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'AGE IS JUST A NUMBER:' HOW CELEBRITY-DRIVEN MAGAZINES MISREPRESENT FERTILITY AT ADVANCED REPRODUCTIVE AGES. S. Willson,[a] K. N. Goldman.[b] [a]New York University School of Medicine, New York, NY; [b]New York University Langone Medical Center, New York, NY.

OBJECTIVE: Reproductive-aged women frequently overestimate the likelihood of fertility at advanced reproductive ages resulting in the devastating consequence of unintended childlessness. We hypothesize that popular media over-represents celebrity pregnancies at advanced reproductive ages and thus contributes to public misconceptions surrounding age-related fertility decline. We sought to characterize the depiction of fertility and pregnancy among celebrities in widely-consumed mainstream print media.

DESIGN: Quantitative and qualitative analysis of three top-read print magazines targeting reproductive-aged women.

MATERIALS AND METHODS: Three top-read print magazines targeting reproductive-aged women were identified using publicly available demographic data: *US Weekly, Cosmopolitan*, and *People Magazine*. All archived magazines from January 2010 to January 2014 were systematically reviewed for any mention in text or photo of pregnancy, infertility, use of assisted reproductive technology (ART), gestational carrier (GC), or adoption. Depictions of mothers with children under the age of 2y at the time of publication and mentions of pregnancy-related health risks were recorded.

RESULTS: In total, 416 print magazines met inclusion criteria and were analyzed, with a total of 1,894 mentions related to fertility, pregnancy, or motherhood. Fertility was highlighted on nearly 1/3 of magazine covers. 240 individual celebrities received at least one fertility-related mention, with a mean and median age at mention of 35 y. The majority (56%) of women mentioned were AMA. In total, only 2 subjects (<0.008%) were reported as having used ART; this number increased to 6 (0.03%) when including celebrities publicly known to have used ART. Among all AMA women (n=135), 10 (7%) were mentioned as having adopted children, and 5 (4%) used GC. There was no mention of infertility prior to adoption/GC. 45 women were over the age of 40 years (33%); 10 used adoption or GC, and only 2 women (4%) over 40 were mentioned as utilizing ART with autologous oocytes. 7 subjects over the age of 44 years were depicted as pregnant or having delivered healthy infants with no mention of ART. The use of donor gametes received no mention. All magazines contained $\geq$ 1 mention of contraception through sponsored advertisements, while only 10 magazines (2%) mentioned any form of ART. There were no mentions of AMA pregnancy-related health risks.

CONCLUSIONS: Widely-consumed popular media downplays the impact of age on fertility and glamorizes pregnancy at advanced ages. Magazines concurrently advertise contraception contrasted with fertility at advanced reproductive ages, with rare or no mention of ART, donor gametes, or AMA-related health risks. Magazine content reflects a continued stigma surrounding the use of ART and further the public's misconceptions about fertility at advanced reproductive ages. This depiction perpetuates the general notion that fertility is 'flexible' and is highly damaging to young women.

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OPIOID PRESCRIBING PATTERNS AFTER EGG RETRIEVAL. P. Bortoletto,[a] M. Prabhu,[b] E. Garry,[c] K. F. Huybrechts,[d] R. M. Anchan,[a] B. T. Bateman.[a] [a]Brigham and Women's Hospital, Boston, MA; [b]Massachusetts General Hospital, Boston, MA; [c]University of North Carolina at Chapel Hill, Chapel Hill, NC; [d]Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital, Boston, MA.

OBJECTIVE: We sought to describe opioid prescribing patterns following egg retrieval (ER).

DESIGN: A retrospective cohort of commercially insured patients from the Truven Marketscan database from 2003-2014.

MATERIALS AND METHODS: We identified a cohort of women who underwent egg retrieval (CPT code 58970) and had filled no more than 1 opioid prescription in the 12 weeks prior to ER (in order to exclude chronic opioid users). We also excluded women with a diagnosis of opioid or substance use disorders. We assessed for factors that might influence the decision to prescribe opioids including mood or anxiety disorder, smoking, use of SSRIs/TCAs, pelvic pain or endometriosis. Patient age, region, and year of ER were also captured. The outcomes of interest were i) proportion who filled an opioid prescription within 3 days of ER and ii) quantity dispensed, expressed as oral morphine equivalents (median, interquartile range [IQR]). Differences in the frequency of opioid fill by patient characteristics were tested using a chi-squared test.

