.1743-6109.2008.00880.x

Nery, S. F., Paiva, S. P. C., Vieira, É. L., Barbosa, A. B., Sant'Anna, E. M., Casalechi, M., … Reis, F. M. (2019). Mindfulness-based program for stress reduction in infertile women: Randomized controlled trial. *Stress & Health, 35*(1), 49–58. https://doi.org/10.1002/smi.2839

Newton, C. R., Sherrard, W., & Glavac, I. (1999). The Fertility Problem Inventory: Measuring perceived infertility-related stress. *Fertility and Sterility, 72*(1), 54-62. https://doi.org/10.1016/S0015-0282(99)00164-8

Nouri, K., Litschauer, B., Huber, J. C., Buerkle, B., Tiringer, D., & Tempfer, C. B. (2011). Saliva cortisol levels and subjective stress are not associated with number of oocytes after controlled ovarian hyperstimulation in patients undergoing in vitro fertilization. *Fertility and Sterility*, *96*(1), 69-72. https://doi.org/10.1016/j.fertnstert.2011.04.063

O'Reilly, K., Wilson, N., Kwok, C., & Peters, K. (2017). FIT 4 PURPOSE: Designing and distributing the women with traumatic brain injury survey. *Journal of the Australasian Rehabilitation Nurses' Association (JARNA), 20*(3), 8-13.

Oxford English Dictionary. (2017a). Stress., n., Retrieved on September 16, 2017 from http://www.oed.com/view/Entry/191511?rskey=aD5vMx&result=1#eid

Oxford English Dictionary. (2017b). Coping, n, adj. Retrieved on November 5, 2017, from http://www.oed.com/search?searchType=dictionary&q=coping&_searchBtn=Search

Pal, L., Bevilacqua, K., & Santoro, N. F. (2010). Chronic psychosocial stressors are detrimental to ovarian reserve: A study of infertile women. *Journal of Psychosomatic Obstetrics & Gynecology, 31*(3), 130–139. https://doi.org/10.3109/0167482X.2010.485258

Pallant, J. (2016). SPSS survival manual: A step by step guide to data analysis using IBM SPSS. (6th ed.). New York: McGraw-Hill.

Panagopoulou, E., Vedhara, K., Gaintarzti, C., & Tarlatzis, B. (2006). Emotionally expressive coping reduces pregnancy rates in patients undergoing in vitro fertilization. *Fertility & Sterility, 86*(3), 672-677. https://doi.org/10.1016/j.fertnstert.2006.02.096

Park, C. L., & Folkman, S. (1997). Meaning in the context of stress and coping. *Review of General Psychology*, *1*(2), 115-144. https://doi.org/10.1037/1089-2680.1.2.115

Pasch, L. A., Gregorich, S. E., Katz, P. K., Millstein, S. G., Nachtigall, R. D., Bleil, M. E., & Adler, N. E. (2012). Psychological distress and in vitro fertilization outcome. *Fertility and Sterility*, *98*(2), 459-464. https://doi.org/10.1016/j.fertnstert.2012.05.023

Pedro, J., Sobral, M. P., Mesquita-Guimarães, J., Leal, C., Costa, M. E., & Martins, M. V. (2017). Couples' discontinuation of fertility treatments: A longitudinal study on demographic, biomedical, and psychosocial risk factors. *Journal of Assisted Reproduction and Genetics*, *34*(2), 217-224. https://doi.org/10.1007/s10815-016-0844-8

Perry, J., VanDenKerkhof, E. G., Wilson, R., & Tripp, D. A. (2017). Guided internet-based psycho-educational intervention using cognitive behavioral therapy and self-management for individuals with chronic pain: A feasibility study. *Pain Management Nursing, 18*(3), 179-189. doi:10.1016/j.pmn.2016.12.003

Peterson, B. D., Newton, C. R., & Rosen, K. H. (2003). Examining congruence between partners' perceived infertility-related stress and its relationship to marital adjustment and depression in infertile couples. *Family process, 42*(1), 59-70. https://doi.org/10.1111/j.1545-5300.2003.00059.x

Peterson, B. D., Newton, C. R., Rosen, K. H., & Skaggs, G. E. (2006). Gender differences in how men and women who are referred for IVF cope with infertility stress. *Human Reproduction, 21*(9), 2443-2449. https://doi.org/10.1093/humrep/del145

Peterson, B. D., Pirritano, M., Block, J. M., & Schmidt, L. (2011). Marital benefit and coping strategies in men and women undergoing unsuccessful fertility treatments over a 5-year period. *Fertility and Sterility, 95*(5), 1759-1763. https://doi.org/10.1016/j.fertnstert.2011.01.125

Peterson, B. D., Pirritano, M., Christensen, U., & Schmidt, L. (2008). The impact of partner coping in couples experiencing infertility. *Human Reproduction*, *23*(5), 1128-1137. https://doi.org/10.1093/humrep/den067

Pew Research Center (2018). Internet & technology. Social media fact sheet. Retrieved from http://www.pewinternet.org/fact-sheet/social-media/

Pezeshki, K., Feldman, J., Stein, D. E., Lobel, S. M., & Grazi, R. V. (2000). Bleeding and spontaneous abortion after therapy for infertility. *Fertility and Sterility, 74*(3), 504-508. https://doi.org/10.1016/S0015-0282(00)00707-X

Pinar, G., & Zeyneloglu, H. B. (2012). Quality of life, anxiety and depression in Turkish women prior to receiving assisted reproductive techniques. *International Journal of Fertility & Sterility, 6*(1), 1-12. https://www.ncbi.nlm.nih.gov/pubmed/25505505

Pochigaeva, K., Druzhkova, T., Yakovlev, A., Onufriev, M., Grishkina, M., Chepelev, A., ... & Gulyaeva, N. (2017). Hair cortisol as a marker of hypothalamic-pituitary-adrenal Axis activity in female patients with major depressive disorder. *Metabolic Brain Disease, 32*(2), 577-583. https://doi.org/10.1007/s11011-017-9952-0

Polit, D. F., & Beck, C. T. (2017). *Nursing research: Generating and assessing evidence for nursing practice.* (10th ed.). Philadelphia: Wolters Kluwer.

Prattke, T. W., & Gass-Sternas, K. A. (1993). Appraisal, coping, and emotional health of infertile couples undergoing donor artificial insemination. *Journal of Obstetric, Gynecologic & Neonatal Nursing*, *22*(6), 516-527. https://doi.org/10.1111/j.1552-6909.1993.tb01837.x

Prokai, D., & Berga, S. L. (2016). Neuroprotection via reduction in stress: Altered menstrual patterns as a marker for stress and implications for long-term neurologic health in women. *International Journal of Molecular Sciences*, *17*(12), 2147. https://doi.org/10.3390/ijms17122147

Pruessner, J., & Ali, N. (2015). Neuroendocrine mechanisms of stress regulation in humans. In J.A. Russell & M.J. Shipston, M. (Eds.). Neuroendocrinology of stress (121-141). West Sussex, United Kingdom: Wiley & Sons. 10.1002/9781118921692

Psaros, C., Kagan, L., Auba, E., Alert, M., & Park, E. R. (2012). A brief report of depressive symptoms and health promoting behaviors among women with infertility attending a clinical mind-body program. *Journal of Psychosomatic Obstetrics & Gynecology*, *33*(1), 32-36. https://doi.org/10.3109/0167482X.2011.643933

Qadir, F., Khalid, A., & Medhin, G. (2015). Social support, marital adjustment, and psychological distress among women with primary infertility in Pakistan. *Women & Health, 55*(4), 432-446. doi:10.1080/03630242.2015.1022687

Radford, J. (2019). Key findings about U.S. immigrants. Pew Research Center. Retrieved from https://www.pewresearch.org/fact-tank/2019/06/17/key-findings-about-u-s-immigrants/

Ranabir, S., & Reetu, K. (2011). Stress and hormones. *Indian Journal of Endocrinology and Metabolism, 15*(1), 18–22. doi:10.4103/2230-8210.77573

Rapoport-Hubschman N, Gidron Y, Reicher-Atir R, Sapir O, & Fisch B. (2009). "Letting go" coping is associated with successful IVF treatment outcome. *Fertility & Sterility, 92*(4). 1384-1388. doi: 10.1016/j.fertnstert.2008.08.012.

