Published in final edited form as:

Am J Obstet Gynecol. 2017 August ; 217(2): 191.e1–191.e19. doi:10.1016/j.ajog.2017.04.034.

Sexual Function in Infertile Women with Polycystic Ovary Syndrome and Unexplained Infertility

Michael P. Diamond, M.D., Richard S. Legro, M.D., Christos Coutifaris, M.D., Ph.D, Ruben Alvero, M.D., Randal D. Robinson, M.D., Peter A. Casson, M.D., Gregory M. Christman, M.D., Hao Huang, M.D., M.P.H., Karl R. Hansen, M.D., Ph.D., Valerie Baker, M.D., Rebecca Usadi, M.D., Aimee Seungdamrong, M.D., G. Wright Bates, M.D., R. Mitchell Rosen, M.D., William Schlaff, M.D., Daniel Haisenleder, Ph.D., Stephen A. Krawetz, Ph.D., Kurt Barnhart, M.D MSCE, J.C. Trussell, M.D., Nanette Santoro, M.D., Esther Eisenberg, M.D., M.P.H., Heping Zhang, Ph.D., and for the NICHD Reproductive Medicine Network

Department of Obstetrics and Gynecology, Georgia Regents University, Augusta, GA (Dr. Diamond); Department of Obstetrics and Gynecology, Pennsylvania State University, Hershey, PA (Dr. Legro); Department of Obstetrics and Gynecology, University of Pennsylvania School of Medicine, Philadelphia, PA (Drs. Coutifaris, Barnhart); Department of Obstetrics and Gynecology, University of Colorado, Denver, CO (Drs. Alvero, Schlaff, and Santoro); Department of Obstetrics and Gynecology, University of Texas Health Science Center at San Antonio, TX (Dr. Robinson); Department of Obstetrics and Gynecology, University of Vermont, Burlington, VT (Dr. Casson); Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, MI (Drs. Christman); Department of Obstetrics and Gynecology, University of Oklahoma College of Medicine, Oklahoma City, OK (Dr. Hansen); Stanford University Medical Center, Stanford, CA (Dr. Baker); Carolinas Medical Center, Charlotte, NC (Dr. Usadi); Rutgers New Jersey Medical School (Dr. Seungdamrong); University of Alabama Birmingham, Birmingham, AL (Dr. Bates); Department of Reproductive Endocrinology and Infertility, University of California, San Francisco, CA (Dr. Rosen); Ligand Core Laboratory University of Virginia Center for Research in Reproduction, Charlottesville, VA (Dr. Haisenleder); Department of Obstetrics and Gynecology, Wayne State University, Detroit, MI (Drs. Diamond, Krawetz); Upstate University Hospital, Syracuse, NY (Dr. Trussell); Fertility and Infertility Branch, Eunice Kennedy Shriver NICHD,

Corresponding Author: Michael P. Diamond, MD, Professor and Chair, Department of Obstetrics and Gynecology, William H. Brooks, MD, Distinguished Chair, Associate Dean for Research, Medical College of Georgia, Senior Vice President for Research, Augusta University, 1120 15th Street, BA-7300, Augusta, GA 30912, Phone: 706-721-3591, michael.diamond@augusta.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Dr. Michael P. Diamond – NIH Funding, AbbVie and Bayer Funding, Board of Directors and Stockholder for Advanced Reproductive Care; **Dr. Richard Legro** – Consultant for Ogeda, Millendo, Kindex, and Bayer; Ferring and Astra Zeneca funding; **Dr. Christos Coutifaris** – NIH Funding; **Dr. Ruben Alvero** – NIH Funding; **Dr. Randal D. Robinson** – NIH Funding, AbbVie Funding, and Speaker's Bureau and Implanon Training for Merck. **Dr. Peter Casson** – NIH Funding; **Dr. Gregory M. Christman** – No conflicts; **Dr. Hao Huang** – No conflicts; **Dr. Karl R. Hansen** – Yale University/ Reproductive Medicine Network/NICHD, Roche Diagnostics and Ferring International Pharmascience Center US funding; **Dr. Valerie Baker** – No conflicts; **Dr. Rebecca Usadi** – No conflicts; **Dr. Aimee Seungdamrong** – No conflicts; **Dr. Wright Bates** – No conflicts; **Dr. Mitchell Rosen** – No conflicts; **Dr. Daniel Haisenleder** – No conflicts; **Dr. Stephen A. Krawetz** – No conflicts; **Dr. Kurt Barnhart** – No conflicts; **Dr. J. C. Trussell** – No conflicts; **Dr. Nanette Santoro** – No conflicts; **Dr. Esther Eisenberg** – NIH Employee ; **Dr. Heping Zhang** – NIH Funding

Rockville, MD (Dr. Eisenberg); Department of Biostatistics, Yale University School of Public Health, New Haven, CT (Drs. Zhang and Huang)

Abstract

Background—While female sexual dysfunction is a frequent occurrence, characteristics in infertile women are not well delineated. Furthermore, the impact of infertility etiology on the characteristics in women with differing androgen levels observed in women with polycystic ovary syndrome and unexplained infertility has not been assessed.

Objective—To determine the characteristics of sexual dysfunction in women with polycystic ovary syndrome and unexplained infertility.

Study Design—Secondary data analysis was performed on two of Eunice Kennedy Shriver National Institute of Child Health and Human Development Cooperative Reproductive Medicine Networks clinical trials, “Pregnancy in Polycystic Ovary Syndrome Study II” and “Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation.” Both protocols assessed female sexual function using the Female Sexual Function Inventory and the Female Sexual Distress Scale.

Results—Women with polycystic ovary syndrome had higher weight and body mass index than women with unexplained infertility (each $p < 0.001$), greater phenotypic (Ferriman-Gallwey Hirsutism score, sebum score, and acne score; each $p < 0.001$), and hormonal (testosterone, free testosterone, and dehydroepiandrosterone; each $p < 0.001$) evidence of androgen excess. Sexual function scores, as assessed by the Female Sexual Function Inventory were nearly identical. The Female Sexual Distress Scale total score was higher in women with polycystic ovary syndrome. The mean Female Sexual Function Inventory total score increased slightly as the free androgen index increased, mainly as a result of the desire subscore. This association was more pronounced in the women with unexplained infertility.

Conclusion—Reproductive age women with infertility associated with polycystic ovary syndrome and unexplained infertility, despite phenotypic and biochemical differences in androgenic manifestations, do not manifest clinically significant differences in sexual function.

Introduction

Sexual dysfunction has been identified in up to 40% of women^{1,2} with hypoactive sexual desire representing at least a quarter of these women^{3–5}. Acknowledging that there has been controversy regarding the definition and diagnosis of hypoactive sexual desire in women, hypoandrogenism^{6–9} has been identified as an etiology of hypoactive sexual desire, consistent with the obligatory role of testosterone to increase libido, frequency of and satisfaction with sexual activity, and orgasm in men.¹⁰ Furthermore testosterone has beneficial effects in women on arousal, pleasure, responsiveness, and satisfaction,^{6–8,10–14} and has been shown to be effective as treatment for hypoactive sexual desire disorder in clinical trials of testosterone administration in women.

Sexual dysfunction has been described to be prevalent in couples with infertility, possibly as a “side effect” of frustration regarding their inability to conceive. However, data on the association of underlying infertility diagnosis with sexual dysfunction is limited. In order to

elucidate sexual dysfunction in well-characterized couples with polycystic ovary syndrome (PCOS) and unexplained infertility (UI) and to assess correlations of sexual function and dysfunction in female partners of infertile couples, we undertook a secondary analysis of data from two studies of the Eunice Kennedy Shriver National Institutes of Child Health and Human Development (NICHD) Cooperative Reproductive Medicine Network (RMN). Additionally, we sought to test the hypothesis that circulating androgen, as assessed by Free Androgen Index (FAI) in women, would be inversely related to the prevalence of sexual dysfunction.

