

# Vulvodynia Pain Management

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# Disclosures

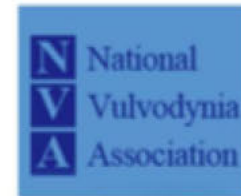
- Provided opinions as a medicolegal expert witness in mesh litigation cases.



# Objectives

- To review vulvodynia definition, etiology, risk factors
- To review different subgroups of vulvodynia
- To review normal and abnormal pain perception in this patient population
- Review current treatment options and future algorithm development





## **2015 Consensus terminology and classification of persistent vulvar pain**

Jacob Bornstein MD, MPA, Andrew Goldstein MD, and Deborah Coady MD  
for the consensus vulvar pain terminology committee

**From the International Society for the Study of Vulvovaginal Disease (ISSVD),  
the International Society for the Study of Women's Sexual Health (ISSWSH),  
and the International Pelvic Pain Society (IPPS)**

**The consensus vulvar pain terminology committee:** For the ISSVD - Jacob Bornstein (co-chair), Gloria A. Bachmann, Ione Bissonnette, Sophie Bergeron, Nina Bohm Starke, David Foster, Hope Katharine Haefner, Micheline Moyal Barracco, Barbara Reed, Colleen Stockdale<sup>1</sup>. For the ISSWSH - Andrew Goldstein (co-chair), , Laura Burrows, Irwin Goldstein, Susan Kellogg-Spadt, Sharon Parish, Caroline Pukall. For the IPPS - Denniz Zolnoun (co-chair), Deborah Coady, A. Lee Dellon, Melissa Farmer, Sarah Fox, Richard Gracely, Richard Marvel, Pam Morrison<sup>2</sup>, Stephanie Prendergast. Observers: Lori Boardman (ACOG), Lisa Goldstein (NVA), Phyllis Mate (NVA)

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<sup>1</sup>Representing also the American Society of Cervical Pathology and Colposcopy (ASCCP)

<sup>2</sup>Representing also the National Vulvodynia Association (NVA)

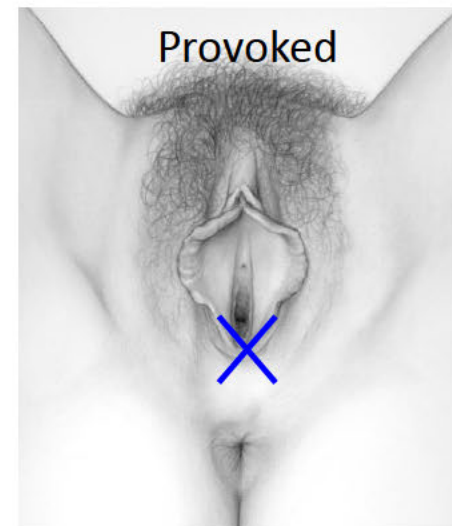
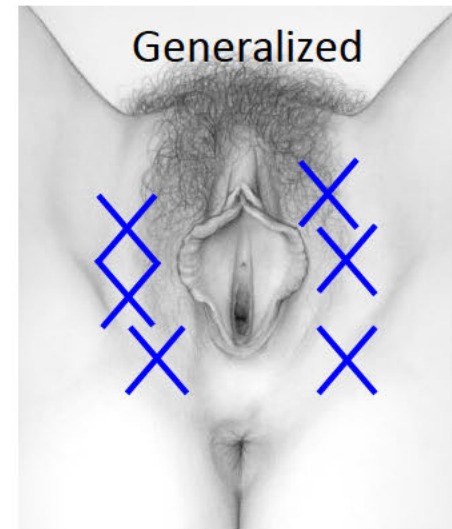


# Nomenclature

Vulvodynia – Vulvar pain of at least **3 months duration, without clear identifiable cause**

Descriptors:

- **Localized** (e.g. vestibulodynia, clitorodynia) or **Generalized** or **Mixed** (Localized and Generalized)
- **Provoked** (e.g. insertional, contact) or **Spontaneous** or **Mixed** (Provoked and Spontaneous)
- Onset (**primary** or **secondary**)
- Temporal pattern (intermittent, persistent, constant, immediate, delayed)



# Potential factors associated with Vulvodynia

**Co-morbidities** and other pain syndromes (e.g. painful bladder syndrome, fibromyalgia, irritable bowel syndrome, temporomandibular disorder)

- **Genetics**
- **Hormonal factors** (e.g. pharmacologically induced)
- **Inflammation**
- **Musculoskeletal** (e.g. pelvic muscle overactivity, myofascial, biomechanical)
- **Neurologic mechanisms:**
  - -Central (spine, brain)
  - -Peripheral
- **Neuroproliferation**
- **Psychosocial factors** (e.g. mood, interpersonal, coping, role, sexual function)
- **Structural defects** (e.g. perineal descent)



# How does the nomenclature update affect **current** treatment?

- Well, it may not.
- However it will guide futures studies to allow phenotyping.
- Longitudinal research is needed to identify risk factors involved in the expression of vulvodynia and designating potential subgroups in order to develop an empirically supported treatment algorithm.

