THE JOURNAL OF
SEXUAL MEDICINE

Recommendations for the Study of Vulvar Pain in Women, Part 2: Methodological Challenges

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ABSTRACT

Introduction: Chronic vulvar pain is a multidimensional condition with great variability in clinical presentation among affected women. In a companion article, part 1, we reviewed and recommended assessment and measurement tools for vulvar pain and related outcomes with a view toward improving consistency and comparison across studies. Yet methodological challenges to conducting research with this population remain and can further hinder conclusions regarding etiology and treatment.

Aim: To discuss methodological challenges to conducting vulvar pain research alongside recommended solutions.

Methods: The expert authors reviewed the scientific evidence related to the study of vulvar pain and made decisions regarding methodological challenges and mitigation strategies via discussion and consensus.

Main Outcome Measure: We articulated key challenges to conducting research in this area and formulated recommendations for mitigating these challenges.

Results: Challenges to the field include selection and sample biases, heterogeneity of the condition, inclusion of the partner, and neglect of the multidimensional aspects of vulvar pain. 2 key recommendations are more careful and detailed tracking and characterization of research samples and greater multidisciplinary collaboration to better capture the complexity of chronic vulvar pain.

Clinical Implications: This methodological critique points to several challenges to clinical research with populations struggling with chronic vulvar pain and makes suggestions for how to mitigate these issues.

Strength & Limitations: Comments in this expert review raise awareness regarding core challenges to the study of vulvar pain and can inform study design of clinical research with this population. The content of this review is based on expert knowledge and opinion rather than a formal systematic review or extended consultation process.

Conclusion: A careful reflection upon methodological challenges facing clinical research of vulvar pain and ways to mitigate such challenges is crucial for improving the quality, generalizability, and uptake of research findings. **Rosen NO, Bergeron S, Pukall CF. Recommendations for the Study of Vulvar Pain in Women, Part 2: Methodological Challenges. J Sex Med 2020; 17:595–602.**

Women with chronic vulvar pain and their romantic partners report sexual, psychological, and relational consequences negatively impacting their health and quality of life.[1,2] In a companion article,[3] we define and describe the characteristics of chronic vulvar pain in more detail. Briefly, there are 2 broad categories of vulvar pain that include (i) vulvar pain caused by a specific disorder (eg, infectious, inflammatory, neoplastic, neurologic, trauma, iatrogenic, or hormonal deficiencies) and (ii) vulvodynia, which is defined as vulvar pain lasting at least for a duration of 3 months without a clear identifiable cause, and which has a prevalence of 8%.[4,5] Provoked vestibulodynia is the most common subtype of vulvodynia in premenopausal women. Provoked vestibulodynia is characterized by an acute recurrent pain triggered by pressure to the vulvar vestibule, primarily during vaginal penetration.[6] We have observed significant progress in understanding the multidimensional etiology of chronic vulvar pain over the last 2 decades, resulting in the development of novel, effective treatments.[2,7–12] Yet several methodological challenges to conducting research with this population remain and may stall further progress.[13]

Received October 1, 2019. Accepted December 13, 2019.

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https://doi.org/10.1016/j.jsxm.2019.12.018