Materials and Methods

Patients

We performed a cross sectional secondary data analysis of the RMNs PPCOS II (Pregnancy in Polycystic Ovary Syndrome Study)^{11,12} and AMIGOS (Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation)^{13,14} clinical trials, which were conducted concurrently at multiple sites in the United States. All PPCOS II women were seeking infertility care and were between the ages of 18 and 39, had oligoovulation, defined by the modified Rotterdam criteria for this disorder, and exclusion of other disorders that could mimic the syndrome, such as congenital adrenal hyperplasia, hyperprolactinemia, or thyroid disease. All participants were required to have a normal uterine cavity and at least one patent fallopian tube. Male partners were required to have at least 14 million sperm per milliliter on screening semen analysis. All AMIGOS women were between the ages of 18 and 40 and had unexplained infertility (UI), defined as one or more years of infertility history with regular menstrual cycles, normal results on fertility testing including evidence of normal uterine cavity and at least one patent fallopian tube, and male partner with at least 5 million motile sperm on semen analysis, and were also seeking infertility care^{15,16}. All couples from both concurrent clinical trials were asked to complete several psychosocial instruments at the time of screening. Each protocol was approved by the Institutional Review Board (IRB) at each study site; all participants gave written informed consent prior to initiating participation in the study. The study design and main outcomes for each protocol has been previously published^{12,13,17,18}.

Briefly, the PPCOS II trial was designed to test whether Letrozole was a superior treatment to clomiphene of ovulation induction and achievement of a live birth in women with PCOS^{11,12}. Seven hundred fifty female participants and their partners enrolled into the PPCOS II trial. Of these, 733 women (97.7%) completed the questionnaires. The AMIGOS trial was designed to test whether Letrozole was more effective at producing monofollicular development and therefore result in fewer multiple pregnancies than either clomiphene or gonadotropins, while being similarly effective to these medications. The AMIGOS trial enrolled 900 women and their partners; 865 women (96.1%) completed the questionnaires.

Sexual Function and Quality of Life Assessments

Female sexual function was assessed in both protocols in an identical fashion as previously described^{17,18}. Briefly, female sexual function was assessed by the Female Sexual Function Inventory (FSFI) along with the Female Sexual Distress Scale (FSDS)¹⁹. The FSFI is

comprised of six domains (desire, arousal, lubrication, orgasm, satisfaction, and pain) with score ranges of 0 (or 1) to 5. The Full Score range is 2.0–36, with higher scores associated with better sexual function. The FSFI measure is considered the “gold standard” assessment of sexual function and has excellent psychometric properties¹⁹. The FSDS is a 13 item questionnaire that measures sexually related personal distress in women, with higher scores indicating greater personal distress.

Quality of life assessment was conducted in identical fashion in both protocols by the Medical Outcomes Survey (Prime MD-PHQ)²⁰ and Short Form 36 (SF-36)²¹. Quality of life relating to infertility was assessed using the FertiQoL survey^{22,23}.

Analytic Measurements

At screening, visits were standardized across all study sites and each site used identical case report forms (CRFs) prepared by the RMN Data Coordination Center at Yale University. Forms and procedures for data collection were identical for both cohorts. BMI was calculated from height and weight measurements performed at the screening visit. Participants were weighed while dressed in light clothing, without shoes. Height was measured without shoes. Couples were administered a basic demographic questionnaire that collected information about educational attainment in categories (high school education or less; college education or some college; graduate level education) and income (household income <or> \$50,000 per year). Hirsutism was assessed in all participants using the Ferriman-Gallwey hirsutism scoring scale²⁴.

Blood specimens for each subject were collected at one time prior to administration of any study medications. All hormone analyses from both protocols were measured by the University of Virginia Core Laboratory as previously described^{11,12,14}. Briefly, subject serum samples were assayed in singlet with 5% run in duplicate (both randomly selected, and for outliers).

Steroid Assays—Total Testosterone (TT), estradiol (E2), progesterone (P4), and 17-OH progesterone (17-OH-P4) were measured using commercial RIAs (Siemens, Los Angeles, CA). DHEAS was measured on the Siemens Immulite 2000 automated chemiluminescent immunoassay analyzer (Los Angeles, CA). The Limit of Quantitation (Functional Sensitivity) was defined as the lowest concentration that demonstrates accuracy within 20% of expected values and intra-assay coefficient of variation (%CV) <20%, and was determined by serial dilutions of a defined sample pool. For TT, intra-assay and inter-assay %CVs were 4.3% and 7.4%, respectively; functional sensitivity was 10 ng/dl. E2, intra-assay and inter-assay %CVs were 5.4% and 6.5%, respectively; functional sensitivity was 10 pg/ml. For P4, intra-assay and inter-assay %CVs were 4.4% and 7.8%, respectively; functional sensitivity was 0.1 ng/ml. 17-OH-P4 was 4.9% (intra-assay), 6.9% (inter-assay) and 0.15 ng/ml (functional sensitivity). For DHEAS, intra-assay and inter-assay %CVs were 5.4% and 6.5%, respectively; functional sensitivity was 15 ug/dl.

Protein Assays—LH, FSH, TSH, and SHBG were measured on the Siemens Immulite 2000. Intra-assay, inter-assay CVs and functional sensitivity for LH was 3.3%, 5.6%, and 0.1 mIU/ml, respectively; 3.2%, 4.9%, and 0.1 mIU/ml, respectively for FSH; 3.6%, 4.7%, and

0.004 uIU/ml respectively for TSH; 2.7%, 5.2%, and 2.0 nmol/L, respectively for sex hormone binding globulin (SHBG).

Quality Controls (QCs)—BioRad (Hercules, CA) Tri-Level human serum QCs were included in all assays used for the present study. In order to identify kit lot-to-lot shifts over the course of the study, all assays included a single lot of BioRad Tri-Level QCs (Lot 270).

FAI—was calculated as TT (in nmol/L) / SHBG (in nmol/L).

Statistical Methods

Analysis was conducted using the combined patients (women only) from the PPCOS II trial (n=750) and AMIGOS trial (n=900). Of these 1650 women, 56 were excluded from analysis because of incomplete data. The combined population was divided into two groups, participants from the PPCOS II study (PCOS patients) and participants from the AMIGOS study (UI patients).

Summary statistics are reported for demographic variables, hormonal parameters, physical and phenotypic characteristics, and sexual function measures, in each of the two groups. Categorical data are reported as frequencies and percentages; differences in these measures between the two groups were assessed by means of a chi-square analysis, with Fisher's exact test used for expected frequencies of less than 5. Continuous data are reported as N, number of participants, and mean (SD), with a Wilcoxon rank-sum test used for testing differences between the two groups. Linear multivariable model analysis was also performed to investigate the association between sexual function measures and patient groups; variables that showed significant differences ($p < 0.05$) between the two groups were included as covariates for the adjustments.

All statistical analyses were performed in SAS V9.4 (SAS Institute, Cary, NC). Statistical significance was defined as a two-sided $p < 0.05$.

Results

Comparing the PCOS and UI populations, many of the demographic characteristics of the female partner, including age, race, ethnicity, marital status, level of education, occupation, annual household income, and insurance type (Table 1) were statistically significantly different. Notably, the PCOS population had an increased prevalence of metabolic syndrome (34.2% vs 13.1% for women with UI, $p < 0.001$). PCOS women reported higher levels of current smoking (34.0% vs 22.1%, respectively), and a lower current alcohol use (71.3% vs 83.5%, respectively, $p = 0.001$).

PCOS women had higher weight ($p < 0.001$) and BMI ($p < 0.001$) than the women with UI (Table 2). Clinical manifestations of androgen excess were also far more common in the women with PCOS, as noted for the Ferriman-Gallwey Hirsutism score, ($p < 0.001$), sebum score ($p < 0.001$), and acne score ($p < 0.001$). Comparing PCOS women to women with UI, LH levels were higher ($p < 0.001$). Androgen levels were higher in PCOS women as compared to UI women, with levels being two fold higher for testosterone ($p < 0.001$), nearly

four-fold higher for free testosterone ($p<0.001$), and DHEAS ($p<0.001$). Consistent with these observation, SHBG levels were nearly double in the women with UI as compared to those with PCOS ($p<0.001$). 17-OH progesterone levels were also considerably higher in PCOS women ($p<0.001$) (Figure 1A, B).

The FSFI total scores (Table 3) in women with PCOS and UI were nearly identical (29.9 ± 4.6 vs 29.9 ± 4.9 , respectively, NS). Among the FSFI subscores, there were no differences in the physiologic arousal, subjective arousal, orgasm, or satisfaction subscores. The desire subscore was statistically higher in the PCOS women ($p=0.007$), while the pain subscore was statistically higher in the UI women ($p=0.001$), although these differences are not likely of clinical significance. Consistent with these observations, there were no differences in the Fertility Quality of Life Questionnaire, with the exception of a statistical difference in the difficulty to express feelings, which was slightly lower in the PCOS group ($p<0.001$). The FSDS total score was higher in women with PCOS than those with UI ($p=0.004$), with a small difference reported in being bothered by low sexual desire, but no difference in satisfaction with their sex life. After the adjustment in the multivariable analyses, none of the above sexual function measures remained significantly different between the two study groups (Table 4).

