Published in final edited form as:

Menopause. 2018 September ; 25(9): 965–967. doi:10.1097/GME.0000000000001170.

Multifactorial: Pain in the Menopause Transition

Nini G.L. Callan, ND, MS and

Department of Family and Child Nursing, University of Washington, Seattle, WA

Helfgott Research Institute, National University of Natural Medicine, Portland, OR

Nancy F. Woods, PhD, RN, FAAN

Department of Biobehavioral Nursing and Health Informatics, University of Washington, Seattle, WA

In their report of the relationship between pessimistic beliefs about back pain and the experience of low back pain and disability, Alyousef and colleagues¹ correctly identified the need for alternative effective treatment options for low back pain (LBP) in women, and in attempting to explore a potential route for this to occur, added to the growing body of literature that has found an increase in pain in the post-menopausal (PM) population. There are many factors to consider when designing a study on pain, given its biopsychosocial nature: these factors are considerably amplified when the population being studied is one transitioning through menopause, which is also biopsychosocial in nature. The research by Alyousef *et al* begins to address some of these factors.

LBP is a major health issue. The lifetime prevalence is estimated to be 84%, of which 5–10% will develop into chronic LBP, resulting in increased disability, suffering, and treatment costs.^{2–3} Women experience more severe LBP and chronic LBP than men, and a higher prevalence of both, with a 50% higher development of chronic LBP compared to men.^{4–5} Thus, we can surmise that women are also experiencing a higher exposure to the often ineffective, often harmful treatment options commonly prescribed for LBP—namely, opioids.

Opioids prescribed for LBP constitute 50% of all opioid prescriptions, and despite limited evidence for their efficacy, well-documented adverse health outcomes, and growing abuse, they continue to be used.^{6–11} In addition, they are particularly deleterious for women, leading to greater psychiatric severity, greater functional impairment, a higher likelihood of using opioids to cope with negative affect and pain, and an increased rate of treatment cessation as a result of adverse effects.^{12–13} As a result of this mix of low effectiveness coupled with potentially harmful impact, polypharmacy of analgesic medications among women is not uncommon. There is a clear need for treatment options that are safe and effective. Alyousef *et al* rightly identified this issue and addressed it by exploring a potential alternative route of pain attenuation in a female population: beliefs about back pain and their effect in the development of chronic LBP and disability.

Alyousef *et al* found that while there was a significant association between negative beliefs about LBP and persistent, high levels of low back disability, there was no association with persistent high intensity pain. This suggests that it is a woman's beliefs about pain, and not

the level of her pain intensity, that contributes to the development of disability from low back pain and support the underlying reality that pain is a biopsychosocial condition, not simply a pathophysiological one. They also found that when adjusting for age, PM status was associated with persistent high intensity pain and persistent low back disability, independent of beliefs, with PM women constituting the majority of each group (pain and disability) at 83.8% and 90.9%, respectively. Taken together, these findings suggest that there is something specific to the PM woman that amplifies both the experience of LBP *and* its likelihood of developing into disability, independent of beliefs about back pain.

Alyousef and colleagues' findings echo those found in three large cohort studies—the Melbourne Women's Midlife Health Project (MWMHP), the Seattle Midlife Women's Health Study (SMWHS), and the Study of Women's Health Across the Nation (SWAN), each of which reported an increase in pain associated with PM status.^{14–16} In addition, all three studies found that pain increased throughout *each stage* of the MT and PM. Yet, despite these stage-dependent increases, reproductive hormones, which change dramatically as a woman transitions through menopause, had no effect on back pain.

So, what is occurring in the MT and PM that contributes to increasing back pain and disability, and how can we best support the women experiencing it? We highlight three critical focus areas to encourage the continued exploration of these questions: validated staging criteria, the biopsychosocial experience of the MT and PM, and the classification of LBP phenotypes.