Table 1. Methodological challenges and recommendations

Challenge	Recommendations
Diagnosing vulvar pain conditions	Confirm diagnosis by study physician who uses a standardized procedure for in-laboratory studies.
	For online studies, compare self-reported symptoms to a standardized list of criteria for the type of vulvar pain under study.
	Consider using a more descriptive term rather than a diagnosis when formal diagnosis has not been made.
Distinguishing and identifying important subgroups	Pilot studies to carefully characterize the future sample, refine, and adapt the inclusion/exclusion criteria as needed.
	Systematically document participant's characteristics for potential use in statistical analyses (eg, covariate analyses).
	Include participants with comorbidities by assessing the medical status of the comorbid condition (when stable, there is minimal bias); document comorbidity status for use as covariates, or group comparisons
Inclusion (or lack thereof) of the partner	Collect detailed information about those who opt to participate or not in dyadic research to determine potential selection biases.
	Reduce self-selection biases by randomization (when appropriate) and wider recruitment efforts.
(Limited) representativeness of samples	Researchers should consider recruiting more diverse samples, across comorbid conditions, culture, sexual orientation, age, and settings (eg, those not involved with health-care system), and those with lower perceived pain intensity and pain duration but who are still distressed.
	Online survey platforms and secure video streaming services may enhance participation outside of urban centers
	Collaboration across multiple research sites to enhance diversity.
	Document participant characteristics for risk of bias and control for it in analyses.
	Track attrition in studies of multiple measurements for nonrandom attrition; use mitigation strategies to enhance retention (eg, reminder calls).
Integration of multiple etiologies	Use multiple methodologies to test the same research question and tease apart the temporal order of associations among biomedical, dyadic, cognitive, affective, and behavioral components of vulvar pain.
	Build multidisciplinary teams to ensure appropriate clinical and methodological expertise.
Different studies using different measures	Refer to recommended guidelines for pain and other key outcomes measures.
	Build multidisciplinary teams that encompass multiple areas of expertise and can inform appropriate measurement.
Power and sample sizes	Conduct a prior power analyses based on effect sizes from pilot data and other studies that have used the same outcome measures.
	Power analyses should take into account primary and secondary outcomes, type of clinical trial, and potential changes in group differences over time.
	Assemble teams to conduct multicenter studies to increase recruitment capacity.

We aimed to review the scientific literature related to the measurement of chronic vulvar pain. This nonsystematic review included an evaluation of the advantages and disadvantages of available measurement tools, as well as methodological challenges to conducting research in this area and potential solutions. Relying on our expert opinion, we reached conclusions and recommendations via discussion and consensus. Our review resulted in 2 companion articles entitled *Recommendations for the Study of Vulvar Pain in Women*. Part 1 reviewed assessment and measurement tools for vulvar pain and associated key outcomes and discussed advantages and potential barriers to use of these tools in research studies.[3] In Part 2—the present article—we review key methodological challenges we consider to be important when conducting research with women and couples coping with vulvar pain. We endeavor to make some recommendations for addressing each of these challenges. A summary of the identified challenges and recommendations can be found in Table 1.

DIAGNOSING VULVAR PAIN CONDITIONS

One of the main questions to consider when researching vulvar pain populations is how to ensure that participants are appropriately diagnosed with the condition under study. Typically, in studies that involve the physical presence of participants in a clinical or laboratory setting, potential participants who have already received a diagnosis of the type of vulvar pain under investigation (via chart review, for example) are invited to participate in the study or are solicited via advertisements and then screened into the study when they meet certain criteria

(eg, moderate to severe provoked pain at the vaginal entrance for a minimum duration of 3 months). For either type of study, the diagnosis can then be confirmed or established by a study gynecologist (or other trained clinician) who conducts a standardized examination appropriate for the diagnosis. For online studies, however, the physical presence of the participants is not likely. In such studies, researchers can ask about the diagnoses received and/or symptoms experienced (eg, via checklists or other kinds of questions). This information can then be compared with an already determined standardized list of criteria that need to be met to be considered as having the type of vulvar pain under study. Research has demonstrated that self-reported symptoms have excellent reliability and validity when predicting vulvodynia diagnoses [14]; however, it is important to ensure that the process of determining diagnoses is clearly explained when reporting results. It may also be worthwhile to use a more descriptive term for the condition under study (eg, "chronic vulvar pain" instead of "vulvodynia") when factors that need to be ruled out to be diagnosed with vulvodynia have not been assessed.