RESULTS: A total of 57,727 women had an ER meeting criteria for analysis. Their mean age was 34.9 (standard deviation 4.8), 2.8% had a diagnosis of anxiety, 3.0% had a diagnosis of mood disorder, 5.7% used SSRI/TCA's, and 5.5% had a diagnosis of endometriosis. Among women having an ER, 11.9% (6,885/57,727) had a post-procedure opioid fill. The most frequently prescribed opioids were hydrocodone (48.8%), codeine (22.5%), and oxycodone (17.4%). The median (IQR) oral morphine equivalents prescribed after ER was 90 (50-125) mg, or 18 tablets of hydrocodone 5 mg. Women with mood disorders, smoking history, or SSRI/TCA use were more likely to fill an opioid prescription, compared to their counterparts without these diagnoses. The frequency of opioids filled over time varied from a low of 10.3% in 2003 to a high of 13.6% in 2006, and was 12.1% for the last year in the study period (2014). Opioids filled after ER varied significantly by region, from a high of 21.2% in the South to a low of 5.3% in the Northeast.

CONCLUSIONS: Whereas only a small proportion of women fill a prescription for opioids after ER, those who do receive a large quantity of opioids. This suggests a disconnect between expected procedural pain and provider prescribing patterns for this subgroup of patients. Patients with a concurrent diagnosis of mood disorder or users of antidepressents were more likely to fill opioid prescriptions, and significant differences existed by region. As most patients tolerate the procedure without using opioids, this should prompt physiciains who routinely prescribe these medications to reevaluate this practice.

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QUALITY OF LIFE AND DEPRESSION IN POLYCYSTIC OVARY SYNDROME. E. A. Greenwood,[a] L. Pasch,[a] R. S. Legro,[b,c] M. Cedars,[d] H. Huddleston.[a] [a]UCSF, San Francisco, CA; [b]Penn State University College of Medicine; [c]Reproductive Medicine Network, New Haven, CT; [d]UCSF, San Francisco, CA.

OBJECTIVE: Polycystic ovary syndrome (PCOS) has known pronounced quality of life effects in the domains of emotional, body hair, infertility, weight, and menstrual problems. The purpose of this study is to examine PCOS-related quality of life in depressed and non-depressed PCOS patients.

DESIGN: Secondary analysis of a randomized clinical trial

MATERIALS AND METHODS: 725 women ages 18-40 with PCOS-Rotterdam, desiring pregnancy, were enrolled in the Pregnancy in Polycystic Ovary Syndrome II (PPCOSII) clinical trial comparing letrozole and clomid. Anthropometric data and hirsutism assessment by modified Ferriman-Gallwey (mFG) scores were obtained. Depression was assessed by the self-administered Patient Health Questionnaire (PHQ), using a validated cutoff algorithm. The PCOS Health-Related Quality of Life (PCOSQ) survey, a validated 26-item questionnaire, was self-administered. PCOSQ scores were calculated for each of five domains: Emotional, Body Hair, Infertility, Weight, and Menstrual Problems. Domain scores range from 1-7, with 1 indicating poorest function and 7 optimal function. Two-sided t-tests compared PCOS QOL symptom scores between depressed and non-depressed patients. Linear regression models assessed the impact of a depression diagnosis on PCOSQ domain scores, controlling for age, BMI and mFG score.

RESULTS: 63/725 (8.7%) of women met the criteria for clinically significant depression. Depressed patients reported significantly lower scores (i.e. poorer function) on all five domains, compared to patients without depression: Emotions (3.1 vs 4.6), Weight (2.0 vs 3.5), Infertility (1.9 vs 3.0), Body Hair (3.5 vs 4.2), Menstrual Problems (3.2 vs 4.1); p<0.001. Depressed PCOS patients reported greater sense of lacking of control over their PCOS than patients without depression. In a multivariate analysis controlling for age, BMI and mFG scores, women with depression reported lower quality of life in all domains.

Effect of depression on PCOS QOL domain scores. *Analysis controlled for age, BMI, hirsutism score.

Domain	Coefficient	95% CI	p-value
Emotions	-1.36	(-1.66, -1.07)	<0.001
Body Hair	-0.49	(-0.83, -0.15)	<0.001
Weight	-1.28	(-1.68, -0.89)	<0.001
Infertility	-1.00	(-1.35, -0.65)	<0.001
Menstrual Problems	-0.83	(-1.11, -0.56)	<0.001

CONCLUSIONS: Depression is associated with poor subjective quality of life from PCOS symptoms. This finding remained after controlling for objective measures of symptoms including weight and hirsutism. Although the direction of the effect cannot be determined, these findings may suggest that depression colors the subjective experience of PCOS symptoms. Treatment of depression may improve subjective assessment of symptoms and quality of life in patients with PCOS.