Rashidi, B., Montazeri, A., Ramezanzadeh, F., Shariat, M., Abedinia, N., & Ashrafi, M. (2008). Health-related quality of life in infertile couples receiving IVF or ICSI treatment. *BioMed Central health services research, 8*(1), 186. https://doi.org/10.1186/1472-6963-8-186

RESOLVE. (2019a). Medical conditions. Retrieved on February 20, 2019 from https://resolve.org/infertility-101/medical-conditions/

RESOLVE. (2019b). Infertility coverage by state. Retrieved on February 20, 2019 from https://resolve.org/what-are-my-options/insurance-coverage/infertility-coverage-state/

Reyes-Foster, B., Carter, S. K., & Hinojosa, M. S. (2015). Milk sharing in practice: A descriptive analysis of peer breastmilk sharing. *Breastfeeding Medicine, 10(5),* 263-269. doi:10.1089/bfm.2015.0009

Rice, V. H. (2012). Addendum: Nursing research using Lazarus's transactional theory of stress and coping and the ways of coping scale 2000-2010. In V. H. Rice, V. H. Rice (Eds.) , *Handbook of stress, coping, and health: Implications for nursing research, theory, and practice* (pp. 223-225). Thousand Oaks, CA: Sage Publications, Inc.

Ried & Alfred (2003). Quality of life, coping strategies and support needs of women seeking Traditional Chinese Medicine for infertility and viable pregnancy in Australia: A mixed methods approach. *BioMed Central Women's Health 13*(17). 1-11. http://www.biomedcentral.com/1472-6874/13/17

Roerink, M. E., Roerink, S. H., Skoluda, N., van der Schaaf, M. E., Hermus, A. R., van der Meer, J. W., ... & Nater, U. M. (2018). Hair and salivary cortisol in a cohort of women with chronic fatigue syndrome. *Hormones and Behavior, 103*, 1-6. https://doi.org/10.1016/j.yhbeh.2018.05.016

Rogers, V. L., Griffin, M. Q., Wykle, M. L., & Fitzpatrick, J. J. (2009). Internet versus face-to-face therapy: Emotional self-disclosure issues for young adults. *Issues in Mental Health Nursing, 30*(10), 596-602. doi:10.1080/01612840903003520

Rossen, L. M., Ahrens, K. A., & Branum, A. M. (2018). Trends in risk of pregnancy loss among US women, 1990–2011. *Paediatric and perinatal epidemiology*, *32*(1), 19-29. https://doi.org/10.1111/ppe.12417

Russell, E., Koren, G., Rieder, M., & Van Uum, S. (2012). Hair cortisol as a biological marker of chronic stress: Current status, future directions and unanswered questions. *Psychoneuroendocrinology*, *37*(5), 589-601. https://doi.org/10.1016/j.psyneuen.2011.09.009

Sandelowski, M. (1987). The color gray: Ambiguity and infertility. *The Journal of Nursing Scholarship, 19*(2), 70-74. doi:10.1111/j.1547-5069.1987.tb00594.x

Sandelowski, M. & Pollock, C. (1986). Women's experiences of infertility. *The Journal of Nursing Scholarship, 18*(4), 140-144. doi:10.1111/j.1547-5069.1986.tb00563.x

Santa-Cruz, D. C., Caparros-Gonzalez, R., & Garcia-Velasco, J. A. (2019). Hair cortisol as a new biomarker of underlying chronic stress, anxiety and depression in infertility: A pilot study. *Fertility and Sterility*, *112*(3), e66. https://doi.org/10.1016/j.fertnstert.2019.07.295

Santos Couto, P. L., Santos Paiva, M., de Oliveira, J. F., Tosoli Gomes, A. M., Argolo Teixeira, M., & Boa Sorte, E. T. (2018). Sexuality and HIV prevention: Consensus and dissent of catholic youths. *Investigacion & Educacion En Enfermeria*, *36*(2), 49-59. doi:10.17533/udea.iee.v36n2e06

Schetter, C. D., & Dolbier, C. (2011). Resilience in the context of chronic stress and health in adults. *Social and Personality Psychology Compass*, *5*(9), 634-652. https://doi.org/10.1111/j.1751-9004.2011.00379.x

Schieve, L. A., Devine, O., Boyle, C. A., Petrini, J. R., & Warner, L. (2009). Estimation of the contribution of non–assisted reproductive technology ovulation stimulation fertility treatments to US singleton and multiple births. *American Journal of Epidemiology*, *170*(11), 1396-1407. https://doi.org/10.1093/aje/kwp281

Schieve, L. A., Tatham, L., Peterson, H. B., Toner, J., & Jeng, G. (2003). Spontaneous abortion among pregnancies conceived using assisted reproductive technology in the United States. *Obstetrics & Gynecology*, *101*(5), 959-967. https://doi.org/10.1016/S0029-7844(03)00121-2

Schmidt, L. (2006). Infertility and assisted reproduction in Denmark. *Danish Medical Bulletin*, *53*(4), 390-417. https://www.ncbi.nlm.nih.gov/pubmed/17150146

Schmidt L, Holstein BE, Christensen U, & Boivin J. (2005a). Communication and coping as predictors of fertility problem stress: Cohort study of 816 participants who did not achieve a delivery after 12 months of fertility treatment. *Human Reproduction. 20*(11), 3248-3256. https://doi.org/10.1093/humrep/dei193

Schmidt, L., Holstein, B., Christensen, U., & Boivin, J. (2005b). Does infertility cause marital benefit?: An epidemiological study of 2250 women and men in fertility treatment. *Patient education and Counseling, 59*(3), 244-251. https://doi.org/10.1016/j.pec.2005.07.015

Schonblum, A., Arnon, L., Ravid, E., Salzer, L., Hadar, E., Meizner, I., ... & Koren, L. (2018). Can hair steroids predict pregnancy longevity? *Reproductive Biology*, *18*(4), 410-415. https://doi.org/10.1016/j.repbio.2018.09.004

Schwerdtfeger, K., & Shreffler, K. (2009). Trauma of pregnancy loss and infertility among mothers and involuntarily childless women in the United States. *Journal of Loss & Trauma*, *14*(3), 211-227. https://doi.org/10.1080/15325020802537468

Selye, H. (1954). The alarm reaction, the general adaptation syndrome, and the role of stress and of the adaptive hormones in dental medicine. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*, *7*(4), 355-367. doi:10.1016/0030-4220(54)90142-5

Sexton, M. B., Byrd, M. R., & von Kluge, S. (2010). Measuring resilience in women experiencing infertility using the CD-RISC: Examining infertility-related stress, general distress, and coping styles. *Journal of Psychiatric Research*, *44*(4), 236-241. doi:10.1016/j.jpsychires.2009.06.007

Sharp, E. (2017). Celebrating the 200 million people of Pinterest. Retrieved on March 13, 2019 from https://newsroom.pinterest.com/en/post/celebrating-the-200-million-people-of-pinterest.