DISTINGUISHING/IDENTIFYING IMPORTANT SUBGROUPS

When studies involve heterogeneous samples and/or subgroups, true effects of treatment efficacy can be masked by those for whom there are no effects (eg, including women with generalized vulvar pain in a study focused mostly on women with provoked pain). Furthermore, some patient subgroups may find it difficult to adhere to study protocols, thereby increasing the risk of selective participant dropout and missing data, which from a statistical perspective, cannot be handled as easily as random missing data, and threaten the internal validity of the study. Hence, researchers often prioritize the homogeneity of participants' clinical characteristics to control for confounding factors such as hormonal influences (eg, physical and sexual changes associated with menopause) or comorbid conditions that may influence the pain or related impairments. Although homogeneous samples are advantageous because they increase experimenter control, focus on research questions of specific, identifiable variables, and allow for better comparison between studies, they increase the risk of limiting the generalizability of findings, that is, external validity, and complicate feasibility with their strict inclusion criteria, for instance, by slowing down the pace of recruitment. Physical and psychological comorbidities are common among women with vulvodynia,[15,16] yet those with significant comorbidities are often screened out of clinical trials.[10,17,18] Consequently, little is known about how women with more complex presentations respond to interventions that have received the most empirical support, such as cognitive-behavioral therapy.

There are potential solutions to this trade-off between internal and external validity. First, the most effective course of action is for researchers to pilot their studies adequately, which helps to characterize a future sample in terms of who calls to take part in the study, what are their clinical presentations—and how to document these if need be—and are the study selection criteria overly stringent. Inclusion/exclusion criteria of the actual study can then be adapted based on these pilot data. Second, participant characteristics need to be surveyed systematically and diligently, to prepare for potential use in statistical analyses (eg, scores on measures of depression can be used as covariates). Third, researchers can include participants with comorbidities by assessing the medical status of the comorbid condition, for example, the stability of antidepressant medication for women with mood disorders. When medication is stable and documented, the risk of bias related to including such participants is minimal. The same can be carried out for relatively large subgroups, such as primary and secondary vulvar pain, or women with antecedents of childhood interpersonal trauma: researchers can document participants' status as carefully as possible and then use specific clinical characteristics as covariates in analyses. When these subgroups are large enough, they can even be compared based on the main study outcomes. However, when subgroups are suspected to be relatively small, studies can be powered in advance for oversampling of these subgroups, for example, same-sex couples, to ensure a large enough subsample to draw meaningful knowledge. In summary, when appropriate controls are in place, heterogeneous samples may be turned into a strength of a study design rather than a weakness.

INCLUSION OF THE PARTNER

Despite strong findings illustrating dyadic consequences for women with vulvodynia and their partners,[2] treatment research has largely focused on affected women only. Partner unwillingness has been reported to be a common reason to decline participation in dyadic studies,[19,20] representing a significant impediment by reducing the generalizability of the findings. Couples who choose to participate may be distinct from those who do not in a variety of ways, including openness to disclosure of personal information and motivation to engage in treatment—some studies involve treatment itself, whereas etiological studies might require refraining from treatment, each acting as a barrier for different couples.[13] On the one hand, couple characteristics such as viewing the problem as a couples' issue, more secure romantic attachment and greater communication and intimacy might increase willingness to participate in research as these couples have existing strengths on which they might hope to capitalize. On the other hand, higher functioning couples might be less likely to participate as they could be less distressed and have developed adaptive ways of coping. Couple therapy studies must carefully screen for intimate partner violence, which is contraindicated for this type of treatment.[21] Couples who are highly distressed by the pain might be less willing to refrain from other treatments to participate. Taken together, it remains unclear whether self-selection biases exist and result in an overestimation or underestimation of the severity of the pain and its relational consequences. Currently, there is limited information about such biases in this population. Future studies should

attempt to collect more detailed information about those who opt to participate or not participate in dyadic research. Self-selection biases are an inherent limitation in vulvar pain research with couples but can be mitigated using randomization when appropriate, and by focusing on wider recruitment efforts in the community (eg, not recruiting only from clinical referrals).[13]

REPRESENTATIVENESS OF SAMPLES

Vulvar pain studies typically include women and couples who are predominantly white, young (ie, aged mid-twenties to mid-thirties on average), and well-educated and who identify as heterosexual and cisgender.[10,17,22,23] However, population-based studies indicate that Hispanic women are more likely to experience chronic vulvar pain than non-Hispanic women, and they are more likely to report pain with first intercourse rather than a later onset.[24,25] Moreover, there are significant racial inequities in pain treatment such that African Americans are undertreated for their pain.[26] Finally, in a small online cross-sectional study, heterosexual women with vulvar pain reported that the pain had more negative consequences for their relationship than lesbian women (75% vs 52%).[27] Inclusion of sexual minorities in vulvar pain sampling is crucial given that there are known gaps in knowledge about physical health among sexual minorities,[28] largely related to a history of excluding sexual minority couples from research [29] and clinical trials.[30] Taken together, findings suggest that there is a serious discrepancy in the representativeness of most etiological and treatment research studies in vulvar pain.

