

NVA Research Update E-Newsletter

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Feature Article

Feasibility of collecting vulvar pain variability and its correlates using prospective collection with smartphones.

Nguyen RH, Turner RM, Sieling J, Williams DA, Hodges JS, Harlow BL.

Pain Res Treat. 2014;2014:659863. doi: 10.1155/2014/659863

<http://www.ncbi.nlm.nih.gov/pubmed/25006458>

Context. Vulvar pain level may fluctuate in women with vulvodynia even in the absence of therapy; however, there is little evidence suggesting which factors may be associated with variability. **Objective.** Determine the feasibility of using smartphones to collect prospective data on vulvar pain and factors that may influence vulvar pain level.

Methods. 24 clinically confirmed women were enrolled from a population-based study and asked to answer five questions using their smartphones each week for one month.

Questions assessed vulvar pain level (0-10), presence of pain upon waking, pain elsewhere in their body, treatment use, and intercourse. **Results.** Women completed 100% of their scheduled surveys, with acceptability measures highly endorsed. Vulvar pain ratings had a standard deviation within women of 1.6, with greater variation on average among those with higher average pain levels ($P < 0.001$). On the weeks when a woman reported waking with pain, her vulvar pain level was higher by 1.82 on average ($P < 0.001$). Overall, average vulvar pain level was not significantly associated with the frequency of reporting other body pains ($P = 0.64$). **Conclusion.** Our smartphone tracking system promoted excellent compliance with weekly tracking of factors that are otherwise difficult to recall, some of which were highly associated with vulvar pain level.

Vulvodynia/Vulvovaginal Pain

Feasibility and Preliminary Effectiveness of a Novel Cognitive-Behavioral Couple Therapy for Provoked Vestibulodynia: A Pilot Study.

Corsini-Munt S, Bergeron S, Rosen NO, Mayrand MH, Delisle I.

J Sex Med. 2014 Jul 24. doi: 10.1111/jsm.12646. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/25059263>

INTRODUCTION: Provoked vestibulodynia (PVD), a recurrent, localized vulvovaginal pain problem, carries a significant psychosexual burden for afflicted women, who report impoverished sexual function and decreased frequency of sexual activity and pleasure. Interpersonal factors such as partner responses to pain, partner distress, and attachment style are associated with pain outcomes for women and with sexuality outcomes for both women and partners. Despite these findings, no treatment for PVD has systematically included the partner. **AIMS:** This study pilot-tested the feasibility and potential efficacy of a novel cognitive-behavioral couple therapy (CBCT) for couples coping with PVD. **METHODS:** Couples (women and their partners) in which the woman was diagnosed with PVD (N = 9) took part in a 12-session manualized CBCT intervention and completed outcome measures pre- and post-treatment. **MAIN OUTCOME MEASURES:** The primary outcome measure was women's pain intensity during intercourse as measured on a numerical rating scale. Secondary outcomes included sexual functioning and satisfaction for both partners. Exploratory outcomes included pain-related cognitions; psychological outcomes; and treatment satisfaction, feasibility, and reliability. **RESULTS:** One couple separated before the end of therapy. Paired t-test comparisons involving the remaining eight couples demonstrated significant improvements in women's pain and sexuality outcomes for both women and partners. Exploratory analyses indicated improvements in pain-related cognitions, as well as anxiety and depression symptoms, for both members of the couple. Therapists' reported high treatment reliability and participating couples' high participation rates and reported treatment satisfaction indicate adequate feasibility. **CONCLUSIONS:** Treatment outcomes, along with treatment satisfaction ratings, confirm the preliminary success of CBCT in reducing pain and psychosexual burden for women with PVD and their partners. Further large-scale randomized controlled trials are necessary to examine the efficacy of CBCT compared with and in conjunction with first-line biomedical interventions for PVD. Corsini-Munt S, Bergeron S, Rosen NO, Mayrand M-H, and Delisle I. Feasibility and preliminary effectiveness of a novel cognitive-behavioral couple therapy for provoked vestibulodynia: A pilot study

Trends in Pharmacy Compounding for Women's Health in North Carolina: Focus on Vulvodynia.

Corbett SH, Cuddeback G, Lewis J, As-Sanie S, Zolnoun D.

South Med J. 2014 Jul;107(7):433-6. doi: 10.14423/SMJ.0000000000000138.

<http://www.ncbi.nlm.nih.gov/pubmed/25010585>

OBJECTIVES:To identify trends in compounding pharmacies with a focus on women's health and, more specifically, the types and combinations of medications used in the treatment of vulvodynia. **METHODS:** This survey study was conducted with 653 nonchain pharmacies that compound medications. Each pharmacy was asked to complete a 19-item online survey assessing general practice and common compounding indications, focusing on women's health. **RESULTS:** Of the 653 pharmacies contacted, 200 (31%) responded to our survey. Women's health issues ranked third (19%) among the common indications for compounding, preceded by otolaryngology (30%) and dermatology (28%). Of the medications compounded for women's health, the most common indication was bioidentical hormone therapy (73%) followed closely by vaginal dryness (70%) and low libido (65%). Vulvodynia, or vulvar pain, was the fourth most common indication for compounding medication for women's health issues (29%). Vulvovaginal infections were reported as an indication for compounding medications by 16% of respondents. **CONCLUSIONS:** Vulvovaginal symptoms are a common indication for compounding medications in women's health. Further research in understanding the rationale for using compounded medications, even when standard treatments are available for some of these symptoms (eg, vaginal dryness, vulvovaginal infections), is warranted.

Prevalence of vulvodynia and risk factors for the condition in Portugal.

Vieira-Baptista, Lima-Silva, Cavaco-Gomes, Beires.