Siegmund, L. A. (2018). Social media: The next research frontier. *Clinical Nurse Specialist*, *32*(2), 62-66. doi:10.1097/NUR.0000000000000354

Smith, A. & Anderson, M. (2018). Social media use in 2018. Pew Research Center. Retrieved March 13, 2019 from http://www.pewinternet.org/2018/03/01/social-media-use-2018-appendix-a-detailed-table/

Smith, C. A., Ussher, J. M., Perz, J., Carmady, B., & de Lacey, S. (2011). The effect of acupuncture on psychosocial outcomes for women experiencing infertility: A pilot randomized controlled trial. *Journal of Alternative and Complementary Medicine*, *17*(10), 923-930. https://doi.org/10.1089/acm.2010.0380

Sobral, M. P., Costa, M. E., Schmidt, L., & Martins, M. V. (2017). COMPI Fertility Problem Stress Scales is a brief, valid and reliable tool for assessing stress in patients seeking treatment. *Human Reproduction*, *32*(2), 375-382. https://doi.org/10.1093/humrep/dew315

Society for Assistive Reproductive Technology. (2019). Frequently asked questions. Retrieved on February 20, 2019 from https://www.sart.org/patients/frequently-asked-questions/

Staffileno, B. A., Zschunke, J., Weber, M., Gross, L. E., Fogg, L., & Tangney, C. C. (2017). The feasibility of using Facebook, Craigslist, and other online strategies to recruit young African American women for a web-based healthy lifestyle behavior change intervention. *Journal of Cardiovascular Nursing*, *32*(4), 365-371. doi:10.1097/JCN.0000000000000360

Staton, A. L. (1991). Cognitive appraisals, coping processes, and adjustment to infertility. In A. L. Stanton & C. Dunkel-Schetter (Eds.), *Infertility: Perspectives from stress and coping research* (pp. 87–108). New York: Plenum Press

Steudte, S., Kirschbaum, C., Gao, W., Alexander, N., Schönfeld, S., Hoyer, J., & Stalder, T. (2013). Hair cortisol as a biomarker of traumatization in healthy individuals and posttraumatic stress disorder patients. *Biological Psychiatry, 74*(9), 639-646. https://doi.org/10.1016/j.biopsych.2013.03.011

Sweeny, K., Andrews, S. E., Nelson, S. K., & Robbins, M. L. (2015). Waiting for a baby: Navigating uncertainty in recollections of trying to conceive. *Social Science & Medicine, 141*, 123-132. https://doi.org/10.1016/j.socscimed.2015.07.031

Tanbo, T., Mellembakken, J., Bjercke, S., Ring, E., Åbyholm, T., & Fedorcsak, P. (2018). Ovulation induction in polycystic ovary syndrome. *Acta Obstetricia et Gynecologica Scandinavica*, *97*(10), 1162-1167. https://doi.org/10.1111/aogs.13395

Turner, K., Reynolds-May, M., Zitek, E. M., Tisdale, R. L., Carlisle, A. B., & Westphal, L. M. (2013). Stress and anxiety scores in first and repeat IVF cycles: A pilot study. *PloS One*, *8*(5), e63743. doi: 10.1371/journal.pone.0063743

Valerian, V., Lotti, F., Vanni, C., Noci, M., Fontanarosa, N., Ferrari, G., . . . Noci, I. (2014). Hatha-yoga as a psychological adjuvant for women undergoing IVF: A pilot study. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, *176*, 158-162. doi:http://dx.doi.org/10.1016/j.ejogrb.2014.02.007

van den Akker, O. B. (2005). Coping, quality of life and psychological symptoms in three groups of sub-fertile women. *Patient Education and Counseling, 57*(2), 183-189. https://doi.org/10.1016/j.pec.2004.05.012

Vashist, S. K. & Schneider, M. (2014). Depression: An insight and need for personalized psychological stress monitoring and management. *Journal of Basic & Applied Sciences, 10*, 177-182. 10.6000/1927-5129.2014.10.25.

Verhaak, C. M., Smeenk, J. M. J., Van Minnen, A., Kremer, J. A. M., & Kraaimaat, F. W. (2005). A longitudinal, prospective study on emotional adjustment before, during and after consecutive fertility treatment cycles. *Human Reproduction*, *20*(8), 2253-2260. https://doi.org/10.1093/humrep/dei015

Vives, A. H., De Angel, V., Papadopoulos, A., Strawbridge, R., Wise, T., Young, A. H., ... & Cleare, A. J. (2015). The relationship between cortisol, stress and psychiatric illness: New insights using hair analysis. *Journal of Psychiatric Research*, *70*, 38-49. https://doi.org/10.1016/j.jpsychires.2015.08.007

Wahlberg, L., Nirenberg, A., & Capezuti, E. (2016). Distress and coping self-efficacy in inpatient oncology nurses. *Oncology Nursing Forum*, *43*(6), 738-746. doi:10.1188/16.ONF.738-746

Walker, L. O., & Avant, K. C. (2011). *Strategies for theory construction in nursing.* (5th ed.). Upper Saddle River, N.J.: Pearson/Prentice Hall

Wang, J. X., Norman, R. J., & Wilcox, A. J. (2004). Incidence of spontaneous abortion among pregnancies produced by assisted reproductive technology. *Human Reproduction*, *19*(2), 272-277. https://doi.org/10.1093/humrep/deh078

Whitehead, L. C. (2007). Methodological and ethical issues in internet-mediated research in the field of health: An integrated review of the literature. *Social Science and Medicine. 65*(4). 782-791. https://doi.org/10.1016/j.socscimed.2007.03.005

Whittemore, R., & Knafl, K. (2005). The integrative review: Updated methodology. *Journal of Advanced Nursing*, *52*(5), 546-553. https://doi.org/10.1111/j.1365-2648.2005.03621.x

Whitworth, J. A., Williamson, P. M., Mangos, G., & Kelly, J. J. (2005). Cardiovascular consequences of cortisol excess. *Vascular Health and Risk Management*, *1*(4), 291–299. doi: 10.2147/vhrm.2005.1.4.291

Wiersema, N. J., Drukker, A. J., Dung, M. B. T., Nhu, G. H., Nhu, N. T., & Lambalk, C. B. (2006). Consequences of infertility in developing countries: results of a questionnaire and interview survey in the South of Vietnam. *Journal of Translational Medicine*, *4*(1), 54. https://doi.org/10.1186/1479-5876-4-54

World Health Organization. (2019a). Sexual and reproductive health. Infertility definitions and terminology. https://www.who.int/reproductivehealth/topics/infertility/definitions/en/

World Health Organization. (2019b). Health statistics and information systems. WHOQOL: Measuring Quality of Life. http://www.who.int/healthinfo/survey/whoqol-qualityoflife/en/

Wright, K. (2005). Researching internet-based populations: Advantages and disadvantages of online survey research, online questionnaire authoring software packages, and web survey services. *Journal of Computer-Mediated Communication*, *10*(3). https://doi.org/10.1111/j.1083-6101.2005.tb00259.x

Xi, J., Chen, H., Peng, Z. H., Tang, Z. X., Song, X., & Xia, Y. B. (2018). Effects of acupuncture on the outcomes of assisted reproductive technology: An overview of systematic reviews. *Evidence-Based Complementary and Alternative Medicine*, *2018*. 1-13. https://doi.org/10.1155/2018/7352735

Xia, J. F., Inagaki, Y., Zhang, J. F., Wang, L., & Song, P. P. (2017). Chinese medicine as complementary therapy for female infertility. *Chinese Journal of Integrative Medicine*, *23*(4), 245-252. https://doi.org/10.1007/s11655-016-2510-5

Yuit Wah Wong, C., & Pang, J., Ser Hua Tan, G., Soh, W., Lim, J., Lau, S., & He, H. (2012). The impact of infertility on women's psychological health: A literature review. *Singapore Nursing Journal*, *39*(3), 11–17.

