A Biopsychosocial Approach to the Clinical Management of Chronic Overlapping Pain Conditions
Notes to Accompany Slides

Slide 1: **Title Slide**

Slide 2: **Faculty**

Slide 3: **Upfront CME Information from Accreditor**

Slide 4: **Learning Objectives**

Slide 5: **Chronic Overlapping Pain Conditions Summary**
Reference [1]

Slide 6: **Terminology Key**

Slide 7: **Section 1: Epidemiology (Transition Slide)**

Slide 8: **Description, Symptom Onset & Gender Disparity (Vulvo, ENDO, IC/PBS, IBS)**
Vulvodynia affects women and girls only. In adult women, vulvodynia symptoms frequently begin between the ages of 18 and 25. [2] Endometriosis affects women and girls only. Sixty percent of women develop symptoms prior to age 20. [3] IC/PBS affects more than twice as many women as men. [4] [5] [6] The average age of symptom onset is 40. [7] Irritable Bowel Syndrome affects twice as many women as men. [8] Adults under the age of 50 are more likely to suffer compared to older adults. [9] (References for diagnostic criteria, including disorder descriptions, can be found on Slides 20-29.)

Slide 9: **Description, Symptom Onset & Gender Disparity (cLBP, FM, ME/CFS)**
Chronic low back pain is 50 percent more common in women, and 3-4 times more likely in people age 50 and older, compared to those between the ages of 18-30. [10] Women are 2-3 times more likely to have fibromyalgia compared to men. [11] [12] FM diagnosis is most likely to occur between ages 20 to 50.[13] ME/CFS affects four times as many women as men. [14] Symptoms begin in two distinct ranges – between the ages of 10-19 and 30-39. [15] (References for diagnostic criteria, including disorder descriptions, can be found on Slides 20-29.)

Slide 10: **Description, Symptom Onset & Gender Disparity (TMD, cMig, cTTH)**
Temporomandibular disorders affect twice as many women as men, and in the most severe cases, at a rate of 9:1. [16] Symptoms typically begin between the ages of 19 and 23. [17] Chronic migraine affects three times as many women as men, and symptoms peak in the 40s. [18] Chronic Tension-Type Headache typically begins in the teenage years, and is 1-2 times more likely to affect women, compared to men. [19] [20] (References for diagnostic criteria, including disorder descriptions, can be found on Slides 20-29.)

Slide 11: **U.S. Prevalence & Total Cost Burden**
Prevalence (listed in order of increasing prevalence):
Chronic Migraine (cMig) affects 1 percent of American adults, equivalent to 2.5 million. [21]
Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) affects between 1-4 million. [22]
Fibromyalgia (FM) occurs in an estimated 2 percent off the general population, equivalent to 4 million. [23] [24]
Chronic Tension-Type Headache (cTTH) affects 2.2 percent of American adults, equivalent to 5.5 million people. [25]
Vulvodynia (Vulv) affects 1 in 4 women over their lifetime [26] and 6 million reproductive-aged women. [27] [28]
Interstitial Cystitis/Painful Bladder Syndrome (IC/PBS) affects between 3-8 million women and 1-4 million men. [29] [30]

The true prevalence of Endometriosis (Endo) is unknown because surgical confirmation is necessary to diagnose the condition; it is estimated that 11 percent of reproductive aged women suffer, equivalent to 11.3 million. [31]
Chronic Low Back Pain (cLBP) affects approximately 10 percent of adults, equivalent to 24 million. [32]
Irritable Bowel Syndrome (IBS) affects 12 percent of the general population, equivalent to 28 million. [33]
Temporomandibular Disorders (TMD) affect approximately 35 million. [34]

Annual U.S. Cost Burden (Direct & Indirect Costs) (listed in order of increasing costs):
Chronic Migraine (cMig) costs $19 billion. [35]
Endometriosis (Endo) costs $22 billion. [36]
Interstitial Cystitis/Painful Bladder Syndrome (IC/PBS) costs $22 billion in direct costs; data on indirect costs is not available. [37]
Temporomandibular Disorders (TMD) cost $32 billion. [38] [39]
Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) cost $37 billion. [40]
Vulvodynia (Vulv) costs range from $31-72 billion, averaging $51 billion. [41]
Fibromyalgia (FM) direct costs are $28 billion and indirect costs $26 billion, totaling $54 billion. [42]
Chronic Low Back Pain (cLBP) costs $100 billion. [43]
Irritable Bowel Syndrome (IBS) direct costs range from $40-182 billion, and indirect costs from $19-187 billion, averaging $213 billion in total costs. [44]
Chronic Tension-Type Headache (cTTH) costs are unknown; one study found that nearly 10,000 lost work days per year were attributed to headache, with 42 percent due to cTTH. [45]

