Self-report of disordered eating and psychological symptoms by women with ovulatory and unexplained infertility compared with women receiving routine health care

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SELF-REPORT OF DISORDERED EATING AND PSYCHOLOGICAL SYMPTOMS BY WOMEN WITH OVULATORY AND UNEXPLAINED INFERTILITY COMPARED WITH WOMEN RECEIVING ROUTINE HEALTH CARE

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Self-Report of Disordered Eating and Psychological Symptoms: Women with Ovulatory and Unexplained Infertility Compared to Women Receiving Routine Health Care by Their Primary Care Providers

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Abstract

Studies suggest that eating disorder (ED) pathology may be linked to ovulatory and unexplained infertility in women who present to reproductive treatment centers. Specifically, studies have linked hypothalamic amenorrhea, oligomenorrhea, and anovulatory cycles to disordered eating. Advances in Assisted Reproductive Technology can lead to successful conception for women with ED; however, they have a higher risk for poor maternal and fetal outcomes.

This descriptive, comparative, quantitative study examined disordered eating and psychological symptoms in women with ovulatory and unexplained infertility compared with women receiving routine health care from their primary care providers. Women ages 20 to 44 were recruited. After providing verbal consent, a study packet was mailed to the study participant's home.

The Eating Disorder Inventory-3-Referral Form and Herman and Polivy Restraint Scale measured disordered eating symptoms. The Speilberger Anxiety Inventory and Beck Depression Inventory-II examined psychological symptoms. Provisional DSM IV TR diagnoses were

ascertained using the Eating Disorder Inventory-3-Symptom Checklist, along with other scale items.

Ninety women were consented and 85 women (51 with infertility; 34 receiving routine health care) returned the packet of instruments. Multivariate analysis of covariance (MANCOVA) confirmed that women with ovulatory and unexplained infertility had significantly higher Desire for Thinness (p = .001) and Bulimia (p = .007) subscale scores putting them at risk for Anorexia Nervosa or Bulimia. Women receiving routine care had significantly higher Body Dissatisfaction (p = .000) subscale scores consistent with their higher weight and tendency toward overeating. Women receiving routine care also had significantly higher Restraint (p = .000) scale scores, leaving them at risk for dietary disinhibition. The groups did not differ on psychological symptoms. Women with infertility had lifetime ED diagnoses many times the national ED prevalence rate, similar to the research findings of Freizinger et al. (2010).

The study results support that women with ovulatory and unexplained infertility are at risk for having an occult ED. The critical import of integrating ED assessment into infertility evaluation, reproductive and primary care was implicated. Further study to isolate biobehavioral markers to better identify women at risk for ED and improve their maternal and fetal outcomes was recommended.

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CHAPTER ONE

Statement of the Problem

Infertility is one of the most common chronic health disorders involving young adults. Infertility is defined as the inability to conceive after a minimum of one year of regular unprotected sexual intercourse (Speroff & Fritz, 2005; Strigh, 2005). Research outcomes reveal a potential link between eating disorders (ED) and infertility. Specifically, ovulatory infertility and unexplained infertility have been linked to ED among women presenting to infertility centers (Abraham, Mira & Llewellyn-Jones, 1990; Bates, Bates & Whitworth, 1982; Couzinet, et al., 1999; Loucks, & Verdum, 1998; Miller, Parulekar, Schoenfeld, Hubbard & Grinspoon, 1998; Stewart, Robinson, Goldbloom, & Wright, 1990). Disordered eating symptoms may be a possible contributor to infertility, and therefore, women experiencing infertility could report more disordered eating symptoms than a comparison group of women receiving routine health care by their primary care providers (PCP). Further study of women experiencing infertility was warranted to determine if disordered eating symptoms were increased in ovulatory and unexplained infertility, when compared to women receiving routine health care by their PCPs, using a carefully controlled comparison research design. To this end, this study was designed to fill the gap in knowledge.

Background and Significance

Infertility

The incidence of infertility in 2002 was 7.4% in women aged 15 to 44 years (National Survey of Family Growth [NSFG], 2002). Eighty-five percent of couples attempting to conceive will have been successful during a 1 year period (Speroff & Fritz,

2005). Clinical assessment of a couple's fertility is indicated if a pregnancy has not occurred within 1 year; although, earlier evaluation is indicated in women with a history of oligomenorrhea or amenorrhea, women older than age 35, and women with suspected pelvic pathology.

For women, gender-related etiologic factors involved in infertility include ovulation disorders, tubal disease, endometriosis and unexplained infertility (Collins et al. 1993). Other factors, such as luteal phase defect, are included among unexplained infertility (Keye, Chang, Rebar, & Soules, 1995; Speroff & Fritz, 2005). Unexplained factors can co-occur with ovulation, tubal, and peritoneal defects. Duration of fertility is an important prognostic feature, as is age (Smith, Pfeifer, & Collins, 2003). Overall, women with infertility have less than a 50% likelihood of proceeding to a live birth without treatment (US Congress Office of Technology Assessment, 1988).

Approximately 25% of infertile women in the US have fallopian tube disease, 5 to 10% of infertile women have endometriosis, and 25% have ovulation disorders (Imani, Eijkemans, te Velde, Habbema, & Fauser, 2002). Another 30% of infertile couples have unexplained infertility, which is defined as having normal basic test results assessing ovulation, tubal patency, and sperm production (Smith et al., 2003; Stewart, Robinson, Goldbloom, & Wright, 1990).

Altered Nutritional Intake in Women with Infertility

Observational studies. Despite limitations of small sample size and lack of control or comparison groups, results from early studies revealed a potential link between altered nutrition associated with disordered eating and ovulatory and unexplained infertility (Abraham, Mira & Llewellyn-Jones, 1990; Bates, Bates, & Whitworth, 1982).

Bates et al. (1982) found that the practice of maintaining a slim body appearance below ideal body weight (IBW) may result in unexplained infertility and abnormal menstrual cycles in otherwise well women. When following a diet designed to increase their body weight to calculated IBW, almost three-fourths of the women with infertility spontaneously conceived and most of the women with secondary amenorrhea resumed their menstrual cycles. Also, Abraham et al. (1990) found evidence of disordered eating or excessive exercise in women with secondary amenorrhea and ovulation failure who were undergoing gonadotropin releasing hormone (GnRH) treatment. However, this study outcome was unclear because excessive exercise often accompanies eating disorders (American Psychiatric Association, 2000; Morgan, 1999).

These early observational studies were limited in their small sample size and lack of adequate power. Lack of comparison groups was also a limitation. Finally, the Bates et al. (1982) study did not specifically investigate disordered eating symptoms.

Biobehavioral studies. Recent biobehavioral research provided additional support for the link between nutritional intake and amenorrhea. Specifically, leptin, a protein hormone expressed mainly by adipocytes, is an important hormone in satiety, metabolism, and reproductive function (Cunningham, Clifton, & Steiner, 1999; Mantzoros & Moschos, 1998). In particular, support for the association between altered nutritional intake and infertility can be found in biobehavioral studies of leptin (Boden, Chen, Mozzoli, & Ryan, 1996; Maffei et al., 1996; Jimerson, Mantzoros, Wolfe, & Metzger, 2000; Wolfe, Jimerson, Orlova, & Mantzoros, 2004).

Decreased leptin has been found in normal weight women with nutritional deficits and functional hypothalamic amenorrhea (FHA; Laughlin, Dominguez, & Yen, 1998).

Functional hypothalamic amenorrhea is defined as the cessation of menstrual cycles with no apparent structural irregularity of the brain, hypothalamus, pituitary or ovaries. Functional hypothalamic amenorrhea results due to a reduction in the hypothalamic gonadotropic-releasing hormone (GnRH) signal to the pituitary gland, resulting in anovulation (Ahima, 2004). The Laughlin et al. (1998) study suggests that adequate nutritional intake is critically important to leptin function and, hence, conception and fertility outcomes.

Leptin levels have been found to be reduced in women with eating disorders, a population characteristically exhibiting amenorrhea or oligoamenorrhea. Women with active anorexia nervosa demonstrated significantly decreased serum leptin levels, which normalized prior to full weight restoration (Eckert et al., 1998; Mantzoros, Flier, Lessem, Brewerton & Jimerson, 1997). Significantly lower leptin levels were also found in women with bulimia nervosa and recovered bulimia nervosa compared to normal controls (Jimerson et al., 2000).

Biobehavioral research outcomes to date suggest that adequate nutritional intake may be a key factor in leptin functioning and, hence, reproductive function. The import of the preceding observational and biobehavioral research outcomes is that disordered eating symptoms may be a possible contributor to infertility. Therefore, disordered eating symptoms may be found in greater numbers of women presenting to infertility centers than in women receiving routine health care from their PCP. Further study using a larger sample size was warranted to determine if disordered eating symptoms are increased in women experiencing ovulatory or unexplained infertility.

Women Experiencing Disordered Eating Symptoms

Disordered eating symptoms may be evidenced in women experiencing infertility in a number of ways. Women may restrict their intake of fat yet maintain a normal weight. Depression or anxiety symptoms may increase or decrease dietary intake. Some woman with infertility may experience EDs defined by the Diagnostic and Statistical Manual, Fourth Edition (DSM IV TR; American Psychiatric Association, 2000) diagnostic criteria. Finally, one infertility diagnosis, specifically Polycystic Ovary Syndrome (PCOS), is associated with beginning metabolic changes that could increase dietary intake (Linne, 2004; Speroff & Fritz, 2005).

Normal weight women with restrictive eating patterns. Women experiencing infertility can have disordered eating symptoms that do not meet full DSM IV TR (American Psychiatric Association, 2000) diagnostic criteria for Axis I ED. Results from a number of studies (Couzinet et al. 1999; Rock, Gorenflo, Drewnowski & Demitrack, 1996; Warren, Holderness, Lesobre, Tzen & Vossoughian, 1994) implicated unbalanced nutritional intake in functional hypothalamic amenorrhea (FHA) and suggested that restoring adequate nutrition might lead to the resumption of menstrual cycles. Additional evidence (Laughlin et al., 1998) pointed to severely restricted fat intake as being a critical factor in neuroendocrine-metabolic abnormalities found in stable weight, nonathletic women with FHA who did not meet DSM IV diagnostic criteria for eating disorder.

Finally, results from two studies of women with FHA and one study of women with hypothalamic amenorrhea (HA) suggested that balancing nutritional intake might restore gonadotropin hormone secretion. Restoring adequate nutrition led to the resumption of normal menstrual cycles and subsequent successful conception in women

with secondary amenorrhea (Abraham et al., 1990). Also, Couzinet et al. (1999) investigated gonadotropin hormonal secretion and biophysiological markers (ferretin, leptin, plasma free T_3, and other assays) of nutrition in women with FHA and healthy controls. Both groups of women were characterized by normal body mass index (BMI) and exercise. The nutritional markers indicated that mild but extended fat restriction interfered with gonadotropin hormone secretion in the women with FHA. Finally, Miller, Parulekar, Schoenfeld, Hubbard, & Grinspoon (1998) examined circulating leptin levels in normal weight women with hypothalamic amenorrhea (HA) and matched controls with normal menstrual cycles. The women with HA, unrelated to fat mass, had significantly lower fat intake and leptin levels. Taken together these studies support the importance of examining women with FHA and HA for disordered eating.

Women experiencing depression and anxiety. Symptoms of depression and anxiety could also contribute to unbalanced nutritional intake in women experiencing infertility. The depression and/or anxiety could be determined by multiple factors, such as the psychological burden of infertility, the negative sequelae of unbalanced nutritional intake, and other situational and biological factors. For example, dieting in healthy volunteers has been associated with lower levels of tryptophan, a metabolite of serotonin which is implicated in depression and possibly impaired in satiety (Wolfe, Metzger, & Stollar, 1997). Also, depressive symptoms were found to be more commonly experienced by women with infertility than by well women receiving routine health care. Domar, Broome, Zuttermeister, Seibel and Friedman (1992) examined women with infertility for symptoms of depression and found significantly elevated depression scores and two times the prevalence of depression.

One of the diagnostic criteria for DSM IV TR (American Psychiatric Association, 2000) Axis I major depression is excess or lack of appetite characterized by a 5% loss or gain of body weight within 1 month. Women who experience appetite changes during periods of anxiety are also at risk for unbalanced nutritional intake (Facchinetti, Fava, Fioroni, & Genazzani, 1993). Therefore, women with infertility who experience depression and anxiety warrant assessment for disordered eating symptoms.

Women experiencing eating disorders. Women who experience anorexia nervosa, bulimia nervosa, and eating disorder not otherwise specified are a high risk group psychologically and biologically (Wolfe, 2006). Women with anorexia nervosa by definition weigh less than 85% of their expected weight and have at least 3 consecutive months of amenorrhea associated with substantial neuroendocrine and psychological imbalance (American Psychiatric Association, 2000). Also, a large proportion of women with bulimia nervosa have amenorrhea and other women with bulimia nervosa experience problems with luteinizing hormone secretion (Devlin et al., 1989).

While in-vitro fertilization can lead to successful conception, women who have DSM IV TR (American Psychiatric Association, 2000) Axis I eating disorders have been found to have poor pregnancy and postpartum outcomes (Abraham et al., 1990; Franko et al., 2001; Lemberg & Phillips, 1989; Little & Lowles, 2000; Mitchell-Gieleghem, Mittelstaedt & Bulik, 2002; Morgan, Lacey, & Sedgwick, 1999; Namir, Melman, & Yager, 1986; Stewart, Raskin, Garfinkle, MacDonald, & Robinson, 1987). Moreover, Franko et al. recommend more frequent assessment of women experiencing a current or past eating disorder to assure successful fertility, pregnancy and postpartum outcomes.

Therefore, it is a reasonable goal to ensure adequate physiologic and psychological stability in women experiencing eating disorders prior to initiating infertility intervention.

Women with Polycystic Ovary Syndrome. Problems with infertility, menstrual irregularity typical of anovulation, and androgen excess most frequently lead women experiencing polycystic ovary syndrome (PCOS) to seek medical evaluation. Additionally, a pattern of androgenic fat distribution, insulin resistance and elevated leptin levels in obese women with PCOS (Ertuck et al., 2004; Sepilian, Crochet, & Nagamani, 2006) warrants examination for disordered eating symptoms in women experiencing this complex disorder.

The observational and biobehavioral research outcomes discussed above implicate disordered eating symptoms as potentially having a role in infertility. These outcomes suggest that women with ovulatory and unexplained infertility could report greater levels of disordered eating symptoms when compared with women receiving routine health care from their PCP. Further study of women with ovulatory and unexplained infertility for eating disordered symptoms was warranted using a large sample and carefully controlled research design.

Purpose of the Study and Research Questions

The overall goal of this descriptive, comparative study was to investigate disordered eating symptoms in women with ovulatory and unexplained infertility in comparison to a group of women receiving routine health care from their PCP. The study answered the following research questions through testing the stated hypotheses:

Research Question 1: Do women with ovulatory and unexplained infertility significantly differ from women receiving routine health care from their PCP in disordered eating

symptoms as measured by the Eating Disorder Inventory-3-Referral Form (EDI-3-RF; Garner, 2004) and Eating Disorder Risk Composite subscale raw scores?

Hypothesis 1: After controlling for selected variables (age, education, income, marital status, work status, race and current BMI), women experiencing ovulatory and unexplained infertility will report significantly more disordered eating symptoms than women receiving routine health care from their PCP.

Research Question 2: Do women with ovulatory and unexplained infertility significantly differ from women receiving routine health care from their PCP in meeting DSM IV TR (American Psychiatric Association, 2000) Axis I eating disorder criteria using participant responses on the Eating Disorder Inventory-3-Symptom Checklist (EDI-3-SC; Garner, 2004)?

Hypothesis 2a: Women experiencing ovulatory and unexplained infertility will report significantly more current DSM IV TR (American Psychiatric Association, 2000) Axis I eating disorders than women receiving routine health care from their PCP.

Hypothesis 2b: Women experiencing ovulatory and unexplained infertility will report significantly more past DSM IV TR (American Psychiatric Association, 2000) Axis I eating disorders than women receiving routine health care from their PCP.

Research Question 3: Do women with ovulatory and unexplained infertility significantly differ from women receiving routine health care from their PCP in symptoms of depression, anxiety, and dietary restraint as measured by participants' total scores on the

Beck Depression Inventory II (Beck, Steer & Brown 1996), the State - Trait Anxiety Inventory (Speilberger, 1989) and the Restraint Scale (Herman & Polivy,1980).

Hypothesis 3: After controlling for selected variables (age, education, income, marital status, work status, race and current BMI), women experiencing ovulatory and unexplained infertility will report significantly more symptoms of depression, anxiety, and dietary restraint than women receiving routine health care from their PCP.

Definitions

Infertility. Infertility is defined as the inability to become pregnant despite efforts to conceive for 1 year duration (Stephen & Chandra, 1998). Etiologic factors involved in infertility include ovulation disorders, tubal disease, endometriosis and unexplained infertility. These factors can co-occur or occur with male factors. Research outcomes indicate that women with ovulation problems or unexplained infertility may have disordered eating symptoms, and thus, women with infertility that have ovulation and explained infertility will be examined and compared with women receiving routine health care from their PCP. The presence of ovulatory or unexplained infertility was determined by the self-report of women who self-refer to the study.

Ovulatory infertility. Infertility related to problems developing oocytes is termed ovulatory infertility. Ovarian function is evaluated by FSH, LH, estradiol (E) and other hormonal tests. Ovulatory dysfunction can be present in women who experience menstrual cycles < 22 days (polymenorrhea), > 35 days (oligomenorrhea), or no menses (amenorrhea). Poly Cystic Ovary Syndrome (PCOS) (estimated occurrence 70%) (Knochenhauser et al., 1998), hypothalamic amenorrhea (10%), hyperprolactinemia

(10%), and premature ovarian failure (10%) are the most frequent etiologies of ovulatory dysfunction (Barbeiri, 2002).

Unexplained infertility. Unexplained infertility is diagnosed when a woman is having difficulty conceiving and her diagnostic infertility tests (semen analysis, tests of ovulation, hormonal profile, uterus and tubal patency) are all normal. Unexplained infertility may represent a problem of having a subthreshold case of one of the infertility diagnoses where the infertility tests remain within the normal range (Templeton, 2000).

Exercise. Exercise is defined as the exertion of the muscles or limbs for purpose of strength, health, and/or weight management. Descriptive information on exercise was characterized by participant's responses to the exercise questions on the EDI-3-SC (Garner, 2004).

Body Mass Index. BMI is a measure of body fat that is the ratio of the weight of the body in kilograms to the square of its height in meters (Gallagher, et al., 2000). BMI is a reliable indicator of total body fat, which is related to the risk of disease and death. BMI categories include: <18.5 indicates an underweight condition, 18.5 to 24.9 is considered healthy, 25.0 to 29.9 is considered overweight, 30 to 39.9 indicates obesity, and over 40 is considered morbidly obese (Janssen, Katzmarzyk, & Ross, 2002). Body Mass Index was calculated from information reported by study participants on the EDI-3-RF (Garner, 2004).

Menstrual Status. Menstrual status describes the temporal characteristic of women's monthly sexual cycles. These characteristics are normal menstrual cycles, oligomenorrhea, and amenorrhea. Menstrual status was operationalized by participants'

report on the Eating Disorder Inventory-3 Symptom Checklist (EDI-3 SC; Garner, 2004) using the following parameters:

Normal menstrual cycles. Normal menstrual cycles are defined as monthly cycles occurring in the range of every 21 – 35 days (Griffin & Ojeda, 1996).

Oligomenorrhea. Oligomenorrhea is defined as menstrual cycles occurring > 35 days.

Amenorrhea. Amenorrhea is defined as the failure of menarche by age 16 (primary amenorrhea) or the cessation of menses for ≥3 months in a woman with a history of periodic menstruation (secondary amenorrhea) (American Psychiatric Association, 2000; Burch, 1994; Griffin & Ojeda, 1996).

Depressive Symptoms. Depressive symptoms include feelings of sadness, pessimism, and failure, punishment and guilt feelings, loss of interest and pleasure, self-dislike and self criticalness, feelings of worthlessness, suicidal thoughts, crying, agitation, irritability, indecisiveness, changes in appetite and sleep, concentration problem, loss of energy, tiredness and fatigue, and loss of interest in sex. Depressive symptoms, a potential psychological influence on disordered eating, were measured by participants' total scores on the Beck Depression Inventory-II (BDI-II; Beck, & Steer, 1987).

Anxiety Symptoms. Anxiety symptoms comprise an uncomfortable emotional state distinguished by personal feelings of pressure or strain, trepidation, apprehension and worry and by autonomic nervous system arousal. Anxiety may be transitory (state) or more enduring where it influences and individual's disposition and reactivity to stress (trait). Anxiety symptoms was measured by participants' total scores for the separate

State (S) and Trait (T) scales on the Speilberger State – Trait Anxiety Inventory (Spielberger, 1989).

State anxiety. State (S) anxiety refers to an obvious uncomfortable emotional reaction taking place at a given time and place.

Trait anxiety. Trait (T) anxiety refers to long-term anxiety traits such as long - term negative self appraisal. Trait anxiety addresses unvarying differences in an individual's anxiety proneness and tendency to identify stressful circumstances as intimidating. The individual tends to respond to the stressful circumstances with elevations in their state anxiety. The concept of trait anxiety also addresses the individual's past experience with anxiety and the likelihood that state anxiety will be experienced in the future.

Disordered Eating Symptoms. Disordered eating symptoms are characterized by perceptions, alterations in food ingestion and/or compensatory behaviors intended to manipulate body weight and/or shape, which significantly impair health and psychological functioning, and are not better accounted for by diabetes, another medical condition (malabsorption syndromes) or another psychiatric illness (Klein & Walsh, 2004). Eating disorder symptoms were measured by participant's raw scores on the Eating Disorder Inventoy-3-RF subscales of the Eating Disorder Risk Composite (Garner, 2004).

Eating disorder diagnoses. Eating disorder diagnoses were determined by participant report of specific eating symptoms on the EDI-3- SC and other selected scale items. Eating disorder diagnosis was assessed by the Principal Investigator transcribing information from the ECI-3-SC and selected other items from the ED scales to the SCID

Module H along with the DSM IV TR (American Psychiatric Association, 2000) manual EDNOS criteria Axis I diagnostic criteria and rated 0 = no diagnosis and 1 = meets diagnostic criteria for a diagnosis. Diagnostic criteria are described for the following eating disorder syndromes: Anorexia Nervosa, Bulimia Nervosa, Eating Disorder Not Otherwise Specified and the provisional diagnosis for further investigation, Binge Eating Disorder. The eating disorder diagnostic criteria below were adapted from the DSM IV TR (American Psychiatric Association, 2000). Participants can meet only one diagnosis currently, although, may have met criteria for a different diagnosis in the past.

Anorexia nervosa. The diagnostic criteria for Anorexia Nervosa includes the following: (A) Refusal to maintain a body weight or weight loss below 85% of expected body weight; (B) intense fear of being fat is expressed despite having an underweight condition; (C) disturbance in how one's body is perceived, excessive influence of weight or shape on self-assessment, or rejection of the gravity of the low weight condition; and (D) amenorrhea of 3 months or more duration. Restricting or binge-eating/purging type must be distinguished.

Bulimia nervosa. The diagnostic criteria for Bulimia Nervosa includes the following: (A) Recurring episodes of binge eating depicted by (1) eating a large amount (more than most people could ingest) of food within a 2 hour period and (2) experiencing a lack of control of the eating episode; (B) engaging in compensatory behaviors to assuage weight gain, which could include purging behavior (vomiting, laxatives, other medication) or extreme exercise; (C) the binges and behavior to recompense the effect of the binges both take place at least two times a week over a temporal period of three months or more; (D) self-perception is disproportionately biased by weight and shape;

and (E) the disturbance does not take place during an occurrence of Anorexia Nervosa. The type of episode must be distinguished by purging or nonpurging.

Eating disorder not otherwise specified. This diagnostic category is for eating symptoms that suggest the person has an eating disorder that does not meet criteria for the eating disorders described above. Exemplars include: (1) individuals who meet criteria for anorexia nervosa except that the they menstruate regularly, (2) individuals who meet all criteria for anorexia nervosa, except they maintain their weight above 85% IBW, (3) individuals who meet criteria for bulimia nervosa, except the binges and compensatory behaviors occur less than two times a week or for less than 3 months duration, (4) the compensatory behaviors occur after ingesting small amounts of food and binges are not evident, and (5) binges occur but the individual does not swallow the food and, instead, spits it out, and (6) binge eating without regular compensatory behavior.

Binge eating disorder. The criteria for Binge Eating Disorder are provided in the DSM TR IV (American Psychiatric Association, 2000) for further study. The criteria are as follows: (A) Recurrent binge episodes where a disproportionate amount of food is ingested in a short period (2 hours) of time with a loss of control over the amount and type of food; (B) three or more characteristics of eating are present; (1) eating more rapidly than normal, (2) eating despite discomfort from fullness, (3) eating large amounts despite lack of physical experience of hunger, (4) eating in isolation to hide shame about one's large intake, and (5) experience of self-disgust and guilt after eating; (C) distress about the binge eating; (D) binges occur 2 days a week for 6 months; and (E) compensatory behaviors are not regularly used to offset binges.