In addition to volunteer biases at play in dyadic studies of vulvar pain, a key selection bias concerns whether recruitment is made within a hospital setting, such as a tertiary care clinic, or in the general population, such as on social media, newspapers, and other advertisements. Women with vulvar pain who consult a specialized clinic may be more distressed, present with pain for a longer duration, and have more comorbidities, in addition to being more persistent in navigating the health-care system. Therefore, the use of clinical samples has been criticized because of these different treatment-seeking behaviors. Nevertheless, given these are the patients that many experts in the field see in their practice, they still need to be included in studies, while carefully documenting the risk of bias and controlling for it in subsequent analyses. Importantly, only 60% of afflicted women seek treatment, and 52% of those never receive a formal diagnosis,[4] such that by focusing on clinical samples exclusively, a large proportion of afflicted women are never studied. Efforts to access those who do not seek help and are not involved with the health-care system should be intensified.

Another challenge that relates to sample representativeness is use of pain during intercourse as the primary outcome of interest.[17,21,31,32] Selecting this measure is not surprising, given that most women report interference with intercourse as the primary cause of distress related to their vulvar pain. However, this outcome is contingent on women engaging in intercourse. Similarly, researchers often use eligibility cutoff points for perceived pain intensity (eg, 4 of 10 on an numerical rating scale) and the length of time since pain onset (eg, a minimum of 6 months).[21,31,33] Therefore, women who are in the early stages of this pain, whose pain is of lower intensity—regardless of the level of distress and interference it causes—and those who are potentially the most impaired or distressed as reflected by their heightened avoidance of intercourse (not necessarily related to their pain intensity) may not be captured in prior research.[13]

Researchers should consider recruiting more diverse samples, across comorbid conditions, culture, sexual orientation, and age (eg, premenopausal, perimenopausal, and postmenopausal women). Broadening inclusion criteria and targeting the recruitment of diverse women may promote a more representative sample, yet may limit internal validity of studies. The use of online survey platforms and secure video streaming services (eg, Zoom) for structured interviews may reduce the reliance on local participants and allow researchers to gather data from those living outside of urban settings, promoting the generalizability of findings. Of course, this strategy is more difficult for studies that require participants to come into the laboratory (eg, for quantitative sensory testing or a psychological intervention). Multisite studies will enhance the diversity of participants in such research.

One strategy to address volunteer bias is to collect data regarding who, of those showing interest in a given study on vulvar pain, decided to participate in the end, and who did not, to make eventual comparisons between participants and nonparticipants. The same holds true for any study involving multiple measurements, including randomized clinical trials: participants need to be tracked and characterized, as any nonrandom attrition poses a threat to the internal validity of a study. Mitigation strategies to retain participants need to be in place from the very beginning of a study. For example, researchers can implement reminder emails and phone calls, make sure that participants consistently interact with the same contact person from the research team, and make use of other participant fidelity procedures (eg, sending birthday cards).

INTEGRATION OF THE STUDY OF MULTIPLE ETIOLOGIES

Despite data and theory suggesting the existence of multiple etiologic pathways leading to the development and persistence of vulvar pain[34] and a growing international trend toward interdisciplinary research, our field lags behind and remains fragmented. Increased dialog among subdisciplines and across disciplines is required, as are research designs that incorporate biomedical and psychosocial factors and questions concerning their interactions.[15] A recent study adopting a biopsychosocial perspective showed that pain catastrophizing was significantly associated with pain intensity, partner support, and pelvic floor musculature flexibility. Fear avoidance, pelvic floor musculature variables, and partner support explained 28.3% of the variance in