Int J Gynaecol Obstet. 2014 Jul 17. pii: S0020-7292(14)00354-3. doi:

10.1016/j.ijgo.2014.05.020. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/25092355>

OBJECTIVE: To investigate the prevalence of vulvodynia in Portugal and factors associated with this condition. **METHODS:** In a cross-sectional study, an online survey was distributed by email and posted on a website and social networks. Women aged at least 18 years who were living in Portugal were eligible to complete the survey between June 1 and November 30, 2013. Participants had to have had symptoms for at least 6 months to be deemed to have vulvodynia. **RESULTS:** Overall, 1229 questionnaires were included in analyses. A total of 80 (6.5%) women had vulvodynia at the time of the survey, and 117 (9.5%) had had it previously; lifetime prevalence was 16.0%. Pregnancy and type of delivery were not associated with vulvodynia. Women who had ever taken oral contraceptives were significantly more likely to have ever had vulvodynia ($P < 0.010$). Candidiasis, genital herpes, urinary tract infections, depression, and premenstrual syndrome were associated with ever having had vulvodynia ($P < 0.01$). Pain syndromes were associated with ever having had vulvodynia, especially fibromyalgia and bladder pain syndrome ($P < 0.001$). Scoliosis and hysterectomy were

also significantly associated ($P < 0.01$). CONCLUSION: The prevalence of vulvodynia in Portugal is similar to that elsewhere. Three main groups of factors might lead to vulvodynia: local inflammatory factors, general pain susceptibility, and pelvic nerve interference.

Toward a better understanding of the relationship between vulvodynia and chronic stressors.

Bachmann G, Brown C, Foster DC.

J Womens Health (Larchmt). 2014 Aug;23(8):634-5. doi: 10.1089/jwh.2014.4943.
<http://www.ncbi.nlm.nih.gov/pubmed/25111855>

Abstract not provided.

Dyspareunia due to medical illness or treatment

Locating pain in breast cancer survivors experiencing dyspareunia: a randomized controlled trial.

Goetsch MF, Lim JY, Caughey AB.

Obstet Gynecol. 2014 Jun;123(6):1231-6. doi: 10.1097/AOG.0000000000000283.
<http://www.ncbi.nlm.nih.gov/pubmed/24807329>

OBJECTIVE: To locate sites of genital tenderness in breast cancer survivors not using estrogen who experience dyspareunia and to test the hypothesis that tenderness is limited to the vulvar vestibule rather than the vagina and is reversed by topical anesthetic. METHODS: Postmenopausal survivors of breast cancer with moderate and severe dyspareunia were recruited for an examination including randomization to a double-blind intervention using topical aqueous 4% lidocaine or normal saline for 3 minutes to the areas found to be tender. Comparisons of changes in patients' reported numerical rating scale values were made with the Wilcoxon rank-sum test with significance set at $P < .05$. RESULTS: Forty-nine patients aged 37-69 years (mean 55.6 ± 8.6 years) had a median coital pain score of 8 (interquartile range 7-9, scale 0-10). On examination, all women had tenderness in the vulvar vestibule (worst site 4 o'clock median 6, 4-7). In addition, one had significant vaginal mucosal tenderness and two had pelvic floor myalgia. All had vulvovaginal atrophy with 86% having no intravaginal discharge. Aqueous lidocaine 4% reduced the vestibular tenderness of all painful sites. For example, pain at the worst site changed from a median of 5 (4-7) to 0 (0-1) as compared with saline placebo, which changed the worst site score from 6 (4-7) to 4 (3-6) ($P < .001$). After lidocaine application, speculum placement was nontender in the 47 without either myalgia or vaginal mucosal tenderness. CONCLUSION: In breast cancer survivors with dyspareunia, exquisite sensitivity was vestibular and reversible with aqueous lidocaine. Vaginal tenderness was rare despite severe atrophy.

Postoperative pain outcomes after transvaginal mesh revision.

Danford JM, Osborn DJ, Reynolds WS, Biller DH, Dmochowski RR.

Int Urogynecol J. 2014 Jul 11. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/25011703>

INTRODUCTION AND HYPOTHESIS: Although the current literature discusses mesh complications including pain, as well as suggesting different techniques for removing mesh, there is little literature regarding pain outcomes after surgical removal or revision. The purpose of this study is to determine if surgical removal or revision of vaginal mesh improves patient's subjective complaints of pelvic pain associated with original placement of mesh. **METHODS:** After obtaining approval from the Vanderbilt University Medical Center Institutional Review Board, a retrospective review of female patients with pain secondary to previous mesh placement who underwent excision or revision of vaginal mesh from January 2000 to August 2012 was performed. Patient age, relevant medical history including menopause status, previous hysterectomy, smoking status, and presence of diabetes, fibromyalgia, interstitial cystitis, and chronic pelvic pain, was obtained. Patients' postoperative pain complaints were assessed. **RESULTS:** Of the 481 patients who underwent surgery for mesh revision, removal or urethrolysis, 233 patients met our inclusion criteria. One hundred and sixty-nine patients (73 %) reported that their pain improved, 19 (8 %) reported that their pain worsened, and 45 (19 %) reported that their pain remained unchanged after surgery. Prior history of chronic pelvic pain was associated with increased risk of failure of the procedure to relieve pain (OR 0.28, 95 % CI 0.12-0.64, $p = 0.003$). **CONCLUSIONS:** Excision or revision of vaginal mesh appears to be effective in improving patients' pain symptoms most of the time. Patients with a history of chronic pelvic pain are at an increased risk of no improvement or of worsening pain.

Sexual disorders in women with MS: assessment and management.

Cordeau D, Courtois F.

Ann Phys Rehabil Med. 2014 Jul;57(5):337-47. doi: 10.1016/j.rehab.2014.05.008.