Dietary Restraint. Dietary Restraint describes cognitive control of eating behavior in individuals who have an enduring focus on dieting. Restrained eating contributes to disinhibited eating behavior (Polivy & Herman, 1985). Research indicated that dieting behavior was clarified to consist of periods of restraint counterbalanced by periods of disinhibited eating. Dietary restraint, a possible influence on disordered eating symptoms, was measured by participants' total scores on the Herman and Polivy (1980) Restraint Scale.

Significance

This study aims to determine if disordered eating symptoms are increased in women with ovulatory and unexplained infertility in comparison with a sample of women receiving routine health care from their PCP. Inquiry in this area might provide important knowledge to inform the assessment process of nurses who assess and counsel women with infertility and inform the assessment and treatment of women with eating disorders by advanced practice psychiatric nurses. Finding a significant difference in the proposed study would provide a foundation to later pursue biobehavioral nursing research of women with ovulatory or unexplained infertility.

Assumptions

The self-report tools assessing eating disorder symptoms, menstrual function, exercise, psychological symptoms, and dietary restraint have been psychometrically validated and utilized extensively in clinical trials. It is assumed that the women will fill out the self-report measures honestly.

Studies show that leptin, a metabolic hormone, has an important role in reproductive functioning. In this study it is assumed that leptin is a candidate link

between energy balance and reproductive functioning (ovarian functioning and endometrial implantation).

Limitations

Limitations of the proposed study include its descriptive, cross-sectional design and use of a non-random sample. However, while obtaining a single assessment in time, the proposed study advances current knowledge by utilizing a larger sample than previous reports and the use of a comparison group to allow for greater generalization of findings.

CHAPTER TWO

Review of the Literature

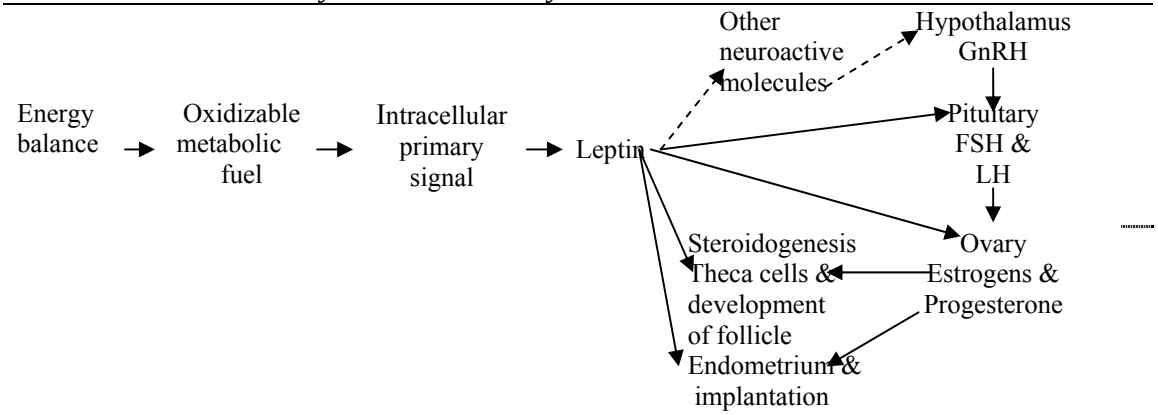
Chapter Two begins with conceptual framework and model for the proposed study. Normal female hormonal function is next reviewed. Areas of the literature related to infertility, energy balance, and disordered eating symptoms are examined. Ovulatory and unexplained infertility is reviewed along with studies at reproductive clinics suggesting the influence of disordered eating. Review of the role of the adipocyte-derived hormone, leptin, on hypothalamic-pituitary-gonadal (HPG) axis functioning provides a possible physiological link between disordered eating symptoms and ovulatory and unexplained infertility.

Conceptual Framework and Model for the Proposed Study

The conceptual framework (Figure 1) provides additional scientific support to pursue research on disordered eating symptoms in women with infertility. The framework contains the investigator's synthesis of normal female hormone functioning, the metabolic fuel hypothesis proposed by Wade, Schneider, and Li (1996) and the developing scientific knowledge of leptin, a hormone marker of energy availability and balance, that has a role in reproduction (Moschos, Chan & Mantzoros, 2002; Schneider, Zhou, & Blum, 2000). Within the conceptual framework, neuroendocrine (hypothalamic and pituitary hormone) control of reproductive physiologic processes (development of the ovarian follicle and the endometruim for implantation) is extremely sensitive to energy balance, as well as to short-term availability of metabolic fuels.

Figure 1

Conceptual Synthesis of Wade's Metabolic Fuel Hypothesis and Leptin's Effect on the Female Hormone System and Fertility



Metabolic Fuel Hypothesis. Wade et al. (1996) posited that reproductive physiologic function responds to short-term fluctuations of metabolic fuel availability. Examining both comparative and human studies of the effect of metabolic manipulation on reproduction, the authors emphasize the vital importance of having a "balance between energy intake and expenditure" (p. E6) rather than requiring a fixed level of either one. Momentary to hourly energetic changes in intracellular metabolic fuel availability and oxidation (rather than energy reserves alone) are relayed by secondary metabolic cues, such as leptin, through neural pathways and neurotransmitters to forebrain effector neurons that regulate hypothalamic GnRH emission. The metabolic fuel hypothesis explains the multiple causes of nutritional infertility, for example, lack of adequate food, extreme exercise, eating disorders, lacatation, certain kinds of obesity, and poorly controlled diabetes mellitus. Wade et al. (1996) also identified potential promise in studying the role of leptin, the then newly identified adipose-derived hormone, on reproduction.

Since Wade et al. (1996) advanced the metabolic fuel hypothesis, outcomes of studies have supported that conditions associated with suboptimal nutritional intake and conditions with excess energy reserves may negatively affect reproductive outcomes (Moschos et al., 2002). Many of the studies focus on the role of leptin as a marker of the adequacy of energy resources and a critical substance for a number of physiologic processes, including reproduction. Suboptimal nutrition was associated with decreased serum leptin levels in women experiencing eating disorders (Considine et al., 1996; Jimerson et al., 2000; Monteleone, Fabrazzo, Tortorella, Fuschino, & Maj, 2002), amenorrhea related to extreme exercise (Landt et al., 1997) and decreased hypothalamic function (Miller et al., 1998).

Excess energy reserves and metabolic problems, such as found in obesity and polycystic ovary syndrome (Pasquali & Gambineri, 2006), has been associated with elevated serum leptin levels and possible leptin resistance (Moschos et al., 2002). The Moschos et al. understanding of leptin raises the question of whether or not a critical level of short-term metabolic fuel availability balanced with energy reserves is required for successful reproductive physiologic processes. Reserves above a critical level may negatively influence reproduction through possible leptin resistance.

Leptin as a link between energy balance and reproduction. Food intake leads to oxidizable metabolic fuel. Short-term fuel availability, energy stores and exercise determine energy balance. Overall energy balance indirectly influences leptin secretion (Cioffe et al., 1997) through a yet to be identified intracellular primary metabolic signal (Schneider et al., 2000). Leptin acts as a cue between the primary metabolic signal and

reproduction (Chehab, Qui, Mounzih, Ewart-Toland & Ogus, 2002; Schneider et al., 2000).

Leptin has a stimulatory effect on the hypothalamic-pituitary-gonadal (HPG) axis. It acts in concert with other neuroactive substances on the hypothalamus and GnRH secretion and directly on pituitary gonadotropes responsible for follicular stimulating hormone (FSH) and luteinizing hormone (LH) (Moschos et al., 2002). Leptin also directly affects both the granulosa cells in the ovary and the uterine endometrium. Therefore, low levels of leptin detected in states of suboptimal nutrition affect sex steroid (estradiol and progesterone) production by the granulosa cells in the ovarian follicle via leptin's reduced effect on LH and to a minor degree FSH secretion and by a direct effect on leptin receptors in the granulosa cells that develop into follicles (the female hormonal system is discussed below).

Excess leptin has a direct inhibitory effect on ovulation through restraining estradiol production. The lower estradiol secretion decreases the elaboration of the granulosa cells, the development of the theca interna, and oocyte maturation. Therefore, high leptin levels found in obesity have been associated with problems in follicular maturation and anovulatory cycles (Mochos et al., 2002).

The Wade et al. (1996) metabolic fuel hypothesis and the understanding of leptin as a critical substance involved in reproductive physiologic processes provide an initial understanding of a link between disordered eating symptoms and infertility.

Figure 2
Conceptual Model for the Proposed Study

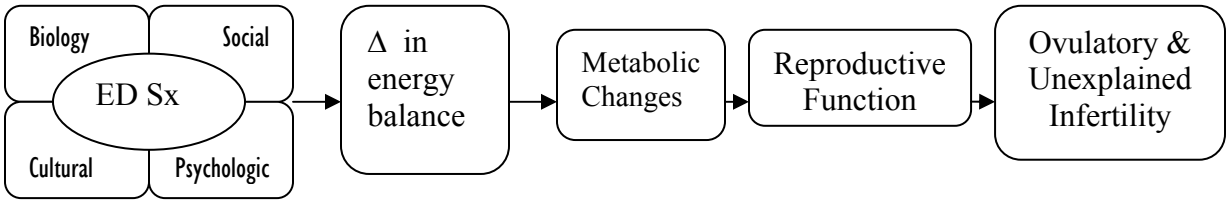


Figure 2 contains the conceptual model for the proposed study. While the focus of the framework has been on the metabolic link to neuroendocrine processes (Wade, Schneider, & Li, 1996; Wade, 1998), the conceptual model for the proposed study recognizes that multiple etiologies, including psychological, cultural, social, and biological factors, may contribute to disordered eating symptoms. The proposed study investigates disordered eating symptoms in women with ovulatory and unexplained infertility and women receiving routine health care from their PCP and examines the continuum of occult disordered eating symptoms through the DSM IV TR (American Psychiatric Association, 2000) Axis I eating disorders.

Normal female hormonal function. Monthly rhythmical alterations in the rates of female hormone release and corresponding changes in the ovaries and other sexual organs characterize the normal reproductive years of women. The regular pattern is referred to as the female monthly sexual cycle (Guyton & Hall, 2006). The average duration of the cycle is 28 days. Cycles could occur as short as 20 days or as long as 45 days; although, decreased fertility has been associated with abnormal cycle length (Speroff & Fritz, 2005). The female sexual cycle is set to produce two important outcomes: the maturation of a single ovum each month, so that one fetus will grow at a time, and the preparation of the uterine endometrium for successful implantation of a fertilized ovum (Tortora & Derrickson, 2006).

The female hormonal system is made up of three hierarchies of hormones: (1) gonadotropin-releasing hormone (GnRH) secreted from the hypothalamus; (2) follicular-stimulating hormone (FSH) and luteinizing hormone (LH), anterior pituitary sex hormones secreted in response to GnRH secretion by the hypothalamus; and (3) estrogen and progesterone, ovarian hormones secreted in response to FSH and LH by the anterior pituitary (Figure 1) (Guyton & Hall, 2006). Secretion of hypothalamic and pituitary hormones varies at different rates or pulses at different times of the monthly cycle. The hormonal pulses vary throughout the proliferative and secretory phases of the monthly cycle. GnRH secretion increases and decreases less drastically during the monthly cycle in short pulses every 90 minutes (Porterfield, 2001). FSH and LH are secreted in a pulsatile fashion at different amounts during different times of the cycle. Both FSH and LH stimulate their ovarian target cells through combining with their respective highly specific receptors in the ovarian target membranes (Guyton & Hall, 2006). The activated receptors in turn increase the cells' rates of secretion, growth and proliferation through activation of the second messenger system causing the formation of key enzymes that simulate sex hormone synthesis (estrogen and progesterone) (Guyton & Hall, 2006).

Effect of the pituitary hormones on sex hormone synthesis. During the first few days of the monthly female sexual cycle, the FSH and LH concentrations are to some extent increased, with FSH being slightly greater and earlier than LH by a couple of days (Guyton & Hall, 2006; Porterfield, 2001; Tortora & Derrickson, 2006). These hormones, especially FSH, enhance the growth of 6 to 12 primary ovarian follicles each month. The initial effect leads to rapid production and elaboration of ovarian granulosa cells (Porterfield, 2001). First, a second mass of cells develops called the theca. The theca

then divides into two layers, the theca interna, which develops the ability to secrete additional estrogen and progesterone, and the theca externa which develops very vascular connective tissue that becomes the exterior of the developing follicle (Guyton & Hall, 2006). In addition to stimulating follicular growth, estrogen also stimulates proliferation of endometrium (Porterfield, 2001).

After the initial growth, the mass of granulosa cells secretes a follicular fluid with a high concentration of estrogen. Positive feedback loops lead to both greater FSH sensitivity and greater estrogen secretion. The FSH and the estrogens combine to promote the development of LH receptors creating a more rapid increase in follicular secretion leading to explosive growth of the follicles (Guyton & Hall, 2006; Tortora & Derrickson, 2006).

After a week of growth, but before ovulation, one follicle outgrows the others and the other follicles involute and become atretic. The large amount of estrogen expressed from the follicle depresses FSH output from the pituitary, which blocks the growth of less developed follicles. The process of atresia generally allows for only one follicle to reach full maturation (Guyton & Hall, 2006; Tortora & Derrickson, 2006).

Two days prior to ovulation, LH secretion by the anterior pituitary increases 6 to 10 fold while FSH increases 2 to 3 fold. The prolonged excessive estrogen secretion ceases one day prior to ovulation (Tortorta & Derrickson, 2006). LH is critical for final follicular growth and ovulation. After ovulation, the granulosa cells become the corpus luteum (Porterfield, 2001) and progesterone secretion from the corpus luteum increases. The pituitary hormones act synergistically to cause rapid swelling of the follicle, and LH affects the theca and granulosa cells converting them to progesterone–secreting cells

(Guyton & Hall, 2006). Progesterone prepares the secretory endometrium in the uterus for implantation and develops the alveolar tissue of the breast (Porterfield, 2001).

In summary, a complex process within the hypothalamus-pituitary-gonadal (HPG) axis is responsible for the development of ovarian follicles and the preparation of the uterine endometrium for implantation of the ova. Since only 20% of fertile couples will conceive in a cycle (Speroff & Fritz, 2005), it is presumed that fluctuations within HPG hormonal axis, associated physiological processes, and other female and male factors explain the low percent of conception per cycle.

Infertility

The NSFG (2002) estimated a 7.4% incidence of infertility in women aged 15 to 44 years. Ovulatory dysfunction, tubal and peritoneal pathology, male factors, infertility unexplained by diagnostic tests, and less commonly occurring uterine factors are the major causes of infertility (Speroff & Fritz, 2005). Speroff and Fritz (2005) identify central factors of the reproductive process requiring evaluation are male factors, ovarian factors, cervical factors, tubal factors and uterine factors. Infertility evaluation is aimed at isolating and examining the components of the human reproductive process as well as discovering problems that could possibly interfere with conception. Since previously insoluble infertility difficulties can now be bypassed by assisted reproductive technologies (ART), the speed and scope of the evaluation are determined by the couple's desires, length of infertility, and individual particularities of the medical history and physical examination (Collins et al., 1993). Because time is of the essence for the infertile couple, less emphasis is situated on determining a precise diagnosis than on implementing the most efficacious and cost-effective treatment (Speroff & Fritz, 2005).

Ovulatory dysfunction. Twenty-five percent of women experiencing infertility have ovulatory problems (Imani et al., 2002). Menstrual cycles between 22 and 35 days, accompanied by bloating, dysmenorrhea, and breast sensitivity imply that ovulation is occurring. Ovulatory dysfunction can be present in women who experience menstrual cycles < 22 days (polymenorrhea), cycles > 35 days (oligomenorrhea), or no cycles (amenorrhea). Polycystic ovary syndrome (PCOS; estimated occurrence of 70% of women with ovulatory problems; Knochenhauser et al., 1998), hypothalamic amenorrhea (10%), hyperprolactinemia (10%), and premature ovarian failure (10%) are the most frequent etiologies of ovulatory dysfunction (Barbieri, 2002).

Polycystic ovary syndrome is characterized as the occurrence of oligoamenorrhea or amenorrhea and hyperandrogenism without evidence of other hyperandrogenic disorders. Polycystic ovary syndrome is also considered a metabolic disorder due to the co-occurrence of symptoms indicative of syndrome X (Linne, 2004). Hypothalamic (HA) amenorrhea is a diagnosis of exclusion (Speroff & Fritz, 2005). Regarded as a central nervous system disorder, hypothalamic amenorrhea generally is suggested by low levels of GnRH emission, withdrawal bleeding only in response to progestational challenge, and low or normal levels of LH and FSH with normal prolactin and thyroid stimulating hormone levels (Barbieri, 2002; Speroff & Fritz, 2005). Hyperprolactinemia with prolactin level greater than100 ng/ml requires Magnetic Resonance Imaging (MRI) for a pituitary secreting adenoma; although, Speroff & Fritz (2005) caution that microadenoma was found in up to 27% of people in an autopsy series. Premature ovarian failure occurs in 1% of women prior to the age of 40, and women experiencing primary amenorrhea have a 10% to 28% incidence of premature ovarian failure. Women with

premature ovarian failure have withdrawal bleeding from progestational challenge but have high gonadotropin levels (Speroff & Fritz, 2005).

Unexplained infertility. When semen analysis, tests of ovulation, uterus and tubal patency are normal, unexplained infertility is diagnosed (Templeton, 2000). This diagnosis represents the lower extreme of normal reproductive efficiency and limitations of the knowledge of the fertilization process (Collins & Crosignani, 1992; Speroff & Fritz, 2005)).

A lesser understood condition thought to occur in some women with unexplained infertility is luteal phase deficiency. Luteal phase deficiency addresses cases of infertility along the continuum between fertility and infertility, is thought to be responsible for cases of subfertility, and may explain some cases of unexplained infertility (Collins & Crosignani, 1992). This is a speculative disorder where ovulation occurs, but the corpus luteum produces levels of progesterone insufficient to support successful implantation (American College of Obstetrics & Gynecology Practice Bulletin, 2002). The lack of controlled trials with women with established fertility renders luteal phase deficiency more of a putative condition than a clear cut disorder.

Another condition that could have a role in unexplained infertility is minimal and mild endometriosis (Speroff & Fritz, 2005). While it is clear that advanced stage endometriosis with endometriomas and adhesions can greatly impair fertility, the effect of mild endometriosis is less understood. Similarly, subthreshold difficulties with characteristics of the semen, the uterus, or fallopian tube patency may be better understood in the future.

Ovulatory dysfunction can preclude conception (anovulation) or be a contributory factor (oligoovulation). However, it must be again noted that only 20% of fertile couples will conceive in a cycle (Speroff & Fritz, 2005); and thus, a diagnosis of ovulatory problems can change over time.

Studies Conducted at Reproductive Clinics

Research outcomes of studies conducted at reproductive clinics revealed a potential link between the altered nutritional intake associated with disordered eating symptoms and the ovulation disorders of infertility. Bates et al. (1982) examined the effect of weight control on menstrual cycles, serum FSH and LH, and infertility, as well as the effect of weight restoration on reproduction. The sample was comprised of 29 women with unexplained infertility (93% with menstrual irregularity) and 18 women referred due to menstrual irregularity but seeking to conceive. Participants were interviewed regarding menstrual history and cycle characteristics, pregnancies, maximum body weight and weight control practices, and physical activity. Serum gonadotropins were measured. Luteinizing hormone and FSH were related to ideal body weight. Nineteen of the 26 women experiencing infertility spontaneously conceived with weight gain. The outcomes suggested that luteal phase deficiency may be associated with dieting behavior, and thus, dieting behavior may be an unrecognized etiology of reproductive problems.

Stewart et al. (1990) prospectively assessed 66 consecutive women with infertility at a university reproductive service. The Eating Attitude Test (EAT) was administered and participants were questioned regarding current and historical weight, menstrual history, and gynecologic history. Participants scoring $\geq$ 20 on the EAT were interviewed

for DSM III (American Psychiatric Association, 1983) diagnosis of an eating disorder. Eleven women (7.6%) were identified as having an eating disorder. When eating disorders not otherwise specified EDNOS was included, 16.7% of the women had an eating disorder. Eating Attitude Test scores were significantly elevated ($p < 0.0001$) in women with menstrual irregularity. Fifty-eight percent (58%) of the women with infertility who had amenorrhea or oligomenorrhea had eating disorders. Stewart et al. highlight the elevated rate of eating disorders in their participants from the reproductive clinic. The rate in their study was 2 to 4 times the rate predicted by population studies. None of the women with an eating disorder in the Stewart et al. study informed their physician of their disordered eating symptoms.

Abraham et al. (1990) examined the eating and exercise histories of 14 women with secondary amenorrhea who were being treated with GnRH after failing Clomid treatment at an infertility clinic. Participants were interviewed for changes in weight, exercise, and eating behaviors, menstrual history, and past physical or psychiatric illness. The EAT and Eating Disorder Inventory were administered and weight, height and body fat were measured. Thirteen of the women met diagnostic criteria for eating disorders. Two women were previously diagnosed with depression. Five of the participants were currently diagnosed with eating disorder not otherwise specified, and two women were compulsive exercisers. Abraham et al. suggested assessing and treating disordered eating and exercise behavior prior to initiating infertility drugs to induce ovulation because of the risk for negative pregnancy outcomes.

Results from the studies discussed above revealed a potential link between disordered eating symptoms and ovulation disorders and unexplained infertility. A

methodological limitation of these early studies was small sample size and lack of adequate power. The studies were also limited by lack of a comparison group. Finally, Bates et al. (1982) did not systematically investigate disordered eating symptoms.

Later research involved investigations in weight stable women with functional hypothalamic amenorrhea (FHA) and comparison groups. Marcus, Loucks and Berga (2001) examined 77 women with amenorrhea (28 with FHA, 18 with primary ovarian failure since menarche, 24 with organic amenorrhea, and 25 healthy volunteers. Participants with DSM IV TR (American Psychiatric Association, 2000) disorders were excluded using the Structured Clinical Interview for the Diagnostic and Statistical Manual IV (SCID; Spitzer, Williams, Gibbon, & First, 1992). The Eating Disorder Inventory-2 (EDI-2; Garner, 1991) was administered. Women with FHA reported more dieting and weight concerns, subclinical binges, and apprehension of weigh gain. Women experiencing FHA also demonstrated more characteristics associated with eating disorders such as, perfectionism and concern regarding judgment by others.

Couzinet et al. (1999) assessed 12 women experiencing functional hypothalamic amenorrhea with normal BMI and exercise activity with 12 age and BMI matched healthy volunteers and 6 women with congenital hypothalamic hypogonadism for comparison of GnRH secretion and possible reversible nutritional contribution. Selected pituitary and gonadal hormones, the GnRH agonist test, dietary intake, body composition, and nutritional markers (ferretin, TSH, leptin and other assays) were assessed. Women with functional hypothalamic amenorrhea consumed significantly less fat than the healthy volunteers; and nutritional markers, including leptin, were significantly decreased. Couzinet et al. (1999) determined mild dieting with extended fat restriction was able to

interfere with gonadotropin emission. The researchers recommended assessment of nutritional markers to identify mild nutritional deficits as a possible reversible etiology of functional hypothalamic amenorrhea.

Verri et al. (1998) studied the relationship between secondary amenorrhea, due to hypogonadotropic, hyperandrogenic, and hyperprolactinemic etiologies, eating disorders and psychiatric comorbidity. None of the participants, recruited from the reproductive clinic, were seeking help for infertility. Modules of the SCID (Spitzer, Williams, Gibbon, M., & First, 1992) assessed mood, anxiety and eating disorders. Eating disorders were significantly increased in women with hypogonadotropic amenorrhea. Also, 40.9% of women with hyperandrogenic amenorrhea had eating disorders. Women experiencing eating disorders had a high incidence of psychiatric comorbidity; however, women who did not have eating disorders demonstrated a similar trend. Verri et al. (1998) questioned what comes first, hormonal dysfunction versus psychiatric problems.

In summary, more recent studies using control groups underscore potential nutritional etiologies in women with secondary amenorrhea. Women with hyperandrogenic amenorrhea also had eating disorders. The nutritional deficits centered on fat restriction. Even when individuals with eating disorders were excluded, some women with functional hypothalamic amenorrhea demonstrated psychological traits similar to individuals experiencing eating disorders. These findings warrant further clinical nursing investigation using a larger sample size and a matched comparison group.

Energy Balance in Women Seeking to Conceive

Eating a healthy diet composed of a variety of foods is important throughout life. However, healthy nutrition is imperative during preconception and pregnancy (Williamson, 2006). Healthy nutrition is important to the production of sex steroid hormones (steroidogenesis), the development of the ova (gametogenesis) and implantation (Schneider & Wade, 2000). Nutritional status at the time of conception is also essential to fetal growth and development (Williamson, 2006). Williamson (2006) identifies that the embryo is at greater risk to the consequences of poor nutrition during the very early weeks (3-7 weeks) of development when rapid cell division and differentiation occurs.