If the total (PCOS and UI) study population is divided into quintiles of FAI, the FSFI total score increases from the first quintile score of 29.1 ± 5.3 to a fifth quintile score of 30.5 ± 4.0 ($p=0.010$; Table 5). This change was most prominently driven by an increase in the desire subscore ($p<0.001$), with a very small but significant increase in the physiological arousal subscore ($p=0.019$) and the subjective arousal subscore ($p=0.026$). Similar observations were observed when data were examined in tertiles as opposed to quintiles (data not shown). Additionally, a similar trend was observed when sexual function was assessed by quintiles of total testosterone levels, but only reached significance for the desire subscore ($p<0.001$; data not shown).

When the relationship between FSFI score and FAI is examined by diagnosis (PCOS vs. UI), the women with PCOS had relatively high FAI values; for example, the lowest FAI quintile include FAI levels up to 3.24. Interestingly, a trend for increasing FSFI score with increasing FAI levels was observed, though, this did not reach statistical significance (data not shown). Among women with UI, the highest quintile had FAI values $>2.53\%$. In this population, FSFI levels were significantly related to FAI quintile ($p=0.001$) with significant differences in the desire subscore ($p=0.005$), physiologic arousal subscore ($p=0.005$), and subjective arousal subscore ($p=0.002$). (Table 6) There were no significant differences in the FSFI orgasm, pain, or satisfaction subscores in relation to FAI quintile. Similarly, there were no significant differences in the FSDS total score, or dissatisfaction with sex life subscore, except bothered by low desire subscores ($p=0.004$) based on FAI quintile.

The relationship between sexual function measures and female BMI and race and ethnicity were investigated. As shown in Table 7, patients with higher BMI had a significantly higher FSFI total and subscores (except the satisfaction score). Hispanic or Latino women had a significantly higher FSFI total and subscores ($p<0.001$), and lower FSDS scores ($p<0.001$), indicating a higher quality of life (Table 8).

Comment

Sexual dysfunction has been associated with low circulating androgen levels both during natural menopause and in relation to surgically induced menopause.^{25–29} Furthermore, improvements in several components of sexual dysfunction are observed with testosterone administration.^{4,6,25,29–32} Limited data is available addressing the relationship of circulating androgens with sexuality in premenopausal women. Thus we sought to assess sexual function in two well characterized populations of women with infertility with markedly different ovulatory and circulating androgen phenotypes.

As expected, and by definition, the PCOS women exhibited greater clinical androgen manifestations, as evidenced by increased hirsutism, sebum, and acne. Consistent with this clinical phenotype, the PCOS women had elevated levels of testosterone (both total and free) and DHEAS, with lower SHBG levels. Although many demographic characteristics differed between the groups with statistical significance, these differences likely did not substantially impact sexual function and dysfunction with the exception of the difference in weight and BMI in the women with PCOS compared to UI. Women with PCOS were more bothered by their weight and were slightly more bothered by lower sex desire than those with UI. Nonetheless, women with higher BMI showed significantly higher FSFI total and subscores (except for the satisfaction subscore).

Interestingly, the androgenic phenotypic and hormonal profile in the PCOS women was not associated with a difference in the FSFI scores as compared to women with UI who were less androgenic. Some contradictions were observed in the PCOS women including a higher sexual desire subscore on the FSFI but being more bothered by low sexual desire on the FSDS, and being bothered by less sexual desire on the Patient Health questionnaire. A possible interpretation is that the PCOS women had greater sexual desire, but were not satisfied with that level of sexual desire. However, while all differences in scores were statistically significant, the absolute differences in each of the scores was small (0.1 increment in each score out of total scores of 6, 4, and 3, respectively), with multivariate analysis indicating no significant differences.. Overall our observations are not consistent with studies demonstrating marked effects of testosterone to increase libido in female animals. This may represent a tamping effect of perceived psychosocial normal human behavior. Alternatively, it may represent a “saturation” of testosterone’s effect on libido in women with high androgen levels as observed in the PPCOS II study, as an increase in sexual desire with rising testosterone levels was more pronounced in the women in the AMIGOS study, in whom there was a greater range in testosterone levels.

We found that increasing FAI was associated with a small but significant increase in FSF scores. Interestingly, the strongest FSFI subscore component correlating with the FAI was for the desire subscore, generally the prominent feature of hypoactive sexual desire disorder, and found by others to be positively impacted by exogenous testosterone treatment^{30–32}, which would increase serum androgens. Significant differences in the physiologic arousal and subjective arousal subscore were also identified. Nevertheless, the FSDS scores were consistent across the FAI quintiles clearly demonstrating that this large population of infertile women did not consider themselves to be dissatisfied with their sex life.

There are many strengths of this secondary analysis. These include the large sample size, the use of validated questionnaires, the measurement of androgens in a single reference laboratory and the well characterized population of reproductive age (not menopausal) women. Additionally, the FSFI and FSDS questionnaires were obtained at a single time point in each study prior to initiation of treatment, which may be considered a limitation of this analysis. Another limitation of the study is the absence of a fertile control group with which to compare these findings in infertile women.

In summary, we have characterized sexual function in two large distinct reproductive age groups of infertile women with the polycystic ovarian syndrome and unexplained infertility. Despite statistically different demographics, and greater phenotypical and hormonal androgenicity in the women with PCOS, the FSFI total scores were nearly identical.

Acknowledgments

FUNDING SOURCE

This work was supported by National Institutes of Health (NIH)/*Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Grants U10 HD39005 (to M.P.D.), U10 HD38992 (to R.S.L.), U10 HD27049 (to C.C.), U10 HD38998 (to R.A.), U10 HD055942 (to R.D.R.), HD055944 (to P.R.C.), U10 HD055936 (to G.M.C.), U10 HD055925 (to H.Z.); and U10 U54-HD29834 (to the University of Virginia Center for Research in Reproduction Ligand Assay and Analysis Core of the Specialized Cooperative Centers Program in Reproduction and Infertility Research). Most importantly, this research was made possible by the funding by American Recovery and Reinvestment Act. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NICHD or NIH.

References

1. Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. *JAMA*. 1999; 281:537–44. [PubMed: 10022110]
2. Shifren JL, Monz BU, Russo PA, Segreti A, Johannes CB. Sexual problems and distress in United States women: prevalence and correlates. *Obstetrics and gynecology*. 2008; 112:970–8. [PubMed: 18978095]
3. West SL, D'Aloisio AA, Agans RP, Kalsbeek WD, Borisov NN, Thorp JM. Prevalence of low sexual desire and hypoactive sexual desire disorder in a nationally representative sample of US women. *Archives of internal medicine*. 2008; 168:1441–9. [PubMed: 18625925]
4. Buster JE, Kingsberg SA, Aguirre O, et al. Testosterone patch for low sexual desire in surgically menopausal women: a randomized trial. *Obstetrics and gynecology*. 2005; 105:944–52. [PubMed: 15863529]
5. Latif EZ, Diamond MP. Arriving at the diagnosis of female sexual dysfunction. *Fertility and sterility*. 2013; 100:898–904. [PubMed: 24012196]
6. Davis SR, Moreau M, Kroll R, et al. Testosterone for low libido in postmenopausal women not taking estrogen. *The New England journal of medicine*. 2008; 359:2005–17. [PubMed: 18987368]
7. Braunstein GD. Safety of testosterone treatment in postmenopausal women. *Fertility and sterility*. 2007; 88:1–17. [PubMed: 17493618]
8. Krapf JM, Simon JA. The role of testosterone in the management of hypoactive sexual desire disorder in postmenopausal women. *Maturitas*. 2009; 63:213–9. [PubMed: 19487090]
9. Clayton AH. The pathophysiology of hypoactive sexual desire disorder in women. *Int J Gynaecol Obstet*. 2010; 110:7–11. [PubMed: 20434725]
10. Reis SL, Abdo CH. Benefits and risks of testosterone treatment for hypoactive sexual desire disorder in women: a critical review of studies published in the decades preceding and succeeding the advent of phosphodiesterase type 5 inhibitors. *Clinics (Sao Paulo)*. 2014; 69:294–303. [PubMed: 24714838]