<http://www.ncbi.nlm.nih.gov/pubmed/24930089>

OBJECTIVES: Summarize the data on sexual disorders in women with multiple sclerosis (MS). **METHOD:** Review of 99 Pubmed articles covering sexual dysfunction in women with MS. **RESULTS:** Prevalence of dysfunction in women with MS varies from 34% to 85%. They include poor vaginal lubrication, poor clitoral erection, and anorgasmia, which correlate with level of disability. Specific brain stem and pyramidal lesions appear to correlate with anorgasmia. Age and duration of the disease correlate with sexual disorders, but not age at onset. Secondary consequences of MS, including bladder and bowel dysfunction, spasticity, pain, fatigue, depression, anxiety, and side effects of medication contribute to sexual dysfunction. Treatments can involve alpha-blockers or phosphodiesterase-5 inhibitors to increase smooth muscle relaxation, while lubricants and oestrogen therapy can help vaginal dryness, burning and dyspareunia. Antidepressants can delay (or abolish) orgasm, suggesting reducing dosage or

combining them with PDE5 inhibitors. Counselling should emphasize planning sexual activities, reducing fatigue, managing positions, preventing incontinence, promoting sexual aids, extra-genital and other sexual options to achieve pleasurable and intimacy. Psychosocial interventions should include couples' relationship and communication skills to increase satisfaction. CONCLUSION: Sexual dysfunctions in women with MS are amenable to treatments covering primary, secondary and tertiary consequences of the disease.

Prevalence of pelvic adhesions on ultrasound examination in women with a history of Caesarean section.

Moro F1, Mavrelou D, Pateman K K, Holland T, Hoo W, Jurkovic D.

Ultrasound Obstet Gynecol. 2014 Jul 14. doi: 10.1002/uog.14628. [Epub ahead of print] <http://www.ncbi.nlm.nih.gov/pubmed/25042444>

OBJECTIVES: To investigate the prevalence and locations of pelvic adhesions following previous Caesarean section (CS), to identify risk factors for their formation and symptoms associated with their presence. **METHODS:** This was a prospective observational study of women with history of one or more previous CS who attended for a gynaecological ultrasound examination. In all women both transvaginal and transabdominal scans were performed in order to identify the presence of pelvic adhesions. Past medical and surgical history was recorded and a structured questionnaire was used to enquire about any history of pelvic pain and urinary symptoms. **RESULTS:** A total of 308 women were recruited into the study. On ultrasound examination 139/308 (45.1%, 95%CI 39.7 - 50.7) women had evidence of adhesions within the pelvis. Adhesions in the vesico-uterine pouch were the most common and they were found in a total of 79/308 (25.6%, 95%CI 20.7 - 30.5) women. In women with no other surgery other than Caesarean section(s) (n = 220), increasing number of CS (OR 3.4, 95% CI 2.1 - 5.5) and a post operative wound infection (OR 11.7, 95% CI 3.5 - 39.5) increased the likelihood of adhesions in the anterior pelvic compartment. There was a significant association between presence of anterior compartment adhesions and chronic pelvic pain. Multivariate logistic regression analysis selected anterior abdominal wall adhesions (OR 2.4, 95% CI 1.6 - 3.7) and any adhesions on scan (OR 2.6, 95%CI 1.2 - 5.7) as independently predictive of chronic pelvic pain. **CONCLUSION:** Pelvic adhesions are present in more than a third of women with a history of previous CS and they are associated with chronic pelvic pain.

Comorbid Disorders

Chronic pelvic floor dysfunction.

Hartmann D, Sarton J.

Best Pract Res Clin Obstet Gynaecol. 2014 Jul 17. pii: S1521-6934(14)00132-1. doi: 10.1016/j.bpobgyn.2014.07.008. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/25108498>

The successful treatment of women with vestibulodynia and its associated chronic pelvic floor dysfunctions requires interventions that address a broad field of possible pain contributors. Pelvic floor muscle hypertonicity was implicated in the mid-1990s as a trigger of major chronic vulvar pain. Painful bladder syndrome, irritable bowel syndrome, fibromyalgia, and temporomandibular jaw disorder are known common comorbidities that can cause a host of associated muscular, visceral, bony, and fascial dysfunctions. It appears that normalizing all of those disorders plays a pivotal role in reducing complaints of chronic vulvar pain and sexual dysfunction. Though the studies have yet to prove a specific protocol, physical therapists trained in pelvic dysfunction are reporting success with restoring tissue normalcy and reducing vulvar and sexual pain. A review of pelvic anatomy and common findings are presented along with suggested physical therapy management.

Pudendal nerve block by transgluteal way guided by computed tomography in a woman with refractory pudendal neuralgia expressed like chronic perineal and pelvic pain.

Ricci P, Wash A.

Arch Esp Urol. 2014 Jul;67(6):565-71.

<http://www.ncbi.nlm.nih.gov/pubmed/25048589>

OBJECTIVE: To demonstrate that the deep infiltration of the pudendal nerve guided by tomography is a good treatment option for patients with refractory neuralgia.

METHOD: Two cases of pudendal neuralgia are presented, both expressed mainly with pain in the perineal and gluteal areas. Both cases had changes in the skin and one with urinary symptoms. A deep trans-gluteal infiltration guided by CT scan was performed, administering bupivacaine 0.25% with 80 mg methylprednisolone. **RESULTS:** In women, after infiltration, there was a decrease in pain from 6 to 3. In man infiltrations were performed monthly, completing 4. He reported pain reduction from 8 to 2.

CONCLUSIONS: Pudendal Neuralgia diagnosis is unknown. The most common cause is inflammation of adjacent structures to the nerve frequently caused by falling.

Diagnosis is mainly clinical. Trans-gluteal infiltration guided by CT scan is an effective option in treatment.

Visceral syndrome in endometriosis patients.