Energy Availability. Reproduction requires greater energy expenditure for women than for men (Schneider & Wade, 2000; Wade, 1996; Wade, 1998). Reproduction in women ultimately demands an adequate food supply to be able to reproduce and, at the same time, maintain other vital homeostatic physiological processes such as, cellular continuation, thermoregulation, movement and growth (Wade 1998). In times of negative energy expenditure when food is less available, such as during starvation or increased physical energetic demand without increased nutritional intake, animals and humans partition their food to those basic processes necessary for survival through an adaptive physiological process (European Society of Human Reproduction & Embryology Capri Workshop Group, 2006). Thus, reproduction is suspended until conditions optimal to conception are reinstated (Wade, 1998).

Nutrition intake provides the body with available metabolic fuel for cellular continuation, thermoregulation, movement and growth along with higher order processes,

such as reproduction (Wade 1998). Nutritional intake must be sufficient to ensure the necessary energy homeostasis for reproduction. Ellison (2003) describes three elements of energy availability and successful conception. The elements include "energy status, energy balance and energy flux" (Ellison, 2004, p. 344). Energy status includes the quantity of stored energy that can be marshaled for reproductive attempt. Energy balance is the remaining energy intake minus energy outflow that likely can be assigned to reproduction (Schneider & Wade, 2000). Energy flux is the actual level of energy turnover independent of energy balance. Ellison (2003) views conception as being sensitive to positive energetic conditions, and ovarian function specifically being sensitive to energy balance and flux.

Body Mass Index and Body Fat Distribution in Women Seeking to Conceive. Normal body weight does not assure successful fertility outcomes. Once thought to be indicative of healthy nutrition, ideal or average body weight according to the Metropolitan Life Tables (Metropolitan Life Insurance Company, 1959) is being replaced by BMI (kilograms/meters^2) (Flegal, Troiano, & Ballard-Barbash, 2001). BMI is a better indication of energy reserves (Gallagher et al., 2000). BMI of at least 22 rather than absolute body weight has been implicated in normal ovulatory function and menstruation (Thomas, 2001). Women who maintain a low body weight associated with eating disorders or recurrent dieting often experience irregular menstrual cycles and may possibly have a longer trajectory to conception (Goldberg, 2002). Conversely, fertility can also decline in women with excessive fat stores. Healthy women with a BMI > 30 presenting for a prospective study of infertility treatment by artificial insemination

demonstrated a lower pregnancy rate than women with a low BMI (< 20) (Zaadstra et al., 1993). Women with a BMI in the range of 20 – 25 had the best pregnancy rate.

Zaadstra et al. (1993) also found that body fat distribution is more likely than obesity itself to affect fertility. Increased waist-to-hip ratio was negatively related to likelihood of conception. Body fat distribution as a predictor of fertility was significant before and after statistical adjustment for age, obesity, parity, characteristics of menstrual cycles and extent of infertility.

A similar outcome was reported by Kirchengast and Huber (2004) in a study of 15 women with secondary amenorrhea associated with anorexia nervosa, 16 women with polycystic ovary syndrome with secondary amenorrhea or oligomenorrhea, 10 women with idiopathic primary amenorrhea and 19 healthy volunteers with regular menstrual cycles from an Austrian university clinic. All groups with amenorrhea were statistically different when compared to healthy controls on body fat and bone mineral paramenters but not lean body mass. Women with anorexia nervosa and healthy women demonstrated a gyneoid (pear shape) fat distribution, and women with polycystic ovarian syndrome had an android (central) distribution. Thus, Kirchengast and Huber (2004) view body fat distribution as an extragenital marker.

Women with a low BMI before and during pregnancy are at greater risk of delivering low birth weight (LBW) babies with greater risk of morbidity and mortality (Institute of Medicine, 1990). Women who are overweight or obese before and during pregnancy are at greater risk of having gestational diabetes, hypertension and pre-eclampsia (Goldberg, 2002). Moreover, as BMI increases, the risk of these complications also increases (Linne, 2004).

Healthy nutrition is critical for successful reproduction. Initially, it was believed that energy stores were the critical for normal menstrual function and fertility (Frisch, 1978). However, energy balance specifically addresses the availability of nutritional fuel. Too little or excess available fuel potentially can negatively influence fertility (Moschos et al., 2002).

Disordered Eating Symptoms

Women experience disordered eating symptoms for a variety of reasons. Women can restrict their dietary intake, engage in obvious dieting behaviors, or utilize compensatory behaviors to offset weight and food intake. Reasons for these behaviors can include the desire to maintain a slim or athletic body size, symptoms of anxiety and/or depression, and the more complex DSM IV TR (American Psychiatric Association, 2000) eating disorders.

Normal weight women with restrictive eating patterns. Normal weight women who achieve a slim body appearance through utilizing restrictive or strict low fat diets are at risk for menstrual disorders (Couzinet et al., 1999: Rock, Gorenflo, Drewnowski, & Demitrack, 1996b; Warren et al., 1994). Laughlin et al. (1998) uncovered evidence of severely restricted dietary fat intake among stable weight, nonathletic women with functional hypothalamic amenorrhea. The women with functional hypothalamic amenorrhea and their matched healthy controls did not meet DSM IV diagnostic criteria (American Psychiatric Association, 2000) for an eating disorder or depression. The Laughlin et al. subjects were specifically selected for no or minimal exercise or weight loss; however, the women with functional hypothalamic amenorrhea and restrictive dietary fat intake had neuroendocrine-metabolic abnormalities

indicative of a hypometabolic state, similar to what is found in exceedingly trained athletes with functional hypothalamic amenorrhea.

Energy deficiency in women who strenuously exercise. Strenuous exercise without a compensatory increase in calories leads to hypoestrogenism and the related physiological consequences of menstrual irregularities, bone loss, and potential cardiovascular risk (De Sousa, 2003). When dietary restraint is coupled with strenuous exercise energy expenditure, energy deficiency results; and the body responds with either weight loss or energy conservation (down-regulation of metabolism). Physiological response to the energy deficits subsequently affect hypothalamic function and lead to suppression of reproductive function (Williams, Helmreich, Parfitt, Caston-Balderrama, & Cameron, 2001). The female athlete triad represents the most extreme case of serious energy deficit associated with physical exercise. The female athlete triad is a syndrome in athletes involving disordered eating, amenorrhea, and osteoporosis (Otis, Drinkwater, Johnson, Loucks & Wilmore, 1997). Menstrual cycle irregularities in athletes and in recreationally physically active women who restrain their dietary intake have been described as existing on a continuum from luteal phase deficiency to amenorrhea (De Sousa, 2003; Ellison, 2003).

Luteal phase defects exist in athletes and physically active women who restrict their dietary intake due to reduced progesterone production during the luteal phase. In essence, the hormonal system functions adequately for ovulation but not for preparation of the uterine endometrium for implantation. Also possible on the continuum of reproductive functioning are anovulatory cycles (McConnell, O'Connor, Brindle &

Williams, 2002), oligoamenorrhea (Cobb et al., 2003; Loucks & Horvath, 1985) and amenorrhea (De Souza, 2003).

Morris et al. (2006) prospectively examined exercise histories and reproductive outcomes in 2,232 women with infertility prior to their first in vitro fertilization cycle. Women who exercised regularly (less than 4 hours a week) were no more likely to have a successful birth outcome than women who did not exercise. However, women who exercised 4 hours or more a week were 40% less likely to have a live birth and were three times more likely to experience cycle cancellation (inadequate ovarian stimulation with oocyte retrieval failed or not performed). The women who exercised 4 or more hours a week were two times as likely to experience implantation failure or pregnancy loss. Cardiovascular exercise reduced the likelihood of a live birth by 30%. The researchers concluded that women who engaged in exercise 4 hours or more a week for 1 to 9 years were more likely than women who did not exercise to have negative IVF outcomes.

Women experiencing depression and anxiety. Women experiencing episodes of depression and anxiety could also be at risk for unbalanced nutritional intake. The depression and/or anxiety could be determined by multiple factors, such as the psychological burden of infertility, the negative sequellae of unbalanced nutritional intake, and other situational and biological factors. For example, dieting in healthy volunteers has been associated with lower levels of tryptophan, a precursor to serotonin, which is implicated in depression and possibly impaired in satiety (Wolfe et al., 1997).

One of the diagnostic criteria for DSM IV TR (American Psychiatric Association, 2000) Axis I major depression is excess or lack of appetite characterized by a 5% loss or gain of body weight within one month (APA, 2000). Kalantaridou, Makrigiannakis,

Zoumakis, and Chrousos (2004) have proposed that stress, through activating the hypothalamic-pituitary-adrenal (HPA) axis, has a restraining effect on reproduction. Stress through its effect on the arousal and autonomic nervous systems leads the hypothalamus to release corticotropin-releasing hormone (CRH) to stimulate adrenocorticotropic hormone (ACTH), which in turn affects cortisol release by the adrenal cortex. When the stress system is activated, reproduction is inhibited through the increased CRH secretion (and other related stress hormones), which inhibits GnRH emission. There is less stimulation of pituitary FSH and LH and subsequent estrogen and progesterone secretion by the ovary. This affects ovarian follicle development and preparation of the endometrium for implantation. Kalantaridou et al. (2004) contend that these effects explain the stress-related hypothalamic amenorrhea exhibited in women experiencing anxiety and depression and women with exercise disorders and eating disorders. Women who experience appetite changes during periods of anxiety are also at similar risk for unbalanced nutritional intake (Facchinetti, Fava, Fioroni, & Genazzani, 1993).

Domar, Broome, Zuttermeister, Seibel, and Friedman (1992) examined women at an infertility clinic and a control group of well women receiving routine health care for symptoms of depression and found that women with infertility commonly experience depressive symptoms. The women completed two depression scales and provided demographic information. The women with infertility scored significantly higher on the depression scales (Beck depression Inventory $p < 0.0003$; Center for Epidemiological Studies Depression Scale $p < 0.0006$). Women with 2 to 3 years of infertility scored the

highest. Also, the women experiencing infertility had twice the prevalence of depression when compared with well women receiving routine medical or gynecologic care.

Women experiencing eating disorders. Women who experience anorexia nervosa, bulimia nervosa, and eating disorder not otherwise specified are a high risk group psychologically and biologically. Women with anorexia nervosa by definition weigh 85% of their expected weight and have at least 3 consecutive months of amenorrhea associated with substantial neuroendocrine and psychological imbalance (American Psychiatric Association, 2000). Normal or over-weight women with bulimia nervosa who utilize binge-purge behaviors or excessive exercise, are another group of women at risk for infertility.

Eating disorders are distinguished in the DSM IV TR by their cardinal criterion of seriously disordered eating symptoms (American Psychiatric Association, 2000). Anorexia nervosa and bulimia nervosa are the most extreme of the eating disorder syndromes. Eating disorder not otherwise specified includes aspects of the two main disorders or the provisional diagnosis associated with over-eating, binge eating disorder (American Psychiatric Association, 2000).

Anorexia nervosa. Anorexia nervosa, an eating disorder first identified in the late 19th century, is associated with psychiatric syndromes with the greatest mortality rates (Harris & Barraclough, 1998). Anorexia nervosa was studied and treated more intensively as a distinct syndrome in the 1970s. Anorexia nervosa affects women at a ratio of 10-20:1, women to men (Klein & Walsh, 2004). The estimated lifetime prevalence of anorexia nervosa among women is 0.5 – 2% (APA, 2000). Because the disorder tends to emerge as the hypothalamic-pituitary-gonadal axis is maturing, Klein

and Walsh (2004) question whether or not some individuals demonstrate sensitivity to this maturation in the development of an eating disorder.

Central symptoms of anorexia nervosa include refusal to maintain a normal body weight body weight (15% below that expected), intense fear of gaining weight, perceptual disturbance in how one's weight and shape is personally experienced, and amenorrhea for three consecutive months (in females postmenarche) (American Psychiatric Association, 2000). Two subtypes of anorexia nervosa have been identified: individuals who restrict their food and individuals with binge-eating and purging episodes. Restriction involves severe dieting and fasting (Klein & Walsh, 2004). Purging episodes can include abuse of laxatives and diuretics.

Bulimia nervosa. In the late 1970s, bulimia nervosa was introduced by Russell (1979); and since its description, the prevalence has exceeded that of anorexia nervosa (Klein & Walsh, 2004). Bulimia nervosa involves repeated binge-eating episodes, behaviors to prevent weight gain, and preoccupation with shape and weight in the absence of anorexia nervosa (American Psychiatric Association, 2000). Individuals with bulimia nervosa usually have a normal weight for their height. While the estimated lifetime prevalence of bulimia nervosa is 1 – 3% among women, some individuals may begin with anorexia nervosa symptoms then move to predominant symptoms of bulimia nervosa (American Psychiatric Association, 2000).

The binge episodes characteristic of bulimia nervosa entail an intake of an unusual amount of food, from 2,000 to 9,000 or more calories, in a short burst of time. Binge episodes must occur two or more times a week for a three month time period to meet DSM IV TR diagnostic criteria (American Psychiatric Association, 2000). The two

subtypes of bulimia nervosa include purging and non-purging subtypes. Abuse of laxatives and self-induced vomiting compensate for the binges of individuals with the purging type of bulimia nervosa. Extreme duration of exercise, extended fasting, and severe dieting compensate for binge episodes in the non-purging subtype.

Women with bulimia nervosa have also been found to have menstrual dysfunction. Pirke et al. (1987) found at least 50% of women with bulimia nervosa in their study suffered from amenorrhea or oligomenorrhea. Changes in luteinizing hormone (LH) secretion can be a problem for some women with bulimia nervosa; although, there is currently a debate in infertility circles as to whether altered LH secretion poses a true infertility problem (Smith, Pfeifer, & Collins, 2003).

Individuals with bulimia nervosa more frequently experience comorbid anxiety and depression, as well as substance use and personality disorders. Brewerton et al. (1995) found a 75% lifetime prevalence of affective disorders in participants with bulimia nervosa in their studies.

Contrasting anorexia nervosa and bulimia nervosa. Women with anorexia nervosa and bulimia nervosa share some psychological attributes (Klein & Walsh, 2004). Concealment of the illness behaviors and shame is common to both groups. Also shared are embarrassment about their weight and body shape, the content of the binge episodes, and the severe measures to avert weight gain can obstruct individuals from seeking appropriate treatment. Klein and Walsh noted that women experiencing anorexia nervosa can experience an unabating desire to be thin along with lack of recognition of illness, two attributes that serve as barriers to seeking psychiatric treatment. Although, women

with bulimia nervosa also tend to avoid treatment until medical sequelae arise. Anorexia nervosa is more refractory to treatment than bulimia nervosa.

Women with anorexia nervosa have amenorrhea for three months or more, and a large proportion of women with bulimia nervosa have amenorrhea, while others experience problems with luteinizing hormone secretion (Devlin et al., 1989). Although in-vitro fertilization can lead to successful conception, women who have DSM IV TR Axis I eating disorders continue to be at higher risk for cesarean section (Franko et al. 2001; Mitchell-Gieleghem et al., 2002), low birth-weight babies (Abraham et al., 1990), postpartum depression (Franko, et al., 2001; Morgan, Lacey, & Sedgwick, 1999), and relapse of their eating disorder exacerbated by the expected weight and fat distribution issues of the postpartum period (Lemberg & Phillips, 1989; Little & Lowles, 2000; Namir et al., 1986; Stewart et al., 1987). Women with eating disorders are classified as at risk and require more frequent assessment to assure successful fertility, pregnancy and postpartum outcomes (Franko et al., 2001). Therefore, it is a reasonable goal to ensure adequate physiologic and psychological stability in women experiencing eating disorders prior to initiating infertility intervention.

Women can exhibit disordered eating symptoms consistent with aspects of DSM IV TR (American Psychiatric Association, 2000) eating disorders. Eating disorder not otherwise specified describes with examples eating disorders that do not meet the full DSM IV TR diagnostic criteria for a Anorexia Nervosa and Bulimia Nervosa. For example, women that experience all of the diagnostic criteria of anorexia nervosa, except menstrual cycles continue to occur, are included under eating disorder not otherwise specified diagnostic criteria.

Eating disorders not otherwise specified. Additionally included in the eating disorder not otherwise specified diagnosis are individuals who have binge eating disorder. The binge eating disorder set of diagnostic criteria is provisional and provided in the DSM IV TR for further research study. Individuals with binge eating disorder may be genetically predisposed to weigh more than the cultural ideal, which currently is unrealistic (American Psychiatric Association, 2000).

Individuals experiencing binge eating disorder describe episodes of ingesting large quantities of food in a short discrete period of time, but they do not exhibit compensatory behaviors commonly seen in women with bulimia nervosa. Women with binge eating disorder do not regularly vomit, over-exercise, or abuse laxatives or diuretics as women with bulimia are prone to do. Women with binge eating disorder must binge on average 2 days week for a period of 6 months (American Psychiatric Association, 2000).

In summary, disordered eating symptoms can be found in a number of circumstances. Some women had been found to restrict components of their dietary intake to maintain a slim or athletic appearance. Other women may restrict their intake and strenuously exercise leading anywhere from brief perturbation to cessation of female hormones. There are women whose dietary intake is increased or decreased due to their experiencing DSM IV TR (American Psychiatric Association, 2000) depressive or anxiety disorders. Women can experience Anorexia Nervosa, Bulimia Nervosa and Eating Disorder NOS, which are particularly severe psychiatric disorders.

Metabolic and Hormonal Signals of Energy Balance

Metabolic signals. Hypothalamic neuronal pathways are responsible for energy homeostasis through regulation of appetite, energy expenditure and metabolism (Flier, 2006). Metabolic building blocks of metabolism include the metabolic fuels that regulate cellular and organism homeostasis: glucose, free fatty acids, and branch-chain amino acids (Coda, 2006; Flier, 2006).

Hormonal signals. Energy homeostasis is accomplished via hypothalamic neural circuits receiving and responding to peripheral signals that express the condition of energy fluxes and balance (Flier, 2006). Many peripheral signals have been identified. Leptin, an adiposite hormone, is a messenger signifying energy availably (Ahima et al., 1996). Leptin effects body weight, eating behavior and satiety, and energy expenditure primarily through its effect on the hypothalamus (Friedman, 2002), and leptin affects reproduction through its effects again on the hypothalamus, anterior pituitary gonadotropes, ovarian follicular development and preparation of the endometrium for implantation (Moschos et al., 2002). Low circulating leptin is a signal to the brain of nutritional shortage, and excess leptin can signify leptin resistance, particularly in obese individuals. Other peripheral regulatory signals (Broberger, 2005) include gut-derived peptide hormones secreted with meals that support appetite (ghrelin) or satiety (Cholecystokinin CCK and peptide YY).

Role of leptin. For the purpose of this research, leptin will be discussed because of its role as a metabolic signal and as a critical hormone/cytokine in reproduction. Leptin has important effects that influence body mass, metabolism and reproductive function among other important physiological processes (Friedman, 2002; Moschos et al.,

2002). Leptin is a protein hormone, which is secreted primarily by adipocytes: Although, leptin is also expressed in the hypothalamus, pituitary, gastric epithelium, skeletal muscle, syncytiotrophoblast (which leads to placenta development), and mammary epithelium (Moschos et al. 2002). Leptin receptors have been found in the hypothalamus, the pituitary gonadotrope cells, ovarian granulosa, theca and interstitial cells, and endometrium. Moschos et al. (2002) view the multiple sites of leptin secretion and existence of leptin receptors at many levels of the HPG axis as support for nutritional and leptin regulation of the reproductive system.

Leptin levels in healthy volunteers. Studies of normal weight healthy study participants provide a foundation to understand physiological responses to low nutritional intake and explain results of leptin studies in women with eating disorders (Wolfe et al., 2004). Circulating leptin was measured in healthy subjects following a short-term fast. The decrease (~50%) in circulating hormone was unexpectedly large compared to the amount of weight loss (0.5%) (Boden et al., 1996). Significantly decreased leptin levels were also found in 28 healthy subjects in response to a one week energy restriction (Dubuc, Phinney, Stern, & Havel, 1998) and in 15 well normal-weight study subjects after following a 4 week low caloric diet (Wolfe et al., 2004). At the end of the 4 week weight loss period, circulating leptin levels were significantly decreased (60.3%).

Leptin in women with eating disorders. Significantly lower serum leptin levels ($p = 0.02$ bulimia; $p = 0.01$ recovered bulimia) were found in 18 women with bulimia nervosa and 15 women with recovered bulimia nervosa compared to normal controls (Jimerson et al., 2000). Grinspoon et al. (1996) examined serum leptin levels in 22 women with anorexia nervosa and in 23 healthy volunteers and found reduced leptin

levels correlated with body fat but not dietary intake. Levels of circulating leptin were also reduced in women with anorexia nervosa, as would be expected relative to their low fat mass (Monteleone, Fabrazzo, Tortorella, Fuschino, & Maj, 2002). Leptin levels (cerebral spinal fluid and serum levels) were found to return to normal prior to normalization of body mass in 11 women with anorexia nervosa (Mantzoros et al., 1997). The study outcome led Mantzoros et al. to question if the early return to normal leptin levels contributes to curtailed weight recovery.

Taken together, the above studies of leptin suggest that circulating leptin measures energy balance. Given the decreases in leptin even with short-term fasting, serum leptin is sensitive measure of current energy balance.

Leptin in women with amenorrhea. Miller et al. (1998) investigated body mass via dual x-ray absorptiometry (DXA) and dietary intake on serum leptin in 21 normal weight women experiencing hypothalamic amenorrhea and in 30 healthy volunteers. Total nutritional intake, fat intake, and insulin levels were significantly lower in the women with hypothalamic amenorrhea. Significant hypoleptinemia was found in women experiencing hypothalamic amenorrhea compared with the healthy volunteers, possibly reflecting inadequate nutritional intake.

Recombinant human leptin was administered to 8 women with hypothalamic amenorrhea associated with demanding physical exercise or low weight (Welt et al., 2004). Six women with hypothalamic amenorrhea served as controls. Reproductive, thyroid, growth hormones, and leptin were assessed in both groups. Three of the eight women ($p < 0.05$) receiving recombinant leptin experienced an ovulatory menstrual cycle. Another two leptin treated women developed a preovulatory follicle without

ovulation. Leptin administration improved reproductive thyroid and growth hormone measures in the treatment group, providing additional support that leptin is necessary for fertility and normal neuroendocrine balance. Finally, Ahima et al. (1996) found that giving leptin restored ovulatory function in a comparative model.

Summary

Infertility is one of the most common health problems facing couples and an estimated 7.4% of women have problems conceiving (NSFG, 2002). Infertility has multiple causes including ovulatory dysfunction, tubal and peritoneal pathology, male causes, endometriosis, and unexplained infertility. Studies conducted at reproductive centers and biobehavioral studies link disordered eating symptoms and ovulatory and unexplained infertility. However, few these studies had control or comparison groups allowing generalization to other women with infertility.

While psychological, biological, social and cultural factors may initiate eating disorders, the effect of too little or too much nutrition on energy balance likely triggers physiologic events ultimately affecting reproduction. Chapter two describes a conceptual model synthesized from an understanding of normal hormonal functioning, Wade's metabolic fuel hypothesis and the role of leptin as a metabolic and reproductive hormone to explicate the link between ED and infertility. Further investigation of ED in women with ovulatory and unexplained infertility is warranted given their risk of poorer maternal and fetal outcomes.

Extending research to the study of disordered eating symptoms in infertility is worthy of clinical nursing research. Investigating women with ovulatory and unexplained infertility and a comparison group of women receiving routine care from

their PCP for evidence of disordered eating symptoms using a larger sample and a comparative, descriptive design may provide definitive support that further nursing research is warranted. Nursing research in the area of disordered eating symptoms and infertility is within the National Institute of Nursing Research's initiatives for reproductive health and at risk populations.

CHAPTER THREE

Method

A descriptive, comparative quantitative design was used to compare disordered eating symptoms in women with ovulatory and unexplained infertility and women receiving routine care from their primary care provider (PCP) at a large metropolitan academic general hospital medical center. This chapter describes the recruitment, recruitment settings, data collection procedures and instruments, human subject protections, and the data analytical methods utilized to answer the research questions.

Research Design

A descriptive, comparative quantitative design was employed to test the stated hypotheses: After controlling for selected variables (age, income, education, marital status, work status, race, and BMI), women experiencing ovulatory and unexplained infertility will report (1) significantly more disordered eating symptoms than women receiving routine healthcare from their PCP; (2a) significantly more current DSM IV TR (American Psychiatric Association, 2000) Axis I eating disorders than women receiving routine healthcare from their PCP; (2b) significantly more past DSM IV TR (American Psychiatric Association, 2000) Axis I eating disorders than women receiving routine healthcare from their PCP; and (3) significantly more symptoms of depression, anxiety, and dietary restraint than women receiving routine healthcare from their PCP.

Sample

The sample size was originally set for 200 women: 100 women with ovulatory or unexplained infertility and 100 women in the comparison group receiving routine healthcare. The proposed sample size was calculated using SamplePower, version *2.0*

(SPSS, 2000). The parameters used to determine the sample size were and alpha set at *.05*, power of *.80* and a low moderate effect size. Following a preliminary analysis, the final sample size was 85 (51 women with infertility and 34 women receiving routine health care), which yielded a power of .82 to 1.0. In addition, the instruments for hypotheses 1 and 3 explained most of the variance in the analyses. Recruitment of women was based on the study inclusion and exclusion criteria.