11. Legro RS, Brzyski RG, Diamond MP, et al. The Pregnancy in Polycystic Ovary Syndrome II study: baseline characteristics and effects of obesity from a multicenter randomized clinical trial. *Fertility and sterility*. 2014; 101:258–69. e8. [PubMed: 24156957]
12. Legro RS, Brzyski RG, Diamond MP, et al. Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. *The New England journal of medicine*. 2014; 371:119–29. [PubMed: 25006718]
13. Diamond MP, Legro RS, Coutifaris C, et al. Letrozole, Gonadotropin, or Clomiphene for Unexplained Infertility. *The New England journal of medicine*. 2015; 373:1230–40. [PubMed: 26398071]
14. Diamond MP, Legro RS, Coutifaris C, et al. Assessment of multiple intrauterine gestations from ovarian stimulation (AMIGOS) trial: baseline characteristics. *Fertility and sterility*. 2015; 103:962–73. e4. [PubMed: 25707331]
15. Rotterdam EA-SPCWG. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertility and sterility*. 2004; 81:19–25.
16. Rotterdam EA-SPCWG. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). *Hum Reprod*. 2004; 19:41–7. [PubMed: 14688154]
17. Diamond MP, Mitwally M, Casper R, et al. Estimating rates of multiple gestation pregnancies: sample size calculation from the assessment of multiple intrauterine gestations from ovarian stimulation (AMIGOS) trial. *Contemp Clin Trials*. 2011; 32:902–8. [PubMed: 21787883]
18. Legro RS, Kunselman AR, Brzyski RG, et al. The Pregnancy in Polycystic Ovary Syndrome II (PPCOS II) trial: rationale and design of a double-blind randomized trial of clomiphene citrate and letrozole for the treatment of infertility in women with polycystic ovary syndrome. *Contemp Clin Trials*. 2012; 33:470–81. [PubMed: 22265923]
19. Rosen R, Brown C, Heiman J, et al. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. *Journal of sex & marital therapy*. 2000; 26:191–208. [PubMed: 10782451]
20. Spitzer RL, Williams JB, Kroenke K, Hornyak R, McMurray J. Validity and utility of the PRIME-MD patient health questionnaire in assessment of 3000 obstetric-gynecologic patients: the PRIME-MD Patient Health Questionnaire Obstetrics-Gynecology Study. *Am J Obstet Gynecol*. 2000; 183:759–69. [PubMed: 10992206]
21. McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Med Care*. 1993; 31:247–63. [PubMed: 8450681]
22. Aarts JW, van Empel IW, Boivin J, Nelen WL, Kremer JA, Verhaak CM. Relationship between quality of life and distress in infertility: a validation study of the Dutch FertiQoL. *Hum Reprod*. 2011; 26:1112–8. [PubMed: 21372046]
23. Santoro N, Eisenberg E, Trussell JC, et al. Fertility-related quality of life from two RCT cohorts with infertility: unexplained infertility and polycystic ovary syndrome. *Hum Reprod*. 2016; 31:2268–79. [PubMed: 27402910]
24. Ferriman D, Gallwey JD. Clinical assessment of body hair growth in women. *J Clin Endocrinol Metab*. 1961; 21:1440–7. [PubMed: 13892577]
25. Sherwin BB, Gelfand MM, Brender W. Androgen enhances sexual motivation in females: a prospective, crossover study of sex steroid administration in the surgical menopause. *Psychosomatic medicine*. 1985; 47:339–51. [PubMed: 4023162]
26. Nathorst-Boos J, von Schoultz B. Psychological reactions and sexual life after hysterectomy with and without oophorectomy. *Gynecologic and obstetric investigation*. 1992; 34:97–101. [PubMed: 1398273]
27. Shifren JL, Nahum R, Mazer NA. Incidence of sexual dysfunction in surgically menopausal women. *Menopause*. 1998; 5:189–90. [PubMed: 9774766]
28. Nathorst-Boos J, von Schoultz B, Carlstrom K. Elective ovarian removal and estrogen replacement therapy--effects on sexual life, psychological well-being and androgen status. *Journal of psychosomatic obstetrics and gynaecology*. 1993; 14:283–93. [PubMed: 8142982]
29. Davis SR, McCloud P, Strauss BJ, Burger H. Testosterone enhances estradiol's effects on postmenopausal bone density and sexuality. *Maturitas*. 1995; 21:227–36. [PubMed: 7616872]

30. Shifren JL, Braunstein GD, Simon JA, et al. Transdermal testosterone treatment in women with impaired sexual function after oophorectomy. *The New England journal of medicine*. 2000; 343:682–8. [PubMed: 10974131]
31. Sherwin BB, Gelfand MM. The role of androgen in the maintenance of sexual functioning in oophorectomized women. *Psychosomatic medicine*. 1987; 49:397–409. [PubMed: 3615768]
32. Braunstein GD, Sundwall DA, Katz M, et al. Safety and efficacy of a testosterone patch for the treatment of hypoactive sexual desire disorder in surgically menopausal women: a randomized, placebo-controlled trial. *Archives of internal medicine*. 2005; 165:1582–9. [PubMed: 16043675]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Figure 1.

A, B. Mean and standard deviation of hormones between patients with Polycystic Ovarian Syndrome and Unexplained Infertility. Free T, free testosterone; 17-OH, 17-hydroxyprogesterone; Total T, total testosterone. * $P < 0.001$.

Table 1

Demographics for Infertile Women from the RMN's PPCOS II (PCOS) and AMIGOS (UI) Studies

Characteristic	PCOS	UI	All	P Value
Age (yr)				
N	734	860	1594	
Mean(SD)	28.9(4.3)	32.2(4.2)	30.6(4.5)	<0.001
Race				<0.001
White	581/734(79.2%)	701/860(81.5%)	1282/1594(80.4%)	
Black	95/734(12.9%)	70/860(8.1%)	165/1594(10.4%)	
Asian	22/734(3.0%)	56/860(6.5%)	78/1594(4.9%)	
American Indian or Alaska Native	7/734(1.0%)	9/860(1.0%)	16/1594(1.0%)	
Native Hawaiian or other Pacific Islander	2/734(0.3%)	0/860(0.0%)	2/1594(0.1%)	
Mixed race	27/734(3.7%)	24/860(2.8%)	51/1594(3.2%)	
Ethnicity				<0.001
Not Hispanic or Latino	608/734(82.8%)	768/860(89.3%)	1376/1594(86.3%)	
Hispanic or Latino	126/734(17.2%)	92/860(10.7%)	218/1594(13.7%)	
Marital status				<0.001
Single	101/734(13.8%)	51/860(5.9%)	152/1594(9.5%)	
Married	627/734(85.4%)	805/860(93.6%)	1432/1594(89.8%)	
Divorced	6/734(0.8%)	3/860(0.3%)	9/1594(0.6%)	
Separated	0/734(0.0%)	1/860(0.1%)	1/1594(0.1%)	
Level of Education				<0.001
High school graduate or less	169/734(23.0%)	66/860(7.7%)	235/1594(14.7%)	
College graduate or some college	481/734(65.5%)	562/860(65.3%)	1043/1594(65.4%)	
Graduate degree	84/734(11.4%)	232/860(27.0%)	316/1594(19.8%)	
Occupation				<0.001
Professional and managerial	309/734(42.1%)	490/860(57.0%)	799/1594(50.1%)	
Sales and clerical	116/734(15.8%)	105/860(12.2%)	221/1594(13.9%)	
Service	124/734(16.9%)	53/860(6.2%)	177/1594(11.1%)	
Manufacturers, operators, farmers, and homemakers	82/734(11.2%)	75/860(8.7%)	157/1594(9.8%)	
Others	103/734(14.0%)	137/860(15.9%)	240/1594(15.1%)	
Annual Household Income				<0.001
<\$50,000	295/734(40.2%)	142/860(16.5%)	437/1594(27.4%)	
>=\$50,000	339/734(46.2%)	574/860(66.7%)	913/1594(57.3%)	
Wish to not answer	100/734(13.6%)	144/860(16.7%)	244/1594(15.3%)	
Insurance type				<0.001
Managed Care Plan or HMO	422/734(57.5%)	594/860(69.1%)	1016/1594(63.7%)	
Other private insurance	103/734(14.0%)	183/860(21.3%)	286/1594(17.9%)	
Medicaid	36/734(4.9%)	9/860(1.0%)	45/1594(2.8%)	
Medicare	6/734(0.8%)	4/860(0.5%)	10/1594(0.6%)	
Self-pay/uninsured	167/734(22.8%)	70/860(8.1%)	237/1594(14.9%)	
Length of time trying to conceive (months)				

