

THE ARIZONA PAIN AND ADDICTION CURRICULUM FACULTY GUIDE

UNDERGRADUATE HEALTH PROFESSIONAL EDITION September 1, 2018

Dear Teaching Faculty:

It is our pleasure to offer this Faculty Guide as a supplement to The Arizona Pain and Addiction Curriculum.

Whether your program is educating future physicians, nurses, physician-assistants, dentists, naturopathic doctors or podiatrists – this *Faculty Guide* can be used to enhance the statewide vision of redefining pain and addiction. The essence of the curriculum rests with its ten Core Components – this *Faculty Guide* provides a further level of detail under each Component and Objective.

As colleagues in health care, we understand that this material represents a significant change from the way we were taught about pain and addiction – or the way we were taught about medicine at all. This curriculum moves from a micro- to a macro- perspective, stressing whole-person care and the societal impact of pain and addiction. It reflects the interrelated nature of pain and addiction – two areas that have been traditionally siloed. It specifically calls for clinicians to be able to critically analyze material, their own practices, and their own biases.

The approach to pain and addiction is advancing rapidly. The material in this *Faculty Guide* is aggressively up-to-date and evidence-based, yet remains in line with the National Pain Strategy, the Institute of Medicine and modern educational theories. As our understanding of pain and addiction changes, so too will this document.

We are proud to have worked with programs' leadership to develop this curriculum and are now excited to work with you to bring it to Arizona learners.

Sincerely,

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INTRODUCTION

PURPOSE

The Arizona Curriculum on Pain and Addiction represents a large-scale culture shift in the education of the next generation of clinicians. While the curriculum aims to bring about focused results such as a reduction in the number of opioid-related overdoses, a reduction in opioids unnecessarily prescribed, and an increase in the number of providers able to treat opioid use disorder – this curriculum moves beyond these discrete goals to redefine pain and addiction as interlinked, complex, public health processes, requiring interprofessional care and involvement of the community and health-based systems.

BACKGROUND

On June 5, 2017, Governor Doug Ducey declared a Statewide Public Health Emergency in Arizona due to the Opioid Epidemic. One of the recommendations from the Arizona Department of Health Services was to create a statewide curriculum on pain and addiction for all clinicians who prescribe opioids.

Beginning in January of 2018, four meetings were held with Deans and Curriculum Representatives from all eighteen MD, DO, PA, NP, DPM, and ND programs in Arizona. A final, modern curriculum was completed in June of 2018, and was based upon the following concepts:

- · The link between pain and addiction
- The use of a macro- to micro- perspective to pain and addiction (the socio-psycho-biological approach)
- The destigmatization of pain and addiction
- · The evidence base of pain and addiction care
- · The influence of the pharmaceutical industry on clinicians
- · The need for clinician and system introspection, both in personal biases and excellence of care

Since its publication, the curriculum has garnered national attention and has been requested by a number of states and program types.

FACULTY DEVELOPMENT

In response to increasing local and national requests for faculty development in regards to pain and addiction, this *Faculty Guide* provides further levels of detail into each Component and Objective.

A Curriculum Summit was held in November of 2018 for all Arizona teaching faculty to introduce methods of conveying this material, including interactive sessions and exploration of the newer concepts presented in the curriculum. Details of this summit are available at www.azhealth.gov/curriculum.

Each summer of 2019, 2020, and 2021, leadership from the Arizona programs will be gathering at the Arizona Department of Health Services to discuss implementation of the curriculum and challenges faced. Specific guidance, concerns or requested adjustments for further faculty support or curricular adjustment can be made at that time.

INTRODUCTION

STRUCTURE AND INTENDED USE

The structure of the original *Arizona Pain and Addiction Curriculum* and this companion *Faculty Guide* are organized by a set of ten *Core Components,* each of which is expanded and detailed into specific *Objectives* and Key Readings. There are a set of Appendices included at the back of this *Faculty Guide,* which include tools and resources, and also a detailed guide to the use of buprenorphine for opioid use disorder. The letter included specifically for medical schools and other health professional schools who intend to include this content in their standard curriculum.

The Arizona Pain and Addiction Curriculum is pertinent to all program types, and the Core Components are able to be expanded and contracted in detail, accordion-style, as pertinent. This Faculty Guide provides a greater level of detail, but it is not exhaustive and certain programs may elect to surpass what is covered. While the Curriculum addresses different types of pain and addiction, there is a primary focus on non-cancer, non-terminal pain and opioid use disorder.

Of note, this *Faculty Guide*, along with the original *Arizona Pain and Addiction Curriculum*, are public materials. They are nonproprietary and can be used outside of the state in any health educational program. Although permission is not required, email notification of programs' use of the materials is appreciated (email: azopioid@azdhs.gov).

DISCLOSURES

All contributors to this Faculty Guide have submitted and declared No Financial Relationships to Disclose.

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VISION + CORE COMPONENTS

CURRICULUM VISION -

To redefine pain and addiction as multidimensional, interrelated public health issues that require the transformation of care toward a whole-person, interprofessional approach with community and systems perspectives.

CORE COMPONENTS

Upon graduation from a health professional education program in Arizona, a student should demonstrate the independent ability to:

REDEFINE PAIN + ADDICTION

1		Define pain and addiction as multidimensional, public health problems.	
	2	Describe the environmental, healthcare systems and care model factors that have shaped the current opioid epidemic and approach to pain care.	
	3	Describe the interrelated nature of pain and opioid use disorder, including their neurobiology and the need for coordinated management.	

APPLY AN EVIDENCE-BASED, WHOLE-PERSON APPROACH TO PAIN + ADDICTION

4	Use a socio-psycho-biological model to evaluate persons with pain and opioid use disorder.	
5	Use a socio-psycho-biological model to develop a whole-person care plan and prevention strategies for persons with pain and/or opioid use disorder.	
6	Reverse the unintended consequences created by the medicalization of chronic pain by empowering persons with self-management strategies, and include an awareness of chemical coping.	
7	Use and model language that destigmatizes, reflects a whole-person perspective, builds a therapeutic alliance and promotes behavior change.	

INTEGRATE CARE WITH A SYSTEMS PERSPECTIVE

8	Employ an integrated, team-based approach to pain and/or addiction care.	
9	Engage family and social support in the care of pain and/or addiction.	
10	Critically evaluate systems and seek evidence-based solutions that deliver quality care and reduce industry influence in the treatment of pain and opioid use disorder.	

COMPONENT 1

1

Define pain and addiction as multidimensional, public health problems.

RATIONALE

This core component sets the tone for the rest of the curriculum by redefining pain and addiction as multidimensional, integrated, population-health based problems. This definition aims to transform education away from the traditionally siloed and reductionist approach to pain and addiction.

OBJECTIVES

A. MESSAGE: Pain and addiction are multidimensional issues.

- A1 Define pain and addiction.
- A2 Describe the established and evolving neurobiological, clinical, psychological, and cultural basis of pain and addiction.
- A3 Describe the social determinants of health and host factors that affect the development of opioid use disorder.
- A4 Describe the social determinants of health and host factors that affect progression from acute pain to chronic pain and disability.
- **B.** MESSAGE: Pain and addiction are public health problems.
 - B1 Describe the impact of chronic pain and opioid use disorder on population morbidity and mortality.
 - B2 Describe the legal landscape in the state and nation for managing pain and opioid use disorder.

KEY READING

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A. MESSAGE: Pain and addiction are multidimensional issues.

A1. Define Pain and Addiction.

Definitions of pain and addiction seek to reflect the modern understanding of these complex conditions, to guide clinical care, research, and education, and to dispel common misconceptions based on outdated models. These definitions have morphed from traditional biomedical characterizations to ones that are multidimensional, and they will continue to evolve with time and discovery.

- The International Association for the Study of Pain defined pain in 1979 as "an unpleasant sensory and emotional experience associated with actual or potential tissue damaged or described in terms of such damage."¹
 - This definition expanded the understanding of pain to include emotion as an essential element, and it recognized that tissue damage was not required.
 - This approach distinguished pain (a perception created by the brain by synthesizing sensory, emotional, and cognitive information) from nociception (nerve activity that results from detection of a stimulus capable of causing tissue damage). Unfortunately, forty years later, pain and nociception continue to be erroneously conflated.
 - This definition is no longer considered complete, as it fails to include the social and cognitive elements of pain and does not acknowledge the protective function of pain.
 - A reconsidered definition of pain has been proposed in 2018: "Pain is a mutually recognizable somatic experience that reflects a person's apprehension of threat to their bodily or existential integrity."²
- The American Society of Addiction Medicine defines addiction as a "primary, chronic disease of brain reward, motivation, memory and related circuits" with socio-psycho-biological components and manifestations. It is "characterized by inability to consistently abstain, impairment in behavior control, cravings, diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response."³
 - This definition seeks to replace prior views of addiction that were rooted in concepts of inherent moral failing and inferiority.
 - Critics of the medical model argue that it removes the responsibility of behavior from the person with addiction and focuses on medication as the only solution.⁴⁵⁶
 - Brain changes are probably less deterministic of behavior than probabilistic (combining with mental activity and environmental factors to influence behavior). For example, an individual with a heroin use disorder who is prepared to inject heroin has an extremely high probability of injecting. However, an individual with a heroin use disorder also has many opportunities to choose to pursue treatment.⁷
 - It is said in the addiction field that, "You are not responsible for your disease, but you are responsible for your recovery."⁸
 - Addiction can be thought of as a more severe manifestation of a substance use disorder. Opioid use disorder is a type of substance use disorder, and is defined as the problematic pattern of opioid use leading to clinically significant impairment of distress as manifested by at least two of the symptoms listed in the DSM-5 (typically remembered by the 3Cs: Loss of Control, Craving, and Use despite negative Consequences.)

A2. Describe the established and evolving neurobiological, clinical, psychological, and cultural basis of pain and addiction.

- · Pain and addiction appear to have some common neurobiological elements.
 - There is an altered reward and anti-reward system in pain and addiction. For an individual in pain, pain relief is experienced as rewarding. For an individual with addiction, the substance is rewarding. In both conditions, there is a deficiency in the reward system and a blunted capacity to experience pleasure from natural rewards. The anti-reward brain system becomes more active, predisposing an individual to aversive states and a heightened sensitivity to stress.
 - Brain changes that involve the same types of molecular processes that underlie learning and memory occur in both pain and addiction. These mechanisms (e.g. long-term potentiation and long-term depression) drive the process of central sensitization in many chronic pain conditions, resulting in smaller peripheral stimuli producing larger amounts of pain.
 [See Component #4 for an explanation of central sensitization.] In addiction, these same mechanisms underlie the process of shifting dopamine activity from the drug itself to drug-related cues.

COMPONENT 1: DEFINITIONS OF PAIN AND ADDICTION

- Executive functioning is impaired in both chronic pain and addiction. In chronic pain, goal-directed behaviors are overtaken by pain-avoidant behaviors. In addiction, impaired inhibitory control contributes to ongoing substance use despite negative consequences.
- [See Component #3 the common neurobiological roots of pain and addiction.]
- The central and interactive roles of psychological states in pain and addiction are supported by an overwhelming amount of evidence. They can no longer be assigned secondary status or viewed as merely reactions to pain or addiction.
 - Emotional distress may predispose people to experience pain and/or addiction, and may be a consequence as well as a precipitating, modulating or perpetuating factor.
 - Strong links have been observed between early traumatic experiences and development of chronic pain and opioid use disorder.
 - [See Component #4 and #5 for the psychological bases and treatment for pain and addiction.]
- Cultural and social factors are key components of pain and addiction.
 - Environmental factors such as the availability of drugs, family and peer dynamics, financial resources, cultural norms, exposure to stress, and access to social support can drive the emergence and progression to chronic pain or addiction.
 - Interpersonal settings (with peers, family, spouse) are perhaps the most potent reinforcers of pain and addiction behaviors.
 - [See Component #9 for the impact of social and cultural factors on pain and addiction development and recovery.]
- A reductionist, biomedical understanding of pain and addiction is insufficient and short-sighted. A whole-person, integrated approach is evidence-based and crucial in successful prevention and recovery.

A3. Describe the social determinants of health and host factors that affect the development of opioid use disorder.

- The World Health Organization has described the social determinants of health as "the conditions in which people are born, grow, work, live and age, and the wider set of forces and systems shaping the condition of daily life."9
- The factors that affect the development of opioid use disorder are being increasingly uncovered.
 - No single determinant predicts problematic drug use. It is more the balance of the number of negative risk factors relative to the number of protective factors that predicts progression to problematic use.
 - Risk factors are characteristics at the biological, psychological, family, community, or cultural level that are associated with a higher likelihood of negative outcomes.¹⁰ They are cumulative across the life course.
 - For drug use, risk factors include genetic disposition, being a victim of child abuse,
 - depression, and suicidal behavior, drug availability, poverty, cultural norms, and others.
 - Protective factors are characteristics that are associated with a lower likelihood of negative outcomes or that reduce a risk factor's impact. Protective factors may be seen as positive countering conditions or events.¹⁰
 - For drug use, protective factors include good coping skills, optimism, ability to resist peer pressure, social support, social integration, and others.
 - The World Health Organization (2004) and the Surgeon General's Report (2016) summarized the risk and protective factors for drug use at the individual and environmental levels.^{11 12} [See TABLE 1 for a summary of the risk factors; see *Appendix C* for an overview of the factors for adolescent and young adult drug use.]

TABLE 1: Risk and protective factors for drug use (Adapted from the World Health Organization)¹¹

DOMAIN	RISK FACTORS	PROTECTIVE FACTORS
INDIVIDUAL	Genetic disposition	Good coping skills
	Victim of child abuse	Self-efficacy
	Personality disorder	Risk perception
	Family disruption and dependence problems	Optimism
	Poor performance at school	Health-related behavior
	Social deprivation	Ability to resist peer pressure
	Depression and suicidal behavior	General health behavior
	Drug availability	Economic situation
	Poverty	Situational control
	Social change	Social support
ENVIRONMENTAL	Peer culture	Social integration
	Occupation	Positive life events
	Drug policies	

- The identification of social determinants underscores the importance of interventions that target multiple factors and populations rather than single factors and single individuals.
 - Research into resilience factors that protect individuals from the development of chronic pain and addiction and subsequent progression to negative outcomes is ongoing. Resilience is the successful adaptation to adverse experiences and may turn out to be one of the more important factors in treatment and prevention of chronic pain and addiction.
 - Areas of investigation include positive attachment styles and development of goal-directed behaviors in the face of challenges.¹³
 - It is particularly important to study these determinants and successful interventions for children.
 - Intervening early in childhood can alter the life course trajectory in a positive direction.^{14 15} Early interventions can increase protective factors and reduce risk factors.¹⁶ Prevention can have particularly strong effects when applied early and at multiple time points in a child's life. This can be seen in the cumulative building of resilience that will have a protective effect later in an individual's life.
 - Prevention is cost-effective: benefit-per-dollar cost ratios for evidence-based interventions range up to \$64 for every dollar invested.¹²

A4. Describe the social determinants of health and host factors that affect the progression from acute pain to chronic pain and disability.

- Acute pain, caused by surgery or an injury, can lead to changes in pain processing that develop into persistent (or chronic) pain.
 - The ability to detect painful or noxious stimuli is a protective mechanism and is essential for survival. Most acute injuries heal with time and treatment, and the pain resolves.
 - But sometimes instead of pain resolution, maladaptive neuroplastic changes occur in the peripheral and central nervous system that can lead to the development of chronic pain. [See *Component #4* for a description of Central Sensitization.]
 - These maladaptive processes are characterized by hyperexcitability and an increased sensitivity and responsiveness to chemical, thermal and mechanical stimuli. This sensitization of the central nervous system can lead to chronic pain being maintained by central processes in the absence of or with minimal peripheral nociceptive input.
 - This means that in the development of chronic pain, the threshold for generating pain decreases and the duration, amplitude and spatial distribution of pain increases.
 - There are several factors that impact whether acute pain progresses to prolonged or chronic pain.
 - Negative social determinants influencing pain chronification include demographics such as level of education, unemployment, and poor job satisfaction.¹⁷
 - Negative host factors include type and severity of pain (e.g. nerve damage), female gender and older age, and psychological factors such as a high baseline fear, anxiety, depression, stress, litigation, fear avoidance, negative beliefs of chronic pain, perceived injustice and catastrophizing.¹⁸
 - There are factors that protect patients against the development of chronic pain. These include social support (e.g. marriage, family), high level of education, coping strategies, work satisfaction, appropriate communication with healthcare providers, high degree of self-efficacy and optimism and adequate self-recognition.
 - When pain progresses from an acute to a chronic condition, it loses its usefulness as an indicator of threat and instead becomes a self-perpetuating toxic influence unto itself.
 - Risk factors influencing the development of pain-related disability include genetics, history of psychological trauma, poor health status, type and severity of pain, number of pain locations, depression, stress, litigation, fear avoidance, perceived injustice, catastrophizing, low self-efficacy, and passive coping strategies.^{18 19 20}
 - These host and environmental factors have been further elucidated in the perioperative period. Chronic post-surgical pain is more likely to develop with the following situations: pain in the pre-operative field, pre-operative pain at a different location, pre-operative stress, depression, anxiety and catastrophizing.^{21,22}
- More research is needed to identify the factors that lead to a favorable adaptation to chronic pain (meaning good functioning and less disability).²³
 - It appears that the mere absence of risk factors does not predict successful adaptation to chronic pain. A recent review indicates that interventions targeted towards specific risk factors are only rarely better than usual care.²³
 - Two primary contributors to better pain adaptation appear to be positive emotional states and meaningful social ties, which may predict lower levels of pain intensity and bolster more effective psychological responses under painful conditions.²⁴
 - Resilience training that focuses on enhancing emotional, cognitive/mental, physical and spiritual adaptability may be a proactive way to protect people from developing worse outcomes from their pain.

B. MESSAGE: Pain and addiction are public health problems.

Public health issues typically affect large numbers of people, exact a substantial societal burden, are amenable to prevention, and have a dimension of social justice such as originating in resource inequities, low socioeconomic status, or social exclusion.²⁵

- Pain and addiction affect millions of Americans and contribute substantially to the morbidity, mortality and disability of the country.
- There are substantial disparities in pain and addiction prevalence, severity, and availability of evidence based treatment across population groups.
- Pain and addiction are costly to the nation, not just in terms of health care expenditures and disability compensation but in terms of lost school and work days, lost productivity and employment, reduced incomes and most importantly – the lost potential and reduced quality of life.
- Pain and addiction raise issues that extend beyond individuals and case-by-case management. Ensuring that opioid medications are available for those than need them (e.g. acute, post-operative, cancer-related and end-of-life pain) while protecting against inappropriate exposure and development of problematic use necessitates cross-governmental efforts at all levels.
- The nation's health is greatly influenced by the graduates of health professions training programs, many of which are publicly funded.
- The ability to reduce pain and addiction's impact on the public's health can be strengthened by new knowledge generated by basic, clinical and translational research, epidemiologic studies, and analysis of care patterns and costs.
- Public health offers an infrastructure for developing strategies for preventing and addressing illness and disease on a population level.

B1. Describe the impact of chronic pain and opioid use disorder on population morbidity and mortality.

- Chronic pain significantly affects the morbidity and mortality of a population.
 - Pain affects the lives of more than 100 million Americans, making its prevention and treatment of enormous value to individuals and society.²⁵
 - For most patients, chronic pain negatively affects overall perceptions of health, interferes with everyday activities, is associated with depressive symptoms, and dramatically and negatively affects relationships and interactions with others.²⁶
 - Chronic pain conditions are the first, third, and fourth top conditions contributing to years lived with disability in the United States.²⁷
 - There are financial consequences to chronic pain, both individually and population-wide.
 - Individuals with moderate to severe chronic pain lose an average of eight days of work every six months.²⁸
 In 2008, more than 100 million adults were affected by chronic pain in the United States, and total costs due to medical care and lost productivity ranged from \$560 billion to \$635 billion in 2010. The annual cost of pain is greater than the combined annual costs of heart disease (\$309 billion), cancer (\$243 billion), and diabetes (\$188 billion).²⁶
 - Substantial disparities exist in the prevalence, seriousness, and adequate treatment of pain.
 - Lack of access to evidence-based pain treatments is more common in vulnerable populations including the elderly, children, racial and ethnic minorities, and others that are a traditional concern of public health agencies and programs.
 - The U.S. veteran population has multiple vulnerabilities to development of chronic pain and represents one notable exception to health care disparities. Interdisciplinary Pain Rehabilitation Programs are the most effective treatment options for people with high-impact chronic pain and while these programs have been steadily declining in the U.S. private sector, they have been steadily increasing within the Veterans Health Administration over the past decade.

COMPONENT 1: DEFINITIONS OF PAIN AND ADDICTION

- Studies have linked chronic pain with a higher risk for fatal and nonfatal suicide attempts.
 - From states participating in the National Violent Death Department System, the overall prevalence of chronic pain in persons who die by suicide has increased over time, with more than 10% categorized as having pain in 2014, the most recent year analyzed.)²⁹
 - This is probably an underestimate of the true prevalence of pain in those who die by suicide.³⁰
 - Convergence of the physical, emotional, and social pain systems may contribute to this increased risk.³¹
- The Centers for Disease Control and Prevention have labeled the opioid overdose deaths as an epidemic.
 - The number of people dying from opioid overdoses increased nearly four-fold between 1999 and 2014.
 - Within the state, more than two Arizonans die every day from an opioid overdose.³² Within the country, more than 115 U.S. residents die per day from an opioid overdose.³³
 - ▶ In 2015, more than 33,000 Americans died from an opioid overdose, including from prescription opioids, heroin, and illicitly manufactured fentanyl.³³
 - In 2015, an estimated 2 million people in the United States suffered from substance use disorders related to prescription opioid pain relievers, and 591,000 suffered from a heroin use disorder (not mutually exclusive).³³
 - It is estimated that 21-29% of patients prescribed opioids for chronic pain misuse them.
 - Between 8-12% develop an opioid use disorder, and an estimated 4-6% of patients who misuse prescription opioids transition to heroin.³³
 - The clinical impact of opioid use disorder goes beyond the single individual.
 - ▶ There is a rising incidence of neonatal abstinence syndrome due to opioid use and misuse during pregnancy.³³
 - Nationally, the percentage of Medicaid-enrolled women who filled at least one opioid prescription during pregnancy increased 23% from 2000-2007, from 18.5% to 22.8%.³⁴
 - The incidence of neonatal abstinence syndrome has increased approximately 400%
 - nationally, from 1.2 per 1000 hospital births in 2000 to 5.8 in 2012. On average, that comes
 - to one infant with neonatal abstinence syndrome born every 25 minutes in the United States.³⁵
 - Arizona has over 60 reports of neonatal abstinence syndrome reported to the Department of Health Services each month.³²
 - The increase in injection drug use has also contributed of the spread of infectious diseases, including HIV and Hepatitis C.³³
 - Like for chronic pain, the financial impact of problematic opioid use to society is significant.
 - The estimated cost of the opioid epidemic was \$504 billion in 2015.³⁶
 - Studies have found that persons with problematic opioid use are generally more likely to utilize medical services, such as the emergency department, outpatient visits and inpatient stays.^{37 38}

B2. Describe the legal landscape in the state and nation for managing pain and opioid use disorder.

- In Arizona, there are statutes and rules that affect the treatment of pain and opioid use disorder. The following are summaries, and do not represent a legal interpretation or analysis. [See *Component #5* for further details of impact on clinical practice.]
 - [Arizona Revised Statutes § 36-2606]²²³ Practitioners must check the prescription drug monitoring database when prescribing controlled substances, including opioids.
 - [Arizona Epidemic Act/ Senate Bill 1001]²²⁴ There are new limits to 90 MME/day prescriptions for opioid-naïve patients, 5-day limit for opioid-naïve patients, requirements for e-prescribing, and requirements for continuing medical education.
 - [A.A.C. R9-10-120]³⁹ Healthcare facilities must adhere to licensing rules on opioid prescribing and treatment, which now include informed consent, discussing alternatives to opioids and performing physical exams.
 - [Arizona Epidemic Act/ Senate Bill 1001 + 9 A.A.C. 10, Article 20]^{39 224} Pain-management clinics are licensed healthcare facilities as of January 1, 2019.
 - [Arizona Medical Marijuana Act]²²⁷ As a result of a voter initiative, chronic pain is a qualifying debilitating condition that qualifies for medical marijuana in Arizona.
 - The Arizona Licensing Boards regulates the practice of medicine (individual practitioners). The Arizona Department of Health Services maintains regulatory authority over licensed-facilities (which include pain-management clinics).

- · Arizona legislation impacts opioid use disorder management in licensed healthcare systems and sober living homes.
 - [Arizona Opioid Epidemic Act / Senate Bill 1001]²²⁴ Sober living homes are required to develop policies and procedures to allow individuals on medication-assisted treatment to continue receiving treatment, health plans must allow at least one medication-assisted treatment without prior authorization, healthcare institutions must refer a patient at discharge after receiving emergency services for a drug-related overdose to a behavioral health services provider and naloxone or other opioid antagonists must be prescribed if a patient is issued a new or continuing prescription above 90 MME/day.
- In the United States, the federal government holds broad powers over the health care industries, mostly exercised through regulatory agencies that interpret and implement laws passed by Congress.
 - Enforcement agencies within the Department of Justice include the Drug Enforcement Administration (DEA), the Federal Bureau of Investigation (FBI) and the Offices of the United States Attorneys.⁴⁰
 - The DEA has the farthest reach and enforcement power of any federal agency when it comes to U.S. drug laws. It works to reduce supply of illicit drugs, whether at the source of illegal "pill mills" or in foreign countries producing and manufacturing drugs like cocaine, heroin, and fentanyl.
 - The FDA is charged with ensuring drug safety, efficacy, marketing, and labeling and is the major enforcer of regulations outside the Department of Justice.
 - The ultimate decision as to which portions of the Controlled Substances Act are enforced, how the government views the prosecution of thousands of Americans, and the balance between incarcerations versus referral for medical treatment lies almost entirely in the Executive Branch, specifically the White House Office of National Drug Control Policy.⁴⁰
 - Treatment of persons with opioid use disorder using evidence-based opioid agonist medications is highly regulated by federal systems.
 - The treatment of opioid dependence using opioid agonist medications is governed by Federal Regulation 42 CFR Part 8, which provides an accreditation and certification-based system for Opioid Treatment Programs.
 - In the year 2000, Congress passed DATA-2000, a law that allows physicians to become eligible to prescribe specially-approved schedule III-IV opioid-based medications for the treatment of opioid addiction. Buprenorphine and buprenorphine/naloxone were the first medications to be approved and affected by this law.
 - DATA-2000 provides a waiver process for which physicians can prescribe this pharmacotherapy for opioid use disorder in their offices. There are multiple pathways to DATA-waiver eligibility, including holding a board certification in addiction psychiatry, holding an addiction certification, or taking a specialized eight-hour course. The waiver caps the number of opioid-dependent patients a physician can treat at any time.
 - In 2016, the Comprehensive Addiction and Recovery Act (CARA) amended the Controlled Substance Act to allow Nurse Practitioners and Physician Assistants to become eligible to prescribe buprenorphine for opioid use disorder, after 24 hours of specialized training.
 - No other medications have such restrictions on use, and these obstacles to providing care stigmatizes both the condition and the treatment.
 - The Mental Health Parity and Addiction Equity Act of 2008 requires insurance groups offering coverage for mental health or substance use disorders to make benefits no more restrictive than the same requirements or benefits offered for other medical care.^{41 42}
 - Privacy of persons with opioid use disorder is highly protected under federal regulations.
 - ► Federal regulations restrict the disclosure and use of patient records pertaining to substance use disorder treatment that federal programs maintain.
 - This is intended for patients' protection, but can be a hindrance to providers in the emergency department or in primary care, as methadone prescribed by Opioid Treatment Programs does not appear in prescription drug monitoring programs.⁴³
 - The Affordable Care Act of 2010 (ACA) significantly expanded prevention and treatment services for substance use disorders. In particular, the ACA enables states to address the opioid epidemic through four primary mechanisms.⁴⁴
 - First, the ACA extends insurance coverage to previously uninsured Americans. It also specifically bans insurers from refusing to sell insurance to individuals with preexisting conditions (including prior treatment admissions for opioid use disorder.)
 - Second, it requires all insurance plans to cover substance use disorder screening and brief interventions, and requires coverage of the Essential Health Benefits package (which includes substance use disorder treatment services under Medicaid expansion programs and qualified health plans offered on state insurance exchanges.)

COMPONENT 1: DEFINITIONS OF PAIN AND ADDICTION

- Third, it extends the 2008 Mental Health Parity and Addiction Equity Act (see earlier bullet point), to apply to all private plans, including those offered on state exchanges and Medicaid expansion programs.
- ▶ Fourth, it promotes integration of substance use disorder treatment and mainstream health care by creating incentives to increase integration of coordination of care and services.

COMPONENT 2

2

Describe the environmental, healthcare systems and care model factors that have shaped the U.S. opioid epidemic and approach to pain care.

RATIONALE

This core component focuses on the complexity of the CDC-described opioid epidemic. There are overlapping factors that have shaped both the development of the epidemic and the current clinical approach to pain. More than providing background, this centers on prevention, in order to avoid a similar epidemic in the future.

OBJECTIVES

A. MESSAGE: Multiple factors shaped the current opioid epidemic.

- A1 Describe the environmental, healthcare systems, industry, legal, and care model factors that have shaped the opioid epidemic. A2 Describe the impact a single provider can have on the opioid epidemic.
- **B.** MESSAGE: Multiple factors shaped the current approach to pain.
 - B1 Describe the origins of "pain is the fifth vital sign" and the cultural, industry, The Joint Commission and other care model factors that have shaped the traditional biomedical approach to pain.
- C. MESSAGE: It will take a comprehensive approach to address the opioid epidemic.
 - C1 Explain the macro (e.g., policy, systems, legal, societal) and micro changes (e.g. clinician prescribing, focus on pain self-management) that are needed to stem this epidemic.
 - C2 Explain how an epidemic like this might be prevented in the future.

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A. MESSAGE: Multiple factors shaped the current opioid epidemic.

A1. Describe the environmental, healthcare systems, industry, legal, and care model factors that have shaped the opioid epidemic.