pain during intercourse.[35] One important caveat of a majority of studies on vulvar pain is the use of cross-sectional, self-report methodologies, which do not allow the establishment of causal relations between distal factors, such as childhood trauma, and current pathophysiology or enable the identification and understanding of mechanisms as they manifest across time. Capitalizing on triangulation, that is, the strategic use of multiple methodologies testing the same idea, would go a long way in resolving this challenge.[36] For instance, in-laboratory observational studies could allow for the (i) integration of physiological measures of psychological factors, such as emotion regulation, through monitoring of the autonomic nervous system (eg, heart rate) and (ii) inclusion of the partner, as well as interactions among these intraindividual and interpersonal variables and their biological underpinnings.[2,37] They can be incorporated with longitudinal or daily diary designs using multiple time points. Such complex paradigms need to be adopted more frequently if we are to find relevant answers to afflicted women's suffering and tease apart the temporal order of the associations among biomedical, dyadic, cognitive, affective, and behavioral components of vulvar pain.

At first glance, these study designs may appear to pose a greater burden on participants. However, with the proper approach, they remain feasible and could mirror the complexity of studies conducted in other interdisciplinary fields, such as psychoneuroendocrinology. Potential ways to mitigate participant burden include offering drinks and snacks, including a break between 2 different measurements (eg, between self-report measures completed on a computer and physiological measures), and, importantly, compensating participants financially for their time. Finally, the rapport established with the research team is key to the success and participant retention in such complex studies, and therefore, they require high quality research personnel who are well trained and closely supervised.

The same holds true for treatment studies. Few studies have examined whether a medical treatment can improve sexual and psychological end points. 4 randomized clinical trials investigated the efficacy of topical and oral medications not only in relieving vulvovaginal pain in women with vulvodynia but also in improving sexuality and psychological secondary end points such as depression and sexual satisfaction.[10,33,38,39] These studies take into account the multidimensional aspects of vulvar pain, which is an important strength. Nevertheless, changes in sexuality outcomes typically have small effect sizes and hence require larger samples to be detected. Studies to date are likely underpowered for sexual function, satisfaction, and distress outcomes as they are typically designed to yield significant effects in the primary outcome only, which is pain. One trial aimed to test whether a behavioral approach, physical therapy, resulted in changes in pathophysiology, that is, pelvic floor muscle morphology.[18] However, only the trial design has been published. In addition, no rigorous, phase III randomized clinical trial to date has focused on whether multimodal, multidimensional approaches are superior to single interventions, whereas this question has significant implications for treatment recommendations, sequence of treatments, and cost effectiveness.

THE PROBLEM OF DIFFERENT STUDIES USING DIFFERENT MEASURES

Another challenge lies in the disparity of measures used in different study protocols, rendering it difficult to make comparisons across studies and to draw firm conclusions. Indeed, the field is plagued with inconsistencies in terms of how central end points, such as pain and sexual function, are assessed. This is perhaps not surprising in light of the fact that published guidelines supporting best research practices, such as findings from the 4th Consultation on Sexual Medicine[40] and guidelines for the choice of outcome measure in clinical trials for vulvar pain [41] are fairly recent. 2 recent studies found moderate correlations among subjective and objective measures of pain: a numeric rating scale of self-reported pain during vaginal penetration, the pain subscale of the Female Sexual Function Index, and pain elicited via a vulvalgesiometer (an objective measure of eliciting pain [42,43]). However, the numeric rating scale was more likely to be associated with measures of emotional functioning including pain catastrophizing and hypervigilance than were the other 2 measures of pain. These findings suggest that the pain measures tap into both a common dimension of women's vulvar pain and distinct aspects of their experiences. Multiple measures of pain should be prioritized.

Still, many medically based studies do not assess important components of sexuality, such as sexual satisfaction and sexual distress.[44] Moreover, many psychological factors are assessed from a psychopathological perspective, that is, in terms of disorders, whereas most women present with subclinical, but nevertheless distressing, levels of depressive and anxiety symptoms and other emotions beyond psychiatric diagnoses, such as shame and guilt. Conversely, some psychosocial studies do not involve a gynecological examination—a core assessment to establish the vulvar pain diagnosis and sample homogeneity. Building multidisciplinary research capacity and teams encompassing multiple areas of expertise such as gynecology, psychology, epidemiology, neuroscience, and physical therapy could help resolve these unfortunate limitations and generate robust findings that can inform much needed novel interventions.