Slide 12: **COPCs Co-Prevalence Rates & Major Findings**

Reported rates of co-occurrence of COPCs vary substantially by study type and design, mainly because most studies are cross-sectional and include patients from specialized tertiary clinics (rather than from the general population). Specialized longitudinal studies, funded by the National Institutes of Health (NIH), are currently underway, which will yield more accurate rates of co-prevalence. As one example, this slide summarizes data from the Multi-Disciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network, which is a NIH-sponsored multi-center study of urological chronic pelvic pain syndrome (e.g., IC/PBS and chronic prostatitis/chronic pelvic pain syndrome). One important aim of this study is to understand comorbidity and how it influences disease trajectory. Of 424 participants, 38 percent were found to have at least one comorbid pain condition, with females suffering at a higher rate (44% vs. 31%). IBS was found to be the most prevalent comorbidity (57%), following by FM (9%) and ME/CFS (8%). Importantly, an additional 25% of bladder pain patients were found to have more than one of these comorbid conditions. Urologic pain patients with comorbidities, compared to those without, were found to: have more severe bladder symptoms; greater pain sensitivity and pain-related interference; increased depression, anxiety and stress; increased disability; and decreased quality of life. [46] Further, MAPP studies have shown that two general constructs are associated with non-urological pain comorbidities – alterations in "Generalized Sensory Sensitivity" and "S.P.A.C.E." (sleep, pain, affect, cognition, energy). [47] [48] These data are consistent with a growing literature base demonstrating the deleterious consequences of suffering from COPCs.

Slide 13: **COPCs Cluster Analysis**

Another large, prospective, multi-site study funded by the NIH on COPCs is the *Orofacial Pain Prospective Evaluation & Risk Assessment (OPPERA) Study,* [49] which identified meaningful patient clusters using a comprehensive array of biopsychosocial measures. Compared with the *Adaptive Cluster*, participants in the *Pain-Sensitive Cluster* showed heightened sensitivity to experimental pain, and participants in the *Global Symptoms Cluster* showed both greater pain sensitivity and psychological distress. Cluster membership was strongly associated with chronic TMD: 91.5% of TMD cases belonged to the *Pain-Sensitive* and *Global Symptoms Clusters*, whereas 41.2% of controls belonged to the *Adaptive Cluster*. TMD cases in the *Pain-Sensitive* and *Global Symptoms Clusters* also showed greater pain intensity, jaw functional limitation, and more comorbid pain conditions. During a median 3-year follow-up period of TMD-free individuals,

participants in the *Global Symptoms Cluster* had greater risk of developing first-onset TMD (hazard ratio = 2.8) compared with participants in the other 2 clusters. [50]

Slide 14: Notable Findings Relative to Comorbidity

Akin to the MAPP & OPPERA Study findings described in the previous slides, a growing body of evidence demonstrates that as the number of pain diagnoses (or body sites of pain) increase, a vicious cycle ensues, which includes: worsening of localized and systemic pain symptoms; decreased treatment effectiveness; reduced health and psychosocial outcomes; increased levels of disability; increased costs (both personal and societal); and markedly diminished quality of life. [51] [52] [53] [54] [55] [56] [57] [58] [59] [60] [61] [62] [63] [64]

Slide 15: Section 2: Pathophysiology (Transition Slide)

Slide 16: Mechanistic Characterization of Pain

Pain mechanisms can be categorized as nociceptive, neuropathic, and centralized. While this classification scheme overly simplifies the vast array of possible mechanisms within each category, it does provide a framework through which clinicians can narrow down treatment options based on each patient's most prevalent signs and symptoms. Although some chronic pain diagnoses are thought to be more centralized (e.g., COPCs) and others more peripheral (e.g., osteoarthritis), the reality is that no chronic pain state falls neatly into a single mechanistic category. [65]

Slide 17: COPCs Pathophysiology

This model depicts likely determinants that contribute to both the risk of developing, as well as the onset and maintenance, of COPCs. [66] Genetic predisposition combined with environmental exposures increases the risk of increased pain amplification and emotional distress, moderated by factors from multiple body systems (neurological, immune, endocrine). Cumulatively, evidence now clearly demonstrates that COPCs are not just an extension of acute pain, but rather, a complex multi-system illness.