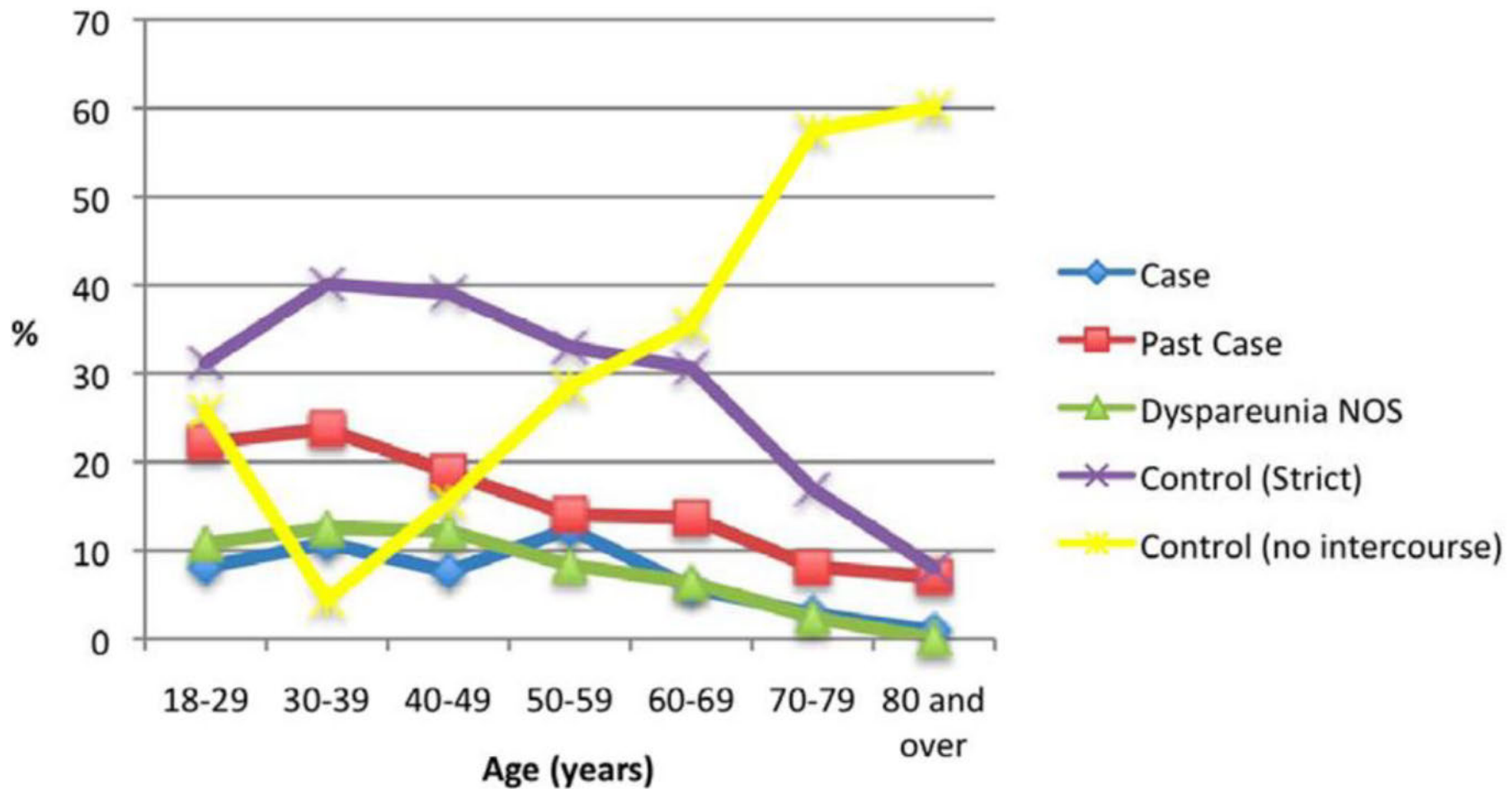


# Magnitude of the Problem

- Lifetime estimates ranging from 10% to 28% in reproductive-aged women in the general population.
- Harlow et al indicated that 8% of women 18 to 40 years old reported a history of vulvar burning or pain upon contact that persisted longer than 3 months and that limited or prevented intercourse.







Reed BD et al., Am J Obstet Gynecol 2013

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# Vulvodynia research

- Four NIH-funded population-based studies estimate that 3-8% of adult women suffer from chronic vulvar pain
- Up to 60% may see three or more doctors before receiving a diagnosis.
- Most common complaint (80%) among sufferers of chronic vulvovaginal pain is discomfort on contact (i.e. intercourse or tampon use)

Reed BD et al., Am J Obstet Gynecol 2011

Harlow BL, et al., J Am Med Women's Assoc 2003



# Insufficient Research to Report Efficacy

**“Vulvodynia interventions – systemic review and evidence grading.”**

- For improvement of pain and/or function in women with PVD, there was fair evidence that vestibulectomy was of benefit, but the size of the effect cannot be determined with confidence.
- There was fair evidence of lack of efficacy for several nonsurgical interventions.
- There were several interventions for which there were insufficient evidence to reliably evaluate.
- There was insufficient evidence to judge harms or to judge long-term benefits.
- For clinically meaningful improvement of pain in women with GV, there was insufficient evidence for benefit or any intervention.

## Summary:

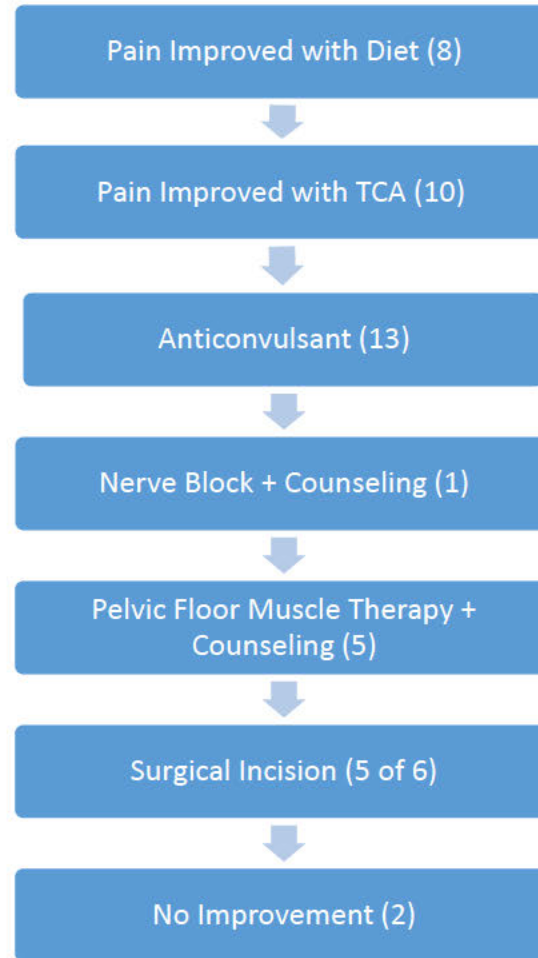
- Providers and patients looking for evidence-based interventions may need to rely on indirect evidences from studies of neuropathic pain and functional pain syndromes.

