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Psychosocial Changes Associated with Weight Loss: An Ancillary Study to the Longitudinal Assessment of Bariatric Surgery (LABS) consortium to be conducted at North Dakota Medical School/Neuropsychiatric Research Institute and the University of Pittsburgh School of Medicine

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1. Purpose

Patients who seek bariatric surgery are often motivated to lose weight to improve their physical health. Many patients also pursue surgery and the resulting weight loss to improve their quality of life and, more specifically, their physical appearance and body image. Studies indicate that bariatric surgery confers these benefits.

Few studies have investigated more specific aspects of extremely obese individuals' quality of life, including sexual function. Obesity, particularly in the presence of common comorbidities such as type II diabetes and hypertension, is associated with impaired sexual functioning. Clinical reports and a small number of studies suggest that obese individuals experience improvements in sexual functioning following weight loss. However, this has yet to be thoroughly investigated with valid and reliable measures in extremely obese persons who undergo bariatric surgery. Similarly, there has been little investigation of changes in sex hormones following bariatric surgery and their potential relationship with changes in sexual behavior.

The first aim of the proposed study is to compare changes in sexual function at 12, 24, 36 and 48 months postoperatively in 120 individuals who undergo a bariatric surgical procedure with changes in 120 extremely obese individuals with similar obesity-related comorbidities who do not seek surgery (treatment comparison group). The second aim of the proposed study is to compare changes in sex hormones in the two groups at 12, 24, 36, and 48 months following surgery. Finally, the proposed study aims to compare changes in body image and relationship satisfaction in the two groups at 12, 24, 36 and 48 months postoperatively.

2. Duration

The total duration of the study is 48 months. At baseline, participants will have a blood test and complete various pen and paper psychosocial assessments. Participants will return at 12, 24, 36, and 48 months to have regularly scheduled annual blood tests and complete annual psychosocial assessments.

3. Participant Recruitment and Selection

This Ancillary Study to the Longitudinal Assessment of Bariatric Surgery (LABS) consortium will be conducted at North Dakota Medical School/Neuropsychiatric Research Institute and the University of Pittsburgh School of Medicine. In addition, control participants who will not undergo bariatric surgery will be recruited at the University of Pennsylvania School of Medicine. One hundred twenty individuals who undergo bariatric surgery as part of the LABS consortium (60 each at the 2 sites) will participate in this study. In addition, 120 persons

with extreme obesity but not undergoing bariatric surgery will participate as controls. These individuals will be recruited through primary care practices at the University of Pennsylvania Health System.

Surgery Patients

Surgical patients will be recruited from individual's who have already decided to undergo bariatric surgery at the respective LABS sites. Consistent with routine standards of care in bariatric surgery practice, all surgery patients will complete the same series of preoperative medical evaluations. Surgery candidates first meet with a bariatric surgeon, who evaluates their medical appropriateness and discusses the surgical procedure with them. Patients judged appropriate by the surgeon undergo a physical exam. In addition, patients complete an upper gastrointestinal examination, ultrasound of the abdomen, electrocardiogram, chest x-ray, complete blood count, and chemistry profile. Patients' medication use prior to the onset of the study and at every assessment point throughout the investigation will be recorded to assess the possible influence of medication changes on weight, sexual function, and sex hormones. Cigarette smokers will not be excluded from the study.

Based on the results of the physical examination, individuals with the following conditions will be excluded from the proposed investigation.

Exclusion Criteria:

- Any major illnesses that the surgical team believes present too great a risk for surgery. These include severe cardiac and pulmonary diseases, as well as uncontrolled type 2 diabetes.
- Evidence of major depression or other psychiatric disorder (schizophrenia, bipolar disorder, major depression, bulimia nervosa, etc.) that significantly interferes with daily living and functioning.
- Use of the following medications: lithium, tricyclic antidepressants, and anti-psychotic agents (The use of selective serotonin re-uptake inhibitors (SSRIs) will not be excluded because of their widespread use and lesser effect on body weight.)
- Any current (past 12 months) substance abuse or dependence disorder.
- Pregnancy or lactation (Those who are pregnant do not undergo bariatric surgery. In addition, the hormone changes induced by pregnancy are known to interfere with the hormones examined in this study, confounding the findings. Participants who become pregnant while in this study will be withdrawn from the study.)