Characteristic	PCOS	UI	All	P Value
N	700	851	1551	
Mean(SD)	41.8(38.0)	34.3(24.6)	37.7(31.6)	0.639
History of previous fertility treatment	407/734(55.4%)	481/860(55.9%)	888/1594(55.7%)	0.847
Presence of metabolic syndrome	250/731(34.2%)	106/807(13.1%)	356/1538(23.1%)	<0.001
Current smoking	107/315(34.0%)	65/294(22.1%)	172/609(28.2%)	0.001
Current alcohol use	464/651(71.3%)	632/757(83.5%)	1096/1408(77.8%)	<0.001

Table 2

Physical and Phenotypic Characteristics of Infertile Women from the RMN's PPCOS II (PCOS) and AMIGOS (UI) Studies

Characteristic	PCOS	UI	All	P Value
Weight(kg)				
N	734	860	1594	
Mean(SD)	95.1(26.3)	72.4(18.5)	82.8(25.1)	<0.001
Body Mass Index(kg/m ²)				
N	734	860	1594	
Mean(SD)	35.2(9.3)	26.8(6.4)	30.7(8.9)	<0.001
<25	118/734(16.1%)	417/860(48.5%)	535/1594(33.6%)	<0.001
25–35	247/734(33.7%)	357/860(41.5%)	604/1594(37.9%)	
>35	369/734(50.3%)	86/860(10.0%)	455/1594(28.5%)	
Waist/hip ratio				
N	732	857	1589	
Mean(SD)	0.9(0.1)	0.8(0.1)	0.9(0.1)	<0.001
Hirsutism score				
N	734	854	1588	
Mean(SD)	17.0(8.6)	7.6(5.7)	11.9(8.6)	<0.001
Sebum Score(mcg/cm ²)				
N	714	833	1547	
Mean(SD)	107.5(55.5)	91.3(49.2)	98.7(52.8)	<0.001
Acne Score				
N	733	859	1592	
Mean(SD)	8.8(16.2)	2.8(6.4)	5.6(12.3)	<0.001

Table 3

Sexual Function Measures for Infertile Women from the RMN's PPCOS II (PCOS) and AMIGOS (UI) Studies

Measure	PCOS	UI	All	P_Value
FSFI total score *				
N	734	860	1594	
Mean(SD)	29.9(4.6)	29.9(4.9)	29.9(4.8)	0.914
Desire subscore				
N	731	860	1591	
Mean(SD)	4.1(1.1)	4.0(1.0)	4.0(1.1)	0.007
Physiologic arousal subscore				
N	731	860	1591	
Mean(SD)	2.5(0.6)	2.5(0.6)	2.5(0.6)	0.800
Subjective arousal subscore				
N	731	860	1591	
Mean(SD)	2.5(0.6)	2.5(0.6)	2.5(0.6)	0.271
Orgasm subscore				
N	733	858	1591	
Mean(SD)	4.9(1.3)	4.9(1.3)	4.9(1.3)	0.978
Pain subscore				
N	734	858	1592	
Mean(SD)	5.3(1.1)	5.5(1.1)	5.4(1.1)	0.001
Satisfaction subscore				
N	734	860	1594	
Mean(SD)	5.3(0.9)	5.3(0.9)	5.3(0.9)	0.268
FSDS total score **				
N	734	860	1594	
Mean(SD)	6.8(8.6)	5.6(7.5)	6.2(8.0)	0.004
FSDS dissatisfied with sex life				
N	733	856	1589	
Mean(SD)	0.6(0.8)	0.5(0.8)	0.6(0.8)	0.265
FSDS bothered by low sexual desire				
N	733	857	1590	
Mean(SD)	0.8(1.2)	0.7(1.0)	0.8(1.1)	0.027
Patient health questionnaire [#]				
Pain or problems with intercourse				
N	731	854	1585	
Mean(SD)	1.2(0.5)	1.1(0.4)	1.2(0.4)	<0.001
Bothered by weight				
N	729	848	1577	
Mean(SD)	2.2(0.7)	1.7(0.6)	1.9(0.7)	<0.001
Bothered by less sex desire				

Measure	PCOS	UI	All	P_Value
N	729	846	1575	
Mean(SD)	1.4(0.6)	1.3(0.5)	1.3(0.5)	0.001
Difficulty with partner				
N	727	846	1573	
Mean(SD)	1.2(0.5)	1.1(0.4)	1.2(0.4)	<0.001
Fertility quality of life questionnaire [†]				
Satisfied with sex relationship				
N	730	857	1587	
Mean(SD)	4.1(1.0)	4.1(1.0)	4.1(1.0)	0.947
Affectionate with partner				
N	728	857	1585	
Mean(SD)	4.4(1.0)	4.4(1.0)	4.4(1.0)	0.077
Fertility problems strengthen commitment to partner				
N	728	848	1576	
Mean(SD)	3.4(1.2)	3.4(1.2)	3.4(1.2)	0.787
Negative impact of fertility problems on relationship				
N	729	856	1585	
Mean(SD)	4.6(0.7)	4.7(0.6)	4.6(0.7)	0.134
Difficulty to express your feeling				
N	728	856	1584	
Mean(SD)	4.4(0.9)	4.6(0.7)	4.5(0.8)	<0.001
Content with current relationship				
N	728	856	1584	
Mean(SD)	4.2(1.1)	4.4(0.9)	4.3(1.0)	0.071

* Full score range 2.0–36.0, subscore ranges 0–6; lower score indicating lower sexual activity or desire.

** Total score ranges 0–52, item score ranges 0–4 (never, occasionally, frequently, or all the time); scores are negatively associated with sexuality.

Score range 1–3, lower score indicating higher quality of life.

[†] Score range 1–5, higher score indicating higher quality of life.

Table 4

Multivariable model analysis for association between sexual function measures and patient group (patients with UI were set as reference group) for women with PCOS and UI*.

Measure	Beta (95% CI)	P Value
FSFI total score	-0.25 (-1.54, 1.05)	0.709
Desire subscore	0 (-0.32, 0.32)	0.993
Physiologic arousal subscore	-0.11 (-0.27, 0.05)	0.195
Subjective arousal subscore	-0.08 (-0.24, 0.08)	0.342
Orgasm subscore	0.19 (-0.15, 0.53)	0.266
Pain subscore	-0.02 (-0.30, 0.27)	0.902
Satisfaction subscore	-0.06 (-0.33, 0.21)	0.667
FSDS total score	0.02 (-2.39, 2.41)	0.992
FSDS dissatisfied with sex life	-0.02 (-0.26, 0.22)	0.864
FSDS bothered by low sexual desire	0.17 (-0.16, 0.50)	0.312
Patient health questionnaire		
Pain or problems with intercourse	0.03 (-0.10, 0.15)	0.688
Bothered by weight	0.10 (-0.08, 0.27)	0.273
Bothered by less sex desire	-0.03 (-0.19, 0.14)	0.724
Difficulty with partner	0.05 (-0.08, 0.18)	0.483
Fertility quality of life questionnaire		
Satisfied with sex relationship	0.13 (-0.14, 0.41)	0.340
Affectionate with partner	0.13 (-0.13, 0.39)	0.319
Fertility problems strengthen commitment to partner	-0.18 (-0.54, 0.18)	0.331
Negative impact of fertility problems on relationship	0.16 (-0.04, 0.35)	0.111
Difficulty to express your feeling	-0.19 (-0.44, 0.05)	0.114
Content with current relationship	-0.05 (-0.33, 0.23)	0.710

* Adjusted for age, ethnicity, race, marital status, occupation, education, insurance type, household income, screening BMI, waist-hip ratio, metabolic syndrome, current smoking, current alcohol use, hirsutism score, sebum score, acne score, FSH, LH, total testosterone, free testosterone, SHBG, DHEAS, and 17-hydroxyprogesterone.