For a thorough literature review, please see Veasley C, et al. [67]

Slide 18: Diagnostic Criteria (Transition Slide)

Slide 19: Diagnostic Criteria for Central Sensitization

COPCs have been recognized by the National Institutes of Health as a set of disorders likely to share common underlying mechanisms of disease across the neurologic, endocrine and immunologic systems, resulting in central sensitization (CS). [68] COPCs are often referred to as 'central sensitivity syndromes.' The International Association for the Study of Pain (IASP) defines CS as: "increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input." [69] CS, as defined by IASP and others, has been translated into clinical diagnostic criteria by Nijs, et al., outlined in this slide. [70] The Central Sensitivity Inventory may be a useful tool for identifying the extent to which CS may be contributing to a patient's pain syndrome.

Slides 20-29 provide specific diagnostic criteria for each of the 10 COPCs addressed in this CME. Of importance, elements of this CS classification can be identified throughout.

Slide 20: Diagnostic Criteria: Temporomandibular Disorders

Reference: Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications: Recommendations of the International RDC/TMD Consortium Network and Orofacial Pain Special Interest Group [71]

Slide 21: Diagnostic Criteria: Temporomandibular Disorders (cont.)

Slide 22: Diagnostic Criteria: Chronic Migraine & Chronic Tension-Type Headaches

Chronic Migraine Headache Reference:

2018 International Headache Society (IHS): International Classification of Headache Disorders (ICHD), 3rd Edition [72]

Chronic Tension Type Headache Reference:

2018 International Headache Society (IHS): International Classification of Headache Disorders (ICHD) 3rd Edition [73]

Slide 23: **Diagnostic Criteria: Chronic Low Back Pain**

Reference: American College of Physicians & American Pain Society Low Back Pain Guidelines Panel [74]

Slide 24: **Diagnostic Criteria: Vulvodynia**

Reference: 2015 ISSVD, ISSWSH & IPPS Consensus Terminology and Classification [75]

Slide 25: **Diagnostic Criteria: Myalgic Encephalomyelitis / Chronic Fatigue Syndrome**

Reference: 2015 National Academies of Sciences, Engineering and Medicine Criteria [76]

Slide 26: **Diagnostic Criteria: Fibromyalgia**

Reference: 2016 American College of Rheumatology Diagnostic Criteria [77]

Slide 27: **Diagnostic Criteria: Interstitial Cystitis/Painful Bladder Syndrome**

Reference: American Urological Association (AUA) Definition[78]; RICE Definition[79] [80]

Slide 28: **Diagnostic Criteria: Endometriosis**

Reference: National Institute of Child Health and Human Development [81] [82]
American College of Obstetricians and Gynecologists [83]

Slide 29: **Diagnostic Criteria: Irritable Bowel Syndrome**

Reference: Rome IV Classification [84]

Slide 30: **Differential Diagnoses**

A review of COPCs' differential diagnoses is beyond the scope of this educational program, however, links for additional learning opportunities on this topic are provided.

Slide 31: **Section 4: Biopsychosocial Assessment of COPCs (Transition Slide)**

Slide 32: **Biopsychosocial Model**

This figure summarizes how one's health/illness perception exists at the intersection of one's biological, psychological and sociological makeup. [85] It also helps to explain why patients with similar types of chronic pain experience living with chronic pain and its consequences very differently. In order to effectively treat COPCs, one cannot focus on biological processes only, but rather, needs to take a more broad and comprehensive approach that recognizes processes and factors from all three domains in assessment and clinical management.

Slide 33: **Rationale for Conducting a Comprehensive Pain Assessment – Consequences of Unrelieved Pain**

Reference: [86]

Slide 34: **Rationale for Conducting a Comprehensive Pain Assessment**

Reference: [87]

Slide 35: **Elements of a Comprehensive Pain Assessment**

Reference: [88] [89]

Slide 36: **Heuristic Model of Pain Assessment**

This model depicts the two major goals of pain assessment: 1) assessment of pain burden, and 2) assessment of pain mechanisms. Domains of pain burden that should be assessed are listed on the left. While these measures primarily fulfill the goal of assessing pain burden (as indicated by the solid arrows), some also provide information on pain mechanisms (as indicated by the dashed arrows). Common and emerging methods of assessing pain mechanisms are listed on the right. A review of these measures is beyond the scope of this educational program, but can be reviewed in detail in Fillingim RB, et al. [90]

Slide 37: **Approaches to Assessing Domains of Pain**

This figure summarizes measures available to assess five key pain-related domains: 1) sensory and affective qualities, 2) perceptual qualities, 3) temporal features, 4) bodily locations, and 5) other pain features. [91]

Slide 38: **Non-Pain Comorbidities & Contributing Factors**

A comprehensive pain assessment also includes an evaluation of non-pain disorders and factors that commonly co-exist with COPCs. These include sleep and mood disorders, as well as fatigue, cognitive impairment, physical disability, social dysfunction and sexual dysfunction. All combinations, and in varying severities, are possible and the interplay among these comorbidities is complex. Effective treatment for COPCs will only result from identification, assessment and management of both pain conditions/symptoms as well as these non-pain comorbidities.