Inclusion criteria. Inclusion criteria for women with infertility were as follows: (a) age 18 to 44 years; (b) reported diagnosis of an ovulation disorder or unexplained infertility; (c) in stable medical condition and (d) able to speak, read and understand English. The comparison group included a real world sample of women receiving routine health care from their PCP at a general hospital medical center. Inclusion criteria for women in the comparison group are (a) age 18 to 44 years, (b) in stable medical condition, (c) not currently experiencing infertility and (d) able to speak, read and understand English.

Exclusion criteria. Women experiencing current unstable major medical illnesses will not be included in either group of participants. Women with tubal disease, endometriosis, or peritoneal effects will not be included unless they also experience co-occurring ovulation or unexplained infertility. Couples seeking infertility treatment due to male factors were included if the women also experienced ovulatory or unexplained infertility.

Setting

Three healthcare sites were utilized to recruit study participants. These sites included a Boston In Vitro Fertilization Center, Brigham and Women's Center for

Infertility and Reproductive Surgery, and the Beth Israel Deaconess Medical Center Internal Medicine sites.

Boston IVF is a highly specialized private fertility treatment center dedicated to in-vitro fertilization located in the metropolitan Boston area. Affiliated with the BIDMC, a major teaching center of Harvard Medical School, Boston IVF has clinics in Brookline, Waltham and Quincy and affiliated practices in three states and Bermuda. The Waltham site was utilized for the recruitment of the group of women experiencing infertility.

Recruitment of women with infertility was expanded in the spring of 2009 to include the recruitment of women with infertility from a general hospital infertility center, the Brigham and Women's Hospital, Center for Infertility and Reproductive Surgery. The Center for Infertility and Reproductive Surgery involves a committed team of academic physicians, embryologists, nurses, social workers, physician care assistants, and other personnel who are dedicated to helping couples build families through offering comprehensive reproductive services.

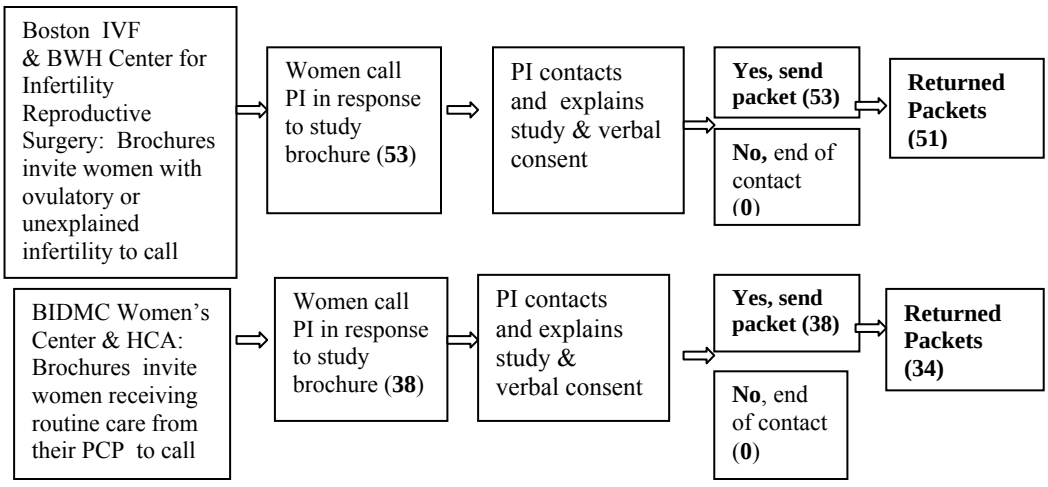
Women receiving routine healthcare from their primary care provider (PCP) were recruited from the Beth Israel Deaconess Medical Center Healthcare Associates and the Women's Center. Healthcare Associates (HCA) is a hospital based primary care teaching practice comprised of faculty physicians, rotating medical house staff, nurse practitioners, triage nurses and clinical social workers. HCA provides medical and mental health care to over 36,000 patients with 100,000 visits annually. The Women's Center provides expert primary care and mental health services that address an extensive scope of women's health issues from preventative care to specialized treatment of disorders and conditions specific to women. The team at the Women's Center is comprised of

physicians, nurse practitioners, mental health specialists, and a professional health educator.

Recruitment

Figure 3

Flow Diagram for Study Recruitment, Consent, and Meeting Goals for Data Collection.



Prior to initiation of the study, the study plan was presented to the clinical staff at BIDMC Healthcare Associates Practice Committee and the Women's Center, Boston IVF Waltham Center, and the Brigham and Women's Hospital Center for Infertility and Reproductive Surgery (Figure 3).

Brochures describing the study were left in the waiting room of each center. The brochures directed women, interested in hearing more about the study, to call a confidential voice mail (or e-mail the PI) and leave a message about convenient days and times of their choosing to receive a return telephone call. The investigator contacted the potential participants by telephone and provided a brief overview of the study. The telephone call was placed at a time requested by the potential participant. The procedures

regarding the number of telephone contacts (limit < 5) to potential participants were strictly followed.

If the woman was interested in participating in the study, verbal informed consent was obtained by telephone (Appendix). Questions about the study were solicited by the PI to ensure that the woman fully understood the material presented. Additionally, the PI was careful to discuss the steps taken to ensure confidentiality of the participant's responses. After the woman provided verbal consent, the study packet containing the self-report tools, a demographic information sheet, a letter containing the information presented in the verbal consent and a stamped investigator-addressed envelope was sent by mail to her home.

A small stipend was sent via US mail to the participant. The woman received a stipend in the form of a gift card ($30.00). Participants were asked to choose a card from CVS, Walgreen's, Dunkin' Donuts, or Starbucks Coffee.

Data Collection Procedures

After the participant provided verbal informed consent, a study packet with the study measures was mailed to her home. A stamped, investigator-addressed envelope was included to facilitate return of the study responses to the investigator. A letter in the packet provided the telephone number of the investigator and dissertation committee chair should the participant require clarification of any questions on the measures. If the packet was not returned within two weeks of the mailing, the investigator contacted the participant by telephone to assure that any remaining questions or concerns were addressed. Most of the study packets were returned within the two week period.

Data Collection Instruments

Study participants were asked to score five self-report instruments and a brief demographic information sheet (Appendix). Participants were asked to complete all of the self-report ratings within a one hour time period. Table 1 lists the study measures to be utilized in the investigation.

Table 1
Study Instruments

Study Measure	Purpose	# of Items	Administration Time	Variables Measured
EDI-3-RF	Measurement of eating disorder risk, BMI	25	5 - 10 minutes	Drive for thinness, Bulimia, and Body Dissatisfaction Scales
EDI-3-SC	Determine DSM-IV-TR Axis I eating disorder diagnostic criteria	9 categories	≤10 minutes	Descriptive responses on specific eating behaviors, dieting, exercise, and, purging
Restraint Scale	Measurement of dietary restraint	10	5 minutes	Long-term dieting behavior
BDI-II	Measurement of depression	20	5 - 10 minutes	Depressive symptoms
STAI form Y	Measurement of anxiety	40	≤12 minutes	Trait anxiety State anxiety

Demographic information sheet. A demographic questionnaire (Appendix C) included questions such as age, education, income, work status, race and ethnicity, highest level of education, and a place to check whether or not they had ovulatory infertility, unexplained infertility, or no infertility (comparison group).

Eating Disorder Inventory-3-Referral Form. The Eating Disorder Inventory-3-Referral Form (EDI-3-RF; Garner, 2004) was used in the study to identify women at risk for developing an eating disorder. The EDI-3-RF was developed to assist with the identification and referral of individuals vulnerable to developing eating disorders. A 4-

page booklet containing an Answer Sheet, a Scoring Sheet, and a Referral Sheet comprised the RF. The Answer Sheet had two sections with 39 items. Information on height and weight was collected on the back page of the booklet to allow for calculation of BMI. The EDI-3-RF was recommended for screening use in new settings, such as infertility centers, and takes 5-10 minutes to complete (Garner, 2004).

The EDI-3-RF utilizes the Eating Disorder Inventory-3 three subscales with 25 questions that make up the Eating Disorder Risk Scales. These subscales are the Drive for Thinness (DT), Bulimia (B), and the Body Dissatisfaction (BD) Scales and comprise the Eating Disorder Risk Composite. The DT scale has seven items that evaluate extreme concern with restraining dietary intake and fear of gaining weight. The B scale has 8 items that evaluate the propensity to consider and engage in bursts of marked out of control eating. The BD scale has 10 items that evaluate distress and dissatisfaction with the size and shape of body regions (buttocks, hips, stomach and thighs).

Information sought by the EDI-3-RF included weight (highest, lowest, and desired), height and weight loss in the past 6 months. Additional questions covered the frequency of binges, making one-self sick (vomiting), laxative use, or exercising for 60 minutes or more to control weight or shape. The EDI-3 Eating Disorder Risk Scales are written at the fourth grade reading level. Information about the EDI-3 DT, B, and BD subscale reliability and sample was used to discuss the EDI-3-RF subscale reliability.

The EDI-3 was developed on a large US clinical multi-site sample separated into four different diagnostic groups, a large international clinical sample, and a US and international nonclinical sample for comparison purposes (Cumella, 2006). Exploratory factor analysis (EFA) examined the underlying relationships of the EDI-3 items in

diagnostic subgroups and in a non-patient sample. The EFA solution for the EDI-3 led to more conceptually precise items and wider conceptual focus for the composites than the previous version (EDI-2; Garner, 2004).

Items on the EDI-3 were presented in a 6 point, forced-choice format that required respondents to indicate whether or not a specific item pertains by selecting one of the following choices: *Always, Usually, Often, Sometimes, Rarely or Never* (Garner, 2004). Each item was scored from 0 to 4 with the most severe replies in the pathologic direction. The pathologic direction of an item is given a 4, determined by the positive *(Always)* or negative *(Never)* direction of the item. The adjoining response is given a 3, the subsequent response is given a 2, the next adjacent response a 1, and the two last responses are given a 0 since they are in contradistinction to the pathology. Scale scores for a particular subscale are achieved by summing the items.

Reliability and validity for the EDI-3 using the 0 to 4 scoring system is available for a US and international sample of adults and adolescents (Garner, 2004). Subscale reliabilities were in the high .80s to low .90s for the normative groups with comparable reliabilities for the four diagnostic groups (Anorexia Nervosa-Restrictive (AN-R), Anorexia Nervosa-Binge/Purge (AN-B/P), Bulimia (BN), and Eating Disorder Not Otherwise Specified (EDNOS)) except for the AN-R group, which expectedly demonstrated a lower score range. Item-total correlations were uniformly high, as can be expected from the fairly high internal consistency reliability estimates (Garner, 2004).

Established parameters identify individuals at risk for developing an eating disorder for referral: the individual's BMI only, BMI along with EDI-3 questions about

intense eating preoccupation, and on the responses given to behavioral questions pertaining to eating disorder pathology (Garner, 2004).

Finally, the willingness of women with eating disorders to honestly respond to self-report measures is likely linked to the fidelity of efforts to maintain confidentiality (Garner, 2004). Garner recommends care be taken to guarantee confidentiality to ensure that participants respond truthfully. He further recommended that the self-report measure not be administered at the recruitment site and be mailed directly to the investigator. For this reason, the consent process and rating scales were not administered at the recruitment sites. Also, care was taken to ensure the participant understood that her responses would remain confidential.

Eating Disorder Inventory -3- Symptom Checklist. The EDI-3-Symptom Checklist (EDI-3-SC; Garner, 2004) was utilized to determine whether or not study participants met DSM IV TR (American Psychiatric Association, 2000) Axis I eating disorder criteria. The EDI-3-SC (Garner, 2004) is a structured self-report inventory requesting current and historical details about the person's eating-related symptoms (binging, vomiting, frequency of exercise, compensatory behaviors) and menstrual history. The EDI-3-SC systematically collects descriptive symptom data that assists in determining if the individual's symptoms meet diagnostic criteria for any of the DSM-IV-TR (American Psychiatric Association, 2000) eating disorders. Items indicated with an asterisk identify information required in making an eating disorder diagnosis by DSM IV TR (American Psychiatric Association, 2000). The EDI-SC is written at a sixth grade reading level and generally takes less than 10 minutes to complete.

The EDI-3-SC was used along with specific questions on the EDI-3-RF subscales to assess provisional lifetime, current and past eating disorders using the SCID (APA, 2000) Module H along with the DSM IV TR manual EDNOS criteria. Specifically, EDI-3-SC symptoms were transcribed to Module H along with the EDNOS criteria from the DSM IV TR. Select items from the EDI-3- RF subscales addressing attitudes in Module H (Appendix). Past AN and BN symptoms were often diagnosed as EDNOS due to limited information.

Beck Depression Inventory II. The Beck Depression Inventory II (BDI-II; Beck, Steer, & Brown, 1996) was utilized in the study to measure the level of depressive symptoms. The BDI II has a strong empirical foundation, supported by 40 years of research. The BDI was also utilized in Domar, Broome, Zuttermeister, Seibel, and Friedman (1992) investigation of depression in women with infertility. The BDI-II is the most recent adaptation of the Beck, Ward, Mendelson, Mock and Erbaugh (1961) original self-report rating scale for depression. The original items of the scale were established from verbal descriptions by patients and were not theory derived. The BDI-II was modified from the widely used BDI I to be more in-line with the major depressive episode concept as characterized in the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) (American Psychiatric Association, 1994). The inventory's items were assessed through an iterated, principal-factor analysis and a promax (oblique) rotation which yielded a 2-factor solution representing a somatic-affective dimension and a cognitive dimension.

Similar to the early versions of the scale, the BDI-II contains 21 items; each item assesses a specific symptom or attitude (Beck et al., 1996). The items are weighted on a

0 to 3 point scale, and the person is asked to endorse statements covering symptoms or attitudes experienced over the past two weeks, which are graded on level of severity. The respondent was asked to circle the highest weighting that applies. A total score was computed by adding weights corresponding to the each of the participant's 21 items. Empirically informed cut off scores, based on responses from outpatients with a diagnosed episode of major depression, are provided.

The BDI II was normed on 500 psychiatric outpatients with mood disorders, anxiety disorders, adjustment disorders and other disorders as well as college students (Beck et al., 1996). Internal consistency was evaluated using corrected item-total correlations (ranges: .39 to .70 for outpatients; .27 to .74 for students) and coefficient alpha (.92 for the 500 outpatients; .93 for 120 students).

The BDI I was written at a sixth grade level and it is assumed that the BDI II is also at the same level (Beck et al., 1996). The BDI-II generally can be completed within 5 to 10 minutes.

Herman and Polivy Revised Restraint Scale. The Herman and Polivy Revised Restraint Scale (Herman & Polivy, 1980) was utilized in the study to measure dietary restraint. Originally designed in 1973 to identify dieters who maintained a weight below set point (the level at which weight tends to stabilize), the Restraint Scale (Herman & Polivy, 1980) is now regarded as a measure of cognitive control of eating, disinhibition, and hunger (Herson & Bellack, 1986). Soon after the introduction of the scale, Polivy and Herman (1985) identified that restrained eating contributes to disinhibited eating behavior. Average dieting behavior was clarified to consist of periods of restraint counterbalanced by periods of disinhibited eating. Therefore, the scale does not give

primacy to successful restrained eaters. Instead, those individuals with a tendency toward disinhibited eating score the highest, and the scale selects dieters that weigh well above set point (Polivy, 1978). The scale best identifies individuals with an enduring focus on dieting.

The Restraint Scale was developed using a sample of college students (166 male; 348 female) (Herman & Polivy, 1986). The scale can be considered unifactorial. Especially with females, the first unrotated factor explained 32% of the variance using principal components analysis. The loadings on the first principal component were high in both genders (male .32 to .72; female .29 to .81) allowing for use as a unidimensional scale. Later varimax rotation provided a 2-factor solution. The first factor covered diet-related cognitions, and the second factor reflected weight fluctuations. However, neither factor alone seemed superior to the total scale (Herman & Polivy, 1986).

The Restraint Scale is comprised of ten items that measure individual focus on weight and dieting (Herman & Polivy, 1986). The multiple choice questions address weight fluctuations, extent of enduring dieting, and associated perspectives regarding weight and eating. The multiple-choice answer format has four (0, 1, 2, 3) or five (0, 1, 2, 3, 4) response options, with no reversed items. Scores range from 0 to 35.

Item total correlations spanned from .41 to .77 for female and .30 to .67 for male students (Herman & Polivy, 1986). Test-retest reliability (1 week) was high ($r = .95$) with satisfactory internal consistency (alpha coefficient = *.82*) in a sample of undergraduates (Alison, Kalinsky, & Gorman, 1992). Most studies have used the median split to contrast restrained and unrestrained subjects.

The restraint scale has been widely used to identify individuals at risk for disinhibition of dieting behavior, such as those who disinhibited in response to preloading, who eat more during an emotional response, and who overeat in response to alcohol (Herman & Polivy, 1986). The Restraint Scale is written at a fourth grade reading level, and can be completed in 5 minutes.

Spielberger State-Trait Inventory. The State-Trait Anxiety Inventory Form Y (STAI; Spielberger, 1989) will be utilized in the proposed study to measure anxiety. The STAI Form Y (Spielberger, 1989) is a 40-item self-report instrument that measures both transitory anxiety (state [S] anxiety) and general long-standing anxiety (trait [T] anxiety) in adults. Development of the instrument initiated in 1964. Items from three widely used scales were rewritten with the psychological intent preserved to differentiate state and trait anxiety. The STAI Form Y (Appendix F), utilized in this investigation, is the third iteration of the state and trait scales.

Normative data for Form Y was collected from 5081 individuals (working adults, college students and military recruits) (Spielberger, 1989). The factor structure for Form Y was assessed using the principle axis method of factor extraction, rotated by varimax to yield a four-factor solution; state-anxiety present items, state-anxiety absent items, trait-anxiety present items and trait-anxiety absent items.

Each item of the STAI Form Y is rated on a four-point Likert-type scale (Spielberger, 1989). The State Anxiety (S-Anxiety) scale consists of twenty statements that assess how respondents feel "right now, at this moment" based on the intensity of anxiety where 1 = *Not At All,* 2 = *Somewhat,* 3 = *Moderately So*, and 4 = *Very Much So.* The S-Anxiety scale contains 20 items. The S-Anxiety scale is comprised of ten anxiety-

present items, which are scored from 1 to 4, and ten anxiety-absent items (1, 2, 5, 8, 10, 11, 15, 16, 19, and 20), which also are scored from 1 to 4 and require reverse scoring prior to statistical analysis (Spielberger, 1989).

The Trait Anxiety (T-Anxiety) scale asks participants to rate the frequency of anxious feeling where 1 = *Almost Never,* 2 = *Sometimes,* 3 = *Often*, and 4 = *Almost Always.* The T- Anxiety scale is composed of eleven anxiety-present and nine anxiety-absent (21, 23, 26, 27, 30, 33, 34, 36, and 39) items scored 1 to 4. The anxiety-absent items of the T-Scale require reverse scoring prior to statistical analysis.

The weighted scores for the twenty items on the T-Anxiety scale are summed and recorded on the allotted space on the test form (Spielberger, 1989). Where one or two items are omitted on the instrument, the mean weighted score is computed, multiplied by 20, and rounded to the next higher whole number. Omitted responses in excess of two place the validity of the scale in question.

Due to the fluctuating nature of anxiety states, measures of internal consistency (alpha coefficients) provide a more meaningful indicator of the S-Anxiety scales than test-retest correlations (Spielberger, 1989). Alpha coefficients across groups and gender ranged from .89 to .93 indicating that Form Y has superior psychometric properties. The alpha coefficient for females in the age range from 19 – 39 was .92.

The STAI Form Y (Spielberger, 1989) will be utilized in this investigation. Form Y- is written at the fourth to fifth grade reading level and takes five minutes to complete.

Human Subjects Protection

Approval of the study was sought through the Boston College (BC) Institutional Review Board (IRB) and the Beth Israel Deaconess Medical Center (BIDMC) Committee

on Clinical Investigations (CCI). The principal investigator (PI) was a nonphysician member of the BIDMC physician group and worked for a BIDMC research group. The BC IRB and the BIDMC CCI approved research at each of the sites designated in the proposed project for data collection: the Boston In-Vitro Fertilization (IVF) infertility clinic and the BIDMC Women's Center and HCA practices. The two IRBs also approved the use of BWH Center for Infertility and Reproductive Surgery as a recruitment site.

Consent Process. Women who call the self-referral telephone number received a return call from the PI on a day and at a time of their choosing. No messages were left on the woman's voicemail. Women were first provided a brief overview of the study by the PI and asked if they would consider participation. A verbal informed consent was then read to women interested in participating in the study (Appendix A). Participants were asked to review the letter containing the informed consent in the packet, prior to filling out the self-report tools. Over 90 women called and were later contacted and consented.

When the woman provided verbal consent, a packet of instruments, the demographic questionnaire, and the verbal consent in letter form were be sent via mail. The return of the completed instruments by US mail to the PI implied consent. No woman who self-referred refused participation at the time of the consent process. However, 5 women did not return their packets and one returned her packet well after data analysis was complete.

Risk/Benefit Assessment. The study had clinical intervention component; and therefore, the study was expected to be of no direct benefit to the study participants. The study posed minimal risk of serious psychological response. Filling out the self-report

instruments may have been tedious for some participants. Study participants with active ED symptoms may possibly be stressed by the nature of the questions covering eating patterns. However, a contact numbers for the principal investigator and the dissertation chair were provided to the study participant along with the study instruments. While the plan was that participants expressing distress would be assessed by the PI (an advanced practice psychiatric nurse) and if necessary, a referral made, no participants called due to stress. Two of the participants called because their packet was lost in the mail and another called requesting feedback on her instrument scores.

All participant responses and total inventory scores to the self-report measures were evaluated by the PI. Participants who meet EDI-3-RF referral criteria or were rated with high scores on the BDI-II (or indication of suicidal thinking) were be re-contacted by telephone, as detailed in the verbal informed consent. The participant was be assessed by the PI and appropriate referral recommended if necessary.

Information obtained from the study could possibly contribute to an increased understanding of the role of disordered eating symptoms in ovulatory and unexplained infertility. A finding of significantly greater disordered eating symptoms in the study participants with infertility may point to the need for further inquiry related assessment of early intervention with this population.

Privacy and Confidentiality. All research materials were stored in locked file cabinets which are located in a locked room. The Screening Form from potential participants were given a 3 digit identification (ID) number. Women who agreed to study participation were assigned a 4 digit study subject number. The subject ID number was used on all data collection measures, and the code chart was kept in locked file separate

from collected study data. Also, screening forms of the study participants were kept in a separate locked file cabinet from the participant study data. All study data were entered in password protected Statistical Package for the Social Sciences (SPSS) for Windows, version 16.0 files on a password protected computer located in a locked room.

Data Analysis Plan

After entering data into SPSS for Windows, version 16.0, all inputted data were checked prior to proceeding to the data analysis. Multivariate analysis of covariance was computed for hypotheses one and three. Chi square was used to test hypothesis two. Chapter IV details preparation of the data to answer the research questions and the results of the statistical tests.

CHAPTER IV

RESULTS

The purpose of the study was to investigate disordered eating symptoms in women with ovulatory and unexplained infertility in comparison to a group of women receiving routine health care by their primary care providers. Chapter 4 describes the study results including sample demographics and the primary analyses for hypothesis-testing. Data were analyzed using SPSS for Windows, version 16.0.

Description of the Sample

Table 2 reports frequencies and percents for the nominal level demographic variables. Nominal demographic variables with insufficient number were recoded and used in subsequent analyses (Table 3). Table 4 reports descriptive statistics for the continuous variables broken out by group. The mean age was 34.4 years (SD 4.8) for the infertility group and 31.2 years (SD 6.5) for the women receiving routine health care. Over 96% (n=49) of the women with infertility were married compared to 18% (n=6) women receiving routine health care. Seventy-eight percent (n=40) of the women with infertility were White as were 62% (n=21) of the women receiving routine health care. Seventy-eight percent (n=40) of the women with infertility were working full or part-time compared with 62% (n=21) of the women receiving routine health care. Ninety-eight percent (n=50) of the women with infertility had post secondary degrees as did 68% (n=22) of the women receiving routine care.