Hansen KE, Kesmodel US, Baldursson EB, Kold M, Forman A.
Eur J Obstet Gynecol Reprod Biol. 2014 Aug;179:198-203. doi:
10.1016/j.ejogrb.2014.05.024.
<http://www.ncbi.nlm.nih.gov/pubmed/24999078>

OBJECTIVE: Pain related to bowel and bladder function is seen more often in endometriosis. This study explored whether employed endometriosis patients experience multiple visceral symptoms more often than reference women without the disease. **STUDY DESIGN:** In a cohort study, 610 patients with diagnosed endometriosis and 751 reference women completed an electronic survey based on the EHP-30 questionnaire. Percentages were reported for all data. Principal component analysis was used to find underlying structures of correlations among variables, and Cronbach's alpha reliability analysis was used to demonstrate internal consistency of each scale. The level of statistical significance was set at $p < 0.025$ in all the analyses. **RESULTS:** Principal component analysis pointed at a specific visceral symptom-complex relating to the abdominal organs. This correlation was called "visceral syndrome" and consisted of the seven symptoms; "abdominal pain with no relation to menstruation", "pain during urination", "pain during defecation", "constipation or diarrhea", "irregular bleeding", "nausea or vomiting" and "feeling tired/lack of energy", with a Cronbach's alpha value $\alpha = 0.85$. More women with endometriosis than reference women suffered between five and seven symptoms from the visceral syndrome (22.7% vs. 2.7%) and more women with endometriosis compared to women with pain from other conditions suffered between five and seven symptoms from the visceral syndrome (22.7% vs. 3.2%). **CONCLUSION:** These data indicate that a significant number of endometriosis patients suffer from a specific symptom correlation, which is uncommon in women without the disease. These findings and previous data may suggest the occurrence of a visceral syndrome in endometriosis.

Urinary symptoms as a prodrome of bladder pain syndrome/interstitial cystitis.

Warren JW, Wesselmann U, Greenberg P, Clauw DJ.
Urology. 2014 May;83(5):1035-40. doi: 10.1016/j.urology.2014.01.012.
<http://www.ncbi.nlm.nih.gov/pubmed/24674116>

OBJECTIVE: To test the hypothesis that more cases than controls report pre-onset urinary symptoms. **METHODS:** In a risk factor study, the date of BPS/IC onset (index date) was systematically determined in 312 female incident cases; the mean age at onset was 42.3 years. Frequency-matched controls were compared on pre-index date medical history. **RESULTS:** Three pre-index date symptoms were more common in BPS/IC cases: pelvic pain with urinary features, frequency, and bladder pain; 178 cases (57%) vs 56 controls (18%) had at least 1 symptom ($P < .001$). Several perspectives suggested that prodromal symptoms were different from BPS/IC symptoms. In prodromal women, the median age of the earliest urinary symptom "more than other people" was 20 years. Women with the

prodrome were significantly more likely than those without to have pre-index date nonbladder syndromes (NBSs). The prodrome predicted not only BPS/IC but also a worse prognosis for it. CONCLUSION: Before the onset of BPS/IC, pelvic pain with urinary features, frequency, and/or bladder pain were reported by more than half the cases. Prodromal women recalled abnormal urinary symptoms decades before the onset of BPS/IC. The prodrome was associated with prior NBSs and predicted not only BPS/IC but also its poor prognosis. These data generated 2 hypotheses: that (1) prodromal symptoms are different from BPS/IC symptoms and (2) pain amplification links NBSs, the prodrome, the appearance of BPS/IC, and its poor prognosis. Recognition of the prodrome might provide opportunities for prevention of fully developed BPS/IC.

Seasonal changes in symptoms in patients with chronic prostatitis/chronic pelvic pain syndrome: a seasonal follow-up study.

Shin JH, Lee G.

Scand J Urol. 2014 Jul 11:1-5. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/25012875>

Abstract Objective. The aim of this study was to evaluate whether seasonal changes aggravate the symptoms of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), by serial administration of the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) questionnaire for an extended period. **Material and methods.** Seventy-seven men with CP/CPPS were serially evaluated with the Korean version of the NIH-CPSI questionnaire every 2-3 months from October 2008 to October 2012. The mean duration of follow-up was 27.11 ± 10.00 months and the mean number of visits per patient was 14.68 ± 5.33 times during the study. **Results.** The number of patients complaining of breakthrough pain during the study was 31 in spring and autumn, nine in summer and 18 in winter. However, there were no significant differences in the mean NIH-CPSI scores across the seasons. In spring, summer and autumn, only urination symptoms correlated with quality of life (QoL) ($r^2 = 0.277$, $p < 0.001$). In winter, both pain items and urination symptoms correlated with QoL (pain: $r^2 = 0.522$, $p < 0.001$; urination symptoms: $r^2 = 0.250$, $p < 0.001$). **Conclusion.** Although fewer severe pain attacks occurred in summer, the mean NIH-CPSI scores did not differ across seasons. The pain from CP/CPPS had a greater impact on QoL during winter than it did in the other seasons. In addition, pain was a more significant determinant of QoL than urination symptoms during winter.

Endometriosis: translation of molecular insights to management.

Langan KL, Farrell ME, Keyser EA, Salyer BA, Burney RO.

Minerva Endocrinol. 2014 Sep;39(3):141-54.

<http://www.ncbi.nlm.nih.gov/pubmed/25003227>

Endometriosis is a debilitating gynecologic disorder causing pelvic pain and infertility and characterized by the implantation of endometrial tissue to extrauterine locations.

Though aspects of the condition remain enigmatic, the molecular pathophysiology of endometriosis appears to be clarifying. Estrogen dependence of the disease is a sentinel endocrine feature and reduction of estrogen bioavailability is the therapeutic principle upon which traditional treatment and prevention approaches have been based. Endometriosis is a chronic inflammatory condition associated with lesional neoangiogenesis and attenuated progesterone action at the level of the endometrium. The elucidation of the molecular pathways mediating these observations has revealed new targets for directed medical and surgical treatment. This paper will review current approaches to the management of endometriosis in the context of the molecular pathophysiology.