Table 5
Sexual Function Measures for Infertile Women from the RMN's PPCOS II and AMIGOS Studies

	FAI	FAI 1.09	FAI 1.09– 1.86	FAI 1.86– 3.64	FAI 3.64– 7.67	FAI > 7.67	All	P Value
FSFI total score*								
N	313	312	311	315	313	1564		
Mean(SD)	29.1(5.3)	29.8(4.9)	30.0(4.7)	30.0(5.1)	30.5(4.0)	29.9(4.8)	0.010	
Desire subscore								
N	313	312	311	313	312	1561		
Mean(SD)	3.8(1.0)	3.9(1.0)	4.1(1.1)	4.2(1.1)	4.2(1.0)	4.0(1.1)	<0.001	
Physiologic arousal subscore								
N	313	312	311	313	312	1561		
Mean(SD)	2.4(0.6)	2.5(0.6)	2.5(0.5)	2.5(0.6)	2.5(0.5)	2.5(0.6)	0.019	
Subjective arousal subscore								
N	313	312	311	313	312	1561		
Mean(SD)	2.4(0.6)	2.5(0.6)	2.5(0.6)	2.5(0.6)	2.5(0.5)	2.5(0.6)	0.026	
Orgasm subscore								
N	313	312	310	314	313	1562		
Mean(SD)	4.8(1.4)	4.8(1.3)	4.9(1.3)	4.8(1.4)	5.1(1.1)	4.9(1.3)	0.162	
Pain subscore								
N	312	311	311	315	313	1562		
Mean(SD)	5.4(1.1)	5.4(1.0)	5.4(1.0)	5.4(1.2)	5.4(1.1)	5.4(1.1)	0.963	
Satisfaction subscore								
N	313	312	311	315	313	1564		
Mean(SD)	5.3(0.9)	5.3(1.0)	5.3(0.9)	5.4(1.0)	5.4(0.8)	5.3(0.9)	0.152	
FSDS total score**								
N	313	312	311	315	313	1564		
Mean(SD)	6.4(8.1)	5.6(7.0)	6.1(8.0)	6.4(8.7)	6.5(8.4)	6.2(8.1)	0.792	
FSDS dissatisfied with sex life								
N	312	311	311	313	313	1560		
Mean(SD)	0.6(0.9)	0.6(0.8)	0.6(0.8)	0.6(0.9)	0.5(0.8)	0.6(0.8)	0.943	
FSDS bothered by low sexual desire								

	FAI	1.09	FAI 1.09–	1.86	FAI 1.86–	3.64	FAI 3.64–	7.67	FAI > 7.67	All	P Value
N	312	311	311	311	311	314	313	313	1561		
Mean(SD)	0.8(1.1)	0.7(1.0)	0.7(1.1)	0.8(1.1)	0.8(1.1)	0.8(1.1)	0.7(1.1)	0.8(1.1)	0.355		
Patient health questionnaire [#]											
Pain or problems with intercourse											
N	312	308	308	308	308	314	313	313	1555		
Mean(SD)	1.2(0.4)	1.2(0.4)	1.2(0.4)	1.2(0.4)	1.2(0.4)	1.2(0.5)	1.2(0.4)	1.2(0.4)	0.192		
Bothered by weight											
N	309	307	307	307	307	312	313	313	1548		
Mean(SD)	1.7(0.6)	1.7(0.6)	1.7(0.6)	1.9(0.7)	1.9(0.7)	2.1(0.7)	2.3(0.6)	1.9(0.7)	<0.001		
Bothered by less sex desire											
N	309	307	306	306	306	312	313	313	1547		
Mean(SD)	1.3(0.5)	1.3(0.5)	1.3(0.5)	1.3(0.5)	1.3(0.5)	1.3(0.6)	1.3(0.6)	1.3(0.5)	0.453		
Difficulty with partner											
N	308	306	307	307	307	312	311	311	1544		
Mean(SD)	1.2(0.4)	1.2(0.4)	1.1(0.4)	1.2(0.4)	1.2(0.4)	1.2(0.4)	1.3(0.5)	1.2(0.4)	0.002		
Fertility quality of life questionnaire [†]											
Satisfied with sex relationship											
N	312	311	310	310	310	314	310	310	1557		
Mean(SD)	4.1(0.9)	4.1(1.0)	4.1(1.1)	4.2(0.9)	4.1(1.0)	4.1(1.0)	4.1(1.0)	4.1(1.0)	0.186		
Affectionate with partner											
N	312	310	310	310	310	313	310	310	1555		
Mean(SD)	4.3(1.0)	4.4(0.9)	4.4(0.9)	4.4(1.0)	4.4(0.9)	4.4(1.0)	4.4(1.0)	4.4(1.0)	0.424		
Fertility problems strengthen commitment to partner											
N	308	307	310	310	310	313	308	308	1546		
Mean(SD)	3.4(1.2)	3.5(1.3)	3.4(1.3)	3.4(1.2)	3.4(1.2)	3.4(1.2)	3.5(1.2)	3.4(1.2)	0.351		
Negative impact of fertility problems on relationship											
N	312	311	310	310	310	314	309	309	1556		
Mean(SD)	4.7(0.6)	4.6(0.6)	4.6(0.7)	4.6(0.6)	4.6(0.7)	4.6(0.6)	4.6(0.8)	4.6(0.7)	0.486		
Difficulty to express your feeling											
N	312	310	310	310	310	313	309	309	1554		
Mean(SD)	4.6(0.7)	4.6(0.6)	4.6(0.8)	4.6(0.6)	4.6(0.8)	4.5(0.9)	4.4(0.9)	4.5(0.8)	0.092		

	FAI	1.09	FAI 1.09–	1.86	FAI 1.86–	3.64	FAI 3.64–	7.67	FAI > 7.67	All	P Value
Content with current relationship											
N	311	310	310	311	312	310	1554				
Mean(SD)	4.4(0.9)	4.3(1.0)	4.3(1.0)	4.3(1.0)	4.3(1.0)	4.1(1.2)	4.3(1.0)				0.190
Feel like you are not sexy because of being overweight-PCOS questionnaire [^]											
N	15	42	123	250	294	724					
Mean(SD)	4.2(2.1)	5.2(2.1)	4.6(2.0)	3.9(2.1)	3.4(2.0)	3.9(2.1)	3.4(2.0)	3.9(2.1)			<0.001

* Full score range 2.0–36.0, subscore ranges 0–6; lower score indicating lower sexual activity or desire.

** Items were scored from 0–4 (never, occasionally, frequently, or all the time) and negatively associated with sexuality.

Score range 1–3, lower score indicating higher quality of life.

[†] Score range 1–5, higher score indicating higher quality of life.

[^] Items are scored on a 7-point Likert scale ranging from none to “severe” or “all of the time.” Lower scores indicate lower health-related quality of life.

Table 6

Female sexual function measures for AMIGOS patients

	FAI	0.82	FAI 0.82–	1.16	FAI 1.16–	1.63	FAI 1.63–	2.53	FAI > 2.53	All	P Value
FSFI total score											
N	167	167	167	168	168	168	168	168	168	838	
Mean(SD)	28.8(5.2)	29.6(5.6)	29.6(4.7)	30.2(5.0)	30.7(4.5)	29.8(5.1)	<0.001				
Desire subscore											
N	167	167	167	168	168	168	168	168	168	838	
Mean(SD)	3.7(1.0)	4.0(1.0)	3.9(1.0)	4.1(1.0)	4.1(1.0)	4.0(1.0)	0.001				
Physiologic arousal subscore											
N	167	167	167	168	168	168	168	168	168	836	
Mean(SD)	2.4(0.6)	2.4(0.7)	2.4(0.6)	2.6(0.5)	2.6(0.5)	2.5(0.6)	0.004				
Subjective arousal subscore											
N	167	167	167	168	168	168	168	168	168	836	
Mean(SD)	2.4(0.6)	2.4(0.7)	2.4(0.6)	2.6(0.5)	2.6(0.5)	2.5(0.6)	0.002				
Orgasm subscore											
N	167	167	167	168	168	168	168	168	168	836	
Mean(SD)	4.7(1.4)	4.8(1.4)	4.8(1.3)	5.0(1.2)	5.0(1.3)	4.9(1.3)	0.056				
Pain subscore											
N	167	166	167	167	167	168	168	168	168	835	
Mean(SD)	5.4(1.1)	5.4(1.2)	5.5(1.0)	5.5(1.0)	5.6(1.1)	5.5(1.1)	0.042				
Satisfaction subscore											
N	167	167	167	168	168	168	168	168	168	837	
Mean(SD)	5.3(0.9)	5.3(0.9)	5.2(1.1)	5.4(0.9)	5.4(0.9)	5.3(0.9)	0.336				
FSDS total score											
N	165	166	168	167	167	167	167	167	167	833	
Mean(SD)	6.7(8.3)	5.5(7.3)	5.6(7.0)	4.9(6.9)	5.3(8.0)	5.6(7.5)	0.152				
FSDS dissatisfied with sex life											
N	164	166	167	167	167	166	166	166	166	830	
Mean(SD)	0.6(0.9)	0.6(0.8)	0.6(0.8)	0.5(0.8)	0.5(0.8)	0.6(0.8)	0.780				
FSDS bothered by low sexual desire											