Andrews. Obstet Gynecol Surv. 2011

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# Step-Wise PVD Treatment Study Results Suggest Heterogeneity



Ventolini. J Obstet Gynaecol. 2009



# Treatments

- Discontinuation of Irritants
- Tricyclic Antidepressants
- Serotonin-Norepinephrine Reuptake Inhibitors
- Anticonvulsants
- Opioids
- Topical Medications
- Topical Hormonal Creams (e.g., estrogen, testosterone)
- Topical Anesthetics (e.g., lidocaine)
- Topical Compounded Formulations (e.g., anticonvulsant, antidepressant)
- Pelvic Floor Muscle Therapy
- Nerve Blocks
- Diet Modification
- Neurostimulation and Spinal Infusion Pump
- Complementary or Alternative Medicine
- Surgery (for women with Vulvar Vestibulitis Syndrome/Provoked Vestibulodynia)



# Current algorithm

- None



# Pathophysiology of Vulvodynia

ORIGINAL ARTICLE

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## Altered Central Sensitization in Subgroups of Women With Vulvodynia

*Zheng Zhang, MS,\* Denniz A. Zolnoun, MD, MPH,† Eric M. Francisco, BS,\* Jameson K. Holden, BS,\* Robert G. Dennis, PhD,\* and Mark Tommerdahl, PhD\**

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**Objective:** To investigate the clinical correlates of central nervous system alterations among women with vulvodynia. Altered central sensitization has been linked to dysfunction in central nervous system-inhibitory pathways (eg,  $\gamma$ -aminobutyric acidergic), and metrics of sensory adaptation, a centrally mediated process that is sensitive to this dysfunction, could potentially be used to identify women at risk of treatment failure using conventional approaches.

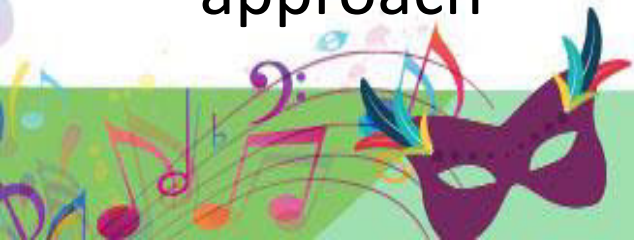
characteristics as provoked versus unprovoked. Although a given patient may experience both provoked and unprovoked pain, the most common symptom is that of provoked pain on contact, precipitated by tampon use or intercourse. Unlike unprovoked pain, where the clinical examination is nonspecific, the majority of women with provoked pain have localized tenderness in vulvar mucosa (ie, vestibule).<sup>2</sup> In addition, women with provoked vulvodynia tend to be



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# Central Sensitization in different subgroups

- Vulvodynia may be triggered by peripheral factors in the skin and underlying musculature
- Varying degrees of central dysregulation may develop
- Hypersensitivity at extragenital sites
- Understanding of the mechanistic (central vs. peripheral) implication of clinical signs and symptoms in vulvodynia is a necessary first step toward individualized, symptom-based treatment approach



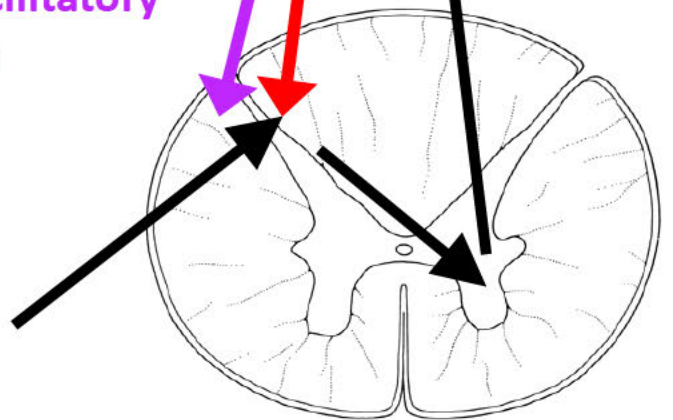
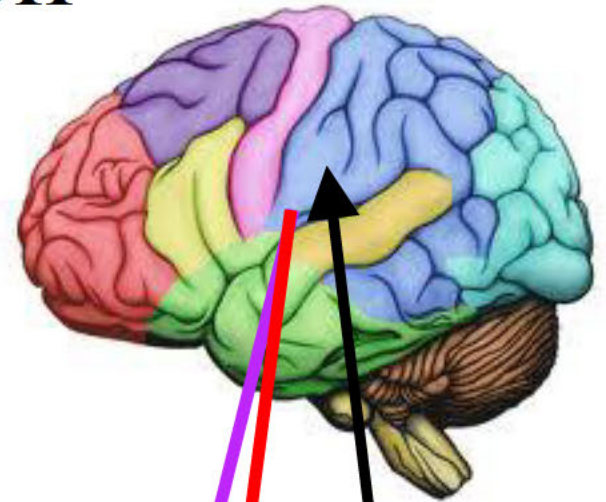


# Abnormal pain perception

- Pathophysiology
- Augmented pain processing has been identified in numerous chronic pain syndromes
  - Fibromyalgia (FM)
  - Temporomandibular disorder (TMD)
  - Irritable bowel syndrome (IBS)
  - Chronic low back pain
  - Vulvodynia