Nutcracker Syndrome Accompanying Pelvic Congestion Syndrome; Color Doppler Sonography and Multislice CT Findings: A Case Report.

Inal M, Karadeniz Bilgili MY, Sahin S.

Iran J Radiol. 2014 May;11(2):e11075. doi: 10.5812/iranjradiol.11075.

<http://www.ncbi.nlm.nih.gov/pubmed/25035694>

Nutcracker syndrome (NCS) is a rare pathology, caused by compression of the left renal vein (LRV) between the abdominal aorta (AA) and the superior mesenteric artery (SMA), due to reduction of the angle between AA and SMA. This leads to LRV varices, left gonadal vein varices and therefore, the pelvic congestion syndrome. For this reason, coexistence of NCS and pelvic congestion syndrome has been described. It manifests by hematuria, proteinuria, and nonspecific pelvic pain secondary to pelvic congestion, dyspareunia and persistent genital arousal. We report a 27-year-old woman who experienced hematuria and left flank pain. The diagnosis of NCS accompanied by pelvic congestion syndrome was missed initially, but later on the diagnosis was made by color Doppler ultrasound, abdominal computed tomography (CT) and CT angiography that were later performed. She refused interventional and surgical treatments, and was lost to follow up.

Evidence of Health Risks Associated with Prolonged Standing at Work and Intervention Effectiveness.

Waters TR, Dick RB.

Rehabil Nurs. 2014 Jul 7. doi: 10.1002/rnj.166. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/25041875>

PURPOSE: Prolonged standing at work has been shown to be associated with a number of potentially serious health outcomes, such as lower back and leg pain, cardiovascular problems, fatigue, discomfort, and pregnancy-related health outcomes. Recent studies have been conducted examining the relationship between these health outcomes and the amount of time spent standing while on the job. The purpose of this article was to provide a review of the health risks and interventions for workers and employers that are involved in occupations requiring prolonged standing. A brief review of recommendations by governmental and professional organizations for hours of

prolonged standing is also included. FINDINGS: Based on our review of the literature, there seems to be ample evidence showing that prolonged standing at work leads to adverse health outcomes. Review of the literature also supports the conclusion that certain interventions are effective in reducing the hazards associated with prolonged standing. Suggested interventions include the use of floor mats, sit-stand workstations/chairs, shoes, shoe inserts and hosiery or stockings. Studies could be improved by using more precise definitions of prolonged standing (e.g., duration, movement restrictions, and type of work), better measurement of the health outcomes, and more rigorous study protocols. CONCLUSION AND CLINICAL RELEVANCE: Use of interventions and following suggested guidelines on hours of standing from governmental and professional organizations should reduce the health risks from prolonged standing.

Dermatological Disorders/Infectious Disease

Vulvar dermatosis.

Moyal-Barracco M, Wendling J.

Best Pract Res Clin Obstet Gynaecol. 2014 Jul 18. pii: S1521-6934(14)00129-1. doi: 10.1016/j.bpobgyn.2014.07.005. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/25132276>

Vulvar dermatoses are inflammatory conditions responsible for chronic or recurrent itching and soreness. The lesions are either circumscribed to the vulva or associated with extragenital localizations which may help to assess the diagnosis. They should be differentiated from infectious or neoplastic diseases which may have clinical similarities. As opposed to the majority of all dermatoses that have a benign and regular course, lichen sclerosus or lichen planus could exceptionally foster the occurrence of an epithelial cancer precursor which may evolve to squamous cell carcinoma. Topical corticosteroids are the mainstay treatment of vulvar dermatosis. We do not know if the treatment of vulvar lichen sclerosus and vulvar lichen planus prevents squamous cell carcinoma.

Vulval pruritus: The experience of gynaecologists revealed by biopsy.

Ozalp SS1, Telli E, Yalcin OT, Oge T, Karakas N.

J Obstet Gynaecol. 2014 Jul 10:1-4. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/25010568>

Pruritus of the vulva is a common symptom among patients attending to outpatient clinics. In the present study, we aimed to assess pathologies causing vulval pruritus in the reliability of biopsy in a tertiary referral centre. A total of 137 patients undergoing vulval colposcopy because of vulval pruritus were reviewed from the hospital records retrospectively. The mean age of the patients was 47.61 ± 11.88 years and 36.5% of the patients were postmenopausal. In 101 (73.7%) of the patients, macroscopic lesions were present. In 88 (64.2%) of the patients, toluidine-positive stained areas were

determined under colposcopy. In total, 68 (49.6%) of the lesions were plain, whereas 51 (37.2%) of them were depigmented. Lichen simplex chronicus, lichen sclerosis and chronic inflammation were the major pathologies associated with vulval pruritus (25.5%, n = 35; 20.4%, n = 28; 14.6%, n = 20). In conclusion, several pathologies out of vulvovaginal candidiasis may lead to vulval pruritus and clinicians should be aware of the impact of biopsy to reveal the underlying pathology.

The role of human Dectin-1 Y238X gene polymorphism in recurrent vulvovaginal candidiasis infections.

Usluogullari B, Gumus I, Gunduz E, Kaygusuz I, Simavli S, Acar M, Oznur M, Gunduz M, Kafali H.