Individuals who meet the above criteria will be invited to participate in this ancillary study by a research assistant at the respective LABS site. The assistant will inform interested persons that the study will involve completing several paper and pencil measures of sexual behavior, body image, and relationship satisfaction prior to surgery and annually for the next 4 years. They will be informed of other requirements, which include a blood draw to assess changes in sex hormones at each assessment point. Participants will receive a $40.00 card (to a local department or bookstore) each year in recognition of their participation. The research assistant will obtain informed consent from individuals who wish to participate. Study participants will complete the baseline questionnaires and blood draw either at this time or within

one week of being enrolled in the study. Eligibility to participate will be determined by the criteria summarized below:

Inclusion Criteria:

- Age: Age of participants must be consistent with the age inclusion criterion for the behavioral modification program in which they are enrolled.
- Gender: Both women and men are eligible to participate.
- Ethnicity and Race: Individuals from all ethnic and racial groups will be invited to participate.
- Body Mass Index: Must be consistent with the BMI inclusion criterion for the behavioral modification program in which they are enrolled.
- Ambulation: Patients must be ambulatory, given the frequent number of assessments (and difficult arranging transportation for non-ambulatory individuals
- Competent: The patient must be able to communicate with the investigator and be legally competent, provide written informed consent.

Treatment-Comparison Participants

Participants in this group will be recruited from lifestyle modification studies already underway at the Center for Weight and Eating Disorders as well as from the Stunkard Weight Management Program . Participants who have already provided informed consent to participate in one of these studies or who are beginning a weight loss program at the Stunkard Clinic will be telephoned by a research assistant to the Psychosocial Changes study. The research assistant will explain to the potential participant that an ancillary study to the larger lifestyle modification program is being conducted examining changes in psychosocial status and sex hormones following weight loss. If the individual is interested in participating in the study, the research assistant will then ask him or her a series of questions geared towards discovering if the individual is appropriate for the study (see attached screening questionnaire). Participants who appear to meet the criteria (i.e. not on certain medications and in a romantic, committed relationship of at least one year), will be told they will meet with the research assistant when they come in for their baseline assessment to go over the details of the present study again and sign the informed consent form.

The same inclusion and exclusion criteria used to select the participants for the larger studies will be used to select the treatment-comparison participants.

4. Location

Behavioral assessments and blood draws of the bariatric surgery patients will be conducted annually at the Neuropsychiatric Research Institute at the University of North Dakota and the University of Pittsburgh School of Medicine. All patients in the treatment-comparison group will complete assessments and have blood draws at University of Pennsylvania's Weight and Eating Disorders Program or at the General Clinical Research Center at the Hospital of the University of Pennsylvania, depending on the protocol of the larger study.

5. Background

Bariatric surgery appears to be the most effective weight control option for extreme obesity. Behavioral weight loss programs and pharmacologic agents typically induce a mean loss of 8% to 10% of initial body weight. These modest weight losses may improve the health and psychosocial status of those with moderate obesity, but likely have little effect on the health and well being of the extremely obese. These and other factors likely have contributed to the growing popularity of bariatric surgery, which is recommended for patients with a BMI $\geq$ 40 kg/m^2 (or a BMI > 35 kg/m^2 in the presence of significant co-morbidities). Approximately 103,000 individuals underwent bariatric surgery in the United States in 2003. Two years postoperatively, patients typically lose 50-60% of excess body weight with GBP procedures and 40-50% with the restrictive procedures.

Many extremely obese persons pursue bariatric surgery for the anticipated health benefits. They also seek surgery because of its likely effects on psychosocial status and quality of life. Studies have suggested that patients experience improvements in psychosocial status postoperatively and health-related quality of life also appears to improve. Studies have also shown that patients report improvements in their marital functioning.

Physical appearance and body image are intricately linked to sexual function in both men and women. Problems with sexual functioning are highly prevalent and are associated with both impaired mood and quality of life. Historically, research on sexual dysfunction has been limited due to several factors, including a lack of consensus on definitions of sexual dysfunction, absence of well-validated measurement instruments, and societal taboos regarding sexuality.

Both psychosocial and physical factors appear to contribute to the development of sexual dysfunction in both men and women. Less is known about the development (and maintenance) of sexual function problems in specific groups of individuals, such as those with obesity. Clinical reports suggest that extremely obese individuals report difficulties with sexual functioning prior to bariatric surgery and experience improvements in functioning postoperatively. These studies, however, have failed to use valid and reliable measures of sexual functioning, as proposed in the current application.

The mechanisms by which extreme obesity affects sexual functioning have received little attention. Intuitively, it is easy to imagine how an obese individual, dissatisfied with his or her body image, would be reluctant to engage in sexual behavior. Similarly, physical limitations associated with excessive body weight may make sexual activity unpleasant, difficult, painful, or impossible. The majority of research on the mechanisms of sexual dysfunction has come from two of the most common comorbities found in those with extreme obesity: diabetes and hypertension.