APPENDIX A: IRB APPROVAL

EAST CAROLINA UNIVERSITY
University & Medical Center Institutional Review Board
4N-64 Brody Medical Sciences Building· Mail Stop 682
600 Moye Boulevard · Greenville, NC 27834
Office **252-744-2914**· Fax **252-744-2284**· **www.ecu.edu/ORIC/irb**

Notification of Initial Approval: Expedited

From: Biomedical IRB
To: Alison Swift
CC: Pamela Reis
Date: 2/11/2019
Re: UMCIRB 18-002301
Relationships between infertility-related stress, coping, and quality of life in women undergoing infertility treatments

I am pleased to inform you that your Expedited Application was approved. Approval of the study and any consent form(s) occurred on 2/10/2019. The research study is eligible for review under expedited category # 3,7. The Chairperson (or designee) deemed this study no more than minimal risk.

Changes to this approved research may not be initiated without UMCIRB review except when necessary to eliminate an apparent immediate hazard to the participant. All unanticipated problems involving risks to participants and others must be promptly reported to the UMCIRB. The investigator must submit a Final Report application to the UMCIRB prior to the Expected End Date provided in the IRB application. If the study is not completed by this date, an Amendment will need to be submitted to extend the Expected End Date. The Investigator must adhere to all reporting requirements for this study.

Approved consent documents with the IRB approval date stamped on the document should be used to consent participants (consent documents with the IRB approval date stamp are found under the Documents tab in the study workspace).
The approval includes the following items:

Name	Description
COMPI-Coping Stategies Scale	Surveys and Questionnaires
COMPI-Fertility Problem Stress Scale	Surveys and Questionnaires
Consent to provide Hair Sample	Consent Forms
Demographic data	Data Collection Sheet
Demographic data	Surveys and Questionnaires
Fertility Quality of Life	Surveys and Questionnaires
Hair Care and Steriod Use Questionnaire for Hair Sample	Surveys and Questionnaires
Hair sample procedure for participants	Additional Items
Research Proposal/Protocol	Study Protocol or Grant Application
Screening Questions	Surveys and Questionnaires
Screenshot of Facebook study page	Recruitment Documents/Scripts
Social Media Script	Recruitment Documents/Scripts
Survey Consent	Consent Forms

The Chairperson (or designee) does not have a potential for conflict of interest on this study.

APPENDIX B: IRB AMENDMENT APPROVAL

EAST CAROLINA UNIVERSITY
University & Medical Center Institutional Review Board
4N-64 Brody Medical Sciences Building· Mail Stop 682
600 Moye Boulevard · Greenville, NC 27834
Office **252-744-2914** · Fax **252-744-2284** · **www.ecu.edu/ORIC/irb**

Notification of Amendment Approval

From: Biomedical IRB
To: Alison Swift
CC:
Pamela Reis
Date: 7/15/2019
Re: Ame3_UMCIRB 18-002301
UMCIRB 18-002301
Relationships between infertility-related stress, coping, and quality of life in women undergoing infertility treatments

Your Amendment has been reviewed and approved using expedited review for the period of 7/14/2019 to 5/4/2020. It was the determination of the UMCIRB Chairperson (or designee) that this revision does not impact the overall risk/benefit ratio of the study and is appropriate for the population and procedures proposed.

Please note that any further changes to this approved research may not be initiated without UMCIRB review except when necessary to eliminate an apparent immediate hazard to the participant. All unanticipated problems involving risks to participants and others must be promptly reported to the UMCIRB. A continuing or final review must be submitted to the UMCIRB prior to the date of study expiration. The investigator must adhere to all reporting requirements for this study.

Approved consent documents with the IRB approval date stamped on the document should be used to consent participants (consent documents with the IRB approval date stamp are found under the Documents tab in the study workspace).

The approval includes the following items:

Document	Description
COMPI-Fertility Problem Stress Scale(0.03)	Surveys and Questionnaires
Demographic data(0.03)	Surveys and Questionnaires
Research Proposal/Protocol(0.03)	Study Protocol or Grant Application
Screening Questions(0.04)	Surveys and Questionnaires

The Chairperson (or designee) does not have a potential for conflict of interest on this study.

APPENDIX C: PERMISSION TO USE TOOLS

Permission to use tools

1. FertiQoL tool was downloaded for free from a public domain, with terms of use followed. Retrieved from http://sites.cardiff.ac.uk/fertiqol/download/

2. The following is the permission to use the COMPI-FPSS and COMPI-CSS:

Dear Alison Swift,
Thank you for your interest in our COMPI scales.

You have my permission to use the psychosocial COMPI scales.

Please, find attached:

1) The COMPI baseline questionnaire for women
2) Overview of the items in each psychosocial COMPI scale. Originally the COMPI Fertility Problem Scales include more items. However, after a cross-cultural validity study (Sobral et al, 2017 and 2018, attached.) the COMPI Fertility Problem Stress Scales is reduced to 9 items.
3) An overview of the COMPI research (summary from my doctor of medical sciences dissertation; DMSc)

We have published a large number of studies based on the COMPI Infertility Cohort data on coping, infertility-specific stress etc. Please, let me know whether you would like me to send you these publications.

You are welcome to contact me again if you have any questions.

Yours sincerely,

Lone Schmidt
Professor wsr, DMSc, PhD, MD
University of Copenhagen
Department of Public Health
Section of Social Medicine
Øster Farimagsgade 5, PO Box 2099
DK-1014 Copenhagen K
Denmark

Phone: +45 35 32 76 31
Mobil: +45 22 41 65 85
Mail: lone.schmidt@sund.ku.dk

Visiting address: Gothersgade 160, 1st floor

APPENDIX D: SOCIAL MEDIA SCRIPT

We are so sorry you are going through a difficult and painful time in trying to conceive. We are researchers at East Carolina University trying to understand the impact infertility and infertility treatments have on your life, to hopefully find ways to help women during this incredibly difficult time. If you are willing to complete an anonymous online survey you might be able to help us, and help others going through similar circumstances. The survey will ask you about what symptoms you might be having related to infertility and ways you might be coping with infertility.

You can find the survey on REDCap survey tool at this link:

For questions, please contact Alison Swift, MSN, RN, CNE, PhD(c) at ecuinfertilitystudy@ecu.edu. We appreciate your time and willingness to help others during this time.

APPENDIX E: CONSENT LETTER FOR SURVEY RESEARCH

Dear Participant,

I am a PhD student at East Carolina University in the College of Nursing, Department of Nursing Science. I am asking you to take part in my research study entitled, "Relationships between infertility-related stress, hair cortisol, coping, and quality of life in women undergoing infertility treatments".