Slide 39: **Vicious Cycle**

If non-pain comorbidities are not evaluated and addressed (in addition to pain) in COPCs patients, a vicious cycle can ensue, leading to sleep disturbance, mood disorders and maladaptive thinking, decreased energy levels and reduced activity, all of which contribute to worsening pain.

Slide 40: **Pain & Sleep: Major Findings**

Evidence demonstrates these major findings about the bidirectional relationship between chronic pain and sleep. [92]

Slide 41: **DSM-V Recognized Sleep-Wake Disorders**

The Diagnostic and Statistical Manual of Mental Disorders (DSM), 5th Edition, recognizes 10 sleep-wake disorders. [93] The prevalence of sleep disorders vary by pain condition and data are irregular. Insomnia, hypersomnia, sleep apneas and restless legs syndrome may be the most common disorders associated with chronic pain.

Slide 42: **Assessment of Sleep Quality**

Differential diagnosis/assessment of sleep disorders is beyond the scope of this educational program. References are provided for further learning opportunities, along with a questionnaire that can be used to screen for the presence of sleep disorders in patients.

Slide 43: **Pain & Mood: Major Findings**

Evidence demonstrates these major findings on the relationship between chronic pain and mood disorders and maladaptive thinking. [94] [95]

Slide 44: **Assessment of Mood & Maladaptive Thinking**

Differential diagnosis and assessment of mood disorders and maladaptive thinking are beyond the scope of this educational program. References are provided for further learning opportunities, as well as screening questionnaires.

Slide 45: **Other Non-Pain Domains Important to Assess**

Also important to evaluate are: physical function and disability, sexual function, fatigue, cognitive impairment and social support. References for learning opportunities on assessment, along with screening questionnaires, are provided.

Slide 46: **Biopsychosocial Treatment of COPCs (Transition Slide)**

Slide 47: **Management & Referral Pathway**

This management and referral pathway begins once known causes for pain resulting from COPCs are ruled out, possibly through referral to other medical specialties (e.g., gastroenterology for IBS, urology for IC/PBS). The differential diagnosis each COPC is beyond the scope of this educational program, however, Slide 30 provides references for further learning opportunities on this topic.

All patients should receive pain education on self-management. Making patients aware of tools that can assist them in the self-management of their pain condition is important for improving quality of life, decreasing reliance on medical care, and empowering them. Patient and family education, instruction in disease self-management, lifestyle modification, and emotional and social support have become increasingly important elements of chronic disease management. [96] An excellent resource from the Integrative Medicine Program at the University of Wisconsin can be found online: http://projects.hsl.wisc.edu/SERVICE/modules/30/M30_EO_Self_Management_of_Chronic_Pain.pdf.

Development of functional goals is addressed on Slide 54.

Following pain education and development of functional goals, pharmacologic, psychological and physical interventions can be individualized based on the findings of the biopsychosocial pain assessment (see Slides 49-53). Progress and review of functional goals should be conducted in 4-8 weeks. If improvement is satisfactory, the patient can be reassessed every 6-12 months for 1-2 years.

Slide 48: **Management & Referral Pathway (cont.)**

If improvement is unsatisfactory and the patient is not making progress towards his/her functional goals, the patient and treatment plan should be reassessed. Options for next steps include: continuing with the current treatment plan (if additional time may provide for improvement, for example, if a patient has not yet reached the recommended dose of a particular medication); seeking advice from a pain specialist; or referring the patient to a pain specialist. The patient should be reassessed in 4-8 weeks, and if progress is satisfactory, can be reassessed annually as needed. If improvement in symptoms/goals is not satisfactory, a referral to a pain specialist may be helpful.