- The U.S. is experiencing an epidemic of drug overdose deaths. There has been a rapid increase in the use of prescription and nonprescription opioid drugs in the United States (beginning in the 1990s and continuing through today), mirrored by a striking increase in opioid-related deaths.^{45 46}
 - The number of overdose deaths involving opioids was five times higher in 2016 than it was in 1999. The CDC estimates that 115 Americans die every day from an opioid overdose.⁴⁵
 - The rise in U.S. opioid overdose deaths has had three distinct waves.
 - ▶ The first wave of the epidemic began with increased prescribing of opioids in the 1990s.
 - Sales of prescription opioids increased 4-fold from 1999 2010, almost exclusively due to increased prescribing for non-terminal chronic pain.⁴⁷
 - ▶ The second wave began in 2010, with rapid increases in overdose deaths involving heroin.⁴⁵
 - The third wave began in 2013, with significant increases in overdose deaths involving synthetic opioids, particularly those involving illicitly manufactured fentanyl.⁴⁵
 - Recent data indicate that overdose deaths due to other substances is increasing as well, including cocaine, methamphetamine, and benzodiazepines. Contamination with fentanyl analogues appears to be driving some of these increases.
 - In 2016, 11.4 million people misused prescription opioids and 2.1 million people had an opioid use disorder.48
- The pharmaceutical industry played a large and obvious role in the opioid epidemic, but this was enabled by relaxed federal regulations and clinician buy-in.
 - In the 1990s, with millions of people affected by chronic pain, the U.S. drug companies and state and federal entities pushed to expand the use of opioids.
 - In 1997, the FDA changed its advertising guidelines to allow direct-to-consumer marketing of drugs. The same cultural shifts that made this possible likely changed the reception of persistent marketing by industry. There was a surge of industry spending on advertising and targeting physicians for opioid marketing.⁴⁹
 - Much of this advertising was focused on OxyContin[®], which was aggressively marketed as an addiction-free painkiller.
 - > The safety claims of the non-addictive quality of opioids were misrepresented by pharmaceutical companies.
 - Pharmaceutical companies and others who were promoting the more widespread use of opioids often cited a fivesentence letter to the editor in the New England Journal of Medicine that described a chart review for hospitalized patients without a history of addiction who received "at least one narcotic preparation" in which the identification of addiction was rare. This letter was subsequently cited 439 times as evidence that addiction was rare in people treated with opioids.^{50 51}
 - There was a concerted effort from pharmaceutical companies to change the prescribing culture towards more widespread use of opioids for non-cancer pain.
 - For example, Purdue Pharma provided physicians with starter coupons that gave patients a free 7- to 30-day supply of OxyContin[®].
 - Purdue Pharma funded more than 20,000 educational programs designed to promote the use of opioids from chronic pain. In general, more non-research payments correlated with more opioid prescriptions in the following year.⁵²
 - Other large companies (e.g. Teva Pharmaceuticals and Janssen Pharmaceuticals) additionally took part in aggressive marketing schemes for opioids. Together, they plied clinicians with speaking fees, free travel and consulting fees.
 - ▶ Prescriptions for OxyContin[®] for non-cancer-related pain went from 670,000 written in 1997 to 6.2 million in 2002.
 - Pharmaceutical companies also provided financial supports for groups such as the American Pain Society, which in turn, launched a campaign calling pain "the fifth vital sign" which changed the landscape of pain care [see next objective.]⁵³
 - Pharmaceutical companies recruited prominent physician "thought leaders" to be part of their "speakers bureau" and paid them to provide talks supporting the use of opioids for chronic pain.⁵⁴
 - A patient advocacy group, The American Pain Foundation, which received 90% of its funding from pharmaceutical and device companies, began promoting the use of opioids for non-cancer pain.⁵⁵
 - Mirroring the positive trend in the prescribed volume of opioid pain relievers has been an increase in the admissions to substance abuse treatment and increase in opioid-related overdose deaths.

- The U.S. overprescription of opioids coincided with a flood of heroin entering the country in the 2000s from Mexico, leading to the second wave of the opioid epidemic.
 - The increased number of people exposed to prescription opioids in the United States and the associated increase in the problematic use of opioids created a wider market for heroin, which was more readily accessible and much less expensive than prescription opioids.
 - In the 1960s, 80% of individuals entering treatment for heroin treatment started with heroin. In 2010, 75% of individuals entering treatment started on a prescription opioid.⁵⁶
 - Cartels tried to avoid detection of federal authorities by basing their U.S. operations out of suburbs and quiet rural areas.
 - Heroin and other illicit drugs including cocaine, methamphetamine, and marijuana later began to be adulterated with fentanyl and analogues, which was not only relatively easy to produce, but was orders of magnitude stronger than heroin.
 - Mexico now dominates the U.S. heroin market.
- There was a lack of United States federal oversight in opioid manufacture, distribution, prescribing, diversion and importation.⁵⁷
 - Between 1996 and 2007, the DEA approved increases in the U.S. production of hydrocodone 4-fold, fentanyl 10-fold, and hydromorphone 4.5-fold but it sanctioned <0.1% of physicians for narcotic-prescribing violations from 1999 to 2003.^{58 59}
 - The Ensuring Patient Access and Effective Drug Enforcement Act weakened DEA enforcement activities against drug distribution companies that were supplying physicians and pharmacists selling narcotics on the black market.⁶⁰ Twentythree of the Act's sponsoring lawmakers had received dollars from industry.
 - The FDA, charged with ensuring drug safety, efficacy, marketing, and labeling was also impacted by pain treatment advocacy. In the 1990s, FDA implemented a protocol to speed the approval process for pain medications and a pharmaceutically-funded group helped develop the protocol. This protocol was criticized for increasing the risks of undetected side effects in new drugs.⁵⁷
 - The FDA missed the implications of a disclosure regarding OxyContin[®] that crushing tablets immediately released 68% of the oxycodone, promoting it to a drug of abuse.⁵⁷
- The U.S. health care and insurance systems also drove the treatment of pain towards opioids.
 - The U.S. health care system financially incentivizes care that is:
 - Episodic (e.g. periodic injections)
 - Single-discipline driven (e.g. orthopedic surgery, pain medicine)
 - Short-term focused (i.e. treatment may provide short-term pain relief but has long-term risks and promotes passive coping)
 - Disease-focused (e.g. identify pathology and ignore patient strengths/resources)
 - ▶ Reductionist (i.e. focus on single body part rather than whole person)
 - Single treatment focused (e.g. procedures and opioids rather than integrated care)
 - The U.S. health care system is not structured to adequately prevent and manage pain and addiction. These complex conditions require a team-based whole-person approach that is difficult to deliver when short, episodic, single discipline care is financially incentivized and cognitive work (education about self-management, psychological therapies) is not.
 - Studies analyzing the coverage of Medicaid plans, Medicare Advantage plans, and other commercial insurers revealed that while many insurers applied "utilization management" rules to both opioid and non-opioid medications, strategies to improve chronic pain care by encouraging non-opioid and nonpharmacologic alternatives was rare.⁶⁰
 - In order to support the type of pain and addiction care that is envisioned by this curriculum [See Component #5], the U.S. health care system must transform to promote care that is:
 - Longitudinal (i.e. working with patient to build gradual health gains over time)
 - Team based (i.e. diverse disciplines working together with patient)
 - Long-term focused (i.e. ensures goals benefit the patient over time and do not have unintended consequences)
 - Based in wellness and prevention (i.e. focus on improving physical, mental, social, spiritual health and well-being)
 - ▶ Whole-Person inclusive (i.e. focus on care plan for person rather having just a "pain plan" and help patient create environment that supports health)
 - Multimodal (i.e. support self-management with use of progressively more intensive physical, mental, social rehabilitation)

- While opioid addiction is often described as an "equal opportunity" problem, there are significant environmental and socioeconomic factors at play.
 - The opioid crisis has affected some of the poorest regions of the country.
 - In an influential paper from Princeton University, authors described drug overdose deaths, suicide and alcohol-related deaths as "deaths of despair", arguing that they "come from a long-standing process of cumulative disadvantage for those with less than a college degree."⁶¹
 - Reversing decades of increasing life expectancy, the mortality rates among mid-life white Americans increased in early 2000s. This trend was most marked in those with less education and was attributed by the authors to "deaths of despair."
 - In an analysis focused on the Midwest, Appalachia and New England (where the heroin, fentanyl epidemics are most pronounced), mortality rates for "diseases of despair" (drug abuse, alcoholism, suicide) increased as country economic distress worsened.⁶¹
 - This research coincides with other research in the U.S. which indicates that happiness is downwardly trending for most subgroups of Americans and pessimism is most prominent in white Americans.⁶⁴
 - According to the U.S. Department of Health and Human Services, persons on Medicaid are more likely to be prescribed opioids, at higher doses, and for longer durations – increasing their risk for addiction and its associated consequences. They are also less likely to have access to evidence-based addiction treatment.⁶²
- The United States is the only country to officially declare an opioid overdose epidemic, although Canada is close behind the U.S. in its prescribing and related abuse and death rates. In contrast, the prescribing of opioids for chronic pain in developing countries is rare.
 - These international differences likely stem from differences in culture, healthcare systems, healthcare availability and access, promotional activities by the pharmaceutical industry, drug availability, drug relationships, and clinical practice standards.⁶³
 - The U.S. is the world's largest consumer of opioids, with some reports that it accounts for 4.4% of the world's population and consumes 30% of the opioid supply (including 83% of the oxycodone and 99% of the hydrocodone in the world).⁶⁵

Americans report more pain than citizens of any other country, suggesting complex underlying cultural and social factors.⁶⁴

- There is an insufficient clinical workforce to treat opioid use disorder in the United States.
 - Federal regulations currently represent a barrier to developing adequate capacity to treat opioid use disorder.
 - Treatment of opioid use disorder has been historically governed by law. The Harrison Act (1914) and subsequent Supreme Court interpretation made it illegal to prescribe opioids for the treatment of addiction. The Narcotic Addict Treatment Act (1974) established methadone clinics, and DATA-2000 (2000) provided a mechanism for physicians to obtain a waiver and dispense medications for the maintenance or detoxification of opioid dependence in an office-based setting. Finally, the Comprehensive Addiction and Recovery Act (2016) increased patient limits and provided a mechanism for nurse practitioners and physician assistants to obtain a waiver.
 - A 2011 survey reported that 43% of counties in the United States had no physicians able to prescribe buprenorphine. Geographical disparities exist in the counties that have at least one waivered physician – with up to a 30-fold difference in the number of waivered physicians per capita.⁶⁶ These geographical disparities are particularly prevalent in the states that have resisted the Affordable Care Act.⁶⁷
 - The majority of physicians who are waivered are not prescribing to their maximum capacity. One study found 48.1% of waivered physicians were prescribing buprenorphine to five patients or fewer.⁶⁸

A2. Describe the impact a single provider can have on the opioid epidemic.

- Know the evidence and develop information mastery. With the volume of literature available, clinicians must be able to pick out and apply the most relevant evidence to their patients and practice. Studies, consensus statements and guidelines must be analyzed for quality and funding sources. As of the writing of this *Faculty Guide:*
 - There is evidence that coordinated management of pain and opioid use disorder benefits patients. [See Component #3.]
 - There is no evidence of benefit in ordering imaging for most uncomplicated, nonspecific chronic back pain and headaches. [See *Component* #4.]

- Evidence-based treatments for opioid use disorder are underutilized. [See Component #5.]
- Nonpharmaceutical approaches to chronic pain are preferred, based on evidence showing favorable benefit-to-risk profiles. [See *Component #5*.]
- There is no evidence of long-term benefit for the use of opioids for chronic pain compared to other treatments. [See *Component* #5.]
- There is evidence that medication-assisted treatment is effective in treating opioid use disorder. [See Component #5.]
- There is evidence that self-management enhances patient outcomes. [See Component #6.]
- There is evidence that motivational interviewing techniques support behavior change. [See Component #7.]
- There is evidence that a team-based approach to pain and addiction is effective. [See Component #8.]
- There is evidence that family and social support impact recovery from pain and addiction. [See Component #9.]
- There is evidence available in all fields, including pain and addiction, that can and should impact patient care. [See *Component* #10.]
- Cultivate intellectual virtue. It is tempting in healthcare to perpetuate the status quo, do what you've always done, and to avoid conflict with patients, systems, and industry. However, in order to impact the opioid epidemic, clinicians must cultivate intellectual virtues that challenge oneself and the surrounding systems.
 - Intellectual curiosity and intellectual humility the drive to seek out answers and to question one's own knowledge. Is there a better way to treat my patients? Do I know the evidence-based treatments of pain and addiction? Is it possible my treatment is causing harm?
 - Intellectual courage the ability to do the right thing, in the face of personal and professional resistance. Do I provide evidence-based, safe care, resisting the pressures of satisfaction surveys, uncomfortable office visits, or industrysponsors?
 - Intellectual creativity the ability to "look outside the box" for solutions. If insurance won't cover physical therapy, what other creative solutions exist?
 - [See Component #10 for the application of these virtues in facing the opioid epidemic.]
- Use therapeutic, person-centered language. Language can impact care and well-being; even unconscious metaphors can hold power. Words need to be chosen and examined carefully.
 - Stigma negatively affects the treatment and outcomes of persons with chronic pain and/or addiction. Stigma has become
 institutionalized and currently lives within the language of large-scale federal policies and among many health care
 professionals [See Component #7 for the impact of stigma.]
 - Clinicians need active reflection to uncover personal biases against persons with pain and/or addiction. It is the role of every clinician to model non-stigmatizing language and correct harmful language.
 - Clinicians must also choose language that doesn't conceptualize pain care as a battle ("attack of back pain" or "eradicate the pain") and doesn't create a sense of fear and helplessness in patients ("crumbling disc" or "frozen shoulder").
 - [See Component #7 for how to recognize and correct damaging metaphors and stigmatizing language.]

B. MESSAGE: Multiple factors shaped the current approach to pain.

B1. Describe the origins of "pain is the fifth vital sign" and the cultural, industry, The Joint Commission and other care model factors that have shaped the traditional biomedical approach to pain.

- Prior to the 1800s, pain was viewed as an existential experience and accepted as a consequence of aging.⁶⁹
- The twentieth century saw the medicalization of pain management [See Component #6] with a growth of the structural pathology paradigm of pain. This paradigm grew in parallel with the increased knowledge of physiology of nociception in peripheral tissues.
 - Unfortunately, the structural pathology paradigm of pain conflated *pain* (a perception created by the brain) and *nociception* (activation of specialized peripheral sensors). This led clinicians and industry to develop and provide invasive treatments intended to eradicate nociception, when in fact pain is much more complex. Due to the inherent complexity of the pain experience, these focal approaches have yielded limited and temporary benefit.
 - The structural paradigm (biomedical model) unwittingly ignored the primary drivers of pain chronification and pain-related disability. [See *Component #4* for the risk and protective factors in developing pain, pain chronification and disability.]⁶⁹

COMPONENT 2: FACTORS INFLUENCING PAIN CARE AND THE OPIOID EPIDEMIC

- Dr. John Bonica, widely considered the father of modern pain management, was originally trained in the "specificity theory of pain" which posited that pain resulted from an identifiable injury. Dissatisfied with the treatments of pain in soldiers during World War II, Bonica consulted with other disciplines and developed the first multidisciplinary pain clinic in the 1950s.⁶⁹
- Multidisciplinary pain clinics became the standard within academic circles in the 1950s, while the biomedical approach
 persisted in the community. Evidence supported the multidisciplinary approach, however, and had a positive impact on
 patients.
 - These multidisciplinary clinics later included operant behavioral conditioning methods that produced marked improvements in patient self-management of pain. These included positive staff feedback and extinction of "pain behaviors."
 - In contrast to only short-term benefits from single discipline treatments, the multidisciplinary pain clinic was shown to produce clinical benefits for more than a decade after completing treatment.⁶⁹
- Development of market forces and specialty trainings led to the decline in multidisciplinary clinics and thus to a gap between evidence and practice.
 - Market forces emerged to reduce reimbursement rates of multidisciplinary clinics. CPT codes became necessary for reimbursement, but inherently emphasized a fee-for-service model of health care delivery. This ran counter to the multidisciplinary pain clinic model of providing a package of services that were necessary for optimal patient outcomes.⁶⁹
 - The growth of managed care in the late 1980s and 1990s led to a "carving out" of specific services in the multidisciplinary pain clinic.
 - For example, physical therapy would not be reimbursable if delivered by the same group on the same day as psychological and other rehabilitation treatments.
 - Subsequent studies showed worse treatment outcomes and overall decreased cost savings outcomes with this approach.
 - Hospitals and academic medical centers that housed and subsidized many of the multidisciplinary pain clinics became increasingly concerned with short-term cost-containment and profits. Institutional support shifted to programs with the highest profit margins, at the expense of multidisciplinary pain treatment programs.⁶⁹
 - The few remaining multidisciplinary clinics have been able to remain solvent by generating revenue from highly reimbursed procedures to subsidize low or non-reimbursed rehabilitation services.
 - Pain fellowship programs developed. Pain medicine came to be recognized as a subspecialty under anesthesiology, and training placed a primary emphasis on procedure-based care than whole-person, integrated care.⁶⁹
 - Many of the multidisciplinary pain treatment clinics closed due to financial concerns, leaving the majority of chronic pain care in the hands of primary care providers and modality-specific pain clinics.⁶⁹

• In 1995, The American Pain Society initiated an influential campaign "Pain, the Fifth Vital Sign" to raise awareness among healthcare providers of pain assessment and management

- At the time, many doctors were afraid to prescribe opioids.
- The Veterans Health Administration, the largest government-run healthcare system in the United States, adopted "Pain, the Fifth Vital Sign" in 1999, giving credibility to the campaign.⁷⁰
- While this campaign led to increases in pain research, education and an important focus on pain relief, unintended consequences resulted in an overreliance on opioids to treat chronic non-cancer pain.
 - Use of the "fifth vital sign" proved to be problematic in practice; rather than seeing the phrase as an analogy to draw attention to the need for improved assessment, some organizations interpreted this to mean that pain needed to be assessed every time vital signs were taken.
 - Use of an oversimplified assessment tool (Numeric Rating Scale in which patients are asked to rate their pain on a scale of 0-10) led to oversimplified treatment (e.g. use of opioids to reduce the pain score).
 - Healthcare facilities also developed polices that liberalized the use of opioids in an attempt to meet JCAHO (now called The Joint Commission) standards.
 - A study later found that routinely measuring pain as the fifth vital sign did not increase the quality of pain management.⁷¹

COMPONENT 2: FACTORS INFLUENCING PAIN CARE AND THE OPIOID EPIDEMIC

- The treatment of chronic non-cancer pain became a new and growing indication for an opioid prescription. Most famously, Purdue Pharmaceuticals introduced OxyContin[®] in 1996, which was marketed aggressively with FDA-approved labeling to claim that iatrogenic addiction was "very rare."
 - As detailed earlier, marketing, advertising, and "education" were funded by Purdue and other pharmaceutical companies to normalize the use of opioids and (incorrectly) state its nonaddictive potential.
- The Federation of State Medical Boards created model guidelines in 1998 that stated physicians would not receive excessive regulatory scrutiny if prescribing notable amounts of opioids "in the usual course of professional practice."⁷²
 - This policy was drawn up with the help of several people with links to opioid makers. Of note, the Federation had received nearly \$2 million from opioid makers since 1997.⁶⁹
 - States passed Intractable Pain Laws, such as California whose law stated "No physician shall be subject to discipline for prescribing or administering controlled substances in the course of treatment for intractable pain."⁷³
- By 2001, the JCAHO (now the Joint Commission) mandated pain assessment and treatment of all patients in accredited healthcare settings in order to receive federal health dollars.^{69 74}
 - Many clinicians were concerned that raising pain treatment to a "patients' rights" issue could lead to an overreliance on opioids. Such concerns were criticized by medical experts, advocacy groups, and pharmaceutical companies as "opioid-phobic."
- The DEA in 2001 agreed to follow a "balanced policy" in examining prescribing practices. This policy encouraged the use of opioids to relieve pain and reduced oversight of physicians that had high rates of opioid prescribing.⁶⁹
- There was increasing public attention to the treatment of pain and a developing expectation for complete pain relief.
 - One cultural example of this was found on the cover of a 1997 issue of U.S. News & World Report: "NO EXCUSE FOR PAIN – Doctors have the means at hand to relieve the suffering of millions of Americans. Why aren't they doing it?"⁷⁵
- Since then, agencies and companies have changed their campaigns and marketing, but the concept that iatrogenic addiction is rare and that long-acting opioids are less addictive has been reinforced and widely repeated.
 - In 2001, the FDA required removal of the unsubstantiated claims of rare addiction from the OxyContin®'s labeling.
 - In 2011, the Joint Commission noted, "Both pharmacologic and nonpharmacologic strategies have a role in the management of pain."
 - "Pain as the Fifth Vital Sign" is no longer used by The Joint Commission, and advocacy has been withdrawn from the American Medical Association, the American College of Surgeons, the American Academy of Family Physicians, and the Centers for Medicare and Medicaid services.⁷⁶
 - In 2018, The Joint Commission finalized and implemented new and revised pain assessment and management standards for accredited hospitals. They require hospitals to "actively engage medical staff and hospital leadership in improving pain assessment and management" and to "improve pain assessment to be concentrating more on how pain is affecting patients' physical function." ⁷⁷
 - In 2018, Purdue Pharma, the largest manufacturer of opioids announced that it would no longer market OxyContin[®] to doctors.
 - Due to the pharmaceutical marketing that improperly minimized addiction potential (OxyContin[®]), and promoted offlabel use (Actiq[®]), and later physician kickback schemes (Subsys[®]), hundreds of lawsuits have been brought against pharmaceutical companies and their distributors.

C. MESSAGE: It will take a comprehensive approach to address the opioid epidemic.

C1. Explain the macro (e.g. policy, systems, legal, societal) and micro changes (e.g. clinician prescribing, focus on pain self-management) that are needed to stem this epidemic.

- There are policy shifts needed in order to impact the availability of treatment for opioid use disorder, financially incentivize long-term, evidence-based care and enhance clinician training on pain and addiction.
 - There needs to be expanded treatment for opioid use disorder. Efficacious medications are available but underutilized due to a number of factors.
 - A survey reported a lack of U.S. providers that can treat opioid addiction; 96% of U.S. states reported higher rates of opioid use disorder or dependence than their buprenorphine treatment capacity.⁷⁸ Primary care clinicians struggle to find DATA-waivered providers that are able to treat their patients, and referral times can reach several months.
 - The DATA-2000 requirement to have a waiver in order to prescribe buprenorphine cannot be removed, as it allows physicians to prescribe it for opioid use disorder treatment in their offices instead of Opioid Treatment Programs. Waiver-qualifications are still a barrier, however -- physicians can apply for the DATA-waiver if they take and pass an eight-hour course and/or meet other specifications; Nurse Practitioners (NPs) and Physician Assistants (PAs) require 24 hours of additional training.
 - In 2018, a Federal Bill adjusted the waiver requirements to allow all graduating physicians from medical and osteopathic schools to be automatically eligible for the DATA-waiver. It does not address or reduce the barrier for NPs and PAs.⁷⁹
 - The DATA-2000 law also caps the number of patients a physician can treat at any one time: 30 patients through the first year after certification, and can expand to 100 patients after the first year. Certain physicians (not NPs and PAs) can apply to treat up 275 patients.

 Of note, no other medication has this "capping" of patient numbers -- including opioids and other controlled substances that drive addiction. The lack of providers and restriction on patient numbers limits access to treatment. Combating the opioid crisis with the reduced provider work force is like "trying to fight World War II with only the Coast Guard."

Dr. Timothy Brennan, Addiction Medicine Fellowship Director at Mountain Sinai Health System treatment⁸⁰

- There needs to be increased training on pain and addiction care for students and increased support for graduating clinicians treating addiction.
 - While most medical schools now offer some education about opioids, less than 20 of 180 American programs teach addiction. Pain and addiction curriculum content in schools varies, ranging from an emphasis on regulatory issues to complete courses on medication-assisted treatment. In medical schools, there is a mean of nine hours of pain education.^{80 81}
 - A report by the National Center on Addiction and Substance Abuse (Columbia University) called out "the failure of the medical profession at every level in medical school, residency training, continuing education and in practice" to adequately address addiction.⁸²
 - Medical schools, osteopathic schools, dental schools, naturopathic schools, nursing schools, podiatry schools and physician assistant programs all graduate clinicians that will encounter patients with pain and/or opioid use disorder. Just as insulin and diets are taught for treatment of diabetes, whole-person care for pain and addiction and medication-assisted treatment for opioid use disorder should be taught.
 - There also needs to be support for providers out in the community who are DATA-waivered and/or treat opioid use disorder. The majority of physicians who are waivered are not prescribing to their maximum capacity. Support of these clinicians has been listed as a way to increase prescribing of medication-assisted treatment.^{68 83}

- There needs to be payment reform that incentivizes cognitive work, integrated and team-based care, and quality.
 - The current system financially incentivizes procedures, single discipline care and quantity of care. Evidence should guide payment models to cover treatments that have been shown to be effective.
 - The Medicare Resource-Based Relative Value Scale, which determines the physician payment system, currently undervalues cognitive office efforts. One study found that office visits for an established patient have Relative Value Unit (RVU) from 0.97-2.11; procedures have an RVU from 3.26-5.24. Thus, the care of patients with chronic complex diseases that requires counseling and office visits, has low compensation.⁸⁴

A good example of evidence-driven policy is seen by Oregon's Health Evidence Review Commission. This Commission reviews medical evidence and only offers coverage for practices that have evidence for their effectiveness.

- The majority of representatives on the American Medical Association Specialty Society Relative Value Scale Update Committee (RUC), whose recommendations to CMS significantly influence the values assigned to physician services are appointed by surgical, procedural or other subspecialties, and a minority represent primary care.⁸⁵
- Health plans have the potential to reduce the use of specific prescription drugs. The judicious deployment of insurer policies related to opioid prescribing would benefit from a commensurate increase in coverage and access to comprehensive pain management.⁸⁶
- Some Medicaid programs have begun to implement value-based payment strategies as part of a wider approach to address to opioid crisis. These strategies have demonstrated the ability to reduce costs and improve the quality of behavioral health care.
- There needs to be a change in the training of pain medicine specialists.
 - Modern understanding of the complex, intersubjective nature of pain requires clinicians and specialists to focus on longitudinal, whole-person care using the chronic care model.
 - The majority of care and management of persons with pain should take place in primary care, and specialty services should focus on care for higher complexity patients who are experiencing a greater degree of pain-related disability.²⁵
 - Specialists in pain medicine should be trained in the prevention, diagnosis and management of opioid use disorder. More than 1 in 4 individuals receiving long-term opioids for chronic pain (in a primary care setting) struggles with addiction.⁸⁷
- Healthcare systems need to promote whole-person, integrated, and team-based care.
 - Chronic pain has often been viewed and treated using an acute care model.
 - Addiction has largely been treated outside of the general healthcare system or using an acute care model that focuses on "detoxification."⁸⁸
 - One option is for systems to adopt a Chronic Care Model⁸⁹ for chronic pain and addiction. The Chronic Care Model is a proactive management strategy that involves multidisciplinary and interdisciplinary teams of healthcare providers to anticipate and prevent recurrence of relapses. There is evidence that this model is more effective than traditional clinical care in the treatment of several chronic illnesses, is appreciated by patients and physicians, and doesn't cost more than traditional care. ^{90 91 92 93 94}
 - Addressing pain and addiction with a Chronic Care Model would entail redesigning the healthcare delivery system to facilitate preventive care, gaining organizational leadership support for the change, providing expert input to generalists to help manage cases, improving clinical information systems to track and coordinate care, fostering patient self-management, and increasing patient access to community sources.⁸⁸
- On the legal side, more work needs to be done in analyzing the criminalization of substance use disorders.
 - There needs to be therapeutic responses to substance use disorders promoted, rather than incarceration.
 - Decriminalization is not the same as legalization. In Portugal, for example, almost all drug use was decriminalized, not legalized. Possession of drugs in Portugal are handled as a public health problem and not as criminal activity. Substance use disorders and addiction rates have been cut in half since decriminalization.⁹⁵
 - Drug courts, specialized diversion programs that permit eligible nonviolent defendants to avoid incarceration if they undergo treatment for addiction, are becoming increasingly prevalent at the state level, but not the federal level.
 - Drug treatment courts have been shown to reduce recidivism rates and save money. One study in California showed that use of drug courts saved the state over \$9 million in criminal justice and treatment costs. The US Government Accountability Office found that drug court participants have rearrest rates 12-58% lower than a comparison group of arrestees that did not participate in drug courts.⁹⁶

- Addiction treatment and rehabilitation is less expensive than incarceration. Further, individuals with substance use disorders are more likely to pursue recovery in treatment programs than in jail.
- The existing treatment resources are not nearly large enough to handle the large population of patients currently in the criminal justice system.
- Societal improvements and public health campaigns could act as prevention. Healthy communities can act as protective factors from the development of pain chronification and opioid use disorders.
 - Reversing the opioid crisis and preventing future drug crises of this scope will require addressing the economic disparities, housing instability, poor education, and lack of access to quality health care (including evidence-based treatment) that currently plague many of America's disadvantaged individuals, families and communities.⁶²
 - Public health campaigns are needed to promote awareness of key concepts such as advice to stay active, practice selfmanagement strategies, and education about the consequences of opioid and drug use.
 - Education is needed to change expectations with respect to the treatment and management of chronic pain. Pain is not the measure of one's health and happiness. Pain is a part of life and it takes long-term care and incremental improvement to expand one's functionality and life enjoyment and decrease the amount of life dedicated to fighting pain.
- A cultural transformation in the way clinicians, patients, government and the public view pain and addiction and its treatment is needed. There are system-level, clinician-level and patient-level barriers to change: macro-barriers take years to change and appear insurmountable, but micro-barriers (clinician and patient-level) can change today.

C2. Explain how an epidemic like this might be prevented in the future.

The interrelated epidemics of chronic pain, opioid misuse and overdose deaths have roots in two sets of factors: self-inflicted factors (healthcare-related policies and actions that contributed to these epidemics of illness) and ecological factors (interactions of the U.S. culture and society with the healthcare system and each other).

- The healthcare system that now fights these epidemics played a role in their development. Between the pharmaceutical
 and device industries pursuing profits, device industry pursuing profits, professionals with conflicts of interest and
 well-intended physician-leaders who advocated for medical care based on ideology ("we need better pain control")
 rather than sound evidence (lack of safety and effectiveness data for long-term opioid treatment) diverse entities from
 individual clinicians to private organizations to federal health agencies are implicated.
- The ecological factors in the U.S. population refer to socioeconomic disparities, social disintegration leading to loneliness, public intolerance for pain and both unconscious and mean-minded stigma. These factors left the population vulnerable to promises of quick fixes for pain and/or despair, and then to the downstream effects of pain-related disability and/or addiction.

Prevention of future epidemics needs to address both sets of factors by strengthening the U.S. healthcare system and the resilience of the U.S. population.

- The healthcare system requires fortification from the ground up.
 - Individual clinicians must have intellectual virtues that keep them searching for excellence, questioning their care and biases, and being able to say no to inappropriate requests from patients and industry alike.
 - Medical and public health professionals need to be information mastery experts with awareness of factors that bias outcomes, such as financial conflicts of interest.
 - Watch-dog groups (e.g. FDA, DEA) must maintain appropriate regulatory oversight and need to be made up of individuals without conflicts of interest.^{97 98}
 - Public health agencies needs high quality and continuously updated data both to serve as an initial alert and to track over time. Diseases of concern should be prioritized and surveillance systems created.

COMPONENT 2: FACTORS INFLUENCING PAIN CARE AND THE OPIOID EPIDEMIC

- The health of and interactions within communities needs to be prioritized it can act as a protective factor for people who are at risk for pain, addiction, or the next epidemic.
 - Social connection and compassion (towards others and self) appear to be important predictors of wellbeing.^{99 100}
 Promoting compassion for self (defined by Neff¹⁰¹ as self-kindness, common humanity, and mindfulness) and others may be one important approach to enhancing social connections.
 - Enhancing the therapeutic alliance between the healthcare team and patients is an important social factor that the healthcare team can cultivate to improve care.¹⁰²
 - Enhancing social connection within healthcare involves promoting integrated team approaches [See *Component* #8 for how a team's integration affects the care of a patient.]
 - Social factors that can drive poor health outcomes (e.g. social isolation, lack of parenting skills, early substance use) need to be addressed.
 - There needs to be a culture change that emphasizes active approaches to health and wellness, rather than relying on passive strategies.
 - Policies and strategies must be developed that improve socioeconomic status and resolve disparities.