	FAI 0.82	FAI 0.82- 1.16	FAI 1.16- 1.63	FAI 1.63- 2.53	FAI > 2.53	All	P Value
N	164	166	167	167	167	831	
Mean(SD)	0.9(1.1)	0.7(1.0)	0.7(1.0)	0.6(1.0)	0.5(0.9)	0.7(1.0)	0.003
Patient health questionnaire Pain or problems with intercourse							
N	167	164	167	165	167	830	
Mean(SD)	1.2(0.4)	1.1(0.4)	1.1(0.4)	1.2(0.4)	1.1(0.3)	1.1(0.4)	0.063
Bothered by weight							
N	163	165	165	166	167	826	
Mean(SD)	1.6(0.6)	1.6(0.6)	1.7(0.7)	1.8(0.6)	1.9(0.7)	1.7(0.6)	0.001
Bothered by less sex desire							
N	162	165	165	166	166	824	
Mean(SD)	1.4(0.6)	1.3(0.5)	1.3(0.5)	1.2(0.5)	1.2(0.5)	1.3(0.5)	0.056
Difficulty with partner							
N	162	164	164	166	167	823	
Mean(SD)	1.2(0.4)	1.1(0.3)	1.2(0.4)	1.1(0.3)	1.1(0.3)	1.1(0.4)	0.144
Fertility quality of life questionnaire Satisfied with sex relationship							
N	166	166	167	168	167	834	
Mean(SD)	4.1(0.9)	4.1(1.0)	4.1(1.0)	4.2(1.0)	4.2(1.1)	4.1(1.0)	0.309
Affectionate with partner							
N	166	166	166	168	168	834	
Mean(SD)	4.3(1.0)	4.3(1.1)	4.4(0.9)	4.3(1.0)	4.5(0.9)	4.4(1.0)	0.271
Fertility problems strengthen commitment to partner							
N	163	164	164	167	167	825	
Mean(SD)	3.3(1.3)	3.4(1.2)	3.4(1.3)	3.6(1.2)	3.4(1.2)	3.4(1.2)	0.250
Negative impact of fertility problems on relationship							
N	166	166	167	168	167	834	
Mean(SD)	4.7(0.6)	4.7(0.6)	4.6(0.6)	4.7(0.6)	4.7(0.6)	4.7(0.6)	0.662
Difficulty to express your feeling							
N	166	166	167	167	167	833	
Mean(SD)	4.6(0.7)	4.6(0.7)	4.7(0.6)	4.7(0.7)	4.6(0.9)	4.6(0.7)	0.447
Content with current relationship							
N	166	165	167	167	168	833	

	FAI	0.82	FAI 0.82– 1.16	FAI 1.16– 1.63	FAI 1.63– 2.53	FAI > 2.53	All	P Value
Mean(SD)	4.3(0.9)	4.4(0.9)	4.3(1.0)	4.4(0.9)	4.4(1.0)	4.4(0.9)	4.4(0.9)	0.694
Physical components								
N	165	164	164	168	165	826	826	
Mean(SD)	57.7(3.7)	57.2(4.7)	56.4(4.6)	56.1(5.5)	55.8(5.5)	56.6(4.9)	56.6(4.9)	0.002
Mental components								
N	165	164	164	168	165	826	826	
Mean(SD)	53.3(6.0)	53.3(6.9)	52.7(6.6)	54.1(6.2)	53.8(7.3)	53.4(6.6)	53.4(6.6)	0.092
Work problem by physical health								
N	167	166	166	168	168	835	835	
Mean(SD)	98.9(8.6)	97.2(13.2)	97.8(10.9)	97.3(13.1)	95.6(18.1)	97.4(13.2)	97.4(13.2)	0.380
Work problem by emotional problem								
N	166	165	166	168	165	830	830	
Mean(SD)	95.8(17.3)	95.6(15.8)	95.6(16.2)	97.6(10.7)	94.9(17.5)	95.9(15.7)	95.9(15.7)	0.630
Social activity was interfered by health and emotion								
N	167	166	165	168	167	833	833	
Mean(SD)	96.1(10.6)	95.0(12.4)	93.9(13.3)	94.9(12.7)	94.9(13.0)	95.0(12.4)	95.0(12.4)	0.500
Normal work was interfered by pain								
N	165	166	166	168	166	831	831	
Mean(SD)	91.1(24.1)	94.0(19.7)	87.3(28.6)	90.9(24.8)	88.6(26.9)	90.4(25.0)	90.4(25.0)	0.204
How you feel and how things have been with you								
N	166	165	164	168	167	830	830	
Mean(SD)	76.9(11.3)	77.6(12.6)	75.4(13.0)	77.7(12.3)	77.6(13.4)	77.0(12.5)	77.0(12.5)	0.243

* Full score range 2.0–36.0, subscore ranges 0–6; lower score indicating lower sexual activity or desire.

** Items were scored from 0–4 (never, occasionally, frequently, or all the time) and negatively associated with sexuality.

*** Physical and mental components score were normalized with a mean of 50 and sample standard deviation of 10; other items score range 0–100. Higher score indicates better health.

Score range 1–3, lower score indicating higher quality of life.

\$ Score range 1–5, higher score indicating higher quality of life.

Table 7
Sexual Function Measures by screening BMI for Infertile Women from the RMN's PPCOS II and AMIGOS Studies

Label	BMI<25	BMI 25–29.9	BMI 30–34.9	BMI 35–39.9	BMI≥40	All	P Value
FSFI total score							0.006
N	535	335	263	188	273	1594	
Mean(SD)	29.3(5.3)	29.7(4.8)	30.2(4.6)	30.7(4.2)	30.4(4.0)	29.9(4.8)	
Desire subscore							0.047
N	535	335	263	186	272	1591	
Mean(SD)	3.9(1.1)	4.0(1.0)	4.0(1.1)	4.1(1.0)	4.1(1.1)	4.0(1.1)	
Physiologic arousal subscore							0.013
N	535	335	263	186	272	1591	
Mean(SD)	2.4(0.6)	2.5(0.6)	2.5(0.6)	2.6(0.5)	2.6(0.5)	2.5(0.6)	
Subjective arousal subscore							0.045
N	535	335	263	186	272	1591	
Mean(SD)	2.4(0.6)	2.5(0.6)	2.5(0.6)	2.5(0.5)	2.5(0.5)	2.5(0.6)	
Orgasm subscore							0.006
N	533	334	263	188	273	1591	
Mean(SD)	4.7(1.4)	4.8(1.3)	5.0(1.3)	5.1(1.2)	5.0(1.1)	4.9(1.3)	
Pain subscore							0.228
N	535	333	263	188	273	1592	
Mean(SD)	5.4(1.1)	5.4(1.1)	5.4(1.1)	5.5(1.1)	5.5(1.0)	5.4(1.1)	
Satisfaction subscore							0.134
N	535	335	263	188	273	1594	
Mean(SD)	5.3(1.0)	5.3(0.9)	5.4(0.9)	5.4(0.9)	5.3(0.9)	5.3(0.9)	
FSDS total score							0.088
N	535	335	263	188	273	1594	
Mean(SD)	5.8(7.2)	6.0(8.2)	5.9(8.4)	5.9(7.5)	7.5(9.2)	6.2(8.0)	
FSDS dissatisfied with sex life							0.189
N	532	334	262	188	273	1589	
Mean(SD)	0.6(0.8)	0.5(0.8)	0.5(0.9)	0.6(0.9)	0.7(0.9)	0.6(0.8)	
FSDS bothered by low sexual desire							0.590