First and foremost, it is imperative that as the body of literature on pain in MT and PM populations grows, we standardize the language used to describe and organize the changes that occur throughout reproductive aging. Without a common and validated vocabulary, menopause research results will continue to be less clear with respect to the influence of the menopausal transition, as will the clinical direction we can glean from it. What one research group calls perimenopause, another calls the climacteric phase, and yet another distinguishes as the early menopausal transition and late menopausal transition stages, each description also accompanied by its own qualifying criteria. This lack of precise terminology makes inter-study comparisons difficult, and perhaps worse, valuable intra-study comparisons may be overlooked due to the lack of specificity that can accompany ill-defined measures. For example, while research has revealed that reproductive hormones do not have an effect on LBP in an MT and PM population, the severity of other MT- and PM-specific symptoms do. These symptoms often increase or decrease according to MT and PM stage. Thus, in order to uncover and better understand potential inroads to better treatment, consistent MT and PM stages must be used. Alyousef *et al* determined whether or not a woman was postmenopausal based on a “hierarchy of information”, yet didn't clearly describe how that hierarchy worked or what qualified a woman as postmenopausal, thus decreasing the applicability of results to the MT and PM population at large. Additionally, reproductive aged women and MT women were grouped together for analysis, thus perhaps masking relationships that might have been apparent with the use of a staging system for the menopausal transition and postmenopause. One such system, the STRAW+10 staging system, differentiates reproductive aging into seven stages: Stage –5, –4, and –3 (early, peak and late reproductive phase, respectively); Stage –2 and –1 (early and late menopausal

transition phase, respectively); and Stage +1 (a–c) and +2 (early and late postmenopause phase, respectively).¹⁷ STRAW+10 provides reliable terminology, qualifying criteria for reproductive aging transition stages, and is widely applicable to women regardless of age, lifestyle, demographic factors, or BMI. Consistent use of the STRAW+10 staging system has the potential to dramatically increase the generalizability and comparability of research results, the cross-pollination of ideas and findings, the amount and specificity of data collected, and the rate of discovery and dissemination of critical findings of reproductive aging research. As pain is already a deep global problem, the quicker we adopt the STRAW+10 staging system, the quicker we may begin to elucidate the answers to some of the questions surrounding pain in the MT and PM.

Secondly, we applaud Alyousef *et al* for their exploration of a potential treatment pathway that takes into consideration the biopsychosocial nature of pain. This is especially important to consider in an MT and PM population, as the menopause transition itself is biopsychosocial in nature, and in turn, has the potential to modify the experience of pain. There is much to learn in this area of research. We know that biopsychosocial effects of the menopause transition—such as stress perceptions, tension, anxiety, depression, and difficulty concentrating—increase throughout the transition, and have been found to be associated with an increase in back pain. It could be the case that the biopsychosocial effects of the MT modulate back pain beliefs, thus increasing the likelihood of developing high intensity LBP and disability. Aspects of women's social context, such as poverty, work demands, and their general health as they age may also modulate their beliefs. Addressing negative beliefs without first addressing the stress, anxiety, or depression that is modifying the negativity may be only a temporary fix. It could also be the case that negative beliefs about back pain increase the likelihood of specific symptoms occurring in the MT and PM, in turn, increasing back pain. At this point, we simply don't know. Gaining a more thorough understanding of this complex issue will help in determining what kind of behavioral interventions can be helpful, and at what point in the menopausal transition administration will be most effective.

Third and finally, it is important that we begin addressing the elephant in the room: there are different classifications of LBP, and each will respond best to different treatments. This seems an obvious point, yet in research, we consistently group patients into one homogeneous group—LBP (or, at best, LBP and chronic LBP)—and explore specific outcomes as if the trends we find will point us towards more effective treatments (and thus, better patient outcomes). Is the LBP from osteoporosis the same as LBP from tissue damage related to a car accident? From endometriosis? From a sports injury? From stress and anxiety? Is LBP from structural pathology any different from LBP due to depression? Are they treated the same? While Alyousef *et al* began exploring the differentiation of LBP over time (no pain, developing pain, resolving pain, and persistent pain)—a productive start—it would be more helpful clinically if researchers also included phenotypes of pain within each temporal classification of pain. Would developing pain result in higher levels of disability in women with LBP *from structural pathology* versus women with LBP *attributable to anxiety*? Such phenotyping would begin to guide more precise interventions. Furthermore, understanding pain histories and the co-occurrence of other types of pain, such as a history of dysmenorrhea, fibromyalgia, or headache, may enhance understanding of both beliefs and

disability, as well as support research about central sensitization to pain.¹⁸ If we continue researching potential treatment options in groups of LBP patients without phenotyping the LBP experienced, the applicability of the treatments that show efficacy may be used as panacea options, when in fact, their effectiveness may extend to only certain classes of LBP, resulting in inconsistent treatment protocols, poor health outcomes for some, increased treatment cost, and patient and practitioner frustration. To enhance the precision of research, and in the service of optimal patient care, we will need to know for which types of back pain specific interventions are best suited. There is no doubt that creating these phenotypes, and the tools that measure them, will be challenging work, but we believe that the current trends in collaboration and interdisciplinary study have the potential to yield fruitful discoveries towards this end.

Acknowledgments

Financial disclosures/ conflicts of interest: Dr. Callan is supported by the National Institutes of Health, National Center for Complementary and Integrative Health, grant #5T90AT008544-03.