COMPONENT 3

3

Describe the interrelated nature of pain and opioid use disorder, including their neurobiology and the need for coordinated management.

RATIONALE

Key to the curriculum's vision, this core component establishes the link between pain and addiction. Pain and addiction are highly comorbid and share neurobiologic mechanisms, clinical manifestations, and treatment approaches. Separation of the research, education, and clinical management of these conditions has led to an unnecessarily narrow understanding and a fragmented approach to care. Integrating these domains enhances the clinician's understanding, assessment, and treatment of persons with pain and/or addiction.

OBJECTIVES

A. MESSAGE: Pain and opioid use disorder are interrelated.

- A1 Describe the neurobiology of pain and addiction, including reward and anti-reward.
- A2 Describe how coordinated management of pain and opioid use disorder benefits patients and their outcomes.

B. MESSAGE: Substance use relates to pain and the risk of developing opioid use disorder.

- B1 Detail the relationship between substance use disorders (including alcohol, tobacco and other drug use), pain and the risk of developing opioid use disorder.
- B2 Explain the relationship between mental illness and trauma with pain and substance use disorders.
- B3 Explain the importance of screening for substance use disorder, when treating someone for acute or chronic pain.

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A. MESSAGE: Pain and opioid use disorder are interrelated.

A1. Describe the neurobiology of pain and addiction, including reward and anti-reward.

Pain and addiction appear to share some common neurobiological mechanisms and vulnerabilities, including an altered reward system, impaired executive function, and dysfunctional learning processes.

- An altered reward homeostasis is central to pain relief and the development of addiction and chronic pain.
 - The reward system is a collection of brain structures and neural pathways that are responsible for motivating and rewarding a person's behaviors.
 - The reward system involves two main processes: hedonic pleasure (i.e. "liking") and motivation to obtain rewards (i.e. "wanting").
 - The neurobiology of the reward system includes endogenous opioids in brain regions including the orbitofrontal cortex, the anterior cingulate cortex, the amygdala, and the nucleus accumbens. Motivation to pursue rewards is primarily driven by dopamine signaling in the mesolimbic circuit.
 - The anti-reward system works opposite and in response to the reward system.
 - The anti-reward system represents an opponent neuroadaptation in response to the aberrant activation of the reward system that occurs in chronic pain and addiction. This system creates a massive outpouring of stressogenic neurochemicals and is manifested in negative affective states (anxiety, distress, depression, fear, withdrawal), anhedonia and narrow focus on seeking urgent pain relief (or taking a drug).^{103 104}
 - The neuroanatomy of the anti-reward system involves the so-called "extended amygdala" (basolateral amygdala, bed nucleus of the stria terminalis and lateral tegmentum), hippocampus and habenula.
 - Addiction is currently understood as a reward-deficient condition.
 - Initial use of an addictive substance causes activation of the brain reward system and is felt as intense pleasure and well-being (i.e. intense "liking"). With continued substance use, this "liking" response to the substance diminishes. This process is called tolerance, and is due to a diminished responsiveness in the reward system and overall depletion of dopamine.
 - Repeated activation of the brain's reward system by the addictive substance changes the way the person responds to stimuli that are associated with use of the substance. A person learns to associate the people, places, things, and internal moods (e.g. anxiety, pain, or sadness) that trigger substance use with the pleasurable "liking" feeling created by the substance over time, these stimuli (also called activate powerful urges to take the substance (i.e. an intense state of "wanting"). Once the brain state of addiction develops, the specific cues continue to trigger the "wanting" of the substance even though the "liking" of the substance has diminished or disappeared.
 - As the anti-reward system ramps up and the "liking" response decreases (reward deficiency), the opposite effects of the drug begin to predominate when the drug wears off (i.e. withdrawal symptoms such as pain, anxiety, distress, irritability, dysphoria in the case of opioids).
 - Thus, as addiction develops, the nature of drug-taking transitions from being impulsive (seeking pleasure) to compulsive (avoiding negative physical and emotional states of withdrawal).
 - Additionally, as the brain transitions to an addicted state and the reward system loses its responsiveness to both drug and natural rewards, normal rewarding activities (such as food, positive relationships, pursuit of important goals, and sex) become less important and enjoyable for a person with addiction.
 - · Opioids for pain relief act on the reward system and can create learned associations that urge continued use.
 - When opioids are prescribed for pain, they not only activate the areas of the brain that process physical pain, but also brain areas involved in emotional pain, social pain (e.g. social isolation or loss of a loved one), and the reward system.
 - They also create learned associations between the taking the opioid and the opioid effects (e.g. sense of well-being, short-term relief of pain, reduced anxiety). This unconscious learned association can become part of the urge to continue using the opioids. With chronic pain, even mild pain can trigger these learned associations and manifests as an urge for short term pain relief and the other short-term effects of well-being and tranquility.
 - Prolonged pain also creates a state of reward deficiency and anti-reward excess.
 - > While the drug or substance is rewarding in addiction, pain relief is rewarding in chronic pain.
 - With addiction, the reward system is activated and in order to maintain homeostasis, the anti-reward system is also activated. With prolonged pain, the anti-reward system appears to be chronically activated and overly sensitive, leading to dysphoria, fear, aversion, social isolation, and a rigid motivational state with near-exclusive focus on pain relief. This activation of the anti-reward system may be driven by the excessive activation of the reward system that happens during chronic pain.¹⁰⁴

- Fear avoidance, or avoiding activities in life, is a significant factor in developing chronic pain-related disability. This can be due to an oversensitive anti-reward system which is evolutionarily meant to be protective, but is now overly protective.¹²⁰
- Fear avoidance behaviors can lead to decreased activity levels and physical deconditioning. The deconditioned state includes a weak and tight musculoskeletal system that can serve to perpetuate chronic pain and fear avoidance.
- In chronic pain, natural rewards become less rewarding (i.e. normally it is enjoyable to hang out with a friend; in chronic pain it may be less enjoyable). While acute pain activates dopaminergic neurotransmission in the reward system, prolonged pain (on the continuum to chronic pain) produces the opposite effect (hypodopaminergic reward deficiency) leading to a blunted capacity to enjoy or experience pleasure from natural rewards such as positive relationships, altruism, appreciating beauty, and accomplishing goals.
- Executive functioning is impaired in both chronic pain and addiction.
 - Impaired executive functioning is manifested in chronic pain by impaired goal-directed behavior. The prefrontal cortices are involved in planning for the future with a particularly important ability to choose a goal (e.g. finish high school) and implement behaviors that will lead to accomplishing the goal sometime in the future (e.g. reading a required book or studying for a test). Individuals with chronic pain often prioritize behaviors that lead to pain avoidance rather than behaviors that lead to accomplishing valued goals.¹⁰¹
 - Impaired executive functioning is manifested in addiction as impaired inhibitory control. The prefrontal cortex works to inhibit impulses driven by the reward/limbic systems (e.g. "the chocolate cake smells good, but I shouldn't eat a third piece.") This impaired ability of the prefrontal cortex to inhibit reward/limbic impulses once addiction develops makes it more difficult for the individual to resist a craving or strong urge to use a substance.¹⁰⁵
- Dysfunctional neuroplastic processes that share the same mechanisms as Learning and Memory also underlie the development of chronic pain and addiction.
 - In chronic pain, there can be Central Sensitization in which the central nervous system amplifies the processing of pain. This means that smaller, peripheral activations of the nociceptive system produce larger amounts of pain in the brain, or that the brain is producing pain in the absence of peripheral nociceptive signals. [See *Component* #4 for a description of pain processing.]
 - In addiction, there are similar neuroplastic changes, such as the shifting of dopamine surge from the drug to drug-related cues, down-regulation of the reward system in response to natural rewards (reward deficiency) and up-regulation of the anti-reward system (negative affect, anxiety, depressed mood, fear).

A2. Describe how coordinated management of pain and opioid use disorder benefits patients and their outcomes

In the current fragmented and siloed systems, individuals with pain and opioid use disorder often present to healthcare settings that are unable to provide integrated care. This leads to a one-size-fits-all approach, rather than an evidence-based, whole-person approach.

- For example, a patient with depression, anxiety, and opioid use disorder who presents with back pain to an interventional pain clinic will often receive back injections (with low likelihood of benefit) rather than integrated treatment of pain, mental health and substance use disorder comorbidities (which will have a much better chance of benefit).
- Management of chronic pain is largely provided by specialized single discipline clinics with a narrow treatment focus that
 is siloed from other aspects of an individual's care. This is problematic, given the inherent risk of developing problematic
 opioid use with long-term opioid therapy and the high rate of comorbid mental health disorders.
- Similarly, management of opioid use disorder often occurs outside the medical system or in isolated settings that cannot provide evidence-based pharmacotherapy for opioid use disorder and cannot manage comorbid conditions that increase the likelihood of relapse (e.g. mental health and chronic pain comorbidities).
- Current fee-for-service payment models that prioritize payments for procedures and brief visits over cognitive work provided in an interdisciplinary environment continue to drive the siloed and fragmented system of care.

COMPONENT 3: INTERRELATEDNESS OF PAIN AND OPIOID USE DISORDER

Integrating pain, mental health, and addiction services is a system factor that facilitates whole-person care for individuals with pain and opioid use disorder. [See *Component #8* for integration of healthcare teams.]

- When integrated care is available, individuals with chronic pain who have unidentified substance use disorders and mental health comorbidities can receive the most appropriate and evidence-based treatments.
- The evolving understanding of substance use disorders has helped reduce the negative attitudes around them and has supported the integration of treatment into mainstream health care. Promising scientific evidence suggests that it can increase the quality, effectiveness and efficiency of care.¹⁰⁶

B. MESSAGE: Substance use relates to pain and the risk of developing opioid use disorder.

B1. Detail the relationship between substance use disorders (including alcohol, tobacco and other drug use), pain, and the risk of developing opioid use disorder.

There is an association between substance use disorders and chronic pain.

- It has been reported that up to 60-80% of patients seeking treatment for opioid use disorder have chronic pain.^{107 108}
- Long-term effects of alcohol use, tobacco use, and opioid use all appear to increase the risk of developing chronic pain and for worsening chronic pain. These substances have both analgesic and hyperalgesic effects.^{109 110 111}
- Chronic pain is highly prevalent in patients with substance use disorders and appears to be risk factor for substance use disorders.¹¹²
- Chronic pain may increase the risk of relapse for patients with substance use disorders and complicates the treatment
 of opioid use disorder.

Substance use and pain are risk factors for developing opioid use disorder.

- Painful conditions contribute to the risk of prescription opioid use disorders.¹¹³ In patients prescribed opioid analgesia for chronic non-cancer pain, the rates of opioid misuse averaged 21-29% and the rates of addiction were 8-12%.¹¹⁴
 Another study found a lifetime prevalence for prescription opioid use disorder of 41%.¹⁵⁴
- In patients with chronic pain, a history of prior problematic substance use including alcohol, tobacco, and illicit drugs increases the risk of developing an opioid use disorder.¹¹⁵

B2. Explain the relationship between mental illness and trauma with pain and substance use disorders.

There is an association between previous emotional or mental trauma and the development of pain and substance use disorders.

- Adverse childhood experiences (ACE) are stressful or traumatic events, including abuse and neglect. They may include household dysfunction such as witnessing domestic violence or growing up with family members who have substance use disorders.
- Adverse childhood experiences in youth have been found to be frequently associated with several chronic pain conditions.¹¹⁵
- Adverse childhood experiences are also a significant risk factor for developing substance use disorders. The cumulative ACE score has a strong, graded relationship to numerous health, social and behavioral problems throughout a person's lifespan, including substance use disorders.¹¹⁵

COMPONENT 3: INTERRELATEDNESS OF PAIN AND OPIOID USE DISORDER

• In a 2003 study, for every additional ACE score, the rate of number of prescription drugs used increased by 62%, and each ACE increased the likelihood of early initiation into illicit drug use by 2-4 fold.¹¹⁵

There is a high comorbidity of mental illness and chronic pain.

- Mental health and physical health are fundamentally linked. People living with a serious mental illness are at higher risk of experiencing a wide range of chronic physical conditions. Conversely, people living with chronic physical health conditions experience depression and anxiety at twice the rate of the general population.¹¹⁶
- Individuals with chronic pain have a higher rate of anxiety, depression, and post-traumatic stress disorder (PTSD) compared with individuals without chronic pain.¹¹⁷
- "Adverse selection" refers to the fact that individuals who are most likely to experience opioid-related adverse events (those with prior substance use disorders or mental health conditions) are more likely to receive opioids, at higher doses, and for longer periods of time than lower risk individuals with chronic pain.¹²¹
- Individuals with chronic pain and a comorbid mental illness are at increased risk for opioid-related adverse events,¹¹⁸ respond to treatments less favorably,¹¹⁹ and are more likely to be disabled by chronic pain¹²⁰ compared with individuals with chronic pain who do not have comorbid mental health conditions.
- Optimizing treatment of mental health conditions can have a direct effect on improving pain in patients with chronic pain.¹²²

There is a high comorbidity of mental illness and substance use disorders.

- National population surveys have found that about half of those who experience a mental illness during their lives will also experience a substance use disorder and vice versa.¹²³
 - Adolescents with substance use disorders have high rates of co-occurring mental illness over 60% of adolescents in community-based substance use disorder treatment programs also meet diagnostic criteria for another mental illness.¹²³
- There are high rates of comorbid substance use disorders with anxiety disorders (generalized anxiety disorder, panic disorder and PTSD) and comorbid substance use disorders with mental disorders (such as depression, bipolar disorder, ADHD, psychotic illness, borderline personality disorder, and antisocial personality disorder).
 - Research indicates that 43% of people in substance use disorder treatment for nonmedical use of prescription painkillers have a diagnosis of symptoms of mental health disorders, particularly depression and anxiety.¹²³
 - Around 1 in 4 individuals with serious mental illness also have a substance use disorder.¹²³ Patients with schizophrenia have higher rates of alcohol, tobacco, and drug use disorders than the general population.

These comorbidities appear to be mutually reinforcing with common mechanisms, and individuals with comorbid (rather than isolated) conditions have worse outcomes and respond less favorably to isolated treatments.

Individuals with substance use disorder, chronic pain, and many mental health conditions respond positively to behavioral therapies. Integrated interdisciplinary rehabilitation is key for individuals with high degrees of comorbidity and dysfunction.^{119 122 124}

B3. Explain the importance of screening for substance use disorder when treating someone for acute or chronic pain.

Substance use disorders and opioid use disorders are common in the general public and are more common patients with chronic pain using long-term opioid treatment.

- In 2014, 21.5 million people aged 12 or older had a substance use disorder in the previous year.¹²⁵
- In 2016, 2.1 million people were estimated to have an opioid use disorder in the United States.⁴⁸
- In people on long-term opioid treatment for chronic pain, the lifetime prevalence for opioid use disorder has been estimated at 41%.¹⁵⁴

COMPONENT 3: INTERRELATEDNESS OF PAIN AND OPIOID USE DISORDER

All patients using opioids are at risk for developing an opioid use disorder, and the diagnosis is under-recognized.

 As many as one in four patients receiving long-term opioid therapy in primary care settings struggle with opioid use disorder.⁸⁷

Among patients with untreated substance use disorders, the use of opioids carries a significant risk for adverse outcomes including opioid use disorder, opioid overdose and death. Presence of a substance use disorder requires additional caution in treatment planning for patients with acute pain.

• For patients already receiving chronic opioid therapy who are diagnosed with an untreated substance use disorder, clinicians should monitor closely, offer or arrange for substance use disorder treatment and proceed with an exit strategy from the use of long-term opioid therapy. [See Component #5 for description of opioid exit strategies.]

Screening for substance use disorders does not take long and can be conducted effectively in a variety of settings. The goal is to identify individuals who have or are at risk for developing alcohol or drug-related problems, and within that group, identify patients who need further assessment, and then develop plans to treat them. [See SBIRT and screening tools in *Component #4*].

Definitions for substance use disorders and opioid use disorders are contained in the DSM-5.¹²⁶

- Of note, the *DSM-5* no longer uses the terms substance abuse and substance dependence which were used in *DSM-4*. Instead, it now refers to substance use disorders with a degree of severity (mild, moderate, severe).
- Opioid use disorder is defined in the DSM-5 and can be remembered through the 3Cs: loss of CONTROL, CRAVING and use despite negative CONSEQUENCES. [See Component #4 for diagnostic criteria and severity classification for opioid use disorder.]

Treatment for substance use disorders and opioid use disorders is effective. Concurrent, integrated treatment for substance use disorders and pain greatly enhances patient outcomes [See *Component #8* for coordinated management strategies; See *Component #5* for treatment of pain and opioid use disorders.]

COMPONENT 4

4

Use a socio-psycho-biological model to evaluate persons with pain and/or opioid use disorder.

RATIONALE

This curriculum flips the traditional biopsychosocial model to instead focus on social, psychological, and physical functioning. This emphasis on the interpersonal and intersubjective domains of pain and opioid use disorder reflects the most recent basic science and clinical evidence that social, emotional, and cognitive aspects of pain are central to chronification and the associated dysfunction and disability – and not a secondary issue or a distraction. Rather than beginning with a reductionist approach that focuses on cellular and molecular mechanisms and then progresses to social and psychological phenomena as merely the result of the microscopic processes, a macroscopic, integrated, whole-person approach is what is recommended in this component.

OBJECTIVES

- A. MESSAGE: Clinical understanding of pain and addiction encompasses social, psychological and biological dimensions.
 - A1 Describe the socio-psycho-biological model of pain, and detail the components of each.
 - A2 Describe the socio-psycho-biological model of opioid use disorder, and detail the components of each.
- B. MESSAGE: Evaluation of pain and opioid use disorder requires a whole-person approach.
 - B1 Perform a whole-person assessment of a person with pain.
 - B2 Describe patient-centered and clinician-centered parts of the pain interview.
 - B3 Discuss red flags noted during a history and physical, and the associated work-up when present.
 - B4 Describe yellow flags and their importance in acute and chronic pain conditions.
 - B5 Discuss the indications for imaging for common pain complaints.
 - B6 Demonstrate ability to screen individuals for opioid use disorder and diagnose them using DSM-5 diagnostic criteria.
 - B7 Demonstrate use of Screening, Brief Intervention, and Referral to Treatment (SBIRT) for persons with addiction.
 - B8 Perform a whole-person assessment of a person with addiction.

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A. MESSAGE: Clinical understanding of pain and addiction encompasses social, psychological and biological dimensions.

A1. Describe the socio-psycho-biological model of pain and detail the components of each.

Clinical models provide a common framework and context that guides understanding and treatment of disease.

- These models are usually implicit and not usually explicitly discussed or considered in clinic, educational or research settings.
- At best, clinical models distill complex sets of data into a practical clinical framework. At worst, they perpetuate outmoded views and practices that then persist for longer than appropriate.

Pain care models seek to provide the context to answer the following questions: What causes pain? What are treatments and treatment goals? Who is responsible for the treatment outcomes, and how does the health care system drive care?

- The Biomedical Model of pain care has its roots in reductionism (i.e. focusing on a disordered part rather than the whole), and can be expressed as an outcropping of the antibiotic era of medicine ("find disease ▶ give pill ▶ kill something.")¹²⁷ This is the primary model that is implicitly taught and that shapes our medical system.
 - The Biomedical Model is a "find it and fix it" approach, assuming a 1:1 correlation between physical pathology and pain.
 - The Biomedical Model establishes the role of the patient as a passive victim of an identifiable disease and the doctor as responsible for urgent and complete pain relief. Treatments are done to the patient.
 - For example, this is how the Biomedical Model would answer questions about pain:
 - ▶ What causes pain? Facet arthritis.
 - What are treatment goals? To reduce nociception (nerve activity that results from detection of stimuli capable of causing tissue damage) from a specific source.
 - ▶ What are the treatments? Nerve ablation or fusion surgery.
 - ▶ Who is responsible for the treatment outcomes? The pain doctor or surgeon.
 - How does the health care system drive care? It incentivizes procedures and high-volume care.
- The Biopsychosocial Model of Pain was generated in response to a recognition that the narrow focus of the Biomedical Model on physical factors does not account for the complexity of the pain experience, and that psychosocial factors must also be considered.
 - The Biopsychosocial Model views pain as a dynamic interaction among and within the biological, psychological and social factors unique to each individual.
 - Often, the biopsychosocial model is taught in a way that prioritizes the "bio" (ion channels, nerve pathways, microscale events) and de-emphasizes the "psycho" and "social" (psychosocial and environmental factors that are key to determining functional and quality of life outcomes for patients with chronic pain).
 - Focus on the "micro" aspects of pain (ion channels and nerve pathways) implies that all "macro" aspects (painrelated disability and suffering) are necessary downstream effects and will resolve once the "micro" factors are addressed. Pain research has not demonstrated this to be accurate.¹²⁸
 - The mechanistic focus on the subcellular and cellular processes poorly prepares trainees to assess and treat pain in everyday practice, as research has found that psychological factors such as context, meaning, expectation, selfefficacy, and catastrophizing and social factors such as family, culture, religion are key components driving pain outcomes.¹²⁸

- The Socio-Psycho-Biological Care Model has grown out of the recognition that the Biopsychosocial Model has been taught and implemented in a way that prioritizes microscopic physiology and the physical domains of pain (i.e. the Biomedical Model with psychosocial factors added on).
 - The Socio-Psycho-Biological Care Model represents a true paradigm shift to a whole-person and whole-system focus on person-centered outcomes such as function and quality of life.
 - The social and psychological dimensions that drive the experience of chronic pain are taught as foundational elements that provide context for understanding neurobiology.
 - In contrast to the Biomedical Model, the Socio-Psycho-Biological Care Model would have the following answers:
 - *What causes pain?* A complex interaction of social, psychological and biological factors.
 - What are treatment goals? To improve function and quality of life.
 - What are the treatments? Education, self-management, movement therapies, psychological therapies, procedures as bridging therapies and judicious use of medications.
 - + Who is responsible for treatment outcomes? The person with pain is the active center of the care team.
 - How does health care system drive care? It does not support this model as the current system devalues cognitive work and often does not cover psychological and interdisciplinary care.
- Reframing the pain curriculum from its current bottom-up "biomedical/biopsychosocial" phenomenon to a top-down "socio-psycho-biological" one is supported by the modern understanding of pain as an inherently interpersonal, social process.¹²⁸
 - Human development, thriving, pain, suffering and survival are all inextricably social. Social environments shape a person's experience of pain, thoughts and feelings related to pain, communication of distress, degree of disability and others' responses.²¹²⁹
 - From an evolutionary perspective, human survival depends on maintaining the integrity of the body and the social structure. Evolutionarily, damage to the body or separation from other humans represent threats to survival.
- The standard pain curriculum resembles an approach to driver education in which classes in combustion chemistry and auto mechanics were mandatory, while on-road training in courtesy and defensive driving amidst traffic were optional.¹²⁸
- Pain itself appears to alert humans to all types of threats to survival, bodily harm as well as social isolation.
- Physical pain and social pain (painful feelings that follow from social rejection, exclusion, or loss) appear to share neurobiological mechanisms.¹³⁰
- The Socio-Psycho-Biological Model clarifies that pain is not a damage detection system (i.e. producing accurate information about tissue damage), but rather functions as a threat detection system (i.e. identifies potential threat to survival and motivates action to protect survival).

Social forces shape a variety of pain-related outcomes.

- Reviews have found that the modulation of pain by interpersonal factors depend on 1) the degree to which the social partners were active or were perceived by the participants to possess possibility for action; 2) the degree to which participants could perceive the specific intentions of the social partners; 3) the type of pre-existing relationship between the social partner and the person in pain; and 4) the individual differences in relating to others and coping styles.
- Of more than a dozen studies, most found that more perceived social support was associated with better pain-related functioning.¹³¹
- Lack of social support at work, dissatisfaction with coworkers, and interactions with the disability compensation system
 are among the most potent predictors of work disability related to pain.¹³¹ [See *Component #8* for the role of social support
 in treatment.]

The central and interactive roles of psychological states are supported by an overwhelming amount of evidence. Unfortunately, in practice, psychological factors are assigned secondary status and viewed largely as reactions to pain or distractions from "real pain" that will spontaneously resolve if pain is cured.

- Emotional distress may predispose people to experience pain, be a precipitant of symptoms, be a modulating factor amplifying or inhibiting the severity of pain, be a consequence of persistent pain, or be a perpetuating factor.^{132 133 134}
 - For example, the literature is replete with studies demonstrating that current mood state modulates reports of pain as well as tolerance for acute pain.¹³²
 - Additionally, anxiety has been shown to influence not only pain severity but also complications following surgery and number of days of hospitalization.¹³²
- Strong links have been observed between early traumatic experiences and the subsequent development of chronic pain.
 - A meta-analysis reported that the presence of past trauma was associated with a 2-3x increase in the subsequent development of chronic widespread pain; nearly 50% of patients with various types of chronic pain reported a history of childhood abuse.¹³⁵
- Psychological processes that modulate the experience of pain are associated with both pain chronification and recovery. These include attention, cognition, catastrophizing, maladaptive behaviors, and self-efficacy.¹³⁴
 - Attention: Individuals direct their attention to experiences that are salient to survival. Pain is a highly salient internal experience which often draws one's attention away from other experiences and activities. Focusing attention on pain can increase one's pain intensity.
 - *Cognition:* Thoughts, beliefs, context, and expectations all influence a person's experience of pain, including pain intensity and pain-related function.^{120 136}
 - Catastrophizing: This is a pain-specific pattern of cognition and emotional distress characterized by the triad of amplification, rumination, and helplessness. Higher degrees of pain catastrophizing are associated with high pain intensity, greater pain-related disability, and worse responses to several different pain treatments.¹³³
 - *Maladaptive behavior:* This is what one does to cope with pain, and it can influence one's perception and perpetuate the cycle of chronic pain. Passive coping strategies and avoidance behaviors may increase disability.
 - *Emotions:* negative feelings and emotional distress may influence the pain as well as fuel cognitions, attention, and maladaptive behaviors. Fear may increase avoidance behavior and disability. Anxiety and depression may increase pain disability. Positive emotions might decrease pain.
 - Self-Efficacy: This is the belief in one's capacity to implement specific behaviors (the belief that you can self-manage)¹³⁷.
 [See Component #5 for how this fits into a framework of active and passive care treatments; See Component #6 for the evidence of its impact on patient outcomes.]

Many of the biological components of acute pain are well established. New understanding about the pathophysiology of chronic pain (e.g. deconditioning, central sensitization) continues to develop.

- Pain has a biologically important protective function. The nervous system relays information about actual or potential tissue damage to the brain, and the brain synthesizes the sensory information with emotional and cognitive information to produce the experience of pain. Pain signifies that a threat is perceived, and a response is required in order to protect the individual.
 - Nociception and pain processing occurs in four steps:
 - Transduction noxious stimuli are translated by afferent nociceptive nerve endings (A-delta and C fibers) into electrical impulses.
 - Transmission electric impulses travel along primary nociceptors to the dorsal horn of the spinal cord where multiples synapses occur. Second-order neurons then may carry the signal from the dorsal horn to the brain.
 - Modulation afferent neural signals are either dampened or amplified at multiple levels of the central nervous system, including the dorsal horn of the spinal cord and brain.
 - Perception there is a conscious awareness of the experience of pain. Sensory, emotional, and cognitive information is synthesized to determine if the organism is in danger and a behavioral response is required.
 - Understanding the pain processing steps can facilitate understanding the mechanisms of different pain medications. [See Component #5 for the evidence-based treatment of pain.]

- Higher brain structures determine whether nociceptive signals from the body should be amplified or suppressed based on threat to survival. The descending neural pathways, which appear to be activated by higher brain structures, are used to modulate pain. This has tremendous implications in our understanding of pain, in that the brain not only passively receives neural signals about pain, it can inhibit or amplify incoming nociceptive signals from the body.
 - Neural circuits that originate in the midbrain (Periaqueductal Grey PAG), relay in the medulla (Rostral Ventral Medulla – RVM), and descend to the spinal cord, provide potent inhibition to spinal nociceptive signals.
 - Higher cortical structures involving cognition and emotion appear to provide input to and initiate the (PAG ► RVM ► spinal cord) descending inhibitory system.¹³⁸ The existence of these connections, along with converging early experimental data, support the concept that this descending pain inhibitory pathway can be influenced by psychological factors like cognition, emotion, attention to modify incoming nociceptive signals.
- Processing of nociception and pain can change, depending on the type of the initial stimulus and degree of chronification.¹³⁹
 - Tissue injury can increase the excitability of neurons in the peripheral and central nervous system, creating a state of peripheral or central sensitization, respectively. These changes can outlast the tissue injury, persisting long after the originally injured tissue has healed.
 - Hyperalgesia (higher than usual degree of pain is produced by a painful stimulus) and allodynia (pain is produced by a non-painful stimulus) can be caused by peripheral and central sensitization that results from tissue injury.
 - Nociceptive pain is when brief (seconds to minutes) noxious stimuli are applied to intact tissue and normal pain processing occurs. This is less relevant in clinical medicine as it occurs in the absence of tissue damage and peripheral/central sensitization.
 - Inflammatory pain occurs after tissue injury but with an intact nervous system. It involves changes to the processing of nociceptive signals in the peripheral and central nervous system.
 - Neuropathic pain occurs when there is damage to the peripheral or central nervous system and also involves changes to the processing of nociceptive signals in the peripheral and central nervous system.
- After an acute injury, the nociception and pain processing system usually return to their normal functional states as soon as healing takes place. Socio-psycho-biological mechanisms and central sensitization (i.e. amplification of pain processing by the central nervous system) drive the transition to chronic pain (i.e. pain chronification).
- The biological component of *chronic pain* recognizes the major role played by the central nervous system and shifts away from the structural pathology paradigm. This shift leads to a more comprehensive, systems view.
 - Pain perception involves the complex integration of information from multiple brain regions including, but not limited to, the primary and secondary somatosensory cortices, insula, thalamus, anterior cingulate cortex (ACC), prefrontal cortex (PFC), cerebellum, amygdala and basal ganglia.
 - Change is a fundamental property of the brain and changes among, between, and within neurons is referred to as neuroplasticity. Neuroplastic changes in the brain can be adaptive (as in learning, memory, and normal health development) or maladaptive (as in the pathological brain changes that occur in addiction or chronic pain).
 - Central sensitization is a major feature in virtually all chronic pain states and sometimes represents the primary driver of persistent pain.
 - Different brain regions are involved in the chronification of pain.
 - Individuals with chronic pain have consistently been shown to have decreases in the grey matter of three cortical regions: anterior cingulate cortex (ACC), prefrontal cortex (PFC), and the insula. Changes have also been demonstrated in the white matter integrity of these brain areas.¹³⁸
 - Individual emotional learning characteristics appear to predict the transition from acute to chronic pain. The strength of functional connectivity between a reward/salience brain region (nucleus accumbens) and a brain region involved in modulation of emotions (medial prefrontal cortex) has been found to predict the development of chronic pain with an accuracy of >80%.¹⁴⁰
 - Brain regions that process subacute back pain (about two months duration) are different from brain regions involved in chronic back pain (>one-year duration)
 - Subacute back pain produces activation in the traditional "acute pain" brain circuits: insula, anterior cingulate cortex, thalamus, and basal ganglia.
 - Chronic back pain shows lessening involvement from the acute pain circuits and shifts to activity in the emotional circuits (PFC, amygdala, and basal ganglia).¹⁴¹

A2. Describe the socio-psycho-biological model of opioid use disorder and detail the components of each.