Regardless of the potential mechanisms for the development of sexual dysfunction in obese individuals, a reduction in body weight and an increase in physical activity may reduce the risk of erectile dysfunction. The proposed study (which also will use the International Index of Erectile Function to assess male sexual function) is designed to determine if the massive weight loss following bariatric surgery is similarly associated with improvements in sexual function in both men and women with extreme obesity.

Obesity appears to be related to changes in sex hormone levels, which also may have a detrimental effect on sexual function. In men, obesity has been associated with a decrease in testosterone and sex-hormone-binding globulin, as well as an increase in estradiol levels. In women, obesity is associated with increased androgen and estrogen production rates.

Whether through improvements in body image, sex hormones, or obesity-related comorbities, the marked weight loss following bariatric surgery may have a profound effect on sexual function. The LABS trial provides an ideal opportunity to study changes in sexual function and its relationship to key psychological and hormonal variables of interest. It will also allow us to investigate potential mechanisms for these relationships. Clearer understanding of the mechanisms of obesity-related sexual dysfunction will have important implications for prevention, as well as contribute to our understanding of some of the psychological and physical conditions associated with extreme obesity.

The present study is designed to investigate changes in sexual function, sex hormones, body image, and relationship satisfaction in persons who undergo bariatric surgery in the main LABS study. The use of valid and reliable measures of these domains, coupled with the inclusion of a control group of extremely obese individuals who do not undergo bariatric surgery, should provide definitive findings concerning the relationships among extreme obesity, weight loss, and sexual function.

6. **Research Design**

Surgery Group

After surgery, patients will visit annually either the Neuropsychiatric Research Institute at the University of North Dakota or the University of Pittsburgh School of Medicine for their yearly assessments and blood tests. Patients will complete pen and paper questionnaires, and their blood will be drawn by a phlebotomist at baseline, 12, 24, 36, and 48 months.

Treatment-Comparison Participants

When the participants come in for their baseline assessment visit, the Psychosocial Changes research assistant will meet with them individually to go over the study completely and obtain informed consent. Once they have provided informed consent, the research assistant will screen them once again to make sure nothing has changed since the previous phone call. After the screening, the participants will have their blood drawn and then complete the various paper and pencil questionnaires. Participants will return at 12, 24, 36, and 48 months to have their blood drawn and to complete the same questionnaires.

Dependent Measures

Participants will complete the following assessments at baseline and 12, 24, 36, and 48 months following surgery or the onset of behavioral treatment.

Weight. Weight will be measured with a digital scale with subjects dressed in light clothing and without shoes. Percent weight loss will be calculated from participants' current weight (at each assessment point) as compared to their baseline weight.

Sexual Functioning. Aspects of male sexual functioning will be assessed using the International Index of Erectile Function Questionnaire. The measure consists of 15 multiple-choice items and assesses sexual functioning in five separate domains: erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall sexual satisfaction. The following additional questions will be incorporated into the measure to assess current treatment of erectile dysfunction: "Have you seen a doctor or other health professional for treatment of erectile dysfunction (impotence)?" and "If yes, are you taking Viagra or receiving another medical treatment for your sexual problem?" Aspects of female sexual functioning will be assessed using the Female Sexual Function Inventory. It consists of 19 multiple-choice items and assesses sexual functioning in six separate domains of sexual functioning: sexual arousal, desire, lubrication, orgasm, pain, and satisfaction. Two questions will be added to the measure to assess current treatment of sexual dysfunction in female participants: "Have you seen a doctor or other health professional for treatment of a sexual problem (e.g. lack of lubrication, pain during sex)?" and "If yes, are you taking medication or receiving therapy for your sexual problem?" Additionally, two questions will be used for the assessment of menopausal status: "Are you still having regular menstrual periods?" and "If yes, what was the date of your last menstrual cycle?" Finally, the question "Have you ever been diagnosed with Polycystic Ovary Syndrome (PCOS)?" and its follow-up question "If yes, when were you diagnosed?" will be added.

Sex hormones: Blood samples for hormonal analysis will be obtained. Specific hormones to be assessed in male patients are: total testosterone, free testosterone, sex-hormone-binding globulin, and luteinizing hormone. For female patients, hormonal analyses will include: total testosterone, sex-hormone-binding globulin, luteinizing hormone, estradiol, DHEA-S, and follicle-stimulating hormone. Total testosterone, free testosterone, sex-hormone-binding globulin, and DHEA-S assays will be analyzed using standard ELISA (IBL Hamburg) assay kits. Estradiol and luteinizing hormone will be analyzed by means of Chemiluminescent (Roche Elecys) laboratory assays.