LEIOMYOMA 2

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REGULATION OF PD-1 AND LEPTIN RECEPTOR EXPRESSION BY ESTROGEN THROUGH AKT3 IN HUMAN UTERINE FIBROIDS. A. El Andaloussi,[a] A. Al-Hendy.[b] [a]Ob/Gyn, Augusta University, Augusta, GA; [b]OB/GYN, Dept of Obstetrics & Gynecology, Augusta, GA.

OBJECTIVE: To study the regulation of PD-1 expression by estrogen and its cross talk with Leptin receptor through AKT3 in human uterine fibroids.

DESIGN: In vitro laboratory study with the use of human uterine fibroid (UF) cells.

MATERIALS AND METHODS: To verify our hypothesis, we stimulated HuLM and primary UF patients cells (n=7) with E2 conjugated with BSA (E2-BSA, is too large to enter the cells and thus cannot bind to nuclear ER) at the following concentration (0.1 ; 1 and 10 nM) at three different time point (30 mn; 1h and 2h). The expression of PD-1, PD-L1, anti-TNFα and anti-TGFβ by intracellular staining was analyzed by FACS. Q-PCR was used for RNA expression analysis for PD-1, PI3K, AKT isoforms and LepR used as marker of obesity.

RESULTS: To examine the cross-talk between ER and PD-1 through the non-genomic pathway of E2, Stimulation of UF cells with E2-BSA significantly induces the expression of PD-1 mRNA (5.7$\pm$ 0.84) at the concentration of 0.1 nM after 1h compared to untreated control (2.2 $\pm$ 0.25) (*P= 0.016*). This effect reached a plateau and the concentrations of 1 and 10 nM doesn't induce further PD-1 induction. The ER-BSA treatment had no effect on the level of PD-L1 mRNA in UF cells. This observation was supported by FACS analysis based on the mean fluorescence intensity of PD-1 in UF cells (77136 $\pm$ 585.4) versus the untreated control (36183 $\pm$ 2917.5) (P= 0.035). Downstream of PD-1, the PI3K expression level was induced significantly after 30 mins at 0.1 nM of E2-BSA (0.084 $\pm$ 0.0014) vs. the control cells (0.029 $\pm$ 0.001) (*P= 0.0009*). For AKT, we analyzed the three isoforms AKT1, AKT2 and AKT3 separately. Surprisingly E2-BSA induced marked up-regulation (300 fold increase) of AKT3 after 30 mins of stimulation with 0.1 nM of E2-BSA (300.25$\pm$ 106.6) vs. the unstimulated control (1.38$\pm$ 0.24) (*P= 0.008*). E2 mediated modest induction of AKT1 and no effect on AKT2 (*P=0.07*) compared to untreated control. E2-BSA induced a significant increase of LepR (14.68 $\pm$ 4.6) vs. (0.22$\pm$ 0.01) under the same conditions. This results is suggesting the cross-talk of non-genomic ER, PD-1 and LepR through AKT3, which are eventually mediate proliferation of UF cells.

CONCLUSIONS: Our work presents novel immunomodulatory functions of estrogen in human UF. Our study introduces interconnection among three majors and important pathways in the pathogenesis of UF Targeting AKT3 directly or indirectly through PD-1, might represent a novel effective anti-fibroid immunotherapeutic strategy.

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A CONTROLLED TRIAL ON UTERINE FIBROIDS TREATMENT COMPARING AROMATASE INHIBITOR PLUS GNRH ANALOGUE VERSUS ULIPRISTAL ACETATE. F. Scarpellini,[a] M. Sbracia.[b] [a]CERM, Rome, Italy; [b]CERM-Hungaria, Roma, Italy.

OBJECTIVE: We have previously showed that combined treatment of uterine fibroids with the aromatase inhibitor Anastrazole plus GnRH analogue (Goserelin) is an effective therapy in these women with a fast reduction of uterine volume and related symptoms especially uterine bleeding. In this controlled study we compared this treatmen with Ulipristal acetate that recently has been introduced in the treatment of fibroids.

DESIGN: A controlled randomized trial on women with uterine fibroids

MATERIALS AND METHODS: 63 women with symptomatic uterine fibroids All patients did not undergo surgery and were medically treated. The mean age of women was 39.1 $\pm$ 2.0. The women were assigned to the combined treatment group or to the Ulipristal group by a computer generated sequence. 30 women were treated with Anastrazole 1 mg/die plus Goserelin 3.6 mg/month. 33 women were treated with Ulipristal acetate 5.0 mg/daily. The women of the two groups were followed up during the treatment, undergoing to serial the assessment ultrasound scan of uterine and fibroids dimensions as well as side effects record.