POWER AND SAMPLE SIZES

Many studies in the field of vulvar pain are underpowered, that is, do not have a sufficiently large sample size to detect statistically significant and clinically meaningful effects. This issue is particularly true of treatment studies, whereby many involve about 15-20 participants per group or less, yet are not pilot studies or open trials.[45] Consequently, the authors might conclude that there are no differences between 2 treatment arms,

or between pretreatment and post-treatment on key end points, when in fact findings may likely be due to a lack of statistical power. Limited power is an important issue because clinical trial findings and conclusions are often interpreted as a definitive scientific fact, when unfortunately many in our field are not designed adequately.

A priori power analyses based on effect sizes yielded by pilot data and other treatment studies in the field using the same outcome measures are relatively simple to conduct and will go a long way to inform the appropriate sampling size. Such power analyses should be based on the primary end point and take into account not only the study aims and the type of clinical trial (eg, superiority vs inferiority trial) but also secondary outcomes. Most trials aim to examine group differences, in addition to changes over time and maintenance of gains. These goals should all be taken into account when conducting power analysis.

This methodological challenge is not entirely in researchers' control. First, collecting large samples in clinical research requires substantial funding, and vulvar pain is notoriously underfunded. Second, gathering such samples in a reasonable number of years is influenced by the location of the researcher. If not in a metropolitan area, this challenge will be greater and may even become a barrier to conducting large scale studies that require any kind of in-laboratory manipulation or treatment. One mitigation strategy is to assemble large teams of investigators and conduct multicenter studies, which increases recruitment capacity substantially. This strategy may also hold the advantage of resolving other research challenges, such as the need for diverse and inclusive samples, as well as multidisciplinary approaches.

CONCLUSIONS

In this article, we outline several key methodological challenges faced by researchers in this field and endeavor to make recommendations for how to rectify these problems (see Table 1). As noted in our companion article,[3] greater consistency in the use of measurement tools will enable better comparisons across studies and allow for the pooling of study results to see the overall strength of effects (eg, of etiological factors, treatment outcomes). 2 additional core themes at the heart of our recommendations include a careful and detailed tracking and characterization of research samples and increasing multidisciplinary collaboration to better capture the complexity of this prevalent and distressing condition.

ACKNOWLEDGMENTS

Natalie O. Rosen is supported by a New Investigator Award from the Canadian Institutes of Health Research. Sophie Bergeron is supported by a Tier 1 Canada Research Chair.*

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Conflict of Interest: None.

Funding: This research was supported by the Canadian Institutes of Health Research.

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REFERENCES

1. Shallcross R, Dickson JM, Nunns D, et al. Women's subjective experiences of living with vulvodynia: A systematic review and meta-ethnography. **Arch Sex Behav 2018;47:577-595.**
2. Rosen NO, Bergeron S. Genito-pelvic pain through a dyadic lens: Moving toward an Interpersonal Emotion Regulation Model of women's sexual dysfunction. **J Sex Res 2019; 56:440-461.**
3. Rosen NO, Bergeron S, Pukall CF. Recommendations for the study of vulvar pain in women, part 1: Review of Assessment Tools. *J Sex Med* https://doi.org/10.1016/j.jsxm.2019.10.023. E-pub ahead of print.
4. Harlow BL, Kunitz CG, Nguyen RHN, et al. Prevalence of symptoms consistent with a diagnosis of vulvodynia: Population based estimates from 2 geographical regions. **Am J Obstet Gynecol 2014;210:e1-e8.**
5. Bornstein J, Goldstein A, Stockdale CK, et al. 2015 ISSVD, ISSWSH, and IPPS consensus terminology and classification of persistent vulvar pain and vulvodynia. **Obstet Gynecol 2016;127:745-751.**
6. Harlow BL, Vazquez G, Maclehose RF, et al. Self-reported vulvar pain characteristics and their association with clinically confirmed vestibulodynia. **J Womens Health 2009;18:1333-1340.**
7. Corsini-Munt S, Bergeron S, Rosen NO, et al. Feasibility and preliminary effectiveness of a novel cognitive-behavioral couple therapy for provoked vestibulodynia: A pilot study. **J Sex Med 2014;11:2515-2527.**
8. Wesselmann U, Bonham A, Foster D. Vulvodynia: Current state of the biological science. **Pain 2014;155:1696-1701.**