The socio-psycho-biological model is applicable in the understanding and clinical approach to opioid use disorders.

• For opioid use disorder, there has been a shift from viewing it as a moral inferiority to understanding it as a brain disease. Because opioid use disorder is multidimensional with biological, psychological, social and spiritual manifestations, doing a whole-person assessment and treatment using the socio-psycho-biological model is key.

Social factors strongly impact the development and trajectory of an opioid use disorder.

- Environmental factors such as the availability of drugs, family and peer dynamics, financial resources, cultural norms, exposure to stress and access to social support can drive the emergence and continuation of opioid use and the progression to problematic use or an opioid use disorder.
- The social milieu of the adolescent has a major effect on how they react and interpret drug use. This peer influence, combined with the psychologically reinforcing effects of opioids (which produce both euphoria as well as relief of negative affect), work to continue the addictive spiral. Earlier use of opioids and other addictive substances is a strong predictor of developing problematic use or an opioid use disorder.
- There is social stigma surrounding the label of "a drug addict." Public fear and misunderstanding of the situation of a person with an opioid use disorder make it harder for a person to gain acceptance socially, find a job or be a part of other productive social functions. [See *Component* #7 on impact of stigma on legal, policy and care outcomes.]
- The War on Drugs ideology and certain federal policies "render drug users the enemies of society" which has left society distanced from those with opioid use disorder.¹⁴²

Psychological factors are often involved in both the early and established stages of problematic opioid use.

- Emotional and psychological distress may lead a person to start using an addictive substance, but once the brain changes indicative of addiction are present – it is as if two entities, each needing targeted treatment, are present. Treatment for both the substance use disorder and the comorbid psychiatric condition is necessary.
- But Helen, of the line of Zeus, called to mind another resource. Into the wine they were drinking she cast a drug which melted sorrow and sweetened gall, which made men forgetful of their pains."
- Four psychological behaviors are central to the addiction cycle:

erring to the mythical drug nepenthe, likely opium. – Odyssey, (Homer & Lawrence, 1991, page 50)

- *Impulsivity* is an inability to resist urges, deficits in delaying gratification and unreflective decision making. It is a tendency to act without foresight or regard for consequences and to prioritize immediate rewards over long-term goals.
- *Positive reinforcement* is the process by which a positive stimulus (e.g. feeling of well-being caused by taking a drug) increases the behavior of taking the drug.
- *Negative reinforcement* is the process by which removal of an aversive stimulus (e.g. relief of negative emotions and withdrawal symptoms due to taking a drugs) increases the behavior of taking the drug.
- Compulsivity refers to repetitive behaviors in the face of adverse consequences and repetitive behaviors that are
 inappropriate to a particular situation. People suffering from compulsion often recognize that the behaviors are harmful, but
 they nonetheless feel emotionally compelled to perform them. Doing so reduces tension, stress and anxiety.
- Mental health conditions can occur as a result of substance use (i.e. substance-induced mental disorders) or as primary (i.e. independent) conditions.
 - Evidence favoring an independent mental disorder include 1) episodes of the disorder preceded the onset of intoxication or withdrawal and 2) the full mental disorder persisted for substantial period of time (at least 1 month) after the cessation of acute withdrawal or intoxication.
 - Evidence favoring an independent mental disorder include a) episodes of the disorder preceding the onset of intoxication or withdrawal and b) the full mental disorder persisted for substantial period of time (at least 1 month) after the cessation of acute withdrawal or intoxication.

The biological components of addiction can be described as a repeating three-stage cycle. This cycle worsens over time and involves dramatic changes in the brain reward, stress and executive function systems (adapted from the *Surgeon General's Report, 2016*).¹⁴³

- Intoxication is the stage at which an individual consumes an intoxicating substance and experiences its rewarding
 or pleasurable effects.
 - The "reward circuitry" of the basal ganglia (e.g. the nucleus accumbens), along with dopamine and naturally occurring opioids, play a key role in the rewarding effects of substances and the ability of stimuli/cues to trigger craving, substance seeking, and use. As substance use progresses, repeated activation of the "habit circuitry" of the basal ganglia (i.e. the dorsal striatum) contributes to the compulsive substance seeking and taking that are associated with addiction. The involvement of these reward and habit neurocircuits helps explain the intense desire for the substance (craving) and the compulsive substance seeking that occurs when actively or previously addicted individuals are exposed to alcohol and/or drug cues in their surroundings.
- Withdrawal/Negative Affect is the stage at which an individual experiences a negative emotional state in the absence of the substance.
 - This stage of addiction involves a decrease in the function of the brain reward systems and an activation of stress
 neurotransmitters such as corticotropin-releasing factor (CRF) and dynorphin, in the extended amygdala. Together, these
 phenomena provide a powerful neurochemical basis for the negative emotional state associated with withdrawal. The drive
 to alleviate these negative feelings negatively reinforces alcohol or drug use and drives compulsive substance taking.
- Preoccupation/Craving, is the stage at which one seeks substances again after a period of abstinence.
 - This stage of the addiction cycle is characterized by a disruption of executive function caused by a compromised prefrontal cortex. The activity of the neurotransmitter glutamate is increased, which drives substance use habits associated with craving, and disrupts how dopamine influences the frontal cortex. The over-activation of the GO system in the prefrontal cortex promotes habit-like substance seeking, and the under-activation of the STOP system of the prefrontal cortex promotes impulsive and compulsive substance seeking.
- It is not known if brain changes associated with addiction are permanent, but it appears that they are quite persistent, likely for years or decades. This corresponds to the clinical experience of prolonged vulnerability to relapse once addiction has developed and that recovery is a prolonged process that takes place over years and decades.

Of note, all components of addiction run together. As the brain moves toward compulsion, the behavioral repertoire becomes narrowed and fewer alternative behaviors are available in response to urges for substance use. Social factors also contribute to both the development and the continuation of the addictive spiral.

B. MESSAGE: Evaluation of pain and opioid use disorder requires a whole-person approach.

One of the common misconceptions among health care professionals is that the intensity or quality of pain experienced directly reflects the type and extent of tissue injury (i.e. a 1:1 correlation between tissue damage and pain experience). This has led clinicians to dichotomize the mind/body experience of pain, often at the expense of a multidimensional understanding of the pain experience.

A whole-person approach can be defined as assessing and treating each individual as a whole person rather than as separate symptoms, diagnoses or body parts. Whole-person treatment involves the coordination of health, behavioral health and social services in a patient-centered manner with the goals of improved health outcomes.¹⁴⁴

B1. Perform a whole-person assessment of a person with pain.

Acute pain typically has a well-defined time course and it occurs as the consequence of injury or disease and resolves with healing; chronic pain has no defined time course and often represents pain that persists after an injury has healed. Both are subjective experiences, however, and their severities can be influenced by many factors, including previous experience of pain, cultural background, context, expectations, coping mechanisms, fear, anxiety, and depression. An assessment of a patient with pain then, is multifactorial and complex.

- The focus of the assessment of acute pain is to determine the etiology of the source of the pain to guide the necessary evaluation and management.
- The focus of the assessment of chronic pain is to understand the person as a whole, including past and current medical, psychiatric, and substance use disorder comorbidities to facilitate matching the patient with the most appropriate intensity of care.

The pain interview starts with patient-centered aspects, which include symptoms and the personal and emotional part of the story. Components of the interview differ slightly between acute and chronic pain.

- For individuals presenting with acute pain, in addition to the pain history (character, intensity, location, underlying cause, etc) clinicians should seek to understand the person's unique factors that contribute to the pain experience and either protect against or promote the development of future chronic pain and disability.
- For individuals presenting with chronic pain, elements of the interview include a pain-related history, assessment of the pertinent medical and psychiatric comorbidities including personal and family history of substance use disorder, coping strategies and psychosocial factors such as the patient's beliefs and expectations about chronic pain and its treatment. This includes an evaluation of medical, psychiatric and co-occurring substance use conditions, and the patient's social support system.
 - The patient should also be questioned about the impact of pain on their function (e.g. in social and physical domains) and overall quality of life. Specific questions to ask include social and recreational functioning, mood, affect and anxiety, relationships, occupation, sleep, exercise, and activities of daily living.
 - If a decision about opioid prescribing is required, it is necessary to review prior medical records and request consent to speak with the prior prescriber, check the prescription drug monitoring database, and obtain a baseline urine drug screen.

Specific components of the physical exam for an individual with pain include mental status exam, inspection, vital signs, posture and gait inspection, palpation, range of motion, neurological examination, and additional tests as appropriate.

• The physical exam complements the history in the process of generating a diagnostic impression and guides the selection of further laboratory tests or imaging. The physical exam aids in excluding serious pathology, quantifies physical impairment, and complements the assessment of psychosocial factors.

For individuals with acute and/or chronic pain, red and yellow flags should be identified.

- Red flags are historical or exam findings that may indicate a serious pathology. Imaging or further workup may be required. [See later objective in *Component* #4.]
- Yellow flags are psychosocial risk factors that hold a higher risk of developing chronic pain and/or pain-related disability. An awareness of these flags may help to prevent adverse outcomes or help clinicians identify the start of unhealthy habits or behavior. [See later objective in *Component #4*.]

Use of imaging should be judicious, with keeping in mind the maxim, "Will the results of this test change my management?" Of note, there is no evidence for routine imaging of most persons with uncomplicated, nonspecific common pain complaints.

• [See later objective for indications for imaging; see Appendix B for an overview of the Choosing Wisely initiative.]

B2. Describe patient-centered and clinician-centered parts of the pain interview.

The pain interview starts with the patient-centered aspects. A patient-centered History and Physical involves the physical symptom history, but also the personal and emotional part of the story. The interviewer encourages the patient to express what is most important to him or her.

 The five steps of patient-centered interviewing include setting the stage for the interview, eliciting the chief concern and setting the agenda, interviewing with non-focusing skills to help the patient to express her/himself, using focusing skills to learn the symptom story, personal context and emotional context, then transitioning to the clinician-centered phase (through summarizing and checking accuracy).

The clinician-centered aspects are when the clinician takes charge of the interaction to acquire specific details not provided already. This includes the past medical history, meds/allergies, social history, family history, review of systems and goals of therapy.¹⁴⁵

B3. Discuss red flags noted during a history and physical, and the associated work-up when present.

Red flags are findings that may indicate serious underlying pathology and when combined with the full clinical picture, may prompt further investigation.

For low back pain, red flags are uncommon. Finding a nociceptive source for the pain is also uncommon.¹⁴⁶

- Low back pain is rarely associated with serious underlying pathology such as malignancy, infection, fracture, or the cauda equina syndrome. While there is limited evidence that identification of specific red flags is associated with improved outcomes, evaluating for the presence of red flag findings can guide evaluation and management.
- For low back pain, the presence of trauma history, unintentional weight loss, immunosuppression, history of cancer, IV drug
 use, steroid use, focal neurologic deficit, saddle anesthesia, bowel/bladder dysfunction, or progressive symptoms should
 prompt consideration for additional work-up.
- Systematic reviews have found that the red flags associated with the highest post-test probability of a vertebral fracture were older age, prolonged use of steroids, severe trauma and presence of contusion or abrasion. Only a history of cancer has been shown to increase the probability of finding spinal malignancy.¹⁴⁷

Red flags for headache should prompt further investigation for a possible underlying disease.

- These include systemic symptoms, illnesses or conditions, neurologic symptoms or abnormal signs, new onset (particularly for age >50 years) or sudden onset, other associated conditions or features (head trauma, illicit drug use or toxic exposure, headache awakens from sleep, worsened with Valsalva or precipitated by cough, exertion or sexual activity) or previous headache history with headache progression or change in attack frequency, severity or clinical features. Any of these findings should prompt further investigation, including brain imaging with magnetic resonance imaging or computed tomography.¹⁴⁷
 - A common mnemonic for headaches is SNOOP (Systemic symptoms, Neurologic symptoms, Onset is new, Other associated features, Previous headache history).

B4. Describe yellow flags and their importance in acute and chronic pain conditions.

Yellow flags refer to the psychosocial risk factors for pain chronification and pain-related disability.

• Evidence is unclear about which psychosocial risk factors are most significant, however awareness of a constellation of risk factors can guide clinicians to focus more on psychosocial rehabilitation and less on a biomedical approach to a specific body part. For example, if a patient is not improving from an episode of subacute low back pain and the clinician determines that the patient is unhappy with her job, is in a relationship with an emotionally abusive boyfriend, and is experiencing moderate depression, the next best course of treatment (in the absence of history or exam findings suggestive of serious pathology), would be to refer to self-management training or psychological therapy (cognitive behavioral therapy, acceptance and commitment therapy, mindfulness based therapy) rather than to advanced imaging or invasive procedures.

Yellow flags for the progression from acute pain to chronic pain include depression, stress, perceived injustice and catastrophizing, a high baseline fear, anxiety and negative beliefs on chronic pain.¹⁸

Yellow flags for low back pain disability include psychiatric symptoms such as depression and anxiety, poor job satisfaction, fear avoidance behaviors, catastrophizing, low self-efficacy, and passive coping strategies.¹⁴⁸

Early recognition of patients who have a high risk of developing chronic pain is imperative in guiding early interventions in hopes of preventing chronification and disability. [See *Component #5* for prevention of chronic pain and its sequelae.]

B5. Discuss the indications for imaging for common pain complaints.

For low back pain, the AAFP Choosing Wisely initiative states: "Don't do imaging for low back pain within the first six weeks, unless red flags are present."¹⁴⁹

- Most episodes of acute low back pain resolve spontaneously.¹⁵⁰
- Imaging findings are very common in asymptomatic individuals, indicating "age-related changes" rather than pathology.
 For example, "disc degeneration" and "disc bulge" are present in 80% and 60% of asymptomatic 50-year old individuals, respectively. Imaging findings are nearly universal in asymptomatic 80-year old individuals.¹⁵¹ This translates to very weak correlation between imaging findings and symptoms.
- Routine imaging does not improve outcomes, exposes patients to unnecessary harms (through identification of incidental findings and subsequent invasive treatments) and increases the cost of care. More frequent imaging is associated with higher rates of spine surgery.^{152 153}

For *headache:* Individuals with the danger signs or other features suggesting a secondary headache source will require imaging. Imaging is usually not warranted for patients with a stable migraine pattern and a normal neurologic examination, although a lower threshold for imaging is reasonable for patients with atypical migraine features or in patients who do not fulfill the strict definition of migraine.¹⁴⁷

B6. Demonstrate ability to screen individuals for opioid use disorder and diagnose them using DSM-5 diagnostic criteria.

The lifetime prevalence for opioid use disorder among patients receiving long-term opioid therapy has been estimated to be up to 25-41%.¹⁵⁴

Although the US Preventive Services Task Force (USPSTF) concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening adolescents, adults, and pregnant women for illicit drug use, there are some agencies that do recommend screening (CDC, WHO, ACOG) in certain populations like in adolescents and pregnancy.

- Using a screening tool or questionnaire may avoid implicit and explicit bias compared to relying on clinical judgment alone. There are different screening tools available: examples include the NIDA Quick Screen and TAPS [See *Appendix B* for these and other clinical tools].
 - Example from the NIDA Screen: "How many times in the past year have you used an illegal drug or used a prescription medication for non-medical reasons (for example, because of the experience of feeling it caused?)"¹⁵⁵ Caveat: This screening may have a low sensitivity for patients taking long-term opioid therapy for chronic pain (screening may produce false negatives).
 - The TAPS (Tobacco, Alcohol, Prescription medication, and other Substance Use) Tool is a two-step screening tool
 designed to screen and evaluate for substance misuse and substance use disorders. The first-step screen is suitable for
 use in primary care given its brief and easy-to-use format. TAPS combines screening and brief assessment for commonly
 used substances, eliminating the need for multiple screening and lengthy assessment tools.¹⁵⁶
 - Of note, the ORT (Opioid Risk Tool) is often cited as a screening tool that can be used in primary care for aberrant behaviors in patients taking opioids, however its low sensitivity (18-44%) limits its usefulness.^{157 158}
- Screening is the "S" in "SBIRT", an acronym for a framework for identifying people at high risk for substance use misuse. [See next objective for the framework; see *Component #4* for the diagnostic criteria for Opioid Use Disorder.]

Opioid use disorder is defined in the *DSM-5* as a problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the symptoms below, occurring within a 12-month period. This can also be remembered through the 3Cs – Loss of CONTROL, CRAVING and Use despite Negative CONSEQUENCES [See TABLE 2.]

Symptoms of opioid use disorders (a type of substance use disorder) include strong desire for opioids, inability to
control or reduce use, continued use despite interference with major obligations of social functioning, use of larger
amounts over time, development of tolerance, spending a great deal of time to obtain and use opioids, and withdrawal
symptoms that occur after stopping or reducing use, such as a negative mood, nausea or vomiting, muscle aches,
diarrhea, fever and insomnia.¹⁵⁹

TABLE 2: DSM-5 Diagnostic Criteria for Opioid Use Disorder¹²⁶

LOSS OF CONTROL	Using larger amounts of opioids or over a longer period than initially intended	EXAMPLE: taking more than prescribed (e.g. repeated requests for early refills)
	Persistent desire or inability to cut down on or control opioid use	EXAMPLE: has tried to reduce dose or quit opioid because of family's concerns about use but has been unable to
	Spending a lot of time to obtain, use or recover from opioids	EXAMPLE: driving to different doctors' offices to get renewals for various opioid prescriptions
CRAVING	Craving or strong desire or urge to use opioids	EXAMPLE: describing constantly thinking about/needing opioid
PHYSIOLOGIC USE DESPITE NEGATIVE CRITERIA CONSEQUENCES	Failure to fulfill obligations at work, school or home due to use	EXAMPLE: not finishing tasks due to effect of taking opioids; getting fired from jobs
	Continued opioid use despite persistent or recurrent social or interpersonal problems related to opioids	EXAMPLE: spouse of family member worried or critical about patient's opioid use
	Activities are given up or reduced because of use	EXAMPLE: no longer participating in weekly softball league despite no additional injury or reason for additional pain
	Recurrent use in situations that are physically hazardous	EXAMPLE: repeatedly driving under the influence
	Continued use despite physical or psychological problems related to opioids	EXAMPLE: unwilling to discontinue or reduce opioid use despite non-fatal accidental overdose
	Tolerance*	EXAMPLE: needing to take more to achieve the same effect
	Withdrawal*	EXAMPLE: feeling sick if opioid not taken on time or exhibiting withdrawal effects

*Tolerance and withdrawal are not counted as DSM-5 criteria for opioid use disorder when the patient is taking opioid medications as prescribed.

• The severity of opioid use disorder is classified by the number of presenting symptoms. This severity scale has replaced the concepts of substance abuse and substance dependence.¹²⁶ [See TABLE 3]

TABLE 3: DSM-5 DIAGNOSTIC CRITERIA FOR SEVERITY OF OPIOID USE DISORDER⁹⁰

Mild Severity of Opioid Use Disorder	Presence of 2-3 symptoms above
Moderate Severity of Opioid Use Disorder	Presence of 4-5 symptoms above
Severe Severity of Opioid Use Disorder	Presence of 6 or more symptoms above

• If there is uncertainty whether a patient meets criteria for opioid use disorder, the patient should be referred to an addiction specialist or psychiatrist for diagnosis.

When assessing for opioid use disorder and discussing opioid agonist therapy, clinicians should also strive to destigmatize the condition and the treatment. Reviewing the brain model of addiction and comparing to other conditions that also require ongoing self-management and medication use (like diabetes) can be helpful.

B7. Demonstrate use of Screening, Brief Intervention, and Referral to Treatment (SBIRT) for persons with addiction.

SBIRT is a comprehensive, integrated, public health approach to the delivery of early intervention and treatment services for persons with substance use disorders, as well as those who are at risk of developing these disorders. Primary care centers, hospital emergency rooms, trauma centers and other community settings provide opportunities for early intervention with individuals at risk for substance related problems before more severe consequences occur.

Screening – Universal pre-screening for patients for alcohol and other drug use identifies people with risky substance use. For those with a positive screening, further evaluation can be through interview and self-report.

 There is no universally accepted process for screening for opioid use disorder. For patients on long-term opioid therapy, however, the presence of high-risk behaviors (e.g. non-concordant urine drug testing, multiple prescribers revealed by the state prescription drug monitoring database, not adhering to the prescription instruction, using opioids for mood, energy, or to relieve anxiety) should prompt an evaluation for opioid use disorder using the DSM-5 criteria.

Brief Intervention – This is provided when a screening indicates risk for substance use problems. A brief intervention utilizes motivational interviewing techniques focused on raising a person's awareness of their substance use and its consequences, then motivating them toward positive behavioral change. A typical brief intervention takes from 5-15 minutes to conduct. Interventions work to 1) educate people about substance use and health risks and 2) encourage those at risk of health and other consequences to think differently about their use and make changes to improve their health.

Referral to Treatment – A referral should be provided for those identified as needing more extensive treatment with access to specialty care.

SBI is evidence-based for alcohol and tobacco per the United States Preventive Services Taskforce, but is rated "I" (the rating that indicates insufficient evidence) for illicit drugs. There are some agencies, however, that recommend screening (e.g. CDC, WHO, ACOG) in certain populations like in adolescents and pregnancy.¹⁶⁰

B8. Perform a whole-person assessment of a person with addiction.

Primary care assessment would include a basic physical and mental status examination, a psychiatric and trauma history, assessment for safety and identification of the domains of life affected by the disease.

Clinicians should seek to obtain a comprehensive substance use history, including all substances (e.g. nicotine, opioids, alcohol, marijuana, sedatives, stimulants, etc), onset and pattern of progression, most recent use, past sequelae and past treatment episodes. Clinicians should also ask about withdrawal symptoms and ascertain the presence of craving, loss of control over substance use, and a pattern of substance use despite adverse consequences. An empathetic and nonjudgmental style is critical [See *Component #7* for the impact of language on care.]

Diagnostic verification of a substance use disorder must be done and staged in severity. The *DSM-5* includes diagnostic criteria, in addition to classification of severity. These are both described earlier in this *Component #4*.

Patient history and results of drug tests provide complimentary information and are key in the assessment of intoxication and withdrawal.

An assessment for safety must be performed, looking for evidence of harm, intoxication, and/or withdrawal.

- The patient should be assessed for suicidal or homicidal ideation. Mental health problems associated with harmful behaviors often co-occur among people who have been treated for substance use disorders (e.g. depression, posttraumatic stress disorder, anxiety disorders, some personality disorders). In particular, suicide is a leading cause of death among people with substance use disorders.¹⁶¹
- Use of validated scales (e.g. COWS for opioid withdrawal and CIWA-Ar for alcohol withdrawal) can provide an objective assessment of withdrawal severity.
- Patients with life-threatening intoxication will require immediate care which may include prehospital resuscitation and use of naloxone.
- Patient who are at risk for imminent severe harm associated with their substance use may be considered medically
 unstable or a risk to oneself or others. Clinicians should ensure patient safety and engage the appropriate care pathway
 for management of medically or psychiatrically unstable patients requiring acute care (e.g. may include transfer to the
 emergency department, psychiatric urgent care, or involvement of police if a medical hold needs to be enforced.)

A comprehensive assessment also includes an identification of the domains of life affected by the disease, which can include interpersonal, social, financial, legal, work, school and physical domains. This may involve information gathering from a variety of sources, which is in contrast to the assessment of most medical or surgical conditions in which the initial history, physical and workup are sufficient sources of assessment.

- Sources that are commonly utilized in assessing addiction include patient history, physical exam, laboratory results, family
 interview, legal history questioning and prescription drug monitoring program data.
- Addiction and substance use disorders are among the most stigmatized disorders in society, and thus there can be issues
 of reliability in patient self-report.

The assessment must include an evaluation for medical and psychiatric diagnoses.

- Co-occurring disorders are common with addiction and must be identified and addressed as part of comprehensive care. These disorders may be comorbid or subclinical, but can occur with and influence the substance use disorder. These diagnoses may threaten the health of patients and complicate their treatment.
- Standard laboratory testing for patients with opioid use disorder include a pregnancy test, liver function tests (as they may impact pharmacotherapy), hepatitis viral panel, and HIV serologies.

Clinicians must assess readiness for behavior change. There are self-report instruments available, that assesses the patient's level of recognition of a problem, ambivalence, or uncertainty about changing and whether the patient is taking steps to change. [See *Component* #7 for the stages of change.]

COMPONENT 5

5

Use a socio-psycho-biological model to develop a whole-person care plan and prevention strategies for persons with pain and/or opioid use disorder.

RATIONALE

Evidence-based treatment of chronic pain focuses on a whole-person approach that emphasizes active treatments and selfmanagement strategies while avoiding unnecessary exposure to opioids. Evidence-based treatment of opioid use disorder centers on medication-assisted treatment, while again employing a whole-person approach to care. This core component is the most involved in this curriculum - it stresses the multimodal nature of treatment care plans and the necessary prevention and risk mitigation strategies to employ before and during treatment.

OBJECTIVES

A. MESSAGE: Treatment for pain and opioid use disorder requires a socio-psycho-biological approach.

- A1 Describe a multimodal treatment plan for a person with acute pain.
- A2 Describe a whole-person treatment plan for a person with chronic pain.
- A3 Discuss the difference between the use of active and passive therapies for a person with chronic pain.
- A4 Discuss the evidence for the use of opioids for acute and chronic pain.
- A5 Discuss the use of non-pharmacologic and non-opioid pharmacotherapy for acute and chronic pain.
- A6 Understand the regulatory requirements when treating pain and/or prescribing opioids for a patient with acute and chronic pain.
- A7 Describe a multimodal treatment plan for a person with opioid use disorder.
- A8 Understand the state and federal regulations when treating opioid use disorder.
- A9 Describe the process of coordinating care and arranging for a higher level of care for a person with opioid use disorder.
- A10 Address the management of acute pain in special populations, including persons in the pre- and post-operative periods, perinatal periods, the elderly, the pediatric population and those with substance use comorbidities.
- **B.** MESSAGE: Specific attention must be given to prevention and risk mitigation strategies as part of a treatment plan for acute pain, chronic pain and/or opioid use disorder.
 - B1 Demonstrate ability to implement risk mitigation strategies to prevent adverse outcomes from the use of opioid therapy for chronic pain.
 - B2 Recognize the clinical presentation of opioid withdrawal and know clinical and community resources to address it.
 - B3 Design strategies to prevent the progression from acute pain to chronic pain and pain-related disability.
 - B4 Demonstrate ability to manage challenging patients and recognize how people-pleasing behavior by clinicians can interfere with providing evidence-based care.
- **C.** MESSAGE: Treatment plans for persons on long-term opioid therapy must include an exit strategy, which transitions persons from long-term opioid therapy to a different treatment strategy, to minimize opioid-related adverse events.
 - C1 Contrast complex persistent opioid dependence with simple dependence and opioid use disorder.
 - C2 Describe three approaches to an opioid exit strategy.
 - C3 Discuss the importance of recognizing and addressing substance use disorders, mental health comorbidities and medical comorbidities when managing a person with chronic pain on long-term opioid therapy.

KEY READING

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A. MESSAGE: Treatment for pain and opioid use disorder requires a socio-psycho-biological approach.

A1. Describe a multimodal treatment plan for a person with acute pain.

- Following a whole-person evaluation of the person with acute pain, realistic expectations regarding the duration and severity of expected pain should be provided to patients.
- When possible, the underlying condition should be addressed with specific treatments.
- In general, a step-wise approach to acute pain management is indicated, combining treatments of different mechanisms as appropriate.
 - Step 1 is the use of non-pharmacologic therapies.¹⁶²
 - Non-pharmacologic therapies are the first line options for patients with acute pain. Since acute pain typically resolves over days to weeks, patients may only need these approaches for a short duration of time.
 - Non-pharmacologic treatment options for acute pain include self-care (ice, heat, rest, elevation of affected limb), complementary and integrative therapies (acupuncture, massage, chiropractic therapy), rehabilitation therapies (physical therapy, occupational therapy), and exercise (stretching, swimming, walking, tai chi, yoga, chair exercises).
 - Some treatments may be more appropriate immediately after an injury (e.g. ice, heat, stretching, and elevation), while others like physical therapy and exercise may be implemented once the patient is able to participate more.
 - Step 2 is the use of non-pharmacologic therapies + non-opioid pharmacotherapy.
 - Non-opioid pharmacotherapy should be considered for all types of acute pain where non-pharmacologic treatments are not effective or are not anticipated to be effective as monotherapy.
 - The two main types of non-opioid pharmacotherapy are topical therapy (usually indicated for patients with localized or regional pain and intact skin) and oral therapy (more indicated for patients with systemic/widespread pain who cannot use or did not respond to topicals).
 - Topical formulations include NSAIDs, lidocaine, methylsalicylate and capsaicin products.¹⁶³
 - Oral therapy includes acetaminophen, NSAIDs, and non-benzodiazepine skeletal muscle relaxants. Therapy should be chosen based on individual patient characteristics (e.g. type of pain, other medications, comorbidities).¹⁶¹
 - Step 3 is the use of non-pharmacologic approaches + non-opioid pharmacotherapy + short-term use (3-5 days) of short-acting opioids.
 - Opioids are no longer first-line treatments for most types of acute pain.
 - Generally, opioids should be considered for patients with severe acute pain only if the pain is not responding to nonpharmacologic or non-opioid treatments or if those treatments are not expected to be sufficient.
 - Not all patients with severe acute pain are good candidates for short-term opioid use. Contraindications to using opioids include life-threatening allergies to opioids, actively prescriptions and use of benzodiazepines, active substance use disorder and elevated suicide risk. An exception may be considered in patients with severe pain in an inpatient setting or controlled environment, but extra precautions would need to be taken to ensure safety.
- Treatment should focus on patient's return to function. When appropriate, clinicians should provide advice to stay active and at work, along with education about self-management.
- Acute pain can progress to chronic pain, and psychosocial factors can help predict the chronification. Prevention requires monitoring and potentially additional forms of treatment.
 - It can only take three days of opioid treatment to see an increase in the risk of acute therapy extending into long-term therapy.¹⁶⁴
 - The three most common and influential factors leading to pain chronification include catastrophizing (exaggerated and irrational thoughts about the pain the patient is experiencing, viewing pain as a serious threat to health and functioning), fear avoidance (avoiding physical activity and movement due to fear of pain and injury progression) and depressed mood.
 - Patients experiencing these psychosocial factors may benefit from psychology-based treatments, including cognitive behavioral therapy (CBT), acceptance and commitment therapy, and mindfulness-based stress reduction.¹⁶²

A2. Describe a whole-person treatment plan for a person with chronic pain.