Nocioceptive pain

Descending  
Inhibitory and Facilitatory  
Pathways



## Environmental Factors

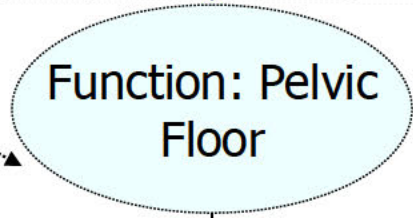
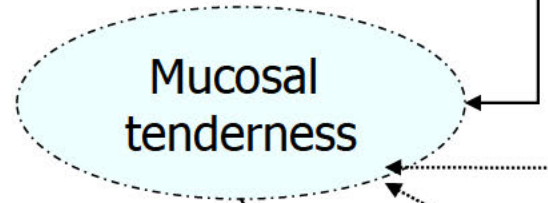
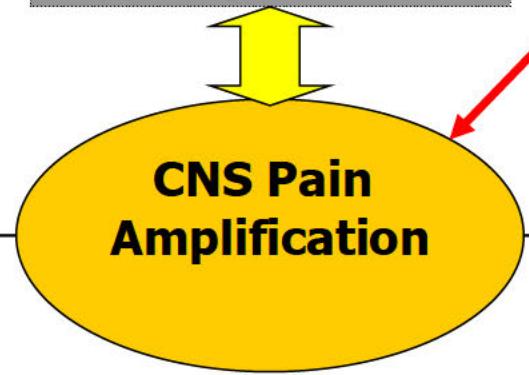
- Abuse/trauma
- Stress
- Marital/Relationship

## Psychological Factors

- Anxiety
- Somatization
- Hyper-vigilance

## Biologic Factors

- BP reactivity
- COMT haplotype
- $\beta$ -adnergic &  $\gamma$  receptor



Provoked Pain (PVD/VVS)



# Localized Provoked Vulvodynia



# Localized Provoked Vulvodynia

- Differences in clinical presentation have identified two subsets of LPVD:
- LPVD 1: Women who experience pain symptoms since the first episode of vaginal penetration
- LPVD2: Women with a history of pain-free penetration and subsequent development of vestibular pain





Pain 140 (2008) 411–419

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**PAIN**

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[www.elsevier.com/locate/pain](http://www.elsevier.com/locate/pain)

## Increased gray matter density in young women with chronic vulvar pain

P. Schweinhardt<sup>a,b,\*</sup>, A. Kuchinad<sup>b</sup>, C.F. Pukall<sup>c</sup>, M.C. Bushnell<sup>a,b,d</sup>

<sup>a</sup> *McGill Centre for Research on Pain, Faculty of Dentistry, McGill University, Room M119, Strathcona Anatomy and Dentistry Building, 3640 University Street, Montreal, Que., Canada H3A2B2*

<sup>b</sup> *Department of Neurology and Neurosurgery, McGill University, Montreal, Que., Canada H3A 2B2*

<sup>c</sup> *Department of Psychology, Queen's University, Kingston, Ont., Canada K7L 3N6*

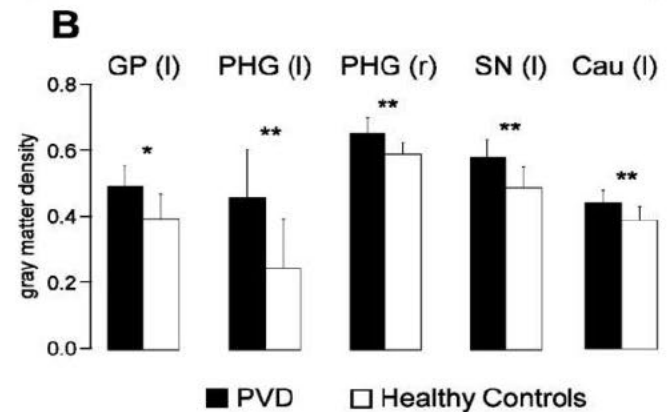
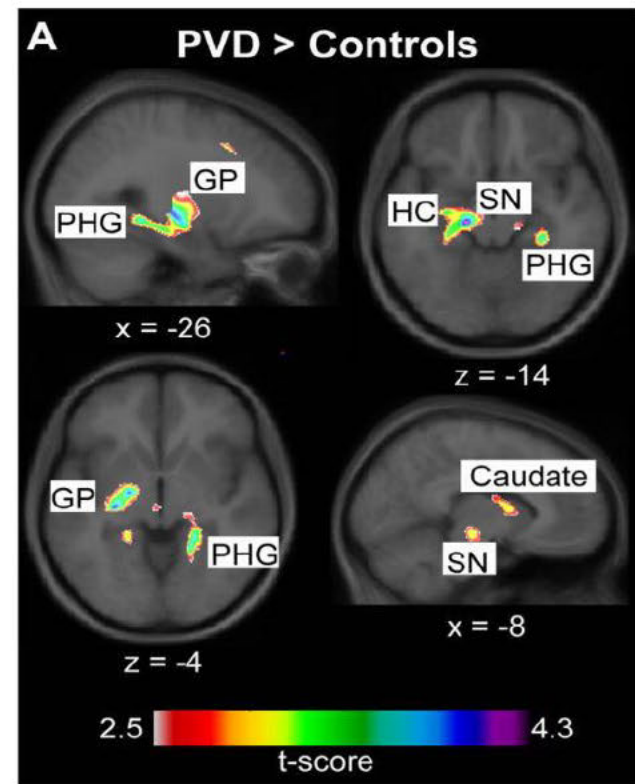
<sup>d</sup> *Department of Anesthesia, McGill University, Montreal, Que., Canada H3A 2B2*

Received 17 March 2008; received in revised form 8 September 2008; accepted 15 September 2008



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- Gray matter (GM) density was investigated in women with PVD (PVD1 and PVD2 subtypes combined) and healthy control women
- In contrast to patterns found in chronic pain patients, women with PVD had significantly *higher* GM density in pain modulatory and stress-related areas.