Body image. Body image will be assessed by the Body Shape Questionnaire and the Body Image Quality of Life Inventory. The Body Shape Questionnaire consists of 34 questions with a 6-point likert scale. The Body Image Quality of Life Inventory consists of 19 questions with a 7-point likert scale for and assesses body image and its influence on one's life.

Relationship satisfaction. The Dyadic Adjustment Survey, consisting of 32 questions, will assess changes in relationship satisfaction.

Quality of life. Quality of life will be assessed by the Medical Outcomes Study 36-item Short Form Survey (SF-36) and the Impact of Weight on Quality of Life-Lite (IWQOL-Lite). The SF-26 has 8 subscales that assess separate domains of life quality. The IWQOL provides more specific information on quality of life particularly as it is related to body weight and weight loss.

Depressive symptoms. The Beck Depression Inventory (BDI) is a 21 item self-report rating inventory measuring characteristic attitudes and symptoms of depression.

Physical Activity. The Stepwatch Activity Diary measures physical activity for 7 consecutive days. It asks participants to indicate if they walked specifically for exercise and what physical activities they engaged in during each day.

7. **Potential Risks**

Bariatric surgery poses several significant risks, including gastric perforation, staple line disruption, disruption of the gastrojejunal anastomosis with a leak, deep vein thrombosis, pulmonary emboluis, and death. **These risks will be addressed with patients as part of their informed consent for surgery. Participation in the proposed study has no impact on the risks associated with surgery.**

Participants in the treatment-comparison group will be exposed to few significant risks as a result of this study. All study participants could experience bruising when having a blood test. This risk, however, is no greater than that experienced in clinical practice. The self-report assessments present minimal psychological risks to subjects.

8. Consent Procedures

Surgery subjects will be recruited during the preoperative assessments at the Neuropsychiatric Research Institute at the University of North Dakota and the University of Pittsburgh School of Medicine. Psychologists will describe the study to potential candidates only after first determining their appropriateness based on fixed enrollment criteria. The psychologists will provide further information about the study and answer any questions that applicants may have. Persons who are interested in participating in the study will meet with the research coordinator, who will inform them further of the study's requirements and obtain their written informed consent.

Subjects for the treatment-comparison group will be recruited as described previously. Potential participant contact information will be obtained from the two larger studies. The research assistant will call potential participants and complete an initial telephone screening. Those who appear appropriate for the study will be met by the research assistant at their scheduled baseline assessment visit for the larger study. The research assistant will obtain subjects' informed consent to participate from those who remain eligible and interested in the study.

9. Protection of Subjects

Study personnel will make it clear that subjects are not obligated to participate in the study. In addition, subjects will be informed that they may withdraw from the study whenever they wish and that their withdrawal will not affect the medical care they receive. Participation in this study will be kept confidential. Name, address, social security number or other information that can identify a participant will only be seen by study personnel at the University of Pennsylvania. Data collection forms will be kept in a locked file cabinet or locked room at the University of Pennsylvania. Research information will be sent to the Data Coordinating Center at the University of Pittsburgh, Graduate School of Public Health in Pittsburgh, Pennsylvania. This information will only be labeled with an ID number and code, which cannot be linked to you. In

addition, samples sent to the General Clinical Research Center at the Hospital of the University of Pennsylvania will be given a code number and will not include personal identifying information.

10. Potential Benefits

Bariatric surgery patients are expected to lose 25%-30% of their initial weight and to experience significant improvements in health complications. Inclusion of the treatment-comparison group will provide further assessments of the benefits of bariatric surgery. All participants will be informed of changes in their cardiovascular risk factors which should help them in judging their progress. Subjects who undergo bariatric surgery will experience improvements in weight and health regardless of whether they participate in the study. Thus, subjects are likely to be motivated by advancing understanding of the effects of bariatric surgery on sexual functioning, body image, and quality of life.

Subjects in the treatment-comparison condition are expected to lose 10%-12% of initial weight and should also experience improvements in weight-related health complications.

11. Risk/Benefit Ratio

The benefits of this research to the subjects studied, and to society at large, far surpass the risks. Results will provide important information on changes in sexual functioning, sex hormones, body image, relationship satisfaction, and quality of life in extremely obese persons who undergo bariatric surgery. **As noted above, bariatric surgery entails significant risks. Subjects in this study who presented for surgery did so of their own volition and were not randomly assigned to surgical treatment. The risks inherent in bariatric surgery are not affected by participation in the proposed study.**