Table 2

Demographic Data by Group for the Original Data with Missing Values

Variable		Infertility group *n=51 (%)*		Comparison group *n* = 34 (%)	
Marital status	Missing	0	(0.0)	1	(2.9)
	Single/never married	2	(3.9)	21	(61.8)
	Married	49	(96.1)	6	(17.6)
	Separated	0	(0.0)	2	(5.9)
	Divorced	0	(0.0)	4	(11.8)
Race	Missing	0	(0.0)	2	(5.9)
	Asian East Southeast	5	(9.8)	1	(2.9)
	Asian Western	2	(3.9)	1	(2.9)
	Black or African American	1	(2.0)	7	(20.6)
	White	40	(78.4)	21	(61.8)
	Multi-racial	3	(5.9)	2	(5.9)
Work status	Missing	0	(0.0)	1	(2.9)
	Full-time	36	(70.6)	15	(44.1)
	Part-time	4	(7.8)	5	(14.7)
	Not working outside home	11	(21.6)	13	(38.2)
Educational level	Missing	0	(0.0)	1	(2.9)
	Some high school	0	(0.0)	1	(2.9)
	High school grad	1	(2.0)	3	(8.8)
	Some college	0	(0.0)	7	(20.6)
	Associate degree	4	(7.8)	1	(2.9)
	Bachelor's degree	14	(27.5)	14	(41.2)
	Master's degree	23	(45.1)	6	(17.6)
	Professional degree	6	(11.8)	1	(2.9)
	PhD	3	(5.9)	0	(0.0)
Income	Missing	3	(5.9)	1	(2.9)
	Under $20,000	8	(15.7)	12	(35.3)
	$20,000 – $30,000	3	(5.9)	5	(14.7)
	$30,000 – $40,000	2	(3.9)	4	(11.8)
	$40,000 – $50,000	5	(9.8)	6	(17.6)
	$50,000 – $75,000	13	(25.5)	5	(14.7)
	$75,000 – $100,000	9	(17.6)	0	(0.0)
	$100,000-$150,000	5	(9.8)	1	(2.9)
	$150,000 and above	3	(5.9)	0	(0.0)

Table 3

Recoded Demographic Variables

Variable		Infertility group (n = 51) *n (%)*	Comparison group (n = 34) *n* = (%)
Recoded Marital Status	Married	49 (96.1)	6 (17.6)
	Single, separated, Divorced	2 (3.9)	28 (82.4)
Recoded Race	White	40 (78.4)	21 (61.8)
	All other races	11 (21.6)	13 (38.2)
Recoded Work	Full or part-time	40 (78.4)	21 (61.8)
	Not working outside home	11 (21.6)	13 (38.2)

Preparation of the Data for Hypothesis-Testing

After entering the study data into SPSS for Windows, Version 16.0, descriptive statistics were computed on all study variables and examined for the presence of random and / or systematic missing data, significant skewness, and outliers. No systematic missing data were found. Minimal random missing data were noted in study variables and were handled by mean substitution.

The continuous variables were next examined for the presence of marked skewness. Fisher's measure of skewness (skewness coefficient ÷ standard error of skewness) was employed to check for marked skewness. As Table 4 reports, three variables were significantly and positively skewed with cut off values greater than ±1.96 standard deviation units, namely: the Desire for Thinness, Bulimia, and BDI scales. Applying the guidelines set forth by Tabachnick and Fidell (2007), logarithmic transformations undertaken to correct the problem were successful. Table 5 reports these results in greater detail.

Table 4

Descriptive Statistics for Continuous Variables

		Age	Desire for Thinness	Bulimia	Body Dissatisfaction	Restraint	State Anxiety	Trait Anxiety	BDI
Infertility	n = 51								
	Mean	34.4	1.00	0.42	1.60	13.69	40.14	40.42	0.99
	Median	34.0	0.57	0.25	1.40	14.00	40.00	39.00	0.57
	SD	4.8	1.01	0.59	0.99	4.93	12.63	10.06	1.01
	Minimum	24.0	0.00	0.00	0.00	4.00	22.00	23.00	0.00
	Maximum	43.0	4.00	3.12	3.70	26.00	77.00	63.00	36.00
	Skewness		1.30	2.45	0.36	-0.08	0.47	0.25	1.30
	SE Skew		0.33	0.33	0.33	0.33	0.33	0.33	0.33
Comparison	n = 34								
	Mean	31.2	1.56	0.82	2.00	17.47	42.51	47.67	1.56
	Median	31.0	1.29	0.63	1.95	16.00	41.82	46.42	1.28
	SD	6.5	1.14	0.80	0.99	6.97	11.11	10.77	1.14
	Minimum	20.0	0.00	0.00	0.00	6.00	21.00	31.00	0.00
	Maximum	44.0	3.71	3.62	3.60	32.00	63.00	69.00	40.00
	Skewness		0.29	1.53	-0.16	0.41	0.13	0.26	0.29
	SE Skew		0.40	0.40	0.40	0.40	0.40	0.40	0.40

Table 5

Fisher's Coefficient of Skewness Prior to and After Logarithmic Transformation

Variable	Desire for Thinness	Log Transformed Desire for Thinness	Bulimia	Log Transformed Bulimia	BDI	Log Transformed BDI
Mean	1.22	.17	.58	.33	13.24	1.73
Median	.75	.17	.25	.36	11.0	1.71
SD	1.10	.03	.71	.05	9.75	.08
Skewness	.82	-.45	1.93	-.50	.87	.52
SE**	.26	.26	.26	.26	.26	.26
Fisher's***	3.12*	-1.74	7.39*	-1.92	3.32*	1.95

* Marked skewness
***SE* = standard error
***Fisher's Measure of Skewness = skewness coefficient ÷ standard error of skewness

Internal consistency reliability of study instruments. Cronbach's alphas, internal consistency reliability coefficients, were next computed for the EDI – 3 – RF subscales (Desire for Thinness, Bulimia, and Body Dissatisfaction), The Herman and Polivy Restraint Scale, the STAI scales (State Anxiety and Trait Anxiety) and the BDI-II scale total scores. The Cronbach alpha coefficients ranged from .82 to .92 as depicted in Table 6. All instruments had reliabilities above 0.80 indicating sufficient reliability to proceed with the formation of subscale and total scores prior to hypothesis-testing.

Table 6

Internal Consistency of Instruments

Instrument	Number of Items	Cronbach's Alpha based on Standardized items
Desire for Thinness Scale	7	.89
Bulimia Scale	8	.86
Body Dissatisfaction Scale	10	.88
Restraint Scale	10	.82
State Anxiety Scale	20	.92
Trait Anxiety Scale	20	.92
Beck Depression Inventory II	21	.92

Hypothesis-Testing

Hypothesis 1: After controlling for participants' age, income, education, marital status, work status, race, and current BMI, women experiencing ovulatory and unexplained infertility will report significantly more disordered eating symptoms than women receiving routine healthcare from their PCP.

Hypothesis 1 was tested using a multivariate analysis of covariance (MANCOVA). The three dependent variables were log transformed Desire for Thinness, log transformed Bulimia, and Body Dissatisfaction subscales. The independent grouping variable was the infertility (ovulatory and unexplained) group (n = 51) and the comparison group (n = 34) of woman receiving routine health care. The covariates were age, education, income, recoded marital status, recoded work, recoded race and current Body Mass Index (BMI). Table 7 reports the omnibus *F* for the three dependent variables was significant (log transformed Desire for Thinness $F = 2.91$, df 15, $p = .001$; log transformed Bulimia $F = 2.41$, df 15, $p = .007$; Body Dissatisfaction F = 4.19, df 15, $p = .000$) using a Bonferroni correction of 0.0167.

Table 8 presents the descriptive statistics by group for the dependent variable prior to and after adjustment for covariance influence. Table 9 reports the results for Box's test for Equality of Covariance Matrices. The nonsignificant *p* of .72 indicates the assumption of equality of covariance matrices was met. Levine's Test of Equality of Error variances, shown in Table 10, was also nonsignificant supporting the assumption of homogeneity of variance of the dependent variables.

Pillai's Trace testing whether the groups significantly differed on the combined dependent variable mean scores was $F = .278$; df 3, 67; $p = .84$ indicating that the two groups were nonsignificant on the combined dependent variables.

Table 7

Summary of Between Subjects Effects

Source	Scale	*F*	*df*	*p*	Partial Eta^2	Observed Power
Corrected Model	Log Transformed Desire for Thinness	2.91	15	.001*	.39	.99
	Log Transformed Bulimia	2.41	15	.007*	.34	.97
	Body Dissatisfaction	4.19	15	.000*	.48	1.00
RECgroup	Log Transformed Desire for Thinness	.087	1	.77	.00	.06
	Log Transformed Bulimia	.82	1	.37	.01	.15
	Body Dissatisfaction	.21	1	.65	.00	.07
Age	Log Transformed Desire for Thinness	.02	1	.90	.00	.05
	Log Transformed Bulimia	.52	1	.47	.01	.11
	Body Dissatisfaction	2.21	1	.14	.03	.31
Education	Log Transformed Desire for Thinness	4.01	1	.05	.06	.51
	Log Transformed Bulimia	2.62	1	.11	.04	.36
	Body Dissatisfaction	.83	1	.37	.01	.15
Incomepart	Log Transformed Desire for Thinness	2.58	1	.11	.04	.35
	Log Transformed Bulimia	.79	1	.38	.01	.14
	Body Dissatisfaction	.01	1	.91	.00	.05
RECmarital	Log Transformed Desire for Thinness	.37	1	.55	.01	.09
	Log Transformed Bulimia	.10	1	.74	.00	.06
	Body Dissatisfaction	.01	1	.95	.00	.05

*Bonferroni adjusted significance is 0.0167

Table 7

Summary of Between Subjects Effects (continued)

Source	Scale	*F*	*df*	*p*	Partial Eta^2	Observed Power
	Log Transformed					
RECwork	Desire for Thinness	1.75	1	.19	.03	.26
	Log Transformed					
	Bulimia	.56	1	.46	.01	.11
	Body					
	Dissatisfaction	1.77	1	.19	.03	.26
	Log Transformed					
RECrace	Desire for Thinness	.00	1	.96	.00	.05
	Log Transformed					
	Bulimia	.02	1	.88	.00	.05
	Body					
	Dissatisfaction	2.87	1	.10	.04	.38
BMIcurr	Log Transformed					
	Desire for Thinness	.00	1	.010*	.09	.75
	Log Transformed					
	Bulimia	.02	1	.003*	.12	.86
	Body					
	Dissatisfaction	25.25	1	.000*	.36	1.00
Group*	Log Transformed					
Age	Desire for Thinness	4.06	1	.05	.06	.51
	Log Transformed					
	Bulimia	.94	1	.34	.01	.15
	Body					
	Dissatisfaction	2.58	1	.11	.04	.35
Group*	Log Transformed					
Education	Desire for Thinness	6.34	1	.010*	.08	.70
	Log Transformed					
	Bulimia	3.433	1	.07	.05	.45
	Body					
	Dissatisfaction	.04	1	.85	.00	.05
Group*	Log Transformed					
Incomepart	Desire for Thinness	1.84	1	.18	.03	.27
	Log Transformed					
	Bulimia	1.66	1	.20	.02	.25
	Body					
	Dissatisfaction	.02	1	.89	.00	.05

*Bonferroni adjusted significance is 0.0167

Table 7

Summary of Between Subjects Effects (continued)

Source	Scale	*F*	*df*	*p*	Partial Eta^2	Observed Power
Group* RECmarital	Log Transformed Desire for Thinness	4.41	1	.04	.060	.544
	Log Transformed Bulimia	2.76	1	.10	.038	.374
	Body Dissatisfaction	.40	1	.53	.006	.096
Group* RECwork	Log Transformed Desire for Thinness	.03	1	.88	.000	.053
	Log Transformed Bulimia	.71	1	.40	.010	.132
	Body Dissatisfaction	.08	1	.77	.001	.059
Group* RECrace	Log Transformed Desire for Thinness	4.90	1	.03	.066	.588
	Log Transformed Bulimia	1/01	1	.32	.014	.168
	Body Dissatisfaction	.72	1	.40	.010	.133
Group* BMIcurr	Log Transformed Desire for Thinness	1.38	1	.25	.020	.212
	Log Transformed Bulimia	1.13	1	.29	.016	.183
	Body Dissatisfaction	9.11	1	.004*	.117	.845

*Bonferroni adjusted significance is 0.0167

Table 8

Descriptive Statistics by Group for the Dependent Variables Prior to and Post Covariate Adjustment

Dependent Variables	Group	Unadjusted Mean (*SD*)	Adjusted Mean (*SE*)
Log Transformed Desire for Thinness Scale	Infertility	.17 (0.03)	.18 (0.01)
	Comparison	.16 (0.03)	.16 (0.01)
	Total	.17 (0.03)	
Log Transformed Bulimia Scale	Infertility	.35 (0.05)	.35 (0.01)
	Comparison	.31 (0.05)	.33 (0.01)
	Total	.33 (0.05)	
Body Dissatisfaction Scale	Infertility	1.60 (0.99)	1.08 (0.22)
	Comparison	2.01 (1.01)	1.92 (0.24)
	Total	1.76 (0.99)	

**SE* = standard error

Table 9

Box's Test for Equality of Covariance Matrices

Box's M	*F*	*df*1	*df*2	*p*
3.9	.62	6	3367	.72

Table 10

Levine's Test of Equality of Error Variances for Dependent Variables: EDI – 3 – RF subscales

Scale	F	*df*1	*df*2	*p*
Log Transformed Desire for Thinness	.32	1	83	.58
Log Transformed Bulimia	.37	1	83	.55
Body Dissatisfaction	.08	1	83	.77

A single factor MANCOVA was used to test the hypothesis. Table 7 displays the results for each between subject effects on the individual dependent variable. Of the covariates, only current BMI was significant (log transformed Desire for Thinness $F = 7.06$; *df 1;* $p = .010$; log transformed Bulimia $F = 9.51$; *df 1;* $p = .003$; Body Dissatisfaction $F = 39.21$; *df 1;* $p = .000$) for all the dependent variables. Of the two way group interactions, only education by group significantly ($F = 6.34$; *df 1;* $p = 0.01$) interacted with the Desire for Thinness subscale score and current BMI by group significantly ($F = 9.11$; *df 1;* $p = .004$) interacted with the Body Dissatisfaction subscale score.

After removal of the covariate and interaction influences, there were significant differences between the groups on all 3 dependent measures. The power for the corrected model ranged from .97 to 1.00. Thus, after removal of the covariate and interaction influences the infertility group had significantly higher Desire for Thinness and Bulimia subscale scores and significantly lower Body dissatisfaction subscale scores than the comparison group.

Hypothesis 2a: Women experiencing ovulatory and unexplained infertility will report significantly more current DSM IV TR (American Psychiatric Association, 2000) Axis I eating disorders than women receiving routine care from their PCP.

Chi Square was utilized to test Hypothesis 2a. As Table 11 reports, women with infertility did not have significantly more Axis I current eating disorders than the comparison group of women receiving routine health care.

Hypothesis 2b: Women experiencing ovulatory and unexplained infertility will report significantly more past DSM IV TR (American Psychiatric Association, 2000) Axis I eating disorders than women receiving routine care from their PCP.

Chi Square was also used to test Hypothesis 2b. As Table 11 reports, women with infertility did not have significantly more Axis I past eating disorders than the comparison group of women receiving routine health care.

Table 12 reports the rate and percent of Lifetime current or past ED diagnosis for the women with infertility and the women receiving routine health care from their PCP for later comparison with other ED studies.

Table 11

Chi-Square of Current and Past Eating Disorder Diagnosis: Infertility and Comparison Groups

		Infertility Group n = 51		Comparison Group n = 34		Total
		n	%	*n*	%	
Current Diagnosis	No Current Diagnosis	44	61.1%	28	38.9%	72
	Current Diagnoses	7	53.8%	6	42.6%	13
	Total	51	60.0%	34	40.0%	85
Past Diagnoses	No Past Diagnoses	37	62.7%	22	37.3%	59
	Past Diagnosis	14	58.3%	12	46.2%	26
	Total	51	60.0%	34	40.0%	85

Current Diagnosis: Pearson $\chi^2(1, N = 85) = .242$, $p = .62$
Past Diagnosis: Pearson $\chi^2(1, N = 85) = .591$, $p = .44$

Table 12

Lifetime Current or Past ED Diagnosis: Infertility and Comparison Groups

	Infertility group (51)		Comparison group (34)	
	n	(%)	*n*	(%)
No diagnosis ever	34	(66.7)	17	(50.0)
Current ED diagnosis	7	(13.7)	6	(17.7)
Past ED diagnosis	10	(19.6)	11	(32.3)
Lifetime diagnosis	17	(33.3)	17	(50.0)

Hypothesis 3: After controlling for selected variables (age, income, education, marital status, work status, race, and current BMI), women experiencing ovulatory and unexplained infertility will report significantly more symptoms of depression, anxiety, and dietary restraint than women receiving routine healthcare by their PCP.

Hypothesis 3 was also tested using (MANCOVA). The four dependent variables were the Restraint, State Anxiety, Trait Anxiety and the recoded BDI-II scale scores. The independent group variable, the fixed factor, included infertility (ovulatory and unexplained) group (n = 51) and the comparison group (n = 34) of woman receiving routine health care. The covariates included age, education, income, recoded marital status, recoded work, recoded race and current BMI. Table 13 reports the omnibus F for the Restraint scale score was significant (F = 3.63, df 1; p = .000) using a Bonferroni correction of 0.0125).

Table 14 presents the descriptive statistics by group for the dependent variable prior to and after adjustment for covariance influence. Table 15 reports the results for Box's test for Equality of Covariance Matrices. The nonsignificant p of .57 indicates the assumption of equality of covariance matrices was met. Levine's Test of Equality of Error variances, shown in Table 16, was also nonsignificant supporting the assumption of homogeneity of variance of the dependent variables.

Pillai's Trace was used to test whether the groups significantly differed on the combined dependent variable mean scores. Pillai's trace was F = .51; df 4, 66; p = .73 indicating that the two groups were nonsignificant on the combined dependent variables.

Table 13

Summary of Between Subjects Effects

Source		*F*	*df*	*p*	Partial Eta^2	Observed Power
Corrected Model	Restraint score	3.63	1	.000*	.44	.999
	State Anxiety score	.53	1	.92	.10	.30
	Trait Anxiety score	1.10	1	.37	.19	.64
	Log Transformed BDI-II score	.90	1	.57	.16	.52
Group	Restraint score	.08	1	.78	.00	.06
	State Anxiety score	.02	1	.89	.00	.05
	Trait Anxiety score	.23	1	.63	.00	.08
	Log Transformed BDI-II score	.17	1	.68	.00	.07
Age	Restraint score	.15	1	.70	.00	.07
	State Anxiety score	3.12	1	.08	.04	.41
	Trait Anxiety score	1.14	1	.29	.02	.18
	Log Transformed BDI-II score	1.60	1	.21	.02	.34
Education	Restraint score	3.04	1	.09	.04	.41
	State Anxiety score	1.99	1	.16	.03	.29
	Trait Anxiety score	1.34	1	.25	.02	.21
	Log Transformed BDI-II score	5.03	1	.03	.07	.60
Incomepart	Restraint score	6.23	1	.02	.08	.69
	State Anxiety score	.00	1	1.00	.00	.05
	Trait Anxiety score	.15	1	.70	.00	.07
	Log Transformed BDI-II score	.10	1	.75	.00	.06

*Bonferroni adjusted significance is 0.0125

Table 13

Summary of Between Subjects Effects (continued)

Source	Scale	*F*	*df*	*p*	Partial Eta^2	Observed Power
RECmarital						
	Restraint score	.82	1	.37	.01	.15
	State Anxiety score	.01	1	.93	.00	.05
	Trait Anxiety score	.07	1	.79	.00	.06
	Log Transformed BDI-II score	.09	1	.77	.00	.06
RECwork	Restraint score	.06	1	.81	.00	.06
	State Anxiety score	.11	1	.74	.00	.06
	Trait Anxiety score	.29	1	.59	.00	.08
	Log Transformed BDI-II score	.09	1	.76	.00	.06
RECrace	Restraint score	5.45	1	.02	.07	.63
	State Anxiety score	.31	1	.58	.00	.09
	Trait Anxiety score	.11	1	.75	.00	.06
	Log Transformed BDI-II score	.04	1	.85	.00	.05
BMIcurr						
	Restraint score	13.79	1	.000*	.17	.96
	State Anxiety score	.19	1	.67	.00	.07
	Trait Anxiety score	.03	1	.87	.00	.05
	Log Transformed BDI-II score	.27	1	.60	.00	.08
Group* Age	Restraint score	39.34	1	.22	.02	.23
	State Anxiety score	31.24	1	.66	.00	.07
	Trait Anxiety score	44.25	1	.54	.00	.09
	Log Transformed BDI-II score	.01	1	.14	.03	.31

*Bonferroni adjusted significance is 0.0125

Table 13

Summary of Between Subjects Effects (continued)

Source	Scale	*F*	*df*	*p*	Partial Eta^2	Observed Power
Group* Education	Restraint score	7.39	1	.008*	.10	.77
	State Anxiety score	.44	1	.51	.01	.10
	Trait Anxiety score	.63	1	.43	.01	.12
	Log Transformed BDI-II score	.28	1	.598	.00	.08
Group* Incomepart	Restraint score	2.13	1	.15	.03	.30
	State Anxiety score	.06	1	.81	.00	.06
	Trait Anxiety score	.39	1	.54	.01	.09
	Log Transformed BDI-II score	.01	1	.94	.00	.05
Group* RECmarital	Restraint score	2.27	1	.14	.03	.32
	State Anxiety score	.79	1	.38	.01	.14
	Trait Anxiety score	.12	1	.73	.00	.06
	Log Transformed BDI-II score	.11	1	.73	.00	.06
Group* RECwork	Restraint score	.30	1	.57	.00	.08
	State Anxiety score	.02	1	.89	.00	.05
	Trait Anxiety score	.01	1	.926	.00	.05
	Log Transformed BDI-II score	.01	1	.91	.00	.05
Group* RECrace	Restraint score	8.99	1	.004*	.12	.84
	State Anxiety score	.29	1	.59	.00	.08
	Trait Anxiety score	2.47	1	.12	.04	.34
	Log Transformed BDI-II score	.89	1	.35	.01	.15

*Bonferroni adjusted significance is 0.0125

Table 13

Summary of Between Subjects Effects (continued)

Source	Scale	*F*	*df*	*p*	Partial Eta^2	Observed Power
Group* BMIcurr	Restraint score	.20	1	.66	.00	.07
	State Anxiety score	.15	1	.69	.00	.07
	Trait Anxiety score	1.48	1	.23	.02	.23
	Log Transformed BDI-II score	1.35	1	.25	.02	.21

*Bonferroni adjusted significance is 0.0125

Table 14

Descriptive Statistics by Group for the Dependent Variables Prior to and After Covariate Adjustment

Dependent Variables	Group	Unadjusted		Adjusted	
		Mean	(*SD*)	Mean	(*SE*)
Restraint scale	Infertility	13.7	(4.93)	12.6	(1.40)
	Comparison	17.5	(6.97)	17.0	(1.52)
	Total	15.2	(6.09)		
State Anxiety scale	Infertility	40.1	(12.63)	42.3	(3.50)
	Comparison	42.5	(11.11)	44.7	(3.80)
	Total	41.1	(12.04)		
Trait Anxiety scale	Infertility	40.4	(10.06)	40.9	(3.01)
	Comparison	47.7	(10.77)	48.1	(3.26)
	Total	43.3	(10.89)		
Log BDI-II scale	Infertility	1.7	(0.08)	1.7	(0.02)
	Comparison	1.7	(0.07)	1.7	(0.02)
	Total	1.7	(0.08)		

**SE* = standard error

Table 15

Box's Test for Equality of Covariance Matrices

Box's M	*F*	*df*1	*df*2	*p*
9.2	.86	10	23400	.57

Table 16

Levine's Test of Equality of Error Variances for Dependent Variables

Scale	*F*	*df*1	*df*2	*p*
Restraint	.68	1	83	.42
State Anxiety	1.39	1	83	.24
Trait Anxiety	1.05	1	83	.31
Log Transformed BDI	.73	1	83	.40

A single factor MANCOVA was used to test the hypothesis. Table 13 displays the results for each between subject effects on the individual dependent variables. When examining for the influence for each main effect on the individual dependent variable of the 7 covariates, only current BMI was significant for all the dependent variables. Of the two way group interactions, only current BMI by group significantly ($F = 13.79$; *df 15;* $p = .000$) interacted with the Restraint scale score.

After removal of the covariate and interaction influences, there was a significant difference between the groups on the Restraint scale score. The power for the corrected model was .999. Thus, after removal of the covariate and interaction influences the infertility group

had significantly lower Restraint scale scores but did not significantly differ on the State Anxiety, Trait Anxiety, BDI-II scale scores than the comparison group.

Summary

Hypothesis 1 was tested using MANCOVA. The infertility and comparison groups were compared in terms of mean scores for the Desire for Thinness, Bulimia and Body Dissatisfaction Subscales, adjusted for the effect of 7 covariates by simultaneously testing each factor effect and interaction effect on the dependent variable. The *F* was significant using a Bonferroni adjustment of 0.0167 for the three subscales. The infertility group had significantly higher Desire for Thinness and Bulimia scale scores than the comparison group. The mean Body Dissatisfaction scale scores for the infertility group were significantly lower than the comparison group scale scores. Thus, hypothesis 1 was partially supported.

Hypotheses 2a and 2b were tested using the Chi Square statistic. The Chi Square results did not find that women with infertility has significantly more current or past Axis I eating disorders than the comparison group. Thus, hypotheses 2a and 2b were not upheld.