The purpose of this research is to study the relationships between infertility-related stress, hair cortisol, coping, and quality of life in women who are having infertility treatments. By doing this research, I hope to learn how infertility-related stress, hair cortisol, coping, and quality of life are related and how stress, coping, and quality of life relate to other aspects of infertility, such as the type of infertility and the length of time of having infertility. Your participation is completely voluntary.

You are being invited to take part in this research because you found the study link or Facebook study page and identify as a woman between 18-55 years of age with infertility and undergoing infertility treatments. The amount of time it will take you to complete this survey is 10 minutes.

If you agree to take part in this survey, you will be asked questions that relate to your feelings about stress, how you cope, and feelings about how infertility and infertility treatments affect your mood and relationships to others. The last question of the survey gives you an option to participate in providing a small hair sample to test for cortisol levels, which is a measure of chronic stress. You may choose to participate by providing an email address, so I may further contact you, or you may choose to not participate by not providing an email address. Should you choose to provide a hair sample, your survey results and hair sample will be coded with a unique number so there will be no identifying information. Once we get the cortisol results, we will compare your hair cortisol results to the survey results.

This research is overseen by the University and Medical Center Institutional Review Board (UMCIRB) at ECU. Therefore, some of the UMCIRB members or the UMCIRB staff may need to review your research data. However, the information you provide will not be linked to you unless you provide your email address to be contacted in the future by the researcher. Therefore, your responses cannot be traced back to you by anyone, including me. Should you provide your email address to be contacted by the researcher, your identity will be evident to those individuals who see this information. However, I will take precautions to ensure that anyone not authorized to see your identity will not be given that information.

If you have questions about your rights when taking part in this research, call the Office of Research Integrity & Compliance (ORIC) at 252-744-2914 (days, 8:00 am-5:00 pm). If you would like to report a complaint or concern about this research study, call the Director of ORIC, at 252-744-1971.

You do not have to take part in this research, and you can stop at any time. If you decide you are willing to take part in this study, check the AGREE box below and the research questions will appear.

Thank you for taking the time to participate in my research.

Sincerely, Alison Swift, PhD(c), MSN, RN, CNE, Principal Investigator

APPENDIX F: INFORMED CONSENT FOR HAIR SAMPLE

Informed Consent to Participate in Research

Information to consider before taking part in research that has no more than minimal risk.

Title of Research Study: Relationships between infertility-related stress, coping, and quality of life in women undergoing infertility treatments

Principal Investigator: Alison Swift (Person in Charge of this Study)
Institution, Department or Division: East Carolina University, College of Nursing
Address: 2205 W. 5th Street Greenville, NC 27834
Telephone #: 252-744-6426

Participant Full Name: _____Date of Birth: _____
Please PRINT clearly

Researchers at East Carolina University (ECU) study issues related to society, health problems, environmental problems, behavior problems and the human condition. To do this, we need the help of volunteers who are willing to take part in research.

Why am I being invited to take part in this research?

The purpose of this research is to study the relationships between infertility-related stress, coping, and quality of life in women who are having infertility treatments. Hair cortisol levels are a measure of chronic stress. You are being invited to take part in this research because you identify as a woman between the age of 18-55 with infertility and undergoing infertility treatments and you indicated your willingness to provide a hair sample. The decision to take part in this research is yours to make. By doing this research, we hope to learn how infertility-related stress, coping, and quality of life are related and how stress, coping, and quality of life relate to other aspects of infertility, such as the type of infertility and the length of time of having infertility.

If you volunteer to take part in this research, you will be one of about __30_____ people to do so.

Are there reasons I should not take part in this research?

I understand I should not volunteer for this study if I am under 18 years of age, do not have an infertility diagnosis, or am not undergoing infertility treatments.

What other choices do I have if I do not take part in this research?

You can choose not to participate.

Where is the research going to take place and how long will it last?

The research will be conducted at East Carolina University (ECU). You do not need to come to any location at any time during the study. The total amount of time you will be asked to volunteer for this study is 10 minutes over the next 1 day.

What will I be asked to do?

You will be asked to do the following: Fill out a survey about personal hair care and if you take steroid medications before providing the hair sample. This is important for the laboratory to determine if the hair

cortisol levels will be accurate. You will be mailed the hair sample collection kit including written instructions and videos on how to collect the hair sample. You will be then be asked to provide a small root hair sample from the crown of your head, about a pencil width and 3 cm long. You can cut the hair sample from the crown of your head yourself or have someone cut it for you. It will then be wrapped in aluminum foil and mailed to the principal investigator, along with the hair care questions and this consent. Once the hair sample arrives to the PI, the hair sample will be coded, have no identifying information, and sent to a laboratory in Massachusetts. The hair root sample will be analyzed for cortisol levels which is a measure of chronic stress. Based on the 3 cm length of hair and the cortisol concentration, we can tell how much cortisol, or stress hormone, you have had over the past 3 months. This will be the only test we will perform with your hair. Remaining hair will be discarded. Once the results are obtained, the hair cortisol results will be compared to the results of the survey.

What might I experience if I take part in the research?
We don't know of any risks (the chance of harm) associated with this research. Any risks that may occur with this research are no more than what you would experience in everyday life. We don't know if you will benefit from taking part in this study. There may not be any personal benefit to you, but the information gained by doing this research may help others in the future.

Will I be paid for taking part in this research?
We will not be able to pay you for the time you volunteer while being in this study.

Will it cost me to take part in this research?
It will not cost you any money to be part of the research. The researcher will pay the costs of the hair collection kit and the analysis of the hair.

Who will know that I took part in this research and learn personal information about me?
ECU and the people and organizations listed below may know that you took part in this research and may see information about you that is normally kept private. With your permission, these people may use your private information to do this research:

- Any agency of the federal, state, or local government that regulates human research. This includes the Department of Health and Human Services (DHHS), the North Carolina Department of Health, and the Office for Human Research Protections.
- The University & Medical Center Institutional Review Board (UMCIRB) and its staff have responsibility for overseeing your welfare during this research and may need to see research records that identify you.

How will you keep the information you collect about me secure? How long will you keep it?
Information collected about you will be kept for a period of 6 years. Electronic data will be stored on a secured and protected server. Physical data will be locked in a filing cabinet in the researchers locked office. Once the hair samples and hair care questions are collected, the hair will be mailed to the independent laboratory for analysis. Results will be returned to the researcher and will be kept electronically on the secured and protected server. If physical results are returned, it will be locked in the filing cabinet in the researcher's locked office. Once the study is concluded, any identifying information (your email address) will be destroyed and only the results will be kept.

What if I decide I don't want to continue in this research?
You can stop at any time after it has already started. There will be no consequences if you stop and you will not be criticized. You will not lose any benefits that you normally receive.

Who should I contact if I have questions?

The people conducting this study will be able to answer any questions concerning this research, now or in the future. You may contact the Principal Investigator at 252-744-6426 Thursdays between 9am-10am, or 12pm-2pm, or Fridays between 12pm-2pm, or by email at ecuinfertilitystudy@ecu.edu

If you have questions about your rights as someone taking part in research, you may call the Office of Research Integrity & Compliance (ORIC) at phone number 252-744-2914 (days, 8:00 am-5:00 pm). If you would like to report a complaint or concern about this research study, you may call the Director of the ORIC, at 252-744-1971.

Is there anything else I should know?

Your information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future studies.