- The National Pain Strategy recommends "a population-based, biopsychosocial approach to pain care that is grounded in scientific evidence, integrated, multimodal, and interdisciplinary, while tailored to an individual patient's needs."¹⁶⁵
- This approach begins by educating patients about chronic pain and the differences from acute pain. [See Component #7 for examples of patient-centered explanations of chronic pain.]
- Because chronic pain is a multidimensional issue, successful management requires addressing the whole person in an
 integrated fashion. Optimized, evidence-based treatment of common comorbidities (psychiatric conditions, insomnia,
 sleep apnea, obesity, diabetes, substance use disorders including tobacco use) is critical when treating patients with
 chronic pain.
 - Interdisciplinary pain rehabilitation has been shown to be the most effective and cost-effective treatment for patients with significant functional impairment due to pain.^{166 167}
 - One study demonstrated that optimized treatment of depression (optimized pharmacotherapy followed by a selfmanagement program) in patients with chronic musculoskeletal pain and depression not only improved depressive symptoms, but also resulted in moderate improvement in pain severity and disability.¹²²
 - There is evidence that integrated multimodal therapies are more effective than any single approach for maintaining long-term gains.¹⁶⁸
- Reevaluation of patients who are taking opioids for chronic pain should be done regularly in order to prevent adverse outcomes.
 - Patients on long-term opioid therapy should be reevaluated regularly for functional improvements, substance use, high-risk behaviors, and psychiatric comorbidities through face-to-face visits, prescription drug monitoring program checks, and urine drug tests.
 - There is a heightened risk for opioid use disorder in persons with concurrent substance use and psychiatric comorbidities.^{169 170 171}
 - Patients on long-term opioid therapy and providers prescribing long-term opioid therapy often fear that tapering will lead to
 worsening pain and function. Recent studies suggest that pain does not worsen and may improve along with function and
 quality of life with opioid tapering/discontinuation. Patients with either opioid use disorder or complex opioid dependence
 will likely require a different exit strategy (see last objective in *Component #5*).
- The primary goal of care for a patient with pain is maximizing function and minimizing pain-related suffering, rather than the elimination of pain.
- A view of living well with chronic pain can be adapted from the definition of recovery from substance use disorder -- "a
 process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach
 their full potential."¹⁷²
 - This concept of recovery is applicable beyond pain and addiction to many other chronic conditions.

A3. Discuss the difference between the use of active and passive therapies for a person with chronic pain.

- Enhancing self-efficacy though self-management strategies is the foundation of chronic pain care and the goal at every stage of treatment.
- The role of the medical system is to support self-efficacy and promote an internal locus of control. This is accomplished by emphasizing active treatments and judiciously using passive treatments as bridging therapies to help the patient adopt active strategies.

COMPONENT 5: PREVENTION AND TREATMENT FOR PAIN AND OPIOID USE DISORDER

- Active treatments are done by the patient and include self-care activities that promote physical (exercise, stretching, anti-inflammatory diet), mental (practicing mindfulness, implementing psychological coping skills), social (cultivating and spending time in supportive and caring relationships), and spiritual (spending time and energy participating in meaningful activities and in pursuit of values) health domains.
 - Active therapies can be grouped into exercise/movement therapies and psychological therapies. These have been shown to be effective at improving pain, function and quality of life in multiple chronic pain conditions.
 - Movement therapies are heterogenous and can include aerobic exercise, strength training, core strengthening, walking, cycling, dancing, swimming, Tai chi, and yoga.
 - Psychological therapies include cognitive behavioral therapy (CBT), acceptance and commitment therapy and mindfulness-based stress reduction.
- Passive treatments are done to the patient by the medical team and include medications, injections, invasive procedures, and surgery).
 - Passive therapies are myriad and should be used judiciously to support adoption of active therapies (listed above).
 Excessive use of passive therapies can lead to overreliance on the medical system and may perpetuate passive coping strategies, which are associated with negative mood and high levels of disability.¹⁹
 - Passive therapies should be recommended based on effectiveness, risk, and cost-effectiveness. Broad categories of
 passive therapies include 1) complementary and integrative health (CIH) approaches; 2) electrical and thermal stimulation
 therapies; 3) medications; 4) invasive procedures; and 5) surgeries.
 - Of note, it is possible to attend treatment sessions for "active treatments" and not implement changes in one's daily life (i.e. attend physical therapy but not implement a home exercise program). In this way, both exercise therapies and psychological therapies can become passive treatments.

A4. Discuss the evidence for the use of opioids for acute and chronic pain.

- Opioids should only be initiated for acute pain after weighing the benefits against the risks of use.
 - There is no absolute safe dose of opioids.
 - There is good evidence to use non-opioid medications and therapies as first-line treatment for mild and moderate acute pain.
 - Opioids have been shown to be effective for very short-term (3–5 days) treatment of severe acute pain (e.g., invasive surgery or significant trauma).^{88 173}
 - Due to the known risks associated with even short-term opioid medication use, the use of opioid medications should be limited to severe pain.
 - > The risks of opioid treatment for acute pain include the development of both adverse short and long-term outcomes.
 - The type, duration and dosage of early opioid exposure can affect chronic outcomes.¹⁶⁴
 - ▶ Evidence shows that the longer duration of early opioid exposure is associated with greater risks for long-term use.¹⁶⁴
 - Each additional day of unnecessary opioid use increases the likelihood of physical dependence without adding benefit.⁸⁸
 - There is a higher risk for overdose among patients who initiate treatment with extended-release/long-acting opioids than among those who initiate with immediate-release opioids.¹⁷⁴
 - Long-acting opioids are associated with an increased risk of all-cause mortality.¹⁷⁵
 - Long-term opioid use can result from opioids initially intended for short-term use.^{176 177}
- For chronic pain, long-term opioid therapy has not been shown to be associated with sustained improvement in pain or function when compared to placebo or other medications, but there is evidence of dose- and durationdependent harms.^{154 178 179}
 - A recent randomized controlled study for patients with moderate to severe chronic pain demonstrated modestly lower pain scores and half the rate of medication side effects with non-opioid medications compared to opioid medications at twelve months. Pain-related function was not significantly different between the two groups if opioids versus non-opioids were used.¹⁸⁰

- Risks to patients with the use of long-term opioid therapy include overdose, addiction, depression, opioid-induced hypogonadism, opioid-induced hyperalgesia, worsening function, and death.^{175 181}
 - Factors increasing the risk of adverse opioid-related outcomes include prescribed opioid dose, mental health comorbidities, and substance use disorder comorbidities.^{118 182 183}
 - ▶ Both short- and long-term opioid use carry the risk of opioid overdose.
- A Cochrane Review found good-quality evidence that use of opioids for greater than two weeks is associated with a significantly increased risk of experiencing an adverse event when compared to placebo and non-opioid pharmacotherapy. It also identified a high absolute rate (78%) for adverse events.¹⁸⁴
- Extended-release/long-acting opioids have not been proven to be safer or more effective than short-acting opioids for managing chronic pain.
- Discontinuing long-term opioid therapy does not appear to worsen pain intensity and opioid tapering may be associated with improvements in pain, function, and quality of life.¹⁸⁵

A5. Discuss the use of non-pharmacologic and non-opioid pharmacotherapy for acute and chronic pain.

- There is evidence that acute pain can be ameliorated by nonpharmacologic and non-opioid therapies, including psychological therapies, exercise treatments (aerobic exercise, physical therapy) and NSAIDs.^{167 175 187 188 189 190 191}
 - Due to their low harm, these therapies should be offered to all patients with mild or moderate pain.
- Exercise, an active therapy, has been shown to be effective at improving pain and function in multiple chronic pain conditions, including spine pain, osteoarthritis, and fibromyalgia.¹⁹² Exercise is also the only treatment that has been shown to prevent future episodes of back pain.¹⁹³
- Some musculoskeletal passive therapies also have relatively good efficacy.
 - Acupuncture has been shown to be safe and effective in many chronic pain conditions^{192 194 195} and is recommended by clinical practice guidelines in the treatment of chronic low back pain.¹⁹⁶
 - Spinal manipulation has been shown to improve pain and function in acute and chronic low back pain¹⁹² and is recommended as an initial treatment option in clinical practice guidelines.¹⁹⁶
 - Although a lower degree of evidence is available with mixed results, massage may provide short-term benefit for low back pain with potential for short-term benefit in other chronic pain conditions (e.g. fibromyalgia, neck pain, temporomandibular disorder, and shoulder pain.) Additional studies are needed.¹⁹⁷
- Psychological therapies have been shown to improve pain, function, and quality of life.^{192 198 199}
 - A systematic review found that biofeedback was more effective than waiting list controls for the treatment of migraine and tension-type headache, with the greatest impact on headache frequency, anxiety and medication consumption.²⁰⁰
- While active therapies are preferred, multiple non-opioid medication options are available and have some evidence of effectiveness.^{201 202} It is important to set realistic expectations about their effectiveness.
 - A recent systematic review evaluated medications for neuropathic pain and calculated the Number Needed to Treat (NNT) in order to achieve a 50% reduction of pain. The NNT indicates the number of patients needed to be treated in order achieve that predetermined outcome.²⁰³
 - NNT for TCA: 3.6 (i.e. For every 3.6 patients treated with a TCA, 1 patient will experience a 50% reduction in pain; 2.6 patients will not.)
 - NNT for SNRI: 6.4 (i.e. for every 6.4 patients treated with a SNRI, 1 patient will experience a 50% reduction in pain; 5.4 will not.)
 - NNT for pregabalin: 7.7 (i.e. for every 7.7 patients treated with pregabalin, 1 patient will experience a 50% reduction in pain; 6.7 will not.)
 - NNT for gabapentin: 7.2 (i.e. for every 7.2 patients treated with gabapentin, 1 patient will experience a 50% reduction in pain; 6.2 will not.)
 - There are multiple adverse effects of these medications and they should not be universally employed. Individual patient characteristics must be considered when prescribing.

- There is evidence that NSAIDs have some benefit for acute and chronic pain, but have risks associated with their use, including gastrointestinal, cardiac, and renal effects.
 - A Cochrane Review found that NSAIDs reduced pain and disability in people with chronic low back pain compared to placebo, with small effect sizes.²⁰⁴ Other reviews state that NSAIDs are effective treatment for acute renal colic²⁰⁵ and dysmenorrhea.²⁰⁶
 - A recent study of moderate-severe acute extremity pain treated in the emergency department found that a single dose of ibuprofen 400mg was non-inferior to 5mg of oxycodone or hydrocodone (each combined with acetaminophen).²⁰⁷
- Anticonvulsants appear somewhat effective in treating migraine and neuropathic pain.
 - Gabapentinoids (gabapentin and pregabalin) have evidence supporting their effectiveness in neuropathic pain and fibromyalgia. They may also be helpful in pain conditions with significant central sensitization. Increased prescriptions rates have raised concerns about the possible abuse of gabapentinoids, as well as concerns for increasing opioid-related adverse events.²⁰⁸
 - ▶ A metanalysis has demonstrated that topiramate can be effective in reducing headache frequency.²⁰⁹
 - A Cochrane Review found that carbamazepine is probably effective in some people with chronic neuropathic pain, particularly facial pain, but needs longer trials.²¹⁰ Carbamazepine is associated with rare but potentially serious side effects (agranulocytosis, aplastic anemia, Stevens-Johnson syndrome).
- Antidepressants have shown some effectiveness in several chronic pain conditions.
 - Tricyclic antidepressants (TCAs) have been shown to be effective in a number of chronic pain conditions including neuropathic pain conditions, fibromyalgia, headache, and possibly chronic visceral pain syndromes. Side effects are common and dose-related and include dry mouth, constipation, urinary retention (often severe in men with prostatic enlargement), QT prolongation, cardiac arrhythmias, and increased intraocular pressure in patients with glaucoma.) Doses used for chronic pain are typically less than the typical antidepressant doses in order to avoid side effects. TCAs should generally be avoided in the elderly and individuals with cardiac disease or at significant risk for suicide (due to potential lethality with intentional overdose.)
 - Selective serotonin reuptake inhibitors (SSRI) medications have been shown to be effective in neuropathic pain conditions, fibromyalgia, and headache.²¹¹
 - Duloxetine has been shown to be effective in the treatment of painful diabetic neuropathy, fibromyalgia and more recently chronic low back and osteoarthritis.^{212,213}
- Topical anesthetics are useful agents when used as part of multimodal analgesia.
 - There is mixed evidence of effectiveness for use topical lidocaine for neuropathic pain conditions.²¹⁴
 - A Cochrane Review found that there is moderate-quality evidence that high-concentration capsaicin patches can give moderate pain relief to a minority of people with postherpetic neuralgia.²¹⁵
 - A Cochrane Review found that topical diclofenac and topical ketoprofen can provide good levels of pain relief in osteoarthritis.²¹⁶
- A Cochrane Review found that muscle relaxants can provide short-term relief for acute non-specific low back pain, but the incidence of adverse effects require that they be used with caution.²¹⁷
 - The use of carisprodol is not recommended given the presence of the metabolite meprobomate, a barbiturate with abuse potential.
- Invasive procedures include epidural steroid injections, radiofrequency denervation and surgeries.
 - Injections may provide short-term analgesia for well-selected patients to facilitate physical therapy, but evidence for significant improvements in long-term outcomes in limited.
 - Epidural steroid injections are the most commonly performed procedures for pain in the United States.
 - Use of epidural steroid injections increased from 1994 to 2001 by 271% and their inflation-adjusted costs increased by 629% during that same time period.²¹⁸
 - The evidence for effectiveness for epidural steroid injections is limited. There has been no benefit found in pain, function, or likelihood of surgery for nonradicular low back pain and spinal stenosis. A small benefit of unclear clinical significance in pain and function was noted to last two weeks for radiculopathy.²¹⁹
 - Radiofrequency denervation is also commonly performed for chronic nonspecific low back pain thought to be due to facet joint pain. A recent Cochrane Review found no high-quality evidence suggesting this procedure provides pain relief and did not find convincing evidence of functional improvement.²²⁰
 - While criticized by a statement from multiple pain societies, a subsequent multicenter trial published in JAMA demonstrated no improvement in pain when radiofrequency denervation was added to a structured exercise program for patients with chronic low back pain.²²¹
 - Surgical neuroablative techniques of the spinal cord pain pathway are mainly used to treat cancer pain. Evidence supporting destructive procedures for non-cancer pain conditions remains limited.²²²

COMPONENT 5: PREVENTION AND TREATMENT FOR PAIN AND OPIOID USE DISORDER

A6. Understand the regulatory requirements when treating pain and/or prescribing opioids for a patient with acute and chronic pain.

- Nationally, federal agencies work to reduce the supply of illicit substances (DEA), monitor illegal "pill mills", and impact the marketing and approval for pharmaceutical opioids (FDA).
 - For individual practitioners, there are more federal requirements for prescribing the treatment for opioid addiction than there are for prescribing opioids.
- In Arizona, there are several key pieces of legislature that affect the prescribing practices from health-care systems to individual providers. [Note: This high-level summary does not serve as legal counsel or advice; reading of the exact language is encouraged and/or consultation with the appropriate licensing board or counsel.]
 - [Arizona Revised Statues § 36-2606]²²³ Highlights: Medical practitioners licensed under Title 32 must check the prescription drug monitoring database before prescribing an opioid or benzodiazepine listed in schedule II, III or IV. Exceptions are listed in the statute.
 - [Arizona Opioid Epidemic Act / Senate Bill 1001]²²⁴ Highlights: Prescribing limits, e-prescribing and continuing medical education.
 - Providers cannot provide new prescriptions for opioid naïve patients that exceed 90 MME per day. There are exceptions listed in the bill, including for cancer, end-of-life care and medication-assisted treatment.
 - Providers cannot provide an initial prescription (any substance dispensed to the patient during the previous 60 days, confirmed by the prescription drug monitoring program) of more than a five-day supply of a Schedule II opioid controlled substances. There are exceptions listed in the bill.
 - E-prescribing is required to dispense Schedule II controlled substances that are opioids.
 - Healthcare professionals are prohibited from dispensing Schedule II controlled substances that are opioids.
 - Healthcare professionals that are authorized to prescribe Schedule II controlled substances or individuals who are authorized to dispense (pharmacists) controlled substances must complete a minimum of three hours of opioidrelated continuing medical education each license renewal period as part of their existing requirements.
 - [Arizona Revised Statutes § 36-405 § 36-406]^{225 226} Highlight: Arizona licensed healthcare facilities must adhere to the Licensing Rules for Healthcare Institutions, now updated to include regulations on opioid prescribing and treatment.
 - These requirements include checking the prescription drug monitoring database, obtaining informed consent, and more.
 - [Arizona Opioid Epidemic Act/ Senate Bill 1001 and 9 A.A.C. 10 Article 20] ^{39 224} Highlight: As of 2019, Pain management clinics are licensed by the Arizona Department of Health Services.
 - A pain management clinic is defined as a healthcare institution of private office or clinic in which a majority of patients in any month are prescribed opioids, benzodiazepines, barbiturates or carisoprodol for more than 90 days in a 12-month period, and does not include medication-assisted treatment.
 - [Arizona Medical Marijuana Act]²²⁷ Highlight: As a result of a voter initiative, chronic pain is listed as a debilitating medical condition that qualifies for medical marijuana in Arizona.
 - ▶ The federal government considers marijuana a Schedule I substance and does not recognize its medicinal use.
 - Multiple states have varying legislation regarding the recreational and medical use of marijuana. In Arizona, qualifying patients with specified debilitating medical conditions (listed in the Act) can seek a written certification from a physician and submit an application for a registry identification care to possess and use medical marijuana.²²⁸
 - ▶ The conflict between state and federal law creates uncertainty for clinicians.
 - The Centers for Disease Control and Prevention states there is "limited evidence that marijuana works to treat most types of chronic pain." More research is needed to know how marijuana compares to other options for managing chronic pain.^{229 230}
 - In general, the Arizona Licensing Boards have authority over individual providers and the practice of medicine and healthcare; the Arizona Department of Health Services has authority over licensed institutions.

A7. Describe a multimodal treatment plan for a person with opioid use disorder.

- Treatment of opioid use disorder requires a whole-person approach, addressing social, psychological and biological aspects of disease. The treatment course is lifelong.
 - The clinical course of opioid use disorder involves periods of relapse and remission, and it is likely that the underlying
 vulnerability never disappears. This is similar to other chronic relapsing conditions like diabetes and hypertension, in which
 cure is rare, complete control of symptoms is difficult, and patient adherence to treatment is often incomplete.
 - Although persons with opioid use disorder are likely to have extended periods of abstinence from opioids and often do
 well, the risk of early death (primarily from an accidental overdose, trauma, suicide, or an infectious disease) is increased by
 a factor of 20. This risk of adverse outcomes decreases markedly with use of pharmacotherapy for opioid use disorder.²³¹
 - The goal of treatment for opioid use disorder is remission, leading to lasting recovery. Recovery is a process of change through which individuals improve their health and wellness and strive to reach their lives' full potential.³⁸
 - This treatment course must be explained to patients and their expectations must be addressed.
- Psychosocial therapies should be individualized for each patient. For patients who are in the pre-contemplative and contemplative stages of change, motivational enhancement approaches should be employed to facilitate readiness to change. For patients who express interest in discontinuing or diminishing drug use, the crux of care depends on the same kinds of cognitive behavioral approaches that are used for other chronic, relapsing conditions.
 - These approaches include working with patients to encourage motivation to change, enhance adherence to medication through education, reward cooperation with treatment, keep motivation high and teach ways to minimize relapse to drug use.²³¹
 - Multiple clinical trials demonstrate that focus on psychosocial treatments alone for opioid use disorder (in the absence of pharmacotherapy) result in high rates of relapse to use opioid within the first year, often with fatal consequences.^{232 233 234 235}
- Pharmacotherapy for opioid use disorder is effective and should be offered to all patients with opioid use disorder.
 - Pharmacotherapy for opioid use disorder is underused.
 - A common misconception associated with pharmacotherapy for opioid use is that it substitutes one addiction for another. In fact, these medications help stabilize the neurobiological imbalances present in opioid use disorder which allows patients to engage more fully in their recovery.²³⁶
 - ▶ Methadone and Buprenorphine can reduce and eliminate withdrawal symptoms.
 - ▶ Methadone, naltrexone and buprenorphine can blunt or block the effects of illicit opioids.
 - ▶ Methadone, naltrexone and buprenorphine can reduce or eliminate cravings for opioids.
 - Pharmacotherapy can reduce illicit use, dramatically increase treatment retention (compared to placebo, medicallysupervised withdrawal and no treatment).
 - Methadone has been shown to reduce the risk of HIV and HCV infection, to lower rates or cellulitis, and to reduce criminal behavior.
 - Pharmacotherapy can reduce opioid overdose deaths and all-cause mortality,²³⁷ compared with psychosocial treatment alone.
 - The main pharmacologic agents used for opioid use disorder include methadone (Methadose[®], Dolophine[®]), buprenorphine (Suboxone[®], Subutex[®]) and naltrexone (Vivitrol[®]). Methadone and Buprenorphine are opioid agonists; naltrexone is an opioid antagonist.
 - Methadone was the first FDA-approved medication for opioid use disorder. It comes in oral form, and can only be ordered, administered and dispensed in Opioid Treatment Programs (OTPs).
 - Buprenorphine is the first medication to treat opioid use disorder that can be prescribed or dispensed in DATAwaivered physician offices. It has excellent evidence of efficacy, and leads to higher retention in treatment, suppression of illicit opioid use, and lower overdose mortality. It is primarily used in a sublingual/buccal form. The risks associated with it include overdoses, (especially if taken with depressant drugs) and diversion.
 - Buprenorphine is now a mainstay of opioid use disorder treatment, and its pharmacology and use are key learning objectives in medical schools.
 - [See *Appendix D* for the clinical use of buprenorphine for opioid use disorder.]
 - Naltrexone is an oral or IM medication, but while it effectively suppresses illicit opioid use, it has an unknown effect on overdose mortality and leads to no better patient retention in treatment (unless using injectable).
 - The duration of therapy for opioid use disorder should be considered indefinite. There is a high rate of relapse and overdose deaths after leaving treatment programs.

- Monitoring of progress toward treatment goals helps to coordinate care and to motivate the patient and the treatment team to identify the gaps and provide opportunities to address emerging problems and change treatment strategies.
 - Indicators of treatment response include patient engagement with important life domains (e.g. family, interpersonal, work, health) and progress toward personal goals.
 - It is helpful to keep key family and other recovery supports. They can attend appointments and discuss how the patient's social network can support progress and treatment goals.
 - Clinicians need to ensure treatment of medical and mental health comorbidities, by providing or referring for evidencebased treatments as indicated.
- Patients should be educated about relapse prevention.
 - Patient should be taught that relapse is a process, with attitudinal, emotional, and behavioral changes that begin to appear in the time leading up to a potential return to substance use.
 - Team members should work with the patient to identify triggers for relapse and coping strategies to either avoid or manage these situations.
- Patients should be encouraged to participate in peer recovery or other social support groups focused on recovery. Patients can find a group that is welcoming to individuals using pharmacotherapy for opioid use disorder as some peer recovery groups may pressure people to stop using pharmacotherapy for opioid use disorder.
- Naloxone should be prescribed to patients and its use explained to family and social support.
 - Naloxone is a key aspect of opioid use disorder treatment. It is a medication approved by the FDA to reverse an overdose by opioids by blocking opioid receptor sites, and can be administered through an injection or nasal inhaler. Families and social support should have naloxone in case of a person's overdose.
 - Naloxone administration has been identified as a life-saving measure following opioid overdose. It is not an over-thecounter medication but many states (including Arizona) have it available through standing orders at pharmacies, so anyone can access it without a specific prescription from their provider.
 - There is moderate evidence that take-home naloxone programs are effective at improving overdose survival and decreasing mortality and it is plausible that effectiveness would be observed in the clinical setting as well.²³⁸
 - Clinicians should consider offering opioid overdose education and naloxone prescriptions for the following groups:
 - All patients receiving long-term opioid therapy
 - All patients who have recently discontinued use of long-term opioid therapy (within the past year)
 - All patients diagnosed with opioid use disorder
 - Particular attention should be given to patients at elevated risk for opioid related overdose including: those with a prior opioid overdose, those with opioid use disorder or substance use disorder, those with a higher prescribed opioid dosage, those with mental health conditions, those who use opioids in combination with other sedating substances, those who have other conditions such as HIV, liver or lung disease, or household members of people in possession of opioids.^{175 259}
 - In Arizona, it is a requirement for providers to prescribe naloxone or other opioid antagonist along with any new and continuing prescription given for over 90 MME. [See *Component #5* for further details on the Arizona Epidemic Act and other legislation.]

A8. Understand the state and federal regulations when treating opioid use disorder.

- Pharmacotherapy for opioid use disorder is governed by Federal Regulation 42 CFR Part 8.
 - Buprenorphine, methadone and naltrexone for opioid use disorder are regulated differently.
 - Federal regulations require methadone-maintenance therapy for opioid use disorder to be performed in Opioid Treatment Programs (OTPs), which must be accredited and SAMHSA-certified.
 - Individual healthcare practitioners are able to prescribe buprenorphine in any medical setting (not just in Opioid Treatment Programs), as long as they receive waivers of the requirements defined in the Controlled Substances Act by meeting the requirements of the Drug Addiction Treatment Act of 2000 (DATA 2000) and the revised Comprehensive Addiction and Recovery Act (CARA). [See Component #1 for the history of and eligibility requirements for the DATA waiver.]

- There are a few exceptions to the requirement to provide methadone (through an OTP) or buprenorphine (through an OTP or waivered practitioner). These include 1) administering an opioid (not prescribing) for no more than three days to a patient in acute opioid withdrawal while doing preparations for ongoing care and 2) administering opioids in a hospital to maintain or detoxify a patient as an adjunct treatment for other conditions.³⁸
- ▶ Naltrexone can be prescribed by any health care provider who is licensed to prescribe medications.
- Healthcare providers with an MD, DO, NP, or PA license can learn how to obtain
- a waiver online: www.samhsa.gov/medication-assisted-treatment.
- While DATA-2000 allows waivered physicians to prescribe pharmacotherapy for opioid use disorder in any office setting, there are limitations to how many patients they can treat. Eligible physicians, nurse practitioners and physician assistants can treat up to 30 patients in their first year of the waiver, and can increase to 100 in the second year. This regulation was adjusted in 2016 to allow qualifying physicians to apply for permission to treat up to 275 patients after two years of treating patients with opioid use disorder. This legislation does not increase the cap for NPs or PAs.
- There are also unique federal confidentiality protections defined by 42 CFR Part 2.²³⁹ These regulations apply to any individual or entity that is federally assisted and holds itself out as providing alcohol or drug abuse diagnosis, or treatment or referral services.
 - 42 CFR Part 2 restricts disclosure of any information from a covered program that identifies an individual directly or indirectly as having a current or past drug or alcohol problem.
 - Exceptions include internal communications, anonymous or non-patient identifying information, crimes on premises or against personnel, medical emergencies, mandated reports on child abuse or neglect, research, special court orders and others.
 - This lack of disclosure means that providers are often not aware if patients are receiving detoxification or maintenance treatment from an Opioid Treatment Program as medications prescribed by the Opioid Treatment Program do not appear in state prescription drug monitoring programs. This unfortunately can act as a "blind spot" for providers providing care for pain or other aspects of a person's health.
- No other medications have such restrictions on use or stringency on privacy.
- In Arizona, licensing and legislative bills impact opioid use disorder diagnosis and management.
 - [Arizona Opioid Epidemic Act / Senate Bill 1001]²²⁴ Highlights: Good Samaritan Act, Sober Living Homes, and Referrals after an overdose.
 - Sober living homes are required to develop policies and procedures to allow individuals on medication-assisted treatment to continue receiving the treatment while living in a structured sober living home.
 - Health plans are required to allow at least one medication-assisted treatment option to be available without prior authorization.
 - There is immunity from prosecution for persons who in good faith seek medical assistance for someone who experiences an overdose or to persons experiencing an overdose.
 - Ancillary law enforcement employees are now added to the list of persons authorized to administer naloxone or other opioid antagonist through a standing order.
 - Healthcare institutions are required to refer a patient who is discharged after receiving emergency services for a drug-related overdose to a behavioral health services provider.
 - If a patient is issued a new prescription above 90 MME per day, the prescriber must also prescribe naloxone or other opioid antagonist.
 - [9 A.A.C. 4 Article 6]²⁴⁰ Healthcare professionals must report a suspected opioid overdose to the Arizona Department of Health Services within five business days.

A9. Describe the process of coordinating care and arranging for a higher level of care for a person with opioid use disorder.

- All clinicians should discuss with their patients the benefits and risks of pharmacotherapy for opioid use disorder as well as the risks and benefits of alternative treatments.
 - The use of medication-assisted treatment (MAT) is not substituting one addiction for another; medication-assisted treatment decreases opioid craving and resolves opioid withdrawal.
 - Medication-assisted treatment (MAT) should be explained as being effective and that it decreases opioid use and opioidrelated deaths.

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- Methadone (and sometime buprenorphine) is dispensed daily at opioid treatment programs (OTPs), buprenorphine (Suboxone[®] and Subutex[®]) is an office-based treatment, and both can assist patients with living full and engaged lives.
- If a decision is made to pursue pharmacotherapy and the clinician is unable to prescribe buprenorphine, it is crucial to coordinate and arrange for appropriate care for the individual.
- All clinicians should discuss with their patients the benefits and risks of pharmacotherapy.
- Clinicians need to facilitate smooth, directional transitions between the current treatment setting and the center providing medication-assisted treatment.
 - · Clinician should contact the local or appropriate treatment program to facilitate each patient's transition.

A10. Address the management of acute pain in special populations, including persons in the pre- and post-operative periods, perinatal periods, the elderly, the pediatric population and those with substance use comorbidities.