Mol Biol Rep. 2014 Jul 10. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/25008994>

Recurrent vulvovaginal candidiasis (RVVC) is defined as having four or more symptomatic vulvovaginal candidiasis (VVC) attacks within a year. This study aimed to investigate whether Human Dectin-1 Y238X Gene Polymorphism plays a role in RVVC pathogenesis. In order to examine and explore this aim, an experimental study was undergone. The clinical study design was conducted with 50 women diagnosed with RVVC and had four or more symptomatic VVC attacks who were included in the experimental group; while 50 women who did not have previous RVVC history and diagnosis and did not have vaginal discharge and itching in the past year were included in the control group. Blood samples were collected from these patients and transferred to EDTA tubes, to investigate the Dectin-1 Y238X gene polymorphism, and stored at -80°. When Dectin-1 genotypes were compared, there was no significant difference between the two groups ($p = 0.452$, $p = 0.615$, $p = 0.275$). History of familial RVVC was significantly higher in the experimental group ($p = 0.001$). When the multivariate analysis was used to evaluate factors that could determine RVVC frequency, history of familial RVVC was found to increase the frequency of RVVC attacks by 3.3 units. This study is the first-of-its-kind to investigate the correlation between Dectin-1 Y238X polymorphism, which has not been previously studied in the Turkish population, and RVVC. The result of this study suggests that there is no correlation between this polymorphism and RVVC.

Epidemiology and Antifungal Susceptibilities of Yeasts Causing Vulvovaginitis in a Teaching Hospital.

Gamarra S, Morano S, Dudiuk C, Mancilla E, Nardin ME, de Los Angeles Méndez E, Garcia-Effron G.

Mycopathologia. 2014 Jul 9. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/25005365>

Vulvovaginal candidiasis is one of the most common mycosis. However, the information about antifungal susceptibilities of the yeasts causing this infection is scant. We studied 121 yeasts isolated from 118 patients with vulvovaginal candidiasis. The isolates were

identified by phenotypic and molecular methods, including four phenotypic methods described to differentiate *Candida albicans* from *C. dubliniensis*. Antifungal susceptibility testing was performed according to CLSI documents M27A3 and M27S4 using the drugs available as treatment option in the hospital. Diabetes, any antibacterial and amoxicillin treatment were statistically linked with vulvovaginal candidiasis, while oral contraceptives were not considered a risk factor. Previous azole-based over-the-counter antifungal treatment was statistically associated with non-*C. albicans* yeasts infections. The most common isolated yeast species was *C. albicans* (85.2 %) followed by *C. glabrata* (5 %), *Saccharomyces cerevisiae* (3.3 %), and *C. dubliniensis* (2.5 %). Fluconazole- and itraconazole-reduced susceptibility was observed in ten and in only one *C. albicans* strains, respectively. All the *C. glabrata* isolates showed low fluconazole MICs. Clotrimazole showed excellent potency against all but seven isolates (three *C. glabrata*, two *S. cerevisiae*, one *C. albicans* and one *Picchia anomala*). Any of the strains showed nystatin reduced susceptibility. On the other hand, terbinafine was the less potent drug. Antifungal resistance is still a rare phenomenon supporting the use of azole antifungals as empirical treatment of vulvovaginal candidiasis.

Tubal ectopic gestation associated with genital schistosomiasis: a case report.

Aminu MB, Abdullahi K, Dattijo LM.

Afr J Reprod Health. 2014 Jun;18(2):144-6.

<http://www.ncbi.nlm.nih.gov/pubmed/25022151>

Schistosoma are trematode blood flukes of the family Schistosomidae affecting the urinary and gastro-intestinal tracts. Riverine areas of the world such as in Africa, Eastern Mediterranean, Central American and East Asia are endemic for the disease, with *S. haematobium* accounting for most of the symptomatic genital infection. A case of a 25-year-old woman with 8 weeks amenorrhoea, lower abdominal pain and per vaginal bleeding was managed for ruptured ectopic pregnancy and discovered to have tubal infection by *Schistosoma* on histological examination is presented.

Probiotic Properties of *Lactobacillus crispatus* 2,029: Homeostatic Interaction with Cervicovaginal Epithelial Cells and Antagonistic Activity to Genitourinary Pathogens.

Abramov V, Khlebnikov V, Kosarev I, Bairamova G, Vasilenko R, Suzina N, Machulin A, Sakulin V, Kulikova N, Vasilenko N, Karlyshev A, Uversky V, Chikindas ML, Melnikov V. Probiotics Antimicrob Proteins. 2014 Jul 16. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/25028263>

Lactobacillus crispatus 2029 isolated upon investigation of vaginal lactobacilli of healthy women of reproductive age was selected as a probiotic candidate. The aim of the present study was elucidation of the role of *L. crispatus* 2029 in resistance of the female reproductive tract to genitourinary pathogens using cervicovaginal epithelial model. *Lactobacillus crispatus* 2029 has surface layers (S-layers), which completely surround cells as the outermost component of their envelope. S-layers are responsible for the

adhesion of lactobacilli on the surface of cervicovaginal epithelial cells. Study of interactions between *L. crispatus* 2029 and a type IV collagen, a major molecular component of epithelial cell extracellular matrix, showed that ¹²⁵I-labeled type IV collagen binds to lactobacilli with high affinity ($K_d = (8.0 \pm 0.7) \times 10^{-10}$ M). *Lactobacillus crispatus* 2029 consistently colonized epithelial cells. There were no toxicity, epithelial damage and apoptosis after 24 h of colonization. Electronic microscope images demonstrated intimate association between *L. crispatus* 2029 and epithelial cells. Upon binding to epithelial cells, lactobacilli were recognized by toll-like 2/6 receptors. *Lactobacillus crispatus* induced NF- κ B activation in epithelial cells and did not induce expression of innate immunity mediators IL-8, IL-1 β , IL-1 α and TNF- α . *Lactobacillus crispatus* 2029 inhibited IL-8 production in epithelial cells induced by MALP-2 and increased production of anti-inflammatory cytokine IL-6, maintaining the homeostasis of female reproductive tract. *Lactobacillus crispatus* 2029 produced H₂O₂ and provided wide spectrum of antagonistic activity increasing colonization resistance to urinary tract infections by bacterial vaginosis and vulvovaginal candidiasis associated agents.

Pain Science

Pain thresholds in women with chronic pelvic pain.

Giamberardino MA, Tana C, Costantini R.