Hypothesis 3 was tested using MANCOVA. Mean Restraint, State Anxiety, Trait Anxiety and BDI-II scale scores, adjusted for the effect of 7 covariates by simultaneously testing each factor effect and interaction effect on the dependent variables, were compared for the infertility and comparison group. The *F* was significant, using a Bonferroni adjustment of 0.0125, for the Restraint scale only. Thus, hypothesis 3, as it was proposed, was not upheld.

Chapter 5 discusses these results in detail. Discussion and interpretation of these findings explores each hypothesis. Limitations and recommendations for future research are incorporated.

CHAPTER V

Discussion

This study was designed to compare disordered eating symptoms in women with ovulatory and unexplained infertility and women receiving routine health care from their PCP at a general hospital medical center. The parameters used in this descriptive, comparative quantitative study were self-report of eating and psychological symptoms on the EDI - 3 - Desire for Thinness, Bulimia, and Body Dissatisfaction subscales, The Herman and Polivy Restraint Scale, The Speilberger State and Trait Anxiety Scales, and the Beck Depression – II Inventory. Additional self-report information of specific ED symptoms and compensatory behaviors was obtained from the EDI – 3 – Symptom Checklist. Group differences were significant for four measures of eating disorder symptoms with women with infertility scoring significantly higher on desire for thinness and bulimia symptoms and scoring significantly lower on body dissatisfaction and dietary restraint. This chapter includes an overview of major study outcomes and a discussion of the results. In addition, limitations of the study as well as recommendations for further study are presented.

Group Characteristics

Study groups evidenced differences on several descriptive characteristics. The infertility group was slightly older, predominately married, and had higher income and education levels; although, two/thirds of the comparison group also had post secondary degrees. BMI was significantly lower in the infertility group $t(42.4) = 2.5$, $p = .019$. The groups were similar on current or past amenorrhea and work status.

Interpretation of the Findings

Hypothesis 1: After controlling for participants' age, income, education, marital status, work status, race, and current BMI, women experiencing ovulatory and unexplained infertility will report significantly more disordered eating symptoms than women receiving routine health care from their PCP.

As, hypothesized, the women with infertility reported significantly more eating disorder symptoms on the Desire for Thinness and Bulimia subscales than women receiving routine health care by their PCP. Thus, eating disorder symptoms putting women at risk for Anorexia Nervosa (Desire for Thinness subscale) and Bulimia (Bulimia subscale) were significantly more evident in the group of women with infertility. Conversely, the women with infertility reported significantly less eating disorder symptoms as measured by the Body Dissatisfaction subscale scores.

The Body Dissatisfaction subscale measures disapproval with body weight and the shape of body areas (hips, stomachs, thighs and buttocks). While these concerns prevail in Western culture, Garner (2004) views the construct of body dissatisfaction as a risk factor, influential in prompting and prolonging extreme weight management behaviors that could foster EDs in predisposed women. Specifically, body dissatisfaction is influenced by weight and weight history. Garner reports that individuals with higher BMIs have higher BD scale scores. Looking at the mean BMI scores for the two groups (infertility *M*=23.81 [*SD* 4.1]; comparison *M*=27.74 [*SD* 8.8]), the BD subscale scores are consistent with the lower BMI of the infertility group. On the other hand, the women receiving routine healthcare had higher BD subscale scores consistent with their higher BMIs and tendency toward overeating.

Hypothesis 2a and 2b: Women experiencing ovulatory and unexplained infertility will report significantly more current and past DSM IV TR (American Psychiatric Association, 2000) Axis I eating disorders than women receiving routine care from their PCP.

Theses hypotheses were not upheld. Women with infertility did not have more current or past Axis I eating disorders than the comparison group. Use of the SCID Module H and the DSM IV EDNOS criteria without an interview to probe for further symptoms may have influenced the nonsignificant result. Some women with infertility reported past EDNOS AN symptoms that were not as well covered by the EDI-3-SC instrument. Specifically, the instrument focuses more on bulimia symptoms and less on historical AN disturbed attitudes, such as of perceived body weight on self-evaluation and denial of the gravity of low weight. Furthermore, lifetime diagnosis may be a better clinical diagnostic perspective to assess women with infertility. Lifetime diagnosis addresses whether or not the participant ever met a threshold ED diagnosis.

Recent prevalence studies provide a basis to better interpret the diagnostic results of the study. These studies are the Hudson, Hiripi, Pope & Kessler (2007) report of national estimated lifetime prevalence data of ED and the Freizinger, Franko, Dacey, Okun and Domar (2010) report of lifetime diagnosis in women with infertility. Hudson et al. examined the National Comorbidity Survey Replication for estimated lifetime prevalence of ED. Using the results of the national, in person, WHO Composite International Diagnostic Interview, the researchers determined the national lifetime prevalence of AN was 0.9%, BN was 1.5%, and the provisional diagnosis BED had a lifetime prevalence of 3.5%. Freizinger et al. reported on research conducted on 82 women with all infertility diagnoses recruited from an infertility center. After providing verbal consent, women were administered the DSM IV Axis I Disorders (SCID I)

Module H along with the DSM IV manual EDNOS criteria by telephone. Freizinger et al. found that 21% (17) of the women with infertility met ED criteria for either a past or current disorder, which was five-times the US estimated prevalence rate of 1-4%.

Over 33% of the infertility group in the present study had a lifetime ED diagnosis based on symptoms transcribed to the SCID Module H along with the DSM IV TR manual EDNOS criteria. Almost 6% (3) women with infertility met full criteria for a current (2; 3.9%) or past (1; 2%) AN or BN. However, over 27% of the women had a current (5; 9.8%) or past (9; 17.6%) EDNOS diagnosis. Women with ovulatory infertility had current diagnoses within the constricting continuum (AN, BN- restricting and EDNOS [AN without amenorrhea]). Past diagnoses were characterized primarily by restriction (4) with only two women having a diagnosis involving binging. Women with unexplained infertility were more likely to report current diagnoses involving binging (3); although, these women reported past diagnoses representing both continuums (restricting [3] and binging eating [3]). These results are in line but higher than the Freizinger et al. (2010) findings.

Sample characteristics and the use of a different ED instrument may explain the higher percentage of women with lifetime ED diagnoses in the present study compared with the Freizinger et al. (2010) study. The present study recruited of only women with ovulatory and unexplained infertility, diagnoses previously reported in early ED studies. Additionally, the EDI-3-SC probes for specific bulimia symptoms and compensatory behaviors. Finally, the study results are also similar to the research findings of Stewart et al. 1990.

Hypothesis 3: After controlling for participants' age, income, education, marital status, work status, race, and current BMI, women experiencing ovulatory and unexplained infertility will

report significantly more symptoms of depression, anxiety, and dietary restraint than women receiving routine care from their PCP.

Although the hypothesis was not upheld, the study found that women with infertility had significantly lower Restraint scale scores than the comparison group. Dietary intake in women with infertility was within the normal range. Therefore, the women receiving routine health care had significantly higher restraint scale score. The dietary intake of women receiving routine health care was characterized by restriction, possibly contributing to dietary disinhibition. In contrast to the infertility group, six of the women receiving routine health care had current ED diagnoses. Three women had BN; three women had EDNOS BED. Three women in the comparison group had full criteria past diagnoses of AN (2) and BN (1); the rest of the subjects (8) had EDNOS diagnoses. Therefore, their diagnoses more commonly fell under the bulimia and BED diagnoses.

The higher rate of ED in the sample of women receiving routine health care from their PCP is also of great concern. The ED diagnostic trend toward the overeating continuum in the comparison group is similar to the Johnson, Spitzer, and Williams (2001) study of ED in women receiving primary care and obstetric gynecology care. The researchers found a 6.2% prevalence rate of BN and BED and noted subjects in their sample experienced higher disability, lower functioning and medical co-morbidity. Worth mentioning, 50% the comparison group in this study had a current or past ED, which was 8 times the percent Johnson, Spitzer, and Williams found. The discrepancy could be explained by their use of a different self-rating instrument, the Spitzer et al. (1999) Patient Health Questionnaire.

Thirty eight percent of the comparison group was comprised of minority women versus 22% in the group of women with infertility. Although previous research reports that minority

women have a similar prevalence of ED to Caucasian women (Franko, Becker, Thomas, and Herzog, 2007), 62% of the sample of minority women (n = 13) receiving routine health care in the present study had a lifetime ED diagnosis. The group of women with infertility had less minority women (n = 11); still, the minority women with infertility also had an unexpectedly high rate (55%) of ED diagnoses. However, 43% of the women receiving routine healthcare that self-reported as White also had ED diagnoses indicating the comparison group had higher lifetime ED diagnoses overall. One explanation for the higher rates could be the age (M 31.2; SD 6.5) of the women participants which is considerably older than the women in other ED studies. Finally, the higher percent of ED could be related to the specific comparison group recruitment setting that integrated mental health and psychiatry services into the internal medicine practices.

The women with infertility in the present study did not report significantly more symptoms of depression than the comparison group, a finding dissimilar to the Domar et al. (1992) study. Domar et al. found higher rates of depression in women with 2 to 3 years of infertility. In contrast, the women in the present study generally reported having infertility for less than two years, a time period generally characterized by greater hope of becoming pregnant. Also, women with a clear cut infertility etiology in the Domar et al. study had higher depression scores than women with unexplained infertility. Sixty-three percent of the infertility group in the present study had unexplained infertility.

Similar to the findings of depression, the women in the infertility group did not report significantly more symptoms of anxiety than the comparison group of women receiving routine health care. In fact, the comparison group of women had slightly higher Spielberger state anxiety and trait anxiety scores than the women with infertility. However, the women with

infertility had elevated state and trait anxiety scores when compared with means of the normative sample of female working adults ages 19 to 39 (state anxiety: infertility [42.3, *SE* 3.5], female working adults [36.17, *SD* 10.96]; trait anxiety: infertility [40.9, *SE* 3.01], female working adults [36.15, SD 9.53].

Studies of anxiety during early infertility treatment had equivocal results (Verhaak, Smeenk, Evers, Kremer, Kraaimaat & Braat, 2007). The studies reporting elevated anxiety found that women with infertility had anxiety prior to initiation of IVF treatment (Beaurepaire, Jones, Theiring, Saunders, & Tennant, 1994; Salvatore, et al., 2001; Slade, Emery, & Lieberman, 1997). In the present study treatment for most of the women with infertility spanned from evaluation up to two years of treatment. Additionally, women with ED have higher rates of comorbid anxiety (Gadalla & Piran, 2008; Pallister & Waller, 2008); and thus, the high prevalence of ED diagnoses in the women with infertility and in the women receiving routine health care may also explain the high anxiety scores.

Study Implications

The study results provide further support that women with ovulatory and unexplained infertility are at risk for having an occult ED. Finding that women with ovulatory infertility had significantly more ED symptoms on the Desire for Thinness and Bulimia subscales and that they had provisional lifetime ED diagnoses many times in excess of the national ED prevalence rate provides support for the conceptual model for the study. The Conceptual Model proposed that individual issues arising out of multiple explanations of behavior predispose women to eating disordered symptoms. The related change in nutritional status leads to metabolic changes affecting reproductive function, specifically ovulatory dysfunction or unexplained infertility. Because the study was at the descriptive, quantitative level, the results cannot be interpreted in

terms of specific physiologic / metabolic processes influencing reproduction. However, the results provide scientific justification to study the physiologic link and markers to better identify women with ED.

The results of this study provide additional support that women with ovulatory and unexplained infertility should be carefully assessed for current and past eating disorders. Assisted reproductive technologies (ART) can lead to pregnancy, but the procedures alone do not confer good pregnancy outcomes. Women with a low BMI before and during pregnancy are at greater risk of delivering low birth weight (LBW) babies with greater risk of morbidity and mortality (Institute of Medicine, 1990). Women who are overweight or obese before and during pregnancy are at greater risk of having gestational diabetes, hypertension and pre-eclampsia (Goldberg, 2002). Moreover, as BMI increases, the risk of these complications also increases (Linne, 2004). Also, women with eating disorders who become pregnant have a higher incidence of cesarean section (CS), postpartum depression (PPD) and small for gestational age babies (Franko, Blais, Becker, Delinsky, Greenwood, Flores, et al., 2001; Moos, Dunlop, Jack, Nelson, Coonrod, Long et al., 2008). Finally, women with eating disorders are at risk for recurrence of their eating symptoms due to body shape changes associated with postpartum fat deposits.

The Center of Disease Control and Prevention's (CDC) Select Panel on Reproductive Health has set forth specific recommendations for health and wellness care of women of reproductive age (Moos et al, 2008). They emphasize the value of integrating reproductive planning into the individual health promotion needs of every woman of childbearing age, regardless of pregnancy intention. The Panel sites the Institute of Medicine's recommendation of a prepregnancy low BMI cut point of < 19.8 km/m^2 and the importance of assessing for eating

disorder symptoms and body shape distortions. The Panel also recommends counseling women with BMIs ≥ 26 kg/m^2 regarding associated health risks, including infertility.

Taking into consideration the results of the current and past studies on eating disorders and infertility, it is critical to integrate assessment for eating disorders into infertility evaluation. Assessment of women with infertility who have had eating disorders is crucial, as these women remain at risk for poor pregnancy outcomes. The current study highlights that normal weight women with infertility can have ED, thus routine assessment of all women with infertility for ED is vital to better ART and pregnancy outcomes. For that reason Andersen and Ryan (2009, p 1353) caution reproductive endocrinologists to develop a "lower index of suspicion" of ED to ensure that ART treatments do not unintentionally contribute to maternal and fetal risk. The use of a self-report tool such as the EDI-3-RF or the EAT would provide a means for discussion of eating issues in the infertility setting. Most important, woman with ED require on-going psychiatric treatment during infertility treatment and pregnancy due to their at risk status.

The higher rate of ED in the sample of women receiving routine health care from their PCP is also of great concern. The ED diagnostic trend toward the overeating continuum in the comparison group is similar to the Johnson, Spitzer, and Williams (2001) study of ED in women receiving primary care and obstetric gynecology care. The researchers found a 6.2% prevalence rate of BN and BED and noted subjects in their sample experienced higher disability, lower functioning and medical co-morbidity. Worth mentioning, 50% the comparison group in this study had a current or past ED, which was 8 times the percent Johnson, Spitzer, and Williams found. The discrepancy could be explained by their use of a different self-rating instrument, the Spitzer et al. (1999) Patient Health Questionnaire.

Thirty eight percent of the comparison group was comprised of minority women versus 22% in the group of women with infertility. Although previous research reports that minority women have a similar prevalence of ED to Caucasian women (Franko, Becker, Thomas, and Herzog, 2007), 62% of the sample of minority women (n = 13) receiving routine health care in the present study had a lifetime ED diagnosis. The group of women with infertility had less minority women (n = 11); still, the minority women with infertility also had an unexpectedly high rate (55%) of ED diagnosis. However, 43% of the women receiving routine healthcare that self-reported as White also had ED diagnoses indicating the comparison group had higher lifetime ED diagnoses overall. One explanation for the higher rates could be the age (M 31.2; SD 6.5) of the women participants which is considerably older than the women studied in other ED research. Finally, the higher percent of ED could be related to the specific comparison group recruitment setting that integrated mental health and psychiatry services into the internal medicine practices.

Limitations

The limitations of the study were the use of convenience sampling, the recruitment settings, the comparison sample of women receiving routine healthcare at a general hospital medical center from their PCP and the use of self-report instruments.

Convenience Sample. The study used a convenience sample which limits generalization to other populations. This sampling method is subject to bias, as people self-refer or volunteer. Additionally, women were given a stipend for participation where they could choose a gift card from one of four stores (two large pharmacy stores and two coffee and tea vendors). Some women could have participated primarily due to the stipend. Finally, the low number of Hispanic study participants also limits generalization. Although overall minority representation

reflected that of the greater Boston area, only 3 women with infertility were Hispanic. Two women in the comparison group were Hispanic, and another 5 women were unsure of their ethnicity.

Recruitment Settings. As with all research, approval to recruit at each site took time to negotiate. The original recruitment plan was to have nurses review the daily patient flow, mention the study to appropriate women, and offer a brochure. Each site reviewed the protocol and expressed realistic concern about the impact of recruitment disrupting patient care flow. All sites finally agreed to allow placement of the study brochures in their waiting rooms for patients to self-refer. Allowing patients to self-refer had a greater impact on the composition of the comparison group.

Comparison group. Women in the comparison group self-referred from the Women's Center and internal medicine outpatient practice sites of a large academic medical center in the Boston metropolitan area. Not as similar in the demographic characteristics, the comparison group had higher rates of ED than the women with infertility. Finding a comparatively well group of women at the medical center was difficult, as not all healthy women under the age of 40 generally have annual exams.

The study brochures and the telephone screening highlighted that participants were to be medically stable. Unfortunately, the notion of being medically stable was in the eye of the beholder, similar to what is clinically seen with women with ED. Even women with BMIs in the extreme obesity range viewed themselves as medically stable. Improved screening at the self-referral contact for current illnesses may have provided a sample more consistent with the wellness of women with infertility. Because the comparison group is also a city sample, it is

difficult to generalize to the overall population of women receiving routine health care by their PCPs.

Use of Self-Report Instruments. The study employed self-report instruments that gathered an array of disordered ED attitudes and symptoms. Garner (2004) suggested that guaranteeing confidentiality provides more truthful response. In the present study participants were guaranteed confidentiality but not anonymity due to the possible need to further assess depression and anxiety symptoms. Use of self-report was successful in the study; however, self-report does not supplant in-person clinical research assessment in the accurate assessment of ED diagnoses.

Recommendations for Future Research

The outcomes of this study provide further support that women with ovulatory and unexplained infertility are at risk for occult ED symptoms. Women with ED may not realistically be able to report their symptoms. Some women in the study, unprompted, openly mentioned their eating symptoms or exercise problem at screening and other women made no mention. Likewise, the comparison group seemed unaware that extreme BMI is not consistent with medical stability. More research is necessary before moving to examining nursing interventions in women with infertility that have ED. Further study is needed to isolate biobehavioral predictor variables to help identify at risk women. Also, qualitative study of women's view of their eating symptoms and wellness may provide greater understanding of the ED population.

Summary

The aim of the study was to investigate disordered eating and psychological symptoms in women with ovulatory and unexplained infertility compared with women receiving routine

health care from their PCP. Hypothesis one stating that women with infertility would report significantly more eating disorder symptoms than the comparison group of women was partially upheld. Women with infertility had significantly higher Desire for Thinness and Bulimia subscale scores. The women receiving routine health care actually had significantly higher Body Dissatisfaction scores. This was consistent with the comparison group having higher BMIs and ED on the overeating continuum. Hypotheses 2a and 2b stating that women with infertility would report significantly more current and past ED diagnoses than the comparison group of women was not upheld. Hypothesis 3 stating that women with infertility would report significantly more symptoms of depression, anxiety and dietary restraint than the comparison group of women was not upheld. Instead, women receiving routine healthcare had higher Restraint scores, possibly contributing to dietary lapses. Further study isolating biobehavioral marker variables identifying women at risk for ED was recommended.

REFERENCES

Abraham, R. S., Mira, N., & Llewellyn-Jones, D. (1990). Should ovulation be induced in women recovering from an eating disorder or who are compulsive exercisers? *Fertility and Sterility, 53*, 566-568.

Ahima, R. S. (2004). Body fat, leptin, and hypothalamic amenorrhea. *New England Journal of Medicine, 351*(10), 959-962.

Ahima, R. S., Prabakaran, D., Mantzoros, C., Qu, D., Lowell, B., Marataos-Flier, E. & Flier, J. S. (1996). Role of leptin in the neuroendocrine response to fasting. *Nature, 382*(250-252).

Allison, D. B., Kalinsky, L. B., & Gorman, B. S. (1992). A comparison of psychometrics of three measures of dietary restraint. *Psychological Assessment, 4*(391-398).

Allison S., Kalucy, R., Gilchrist, P., & Jones, W. (1988). Weight preoccupation among infertile women. *International Journal of Eating Disorders, 7*, 743-748.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders, text revision* (4th Ed.). Washington, DC: American Psychiatric Association.

American Society of Reproductive Medicine Practice Committee, (2000). *Optimal evaluation of the infertile female*. Birmingham, AL: American Society of Reproductive Medicine.

Andersen, A. E., & Ryan, G. L. (2009). Eating disorders in the obstetric and gynecologic patient population. *Obstetrics & Gynecology, 114*, 1353-1367.

Barbieri, R. (2002). Management of infertility caused by ovulatory dysfunction. *American College of Obstetricians and Gynecologists Practice Bulletin, 34,* 1-12.

Balasch, J., Fabreques, F., Creu, M., & Vanrell, J. A. (1992). The usefulness of endometrial biopsy for luteal phase evaluation in infertility. *Human Reproduction 7,* 973-997.

Bates, G. W., Bates, S. R., & Whitworth, N. S. (1982). Reproductive failure in women who practice weight control. *Fertility and Sterility, 37*, 373-378.

Beaurepaire, J., Jones, M., Thiering, P. Saunders, D., & Tennant, C. (1994). Psychosocial adjustment to infertility and its treatment: Male and female responses at different stages of IVF / ET treatment. *Journal of Psychosomatic Research, 38,* 229-240.

Beck, A. T., Steer, R. A. & Brown, G. K. (1996). *Beck Depression Inventory II* Manual. San Antonio, Texas: the Psychological Corporation.

Beck, A. T., & Steer, R. A. (1987). *Beck Depression Inventory Manual*. San Antonio, TX: The Psychological Corporation.

Blais, M. A., Becker, A. E., Burwell, R. A., Flores, A. T., Nussbaum, K. M., Greenwood, D. A., Ekevblad, E. R., & Herzog, D. A. (2005). Pregnancy: Outcome and impact on symptomatology in a cohort of eating-disordered women. *International Journal of Eating Disorders, 37*(2), 92-99.

Boden, G., Chen, X., Mozzoli, M., & Ryan, I. (1996). Effects of fasting on serum leptin in normal human subjects. *Journal of Clinical Endocrinology and Metabolism, 81*, 3419-3423.

Borenstein, M., Rothstein, H., Cohen, J., Schoenfeld, D., & Berlin, J. (2000). *Sample power 2.0*. Chicago: SPSS.

Brewerton, T. D., Lydiard, R. B., Herzog, D. B., Brotman, A. W., O'Neil, P. M., & Ballenger, J. C. (1995). Comorbidity of axis I psychiatric disorders in bulimia nervosa. *Journal of Clinical Psychiatry, 56,* 77-80.

Broberger, C. (2005). Brain regulation of feed intake and appetite: molecules and networks. *Journal of Internal Medicine, 258,* 301-327.

Chehab, F. F., Qui, J. Q., Mounzih, K., Ewart-Toland, A., & Ogus, S. (2002). Leptin and reproduction. *Nutrition Reviews, 60*(10), 39-S46.

Cioffe, J. S., Van Blerkom, J., Antczak, M., Shafer, A., Wittmer, S., & Snodgrass, H. R. (1997). The expression of leptin and its receptor in preovulatory human follicles. *Molecular Human Reproduction, 3*, 467-472.

Cobb, K. L., Bachrach, L. K., Greendale, G., Marcus, R., Neer, R. M., Nieves, J., Sowers, M. F., Brown, B. W., Gopalakrishnan, G., Leutters, C., Tanner, H. K., Ward, B., & Kelsey, L. (2003). Disordered eating, menstrual irregularity, and bone mineral density in female athletes. *Medical Science and Sports Exercise, 35*, 711-719.

Coda, D., Proulx, K., Blake Smith, K. A., Kozma, S. C., Thomas, G. Woods, S. C. & Seely, R. J. (2006). Hypothalamic mTOR signaling regulates food intake. *Science, 312,* 927-930.

Collier, D., & Treasure, J. (2004). Aetiology of eating disorders. *British Journal of Psychiatry, 185*, 363-365.

Collins, J., Burrows, E., & Willan, A. (1993). *Infertile couples and their treatment in Canadian academic infertility clinics* (Vol. 10). Ottawa, Ontario: Minister of Supply and Services.

Collins, J. A., & Crosignani, P. G. (1992). Unexplained infertility: a review of diagnosis, prognosis, treatment efficacy and management. *International Journal of Gynecology and Obstetrics, 39*, 267-275.

Considine, R. V., Sinha, M. K., Heiman, M. L., Kriauciunas, A., Stephens, T. W., Nyce, M. R., Ohannesian, J. P., Marco, C. C., McKee, L. J., Bauer, T. L., & Caro, J. F. (1996). Serum immunoreactive-leptin concentrations in normal weight and obese humans. *New England Journal of Medicine, 334*, 292-295.

Conti, J., Abraham, S., & Taylor, A. (1998). Eating disorder and pregnancy outcome. *Journal of Psychosomatic Research, 44*, 465-477.

Couzinet, B., Young, J., Brailly, S., Le Bouc, Y., Chanson, P., & Schaison, G. (1999). Functional hypothalamic amenorrhea: A partial and reversible gonadotropin deficiency of nutritional origin. *Clinical Endocrinology, 50*, 229-235.