- In the perioperative period, there are special considerations for analgesia and the prevention of adverse outcomes.
 - Several studies have found that post-operative opioid prescriptions can be reduced without compromising post-operative pain control or increasing the number of requests for a refill.²⁴¹
 - A systematic review found that post-operative prescription opioids often go unused, unlocked and undisposed.²⁴²
 - More than ²/₃ rds of patients reported unused prescription opioids following surgery, consistent across several studies of general, orthopedic, thoracic and obstetric inpatient and outpatient surgeries.²⁴²
 - The following recommendations were created by surgeons and anesthesiologists for perioperative safety and pain control:
 - Preoperative patient education must be given, addressing realistic expectations about pain and healing after surgery, norms of opioid needs, the use of non-opioid, information about adverse events from opioids, and safe disposal of opioids.²⁴³
 - ▶ There are several recommended analgesic strategies.
 - Multimodal analgesia is indicated for the treatment of postoperative pain, including nonpharmacologic options, NSAIDs and/or acetaminophen, anticonvulsants.
 - Other perioperative strategies include use of gabapentinoids immediately prior to surgery, long-acting local anesthetics, and regional anesthesia.
 - Procedure-specific opioid prescription strategies have been developed. Online tools such as Michigan-open.org can guide post-operative prescribing habits.^{243 244}
 - It is not necessary to provide enough pain medications to "tide someone over;" clinicians should prescribe what is medically necessary.
 - For opioid-tolerant patients undergoing elective surgery, consultation with pain medicine or addiction specialists is encouraged.
- For women of reproductive age, opioid therapy is generally avoided for chronic non-terminal pain. Evidence-based non-pharmacologic and non-opioid pharmacotherapy should be optimized.
 - Reproductive plans and the risk of neonatal opioid withdrawal syndrome (NOWS, a specific form of neonatal abstinence syndrome) and other adverse neonatal outcomes should be discussed with women of reproductive age before prescribing an opioid.
 - Additionally, for women of reproductive age, contraceptive counseling and access to contraceptive services should be a routine part of substance use disorder treatment to minimize the risk of unplanned pregnancy.
 - In 2017, the American College of Obstetrics and Gynecology and the American Society of Addiction Medicine published a *Committee Opinion* to avoid or minimize the use of opioids for chronic pain management in pregnancy and to highlight alternative pain therapies such as non-pharmacologic and non-opioid pharmacologic treatment.²⁴⁵
 - Studies have shown an association of opioid use in pregnancy with birth defects, including neural tube defects, congenital heart defects, gastroschisis, preterm delivery, poor fetal growth, stillbirth and neonatal opioid withdrawal syndrome.²⁴⁶

- For older adults, chronic or persistent pain is a common problem. Treatment recommendations are based on the differences in the effectiveness and toxicity of opioid therapy due to the age-related alterations in drug absorption, distribution, metabolism and excretion.
 - Nonpharmacologic therapies and topical therapies are the first-line treatment for management of acute pain.
 - Opioids should be avoided if there is a history of falls or fractures, unless it is being used for recent fractures or joint replacement.
 - If opioids are indicated, it is important to anticipate, assess for and identify potential opioid-associated adverse effects.²⁴⁶
 - If opioids are being used, clinicians should reduce the use of dosage of other CNS medications.
 - Polypharmacy (use of multiple drugs or more than are medically necessary) is a growing concern for older adults. The burden of multiple medications has been associated with greater healthcare costs and an increased risk of adverse drug events, drug-interactions, reduced functional capacity, and multiple geriatric syndromes. Opioids and other non-opioid medications for pain can particularly have negative effects in combination with other drugs.
- There are two primary areas of concern with pediatrics: the accidental opioid poisonings of young infants and children, and the exposure/experimentation that may lead to ongoing opioid use and opioid use disorders in adolescents.
 - Cohort and survey studies have found that opioid use disorder is a leading cause of morbidity and mortality among U.S. youth.²⁴⁷
 - Parents need to be counseled about the need for safe storage of their own opioids and controlled substances. Most adolescents who misuse opioids often access them through a friend or family member.²⁴⁸
 - For acute pain management, opioids should only be used for moderate or severe pain, or for pain that is refractory to nonopioid analgesics.
 - Opioids are not recommended to treat most types of chronic pain in pediatric patients. The pediatric population may
 have unique vulnerabilities and inappropriate and/or prolonged exposure to opioids may lead some to develop misuse of
 prescription opioids or addiction.
 - The use of prescribed opioids before the 12th grade is independently associated with future opioid misuse among patients with little drug experience and the vast majority of substance use is initiated in adolescence.^{249 250 251 252}
 - The use of opioids to treat chronic pain may lead to opioid-induced hyperalgesia and catalyze the sensitization process, leading to progression of the child's pain.
 - ► A multimodal approach to treat chronic pain in pediatric patients is indicated: non-opioid supplements, integrative medicine techniques and physical therapy are recommended.
 - Pediatric patients with chronic pain can be referred to psychology to decrease catastrophizing, provide coping mechanisms and teach relaxation and distraction techniques.
 - Family therapy is useful, and nutrition and daily exercise should be incorporated into the treatment plan.
- For individuals with substance use comorbidities, the treatment of acute and chronic pain can be more complex.
 - There is an increased risk of poor outcomes including opioid overdose, opioid use disorder and death for patients taking opioids that have substance use disorders or behavioral health conditions.^{176 177 253 254 255}
 - For acute severe pain from major trauma or surgery, opioid medications can be administered in the acute care setting with caution and close follow-up. For patients dependent on prescribed or illicit opioids, higher than usual doses opioid medications will be required.
 - For the treatment of chronic pain, long-term opioid therapy should be avoided. The recommendation against the use of long-term opioid therapy for patients with substance use disorders is supported by at least five large studies and national recommendations.¹⁷⁷ ¹⁷⁸ ¹⁷⁹ ²⁵⁴ ²⁵⁵
 - > Treatment of pain in these patients should optimize non-pharmacologic and non-opioid pharmacotherapy.
 - For patients already receiving long-term opioid therapy who are diagnosed with an untreated substance use disorder, clinicians should monitor closely, offer or arrange for substance use disorder treatment, and proceed with an exit strategy from the use of long-term opioid therapy. If the patient has an opioid use disorder, then pharmacotherapy for opioid use disorder should be strongly considered.

B. MESSAGE: Specific attention must be given to prevention and risk mitigation strategies as part of a treatment plan for acute pain, chronic pain and/or opioid use disorder.

B1. Demonstrate ability to implement risk mitigation strategies to prevent adverse outcomes from the use of opioid therapy for chronic pain.

- For patients on long-term opioid therapy, informed consent should be documented and risks regularly reevaluated.
 - The degree of risk associated with long-term opioid therapy warrants informed consent. Informed consent should be obtained prior to initiation and following any changes to the treatment plan.
 - A risk assessment should be performed prior to initiating or continuing opioid therapy in patients with chronic pain. Existing tools have limitations of their usefulness due to low sensitivity (e.g. Opioid Risk Tool). A clinical assessment for known risk factors should be performed, ncluding prior and current medical, psychiatric and substance use disorder morbidities, and high risk opioid-related behaviors (e.g. not taking medications as prescribed, obtaining controlled substances from multiple sources, lost/stolen prescriptions, and non-concordant results on urine drug testing and query of the prescription drug monitoring database.)
- If opioids are used to treat acute or chronic pain, opioids should be prescribed at the lowest possible dose and for the shortest possible time.
 - There is no absolutely safe dose of opioids.256
 - Risk for opioid use disorder increases with duration and dose.^{166 178 179}
 - Risk of prescription opioid overdose and death exists even at low opioid dosage level and increases with prescribed dose.
 - Opioid dosages between 50-99 MMEs have been found to increase risks for opioid overdose by factors of 1.9-4.6 compared with dosages <20 MMEs. Dosages >100 MMEs are associated with increased risks of overdose 2-8.9 times the risk at <20 MMEs.^{176 177 254 257}
 - Because lower dose opioid therapy is much more prevalent than high-dose opioid therapy, higher numbers of opioid overdose deaths occur with lower opioid doses.²⁵⁸ Mental health and substance use disorder comorbidities appear to be particularly strong risk factors for adverse opioid related events including overdose.
 - Long-term opioid therapy should not be used in patients with untreated substance use disorders. [See *Component #2* for the increased risk of poor outcomes in this population.]
- Patients should be counseled on safety, including safe storage and disposal of medications and not sharing
 opioids with others.
 - Some of the dangers from opioid used can extend from the patient into the public.
 - Household members of persons in possession of opioids are themselves at increased risk of an opioid overdose.²⁵⁹
 - Children are in danger of initiating opioids or having opioid poisoning.260
 - The public is at risk from a driver than is impaired.²⁶¹
 - · Sharing of controlled substances is a felony, subject to imprisonment or fines.
- Patients on long-term opioid therapy should be reevaluated at least every 90 days for functional improvements, substance use, high-risk behaviors, and psychiatric comorbidities.
 - This can be done with face-to-face visits, prescription drug monitoring database checks and urine drug tests.
 - There is a heightened risk for developing opioid use disorder in patients who take opioids for more than 90 days.^{262 263}
 - There is a heightened risk for opioid use disorder in persons with concurrent substance use and psychiatric comorbidities.^{169 170 171}
 - While there is no clear evidence that urine drug testing improves outcomes, it can help identify patients with substance use disorders and other high-risk behaviors so that evidence-based therapy and risk mitigation strategies can be implemented.
- Opioids and benzodiazepines should not be used together. Concurrent use of opioids and benzodiazepines has an FDA Black Box Warning, the FDA's strongest warning, against it.²⁶⁴
 - Both opioids and benzodiazepines cause central nervous system depression and can decrease respiratory drive, and their combined use is associated with a 4-10 fold increased risk of opioid overdose and death.^{265 266 267} The greatest risk is associated with the use of higher doses of opioids.²⁶⁸

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- Particular caution should be exercised when opioids are used with other sedatives/hypnotics.
- Many patients with chronic pain have other psychological comorbidities. It is important to note that there is a lack of evidence of efficacy for benzodiazepines in the management of PTSD or chronic anxiety.²⁶⁹
- Patients who are receiving concurrent opioid and benzodiazepine therapy need to be assessed for exiting or tapering
 one or both agents, but abrupt discontinuation is not recommended. Abrupt discontinuation of benzodiazepines may be
 associated with serious adverse events, including seizures and death.
- The Arizona Controlled Substances Prescription Monitoring Program should be checked before initiating an opioid or benzodiazepine, and then regularly thereafter.
 - Checking the Arizona Controlled Substances Prescription Monitoring Program before prescribing is good medical practice and a mandate under Arizona Revised Statutes.
 - Data comparing states with an implemented prescription database compared to states without one showed 1.55 fewer deaths per 100,000 people.²⁷⁰
- All patients using opioids are at risk for developing an opioid use disorder²⁵⁶ and longer duration of therapy and higher dose
 prescriptions are associated with a higher risk of developing opioid use disorder. Longer duration of therapy and higher
 dose prescriptions are associated with a higher risk of developing opioid use disorder.¹⁷⁸
 - Patients taking long-term opioids (and short-term) should be assessed for opioid use disorder and treatment should be
 offered or arranged if diagnosed. There is strong evidence to support the use of opioid agonist therapy (i.e. methadone of
 buprenorphine) for patient with opioid use disorder.

B2. Recognize the clinical presentation of opioid withdrawal and know clinical and community resources to address it.

- Opioid withdrawal can be very uncomfortable and distressing, but it is rarely a medical emergency (except in pregnant women and in neonates).
 - Prolonged use of opioid medications (several weeks or longer) produces a state of physical dependence, a physiologic adaptation that manifests as a characteristic opioid withdrawal syndrome upon abrupt discontinuation or sudden decrease in dose of opioids.²⁷¹
 - The withdrawal syndrome can be thought of as experiencing gastroenteritis, severe influenza, arthritis, fibromyalgia, anxiety, impending doom, insomnia, and dysphoria all at the same time.

The classic phrase is: "Opioid withdrawal does not kill you, but you can feel like you are going to die."

- Symptoms of opioid withdrawal are generally opposite to the acute effects of opioids and can include autonomic symptoms (sweating, tachycardia, myoclonus), anxiety, dysphoria, lacrimation, rhinorrhea, myalgias, sleep disturbances, nausea, abdominal cramping and diarrhea) and can be quantified by using the Clinical Opiate Withdrawal Scale (COWS). [See Appendix B for this and other clinical tools for pain and addiction.]
- Symptoms after discontinuation of shorter-acting opioids (e.g. heroin) begin within hours after receiving the prior dose and usually decrease after 7-10 days, whereas with misuse of longer-acting opioids, withdrawal begins after several days.
- Acute withdrawal symptoms are often followed by weeks to months of a protracted withdrawal syndrome that include anxiety, depression, fatigue, anhedonia, sleep disturbances, dysphoria irritability, and pain.²⁷²
- Opioid withdrawal can and should be effectively managed with both pharmacologic and non-pharmacologic approaches (e.g. meditation, relaxation, deep breathing).^{154 163 273 274 275}
 - Withdrawal symptoms should not be treated with an opioid or benzodiazepine.
 - Treatment of acute opioid withdrawal (called medically-supervised withdrawal and formerly referred to as detoxification) should not be performed in isolation. Patients who complete medically-supervised withdrawal usually return to use of opioids, are at higher risk for opioid overdose (due to loss of tolerance), and rarely complete recommended treatments.³⁸ [See TABLE 4.]
 - Treatment of acute opioid withdrawal should always occur in the context of a long-term treatment plan, usually with pharmacotherapy for opioid use disorder. If a patient declines opioid agonist therapy with buprenorphine or methadone, he or she should be offered Injectable Extended-Release Naltrexone (XR-NTX), which can be started after 7-10 days of abstinence.
 - If patient declines all pharmacotherapy, encourage close monitoring, intensive psychosocial therapy, and communicate to the patient that pharmacotherapy is always a future option.

TABLE 4: Treatment of opioid withdrawal symptoms

Indication	Treatment Options
Autonomic symptoms (sweating, tachycardia, myoclonus)	First line: Clonidine; Alternatives: Baclofen, Gabapentin, Tizanidine
Anxiety, dysphoria, lacrimation, rhinorrhea	Hydroxyzine, Diphenhydramine
Myalgias	NSAIDs, Acetaminophen, Topical medications like menthol/methyl salicylate cream, lidocaine cream/ointment
Sleep disturbance	Trazodone
Nausea	Prochloperazine, Promethazine, Ondansetron
Abdominal cramping	Dicyclomine
Diarrhea	Loperamide, Bismuth subsalicylate

- Withdrawal symptoms can be minimized or avoided with gradual tapers.
- Community resources exist to help with guiding clinicians in treating withdrawal and to help patients find care and support during withdrawals.

B3. Design strategies to prevent the progression from acute pain to chronic pain and pain-related disability.

- Most episodes of acute pain resolve as the underlying injury or disease heals, however any painful condition can lead to the chronification of pain. [See Component #1 for the risk factors for progression; See Component #4 for the neurological changes involved.]
- There is limited evidence to guide strategies to prevent pain chronification, but early identification of risk factors and treatment with evidence-based therapies is advisable.
 - When psychosocial risk factors are identified in the presentation of an acute injury, evidence-based therapy and support should be applied early in the course of treatment and excessive use of passive invasive procedures should be avoided.
 - Early intervention includes advice to stay active and return to usual activity as soon as possible, reassurance and use of language that supports recovery rather than fear (e.g. avoid medicalizing terms such as "degenerative disc disease" in favor of terms such as "age-related changes.") [See *Component* #7 for example language.]
 - When pre-operative risk factors are identified, consider delaying or avoiding elective surgery on a painful body part if the surgery is not medically required (e.g. total knee arthroplasty in a patient with BMI 35, depression, fibromyalgia, and high degree of catastrophizing).
- More research is needed into the strategies that would prevent pain-related disability.²³
 - Constructs from Positive Psychology (the study of strengths that enable individuals and communities to thrive) suggest that resilience and coping resources might protect against the development of disability in patients.²⁴
 - Resilience can involve a set of personal, social or societal protective factors that lead to the successful adaptation to adverse experiences, which can be singular (e.g. a trauma) or continuous (e.g. chronic pain). Resilience is generally associated with less depression and greater mental well-being.
 - Three components of successful adaptation have been identified: recovery (bouncing back from stressful events), sustainability (maintaining values and actions towards goals during difficulties), and growth (new insights and enhancing capacity for adaptation in response to difficulties).²⁷⁶
 - Positive emotional states,²⁴ optimism,²⁷⁷ self-efficacy,²⁷⁸ and meaningful social ties²⁴ are primary contributors to successful pain adaptation and may predict lower levels of pain and pain-related disability.¹²⁰
 - Coping resources might also be protective, defined as a patient's potentials in dealing with the chronic disease successfully. In patients with pain, adaptive coping is associated with higher pain-related self-efficacy, increased functioning and lower levels of impairment.²³

B4. Demonstrate ability to manage challenging patients and recognize how people-pleasing behavior by clinicians can interfere with providing evidence-based care.

- Several patient characteristics have been perceived as challenging: those with mental health disorders, multiple physical symptoms, severe symptoms, chronic pain, and/or poor functional status.²⁷⁵
 - Factors contributing to difficult encounters include system issues (overstretched systems, lack of resources, cancellations, lack of time), clinician characteristics (personality/feelings, difficulty with setting boundaries, lack of confidence about how to help patient, communication style, and compassion fatigue) and patient characteristics (past medical and psychosocial history, expectations, personality, feelings, impaired quality of life, etc).
 - Tips on managing difficult interactions include:
 - Planning interactions in advance and structuring one's thoughts
 - Paying attention to patient nonverbal communication
 - Identifying emotions and meaning behind the patient's words
 - Maintaining clinician self-awareness (e.g. negative emotions stimulated by interaction with patient)
 - Setting clear boundaries while maintaining professional and kind demeanor
 - Seeking to align with patient values and building trust
 - Maintaining professional mindset of "how to best help the patient"
 - Clinician breath awareness can assist with maintaining therapeutic stance.
 - Suggesting taking a brief break can allow the patient to modulate emotions.
 - Focusing on moving forward to improve patient's health and well-being rather than on frustrations from the past
 - Bringing a second member of the care team into the exam room with the patient, if appropriate
 - Ensuring a safe setting; discontinuing interaction if safety is a concern
- Even without challenging patients, people-pleasing behavior by clinicians is common, and can interfere
 with providing excellent, evidence-based care.
 - Clinicians try to work collaboratively with patients to reach the best treatment plans. Sometimes clinicians provide nonevidence-based treatment (e.g. provide a prescription, increase dosages) from a sense of wanting to help, a need to please, and even to avoid hurting someone's feelings. Factors such as financial incentives, patient satisfaction, lack of time, and the changing nature of the doctor-patient relationship to a merchant-customer relationship create additional challenges.
 - It has been found that when clinicians deny requests, scores on patient satisfaction surveys after office visit are significantly lower than when requests were fulfilled.²⁸⁰
 - Patient-pleasing behavior by clinicians is not necessarily good for patients' health.
 - A gap between evidence and practice exist with an inappropriately high use of opioids, imaging, invasive treatments, and advice to rest. Clinicians' desire to fulfill patient requests may be one factor in this gap.²⁸¹
 - After reviewing doctor satisfaction ratings, one study found that people who are the most satisfied with their doctors are more likely to be hospitalized, have higher health care expenditures, and have higher death rates than patients who are less satisfied with their care.²⁸²
 - Performing imaging studies and being given imaging results result in higher patient satisfaction, despite being associated with worse outcomes.²⁸³
 - The Institute of Medicine (now the National Academy of Medicine) estimated that 31% of healthcare spending (\$765B) in 2009 was due to waste, with \$210B of wasted expenditures due to unnecessary services.²⁸⁴ Physicians estimated that 20% of all medical care was unnecessary, citing the fear of malpractice and pressure from patients as primary reasons.²⁸⁵
 - Medical care is a leading cause of morbidity and mortality, and unnecessary tests and medical care can be harmful. ^{286 287 288 289 290}
 - Other studies have found that patients are consistently satisfied with testing and the potentially harmful downstream events that follow. Overtesting is known to lead to overdiagnosis, invasive tests and overtreatment, and often in the end - poorer outcomes for patients.²⁹¹
 - There needs to be more training to provide clinicians with communication approaches that foster a positive patient experience without acquiescing to requests for low-value care, thereby avoiding the harms of unnecessary evaluation and treatment, reducing costs for unnecessary care, and maintaining good stewardship of resources.
- The well-being of clinicians is essential for safe, high-quality patient care.
 - Across all specialties and care settings, clinicians are experiencing alarming rates of burnout.292

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- Clinicians themselves need to foster resilience to adapt to more administrative work, more complex patients, more patient numbers, less time and less resources. Without this, clinician communication, empathy, compassion and clinical decisionmaking will suffer.
- There is now a National Academy of Medicine Action Collaborative on Clinician Well-Being and resilience, a network of more than sixty organizations committed to reversing trends in clinician burnout (see reference above).
- C. MESSAGE: Treatment plans for persons on long-term opioid therapy must include an exit strategy, which transitions persons from long-term opioid therapy to a different treatment strategy, to minimize opioid-related adverse events.

C1. Contrast complex persistent opioid dependence with simple dependence and opioid use disorder.

- Complex persistent opioid dependence is a condition recently described in the literature as a clinical and physiologic state that exists on the continuum between simple opioid dependence (which presents with short-lived and self-limited withdrawal symptoms after opioids are discontinued) and opioid use disorder (defined by DSM-5 criteria).¹²⁶
- In patients with complex persistent opioid dependence, opioid tapering or cessation may lead to worsening pain, function, affective symptoms and sleep disturbances.²⁹³

C2. Describe three approaches to an opioid exit strategy.

- Because long-term opioid therapy is associated with known risks and unproven benefits, patients on long-term opioid therapy should receive an individualized treatment plan to minimize opioid-related adverse events. Treatment plans include the development of a tailored opioid exit strategy, which transitions patients from long-term opioid therapy to a different treatment strategy.
 - The choice of an exit strategy cannot be done casually or with a "one-size-fits-all" approach; it should be guided by a socio-psycho-biological assessment of the patient, including evaluation of co-occurring medical and psychiatric conditions, substance use disorders and the patient's social support system.
 - While there is clear evidence for the effectiveness of treating opioid use disorder with medication-assisted treatment, there is no established evidence to otherwise guide the best opioid exit strategy approach for an individual.
- The first exit strategy is to taper the opioid dose.
 - While seemingly a logical intervention, tapering may not be optimal for all patients.
 - Generally, patients with lower MME prescriptions, lower pain-related dysfunction and lower psychiatric comorbidities can be candidates for a gradual taper.
- The second exit strategy is to rotate to buprenorphine and then gradually taper the buprenorphine dose.
 - This strategy is often best for patients with higher MME and higher pain-related dysfunction and comorbidities, but without a diagnosis of opioid use disorder.
- The third exit strategy is to offer or arrange medication-assisted treatment for patients with opioid use disorder.
 - This strategy best applies to patients with opioid use disorder.
- After initiating an exit strategy, ongoing socio-psycho-biological assessment may guide the clinician to switch to a different strategy.
- Abrupt opioid discontinuation is not recommended as an exit strategy, unless required for immediate safety concerns (e.g. evidence of diversion, threatening behavior, seriously disruptive behavior, suicidal ideation or behaviors).

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C3. Discuss the importance of recognizing and addressing substance use disorders, mental health comorbidities and medical comorbidities when managing a person with chronic pain on long-term opioid therapy.

- Mental health and substance use disorder comorbidities are common and each condition increases the risk for the other compared to the general population. Many people who have a substance use disorder also develop other mental illnesses, just as many people who are diagnosed with mental illness are also diagnosed with a substance use disorder.
- These clinical situations can be challenging to manage, and are further complicated by the possibility of providers inadvertently exposing the patient to dangerous drug-drug interactions.
 - This is often seen with the concurrent use of opioids and benzodiazepines, which has a FDA Black Box Warning, the FDA's strongest warning, against it. Combined use of opioids and benzodiazepines is associated with a 4-10 fold increased risk of opioid overdose death.^{264 265 266 267}
- Having one disorder may worsen the symptoms and course of the other, and may impair compliance with treatment of both conditions.
- There is an increased risk of poor outcomes including opioid overdose, opioid use disorder and death, for patients taking opioids that have substance use disorders or behavioral health conditions.^{176 177 253 254 255}
- Interdisciplinary care for patients is advised, even as more research is needed on efficacy and feasibility of arranging such care.
- Further information about the treatment of other substance use disorders, see *The ASAM Principles of Addiction Medicine*. 6th ed. American Society of Addiction Medicine; 2019.
 - In general, alcohol use disorders are treated with psychosocial treatment and medications (e.g. naltrexone, acomprosate, disulfiram), tobacco use disorder is treated with psychosocial treatment and medications (e.g. varenicline, bupropion, and nicotine replacement), and stimulant use disorder is treated alone with psychosocial medications.

COMPONENT 6

6

Reverse the unintended consequences created by the medicalization of chronic pain by empowering persons with self-management strategies, and include an awareness of chemical coping.

RATIONALE

The medicalization of pain describes the process over the past century whereby the understanding and management of pain has been removed from the lay public and co-opted by the medical profession. This has transformed the clinician and the medical system into the primary, active manager of pain with the implicit understanding that the person experiencing pain takes a passive role. Additionally, the commonly practiced structural pathology paradigm erroneously focuses resources toward identifying and eliminating anatomic abnormalities long after acute pain has transitioned to a chronic condition requiring active lifestyle management approaches. Recognizing that medicalization of chronic pain has offered some benefits, the demedicalization of chronic pain aims to reestablish the self-efficacy of the person with pain who then takes the active role at the center of a care team. Self-management strategies form the foundation for improving function and quality of life for persons with chronic pain.

OBJECTIVES

- **A.** MESSAGE: In order to reverse the medicalization of chronic pain, the role of active management of pain must be transferred from the medical system to the person with chronic pain.
 - A1 Describe the medicalization of chronic pain, recognizing the role of the biomedical model in promoting passive treatments for chronic pain and how this model is perpetuated by industry, financial incentives, specialty training, and governmental decisions.
 - A2 Describe how the demedicalization of chronic pain enhances patient outcomes.
 - A3 Describe several self-management strategies for chronic pain and the evidence behind them.
 - A4 Counsel persons with pain on self-management strategies.
- **B.** MESSAGE: Patient strategies to avoid unpleasant physical sensations and emotional distress include "chemical coping" that can lead to poor outcomes.
 - B1 Describe the agonist and withdrawal effects of opioids and other controlled substances on multiple systems including social bonding, affective dimension of pain, anxiety, mood and sleep.
 - B2 Define chemical coping, its prevalence in different populations, risk factors, clinical presentation and how it differs from addiction.
 - B3 Describe a therapeutic approach to chemical coping, including addressing the underlying suffering causing the behavior.

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COMPONENT 6: SELF-MANAGEMENT AND CHEMICAL COPING

A. MESSAGE: In order to reverse the medicalization of chronic pain, the role of active management of pain must be transferred from the medical system to the person with chronic pain.

A1. Describe the medicalization of chronic pain, recognizing the role of the biomedical model in promoting passive treatments for chronic pain and how this model is perpetuated by industry, financial incentives, specialty training, and governmental decisions.

- Medicalization is the process by which common human problems become defined and treated as medical problems. While this process is often beneficial, it has created more unintended consequences in the case of chronic pain.
 - The cultural ownership of chronic pain gradually shifted from the lay public to the medical field throughout the 1900s and early 2000s.
 - In the 1960s, changes in the understanding of pain and its treatment expanded possibilities for the establishment of persistent pain as a distinct medical condition. The gate-control theory of pain played a key role in explaining pain experiences that were seen to lack a physiological cause.²⁹⁴
 - As pain became increasingly understood as a neurogenic phenomenon, medical specialization evolved and biomedical pain treatment expanded.
 - Advancements in neuroanatomy and medicine culminated in the 1990s and 2000s with the message that modern medical technology has the power to enable humans to be "pain free."
 - Some of the benefits of the medicalization of chronic pain include 1) progress in the understanding of the underlying neurobiology of chronic pain and recognition that these mechanisms can be separate from the original underlying condition 2) development of interdisciplinary pain clinics and 3) development of new medications and technologies to address chronic pain.
 - The unintended consequences of the medicalization of chronic pain are the focus of this Component. They include the creation of cultural messages that erode self-management and the delivery of low-value pain care driven by economic factors rather than evidence.
 - Implicit and explicit cultural messages that have resulted from the medicalization of chronic pain include that humans can and should be free from pain. While this is realistic during surgery, complete freedom from pain is not realistic. This message has created unrealistic expectations with inevitable disappointment on the part of the both the patient and medical provider. It has also resulted in taking treatments to extremes, as seen in the recent widespread use of high-dose, long-term opioid therapy for musculoskeletal pain.
 - A second implicit cultural message is that since pain is under the purview of the medical establishment, people with pain should not self-manage, but rather expect the medical profession to treat and/or cure their pain.
 - In fact, biomedical reductionism, the misplaced application of acute pain concepts to chronic pain conditions, and reimbursement structures that favor procedures over professional time spent with patients have led to a dramatic expansion of pain care that relied on simple, episodic treatments (e.g. steroid injections) that were focused on a single painful body part rather than the person suffering from chronic pain.
 - The establishment of the passive patient role and the active medical professional role is often perpetuated by perverse economic incentives where the medical professional is reimbursed more for ordering procedures than counseling self-management strategies.
 - There are other issues that need exploration, like the professional boundaries of pain treatment, the role of the pharmaceutical industry in promoting pain treatment, and the patient experience of medicalized pain treatment.
- Disorders with imprecise diagnostic criteria can provide ground for lawsuits, which leads to the legal industry indirectly
 fostering medicalization. Defensive medicine often prevails and extensive costs are generated by ordering unnecessary
 tests and treatments.²⁹⁵

A2. Describe how the demedicalization of chronic pain enhances patient outcomes.

• Demedicalizing chronic pain refers to re-establishing self-management as the foundation of pain care and re-educating providers and people with pain about appropriate expectations.

COMPONENT 6: SELF-MANAGEMENT AND CHEMICAL COPING

- There needs to be a shift away from the reductionist, biomedical care pathway that primarily relies on interventions such as medications, radiological examinations, injections and surgical procedures. These interventions may heighten patients' expectations and demands, ultimately leading to a dependence on the medical system.²⁹⁸
 - Part of the road to demedicalization is the terminology used. There is a strong association between a sense of threat (e.g. knowledge that you have been told you have a crumbling disc) and pain perceptions.²⁹⁶ [See Component #7 for person-centered language and non-threatening terminology.]
 - A seminal critique of the reductionist biomedical model was provided by George Engel in his 1977 paper: "The Need for a New Medical Model: A Challenge for Biomedicine."
- The biomedical management of chronic pain, a result of the medicalization of chronic pain, has not led to successful patient outcomes.
 - Medications and interventions have poor evidence of effectiveness for chronic pain.^{219 297} There is a lack of evidence showing any sustained functional benefit of long-term opioid therapy for chronic pain, but there is evidence of dose- and duration-dependent harms.
 - In contrast, self-efficacy is associated with a favorable prognosis²⁹⁸ and inversely associated with impairment, distress and pain severity in patients with chronic pain.²⁹⁹
 - [See Component #5 for the whole-person treatment approach.]

A3. Describe several self-management strategies for chronic pain and the evidence behind them.

- Self-management can be defined as the ability to manage the symptoms, treatment, physical and psychosocial consequences and lifestyle changes inherent in living with a chronic condition.
 - Self-management is not simply self-care or patient education; it specifically emphasizes patient skill development, which serves to increase confidence or self-efficacy to manage symptoms, one's response to symptoms (e.g., behavioral, emotional, cognitive and social) and to make lifestyle changes to improve one's health. In other words, self-management includes everything a person can do on their own to manage their health (including pain) and live their life as fully as possible.
- Self-management includes engagement in general health activities and pain management strategies.
 - General health activities: developing and maintaining supportive relationships; attention to sleep hygiene and adequate sleep; eating a health diet (e.g. anti-inflammatory diet); regular physical movement every day in order to maintain and improve strength; pleasant activities aligned with individual values; smoking cessation; mindfulness, and other active relaxation strategies.
 - Pain management activities: mindfulness of body posture and movement, weight loss (if BMI > 25 or centripetal obesity), home exercise program such as yoga, stretching, Tai Chi, etc; diaphragmatic and mindful breathing and relaxation exercises; use of cold packs or heat; attending pain management classes; pacing activity and appropriate rest.
- Self-management skills have been effective in patients with chronic pain.
 - Enhancing patient self-management skills has shown to decrease pain severity and improve functional status,300 depression,³⁰¹ and pain catastrophizing.^{302 303}
 - Evidence shows self-management approaches improve self-efficacy in multiple chronic conditions and that opioid treatment of chronic pain may undermine self-care.^{304 305 306 307}
- The Institute of Medicine has identified self-management as a means to promote health care system improvements in the United States.
- Enhancing self-management and self-efficacy, including appropriate management of flares of chronic pain, are the ultimate goals for virtually all types of chronic non-terminal pain.