The following research results will be provided to you: hair cortisol level results. These results will be shared with you via the email address you provided within 4 weeks from when the results are available to the researcher. Only the result will be shared with you and will not include any interpretation of the result. Should you have questions about the result, please ask your primary healthcare provider.

Will I receive anything for the use of my private identifiable information or identifiable biospecimens?

If the research conducted on your private identifiable information or identifiable biospecimens leads to a commercially valuable product, you will not be eligible for any of the profits either because it will be impossible to identify the information or biospecimen that led to the product or because you are transferring ownership of that sample.

Will my identifiable biospecimen be used for whole genome sequencing?

Whole genome sequencing is the process of determining the complete DNA sequence of an individual at a single time. However, further analysis must usually be performed to provide any biological or medical meaning of this sequence. For this research, whole genome sequencing will not occur.

I have decided I want to take part in this research. What should I do now?

The person obtaining informed consent will ask you to read the following and if you agree, you should sign this form:

- I have read (or had read to me) all the above information.
- I have had an opportunity to ask questions about things in this research I did not understand and have received satisfactory answers.
- I know that I can stop taking part in this study at any time.
- By signing this informed consent form, I am not giving up any of my rights.
- I have been given a copy of this consent document, and it is mine to keep.

_____ _____

Participant's Name (PRINT) **Signature** **Date**

Person Obtaining Informed Consent: I have conducted the initial informed consent process. I have orally reviewed the contents of the consent document with the person who has signed above and answered all of the person's questions about the research.

_____

Person Obtaining Consent (PRINT) **Signature** **Date**

APPENDIX G: SCREENING QUESTIONS

Screening Questions

1. Have you been diagnosed with infertility?

 Yes

 No

 No. I have been trying to get pregnant for more than 1 year, but I have not seen a doctor.

2. Are you currently in treatment for infertility or have you been in treatment for your infertility within the past 6 months (may include consultation, surgery, medications, or other interventions to achieve pregnancy)?

 Yes

 No

3. What is your sex?

 Female

 Male

 Other_____

 Prefer not to say

4. What is your current age (at last birthday?) _____

5. Where do you currently live?

 . In the United States
 . Outside (not in) the United States

APPENDIX H: COPENHAGEN MULTI-CENTRE PSYCHOSOCIAL INFERTILITY FERTILITY PROBLEM SCALE SCORE (COMPI-FPSS)

Personal Domain

Please respond to the following as to how you are feeling currently:

	Strongly Disagree	Somewhat Disagree	Neither Agree or Disagree	Somewhat Agree	Strongly Agree
1. It is very stressful for me to deal with this fertility problem.					

Please respond to the following as to how you are feeling currently. How much stress has your fertility problem placed on the following…

	Not at all	A little	Some	A great deal
2. Your physical health?				
3. Your mental health?				

Marital Domain

Please respond to the following as to how you are feeling currently What consequences has your childlessness for your marriage/partnership?

	Strongly Disagree	Somewhat Disagree	Neither Agree or Disagree	Somewhat Agree	Strongly Agree
4. The childlessness has caused a crisis in our relationship.					

Please respond to the following as to how you are feeling currently. How much stress has your fertility problem placed on the following…

	Not at all	A little	Some	A great deal
5. Your marriage/partnership?				
6. Your sex life?				

Social Domain

7. Your relationships with your family?				
8. Your relationships with your family-in-law?				
9. Your relationships with your friends?				

Additional Question:

If you have other types of stress, related to infertility, please list:_____

APPENDIX I: COPENHAGEN MULTI-CENTRE PSYCHOSOCIAL INFERTILITY COPING STRATEGY SCALE (COMPI-CSS)

People cope with their fertility problem in different ways. How do you cope? I.....

Active-avoidance Coping Scale	Not used	Used Somewhat	Used quite a bit	Used a great deal
1. avoid being with pregnant women or children				
2. leave, when people are talking about pregnancies and children				
3. try to keep my feelings to myself				
4. turn to work or substitute activity to take my mind off things				
Active-confronting Coping Scale				
5. let my feelings out somehow				
6. accept sympathy and understanding from someone				
7. ask other childless people for advice				
8. ask a relative or friend for advice				
9. read or watch television about childlessness				
10. talk to someone about my emotions as childless				
11. talk to someone about how tests and treatments affect me emotionally				
Passive-avoidance Coping Scale				
12. hope a miracle will happen				
13. feel that the only thing I can do is to wait				
14. have fantasies and wishes				
Meaning-based Coping Scale				
15. have grown as a person in a good way				
16. think about the infertility in a positive light				
17. find my marriage/partnership even more valuable now				
18. find other life goals				
19. believe there is a meaning in our difficulties in having children				

APPENDIX J: FERTILITY QUALITY OF LIFE SCALE (FERTIQOL)

For each question, kindly check for the response that most closely reflects how you think and feel. Relate your answers to your current thoughts and feelings. Some questions may relate to your private life, but they are necessary to adequately measure all aspects of your life.

For each question, check the response that is closest to your current thoughts and feelings.

	Very Poor	Poor	Neither Good nor Poor	Good	Very Good
A. How would you rate your health?					

For each question, check the response that is closest to your current thoughts and feelings.

	Very Dissatisfied	Dis-satisfied	Neither Satisfied nor Dissatisfied	Satisfied	Very Satisfied
B. Are you satisfied with your quality of life?					

For each question, check the response that is closest to your current thoughts and feelings.

	Completely	A Great Deal	Moderately	Not much	Not at All
1. Are your attention and concentration impaired by thoughts of infertility?					
2. Do you think you cannot move ahead with other life goals and plans because of fertility problems?					
3. Do you feel drained or warn out because of fertility problems?					
4. Do you feel able to cope with your fertility problems?					

For each question, check the response that is closest to your current thoughts and feelings.

	Very Dissatisfied	Dis-satisfied	Neither Satisfied nor Dissatisfied	Satisfied	Very Satisfied
5. Are you satisfied with the support you receive from friends with regard to your fertility problems?					
6. Are you satisfied with your sexual relationship even					

though you have fertility problems?					

For each question, check the response that is closest to your current thoughts and feelings.

	Always	Very Often	Quite Often	Seldom	Never
7. Do your fertility problems cause feelings of jealousy and resentment?					
8. Do you experience grief and/or feelings of loss about not being able to have a child (or more children)?					
9. Do you fluctuate between hope and despair because of fertility problems?					
10. Are you socially isolated because of fertility problems?					
11. Are you and your partner affectionate with each other even though you have fertility problems?					
12. Do your fertility problems interfere with your day-to-day work or obligations?					
13. Do you feel uncomfortable attending social situations like holidays and celebrations because of your fertility problems?					
14. Do you feel your family can understand what you are going through?					

For each question, check the response that is closest to your current thoughts and feelings.

	An Extreme Amount	Very Much	A Moderate Amount	A Little	Not at All
15. Have fertility problems strengthened your commitment to your partner?					
16. Do you feel sad and depressed about your fertility problems?					

17. Do your fertility problems make you inferior to people with children?					
18. Are you bothered by fatigue because of fertility problems?					
19. Have fertility problems had a negative impact on your relationship with your partner?					
20. Do you find it difficult to talk to your partner about your feelings related to infertility?					
21. Are you content with your relationship even though you have fertility problems?					
22. Do you feel social pressure on you to have (or have more) children?					
23. Do your fertility problems make you angry?					
24. Do you feel pain and physical discomfort because of your fertility problems?					