Curr Opin Obstet Gynecol. 2014 Aug;26(4):253-9. doi:

10.1097/GCO.0000000000000083.

<http://www.ncbi.nlm.nih.gov/pubmed/24921647>

PURPOSE OF REVIEW: To update on the latest developments in sensory changes of female patients with chronic pelvic pain (CPP). CPP is very common, but its pathophysiology is still controversial. Evaluation of pain sensitivity in painful and nonpainful areas is key to understanding the underlying peripheral vs. central contributions to the symptom. This in turn is fundamental to improving the treatment strategies. **RECENT FINDINGS:** We reviewed the experimental studies published over the last year on pain thresholds to different stimuli measured at both the somatic and visceral level in women with different forms of recurrent or CPP. The majority of the studies indicate a pain threshold decrease to most stimuli in skin, subcutis and muscle in painful pelvic areas, the site of referred pain from pelvic viscera, as well as a decreased pain threshold in most viscera (colon and urinary bladder). A significant threshold decrease is also found in deep somatic tissues (subcutis and muscle) outside the painful zone in the most severe cases, indicating a state of central sensitization. **SUMMARY:** These findings have important implications for clinical practice: pain threshold measurement in both painful and nonpainful sites could have important predictive value of the clinical evolution and response to therapy of CPP.

Responses to the McGill Pain Questionnaire Predict Neuropathic Pain Medication Use in Women in With Vulvar Lichen Sclerosus.

Berger MB, Damico NJ, Haefner HK.

J Low Genit Tract Dis. 2014 Jul 17. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/25036743>

OBJECTIVE: The goal of this study was to test the hypothesis that responses to the McGill Pain Questionnaire are predictive of adjunctive neuropathic pain medication use by women with lichen sclerosus (LS). **MATERIALS AND METHODS:** This is a retrospective chart review of 430 women with vulvar LS treated at a tertiary referral vulvar care clinic. Demographics, responses to the McGill Pain Questionnaire, and use of neuropathic pain medications were collected. Bivariate and multivariable logistic regression analyses were performed to identify factors significantly associated with use of neuropathic pain medications. **RESULTS:** Of the 430 subjects, 119 (27.7%) used neuropathic pain medications for vulvar pain. Factors significantly associated with use of these medications include lower body mass index (odds ratio [OR] = 0.96, $p = .02$), non-White race (OR = 2.97, $p = .05$), and total McGill Pain Questionnaire score (OR = 1.05, $p < .001$). **CONCLUSIONS:** Vulvar pain is a common presenting symptom in women with LS. Responses to the McGill Pain Questionnaire may be helpful in the long-term management of women with LS as a screen to identify those patients who might benefit from adjunctive neuropathic pain medication use.

Pudendal nerve block by transgluteal way guided by computed tomography in a woman with refractory pudendal neuralgia expressed like chronic perineal and pelvic pain.

Ricci P, Wash A.

Arch Esp Urol. 2014 Jul;67(6):565-71.

<http://www.ncbi.nlm.nih.gov/pubmed/25048589>

OBJECTIVE: To demonstrate that the deep infiltration of the pudendal nerve guided by tomography is a good treatment option for patients with refractory neuralgia. **METHOD:** Two cases of pudendal neuralgia are presented, both expressed mainly with pain in the perineal and gluteal areas. Both cases had changes in the skin and one with urinary symptoms. A deep trans-gluteal infiltration guided by CT scan was performed, administering bupivacaine 0.25% with 80 mg methylprednisolone. **RESULTS:** In women, after infiltration, there was a decrease in pain from 6 to 3. In man infiltrations were performed monthly, completing 4. He reported pain reduction from 8 to 2. **CONCLUSIONS:** Pudendal Neuralgia diagnosis is unknown. The most common cause is inflammation of adjacent structures to the nerve frequently caused by falling. Diagnosis is mainly clinical. Trans-gluteal infiltration guided by CT scan is an effective option in treatment.

Assessment of deep tissue hyperalgesia in the groin - a method comparison of electrical vs. pressure stimulation.

Aasvang EK1, Werner MU, Kehlet H.

Acta Anaesthesiol Scand. 2014 Sep;58(8):986-96. doi: 10.1111/aas.12361.

<http://www.ncbi.nlm.nih.gov/pubmed/25041382>

BACKGROUND: Deep pain complaints are more frequent than cutaneous in post-surgical patients, and a prevalent finding in quantitative sensory testing studies. However, the preferred assessment method - pressure algometry - is indirect and tissue unspecific, hindering advances in treatment and preventive strategies. Thus, there is a need for development of methods with direct stimulation of suspected hyperalgesic tissues to identify the peripheral origin of nociceptive input. **METHODS:** We compared the reliability of an ultrasound-guided needle stimulation protocol of electrical detection and pain thresholds to pressure algometry, by performing identical test-retest sequences 10 days apart, in deep tissues in the groin region. Electrical stimulation was performed by five up-and-down staircase series of single impulses of 0.04 ms duration, starting from 0 mA in increments of 0.2 mA until a threshold was reached and descending until sensation was lost. Method reliability was assessed by Bland-Altman plots, descriptive statistics, coefficients of variance and intraclass correlation coefficients. **RESULTS:** The electrical stimulation method was comparable to pressure algometry regarding 10 days test-retest repeatability, but with superior same-day reliability for electrical stimulation ($P < 0.05$). Between-subject variance rather than within-subject variance was the main source for test variation. There were no systematic differences in electrical thresholds across tissues and locations ($P > 0.05$). **CONCLUSION:** The presented tissue-specific direct deep tissue electrical stimulation technique has equal or superior reliability compared with the indirect tissue-unspecific stimulation by pressure algometry. This method may facilitate advances in mechanism based preventive and treatment strategies in acute and chronic post-surgical pain states.

Measurement of pain and anthropometric parameters in women with chronic pelvic pain.