Cumella, E. J. (2006). Review of the Eating Disorder Inventory-3. *Journal of Personality Assessment, 87*(1), 116-117.

Cunningham, M. J., Clifton, D.K., & Steiner, R. A. (1999). Leptin's actions on the reproductive axis: Perspectives and mechanisms. *Biology of Reproduction, 60*, 216-222.

D'Abundo, M., & Chally, P. (2004). Struggling with recovery: Participant perspectives on battling an eating disorder. *Qualitative Health Research Qualitative Health Research, 18*(8), 1094-1106.

De Souza, M. J. (2003). Menstrual disturbances in athletes. A focus on luteal phase defects. *Medical Science Sport Exercise, 35*, 1553-1563.

DeCree, C. (1998). Sex steroid metabolism and menstrual irregularities in the exercising female: A review. *Sports Medicine, 25*, 369-406.

Devlin, M. J., Walsh, B. T., Katz, J. L., Roose, S. P., Linkie, D. M., Wright, L., Vande Wiel, R., & Glassman, A. H. (1989). Hypothalamic-pituitary-gonadal function in patients with bulimia. *Psychiatry Research, 28*, 11-24.

Domar, A. D., Broome, A., Zuttermeister, P. C., & Seibel, M. (1992). The prevalence and predictability of depression in infertile women. *Fertility & Sterility, 58,* 1158-1163.

Dubuc, G. R., Phinney, S. D., Stern, J. S., & Havel, P. J. (1998). Changes of serum leptin and endocrine and metabolic paramenters after 7 days of energy restriction in men and women. *Metabolism, 47*, 429-434.

Eckert, E. D., Pomeroy, C., Raymond, N., Kohler, P., Thuras, P., & Bowers, C. Y. (1998). Leptin in anorexia nervosa. *Journal of Clinical Endocrinology and Metabolism, 83*(3), 791-795.

Ellison, P. T. (2003). Energetics and reproductive effort. *American Journal of Human Biology, 15*, 342-351.

Erturk, E., Kuru, N., Savci, V., Tuncel, E., Ersoy, & Imamoglu, S. (2004). Serum leptin levels correlate with obesity paramenters but not with hyperinsulinism

in women with polycyctic ovary syndrome. *Fertility and Sterility, 82*(5), 1364 -1368.

European Society of Human Reproduction and Embryology (2006). Nutrition and reproduction in women. *Human Reproduction Update, 12*(3), 193-207.

Facchinetti, F., Fava, M., Fioroni, L., & Genazzani, A. D. (1993). Stressful life events and affective disorders inhibit pulsatile LH secretion in hypothalamic amenorrhea. *Psychoneuroendocrinology, 18*(5-6), 397-404.

Fairburn, C. G., & Harrison, P. J. (2003). Eating disorders. *Lancet, 361*, 407-416.

Falsetti, L., Gambera, A., Barbetti, L., & Specchia, C. (2002). Long-term follow-up of functional hypothalamic amenorrhea and prognostic factors. *The Journal of Clinical Endocrinology and Metabolism, 87*(2), 500-505.

Favaro, A., Ferrara, S., & Santonastaso, P. (2000). The spectrum of eating disorders in young women: A prevalence study in a general population sample. *Psychosomatic Medicine, 65*, 701-708.

Feight, C. B., Johnson, T. S., Martin, B. J., Sparkes, K. E., & Wagner Jr., W. W. (1978). Secondary amenorrhea in athletes. *Lancet, 2*, 1145-1146.

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. (2002). Structured Clinical Interview for the DSM IV TR axis I disorders, research version (SCID-I/P). New York: Biometrics Research, New York State Psychiatric Institute.

Flegal, K. M., Troiano, R. P., & Ballard-Barbash, R. (2001). Aim for a healthy weight: What is the target? *Journal of Nutrition, 131*, 440S-450S.

Flier, J. S. (1997). Leptin expression and action: New experimental paradigms. *Proceedings of the National Academy of Sciences USA, 94*, 4242-4245.

Flier, J. S. (2006). Regulating energy balance: The substrate fights back. *Science, 312(5775)*, 861.

Franko, D. L., Blais, M. A., Becker, A. E., Delinsky, S. S., Greenwood, S. N., Flores, A. T., Ekeblad, E. R., Eddy, K. E., & Herzog, D. B. (2001). Pregnancy complications and neonatal outcomes in women with eating disorders. *American Journal of Psychiatry, 158*, 1461-1466.

Franko, D. L., Becker, A. E., Thomas, J. J., & Herzog, D. B. (2007). Cross-ethnic Differences in Eating Disorder Symptoms and Related Distress. *International Journal of Eating Disorders, 40, 2*,156-164. DOI 10: 1002eat.

Freizinger, M., Franko, D. L., Dacey, M., Okun, B., & Domar, A. (2010). The prevalence of eating disorders in infertile women. *Fertility & Sterility, 93*, 1, 72-78.

Friedman, J. M. (2002). The function of leptin in nutrition, weight, and physiology. *Nutrition Review, 60*, S1-14.

Frisch, R. (1978). Population, food intake, and fertility. *Science, 199,* 22-33.

Gallagher, D., Heymsfield, S. B., Heo, M., Jebb, S. A., Mrugatroyd, P. R., & Sakamoto, Y. (2000). Healthy percentage body fat ranges: an approach for developing guidelines based on body mass index. *American Journal of Clinical Nutrition, 72,*694-701.

Gadalla, T., & Piran, N. (2008). Psychiatric comorbidity in women with disordered eating behavior: a national study. *Women & Health, 48*(4),467-484.

Garfinkel, P. E., Lin, E., Goering, P., Spegg, C., Goldbloom, D. S., Kennedy, S., Kaplan, A. S., & Woodside, D. B. (1995). Bulimia nervosa in a Canadian community sample: Prevalence and comparison of subgroups. *American Journal of Psychiatry* (152), 1052-1058.

Garner, D. M. (1991). *EDI-3 Eating Disorder Inventory-2* Professional Manual. Lutz, FL: PAR Psychological Assessment Resources.

Garner, D. M. (2004). *EDI-3 Eating Disorder Inventory-3* Professional Manual. Lutz, FL: PAR Psychological Assessment Resources, Inc.

Garner, D. M., Olmstead, M. P., & Polivy, J. (1983). Development and validation of a multidimensional Eating Disorder Inventory. *International Journal of Eating Disorders, 2*, 15-24.

Goldberg, G. (2002). Nutrition in pregnancy and lactation. In P. Sherry (Ed.), *Nutrition through the life cycle*. Leatherhead, UK: Leatherhead Publishing.

Gonzalez., L. O. (2002). Infertility as a transformational process: A framework for psychotherapeutic support. *Issues in Mental Health Nursing, 20*(6), 619-633.

Guyton, A. C., & Hall, J. E. (2006). *Textbook of Medical Physiology*. Philadelphia: Elsevier Saunders.

Harris, E. C., & Barraclough, B. (1998). Excess mortality of mental disorder. *British Journal of Psychiatry*. 173(7):11-53, July 1998.

Herman, C. P., & Mack, D. (1975). Restrained and unrestrained eating. *Journal of Personality, 43,* 647-660.

Herman, C. P., & Polivy, J. (1980). Restrained eating. In A. J. Stunkard (Ed.), *Obesity*. Philadelphia: W. B. Saunders.

Hersen, M., & Bellack, A. S. (1986). *Dictionary of Behavioral Assessment Techniques*. New York: Pergamon Press.

Hilton, L. K., & Loucks, A. B. (2000). Low energy availability, not exercise stress, suppresses the diurnal rhythm of leptin in healthy young women. *American Journal of Physiology Endocrinology and Metoabolism, 278*, E-43-E49.

Hoek, H. W., & van Hoeken, D. (2003). Review of the Prevalence and Incidence of Eating Disorders. *International Journal of Eating Disorders.* 34: 383-396.

Hollander, E. (1998). Treatment of obsessive-compulsive spectrum disorders with SSRIs. *British Journal of Psychiatry, 35*(Suppl.), 7-12.

Hudson, J. I., Hiripi, E., Pope, H. G., Kessler, R. C. (2007). The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. *Biological Psychiatry, 61*(3): 348-358.

Hunault, C., Eijkemans, M. J. C., te Velde, E. R., Habbema J.D., & Collins, J. A. (2002). Validation of a model predicting spontaneous pregnancy among subfertile untreated couples. *Fertility and Sterility, 78*, 500-506.

Imani, B., Eijkemans, M. J., te Velde, E. R., & Habbema, J. D (2002). A nomogram to predict the probability of live birth after clomiphene citrate induction of ovulation in normogonadotropic oligomenorrheic infertility. *Fertility and Sterility, 77*, 91-97.

Institute of Medicine. (1990). *Nutrition during Pregnancy*. Washington, D.C.: National Academy Press.

Institute for the Future. (2003). *Health and Health Care 2010: The Forecast, the Challenge*. Princeton, N.J.: Jossey-Bass.

Janssen, I., Katzmarzyk, P. T., & Ross, R. (2002). Body mass index, waist circumference, and health risk; Evidence in support of current National Institutes of Health guidelines. *Archives of Internal Medicine, 162,* 2074-2079.

Jimerson, D. C., Mantzoros, C., Wolfe, B. E., & Metzger, E. R. (2000). Decreased serum leptin in bulimia nervosa. *Journal of Clinical Endocrinology and Metabolism, 85*(12), 4511-4514.

Kadva, A., Djahanbakhch, O., Monson, J., Di, W. L. & Silman, R. (1998). Elevated nocturnal melatonin is a consequence of gonadotropin-releasing hormone deficiency in women with hypothalamic amenorrhea. *Journal of Clinical Endocrinology and Metabolism, 83*(10), 3653-3659.

Kalantaridou, S. N., Makrigiannakis, A., Zoumakis, E., & Chrousos, G. P. (2004). Review - stress and the female reproductive system. *Journal of Reproductive Immunology, 62*, 61-68.

Kaye, W. H. (1997). Anorexia nervosa, obsessional behavior, and serotonin. *Psychopharmacological Bulletin, 33*, 335-344.

Kendler, K. S., MacLean, C, Neal, M., Kessler, R. Heath, A, & Eaves, L. (1991). The genetic epidemiology of bulimia nervosa. *American Journal of Psychiatry, 148*(1627-1637).

Keye, W. R., Chang, R. J., Rebar, R. W., & Soules, M. R. (1995). *Infertility Evaluation and Treatment.* Philadelphia: W.B. Saunders Company.

King, J. C. (2000). Physiology of pregnancy and nutrient metabolism. *American Journal of Clinical Nutrition, 71 (supp)*, 121S-125S.

Kirchengast, S., & Huber. J. (2004). Body composition characteristics and fat distribution patterns in young women infertile women. *Fertility and Sterility, 81,* 539-544*S.*

Klein, D. A., & Walsh, B. T. (2004). Eating disorders: Clinical features and pathology. *Physiology and Behavior, 81*, 359-374.

Kolaczynski, J. W., Considine, R. V., Ohannesian, J., Marco, C., Opentanova, I., Nyce, M. R., Myint, M., & Caro, J. F. (1996). Responses of leptin to short-term fasting and refeeding in humans. *Diabetes, 45*, 1511-1515.

Knochenhauer, E. S., Key, T. J., Kahsar-Miller, M., Waggoner, W. Boots, L. R., & Azziz, R. (1998). Prevalence of the polycystic ovary syndrome in unselected black and white women of the southeastern Untied States: A prospective study. *Journal of Clinical Endocrinology and Metabolism, 83*, 3078-3082.

Kotsuji, F., Kubo, M., & Takeuchi, Y., & Tominaga, T. (1993). Alternate-day GnRH therapy for ovarian hypofunction induced by weight loss: Treatment of six patients who remained amenorrheic after weight gain. *Clinical Endocrinology and Metabolism, 39*, 641-648.

Lacey, H. J., & Smith, G. (1987). Bulimia nervosa: The impact of pregnancy on mother and baby. *British Journal of Psychiatry, 150*, 777-781.

Landt, M., Lawson, G. M., Helegeson, J. M., Davilla-Roma, V. G., Ladenson, J. H., Jaffe, A. S., & Hickner, R. C. (1997). Prolonged exercise decreases leptin concentrations. *Metabolism, 46*, 1109-1112.

Laughlin, G. A., Dominguez, E., & Yen, S. S. C. (1998). Nutritional and endocrine-metabolic aberrations in women with functional hypothalamic amenorrhea. *Journal of Clinical Endocrinology and Metabolism, 83*(1), 25-32.

LeGrange, D., Telch, C., & Tibbs, J. (1998). Eating attitudes and behaviors in 1435 South African Caucasian and Non-Caucasian college students. *American Journal of Psychiatry, 155*(2), 250-254.

Legro, R. S. (2002). Polycystic ovary syndrome. *American College of Obstetricians and Gynecologists Practice Bulletin, 41,* 1-14.

Levine, A., Pomeroy, J., & Wilson, T. (1994). Hypothalamic dysfunction at ideal body weight simulating anorexia nervosa. *Journal of Pediatric Endocrinology, 7*(357-360).

Linne, Y. (2004). Effects of obesity on women's reproduction and complications during pregnancy. *Obesity Reviews, 5*, 137-143.

Little, L., & Lowkes, E. (2000). Critical issues in the care of pregnant women with eating disorders and the impact on their children. *Journal of Midwifery & Women's Health, 45*(4), 301-307.

Loucks, A. B., & Horvath, S. M. (1985). Athletic amenorrhea: A review. *Medical Science Sport Exercise, 17*, 56-72.

Loucks, A. B. (1990). Effects of exercise training on the menstrual cycle: Existence and mechanisms. *Medicine and science in sports and exercise, 22*(3), 275-280.

Loucks, A. B., & Verdum. (1998). Slow restoration of LH pulsatility by refeeding in energetically disrupted women. *American Journal of Physiology -*

Regulatory, Integrative and Comparative Physiology and Clinical Nutrition, 275, 1218-1226.

Maffei, M., Halaas, J. Ravussin, E., Pratley, R. E., Lee, G. H., Zhang, Y., Fei, H., Kim, S., Lallone, R., Ranganathan, S., Kern, P. A., & Freidman, J. M. (1996). Leptin levels in human and rodent: Measurement of plasma leptin in *ob* RNA in obese and weight reduced subjects. *Nature Medicine, 1*, 1155-1161.

Mantzoros, C., Flier, J. S., Lessem, M. D., Brewerton, T. D., & Jimerson, D. C. (1997). Cerebrospinal fluid leptin in anorexia nervosa: Correlation with nutritional status and potential role in resistance to weight gain. *Journal of Clinical Endocrinology and Metabolism, 82*(6), 1845-1841.

Mantzoros, C. S., & Moschos, S. J. (1998). Leptin: In search of role(s) in human physiology and pathophysiology. *Clinical Endocrinology, 49*, 551-567.

Marcus, M. S., Loucks, T. L., & Berga, S. L. (2001). Psychological correlates of functional hypothalamic amenorrhea. *Sterility & Fertility, 26*, 310-316.

McConnell, H. J., O'Connor, K. A., Brindle, E., & Williams, N. I. (2002). Validity of methods for analyzing urinary steroid data to detect ovulation in athletes. *Medical Science Sports Exercise, 34*, 1836-1844.

Metropolitan Life Insurance Co. (1959). New weight standards for men and women. *Metropolitan Life Statistical Bulletin, 40*, 1-4.

Miller, K., Parulekar, M., Schoenfeld, E. A., Hubbard, J., & Grinspoon, S. K. (1998). Decreased leptin levels in normal weight women with hypothalamic

amenorrhea: The effects of body composition and nutritional intake. *Journal of Clinical Endocrinology and Metabolism, 83*(7), 2309-2312.

Mitchell-Geileghem, A., Mittelstaedt, M. E., & Bulik, C. (2002). Eating disorders and childbearing: Concealment and consequences. *Birth, 29*(3), 182-191.

Mitchell, J. E., Seim, H. C., Glotter, D., Soll, E. A., & Pyle, R. L. (1991). A retrospective study of pregnancy in bulimia nervosa. *International Journal of Eating Disorders, 10*(2), 209-214.

Monteleone, P., Fabrazzo, M., Tortorella, A., Fuschino, A., & Maj, M. (2002). Opposite modifications in circulating leptin and soluble leptin receptor across the eating disorder spectrum. *Molecular Psychiatry, 7*, 641-646.

Moos, M-K., Dunlop, A. L., Jack, B. W., Nelson, L., Coonrod, D. V., & Long, R., et al. (2008). Healthier women, healthier reproductive outcomes: recommendations for the routine care of all women of reproductive age. *American Journal of Obstetrics & Gynecology,* Dec. supplement, S280-S289.

Morgan, J. F. (1999). Eating disorders and reproduction. *Australian and New Zealand Journal of Obstetrics and Gynecology, 39*(2), 167-173.

Morgan, J. F., Lacey, J. H., & Sedgewick, P. M. (1999). Impact of pregnancy on bulimia nervosa. *British Journal of Psychiatry, 174,* 135-140.

Morris, S. N., Missmer, S. A., Cramer, D. W., Powers, D., McShane, P. M., & Hornstein, M. D. (2006). Effects of lifetime exercise on the outcome of in vitro fertilization. *Obstetrics and Gynecology, 108,* 938-945.

Moschos, S., Chan, J. L., & Mantzoros, C. S. (2002). Leptin and reproduction: A review. *Fertility and Sterility, 77*(3), 433-443.

Namir, S., Melman, K. N., & Yager, J. (1986). Pregnancy in restricter-type anorexia nervosa: A study of six women. *International Journal of Eating Disorders, 5*(5), 837-845.

Oshansky, E. (2003). A theoretical explanation for previously infertile mothers' vulnerability to depression. *Journal of Nursing Scholarship, 35*(3), 263-268.

Otis, C. L., Drinkwater, B. L., Johnson, M., Loucks, A. B., & Wilmore, J. H. (1997). ACSM position stand on the female athlete triad. *Medical Science Sports Exercise, 29*, i-ix.

Pallister, E., & Waller, G. (2008). Anxiety in the eating disorders: Understanding the overlap. *Clinical Psychology Review, 28*(3), 366-386.

Pasquali, R., & Gambineri, A. (2006). Polycystic Ovary Syndrome. *Anals of the New York Academy of Sciences, 1092,* 158-174.

Perkins, R., Hall, J., & Martin, K. (2001). Aetiology, previous menstrual function and patterns of neuro-endocrine disturbance as prognostic indicators in hypothalamic amenorrhea. *Human Reproduction, 16*(10), 2198-2305.

Pirke, K. M., Fichter, M. M., Schweiger, U., Fruth, C., Streitmatter, A., & Wolfram, G. (1987). Gonadotropin secretion patter in bulimia nervosa. *International Journal of Eating Disorders, 6,* 655-661.

Polivy, J., & Herman, C. P. (1983). *Breaking the Diet Habit: The Natural Weight Alternative*. New York: Basic Books.

Polivy, J., & Herman, C. P. (1985). Dieting and binging: A causal analysis. *American Psychologist, 40*, 193-201.

Porterfield, S. P. (2001). *Endocrine Physiology* (2nd ed.). St. Louis: Mosby, A Hartcourt Health Sciences Co.

Reifsnider, E., & Gill, S. L. (2000). Nutrition for the childbearing years. *Journal of Obstetrical Gynecological and Neonatal Nursing, 29*(1), 43-55.

Reiger, E., Touyz, S., Swain, T., & Beumont, P. J. V. (2001). Cross-cultural research on anorexia nervosa: Assumptions regarding the role of body weight. *International Journal of Eating Disorders, 29*, 205-215.

Rock, C. L., Gorenflo, D. W., Drewnowski, A., & Demitrack, M. A. (1996b). Nutritional characteristics, eating pathology, and hormonal status in women. *American Journal of Clinical Nutrition, 64*, 566-571.

Russell, G. F. (1979). Bulimia nervosa: An ominous variant of anorexia nervosa. *Psychological Medicine, 9*, 429-448.

Santor, D. A., Ramsay, J. O., & Zuroff, D. C. (1994). Nonparametric item analyses of the Beck Depression Inventory: Evaluating gender item bias and response option weights. *Psychological Assessment, 6*, 255-270.

Schneider, J. E., & Wade, G. N. (2000). Inhibition of reproduction in the service of energy balance. In K. Wallen, & Schneider, J. E. (Ed.), *Reproduction in Context*. Cambridge, MA: The MIT Press.

Schreiber, C., Florin, I., & Rost, W. (1983). Psychological correlates of functional secondary amenorrhea. *Psychotherapy and Psychosomatics, 39*(2), 106-111.

Salvatore, P., Gariboldi, S., Offidani, A., Coppola, F., Amore, M., & Maggini, C. (2001). Psychopathology, personality, and marital relationship in patients undergoing in vitro fertilization procedures. *Fertility & Sterility, 75,* 1119-1125.

Sepilian, V. P., Crochet, J. R., & Nagamani, M. (2006). Serum soluble leptin receptor levels and free leptin index in women with polycystic ovary syndrome: Relationship to insulin resistance and androgens. *Fertility and Sterility, 85*(5), 1441-1447.

Slade, P., Emery. J., & Lieberman, B. (1997). A prospective, longitudinal study of emotions and relationships in in-vitro fertilization treatment. *Human Reproduction, 12,*183-190.

Smith, S., Pfeifer, S. M., & Collins, J. A. (2003). Diagnosis and management of female infertility. *Journal of the American Medical Association, 290*(13), 1767-1770.

Speroff, L., & Fritz, M. A. (2005). *Clinical Gynecologic Endocrinology and Infertility.* (7th ed.) Philadelphia: Lippincott Williams and Wilkins.

Spielberger, C. D. (1989). *Manual for the State-Trait Anxiety Inventory (Form Y).* Palo Alto, CA: Consulting Psychologists Press, Inc.

Spitzer, R. L., Williams, J. B. W., Gibbon, M., & First, M. B. (1992). Structured Clinical Interview for the DSM-III-R (SCID). I: History, rational and description. *Archives of General Psychiatry*, 49, 624-629.

SPSS (2000). *Sample Power,* Version 2.00. Chicago, IL: SPSS Inc.

Stephen, K. S., & Chandra, A. (1998). Updated projections of infertility in the United States: 1995-2025. *Fertility and Sterility, 70*, 30-34.

Stewart, D. E., Raskin, J., Garfinkel, P.E., MacDonald, O. L., & Robinson, G. E. (1987). Anorexia nervosa, bulimia and pregnancy. *American Journal of Obstetrics and Gynecology, 157*, 1194-1198.

Stewart, D. E., Robinson, G. E. Goldbloom, D. S., & Wright, C. (1990). Infertility and eating disorders. *American Journal of Obstetrics and Gynecology, 163*, 1196-1199.

Striegel-Moore, R. H., Dohm, F. A. Kraemer, H. C., Taylor, C. B., Daniels, S., Crawford, P. B., & Schreiber, G. B. (2003). Eating disorders in black and white women. *American Journal of Psychiatry, 160*, 1326-1331.

Stright, B. R. (2005). *Maternal-Newborn Nursing*. Philadelphia, PA: Lippincott, Williams & Wilkins.

Tabachnick, B. G., & Fidell, L. S. (2007). *Using Multivariate Statistics* (5th ed.). New York: Harper Collins.

Templeton, A. (2000). Infertility and the establishment of pregnancy - overview. *British Medical Journal, 56*(3), 577-587.

The American Society of Reproductive Medicine Practice Committee. (2000). *Optimum evaluation of the infertile female*. Birmingham, AL: American Society for Reproductive Medicine.

Thomas, B. (2001). *Manual of Dietetic Practice* (3rd ed.). Oxford, England: Blackwell Publishing.

Tortora, G. J., & Derrickson, B. (2006). *Principles of Anatomy and Physiology* (11th ed.). Hoboken, NJ: John Wiley & Sons.

US Congress Office of Technology Assessment. (1988). *Infertility: Medical and Social Choices*. Washington, D.C.: US Government Printing Office.

Verhaak, C. M., Smeenk, J. M., Evers, A. W., Kremer, J.A. Kraaimaat, F. W., & Braat. (2007). Women's emotional adjustment to IVF: a systematic review of 25 years of research. *Human Reproduction Update, 13*(1), 27-36.

Verri, A. Nappi, R. E., Cecchini, A. P., Vallero, E., Luzi, S., & Zara, C. (1998). Eating disorders and Axis I psychiatric comorbidity in amenorrheic women. *International Journal of Eating Disorders, 24,* 137-146.

Wade, G. N. (1998). Energy balance, effects on reproduction. In E. Knobil, & Neill, J. D. (Ed.), *Encyclopedia of Reproduction* (pp. 1091-1099). New York: Academic Press.

Wade, G. N., Schneider, J. E., & Li, H-Y. (1996). Control of fertility by metabolic cues. *American Journal of Physiology-Endocrinology and Metabolism, 270*(1), E1-E19.

Walsh, B. T., & Devlin, M. (1998). Eating disorders: Progress and problems. *Science, 280*, 1387-1390.

Warren, M. P., Vossoughian, F., Geer, E. B., Hyle, E.P., Adberg, C. L., & Ramos, R. H. (1999). Functional hypothalamic amenorrhea: Hypoleptinemia and disordered eating. *Journal of Clinical Endocrinology and Metabolism, 84*(3), 873-877.