Treatment Module

For each question, check the response that is closest to your current thoughts and feelings.

	Always	Very Often	Quite Often	Seldom	Never
25. Does infertility treatment negative affect your mood?					
26. Are the fertility medical services you would like available to you?					

For each question, check the response that is closest to your current thoughts and feelings.

	An Extreme Amount	Very Much	A Moderate Amount	A Little	Not at All
27. How complicated is dealing with the procedures and/or administration of medication for your infertility treatment(s)?					

28. Are you bothered by the effect of treatment on your daily or work-related activities?					
29. Do you feel the fertility staff understand what you are going through?					
30. Are you bothered by the physical side effects of fertility medications and treatment?					

For each question, check the response that is closest to your current thoughts and feelings.

	Very Dissatisfied	Dissatisfied	Neither Satisfied nor Dissatisfied	Satisfied	Very Satisfied
31. Are you satisfied with the quality of services available to you to address your emotional needs?					
32. How would you rate the surgery and/or medical treatment(s) you have received?					
33. How would you rate the quality of information you received about medication, surgery, and/or medical treatment?					
34. Are you satisfied with your interactions with fertility medical staff?					

APPENDIX K: BACKGROUND AND DEMOGRAPHIC DATA

1. What type of infertility do you have?
   - . Primary (no living children)
   - . Secondary (previously had a child(ren), but now have infertility)
   - . I don't know.

2. How many years have you had infertility (include all time spent trying to get pregnant currently)? _____

3. How long (months or years) have you been undergoing infertility treatment? _____

4. What is the cause of your infertility?
   - . Female Factor
   - . Male Factor
   - . Female and Male Factor (combination)
   - . Unknown

5. What type of infertility treatment are you currently undergoing?
   - . Non-In vitro fertilization treatments (medications and/or inseminations)
   - . In Vitro Fertilization (IVF) treatments (includes all IVF types)
   - . Surgical treatments
   - . Other Procedures
   - . No treatment
   - . Other _____(please list)

6. If you listed "other" type of treatment above, please describe. _____

7. If you listed "no treatment", please describe why you are not in treatments currently._ ____

8. What is your current state or point in your treatment cycle?
   - . Not in treatments
   - . At the beginning of a cycle waiting to take medications or taking birth control pills for suppression
   - . Taking Medications to produce ovulation or egg production/stimulation
   - Waiting for ovulation to occur, at ovulation (trigger), or at egg retrieval, or egg fertilization
   - . In the "2-week wait" or post-ovulation, post intrauterine insemination (IUI), or post-embryo transfer
   - . Failed Cycle or waiting/expected period to begin
   - . Positive pregnancy urine test or blood test
   - . Pre-, Current, or just Post-surgical treatment or other procedures
   - . Consultation.

□. Other.

9. If you listed “other” for the current state or point in your treatment cycle, please list or describe. _____

10. Have you experienced pregnancy loss or miscarriage since you’ve been trying to conceive?
    □. Yes
    □. No
    □. Unsure

11. If you have experienced pregnancy loss, how many pregnancy losses have you had? _____

12. Please indicate if a mental health provider (e.g. psychologist, therapist, counselor) or medical doctor (e.g. psychiatrist, obstetrician/gynecologist, primary care physician) has diagnosed you (current diagnosis) with any of the following emotional or mental health conditions. Check all that apply.

    □. Depression
    □. Generalized Anxiety Disorder
    □. Social Anxiety Disorder
    □. Post-traumatic stress syndrome (PTSD)
    □. Panic Disorder
    □. Bipolar Disorder
    □. Obsessive Compulsive Disorder
    □. Other. Please Describe_____
    □. I do not have a current diagnosis with a mental/emotional health condition.

13. Please select the coping strategies you may use to cope with infertility (Select all that apply):
    □. Talk about it with others (family, friends, husband)
    □. Participate in a support group
    □. Therapy/Counseling
    □. Spiritual/religious practice
    □. Meditate/Mindfulness
    □. Physical Activity (exercise, yoga, etc).
    □. Alternative therapies (such as acupuncture, massage, reflexology, chiropractor)
    □. Journal Writing
    □. Reading
    □. Try not to think about it
    □. Find/Look for other solutions to helping with my infertility
    □. Planning/organizing my schedule related to infertility or infertility treatments
    □. Look for information to help me understand my infertility
    □. Keep myself busy with other activities

. Substance Use (tobacco, alcohol, drugs)
. Other_____

DEMOGRAPHIC DATA

14. Ethnicity:
 Hispanic or Latino
 Non-Hispanic or Latino
 Other

15. Race:
 African-American/Black
 American Indian or Alaska Native
 Asian
 Caucasian/White
 Native Hawaiian or Other Pacific Islander
 Multi-Race or Mixed Race
 Other

16. Marital status:
 Never married
 Committed relationship
 Married
 Divorced/separated
 Widowed

17. Education (highest level of schooling completed)
 8 years or less
 9-11 years
 High school graduate (or GED)
 Some technical school or community college
 Technical school/Associate degree graduate
 Some college
 Baccalaureate degree
 Some graduate school
 Graduate degree or higher

18. Employment Status:
 Unemployed
 Seeking Employment
 Currently Employed Part-Time (1-30 hours)

. Currently Employed Full-Time (31+ hours)

19. Annual household income range:
    . less than $25,000 per year
    . $26,000-50,000 per year
    . $51,000-75,000 per year
    . $76,000-100,000 per year
    . $101,000-150,000 per year
    . $151,000-200,000 per year
    . more than $201,000 per year
20. How many people are in your household (including yourself)? _____

21. Type of insurance coverage:
    . I do not have any medical insurance.
    . I have medical insurance, but it does not cover any costs related to fertility treatments.
    . I have medical insurance, but it only covers part of the costs related to fertility treatment.
    . I have medical insurance and it covers all the costs related to fertility treatments.

22. What state do your currently live?
    . [Drop Down menu for 50 states and Washington D.C.]

23. What type of area do you live in?
    . Rural (outside or not near a city)
    . Urban (city)
    . Sub-urban (near a city)

24. How did you hear about or see the study?
    An OB/GYN Facebook page
    An infertility support group page
    An infertility information page
    I saw study page on Facebook
    A friend/family member shared the page
    A friend/family member told me about the study
    Other

25. Would you be willing to cut and send a small hair sample to test for a chronic stress hormone called cortisol? If yes, you will be emailed the cortisol level result. Please provide your email so a nurse researcher can contact you.
    Yes, my email is _____
    No

APPENDIX L: HAIR CARE QUESTIONNAIRE

Hair Care and Steroid Use Questionnaire for Hair Sample (per UMass) for those agreeing to give a hair sample.

1. Are you currently receiving health care for a medical condition?

___ Yes ___ No

If yes, please describe your medical conditions and list any medications that you are taking for each condition.

_____
_____
_____
_____

2. Are you currently taking any steroid medications <u>in pill form</u>? *Examples include hydrocortisone, cortisone, dexamethasone, methylprednisolone (Medrol), prednisone, and prednisolone (Orapred)*

___ Yes ___ No

If yes, please list the medication(s).

1. _____
2. _____

3. Are you currently taking any steroid medications by <u>nasal spray</u>?
Examples of nasal sprays include Flonase, Rhinocort, Nasacort, Nasonide, Nasarel, Beconase, Omnaris, Allernaze, Ticanase, Vancenase, Symbicort, Asmanex, Azmacort, Advair, Flovent, and Veramyst

___ Yes ___ No

If yes, please list the medication(s).