A4. Counsel persons with pain on self-management strategies.

- Self-management approaches should be recommended to all patients with chronic pain. It can be taught through individual, group, or online formats.
- Self-management of chronic illness exists within the context of other people and influences. Fundamental to its success
 are the relationships among the patients, providers, friends, community and family members.³⁰⁶
- Barriers to patients using pain self-management strategies include an overreliance on medications, limitations related to depression, fear of activity, time constraints and limited resources. Each of these must be fought, mainly through supportive family, friends and community.³⁰³
- There are evidence-based principles which have been found to improve clinicians' support of patient self-management, including the use of a nonjudgmental approach, collaborative problem solving, enhancing patient self-efficacy, ensuring active follow-up and multifaceted interventions (vs single-component).³⁰⁸
- **B.** MESSAGE: Patient strategies to avoid unpleasant physical sensations and emotional distress include "chemical coping" that can lead to poor outcomes.

B1. Describe the agonist and withdrawal effects of opioids and other controlled substances on multiple systems including social bonding, affective dimension of pain, anxiety, mood and sleep.

- In addition to their analgesic properties, opioids and their receptors are implicated in reward and addiction. Human
 opioid ligands and receptors are anatomically located in strategic positions to control the expression of fear and anxiety
 responses in fact, virtually all the brain areas highly involved in emotional regulation are under extensive opioidergic
 control.^{309 310}
- Opioid withdrawal in human opioid addicts can result in a number of well-characterized autonomic, somatic, and affective symptoms. The affective distress often involves irritability, anxiety, dysphoria, and restlessness.³⁰⁹
- Aversive affective symptoms of opioid withdrawal, such as anxiety or dysphoria, may contribute to escalation of opioid drug use and relapse after periods of abstinence. For individuals previously exposed to opioids, natural life experiences that involve stress, anxiety, or sadness can trigger a drive to seek opioids in order to recreate the sense of emotional wellbeing that was experienced with prior opioid use (which may have been prescribed for a minor physical injury).³⁰⁹
- Because opioids cause sedation, patients often seek their use to help initiate sleep. However, similar to alcohol and benzodiazepines, the short-term sedation is overshadowed by overall negative effects on sleep.
 - Studies show that opioids actually interrupt sleep by disrupting sleep architecture and contributing to sleep-disordered breathing. There is evidence that opioids decrease deep sleep (slow wave sleep), sleep efficiency and total sleep time and increase arousal.³¹¹
 - · Long-term opioid use is an established risk factor for sleep-disordered breathing, particularly central sleep apnea.
 - Opioid effects on sleep architecture and sleep-disordered breathing both appear to be dose dependent.³¹²
- Endogenous opioids appear to be key to regulating human social bonding.
 - Animal and human research suggests that the endogenous opioid system is involved in loneliness, social pain (pain resulting from social isolation or loss of a loved one), and the pleasure associated with social connections.
 - Additionally, exogenous opioids can both reduce feelings of loneliness as well as reduce the drive for social affiliation (i.e. promote social isolation).^{130 313 314 315}

B2. Define chemical coping, its prevalence in different populations, risk factors, clinical presentation and how it differs from addiction.

- Chemical coping refers to the use of medication in nonprescribed or inappropriate ways to manage psychological or other distress, and does not include the craving and behavioral issues associated with addiction. Persons addicted to opioids are often chemically coping, but not all people that chemically cope are addicted.^{316 317}
- There are complex biobehavioral interactions that can lead to chemical coping.
 - When opioids are prescribed for pain, they not only activate the areas of the brain that process physical pain, they also activate brain areas that process emotional pain, social pain (e.g. social isolation or loss of a loved one), and the reward system.
 - They also create a learned association between the taking the opioid and the opioid effects (e.g. sense of well-being, short-term relief of pain, reduced anxiety). This unconscious learned association can become part of the urge to continue using opioids. With chronic pain, even mild pain can trigger this learned association and manifests as an urge for short-term pain relief and the other short-term effects of well-being and tranquility.

In 1804, a 19-year old Oxford University student named Thomas De Quincey swallowed a prescribed dose of opium to relieve rheumatic pain. That the drug took away his physical pain was "a trifle", compared to, as he wrote, "the immensity of those positive effects which had opened before me."³¹⁸

- There is a spectrum of severity of chemical coping: it can range from the occasional overuse of opioids to cope with
 emotional distress or suffering (mildest form) to essentially a component of addiction. This is because the lack of opioids
 results in severe emotional distress that, in turn, drives the excessive and inappropriate use of opioids and
 dysfunctional behaviors.³¹⁹
- Adverse consequences of chemical coping include avoidance of difficult emotions and interpersonal interactions, which lead to progressive increases in distress, risk for addiction, increased use of other hazardous substances, diversion, and death.
- Risk factors for chemical coping include a history of smoking, substance use disorders, history of trauma, psychiatric comorbidities, impulsivity, pain catastrophizing, lack of acceptance, or avoidant coping strategies.^{320 321}

B3. Describe a therapeutic approach to chemical coping, including addressing the underlying suffering causing the behavior.

- Chemical coping may be difficult to detect, interpret, and address. Clinical monitoring of a patient depends on both the patient's self-report and the observations of health care providers, often supplemented by drug testing.^{322 323}
- Chemical coping can complicate opioid therapy. When identified, clinicians should focus treatment on the underlying
 distress, psychiatric comorbidities, and sleep disturbances through evidence-based treatments (cognitive behavioral
 therapy, evidence-based pharmacotherapy, and self-management training).
 - Clinicians can explain to patients that opioids affect multiple brain regions related to pain processing including sensory discrimination, emotional unpleasantness, reward system, and social bonding. When opioids are prescribed for chronic pain, all of these areas are affected with short-term effects of reduction in pain intensity, alleviation of negative affect, mood elevation, and social bonding. These are short-term solutions on psychosocial distress, but they create long-term worsening of underlying symptoms.³²⁴
- Whenever possible, clinicians should simplify drug regimens, deemphasize opioid use in patients that are chemically-coping, encourage psychotherapy, implement evidence-based modalities as part of the treatment approach, and focus on teaching coping strategies as alternate choices in times of stress or emotional distress.³¹⁹

COMPONENT 7

7

Use and model language that destigmatizes, reflects a whole-person perspective, builds a therapeutic alliance and promotes behavior change.

RATIONALE

Chronic pain, substance use and addiction are often associated with negative perceptions that are furthered by stigmatizing language. The use of nonjudgmental, person-first language with patients and colleagues is necessary for cultural transformation and to reduce the negative impact of stigma on the community. Person-first language should be paired with language that reflects a whole-person, evidence-based approach to mental health conditions, addiction and chronic pain, while moving away from the structural pathology paradigm of chronic pain.

OBJECTIVES

- A. MESSAGE: Stigma negatively affects the treatment and outcomes of persons with chronic pain and/or addiction.
 - A1 Describe the impact of stigma on legal, policy, research and care services for persons with pain and/or addiction.
 - A2 Contrast the science-based nature of addiction and chronic pain with commonly held perceptions.
 - A3 Model respectful and nonjudgmental communication with persons with pain and addiction.
 - A4 Use active reflection to uncover personal biases to persons with chronic pain and/or addiction.
- B. MESSAGE: Language must be tailored to attend to the patient's unique socio-psycho-biological factors.
 - B1 Explain the diagnosis of pain and/or opioid use disorder using patient-centered language.
 - B2 Describe the impact of language and expectations on a patient's experience with pain.
 - B3 Describe the effectiveness of motivational interviewing for substance use disorders and chronic pain.
 - B4 Demonstrate techniques of motivational interviewing techniques to support behavior change.
 - B5 Assess an individual's readiness for change and tailor treatment approaches to the patient's stage of change.
- C. MESSAGE: A therapeutic alliance with persons with pain and/or addiction enhances treatment outcomes.
 - C1 Describe the importance of the therapeutic alliance in working with persons with pain and/or addiction.
 - C2 Model the development of a therapeutic alliance by demonstrating empathy as well as reaching agreement on functional goals and approaches to reach these goals.
 - C3 Demonstrate validation, partnering, and boundary setting in situations with a high degree of negative affect.

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A. MESSAGE: Stigma negatively affects the treatment and outcomes of persons with chronic pain and/or addiction.

A1. Describe the impact of stigma on legal, policy, research and care services for persons with pain and/or addiction.

- Stigma is the prejudicial attribution of negative qualities to an individual based on his/her social identity in an undesirable social category.
- Institutionalization of stigma worsens patients' sense of isolation and marginalization, undermines their resilience and further diminishes their self-esteem and quality of life.
- The clinical community has unintentionally worsened the stigma of persons with chronic pain.
 - The traditional biomedical model has enculturated clinicians to believe that pain is always due to a specific pathology and that treatment should fix it ("find it and fix it" mentality). Most patients with chronic pain do not fit this biomedical paradigm, and unmet expectations for improvement can lead to mutual distrust between providers and patients.
 - Providers can doubt the legitimacy of their patients and have feelings of frustration, helplessness, anger, and fear of their inability to help.
 - Patients can doubt the competency of their medical providers with feelings of frustration, helplessness, anger, and fear of unresolved health concerns.

Provider's perspective of patient: *"Another crock."* Patient's perspective of provider: *"Another quack."*

- The answer to this problem is not to change the provider or the patient -- it is to change the approach to pain itself. [See Component #4 for strategies to transform the model.]
- The language that providers use with one another has also unintentionally led to stigma. Stigmatizing concepts like "it's all in their head" or "making it up" or even "this patient's pain is real" implies that others' pain is not real.
 - To counter this potential misunderstanding when relating to patients, straightforward language such as "Your pain is very real" can help patients feel validated.
- Stigma and fear of discrimination are key barriers that keep many people from seeking care and influence the care that is provided.
 - Clinicians have lower expectations for health outcomes for patients with substance use disorders; this can affect whether the provider believes the patient is deserving of treatment.
 - Stigma can influence the care provided by health care professionals, including not offering evidence-based therapies (such as pharmacotherapy for opioid use disorder).
 - A comparison can be made between with individuals with substance use disorders and individuals with other biological diseases such as Type 2 Diabetes, Hypertension, and Asthma, in that all these diseases have strong behavioral components. Like persons with addiction, persons with Type 2 Diabetes often do not follow clinical advice to modify their behavior or take recommended medications as prescribed, resulting in poorer health outcomes. In the realm of diabetes care, this person is not thought of as having a moral failing and the healthcare team continues to treat the person by "meeting them where they are at."
- Stigma has been furthered by large-scale federal policies.
 - The development of anti-drug legislation unintentionally sent the message that using drugs was immoral, thus associating it with other forms of criminal activity such as violence, drug trafficking, and prostitution.
 - When people recover from addiction, anti-drug laws make it difficult to reintegrate into society. It can be hard for people with drug convictions to find jobs, gets licenses, receive welfare benefits and support services.
 - The U.S. budgetary federal spending has been 65% on interdiction and criminal sanctions compared to 35% on treatment, prevention and research on substance use disorders.³²⁵

A2. Contrast the science-based nature of addiction and chronic pain with commonly held perceptions.

- Two main factors can drive stigmatizing beliefs and attitudes: the perceived control that a person has over the condition and perceived fault a person has in acquiring the condition.
 - Persons with chronic pain and addiction are often characterized as "drug-seekers" and as having a moral failing.
 - Many Americans blame people who use opioid medications for the opioid epidemic.³²⁶
- The science behind pain reveals a complex, multidimensional disease with significant brain changes.
 - [See Component #3 for aspects of brain reward and anti-reward processes.]
 - Generally, pain relief acts as the reward in the brain reward system, and the anti-reward process becomes chronically activated, leading to fear avoidance, social isolation, depression and anxiety.
 - [See Component #4 for the social, psychological and biological aspects of pain.]
 - Generally, the social aspects of pain include the evidence that social support and interpersonal relationship significantly facilitate or impair adjustment to chronic pain.
 - Generally, the psychological aspects of pain include the link between early traumatic experiences and the development of chronic pain, impaired attention, cognition, emotions and overt behavior. There are both comorbid conditions and subclinical diagnoses found in individuals with chronic pain.
 - Generally, the biological aspects of pain include the structural alterations that lead to central sensitization, deconditioning and other areas involving affect, cognition, reward and stress.
- The science-based understanding of addiction is that it's a biological disease that changes the brain, causing cravings
 and compulsive behavior. In the setting of these brain changes, using opioids and other substances despite negative
 consequences is not merely lack of willpower.
 - While initial drug taking behavior is usually voluntary, once addiction develops with its corresponding brain changes, behavioral control is significantly impaired.
 - Brain changes in addiction include 1) resetting the reward system such that it becomes less sensitive and responsive to both drug and natural rewards; 2) changes in the extended amygdala such that it has an increased reactivity to stress and development of negative emotions; and 3) impairment of the prefrontal regions that manifest as reduced ability to resist strong urges and follow through on goal-directed behaviors. All of these brain changes lead to impairment in an individual's ability to reduce drug-taking behavior despite negative consequences. [See *Component #3* for the neurobiological processes underlying pain and addiction.]
 - Recovery from addiction likely involves normalization of brain functions that correspond with normalization of goal-directed behaviors. Both medications and behavioral interventions can assist with the process.
 - Pharmacotherapy for opioid use disorder can assist with preventing relapse while the brain is healing and emotional and decision-making capacities are being restored.^{327 328} [See *Component #5* and *Appendix D* for treatment of opioid use disorder.]
- Society is slowly overcoming its fear of many mental health conditions, but it appears to be moving slower in regards to addiction.

A3. Model respectful and nonjudgmental communication with persons with pain and addiction.

- Language that supports health and healthy behaviors, even if a person is actively using substances, can help decrease stigma.³²⁹
- Respectful and nonjudgmental communication includes using appropriate terminology.
 - Use "person-first language" ("a person with chronic pain" instead of "a chronic pain patient"). Person-first language clarifies that the person has a disease, not that the person is the disease.
 - Do not conflate substance use and substance use disorder. Language about substance use disorders should be limited to situations where a clinical diagnosis has been made.

- Use technical language with a single, clear meaning instead of colloquialisms: use "negative urine drug screen" instead of "clean urine"; use "medication-assisted treatment" instead of "opioid replacement."
- Do not perpetuate drug-related moral panic. Moral panics marginalize people who are vulnerable. Avoid using the terms "crack babies", "opioid babies" or "addicted babies" which are stigmatizing and inaccurate.
 - Babies cannot be addicted; they can be born physically dependent on opioids or other drugs with manifestations of a withdrawal syndrome. Use accurate terms such as "neonatal abstinence syndrome" or the newer, more specific term "neonatal opioid withdrawal syndrome."
- Use mindful self-awareness to recognize emotions such as anger or disgust that come up for the clinician during a visit. Simply note the emotion without judgment and remain focused on the therapeutic goals for the patient. Recognize that the disease of addiction can involve unpleasant behaviors and despite these behaviors, the goal is to provide therapeutic recommendations while maintaining appropriate boundaries.
- The next generation of clinicians have a responsibility not only to their patients to use respectful and nonjudgmental communication, but also to their colleagues and mentors to correct harmful, stigmatizing language.

A4. Use active reflection to uncover personal biases to persons with chronic pain and/or addiction.

- The language clinicians use to talk about substance use disorders and chronic pain shapes how the public views these conditions. Unintentionally stigmatizing language can perpetuate negative stereotypes.
- The first step toward overcoming a bias is to recognize it in oneself. It is important to articulate how one feels about the opioid epidemic and patients with chronic pain and/or addiction and to start to contextualize (socially, politically, economically, biologically) the patients one will encounter in practice.
- Empathy comes with understanding the context of one's pain or opioid use disorder, as well as the fact that all humans are
 vulnerable to these conditions. This awareness can make the patient's actions more intelligible to clinicians and can foster
 a desire to help in a real way.
- B. MESSAGE: Language must be tailored to attend to the patient's unique socio-psycho-biological factors.

B1. Explain the diagnosis of pain and/or opioid use disorder using patient-centered language.

- Provider language can have a lasting impact on a patient's thoughts, actions and beliefs about their condition, prognosis and ability to influence the course of their recovery.
 - Disease-centered language can contribute to a person's fear, anxiety, beliefs and lead to the perception that she/he is a passive victim of a disease, thereby creating a barrier to self-management and recovery.
 - Person-centered language implicitly affirms the intrinsic value, dignity, and self-efficacy of each person, thereby fostering self-management and supporting recovery.
 - One aspect of person-centered language includes not using disorders to name people (e.g. "alcoholics" or "drug addicts") but identifying the person (e.g. person with substance use disorder.")
 - When discussing chronic pain conditions, person-centered language recognizes the complexity of the mind, brain and body interconnections (i.e. the socio-psycho-biological model) and does not reduce the complex human experience of pain to anatomical pathology (i.e. the structural pathology paradigm).
 - Person-centered language also uses normative terms rather than disease-centered terms.
 - For example: prior to ordering a lumbar spine MRI, the clinician can explain that most individuals will have agerelated changes (e.g. changes to the intervertebral discs and facet joints). When discussing the results (and if there is no evidence of serious pathology), rather than detailing findings of "degenerative disc disease," "facet arthritis," and "disc bulges" (which are unlikely to correlate with the person's pain complaint and are highly prevalent in the normal population), the clinician can describe "age-related changes" and that there is "no evidence of serious problems."

- Patients often recall the language that a surgeon or other health care provider told them that they have internalized as part of their somatic self-image, contributing to a dysfunctional perception of their body.^{330 331} Such patients may remember being told that their "spine is crumbling" and have a perception of their body that is weak, easily damaged and on the verge of becoming paralyzed. These words and images can lead patients to an activity-restricted and sedentary lifestyle, driven by fear of injury.
- Clinicians should also strive to use simple, non-medicalese words and phrases when discussing illness and wellness with patients.
- In total, employing person-centered language to explain chronic pain diagnoses involves 1) describing the complexity of the body-mind-brain-relationship interconnections; 2) describing neuroplastic brain changes associated with chronic pain and recovery; and 3) fostering greater integration in the person with chronic pain rather than reductionism. Examples include:
 - "Chronic pain is complex, and your brain and body and mind all play a role in what you're experiencing. Our nervous system processes physical pain along with emotional pain and social pain. That's why it is important to look at you as a whole person to help you feel better and be able to do more of what is important to you. In fact, when pain persists for many months and years, we can see changes in the brain. Much of our goals of treatment will be to help you build greater physical, emotional, and social health. This will help get your brain, body, and relationships back to a healthier state."
 - "If we just focus on eliminating your pain from one body part (with more injections and medications), we probably won't be able to help you move forward. On the other hand, if we work on a plan for helping you build greater health and strength, my experience (and science shows) that we can be successful in helping you get back engaged in the activities that are most important to you."
 - Explain Pain (EP) refers to a range of educational interventions that aim "to change someone's understanding of what pain actually is, what function it serves and what biological processes are thought to underpin it, and it appears to improve outcomes. "The core objective is to shift one's conceptualization of pain from that of a marker of tissue damage or pathology to that of a marker of the perceived need to protect body tissue."²⁷⁸
- In the current environment of stigma associated with opioid use disorder and its treatment, patient-centered language to
 explain the diagnosis of opioid use disorder focuses on 1) normalizing opioid use disorder as a socio-psycho-biological
 disorder, similar to other more accepted disorders (e.g. diabetes); 2) describing neuroplastic brain changes associated with
 opioid use disorder and recovery; and 3) fostering recovery through supporting self-directed improvements in global health
 and wellness. Examples include:
 - "Long-term exposure of any person's brain to opioids can cause brain changes in the areas that process physical pain, emotions, relationships and motivation. These changes can make it very hard to stop using opioids without help from medications, peers, families, providers, allies and others to foster a self-directed recovery."
 - "Having an opioid use disorder or using medications to treat it does not mean you are a weak or bad person."
 - "Feeling ashamed about having an opioid use disorder can backfire and lead to return to taking opioids. Let's work on letting go of feelings of shame. I would like you to think of opioid use disorder as an illness similar to diabetes that is not your fault, but requires hard work to improve the person's health."
 - ▶ "You are not responsible for the disease of opioid use disorder, but you are responsible for your own recovery."

B2. Describe the impact of language and expectations on a patient's experience with pain.

- Metaphors are often used in conversations with patients with serious illnesses.³³² Military metaphors with pain are common ("attack of back pain", "painkiller", "eradicate the pain") and lead to the unconscious belief that pain is the enemy.
 - Conceptualizing pain as the enemy becomes an inherent problem when the pain is coming from within one's own body. Making pain the enemy can be a barrier to healing and to moving forward. For change to happen, one has to accept where one is now. Part of the therapeutic process is coming to a point of acceptance.
- The language used to describe pain can also be confusing, and they can create undue fear and sense of helplessness ("frozen shoulder", "blown disc", "degenerative spine", "wear and tear.") Use understandable, clear terms like "age-related changes".

- Expectations have a powerful influence on a person's experience of pain and on their response to treatment. In fact, a large part of the therapeutic response to drugs, surgery, therapy, and other treatments may be due to the treatment context rather than the specific effects of the treatment itself.³³³
 - Patient expectations are complex and influenced by prior experience, beliefs, context, social observation, sensory cues and learning.
 - Placebo and nocebo responses are an excellent model to understand how psychosocial factors influence the experience
 of pain. Pain, along with other illnesses that affect the brain such as depression and anxiety, are particularly responsive to
 placebo and nocebo effects.
 - Placebo effects are the beneficial effects that are attributable to the brain and mind's responses to the context in which a treatment is delivered rather than to the specific actions of the treatment.³³³
 - Nocebo effects are adverse effects related to negative expectations and learning processes associated with the context of a treatment rather than the specific actions of treatment.
 - Placebo and nocebo effects are mediated by neurobiological mechanisms.136 Positive expectations can reduce pain by activating brain circuits involving opioids, endocannabinoids, dopamine, and prosocial hormones (e.g. oxytocin/vasopressin).
 - Negative expectations can increase pain by activation of the cholecystokinin system, deactivation of endogenous dopamine/opioid systems and increase in the cyclooxygenase/prostaglandin pathways.
 - Placebo treatments activate a variety of brain regions that are involved processing pain, including the medial prefrontal cortex (vmPFC), dorsolateral PFC (dIPFC), lateral orbitofrontal cortex (IOFC), nucleus accumbens-ventral striatum (NAc–VS), PAG and rostroventral medulla (RVM).
 - Knowledge that a large portion of the therapeutic response to many pain treatments involves placebo neurobiology can help clinicians prioritize safe, evidence-based therapies over invasive procedures for most chronic pain conditions.
 - Awareness of the influence that expectations and context have on the experience of pain can be used to enhance therapeutic response and avoid unnecessary harms. Building the therapeutic relationship can be a powerful way to harness the beneficial effects of placebo neurobiology.

B3. Describe the effectiveness of motivational interviewing for substance use disorders and chronic pain.

- Motivational interviewing is a collaborative, person-centered approach to elicit and strengthen motivation to change. It is rooted in an understanding of how hard it is to change learned behaviors.
 - No patient is completely unmotivated; motivation for change is malleable and can be shaped within the context of the patient-clinical relationship.
- Motivational interviewing has been used in a range of treatment settings for various types of substance use, including
 opioids, and it has been linked to improved treatment engagement and outcomes, increased medication adherence and
 decreased illicit drug use.
- Motivational interviewing can enhance engagement in treatments for chronic pain and addiction.³³⁴
- There is at least moderate evidence that motivational interviewing is effective at improving outcomes in alcohol, tobacco, and marijuana use and modest evidence that it improves engagement with treatment recommendations for patients with chronic pain.³³⁴

B4. Demonstrate techniques of motivational interviewing techniques to support behavior change.

• Motivational interviewing is an approach to communication rather than a rigid set of techniques.

REDS mnemonic for Motivational Interviewing: Roll with resistance, Express empathy, Develop discrepancy, and Support Self-efficacy.

Motivation interviewing consists of a number of steps:
 1) Set the agenda (find the target behavior); 2) Determine the current stage of change; 3) Ask about the positive aspects of the target behavior; 4) Ask about the negative aspects of the target behavior; 5) Explore how the target behavior impacts goals for chronic pain treatment; 6) Assess patient's decision about behavior change; and 7) Set goals.

B5. Assess an individual's readiness for change and tailor treatment approaches to the patient's stage of change.

- Stages of change include Precontemplation, Contemplation, Preparation, Action and Maintenance.335
 - *Precontemplation:* this is when individuals are not considering change and do not intend to change behaviors in the foreseeable future. They may be partly or completely unaware that a problem exists, that they have to make changes, and that they need help in this endeavor. Alternatively, they may be unwilling or too discouraged to change their behavior.
 - Contemplation: As individuals become aware that a problem exists, they begin to perceive that there may be cause for concern and reasons to change. They are considering the possibility of stopping or cutting back in the near future.
 - Preparation: When an individual perceives that the advantages of change and adverse consequences of substance use outweigh any positive features of continuing use at the same level, the decisional balance tips in favor of change. They begin to set goals for themselves and make commitments to stop using.
 - Action: Individuals in the action stage choose a strategy for change and begin to pursue it. At this stage, persons are actively modifying their habits and environment, making drastic lifestyle changes and may be faced with challenging situations and the physiological effects of withdrawal.
 - *Maintenance:* During the maintenance stage, efforts are made to sustain the gains achieved during the action stage. This is the stage at which people work to sustain sobriety and prevent recurrence. Extra precautions may be necessary to keep from reverting to problematic behaviors.
 - Recurrence: Most people do not immediately sustain the new changes they are attempting to make, and a return to substance use after a period of abstinence is the rule rather than the exception. This event triggers the individual's return to earlier stages of change and recycling through the process. Most persons using substances will require several revolutions through the stages of change to achieve successful recovery.
- Patient can be assessed using a "readiness-to-change" meter. For example, this can be done by asking: "On a scale of 0 10, how ready are you to do [action]?" If a patient answers "2", the provider could follow up with: "Tell me more about why you are a 2 and not a 1."
 - Motivational interviewing is about finding patients' own internal reasons and readiness for change. If someone is a "2" and not a "1" or a "0", there is some readiness to change. Approaching the discussion this way invites the patient to talk about their reasons for wanting to change -- rather than the clinician talking about reasons to change and the patient talking about reasons not to change. This is most useful for patients that are in a contemplative or precontemplative stage.
- **C. MESSAGE:** A therapeutic alliance with persons with pain and/or addiction enhances treatment outcomes.

C1. Describe the importance of the therapeutic alliance in working with persons with pain and/or addiction.

- The therapeutic alliance is commonly conceptualized as consisting of three main variables: the collaborative nature of the relationship, the affective bond between the patient and provider, and the patient's and provider's ability to agree on treatment goals and tasks.³³⁶
- Therapeutic alliance has been correlated with treatment adherence and positive outcomes in several disciplines, including medicine, psychotherapy and pain medicine.³³⁷ In addiction treatment, persons who develop a stronger alliance have achieved greater reductions in distress during treatment.³³⁸

C2. Model the development of a therapeutic alliance by demonstrating empathy as well as reaching agreement on functional goals and approaches to reach these goals.

- Mindful self-awareness, a science-based socio-psycho-biological understanding of pain and addiction, and clear therapeutic boundaries allow the clinician to connect with natural human impulses of empathy and compassion. Without setting clear boundaries, clinicians may feel uncomfortable or defensive which will inhibit their natural empathy. [See next objective about boundaries.]
- Empathy can be considered the competence of a clinician to understand the patient's situation, perspective and feelings; to communicate that understanding; and to act on it in a helpful, therapeutic way. It is thus an attitude, a competency, and a behavior.³³⁹

- The attitude is based on respectfulness of the authenticity of the other person, interest in the other person, impartiality and receptivity.
- The competency refers to skills in communication and the ability to build up a relationship based on mutual trust. That
 means the clinician can elicit the inner world of the patient and get as much information as possible while at the same
 time recognizing if there is a problem. Communication skills are then used to clarify, support, understand, reconstruct and
 reflect on patient's thoughts and feelings.³⁴⁰
- There is empirical evidence that the therapeutic relationship is a significant factor in treatment outcomes. There is a relationship between empathy and patient satisfaction and adherence, patient anxiety and distress, better diagnostic and clinical outcomes, and strengthening of patients' enablement.³³⁹
- Overidentification, without clear therapeutic boundaries, can lead to projection of negative emotion and judgment, contributing the complex process of stigmatization of persons with chronic pain and addiction.
- Asking patients about what matters most to them (i.e. their values) lays the foundation for identifying specific health goals related to pain and opioid use.
 - [See Appendix B for a Personal Health Inventory tool that can assist with eliciting these patient values.]³⁴¹

C3. Demonstrate validation, partnering, and boundary setting in situations with a high degree of negative affect.

- Validation can be a powerful first step in developing a therapeutic relationship. Fear of reinforcing unhealthy patient behaviors may prevent clinicians from validating the suffering experienced by the patient. When a patient does not feel that their clinician understands their suffering, he/she may spend much of the encounter trying to convince the clinician of it.
 - An example of how to demonstrate validation includes: "I hear that you are really suffering because of your back pain and the lack of improvement from previous treatments."
- Partnering describes the relationship between patient and clinician and serves to foster a strong therapeutic alliance. By
 including the patient when it comes to treatment planning and goal setting, patients feel more empowered and in control of
 their pain experience.
 - An example of partnering is "This has been very hard/frustrating/etc. for you. Let's work together to help you feel better and be able to do more of what is important to you, despite having some pain."
- All relationships, including those of a provider and patient, are guided by boundaries. The provider has the responsibility to make certain that appropriate boundaries are set and maintained.
 - Most commonly, there is a need to set a boundary about how controlled substances will be handled. Clearly identifying ahead of time the processes that the clinician will follow for medication refills and the responses to aberrant behaviors creates space for the clinician to express empathy and prevents feelings of being pressured or defensive.
 - There is also a less common but important need to set boundaries for aggressive or other negative behaviors. If a clinician is anticipating a clinical encounter where they expect to have a challenging interaction or if inappropriate behavior occurs during a clinical encounter (e.g. inappropriate language, raising one's voice) it's important to set clear boundaries by stating the expected behavior and the consequences if unable to comply.
 - Example: "Mr. Smith, I'd like to ask you to lower your voice and not use any profanity. Do you think you'll be able to do that? If not, we may have to end this appointment."
- Provider self-care is important to maintain empathy. Clinician burnout, poor boundary setting, and overidentification with a patient's suffering can lead to negative emotions and unintentional resentment and stigma.

COMPONENT 8

8

Employ an integrated, team-based approach to pain and addiction care.

RATIONALE

Integrated, team-based care is the future direction of medical care, and there is good evidence that this approach to pain and addiction leads to the best outcomes. The silos of care that characterize conventional medical approaches create obstacles to successful care coordination.

OBJECTIVES

A. MESSAGE: Team-based approach to pain and addiction care is effective.

- A1 Define integration and its relationship to the team structure and function of a healthcare team.
- A2 Describe the components and characteristics of an effective team to assist in the care of someone with pain and/or addiction.