9. Morin M, Carroll MS, Bergeron S. Systematic review of the effectiveness of physical therapy modalities in women with provoked vestibulodynia. **Sex Med Rev 2017;5:295-322.**
10. Bergeron S, Khalifé S, Dupuis MJ, et al. A randomized clinical trial comparing group cognitive-behavioral therapy and a topical steroid for women with dyspareunia. **J Consult Clin Psychol 2016;84:259-268.**
11. Rosen NO, Dawson SJ, Brooks M, et al. Treatment of vulvodynia: Pharmacological and non-pharmacological approaches. **Drugs 2019;79:483-493.**
12. Brotto LA, Bergeron S, Zdaniuk B, et al. A comparison of mindfulness-based cognitive therapy vs cognitive behavioral therapy for the treatment of provoked vestibulodynia in a hospital clinic setting. **J Sex Med 2019;16:909-923.**
13. Corsini-Munt S, Rancourt K, Dubé J, et al. Vulvodynia: A consideration of clinical and methodological research challenges and recommended solutions. **J Pain Res 2017;10:2425-2436.**
14. Reed BD, Haefner HK, Hope K, et al. Reliability and validity of self-reported symptoms for predicting vulvodynia. **Obstet Gynecol 2006;108:906-913.**
15. Bergeron S, Corsini-Munt S, Aerts L, et al. Female sexual pain disorders: A review of the literature on etiology and treatment. **Curr Sex Health Rep 2015;7:159-169.**
16. Pukall CF, Goldstein A, Bergeron S, et al. Vulvodynia: Definition, prevalence, impact, and pathophysiological factors. **J Sex Med 2016;13:291-304.**
17. Masheb RM, Kerns RD, Lozano C, et al. A randomized clinical trial for women with vulvodynia: Cognitive-behavioral therapy vs. supportive therapy. **Pain 2009;141:31-40.**
18. Morin M, Dumoulin C, Bergeron S, et al. Randomized clinical trial of multimodal physiotherapy treatment compared to overnight lidocaine ointment in women with provoked vestibulodynia: Design and methods. **Contemp Clin Trials 2016;46:52-59.**
19. Bois K, Bergeron S, Rosen NO, et al. Intimacy, sexual satisfaction and sexual distress in vulvodynia couples: An observational study. **Health Psychol 2016;35:531-540.**
20. Rosen NO, Bergeron S, Sadikaj G, et al. Impact of partner responses on sexual function in women with vulvodynia and their partners: A dyadic daily experience study. **Health Psychol 2013;33:823-831.**
21. Corsini-Munt S, Bergeron S, Rosen NO, et al. A comparison of cognitive-behavioral couple therapy and lidocaine in the treatment of provoked vesibulodynia: Study protocol for a randomized clinical trial. **Trials 2014;15:506-516.**
22. Rosen NO, Muise A, Impett EA, et al. Sexual cues mediate the daily relations between interpersonal goals, pain, and well-being in couples coping with vulvodynia. **Ann Behav Med 2018;52:216-227.**
23. Ponte M, Klemperer E, Sahay A, et al. Effects of vulvodynia on quality of life. **J Am Acad Dermatol 2009;60:70-76.**
24. Harlow BL, Stewart EG. A population-based assessment of chronic unexplained vulvar pain: Have we underestimated the prevalence of vulvodynia? **J Am Med Womens Assoc 2003;58:82-88.**
25. Nguyen RHN, Reese RL, Harlow BL. Differences in pain subtypes between Hispanic and non-Hispanic white women with chronic vulvar pain. **J Womens Health 2015;24:144-150.**
26. Singhal A, Tien Y-Y, Hsia RY. Racial-ethnic disparities in opiod prescriptions at emergency department visits for conditions commonly associated with prescription drug abuse. **PLoS One 2016;11:e0159224.**