# LPVD1

- Younger
- Greater anxiety
- Lower pain thresholds
- More likely to catastrophize
- More comorbid pain conditions



# LPVD1

- Women with LPVD1 displayed heightened experimental pain sensitivity
  - lower heat pain tolerance at a nonvulvar site
  - lower heat detection and heat pain thresholds at the vulvar vestibule

Sutton KS et al. J Sex Med 2009

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# Differences in LPVD

- LPVD1 appears to be more centralized
- LPVD2 appears to be more peripheral
- **But no study has evaluated interventional response between subtypes**



# Peripheral

- Topical agents have been evaluated in the management of vulvodynia with mixed results, and no study has evaluated interventional response between subtypes.
- Topical application of lidocaine 5% ointment nightly for seven weeks has been shown to decrease dyspareunia in women with vulvodynia.
- Additionally, only a few randomized controlled trials have been performed in women with vulvodynia.
  - Bergeron et al randomized women to cognitive behavioral therapy, surface electromyographic (sEMG) biofeedback, and vestibulectomy with all treatments improving sexual function.
    - Vestibulectomy resulted in the decreasing vestibular pain more than biofeedback, there was a high drop out rate in the surgical group compared to the others. The sexual and psychologic improvements across all groups were sustained at six months.
  - Danielson et al randomized women to four months of topical lidocaine (2% gel for two months then 5% ointment for two months, with application five to seven times daily to vestibule) versus sEMG for four months without a difference in outcome



# Peripheral

- In 2010, Foster et al randomized controlled trial between oral desipramine, topical lidocaine, and the medications combined. No symptom improvement over twelve weeks in any group.



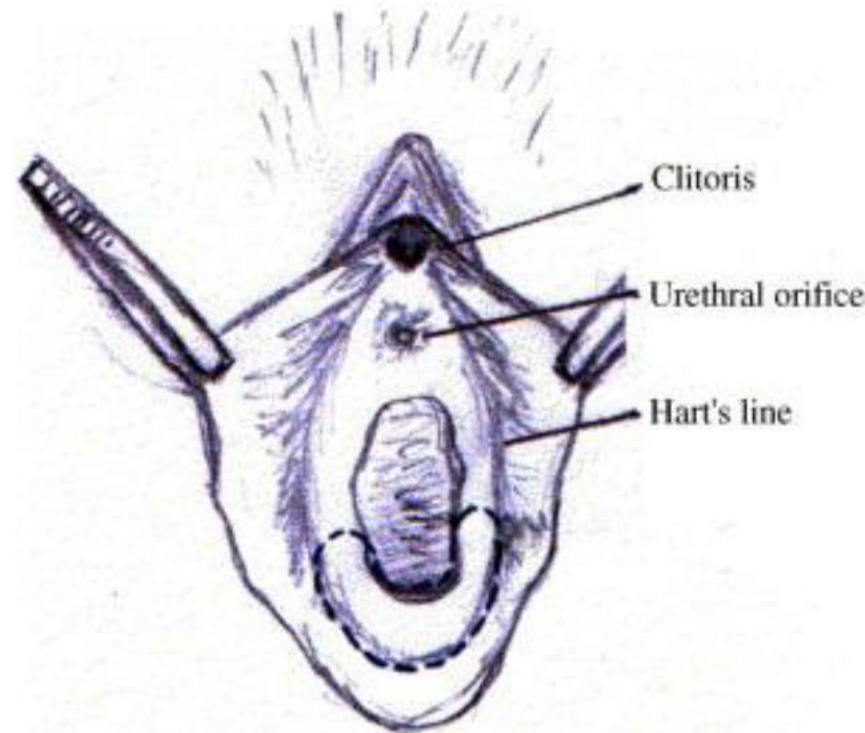
# Peripheral

- Physical therapy is also an established peripheral treatment for women with vulvodynia as most women with provoked vestibular pain have at least superficial muscular dysfunction:
  - Treatment courses as short as 7-12 weeks have been shown to decrease dyspareunia. It has also been described as a component of a multi-disciplinary approach, with systemic or topical medication and/or surgery for symptom management.



# Peripheral

- Vestibulectomy remains a core treatment for women with LPVD who have failed conservative measures, with at least some improvement of vestibular pain in upwards of 90% of women post-operatively.
- While suggestive of high efficacy, few are prospective, randomized studies, and often no control group exists.
- Also, most women continued on topical or oral medication pre and post-operatively which may affect outcome measurements:



# Central

- Despite variable efficacy, oral tricyclic antidepressants are a primary treatment option according to current vulvodynia guidelines



# Central

- SNRI (Duloxetine)
- TCA

| Drug          | Serotonin | Norepinephrine | Dopamine | Sedative | Antimuscarinic |
|---------------|-----------|----------------|----------|----------|----------------|
| Amitriptyline | +++       | +              | -        | +++      | +++            |
| Nortriptyline | +++       | ++             | -        | ++       | ++             |
| Desipramine   | -         | +++            | -        | +        | +              |
| Imipramine    | +++       | ++             | -        | ++       | ++             |