RESULTS: The two groups of patients did not show statistical significant differences for any of epidemiological data. The time of pain symptom disappearance was shorter in the group treated with the combined therapy than in the Ulipristal group (2.8$\pm$0.9 vs 4.1$\pm$1.2, P<0.01). After three months treatment there was a significantly bigger reduction in uterine and fibroids volume in the women treated with the combined therapy than in the Ulipristal group (41.8% vs 14.3%, P<0.01). The side effects rate observed was significantly lower in the patients treated with the combined therapy than controls especially regarding uterine bleeding during treatment (3.3% vs 30.3%; P<0.01).

CONCLUSIONS: The combined treatment of uterine fibroids with Anastrazole plus GnRH analog showed better results than Ulipristal acetate group with a bigger fibroids reduction, in a shorter time and with lower side effects, especially for uterine bleeding The combined treatment seems to be the treatment of choice in these women even though these data should be confirmed in larger study.

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SYNERGISTIC EFFECTS OF SIMVASTATIN AND ULIPRISTAL ACETATE ON UTERINE LEIOMYOMA. M. Malik,[a] W. H. Catherino,[a] A. Laknaur,[b] M. Ali,[b] A. Al-Hendy,[b] J. Segars,[c] M. A. Borahay.[d] [a]OB/GYN, Uniformed Services University of the Health Scienc, Bethesda, MD; [b]OB/GYN, Augusta University, Augusta, GA; [c]OB/GYN, Johns Hopkins School of Medicine, Baltimore, MD; [d]Obstetrics and Gynecology, Johns Hopkins University, Baltimore, MD.

OBJECTIVE: Human fibroids are highly prevalent uterine tumors composed of proliferating transformed myometrial cells and excessive disordered extracellular matrix (ECM). The gonadal hormone progesterone is known to induce and maintain leiomyoma growth. Simvastatin, primarily used to treat hyperlipidemia, was recently shown to have anti-proliferative and pro-apoptotic effect on leiomyoma cells and xenograft model. Moreover, simvastatin is thought to modulate progesterone levels. Our objectives are to examine effect of simvastatin on ECM production and leiomyoma stem cells, and evaluate the combined effect of simvastatin and ulipristal acetate (UPA), a progesterone receptor modulator.

DESIGN: In-vitro laboratory study

MATERIALS AND METHODS: Patient-derived leiomyoma cell lines were treated with simvastatin at different concentrations for 24 and 48 hours. Expression of ECM proteins and regulating pathways was determined using western blot. Patient-derived stro-1$^+$/CD44$^+$ tumor initiating stem cells were treated with simvastatin, UPA and combinations for 48 hours. Proliferation was examined using MTT assay.

RESULTS: Simvastatin affected the expression of collagen 1A (COL1A) in leiomyoma cells, as early as 24hrs of treatment. A clear concentration dependent effect was observed at 48hr of exposure, with leiomyoma cells demonstrating a 2.5-fold (0.4 +/- 0.03) reduction in COL-1A at 10^{-7}M simvastatin, compared to untreated controls. At similar concentration and time point, versican (VCAN) was reduced by 1.25-fold whereas fibronectin (FN1) protein did not demonstrate a significant change. Fibromodulin (FMOD) demonstrated significant change at higher concentrations of simvastatin. A significant 2-fold decrease in transforming growth factor beta3 (TGFβ3) protein indicated that simvastatin may affect the production of the ECM proteins by inhibition of the fibrosis-inducing pathway. Its pro-apoptotic role was supported by a concentration-dependent increase in cleaved caspase-3, in treated cells. We have previously demonstrated that leiomyoma cells exposed to UPA demonstrated a decrease in expression of ECM proteins and various components of the TGF pathway. Treatment of leiomyoma stem cells by simvastatin or UPA for 48 hours inhibited proliferation with effects significant at 10^{-7}M (81$\pm$4% of control) and lower. With simvastatin/UPA combination, proliferation was significantly inhibited to 39$\pm$25% of control at 10^{-7}M concentrations.

CONCLUSIONS: Simvastatin inhibits production of leiomyoma ECM and inhibits proliferation of leiomyoma cells. Simvastatin/ulipristal acetate synergism appears to be a promising approach in leiomyoma therapy. To improve efficacy, combination therapy may work by focusing on different steps in leiomyoma cell stimulation.