Warren, M. P., Holderness, C. C., Lesobre, V., Tzen, R., & Vossoughian, F. (1994). Hypothalamic amenorrhea and hidden nutritional insults. *Journal of the Society of Gynecologic Investigation, 1*, 84-88.

Williams, N. I., Helmreich, D. L., Parfitt, D. B., Caston-Balderrama, A., & Cameron, J. L. (2001). Evidence for a causal role of low energy availability in the induction of menstrual cycle disturbances during strenuous exercise training. *Journal of Clinical Endocrinology and Metabolism, 86*, 5184-5193.

Williamson, C. S. (2006). Nutrition in pregnancy. *Nutrition Bulletin, 31*, 28-59.

Willis, D. C., & Rand, C. S. (1988). Pregnancy in bulimic women. *Obstetrics and Gynecology, 71*, 708-710.

Wolfe, B. E. (2006). Reproductive health in women with eating disorders. *Journal of Obstetric, Gynecologic and Neonatal Nursing, 34,* 255-263.

Wolfe, B. E., Jimerson, D. C., Orlova, C., & Mantzoros, C. S. (2004). Effect of dieting on plasma leptin, soluble leptin receptor, adiponectin, and resistin levels in healthy volunteers. *Clinical Endocrinology, 61*, 332-328.

Wolfe, B. E., Metzger, E. D., & Jimerson, D. C. (2003). Eating disorders. In T. M. Buttaro, J. Tribulski, P. P. Bailey, & J. Sandberg-Cook (Ed.), *Primary Care: A Collaborative Practice* (2nd ed., pp. 1237-1241). St. Louis, MO: Mosby Year Book.

Wolfe, B., Metzger, E., Levine, J., & Jimerson, D. (2001). Laboratory screening for electrolyte abnormalities and anemia in bulimia nervosa: A controlled study. *International Journal of Eating Disorders, 30*, 288-293.

Wolfe, B. E., Metzger, E. D., & Stollar, C. (1997). The effects of dieting on plasma tryptophan concentration and food intake in healthy women. *Physiology and Behavior, 61*, 537-541.

Wolk, S. L., Loeb, K. D., & Walsh, B. T. (2005). Assessment of patients with anorexia nervosa: Interview versus self-report. *International Journal of Eating Disorders, 37*, 92-99.

Zaadstra, B. M., Seidell, J. C., Van Noord, P. A. H., te Velde, E. R., Habbema, J. D. F., Vrieswijk, B., & Larbaat. J. (1993). Fat and female fecundity: Prospective study of effect of body fat distribution on conception rates. *British Medical Journal, 306*(6876), 484-488.

Appendix

Institutional Review Board Approvals

- Boston College
- Beth Israel Deaconess Medical Center

Verbal Informed Consent documents

Study Instruments

- Demographic Information Sheet
- Herman and Polivy Revised Restraint Scale
- Contact information for other instruments

Brochures

- Women with infertility
- Women receiving routine health care

Study Advertisements

- Women with infertility
- Women receiving routine health care

BOSTON COLLEGE
Institutional Review Board
Office for Research Protections
Waul House, 3rd Floor
Phone: (617) 552-4778, fax: (617) 552-0948

IRB Protocol Number: 08.296.01

DATE: June 2, 2008

TO: Ann Cousins

FROM: Institutional Review Board – Office for Research Protections

RE: Self-Report Of Dietary And Psychological Symptoms By Women With Ovulatory And Unexplained Infertility

Notice of IRB Review and Approval
Expedited Review as per Title 45 CFR Part 46.110, FR 60366, FR, # 7
Waiver of Documentation of Informed Consent [Title 45 CFR 46.117 (c)]

The project identified above has been reviewed by the Boston College Institutional Review Board (IRB) for the Protection of Human Subjects in Research using an expedited review procedure. This is a minimal risk study. This approval is based on the assumption that the materials, including changes/clarifications that you submitted to the IRB contain a complete and accurate description of all the ways in which human subjects are involved in your research.

This approval is given with the following standard conditions:

1. You are approved to conduct this research only during the period of approval cited below;
1. You will conduct the research according to the plans and protocol submitted (approved copy enclosed);
2. You will immediately inform the Office for Research Protections (ORP) of any injuries or adverse research events involving subjects;
3. You will immediately request approval from the IRB of any proposed changes in your research, and you will not initiate any changes until they have been reviewed and approved by the IRB;
4. The IRB has waived the requirement for obtaining the signature as allowed under 45CFR 46.117 (c) (1). The only record linking the subject and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of

confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern.

5. You will give each research subject a copy of the informed consent document;
6. You may enroll up to 200 participants.
7. **If your research is anticipated to continue beyond the IRB approval dates, you must submit a Continuing Review Request to the IRB approximately 60 days prior to the IRB approval expiration date. Without continuing approval the Protocol will automatically expire on June 2, 2009.**

Additional Conditions: Any r*esearch personnel that have not completed CITI education certificates should be removed from the project until they have completed the training. When they have completed the training, you must submit a Protocol Revision and Amendment Form to add their names to the protocol, along with a copy of their CITI education certificate.*

Approval Period: **June 2, 2008- June 1, 2009**

Boston College and the Office for Research Protections appreciate your efforts to conduct research in compliance with Boston College Policy and the federal regulations that have been established to ensure the protection of human subjects in research. Thank you for your cooperation and patience with the IRB process.

Sincerely,

Stephen Erickson
Interim Director
Office for Research Protections
COC

BETH ISRAEL DEACONESS MEDICAL CENTER
A member of CAREGROUP

Beth Israel Deaconess Medical Center
330 Brookline Avenue
Boston, MA 02215
(617) 667-7000

Notification of Activation

Protocol #: 2008-P-000095; BIDMC
Legacy #: West Expedited

To: Ann Cousins, MSN, APRN, BC

Title: **Self-Report of Dietary and Psychological Symptoms by Women with Ovulatory and Unexplained Infertility**

IRB Approval Date: 04/4/2008
Expiration Date: 04/3/2009

All committee requirements for the research application referenced have been met. This research application is activated for recruitment and enrollment of subjects. This certifies that the research application was reviewed by the Committee on Clinical Investigations (CCI), the appropriately authorized Institutional Review Board (IRB) and Privacy Board appointed to review research involving human subjects at a convened CCI meeting. The IRB voted to approve this research application. In their review, the IRB specifically considered the rights and welfare of the individual(s) involved; the appropriateness of methods used to secure informed consent; and the risks and potential medical benefits of the investigation.

This study is approved for one year unless otherwise stated.

This study was approved with waiver of written consent and authorization.

The following have been reviewed and approved:

Research Application received 3/14/08:

- Part A – Basic information, dated 2/28/08
- Part B – Study Description
- Part C – Nursing Assistance
- Verbal Informed Consent Script, revised 3/26/08
- Study Summary Letter, revised 3/26/08
- Part M – Expedited Review (Category 7)
- Part P – Data Safety Monitoring Plan
- Part Q – Co-Investigators/Key Study Personnel (Barbara Wolfe)
- Two recruitment brochures (BIDMC and Boston IVF), revised 3/26/08

BETH ISRAEL DEACONESS MEDICAL CENTER
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- Survey Instruments (Demographic Information, Eating Disorder Inventory 3 Referral Form and Symptom Checklist, Beck Depression Inventory, Revised Restraint Scale, State-Trait Anxiety Inventory)

Please note: When the blanks are filled in on the recruitment flyers, they must be submitted for approval as study amendments.

HIPAA Waiver of Authorization:

The CCI/Privacy Board has determined that the Request for Waiver of Authorization dated 3/26/08 satisfies the criteria for waiver. This waiver of authorization is approved for the use and/or disclosure of Protected Health Information (PHI) for the referenced protocol in the manner described below.

Recruitment:

- Conversations with prospective research subjects

Verbal consent only (waiver of written consent)

The following persons or class of persons at BIDMC will have access to (use of) PHI:

- Principal Investigator and Co-Investigator

The PHI to be used includes:

- Names
- Telephone Numbers
- Geographic Identifiers and Dates:
  - Street
  - City
  - Zip Code

<u>While this waiver is approved for the duration of the study, IRB approval for this protocol expires 4/3/09 and will require continuing review prior to this date. It is the responsibility of the investigator to complete the necessary requirements to secure this approval.</u>

INVESTIGATOR, please note the following:

1. Use only IRB approved copies of the consent form(s), questionnaire(s), letter(s), advertisement(s), etc. in your research. Do not use expired consent forms.
2. Any modifications or changes made to the study must be submitted to the IRB in writing for review. The IRB must approve all changes before they can be initiated.

BETH ISRAEL DEACONESS MEDICAL CENTER
A member of CAREGROUP

Beth Israel Deaconess Medical Center
330 Brookline Avenue
Boston, MA 02215
(617) 667-7000

3. Any serious and/or unexpected adverse event in a study subject and/or death of a subject is to be reported to the IRB within 24 hours followed by a written report within 10 working days of the event. Any moderate or mild adverse event in a study subject is to be reported to the IRB within 14 working days of the event.
4. The BIDMC assurance number is: FWA00003245. Form FDA 1572 and NIH grant submissions or follow-up certifications for this research application should reference the appropriate institutional assurance number.
5. This research application expires a year from date of review and will require continuing review prior to that date. It is the responsibility of the investigator to complete the necessary requirements to secure this approval.

Please contact the Committee on Clinical Investigations (CCI) at E/FN 201, or call (617) 667-0476, with any questions you may have. Information can also be found on the CCI website: http://research.bidmc.harvard.edu/OST/ClinicalTrials/default.asp.

Alan Lisbon, M.D.
Chairman, Committee on Clinical Investigations

4/14/2008
Date of Correspondence

Verbal Informed Consent

Study: **Self-Report of Dietary and Psychological Symptoms by Women with Ovulatory and Unexplained Infertility**

Participant: _____

You have been invited to take part in a research study titled, *Self-Report of Dietary and Psychological Symptoms by Women with Ovulatory and Unexplained Infertility*. The study explores aspects of dietary and emotional symptoms in women. You are being invited to take part in this research study because you are embarking on infertility treatment or have recently sought routine health care. If you take part in this study, you will be one of 200 women to do so.

Your participation is completely voluntary. Your decision whether or not to participate will have no effect on your relationship with your health care provider or affect your health care in any way. If there is anything you do not understand, please do not hesitate to ask questions. You may decide to not participate at any time.

The person doing this study is Ann Cousins, an advanced practice psychiatric nurse at BIDMC and a doctoral candidate at Boston College. No funding has been received in this study. Neither Ms. Cousins nor Professor Wolfe expects to receive any extra money from companies because of the research study.

To participate, please fill out the attached survey. The survey involves your report of dietary/eating and psychological symptoms you may have experienced. There is no cost to you for participation. The information containing your responses to the survey will go directly to Boston College.

The survey takes from 30 to 40 minutes to complete. If you need more time, please limit yourself to 1 hour. Participating in the survey is not the same as seeking a professional evaluation or treatment. Should your responses suggest that consultation is recommended, I will call you to discuss possible referral. Please send the survey forms back in the postage-paid envelope addressed to Ann Cousins at Boston College.

Your name and your responses are confidential. No information is entered into your medical record. Additionally, your name will not be on the survey forms. Instead, your self-report forms will have a study ID number. Please leave your name off the survey documents and the return mailing envelope. Your responses will be kept in locked files in a locked room at Boston College, and the key to the study ID will be in a separate locked cabinet.

To the best of my knowledge, filling out the survey will cause you no additional harm to you than what you would experience in everyday life. Your will receive a $30.00 gift card in recognition of your participation. There will be no direct benefit to you for participating.

Returning your responses on the study questionnaires implies your consent. By consenting, you are allowing the investigators and other authorized personnel to use and disclose [to people at BIDMC and Boston College] Protected Health Information about you. This may include information about you that already exists such as the infertility type

you may or may not currently experience, demographic information, as well as any new information generated from your responses on the questionnaires. This is your Protected Health Information.

Your Protected Health Information may be shared with investigators listed on this consent form as well as the supporting research team [i.e. research assistants and statistician]. Your Protected Health Information may also be shared with the Committee on Clinical Investigations of Beth Israel Deaconess Medical Center and the Boston College Institutional Review Board, as they are responsible for reviewing studies for the protection of the research subjects. The main reason for using and sharing your Protected Health Information is to conduct and oversee the research as described in this verbal Informed Consent. Your Protected Health Information may also be shared to ensure that the research meets legal, institutional and accreditation requirements and to conduct public health activities.

If you decide to take back your authorization so that your Protected Health Information can no longer be used in this study, please send a letter notifying the Principal Investigator of your withdrawal of your authorization to Ann Cousins, PhD candidate, APRN at Cushing Hall, Boston College, 140 Commonwealth Avenue, Chestnut Hill, MA 02467. However, the investigators in this study will not be required to destroy or retrieve any of your Protected Health Information that has already been used or disclosed before the Principal Investigator receives your letter.

You are encouraged to ask questions now and at any time. If you have further questions, please contact Ann Cousins at 617-785-0411 or Professor Wolfe at (617) 552-1804. If you have questions about your rights as a research participant, please contact Boston College Office for Human Research Participant Protection at (617) 552-4778 or Beth Israel Deaconess Medical Center Office for Human Research Participant Protection at (617) 667-0469. Thank you very much. I look forward to hearing back from you. A letter summarizing this informed consent will be sent with the study packet.

Ageed to participate? _____ Yes _____ No

_____ _____

Date Time

[BC Letterhead]

April 15, 2008

Dear Study Participant:

You have been invited to take part in a research study titled, *Self-Report of Dietary and Psychological Symptoms by Women with Ovulatory and Unexplained Infertility*. The study explores aspects of dietary and emotional symptoms in women. You are being invited to take part in this research study because you are embarking on infertility treatment or have recently sought routine health care. If you take part in this study, you will be one of 200 women to do so.

Your participation is completely voluntary. Your decision whether or not to participate will have no effect on your relationship with your health care provider or affect your health care in any way. If there is anything you do not understand, please do not hesitate to ask questions. You may decide to not participate at any time.

The person doing this study is Ann Cousins, an advanced practice psychiatric nurse at BIDMC and a doctoral candidate at Boston College. No funding has been received in this study. Neither Ms. Cousins nor Professor Wolfe expects to receive any extra money from companies because of the research study.

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Returning your responses on the study questionnaires implies your consent. By consenting, you are allowing the investigators and other authorized personnel to use and disclose [to people at BIDMC and Boston College] Protected Health Information about you. This may include information about you that already exists such as the infertility type you may or may not currently experience, demographic information, as well as any new information generated from your responses on the questionnaires. This is your Protected Health Information.

Your Protected Health Information may be shared with investigators listed on this consent form as well as the supporting research team [i.e. research assistants and statistician]. Your Protected Health Information may also be shared with the Committee on Clinical Investigations of Beth Israel Deaconess Medical Center and the Boston College Institutional Review Board, as they are responsible for reviewing studies for the protection of the research subjects. The main reason for using and sharing your Protected Health Information is to conduct and oversee the research as described in this verbal Informed Consent. Your Protected Health Information may also be shared to ensure that the research meets legal, institutional and accreditation requirements and to conduct public health activities.

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You are encouraged to ask questions now and at any time. If you have further questions, please contact Ann Cousins at 617-785-0411 or Professor Wolfe at (617) 552-1804. If you have questions about your rights as a research participant, please contact Boston College Office for Human Research Participant Protection at (617) 552-4778 or Beth Israel Deaconess Medical Center Office for Human Research Participant Protection at (617) 667-0469. Thank you very much. I look forward to hearing back from you. A letter summarizing this informed consent will be sent with the study packet.

Sincerely,

Ann Cousins, PhD(c), RN, CS.

Barbara Wolfe, PhD, RN, CS, FAAN
Dissertation Advisor
Professor of Nursing

Study ID _____ **Demographic Information Sheet** Date: __ __/__ __/__ __ __ __
MM DD YYYY

1. Age in whole years: _____ years old

2. What is your marital status (circle one)?
1 Single/Never married
2 Married *(including common law)*
3 Separated
4 Divorced
5 Widowed

3. What is your highest level of education (circle one)?

1	Some high school	5	Bachelors degree
2	High school grad	6	Masters degree
3	Some college	7	Professional degree
4	Associate degree	8	PhD

4. What is your current work status (circle one)?
1 Currently working full-time
2 Currently working part-time (20 hours or less)
3 Not currently working outside of home

5. What is your income (circle one)?
1 Under $20,000
2 $20,000 - $30.000
4 $30,000 - $40,000
5 $40,000 - $50,000
6 $50,000 - $75,000
7 $75,000 - $100,000
8 100,000 - $150,000
9 150,000 and above

6. Yours & spouse/partner combined income?
1 Under $20,000
2 $20,000 - $30.000
4 $30,000 - $40,000
5 $40,000 - $50,000
6 $50,000 - $75,000
7 $75,000 - $100,000
8 $100,000 - $150,000
9 $150,000 and above

7. Are you currently experiencing infertility (circle one)?

1 Yes If yes, were you told that the infertility was (circle one)
1A Ovulatory or hormonal related?
1B Unexplained?
1C Other? Specify:_____

2 No

continued on the next page

Study ID _____ **Demographic Information Sheet** Date: __ __/__ __/__ __ __ __
MM DD YYYY

8. What is your ethnicity (circle one)?
1 Hispanic or Latino
2 Not Hispanic or Latino
3 Unknown

9. What is your race?

Self-Reported Race of <u>All</u> Participants:	**Self reported Race of All Hispanic and Latino Participants**
1 American Indian or Alaskan Native	**1** American Indian or Alaskan Native
2 Asian, East Southeast	**2** Asian, East Southeast
3 Asian, Western	**3** Asian, Western
4 Native Hawaiian or Other Pacific Islander	**4** Native Hawaiian or Other Pacific Islander
5 Black or African American	**5** Black or African American
6 White	**6** White
7 Multi-Racial	**7** Multi-Racial
8 Unknown	**8** Unknown
9 Other	**9** Other

See definitions below:

Ethnic and Racial Definitions for the Categories Above:

Hispanic and Latino:	*A Person of Cuban, Mexican, Puerto Rican, South or Central America or other Spanish culture or origin, regardless of race.*
American Indian or Alaska Native:	*A person having origins in any of the original peoples of North, Central, or South America, and who maintains tribal affiliations or community attachment.*
East/Southeast Asian:	*A person having origins in any of the original peoples of the Far East or Southeast Asia.*
Western Asian:	*A person having origins in any of the original peoples of the Indian subcontinent. This area includes, for example, India and Pakistan.*
Native Hawaiian or Other Pacific Islander:	*A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.*
Black or African American:	*A person having origins in any of the black racial groups of Africa.*
White:	*A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.*

Thank you! Please compete the self-rating questionnaires and use the enclosed investigator addressed envelope to mail back to Boston College.

For questions please call Ann Cousins, PhDc, RN, CS at 617-785-0411

SUBJECT ID#: _____
DATE: _____
TIME: _____

Herman & Polivy Scale

The following questions refer to your **normal** eating pattern and weight fluctuations. Please answer accordingly.

Age _____ Sex _____

Height _____ Weight _____

1. How often are you dieting? (Circle one)
   Never Rarely Sometimes Usually Always

2. What is the maximum amount of weight (in lbs) you have ever lost in one month? (Circle one)
   0—4 5—9 10—14 15—19 20+

3. What is your maximum weight gain (in lbs) within a week? (Circle one)
   0—1 1.1—2 2.1—3 3.1—5 5.1+

4. In a typical week, how much does your weight fluctuate (in lbs)? (Circle one)
   0—1 1.1—2 2.1—3 3.1—5 5.1+

5. Would a weight fluctuation of 5 lbs. affect the way you live your life? (Circle one)
   Not at all Slightly Moderately Very Much

6. Do you eat sensibly in front of others and splurge alone? (Circle one)
   Never Rarely Often Always

7. Do you give too much time and thought to food? (Circle one)
   Never Rarely Often Always

8. Do you have feelings of guilt after overeating? (Circle one)
   Never Rarely Often Always

9. How conscious are you of what you're eating? (Circle one)
   Not at all Slightly Moderately Very Much

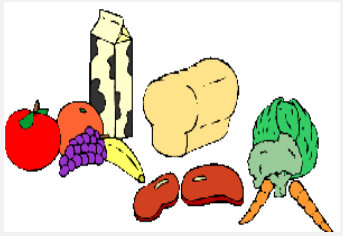
10. What is your maximum weight ever? _____

11. How many pounds over your desired weight were you at your maximum weight? (Circle one)
    0—1 1—5 6—10 11—20 21+

12. If applicable, what is the usual way you respond when your diet is broken: (Check one)
    _____ I go right back on the diet
    _____ I compensate by eating less for a while
    _____ I continue to eat non-diet foods and start the diet another day
    _____ I get rid of non-diet food by vomiting or taking laxatives
    _____ I exercise

Instruments	Available Through
Eating Disorder Inventory-3-Referral Form	Psychological Assessment Resources www.parinc.com 1.800.331.8378
Eating Disorder Inventory-3-Symptom Checklist	Psychological Assessment Resources www.parinc.com 1.800.331.8378
Beck Depression Inventory	www.pearsonassessments.com
Spielberger State-Trait Anxiety Inventory	www.mindgarden.com

This clinical research study asks women with infertility for their confidential self-report of how they relate to food, patterns of eating and emotions.



Who can participate?

- Women currently experiencing ovulation problems or unexplained infertility;
- Ages 18 to 44; and in
- Stable medical condition.

Interested in learning about the study?

- Leave a message on the confidential voicemail:

  617-785-0411

- An advanced practice nurse will return your call on a *day* and *time* of *your choosing* to explain the study.
- More information will be provided if you are interested in taking part in the study.
- If you agree to take part, the questionnaires will be sent to you to fill out.
- A postage paid envelope is provided for return of the questionnaires to Boston College.
- Your responses are confidential and private. They will not be made part of your medical record.

What's involved?

- Giving your confidential response to items on questionnaires;
- 30 to 40 minutes of your time; and
- Mailing the packet back to Boston College.
- You will receive a $30.00 gift card to CVS or Walgreen's, Starbuck's Coffee or Dunkin' Donuts.

Your participation in this study will help us learn whether or not certain lifestyle patterns and emotional symptoms occur more often in women with certain types of infertility compared to healthy women volunteers.

Participation is confidential!

Contact Information:

To discuss participation or to receive more information, please contact:

Ann Cousins, PhDc, RN, CS

617-785-0411

The nurse conducting the study:

Ann Cousins, PhDc, RN, CS is a certified advanced practice nurse with a Beth Israel Deaconess Medical Center research group.

Ms. Cousins is a PhD candidate at:

William F. Connell School of Nursing
Boston College
140 Commonwealth Avenue
Chestnut Hill, MA 02467

617-785-0411

ann.cousins.1@bc.edu

Revised 11/24/08

Women Volunteers

Ages 18 to 44

Needed

For a

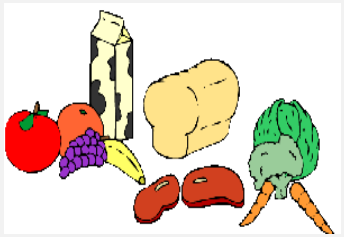
Research Study

Involving a

Confidential Survey

Complete the survey in the privacy of your own home.

This clinical research study asks healthy women volunteers for their confidential self-report of how they relate to food, patterns of eating and emotions.



Who can participate?

- Healthy women receiving routine health care,
- Not currently experiencing infertility;
- Ages 18 to 44; and in
- Stable medical condition.

Interested in learning about the study?

- Leave a message on the confidential voicemail:

  617-785-0411

- An advanced practice nurse will return your call on a *day* and *time* of *your choosing* to explain the study.
- More information will be provided if you are interested in taking part in the study.
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Boston College
140 Commonwealth Avenue
Chestnut Hill, MA 02467

617-785-0411

ann.cousins.1@bc.edu

11/24/08

Healthy Women Volunteers

Ages 18 to 44

Needed

For a

Research Study

Involving a Confidential Survey

Complete the survey in the privacy of your own home.

Volunteers Needed

Ages 18 to 44

For a

Research Study

Involving a

Confidential Survey

Complete the survey in the privacy of your own home.

The study asks for your confidential self-report of dietary patterns, other lifestyle patterns and emotions.

Women coming to the infertility center for evaluation and treatment are invited to consider participation in the study.

For more information, please help yourself to a brochure.

Principal Investigator: Ann Cousins, PhD Candidate, RN, CS

This study is approved by the Beth Israel Deaconess Medical Center and Boston College.

07/23/08

Healthy Women Volunteers Needed

Ages 18 to 44

For a

Research Study

Involving a

Confidential Survey

Complete the survey in the privacy of your own home.

The study asks for your confidential self-report of dietary patterns, other lifestyle patterns and emotions.

Women coming to the center for a routine health visit are invited to consider participation in the study.

For more information, please help yourself to a brochure.

Principal Investigator: Ann Cousins, PhD Candidate, RN, CS.
This study is approved by Beth Israel Deaconess Medical Center and Boston College.

07-23-08