Label	BMI<25	BMI 25–29.9	BMI 30–34.9	BMI 35–39.9	BMI≥40	All	P Value
N	532	335	263	188	272	1590	
Mean(SD)	0.8(1.0)	0.8(1.1)	0.8(1.2)	0.7(1.1)	0.8(1.1)	0.8(1.1)	
Patient health questionnaire							
Pain or problems with intercourse							0.992
N	532	330	263	188	272	1585	
Mean(SD)	1.2(0.4)	1.2(0.5)	1.2(0.4)	1.2(0.4)	1.2(0.4)	1.2(0.4)	
Bothered by weight							0.000
N	528	329	262	187	271	1577	
Mean(SD)	1.5(0.6)	1.9(0.6)	2.1(0.6)	2.2(0.6)	2.3(0.6)	1.9(0.7)	
Bothered by less sex desire							0.756
N	527	328	261	188	271	1575	
Mean(SD)	1.3(0.5)	1.3(0.5)	1.3(0.6)	1.3(0.5)	1.3(0.6)	1.3(0.5)	
Difficulty with partner							0.000
N	526	329	262	185	271	1573	
Mean(SD)	1.2(0.4)	1.1(0.4)	1.2(0.4)	1.2(0.4)	1.3(0.5)	1.2(0.4)	
Fertility quality of life questionnaire							
Satisfied with sex relationship							0.366
N	533	334	261	187	272	1587	
Mean(SD)	4.1(1.0)	4.2(1.0)	4.1(1.0)	4.2(0.9)	4.1(0.9)	4.1(1.0)	
Affectionate with partner							0.527
N	531	335	261	186	272	1585	
Mean(SD)	4.4(1.0)	4.4(1.0)	4.5(0.9)	4.3(1.0)	4.4(0.9)	4.4(1.0)	
Fertility problems strengthen commitment to partner							0.022
N	528	331	259	186	272	1576	
Mean(SD)	3.3(1.3)	3.6(1.2)	3.4(1.3)	3.6(1.2)	3.4(1.2)	3.4(1.2)	
Negative impact of fertility problems on relationship							0.127
N	532	335	260	187	271	1585	
Mean(SD)	4.7(0.6)	4.7(0.7)	4.6(0.7)	4.6(0.7)	4.5(0.8)	4.6(0.7)	
Difficulty to express your feeling							0.298
N	530	335	261	187	271	1584	
Mean(SD)	4.6(0.7)	4.6(0.8)	4.5(0.9)	4.5(0.8)	4.4(1.0)	4.5(0.8)	

Label	BMI<25	BMI 25–29.9	BMI 30–34.9	BMI 35–39.9	BMI≥40	All	P Value
Content with current relationship							0.113
N	531	334	261	187	271	1584	
Mean(SD)	4.4(0.9)	4.4(1.0)	4.3(1.1)	4.2(1.1)	4.2(1.1)	4.3(1.0)	
Feel like you are not sexy because of being overweight-PCOS questionnaire							0.000
N	118	115	124	141	228	726	
Mean(SD)	6.1(1.4)	4.2(2.0)	3.3(1.9)	3.7(1.8)	3.1(1.9)	3.9(2.1)	

* Full score range 2.0–36.0, subscore ranges 0–6; lower score indicating lower sexual activity or desire.

** Items were scored from 0–4 (never, occasionally, frequently, or all the time) and negatively associated with sexuality.

Score range 1–3, lower score indicating higher quality of life.

† Score range 1–5, higher score indicating higher quality of life.

^ Items are scored on a 7-point Likert scale ranging from none to “severe” or “all of the time.” Lower scores indicate lower health-related quality of life.

Table 8
Sexual Function Measures by race and ethnicity for Infertile Women from the RMN's PPCOS II and AMIGOS Studies

	White	Hispanic or Latino	Black	Asian	Mixed race or others	All	P Value
FSFI total score *							
N	1089	218	161	76	50	1594	
Mean(SD)	29.7(4.8)	31.0(4.5)	30.4(4.4)	27.6(5.7)	30.8(3.4)	29.9(4.8)	<0.001
Desire subscore							
N	1087	217	161	76	50	1591	
Mean(SD)	3.9(1.1)	4.3(1.1)	4.3(1.1)	3.8(0.9)	4.2(1.0)	4.0(1.1)	<0.001
Physiologic arousal subscore							
N	1087	217	161	76	50	1591	
Mean(SD)	2.5(0.6)	2.5(0.5)	2.5(0.6)	2.2(0.6)	2.6(0.4)	2.5(0.6)	<0.001
Subjective arousal subscore							
N	1087	217	161	76	50	1591	
Mean(SD)	2.5(0.6)	2.6(0.5)	2.6(0.5)	2.2(0.6)	2.6(0.4)	2.5(0.6)	<0.001
Orgasm subscore							
N	1086	218	161	76	50	1591	
Mean(SD)	4.9(1.3)	5.2(1.2)	5.0(1.3)	4.3(1.5)	5.1(1.1)	4.9(1.3)	<0.001
Pain subscore							
N	1088	218	160	76	50	1592	
Mean(SD)	5.4(1.1)	5.4(1.1)	5.3(1.1)	4.9(1.3)	5.6(0.7)	5.4(1.1)	<0.001
Satisfaction subscore							
N	1089	218	161	76	50	1594	
Mean(SD)	5.3(1.0)	5.5(0.9)	5.4(0.9)	5.3(0.9)	5.4(0.7)	5.3(0.9)	<0.001
FSDS total score **							
N	1089	218	161	76	50	1594	
Mean(SD)	6.6(8.1)	4.8(7.4)	5.2(8.9)	6.4(8.0)	5.1(6.3)	6.2(8.0)	<0.001
FSDS dissatisfied with sex life							
N	1086	218	160	75	50	1589	
Mean(SD)	0.6(0.9)	0.4(0.8)	0.4(0.8)	0.5(0.7)	0.7(0.8)	0.6(0.8)	<0.001

	White	Hispanic or Latino	Black	Asian	Mixed race or others	All	P Value
FSDS bothered by low sexual desire							
N	1088	218	159	75	50	1590	
Mean(SD)	0.8(1.1)	0.6(1.0)	0.6(1.1)	0.7(1.1)	0.7(1.1)	0.8(1.1)	<0.001
Patient health questionnaire [#]							
Pain or problems with intercourse							
N	1085	216	160	75	49	1585	
Mean(SD)	1.2(0.4)	1.2(0.4)	1.3(0.5)	1.2(0.5)	1.2(0.5)	1.2(0.4)	0.179
Bothered by weight							
N	1077	217	158	76	49	1577	
Mean(SD)	2.0(0.7)	1.9(0.7)	1.9(0.7)	1.6(0.6)	2.0(0.7)	1.9(0.7)	<0.001
Bothered by less sex desire							
N	1077	217	156	76	49	1575	
Mean(SD)	1.3(0.6)	1.3(0.5)	1.3(0.5)	1.3(0.6)	1.2(0.5)	1.3(0.5)	0.156
Difficulty with partner							
N	1074	216	158	76	49	1573	
Mean(SD)	1.2(0.4)	1.2(0.4)	1.2(0.4)	1.1(0.3)	1.2(0.4)	1.2(0.4)	0.649
Fertility quality of life questionnaire [†]							
Satisfied with sex relationship							
N	1084	218	159	76	50	1587	
Mean(SD)	4.1(0.9)	4.1(1.1)	4.1(1.1)	3.9(1.1)	4.4(0.7)	4.1(1.0)	0.049
Affectionate with partner							
N	1083	218	159	75	50	1585	
Mean(SD)	4.4(0.9)	4.4(1.1)	4.4(1.0)	4.2(1.2)	4.4(1.0)	4.4(1.0)	0.203
Fertility problems strengthen commitment to partner							
N	1080	214	157	75	50	1576	
Mean(SD)	3.4(1.2)	3.7(1.3)	3.4(1.3)	3.4(1.3)	3.3(1.1)	3.4(1.2)	0.004
Negative impact of fertility problems on relationship							
N	1083	217	159	76	50	1585	
Mean(SD)	4.6(0.7)	4.7(0.6)	4.5(0.8)	4.6(0.8)	4.7(0.5)	4.6(0.7)	0.316
Difficulty to express your feeling							

	White	Hispanic or Latino	Black	Asian	Mixed race or others	All	P Value
N	1083	218	157	76	50	1584	
Mean(SD)	4.6(0.8)	4.5(0.8)	4.3(1.1)	4.6(0.9)	4.7(0.5)	4.5(0.8)	0.050
Content with current relationship							
N	1082	218	158	76	50	1584	
Mean(SD)	4.4(0.9)	4.3(1.1)	4.1(1.2)	3.8(1.4)	4.1(1.3)	4.3(1.0)	<0.001
Feel like you are not sexy because of being overweight-PCOS questionnaire [^]							
N	464	125	91	21	25	726	
Mean(SD)	3.8(2.1)	3.8(2.0)	4.2(2.2)	5.0(2.0)	4.4(2.3)	3.9(2.1)	0.035

* Full score range 2.0–36.0, subscore ranges 0–6; lower score indicating lower sexual activity or desire.

** Items were scored from 0–4 (never, occasionally, frequently, or all the time) and negatively associated with sexuality.

Score range 1–3, lower score indicating higher quality of life.

[†] Score range 1–5, higher score indicating higher quality of life.

[^] Items are scored on a 7-point Likert scale ranging from none to “severe” or “all of the time.” Lower scores indicate lower health-related quality of life.