1. _____
2. _____

4. Are you currently taking any steroid medications by <u>skin cream or ointment</u>?
Examples of creams/ointments include hydrocortisone (Cortaid, Cortizone-10, Caldecort), dexamethasone, betamethasone (Diprolene), triamcinolone (Aristocort), and fluocinolone (Capex)

___ Yes ___ No

If yes, please list the medication(s).

1. _____

2. _____

5. Have you washed your hair in the last 24 hours? ___Yes ___ No

6. How often do you usually wash your hair?

___ daily ___ every other day ___ less frequently than every other day

7. Have you used a hair coloring, bleaching, straightening, or other hair product in the past 3 months?

___Yes ___ No

If yes, please indicate what type of product(s) you used.

1. _____
2. _____

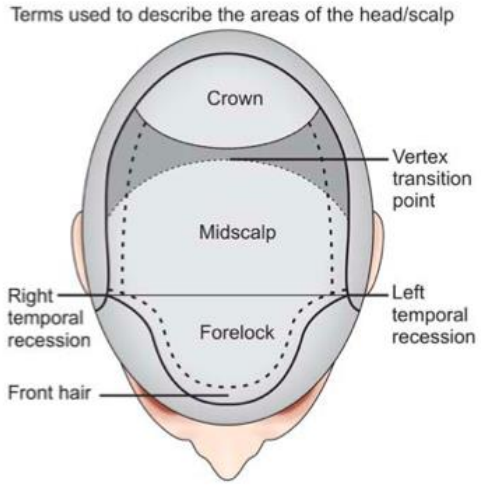
8. Have you been swimming once a week or more often in a chlorine pool over the past 3 months? ___Yes ___ No

9. Do you typically exercise 2 or more hours per day? ___Yes ___ No

APPENDIX M: HAIR SAMPLE PROCEDURE FOR PARTICIPANTS

Hair Sampling Procedure

Hair should be cut as close to the scalp as possible (taking care not to nick the skin) with a clean scissors. The total amount of hair to take is roughly the width of a pencil and cut from the "crown" of the head, as located in the image below.



1. There are 2 ways to cut the hair sample. One way is to cut the entire hair sample at once by cutting 1 small section of hair on the crown of the head. It is ok to cut the sample underneath other hair, so that longer hair can cover the sample area. Another option is to cut several small samples of hair from several places around the scalp at the crown of the head. You may wish to secure the hair you cut with a tight rubber band before making the cut at the scalp level if you think that is helpful. The following videos can be viewed to help in further instruction on how to collect the hair sample from your scalp. Remember, it is important to cut as close to the scalp as possible, without cutting or nicking the skin.

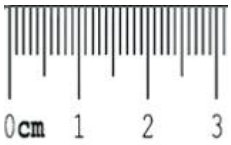
Videos of hair sample collection for further instruction

A. Hair sample taken from 1 area on crown of head:

https://www.youtube.com/watch?v=qE8ivQMU8pA

B. Hair sample taken from multiple areas on crown of head:
https://www.dropbox.com/s/inza7q7usa6m1fl/Hair%20Sample%20Collection%20Instructional%20Final.mp4?dl=0

2. After making the first cut, use a ruler to measure 3 cm from the cut end (the root of the hair). You can use the 3 cm ruler below to help you measure the length of hair needed. Cut the ends of the hair off, so that only 3 cm of hair that was closest to the scalp is taken for the sample. Once the hair has been cut to length, you can throw away the remaining hair in the trash. You do not need to mail the discarded hair.



3. Place the 3 cm of hair sample in the aluminum foil pouch. Return the foil pouch to the pre-stamped mailing envelope, and place in the mailbox.

Please contact the researcher below for any questions or concerns related to hair sample.

Alison Swift, MSN, RN, CNE, PhD(c) at ecuinfertilitystudy@ecu.edu or 252-744-6426

APPENDIX N: STUDIES INCLUDED IN REVIEW

Table 4.
Studies Included in Review

Author and Year	Design	Topic	Sample Size	Strategy	Consent obtained
Al Qadire 2019	Quantitative	Nursing Education	316	Snowball Sharing	Unknown
Akard et al. 2015	Quantitative	Parents of Children	45	Banner Ads	Yes
Atarhim et al. 2019	Quantitative	Nurses	208	Closed Group	Yes
Benham-Hutchins et al. 2017	Mixed Methods	Chronic Diseases	34	Snowball Sharing and Email Invites	Yes
Berry & Rutledge 2016	Quantitative	Women's Health	143	FB Page, Snowball Sharing	Unknown
Books et al. 2017	Quantitative	Nurses	101	FB Contacts and Email	Yes
Carter-Harris et al. 2016	Quantitative	Cancer	361	Banner Ads, Newspaper Ads	Unknown
Close et al. 2013	Quantitative	Pediatrics	43	Brochures/Flyers, Face to Face, Websites, Banner Ads	Unknown
du Plessis 2016	Qualitative	Nurses	Unknown	Articles, FB page	Yes
Fowler et al. 2019	Qualitative	Parents of Children	10	Public Page	Yes
Gage-Bouchard et al. 2017	Qualitative	Cancer	Unknown (18 pages with 15,852 posts but unknown # of participants)	Public Pages	No

Author and Year	Design	Topic	Sample Size	Strategy	Consent obtained
Gribble 2013	Qualitative	Women's Health	138	Banner Ads	Yes
Gribble 2014	Qualitative	Women's Health	138	Banner Ads	Yes
Helbing et al. 2017	Quantitative	Nurses	89	Public Page	Unknown
Hetland et al. 2018	Qualitative	Nurses	374	Public Page and Email	Yes
Jones et al. 2012	Quantitative	Pediatrics	70	Messenger, Study Page, Email	Unknown
Jones et al. 2015	Quantitative	Sexual Health/HIV	230	Banner Ads	Yes
Jones et al. 2017	Quantitative	Sexual Health/HIV	247	Banner Ads and Face to Face	Yes
Khumsaen & Stephenson 2017	Quantitative	Sexual Health/HIV	469	Banner Ads	Yes
Kim et al. 2016	Qualitative	Parents of Children	23	Public Pages, Websites, Blogs	No
Ko et al. 2013	Quantitative	Sexual Health/HIV	1,037	Banner Ads, Email	Yes
Ladores & Aroian 2015	Qualitative	Women's Health	12	Snowball Sharing/Flyers	Unknown
Marks et al. 2014	Quantitative	Parents of Children	66	Study Page	Unknown
Mitchell 2014	Quantitative	Sexual Health/HIV	361	Banner Ad	Yes
Moreno et al. 2012	Quantitative	Mental Health	224	Public Pages then Email	Yes

Author and Year	Design	Topic	Sample Size	Strategy	Consent obtained
O'Reilly et al. 2017	Mixed Methods	Traumatic Brain Injury	Unknown	Public Page	Yes
Perry et al. 2017	Quantitative	Chronic Disease	41	Banner Ads, Email	Yes
Rogers et al. 2009	Quantitative	Mental Health	328	Banner Ads	Yes
Santos Couto et al. 2018	Mixed Methods	Sexual Health/HIV	84	Public Group/Messenger	Yes
Staffileno et al. 2017	Quantitative	Women's Health	35	Banner Ads, Flyers, Websites	Yes
Wahlberg et al. 2016	Mixed Methods	Nurses	163	Public Pages, Flyers	Yes