Slide 49: **COPCs Treatment Paradigm**

Developing an individualized treatment plan for COPCs patients begins with considering the FDA-approved treatment options available for specific conditions that each patient has. (Six of the 10 COPCs discussed in this educational program have FDA-approved treatments options; please see Slides 50-52.) Next, one can incorporate other disorder-specific treatments approaches. (References on off-label and other treatment approaches for each of the 10 COPCs are provided for review.) Following, universal chronic pain treatment approaches can be utilized, summarized on Slide 53. Finally, treatment of non-pain comorbidities should also be included as part of a comprehensive regimen, which may require referral to other medical professionals.

Slide 50: **FDA-Approved Treatments for COPCs**

There are no FDA-approved treatments for Vulvodynia, TMD, Chronic Tension-Type Headache and ME/CFS. A summary of FDA-approved treatments for Chronic Low Back Pain, Chronic Migraine Headache and IC/PBS is provided.

Slide 51: **FDA Approved Treatments for COPCs (cont.)**

A summary of FDA-approved treatments for IBS-D, IBS-C and Fibromyalgia is provided.

Slide 52: **FDA-Approved Treatments for COPCs (cont.)**

A summary of FDA-approved treatments for endometriosis is provided.

Slide 53: **Treatment Approaches for Chronic Pain**

This figure summarizes the various treatment approaches for chronic pain. It is by no means an exhaustive list. Rigorous data are lacking for most chronic pain treatments, and the best approaches for each individual are typically identified through a trial-and-error process. The most common approaches for the treatment of COPCs include those that target the central nervous system, and include adjuvant medications, such as tricyclic antidepressants, selective serotonin-norepinephrine reuptake inhibitors (SNRIs), anticonvulsants, and muscle relaxants, specifically antispasmodics. Physical and occupational therapy is often utilized to maximize and maintain one's functional ability, without increasing pain severity, and to help patients perform activities of daily living. Psychiatric/psychological counseling can be helpful, particularly for those with comorbid mood disorders and/or maladaptive thinking. Interventional pain management approaches, such as peripheral and spinal cord neurostimulation can be helpful for some patients, but invasive approaches are typically reserved for after more conservative treatments are tried. Some find various complementary health approaches, such as chiropractic care, massage, yoga and acupuncture, to be helpful in managing symptoms.

Slide 54: **Functional Goal-Setting**

Setting small attainable goals that patients can work towards accomplishing in between visits helps to keep them focused on moving forward with their lives, rather than focusing on how bad they feel each day. Major research findings related to goal setting approaches are summarized. [97]

There are several steps involved in working with patients to set functional goals. First, addressing faulty beliefs that may hinder patients from setting effective goals is essential. Helping patients to understand that their pain does not need to be ameliorated before goals can be set or they can become more active is important, as well as educating them on the difference between what "hurts" versus what "harms" their bodies. Next, a Focus Area that patients feel they can change is selected; common areas include: 1) exercise; 2) relaxation; 3) social support/activity; 4) meaningful life activities; 5) pleasurable activities; and/or 6) attitude. Next, the SMART goal setting system is used to narrow down focus and set specific goals. ("SMART" stands for: Specific, Measurable, Action-Oriented, Realistic, and Timed.) A well-developed goal allows one to track progress and answer the question, "Did I achieve this goal?" with a clear "yes" or "no" answer. By successfully achieving smaller goals, over time, patients gain the confidence to tackle larger goals in the future. Next, patients write down their personal SMART goal, and break it down into three small achievable steps, using the 90% rule to assess whether the goal is realistic and achievable (i.e., if a patient is not 90% sure that s/he can reach the smaller goal within two weeks, then the goal is set too high and needs to be scaled back.) Even with the best of intentions, the very unpredictable nature of chronic pain can create obstacles. As such, the final step is for patients to write down potential obstacles and specific steps they'll take to deal with those obstacles to stay on track.

For additional information on this tool, along with a downloadable patient worksheet, visit: http://projects.hsl.wisc.edu/SERVICE/modules/30/M30_CT_Goal_Setting_for_Pain_Rehabilitation.pdf.

Slide 55: **Shared Decision-Making & Tracking Progress (Transition Slide)**

Slide 56: **Shared Decision-Making**

The figure outlines the patient-centered shared decision-making approach (SHARE) from the Agency for Healthcare Research and Quality. This excellent curriculum, along with resources and handouts, is available here: https://www.ahrq.gov/professionals/education/curriculum-tools/shareddecisionmaking/index.html.

Slide 57: **Summary (Transition Slide)**

Slide 58: **Key Summary Points**

Slide 59: **Key Summary Points (cont.)**

Slide 60: **Resources (Transition Slide)**

Slide 61: **Resources**

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