27. Blair KL, Pukall CF, Smith KB, et al. Differential associations of communication and love in heterosexual, lesbian, and bisexual women's perceptions and experiences of chronic vulvar and pelvic pain. **J Sex Marital Ther 2014;41:498-524.**
28. Lick DJ, Durso LE, Johnson KL. Minority stress and physical health among sexual minorities. **Perspect Psychol Sci 2013;8:521-548.**
29. Andersen JP, Zou C. Exclusion of sexual minority couples from research. **Health Sci J 2015;9.**
30. Egleston BL, Dunbrack RL Jr, Hall MJ. Clinical trials that explicitly exclude gay and lesbian patients. **N Engl J Med 2010;362:1054-1055.**
31. Bergeron S, Binik YM, Khalifé S, et al. A randomized comparison of group cognitive-behavioral therapy, surface electromyographic biofeedback, and vestibulectomy in the treatment of dyspareunia resulting from vulvar vestibulitis. **Pain 2001;91:297-306.**
32. Pukall CF, Binik YM, Khalifé S. A new instrument for pain assessment in vulvar vestibulitis syndrome. **J Sex Marital Ther 2004;30:69-78.**
33. Foster DC, Kotok MB, Huang LS, et al. Oral desipramine and topical lidocaine for vulvodynia: A randomized controlled trial. **Obstet Gynecol 2010;116:583-593.**
34. Bergeron S, Rosen NO, Morin M. Genital pain in women: Beyond interference with intercourse. **Pain 2011;152:1223-1225.**
35. Benoît-Piau J, Bergeron S, Brassard A, et al. Fear-avoidance and pelvic floor muscle function are associated with pain intensity in women with vulvodynia. **Clin J Pain 2018;34:804-810.**
36. Munafo MR, Davey Smith G. Robust research needs many lines of evidence. **Nature 2018;553:399-401.**
37. Dewitte M, Schepers J, Melles R. The effects of partner presence and sexual stimulation on the appraisal of vaginal pressure and sexual arousal. **J Sex Med 2018;15:539-549.**
38. Danielsson I, Torstensson T, Brodda-Jansen G, et al. EMG biofeedback versus topical lidocaine gel: A randomized study for the treatment of women with vulvar vestibulitis. **Acta Obstet Gynecol Scand 2006;85:1360-1367.**
39. Bachmann GA, Brown CS, Phillips NA, et al. Effect of gabapentin on sexual function in vulvodynia: A randomized, placebo-controlled trial. **Am J Obstet Gynecol 2019;220:89 e1-e8.**
40. Goldstein A, Pukall CF, Brown C, et al. Vulvodynia: Assessment and treatment. **J Sex Med 2016;13:572-590.**
41. Pukall CF, Bergeron S, Brown C, et al. Recommendations for self-report outcome measures in vulvodynia clinical trials. **Clin J Pain 2017;33:756-765.**
42. Wammen Rathenborg FL, Zdaniuk B, Brotto LA. What do different measures of pain tell us? A comparison in sexually

active women with provoked vestibulodynia. **J Sex Med 2019; 16:278-288.**

43. Aerts L, Bergeron S, Pukall CF, et al. Provoked vestibulodynia: Does pain intensity correlate with sexual dysfunction and dissatisfaction? **J Sex Med 2016;13:955-962.**
44. Brown CS, Bachmann GA, Wan J, et al; Gabapentin Study Group. Gabapentin for the treatment of vulvodynia: A randomized controlled trial. **Obstet Gynecol 2018; 131:1000-1007.**
45. Guillet AD, Cirino NH, Hart KD, et al. Mindfulness-based group cognitive behavior therapy for provoked localized vulvodynia: A randomized controlled trial. **J Low Genit Tract Dis 2019; 23:170-175.**