References

1. Alyousef B, Cicuttini FM, Davis SR, Bell R, Botlero R, Urquhart DM. Negative beliefs about back pain are associated with persistent, high levels of low back disability in community-based women. *Menopause*. 2018; 25(9):xxx-xxx.
2. Musial F, Spohn D, Rolke R. Naturopathic Reflex Therapies for the Treatment of Chronic Back and Neck Pain – Part 1: Neurobiological Foundations. *Forsch Komplementmed*. 2013; 20:219–224. *Prev of CLBP: Sys Rev* 2015. [PubMed: 23860024]
3. Chou R, Ballantyne JC, Fanciullo GJ, Fine PG, Miasowski C. Research gaps on use of opioids for chronic noncancer pain: findings from a review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline. *J Pain*. 2009; 10:147–159. [PubMed: 19187891]
4. Meucci RD, Fassa AG, Faria NM. Prevalence of chronic low back pain: systematic review. *Rev Saude Publica*. 2015; 49:73. Epub 2015 Oct 20. doi: 10.1590/S0034-8910.2015049005874
5. Hoy D, Bain C, Williams G, et al. A systematic review of the global prevalence of low back pain. *Arthritis Rheum*. 2012; 64(6):2028–2037. [PubMed: 22231424]
6. Deshpande A, Furlan A, Mailis-Gagnon A, Atlas S, Turk D. Opioids for chronic low-back pain. *Cochrane Database Syst Rev*. 2007 CD004959.
7. Kuijpers T, van Middelkoop M, Rubinstein SM, Ostelo R, Verhagen A, Koes BW, van Tulder MW. A systematic review on the effectiveness of pharmacological interventions for chronic non-specific low-back pain. *Eur Spine J*. 2011; 20:40–50. [PubMed: 20680369]
8. Martell BA, O'Connor PG, Kerns RD, Becker WC, Morales KH, Kosten TR, Fiellin DA. Systematic review: opioid treatment for chronic back pain: prevalence, efficacy, and association with addiction. *Ann Intern Med*. 2007; 146:116–127. [PubMed: 17227935]
9. Ashworth J, Green DJ, Dunn KM, Jordan KP. Opioid use among low back pain patients in primary care: Is opioid prescription associated with disability at 6-month follow-up? *Pain*. 2013; 154(7): 1038–1044. [PubMed: 23688575]
10. Deyo RA, Smith DHM, Johnson ES, Donovan M, Tillotson CJ, et al. Opioids for Back Pain Patients: Primary Care Prescribing Patterns and Use of Services. *J Am Board Fam Med*. 2011; 24:717–727. [PubMed: 22086815]
11. VanTulder MW, Koes B, Malmivaara A. Outcome of non-invasive treatment modalities on back pain: an evidence-based review. *Eur Spine J*. 2006; 15:S64–S81. [PubMed: 16320031]
12. McHugh KR, DeVito EE, Dodd D, Carroll KM, Potter JS, et al. Gender Differences in a Clinical Trial for Prescription Opioid Dependence. *J Subst Abuse Treat*. 2013; 45(1):38–43. [PubMed: 23313145]

13. Sagy I, Friger M, Sagy TP, Rudich Z. Gender-based differences in the management of low back pain. *Harefuah*. 2014; 153(7):380–384. 434. [PubMed: 25189025]
14. Dennerstein L, Dudley EC, Hopper JL, Guthrie JR, Burger HG. A prospective population-based study of menopausal symptoms. *Obstet Gynecol*. 2000; 96:351–8. [PubMed: 10960625]
15. Dugan SA, Powell LH, Kravitz HM, Everson-Rose SA, Karavolos K, Luborsky J. Musculoskeletal pain and menopausal status. *Clin J Pain*. 2006; 22:325–31. [PubMed: 16691084]
16. Mitchell ES, Woods NF. Pain symptoms during the menopausal transition and early postmenopause. *Climacteric*. 2010; 13:467–78. [PubMed: 20497030]
17. Harlow SD, Gass M, Hall JE, Lobo R, Maki P, et al. EXECUTIVE SUMMARY of STRAW+10: Addressing the Unfinished Agenda of Staging Reproductive Aging. *Climacteric*. 2012; 15(2):105–14. [PubMed: 22338612]
18. Vincent K, Warnaby C, Stagg CJ, Moore J, Kennedy S, Tracey I. Dysmenorrhoea is associated with central changes in otherwise healthy women. *PAIN*. 2011; 152:1966–1975. [PubMed: 21524851]