# Central

| Class/Medication                                    | Dosing   | Side effects   | Considerations   |
|---|--|--|--|
| Tricyclic Antidepressants (TCA)                     |  | Sedation, dry mouth, constipation, weight gain, tachycardia, hyperglycemia | Urinary retention<br>Uncontrolled diabetes,  |
| Amitriptyline                                       | 10-25 mg qhs<br>Titrate 10-25 mg/week to 75-150mg qhs  |  |  |
| Nortriptyline                                       | 10 mg qhs<br>Titrate 10 mg/week to 50-100 mg qhs       |  |  |
| Desipramine   | 25 mg daily<br>Titrate 10-25 mg/week to 75-100mg daily |  |  |
| Selective norepinephrine reuptake inhibitors (SNRI) |  | Sedation, headache, dizziness  | Hepatic dysfunction, caution with serotonergic drugs (risk for serotonin syndrome), rapid-cycling bipolar. Taper off required. |
| Duloxetine  | 20 mg daily<br>Titrate 20 mg/week to 60-90 mg daily    |  |  |





# Central

- Anticonvulsant therapy and vulvodynia
- Systematic review by Leo et al reported that while some vulvodynia patients derive symptom relief from anticonvulsants, there is, insufficient evidence to support the recommendation of anticonvulsant pharmacotherapy in the treatment of vulvodynia



# Central

- Gabapentin and Pregabalin
- MOA: binds  $\alpha_2\text{-}\delta_1$  subunit of Ca channel, blocking neurotransmitter release
- Efficacy: neuropathic pain, FM, MS, myofascial pain, LBP
- Other: Topiramate, Oxcarbazepine
- Side effects: sedation, dizziness, lower extremity edema
  - Because gabapentin/pregabalin is eliminated primarily by renal excretion, the dose should be adjusted for patients with reduced renal function.
  - Caution with patients who are at fall risk



# Central

- Gabapentin dosing
- Month 1:
  - Week1: 100 mg po qhs
  - Week2: 200mg po qhs
  - Week3: 300 mg po qhs
  - Week4: 100 mg po q am, 300 mg po qhs
- Month 2:
  - 300 mg po tid
- Month 3:
- The dose may be titrated up as needed for pain relief



# Central

- Pregabalin dosing
- Month 1:
  - Week1: 25 mg po qhs
  - Week2: 50 mg po qhs
  - Week3: 25 mg po q am, 50 mg po qhs
  - Week4: 50 mg po bid
- Month 2:
  - 75 mg po bid

The dose may be increased to 150 mg two times a day (300 mg/day) within one month based on efficacy and tolerability. Patients who do not experience sufficient benefit with 300 mg/day may be further increased to 225 mg two times a day (450 mg/day). Recommended dose: 300 to 450 mg/day Although pregabalin was also studied at 600 mg/day, there is no evidence that this dose confers additional benefit and this dose was less well tolerated. In view of the dose-dependent adverse reactions, treatment with doses above 450 mg/day is not recommended.



# Central

- Cognitive behavior therapy (CBT) programs are based on fear-avoidance pain responses women associate with intercourse.
- Both CBT and self-management programs allow the patient to control their feelings and emotional response to pain and have been successfully used in women with vulvodynia.
- CBT for vulvodynia has been shown to improve sexual pain immediately after therapy and up to two and a half years in follow.



# Central

- Opioids
- MOA: Analgesic effect by binding to G protein coupled receptors

## Short-acting Opioids

## Long-acting Opioids

### Advantages

Fast-acting; appropriate for acute pain, breakthrough pain

May be more appropriate for patients with a constant pain component; analgesic stability

### Disadvantages

Need for repetitive dosing

Initial delayed onset of action



# Opioid Risk Tool (ORT)

|  |  | Mark each<br>box that applies | Item Score<br>If Female | Item Score<br>If Male |
|--|--|-------------------------------|-------------------------|-----------------------|
| 1. Family History of Substance Abuse     | Alcohol  | [ ]                           | 1                       | 3                     |
|  | Illegal Drugs  | [ ]                           | 2                       | 3                     |
|  | Prescription Drugs   | [ ]                           | 4                       | 4                     |
| 2. Personal History of Substance Abuse   | Alcohol  | [ ]                           | 3                       | 3                     |
|  | Illegal Drugs  | [ ]                           | 4                       | 4                     |
|  | Prescription Drugs   | [ ]                           | 5                       | 5                     |
| 3. Age (Mark box if 16 – 45)             |  | [ ]                           | 1                       | 1                     |
| 4. History of Preadolescent Sexual Abuse |  | [ ]                           | 3                       | 0                     |
| 5. Psychological Disease                 | Attention Deficit<br>Disorder                                | [ ]                           | 2                       | 2                     |
|  | Obsessive Compulsive<br>Disorder<br>Bipolar<br>Schizophrenia |                               |                         |                       |
|  | Depression   | [ ]                           | 1                       | 1                     |
| <b>TOTAL</b>                             |  | [ ]                           |                         |                       |

**Total Score Risk Category**

Low Risk 0 – 3

Moderate Risk 4 – 7

High Risk  $\geq 8$



# Opioid Side Effects

## Side Effects

- Nausea and vomiting
- Sedation
- Constipation

## Amelioration

- Switch opioids; anti-emetics
- Lower dose (if possible); add co-analgesics; add stimulants
- Treat prophylactically with stool softeners, bowel stimulants; non-pharmacological measures; switch opioids





# Opioid Side Effects

## Side Effects

- **Itching**
- **Endocrine dysfunction/  
reduced libido**
- **Edema and sweating**
- **Dizziness**
- **Confusion**

## Amelioration

- **Switch opioids;  
antihistamines**
- **Endocrine monitoring;  
hormone replacement;  
endocrine consultation**
- **Switch opioids**
- **Antivertiginous agents  
(eg, scopolamine)**
- **Titrate dose; switch opioids**

# DEA drug classes

- **Schedule I**

- Drugs with no currently accepted medical use and a high potential for abuse. Schedule I drugs are the **most dangerous** drugs heroin, lysergic acid diethylamide (LSD), marijuana (cannabis), 3,4-methylenedioxymethamphetamine (ecstasy), methaqualone, and peyote

- **Schedule II**

- High potential for abuse, less abuse potential than Schedule I drugs, with use potentially leading to severe psychological or physical dependence. These drugs are also considered **dangerous**. Cocaine, methamphetamine, methadone, hydromorphone (Dilaudid), meperidine (Demerol), oxycodone (OxyContin), fentanyl, Dexedrine, Adderall, and Ritalin

- **Hydrocodone**

- **Schedule III**

- Moderate to low potential for physical and psychological dependence.