Gurian MB, Mitidieri AM, da Silva JB, Silva AP, Pazin C, Poli-Neto OB, Nogueira AA, Dos Reis FJ, Rosa-E-Silva JC.

J Eval Clin Pract. 2014 Jul 5. doi: 10.1111/jep.12221. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/25040704>

RATIONALE, AIMS AND OBJECTIVES: To analyse anthropometric parameters, clinical pain and experimental pain in women with chronic pelvic pain (CPP). **METHODS:** Ninety-one women with a clinical diagnosis of CPP, mean age of 40.03 ± 9.97 years, submitted to anthropometric evaluation based on body mass index (BMI) and percent body fat (%BF) using bioimpedance body composition monitor; pain intensity was determined by visual analogue scale (VAS), numerical categorical scale (NCS) and McGill Pain Questionnaire; experimental pain was determined by transcutaneous electrical nerve stimulation (TENS), and anxiety and depression symptoms were

determined by the Hospital Anxiety and Depression scale. RESULTS: A total of 54.8% of the women showed %BF >32 risk of disease associated with obesity. Regarding the anthropometric data, a statistically significant difference was observed between groups for both BMI and %BF ($P < 0.0001$). In the analysis of pain intensity by the VAS, NCS and total McGill, there was no significant difference between the groups, and experimental pain by TENS revealed significant difference only between the normal weight and overweight groups ($P = 0.0154$). The results of anxiety symptoms were above the cut-off point in all groups, with no significant difference between them ($P = 0.3710$). The depression symptoms were below the cut-off point in the normal weight group and above the cut-off point in the overweight and obese groups, 9.469(4.501) and 9.741(4.848), respectively, with no significant difference between them ($P = 0.6476$). CONCLUSION: Evaluation of anthropometric parameters and pain measurements can be applied in clinical practice, making a contribution to the diagnosis and influencing the choice of a more effective treatment for women with CPP.

Elevated peritoneal expression and estrogen regulation of nociceptive ion channels in endometriosis.

Greaves E1, Grieve K, Horne AW, Saunders PT.

J Clin Endocrinol Metab. 2014 Jul 16:jc20142282. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/25029427>

Context: Ovarian suppression is a common treatment for endometriosis-associated pelvic pain. Its exact mechanism of action is poorly understood although it is assumed to reflect reduced production/ action of estrogens. Objective: To measure expression of mRNAs encoded by nociceptive genes in the peritoneum of women with chronic pelvic pain (CPP) with or without endometriosis; to investigate whether estrogens alter nociceptive gene expression in human sensory neurons. Design: Human tissue analysis and cell culture. Setting: University Research Institute Patients: Peritoneal biopsies were obtained from women with CPP and endometriosis ($n=12$), CPP and no endometriosis ($n=10$), and with no pain or endometriosis ($n=5$). Endometriosis lesions were obtained from women with endometriosis ($n=18$). Main outcome measures: mRNAs encoding ion channels (P2RX3, SCN9A, SCN11A, TRPA1, TRPV1) and the neurotransmitter TAC1 were measured in tissue samples and in human embryonic stem cell-derived sensory neurons treated with estrogens. Results: TRPV1, TRPA1 and SCN11A mRNAs were significantly higher in the peritoneum from women with endometriosis ($p < 0.001$, $p < 0.01$). TRPV1, SCN9A and TAC1 were elevated in endometriosis lesions ($p < 0.05$). P2RX3 mRNA was increased in the peritoneum of women with CPP, with and without endometriosis ($p < 0.05$). Incubation of sensory neurons with E2 increased TRPV1 mRNA ($p < 0.01$); the ER β -selective agonist DPN increased concentrations of TRPV1, P2RX3, SCN9A and TAC1 mRNAs. Conclusions: Estrogen-dependent expression of TRPV1 in sensory neurons may explain why ovarian suppression can reduce endometriosis-associated pain. Strategies directly targeting ion channels may offer an alternative option for management of CPP.

Sex Differences

Sex differences in the incidence of severe pain events following surgery: a review of 333,000 pain scores.

Tighe PJ, Riley JL, Fillingim RB.

Pain Med. 2014 Aug;15(8):1390-404. doi: 10.1111/pme.12498.

<http://www.ncbi.nlm.nih.gov/pubmed/25039440>

OBJECTIVE/BACKGROUND: Prior work has not addressed sex differences in the incidence of severe postoperative pain episodes. The goal of this study was to examine sex differences in clinical postoperative pain scores across an array of surgical procedures using direct comparisons of numeric rating scale pain scores as well as using the incidence of severe pain events (SPEs). **DESIGN/SETTING:** Retrospective cohort study of over 300,000 clinical pain score observations recorded from adult patients undergoing nonambulatory surgery at a tertiary care academic medical center over a 1-year period. **METHODS/PATIENTS:** To test the hypothesis that the number of SPE on postoperative day (POD) 1 differed by sex after controlling for procedure, we calculated Cochran-Mantel-Haenszel statistics of sex by count of SPE, controlling for type of surgery. **ASSESSMENT TOOLS/OUTCOMES:** Pain scores were collected from clinical nursing records where they were documented using the numeric rating scale. **RESULTS:** In female patients, 10,989 (25.09%) of 43,806 POD 1 pain scores were considered SPE compared with 10,786 (22.45%) of 48,055 POD 1 pain scores in male patients. This produced an overall odds ratio of 1.16 (99% confidence interval 1.11-1.20) for females vs males to report an SPE for a pain score on POD 1. Estimates of the odds that a given pain observation represents an SPE for female vs male patients after controlling for type of surgery yielded an odds ratio of 1.14 (99% confidence interval, 1.10-1.19). **CONCLUSION:** Female patients experience greater mean pain scores, as well as a higher incidence of SPE, on POD 1 for a variety of surgical procedures.