- **Hydrocodone**

- (Tylenol with codeine), ketamine, anabolic steroids, testosterone

- **Schedule IV**

- Low potential for abuse and low risk of dependence.

- Xanax, Soma, Darvon, Darvocet, Valium, Ativan, Talwin, Ambien

- **Tramadol**

- **Schedule V**

- Schedule V drugs are generally used for antidiarrheal, antitussive, and analgesic purposes. cough preparations with less than 200 milligrams of codeine or per 100 milliliters (Robitussin AC), Lomotil, Motofen, Lyrica, Parepectolin



# Opioid changes that will affect your practice

- **Prescription drug monitoring programs (PDMP)-**
  - 37 states have operational PDMPs that have the capacity to receive and distribute controlled substance prescription information to authorized users
- **Some states require a state AND DEA prescribing certificate**
- **May be new legislature to have prescriber training to provide scheduled medications, particularly schedule II**

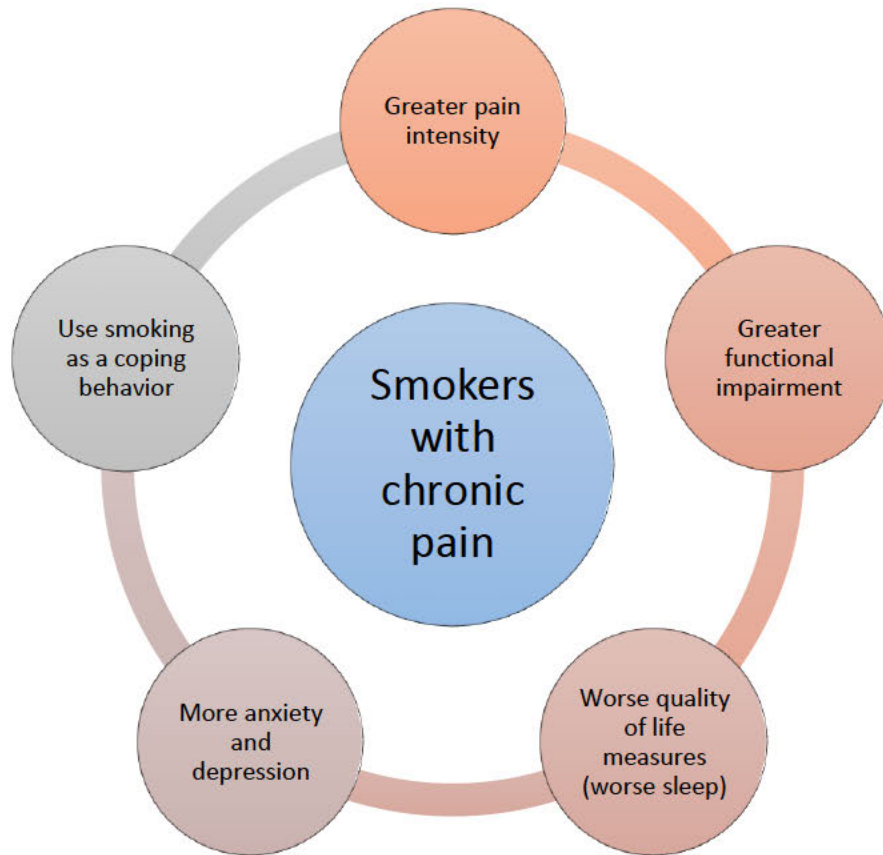


# Placebo

- Patient's belief they will be better is POWERFUL
- Characteristics of the placebo
  - If the pill (or treatment) looks real, more likely to believe it contains active ingredients
  - Larger sized pills suggest a stronger dose than smaller pills
  - Taking two pills appears more potent than just one
  - Injections have a more powerful effect than pills



# Tobacco abuse



- Why does smoking increase pain?
  - HPA is down-regulated in smokers
  - Accelerates degenerative change
  - Impairs healing
- Psychosocial factors

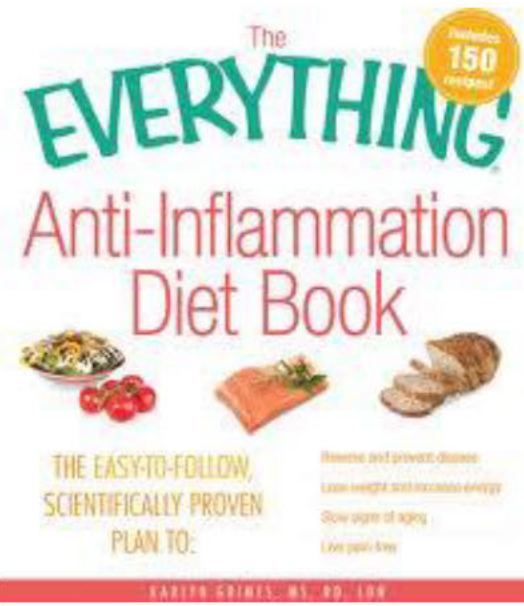
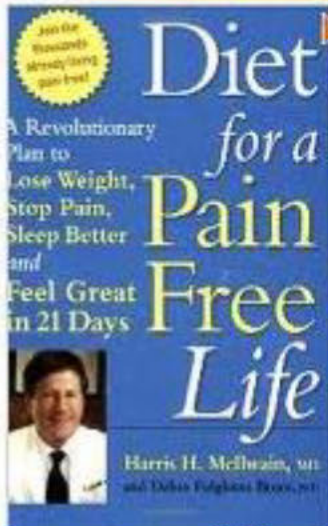
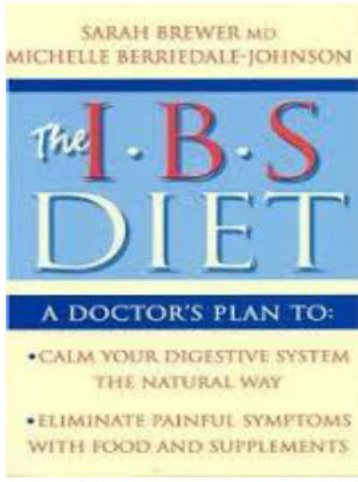


# Sleep

- Provide instruction on **sleep hygiene** and limit the drugs that alter restorative sleep
  - **Prevent REM sleep:** long acting opioids, beta blockers, clonidine, SSRIs
  - **Prevents paralysis and timing of sleep:** Dopaminergic blockers
- Vitamin D deficiency (and toxicity) associated with poor sleep



# Diet



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# Exercise

- Anti-inflammatory (improvement of inflammatory markers)
- Release of natural 'endorphins'
- Improves sleep/depression symptoms
- Can be a narrow therapeutic window





# Case

- 33 year old P2 female presents with 6 months of provoked burning vulvar pain following the birth of her last child. She recently stopped breastfeeding. Normal bowel and bladder habits. No vaginal d/c or odor.
- Alleviating factors: loose clothing, Monistat
- Aggravating factors: intercourse, tight clothing
- PMH: Depression
- PSH: None



# Case

- Meds: PNV, Prozac, OCP
- All: None
- Exam:
- External genitalia wnl.
  - Mild erythema of the vestibule, TTP with qtip. Reproduces burning sensation with intercourse primarily from 4 to 8 o'clock.
- Muscles:
  - Moderately tender levator ani muscles bilaterally, nontender obturators, nontender piriformis
- Bimanual exam wnl



# Case

Peripheral treatment:  
Topical anesthetic+  
pelvic floor physical  
therapy

Reassess pt.  
Continue PT.  
Consider adding  
muscle relaxer

Central treatment:  
Transition Prozac to SNRI,  
continue pelvic floor  
physical therapy +/- CBT

Vestibulectomy

Week0

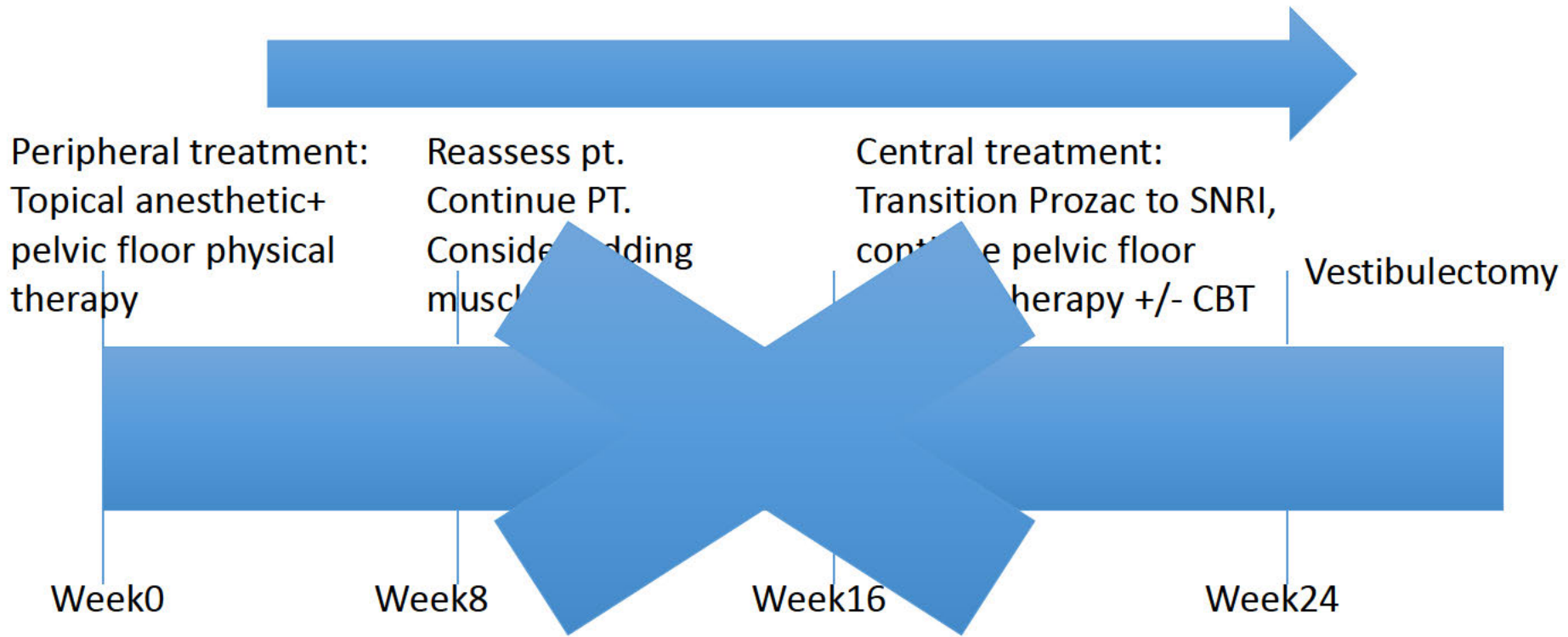
Week8

Week16

Week24



# Case



# Conclusions

- Numerous factors have been implicated in the development and maintenance of vulvar pain.
- For many women, peripheral and central therapies may be beneficial depending on symptom profile
- Further phenotyping will allow phenotypic specific interventions to be identified for improved outcomes.



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