B. MESSAGE: Interdisciplinary, integrated care has a role in the care of all patients.

B1 Describe the process of creating an interdisciplinary care team in the outpatient setting.

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A. MESSAGE: Team-based approach to pain and addiction care is effective.

A1. Define integration and its relationship to the structure and function of a healthcare team.

- Integration has been defined as "the linkage of differentiated parts of a system" (adapted from Siegel DJ, 2012). This
 definition resonates on multiple levels: in physics (e.g. water molecules interacting in a cloud), neurobiology (e.g. regions of
 the brain), intrapersonal functions (e.g. functions of the mind), and organizations (e.g. members interacting in a team).
- Healthcare teams are composed of members from different disciplines with highly specific training who perform different, specialized functions. The degree of linkage in a team is determined by the communication, interaction, structural organization, and philosophical approach of the team members. The degree of linkage then determines the degree of team integration.
- Healthcare team integration can be seen on a spectrum, from a single discipline clinic (minimal integration) >
 multidisciplinary clinic > interdisciplinary program > interprofessional team (maximal integration).
 - Single-discipline clinics have clinicians from one discipline that provide care (e.g. cardiology, orthopedic, or pain clinics) and need to connect with outside clinicians in order to integrate care. They can maximize integration by developing networks of diverse health professionals that have a common way of understanding and managing patient care. A high degree of communication (verbal, electronic, and through the medical record) is necessary to develop and cultivate this type of virtually-integrated team.
 - Multidisciplinary clinics involve multiple clinicians from different disciplines -- often in the same physical space -- that may be working from different treatment models (biomedical vs socio-psycho-biological) and without coordinated discussion of the treatment plan. Opportunities for communication (e.g. regular team meetings to discuss treatment planning and process improvement) are lacking, and treatment plans are episodic and not coordinated between disciplines.
 - Interdisciplinary programs include multiple clinicians from different disciplines who share a common treatment model (e.g. socio-psycho-biological) and develop a coordinated treatment plan. This is usually done through a patient assessment process that involves members from multiple disciplines and through daily interactions and communication and regularly scheduled team meetings (which additionally provide a forum for continuous process improvement). The organizational structure of interdisciplinary programs fosters a high degree of integration by arranging clinicians' schedules to prioritize and allow for co-disciplinary assessments, daily team huddles, weekly team meetings, and shared professional and program development.³³⁸
 - Interprofessional teams include many of the aspects of interdisciplinary programs while also placing the highest value on mutual respect, trust, excellent communication skills, and an interest to collaborate among clinicians from diverse disciplines. Interprofessional collaboration entails mutual contribution from different disciplines to the overall treatment plan and an openness to contributions from each other. Over time, while each team member retains the unique differentiated expertise of their own discipline, their professional growth includes incorporating insights from other disciplines.

A2. Describe the components and characteristics of an effective team to assist in the care of someone with pain and/or addiction.

- The care of someone with complex pain and/or addiction is ideally done in a team-based setting. The components of these teams are similar.
 - Depending on the needs of the patient, the key disciplines that benefit patients with higher complexity chronic pain and/ or addiction can include primary care, substance use specialties, pain medicine, mental health, nutrition and diet, health coaching, social work, and movement specialties (e.g. physical therapy).
 - If interdisciplinary care is not available in a single care setting, it should be coordinated virtually between distinct care sites.
- The characteristics of these teams that make them effective include shared commitment and across providers and disciplines.³⁴³
 - A team must have leadership and organization commitment (commitment to integrated care), team development (jointly developed values of quality patient and patient-centered care), team relationships and personal rapport, team process (clinical care reviews, transparency and continued assessment of team) and team outcomes (tracking patients' treatment through objective, evidence-based measures).

- Integrated care for pain and/or addiction is effective.³⁴⁴
 - Collaborative care has been shown in randomized clinical trials to increase the proportion of primary care patients receiving evidence-based treatment for opioid and alcohol use disorders and the number of patients achieving abstinence at six months.³⁴⁵
 - A Cochrane Review has showed that multidisciplinary care is more effective than usual care in reducing low back pain and disability and has a positive influence on work status.¹⁶⁷
 - A recent Cochrane meta-analysis showed that interprofessional collaboration was associated with small improvements in patient functioning, professionals' adherence to recommended practices, and utilization of healthcare resources.³⁴⁶

B. MESSAGE: Interdisciplinary, integrated care has a role in the care of all patients.

B1. Describe the process of creating an interdisciplinary care team in the outpatient setting.

- The current health care system is financially incentivized and designed to deliver episodic, single discipline, disease-focused care.
- Top-down (change from leadership, governmental organizations, and payers) and bottom-up (grassroots change from patients and providers) efforts are needed to transform the health care system to drive care that is whole-person, team-based, interdisciplinary, longitudinal, and focused on health promotion and illness prevention.
- For large organizations, this transformation of care centers around maximizing health care value and patient outcomes rather than simple market forces.
- Creation of an interdisciplinary care team within an organization includes processes such as 1) Define goals and develop
 a shared aim; 2) Define specific, measurable outcomes and objectives; 3) Assign roles for each team member and define
 and delegate functions and tasks; 4) Ensure that each team member is competent to perform their defined and delegated
 functions and tasks; 5) Ensure that clinical and administrative systems support team members in their defined work; 6)
 Create communication structure and processes; and 7) Use data to assess team progress and performance regularly.³⁴⁷
- Integrated care can be provided within the same physical space or can be separated by location.
 - Co-located care (different disciplines working in the same physical space) does not necessarily translate to integrated care. Often disciplines remain siloed in their philosophies and care approaches despite being located in the same physical space.
 - An interventional pain clinic may employ a psychologist, but if the practice of the interventional pain physician does not incorporate a behavioral perspective with a focus on active therapies and self-management, the practice is colocated but not integrated.
 - On the other hand, a primary care provider (PCP) may be practicing in a solo environment, and create a virtual team which includes a psychologist practicing in a different physical location. Although the PCP and psychologist are practicing in separate locations, if they incorporate the team elements of common rehabilitation treatment goals, collaborative communication, and a high degree of mutual respect, this clinical pair will be delivering integrated care.
 - Virtual (meaning, not same physical space) integrated care teams can be created by any core provider type, but the primary care provider may be best suited within the health care system. This type of care has also been termed a "distributive model."
 - Key elements to create a virtual integrated team include: 1) the team leader works with the patient to determine the treatment goals; 2) the team leader establishes relationships with various providers of different disciplines who are open to supporting the common treatment goals (improved function, rehabilitation approach, focus on active strategies, de-emphasizing invasive treatments for most chronic pain conditions, supportive of evidence based pharmacotherapy and psychosocial treatments; 3) care manager who guides the patient through the virtual care team; and 4) excellent communication amongst care team and with the patient.
 - A recent Cochrane meta-analysis showed interprofessional collaboration was associated with small improvements in patient functioning, professionals' adherence to recommended practices, and utilization of healthcare resources.³⁴⁶

COMPONENT 9

COMPONENT 9

9

Engage family and social support in the care of pain and addiction.

RATIONALE

Beyond the clinician-patient relationship, community is centrally important to the sustained recovery of persons with pain and addiction. This core component pointedly focuses on the need for family and social support.

OBJECTIVES

A. MESSAGE: Family and social support play an important role in the care of a person with pain and/or addiction.

- A1 Describe the impacts of pain, addiction and disability on family members including potential for and consequences of caregiver burnout.
- A2 Describe the impact family and social support can have on recovery from pain and addiction.
- **B.** MESSAGE: Resources and education can empower family and social supports to care for themselves and build healthy relationships with persons with pain or addiction.
 - B1 Detail family resources for care, including family therapy and crisis response numbers.
 - B2 Describe illness and wellness behaviors in persons with chronic illness, including their significance within the family and social spheres.
 - B3 Discuss the importance/use of naloxone for a family member or social support figure, and how to access it.

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A. MESSAGE: Family and social support play an important role in the care of a person with pain and/or addiction.

A1. Describe the impacts of pain, addiction, and disability on family members including the potential for and consequences of caregiver burnout.

- Chronic pain may disrupt previously established roles and relationships within families.³⁴⁸
 - Family members often find that they need to undertake activities, such as care duties, participation in and evaluation of treatments and managing medications. They also must become involved in decision-making when consulting doctors. As a result of these new obligations, which they often find difficult to cope with, relatives may suffer a physical and psychological deterioration.
 - Studies that analyzed the impact of oncological and non-oncological pain on relatives who act as caregivers found that over 30% of caregivers admitted that they could not cope with the pain-related problems affecting their relative. Many caregivers had problems with anxiety and depression.³⁴⁹
 - In another study, it was observed that a high proportion of the relatives of patients with chronic pain patients suffered anxiety or sadness, and that they had stopped taking part in social activities because of the presence of pain in their family.³⁴⁹
 - It was also demonstrated that 60-70% of caregivers for patients with chronic pain displayed one or more related pathologies, and that the discomfort suffered by the caregiver was sometimes even greater than that reported by the patient.³⁴⁹
 - Stressors that a patient with chronic pain puts on their family members include: 1) Family loss (financial, family, friendships, social activities); 2) Life changes (relationships, role reversals, career/employment prospects; 3) Emotional impacts (self-blame, anger, fear);and 4) and Future plans (expected outcomes of the condition, ability to survive the experience).³⁵⁰
- The relationships between children and parents may become strained, with potentially lasting effects, when an individual is experiencing chronic pain and/or addiction.
 - Children with parents who have chronic pain are at risk for poorer outcomes in areas of pain, health, psychological and family functioning compared to children with parents without chronic pain. This may be directly related to parental pain or to other characteristics associated with chronic pain, such as comorbid mental health issues, medication use, pain-related disability, or dysfunctional parenting strategies.^{351 352}
 - Children with parents with *substance use disorders* face elevated risks for poorer academic functioning; emotional, behavioral, and social problems; an earlier onset of substance use; faster acceleration in substance use patterns; and higher rates of alcohol and drug use disorders.
 - Children of parents with substance use disorders are potentially at greater risk for poorer outcomes due to parenting deficits (less warmth, responsiveness, and physical and verbal engagement as well as harsher and over-involved interaction styles), greater risk for child maltreatment, and less secure attachment patterns.³⁵³
 - Frequently, children may act as surrogate spouses for the parent that has a substance use disorder. Children
 - may also develop elaborate systems of denial to protect themselves against the reality of the parent's addiction.
 A parent of small children may attempt to compensate for deficiencies that his or her spouse with a substance use disorder has developed as a consequence of that substance use.
 - Aging parents of adults with substance use disorders may maintain inappropriately dependent relationships with their grown offspring, missing the necessary "launching phase" in their relationship.354
- Evidence suggests that the effects of substance use disorders frequently extend beyond the nuclear family.
 - Extended family members may experience feelings of abandonment, anxiety, fear, anger, concern embarrassment or guilt. Some may feel the need for legal protection from the person with the substance use disorder.354
 - The effects on families may continue for generations. Intergenerational effects of substance use disorder can have a negative impact on role modeling, trust, and concepts of normative behavior.
 - In most cases, a restructuring of the entire family system is needed, including the relationship between the parents and the relationships between the parents and the children.

A2. Describe the impact family and social support can have on recovery from pain and addiction.

- Family-involved treatment is a distinct shift from the typically minimal involvement of families in the treatment of other chronic conditions.
 - Involving the family (with patient's consent) for the precontemplative patient can help with moving the patient along the stages of change.
 - As change takes place during a patient's diagnosis and treatment, family therapy helps all family members understand what is occurring. This transparency also removes any suspicion that the family is "ganging up" on the person abusing substances.³⁵⁴
 - While there are limited studies of the effectiveness of family therapy in the treatment of substance use disorder generally, substance use disorder treatment that includes family therapy works better than treatments that do not. It increases engagement and retention in treatment, reduces the patient's drug and alcohol use, improves both family and social functioning, reduces the impact of harm for family members and others affected (including children) and discourages relapse.³⁵⁴
 - Another goal of family therapy in substance use disorder treatment is prevention, especially keeping substance misuse from moving from one generation to another. Some studies have found this to be successful.
- Interpersonal settings (with peers, family, spouse) are perhaps the most potent reinforcers of substance use, abstinence, pain behaviors, illness behaviors and wellness behaviors.
 - Helping patients identify the interpersonal factors that are supporting and impeding their recovery is critical. All aspects
 of treatment must be aware of and work to enhance interpersonal factors supporting recovery and managing barriers
 to recovery.
 - Transformation of a patient's relationship with these factors is not trivial. It can mean avoiding or changing relationships. Providers can help their patients create a positive environment that is supportive of treatment and recovery.
 - A common mantra is the Serenity Creed: accept with serenity what you cannot change, have the courage to change what you can, and develop the wisdom to know the difference.
 - Adverse childhood events are important predictors for both the development of chronic pain and substance use disorders. This underscores the importance of the interpersonal environment, particularly in the early developmental period as well as the effects of stress and threat detection as risk factors for the development of chronic pain and addiction.
- Twelve-Step Programs (TSP) are mutual help groups open to anyone desiring not to drink or use drugs. Participation in TSP is associated with improved abstinence rates compared to non-participation and shows a dose-response relationship. Participation is anonymous, there is no cost, and questions are not asked of newcomers. The active ingredients of TSP are thought to be involvement and attendance, having a sponsor, studying and following the direction of the steps, telling one's story at a meeting, and social/network support.³⁵⁵
- **B.** MESSAGE: Resources and education can empower family and social supports to care for themselves and build healthy relationships with persons with pain or addiction.

B1. Detail family resources for care, including family therapy and crisis response numbers.

- Family members benefit from education and support that helps them assist their relatives achieve specific goals. Groups for chronic pain patients and their spouses have proved helpful in reducing anxiety, depression, and interpersonal relationships.³⁴⁸
- A small but growing body of data has demonstrated the cost-benefit of family therapy for substance abuse problems.³⁵⁴
- There are national and local resources for family members.
 - Arizona has a Crisis Response Network that is part of the National Suicide Prevention Lifeline network. From within Arizona, calls are routed to the Crisis Response Network locally: 800-273-TALK.³⁵⁶
 - Arizona has a local Opioid Assistance and Referral Line (OAR Line) to assist community members and physicians on complicated cases with pain and addiction. Arizona specialists can be called 24/7 to assist with questions about medications, linkage to care, rehabilitation facilities, and risk mitigation strategies: 888-688-4222.

- Al-Anon is a Twelve Step Program for friends and relatives of persons who have been impacted by another's drinking. Al-Anon is not family therapy and does not focus on the person with the substance use disorder, but rather focuses on helping the family member or friend to recover from the effects of someone else's drinking.
- Network Therapy and Community Reinforcement And Family Training (CRAFT) are specific approaches that aim to enlist social support networks to support the patient's recovery from substance use disorders. It teaches family and friends effective strategies that help to affect the loved one's behavior. See https://motivationandchange.com/.

B2. Describe illness and wellness behaviors in persons with chronic illness, including their significance within the family and social spheres.

- Illness behaviors refer to the varying ways individuals respond to bodily symptoms, how they monitor internal states, define and interpret symptoms, make attributions, take remedial actions and utilize sources of care. These behaviors are influenced by symptom perception, symptom interpretation, symptom expression, and coping behaviors. This concept recognizes the distinction between illness and disease as well as the social, psychological, and cultural factors that shape an individual's response to symptoms and disease.³⁵⁷
 - When a person is defined by themselves or society as "sick," they are relieved of otherwise normal responsibilities such as working, supporting themselves and their family, contributing to the community, exercising, and maintaining a healthy social network.
 - Pain behaviors are a type of illness behavior, and represent the broad range of behaviors that people display to communicate to others that they are experiencing pain, distress or suffering ("all behaviors that tell us or another person that we are in pain"). Examples include facial grimacing, paralinguistic vocalizations such as sighs and moans, rubbing the painful body part, moving very slowly, taking medications to reduce pain, withdrawing, excessive resting, cancelling plans, and describing pain symptoms and/or pain history and their impact on suffering).
- Wellness behaviors are all behaviors that are incompatible with the expression of pain (all behaviors that signal to others that you are feeling okay and they do not have to worry about you). Examples include exercise, talking about health goals, eating healthy, smiling, appropriate activity pacing and relaxation techniques.
- Social responses to a person's behaviors can serve to either maintain or reduce the behaviors (operant conditioning). One of the treatment goals for patients with chronic pain is to reduce pain behaviors and encourage wellness behaviors. Both the treatment team as well as the patient's social network should be involved in working towards this goal.
 - Facilitative responses or encouragement of wellness behaviors from others (e.g. "you're doing a good job", "I'm happy you're more active") is related to lower levels of patient-reported pain behaviors. In contrast, negative responses to pain behaviors (e.g. being critical, ignoring someone), as well as higher levels of solicitous responses to pain behaviors (e.g. trying to keep stress out of the house, offering to cover normal life responsibilities) are generally related to poorer patient functioning.
 - Responses that increase pain behaviors: offering to help with tasks or taking over roles, monetary compensation, avoidance of unpleasant activities or emotional demands, increased caretaking and expressing concern for ability to carry out activities.³⁵⁸ While these behaviors are often seen in spouses, they can also be seen in healthcare providers.
 - Responses that reduce pain behaviors: being neutral (e.g. not paying attention) to the pain behavior while increasing attention and communication toward wellness behaviors.
 - Spousal pain beliefs about disability, emotion, control, and medication have been significantly correlated with partners' pain severity and other indicators of pain adjustment. Emotion, disability, and other beliefs have been related to spousal responses to pain, and spouses' depressive symptoms and marital dissatisfaction.³⁵⁹
 - Higher levels of solicitousness of spouses were related to heightened pain perception in patients with chronic pain.³⁵⁸

B3. Discuss the importance/use of naloxone for a family member or social support figure, and how to access it.

- Naloxone administration has been identified as a life-saving measure following opioid overdose. There is moderate evidence that take-home naloxone programs are effective at improving overdose survival and decreasing mortality.²³⁸
- Distribution of naloxone is supported by Centers for Disease Control and Prevention, Substance Abuse and Mental Health Services Administration, Veterans Administration, Department of Defense, the American Medical Association and other associations.
- Multiple clinics already have standing orders for naloxone and should create one if it does not currently exist. Other
 insurance companies and state health departments may have standing orders for naloxone, not requiring persons or family
 member to have a personalized prescription from a doctor's office in order to access it.

COMPONENT 10

10

Critically evaluate systems and seek evidence-based solutions that deliver quality care and reduce pharmaceutical influence in the treatment of pain and opioid use disorder.

RATIONALE

An awareness of and responsiveness to the larger context and system of health care has been established in this curriculum; this core component ensures that learners can evaluate these systems and find solutions to inevitable barriers to the safe, quality care of patients. This requires the learner to be proactive and reflective and to critically evaluate the evolving field of health care.

OBJECTIVES

A. MESSAGE: Systems and individual clinician care require continual, critical evaluation.

- A1 Explain how use of patient-centered outcomes can enhance pain and/or addiction care.
- A2 Demonstrate skill in appraising sources, content and applicability of evidence with an emphasis on quality, safety, population health and cost-effectiveness.
- A3 List ways a provider can evaluate his/her own practice, including use of a data registry of patients with chronic pain and morbidity reviews.
- B. MESSAGE: Quality pain and addiction care requires resourceful efforts to overcome obstacles to care.
 - B1 Describe clinical resources within the healthcare system, governmental entities and private organizations that can assist with care management and treatment.
- C. MESSAGE: Pharmaceutical companies have an impact on clinical care.
 - C1 List examples of how pharmaceutical companies influence continuing medical education, published evidence and clinical guidelines.
 - C2 Summarize how pharmaceutical companies have impacted prescribing practices and clinical practice.
 - C3 Detail ways to reduce pharmaceutical influence on clinical practice at the level of individual clinician and health care systems.

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A. MESSAGE: Systems and individual clinician care require continual, critical evaluation.

A1. Explain how use of patient-centered outcomes can enhance pain and/or addiction care.

- Patient-centered outcomes focus on outcomes that are important to patients. It is an umbrella term that encompasses POEMs (Patient Oriented Evidence that Matters) and PROs (Patient-Reported Outcomes).³⁶⁰
 - POEMs, or Patient Oriented Evidence that Matters, represent a framework to guide clinicians toward highly relevant medical evidence, looking at outcomes that are important to patients (Patient Oriented Evidence, not Disease Oriented Evidence) and that has potential to change their practice (evidence that Matters).
 - A study is called a POEM if the answer to the following three questions is yes: 1) Will this information have a direct bearing on the health of my patients? 2) Is the problem common in my practice? 3) If valid, will this information require me to change my current practice?³⁶⁰
 - By using the POEM framework to identify useful articles, providers can focus their browsing and literature reviews to the most relevant and impactful articles for practice change.
 - PROs, or Patient-Reported Outcomes, are reports of a patient's health, quality of life, or functional status associated with health care or treatment that are directly reported by the patient and that are important to the patient.³⁶¹
 - There are measures based on PROs that act as validated tools -turning a patient's report of symptoms, function, or well-being into a score that can be used to track a patient's progress over time, compare a patient to a particular population, compare treatments to each other, and create benchmarks for treatment centers.
 - PROMIS®, or Patient-Reported Outcomes Measurement Information System, is a set of patient-centered measures that evaluates and monitors physical, mental and social health in adults and children. It is designed to enhance communication between clinicians and patients and to be relevant across all conditions for the assessment of symptoms and function.³⁶²
 - > Providers can implement PROs to track patient's progress in terms of outcomes that are important to the patient.
 - Outcomes includes sleep interference, physical function, pain interference, social functioning, anger, depression, and anxiety.
 - For patients with chronic pain, they can help identify other dimensions of the person's life that are dysfunctional and would benefit from attention.
- The PICO process is a technique used in evidence-based practice to frame and answer a clinical or health care related question. The PICO acronym stands for <u>Patient</u>, <u>Problem or Population</u>; <u>Intervention</u>; <u>Comparison</u>, <u>Control or Comparator</u>; and <u>Outcome</u>.
 - Providers should frame their clinical questions in terms of PICOs, making the literature search directly relevant to the patient or problem at hand.

A2. Demonstrate skill in appraising sources, content and applicability of evidence with an emphasis on quality, safety, population health and cost-effectiveness.

- With the vast amount of information bombarding clinicians, information mastery is needed in order to effectively and efficiently identify, evaluate and use new information. Information mastery is the application of evidence-based medicine concepts and techniques to the daily practice of medical care.
 - The first principle of Information Mastery is that some information sources are more useful to clinicians than others. Patient-Oriented Evidence that Matters (POEMs) are addressed in the prior objective, and are studies that provide direct evidence that a medical intervention, on average, lengthens life, decreases symptoms, and/or improves life quality.³⁶³
 - The second principle is that the most useful information must have three attributes: it must be relevant to everyday practice, it must be correct (valid) and it should require little work to obtain. The common equation used is "Usefulness of the Medical Information = (Relevance x Validity) / Work."³⁶⁰
 - Regarding relevance is it a common/important problem, does the study address a relevant population, did it report POEMs?
 - Regarding validity did the authors minimize bias, was the study funded or performed by individuals or entities with a financial interest in the results, did the study report all outcomes and did they match what they were looking for, and does the math work?
 - Regarding work is it easy to read and is it available anywhere (bedside, consulting room)?

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- The third principle is that clinicians always need two types of information tools: a resource in which to hunt for information at the point of care,³⁶⁴ and another "keeping up" resource that finds and presents new research findings that are both relevant and valid.³⁶⁵
- The fourth principle is that clinicians must mix the best available evidence with the clinical experience necessary to understand what each patient needs.³⁶⁶
- Information mastery helps clinicians interpret the overall body of literature.
 - For example, research has shown author bias can affect research results. Knowing the financial and other conflicts of interest of studies are necessary in order to determine the utility and validity of published literature.
 - An example relevant to pain is that research performed by interventional pain doctors are nearly three times as likely to demonstrate positive outcomes versus studies performed by non-interventionalists.^{367 368}
 - There is also evidence that funding sources correlate with the outcomes of clinical trials.
 - One study analyzed randomized cardiovascular trials that had been published in medical journals between 2000-2005, and found that 67.2% of studies funded by for-profit organizations favored the newer treatment, whereas only 49% of non-profit organizational studies showed results in favor of the newer treatment.³⁶⁹
 - This contrast was even more pronounced for pharmaceutical drugs: 65.5% of industry-sponsored studies showed benefits of a newer treatment, but 39% of non-profit funded studies did.³⁶⁹
 - A meta-analysis found that research supported by the drug industry was more likely to produce results favoring the product made by the company sponsoring the research than studies funded by other sources (summary odds ratio: 4.05). The results play across a range of diseases and drugs and over two decades of research.³⁷⁰
- Poor appraisal of the literature can result in adoption of unsafe practices. This was exemplified in the pharmaceutical industry's misrepresentation of a letter to the editor demonstrating that iatrogenic addiction from opioids was "very rare."⁵⁰
- Didactic dissonance can occur when learning new concepts, and the stance of the educator towards this dissonance can either erode or support evidence-based practice.
 - Didactic dissonance occurs when learners see or hear opposing didactic messages. For example, learners may learn about the lack of evidence for long-term opioid treatment for chronic pain in the classroom, but they see providers starting such treatment in the clinical setting. Another example is that learners may be tested on the black box warning of concurrent benzodiazepines and opioid use, but they see it regularly prescribed on their rotations.
 - When educators sidestep the discomfort caused by dissonance, learners miss an opportunity to develop critical assessment skills and evidence-informed practice may suffer.
 - Rather than avoiding dissonance, educators should encourage learners to identify and explore opposing didactic messages, and theorize why a potential evidence-practice gap exists.
 - Evidence-practice gaps can be found throughout medicine, and exploring why they exist may prevent learners from developing large gaps in their own future practice.

A3. List ways a provider can evaluate his/her own practice, including use of a data registry of patients with chronic pain and morbidity reviews.

- Creation and maintenance of a data registry of patients with chronic pain is a useful evaluation tool. The registry can be
 used to track data for prescription management, which helps ensure that care is appropriate and provides measures to
 track improvement and activities.³⁷²
 - Some common elements in registries include the date of renewal of patient agreement, current morphine milligram
 equivalent dose of opioid medications, date of most recent prescription drug monitoring database check, date and result of
 most recent urine drug tests, date of last visit, date that naloxone was prescribed, a medication list to review for concurrent
 use of sedatives and screens for depression.
- State Boards of Pharmacy and other care organizations (e.g. Kaiser) often have report cards that compare providers' controlled substance prescribing practices. The Board of Pharmacy in Arizona performs this service and offers awareness to a provider on his/her prescribed opioid doses and the presence of any dangerous combinations.³⁷³

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- Morbidity reviews, or group presentation and discussions about particular patients with poor outcomes, are useful for the
 provider and their colleagues. There are multiple ways to structure a morbidity or mortality review, but all require a safe
 learning environment and openness to identify issues and concerns. Reviews are only impactful if following a review there
 are specific actions identified and assigned.
- No matter what tool, the imperative part is to evaluate one's practice. This evaluation requires identification of key process
 and outcome measures to monitor practice change implementation and agreed upon patient care data. Commonly
 monitored measures include the proportion of patients with an up-to-date agreement in the chart and the proportion of
 patients with prescription drug monitoring database checks in the past quarter. Clinics can discuss these measures during
 monthly staff meetings and leadership team meetings.³⁷²
- [See Component #2 for the roles of intellectual curiosity and humility in evaluations.]

B. MESSAGE: Quality pain and addiction care requires resourceful efforts to overcome obstacles to care.

B1. Describe clinical resources within the healthcare system, governmental entities, and private organizations that can assist with care management and treatment.

- The healthcare system is complex, and the location and level of resources available to individuals is often unknown or unrecognized.
- It is the role of the clinician and healthcare team to help a person utilize resources to overcome obstacles to care. It is not
 the role of the clinician or system to navigate the obstacles on behalf of the patient.³⁷⁴
- There is evidence that care management interventions improve outcomes across chronic diseases (most commonly studied for diabetes, asthma, CHF, COPD and CAD).
- There are several potential avenues for clinical support and services that patients with pain and addiction can explore.
 - Clinical resources within the health care system in which the person is receiving care (contact social services, patient advocates)
 - Insurance companies (contact social services, patient advocates)
 - Self-help and peer recovery groups (search for in-person and online groups)
 - · Community-based treatment and recovery resources (search online)
 - Schools and Student Assistance Programs (contact counselors)
 - · Employers and Employee Assistance Programs (contact employee wellness and human resources)
- [See Component #2 for the roles of intellectual curiosity and creativity in resource findings.]

C. MESSAGE: Pharmaceutical companies have an impact on clinical care.

C1. List examples of how pharmaceutical companies influence continuing medical education, published evidence and clinical guidelines.

- Clinical trials funded by for-profit organizations are more likely to report positive findings than trials funded by not-for-profit organizations.³⁷⁰
- Clinical practice guidelines are generally accepted as an objective consensus on evidence, but they are often influenced by industry. Out of 44 North American Guidelines studied in 2002, 87% of authors had some form of interaction with the pharmaceutical industry.³⁷⁵

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- Academic journals have advertising which is often misleading, and contain editorials favorable to industry, leading to
 accusations that they are "corrupting science to promote drugs." Drug-sponsored trials are also commonly published in
 these journals.³⁷⁶
- Continuing Medical Education is often sponsored by pharmaceutical companies. It has been found that sponsorship
 influenced behavior of conference attendees, leading to attendees prescribing more drugs from the sponsoring companies,
 without sufficient evidence supporting superiority of those drugs. The majority of attendees failed to identify inaccurate
 information about the company drug.³⁷⁷
 - Accepting funding to attend a symposium was independently associated with increased formulary requests for the sponsor's drug. This interaction was also found to impact hospital prescribing practices two years after groups of physicians accepted all-expenses-paid trips to a drug-sponsored symposium. This occurred despite the continued prescribing of the two drugs that the new ones were to replace.³⁷⁸

C2. Summarize how pharmaceutical companies have impacted prescribing practices and clinical practice.

- It has been estimated that \$8,000 to \$13,000 is spent per year by pharmaceutical companies on each physician.³⁷⁹
- Pharmaceutical representatives provide selected, usually positive, information about their products.³⁸⁰
 - For example, Purdue Pharma funded over 20,000 pain-related educational programs through direct sponsorship or financial grants from 1996, when OxyContin® was introduced to the market, to July 2002.³⁸¹
 - In 2007, Purdue plead guilty to felony charges of misbranding OxyContin[®] with the intent to mislead and defraud physicians and consumers.³⁸²
- 84% of physicians have some relationship with the pharmaceutical industry, from contacts with drug representatives to
 research collaborations. Accepting samples leads to higher branded drug prescription rather than generic prescribing. Drug
 samples do not reduce prescription costs for patients and most likely raise the cost of drugs and contribute to
 health care overspending.^{383 384}
- Interactions with pharmaceutical representatives were found to affect the prescribing practice of residents and physicians in terms of prescribing cost, nonrational prescribing, awareness, preference and rapid prescribing of new drugs, and decreased prescribing of generic drugs.³⁷⁸
- The majority of physicians do not believe that they are affected by pharmaceutical industry and representative interaction. They believe, however, that their colleagues are more susceptible to pharmaceutical industry marketing strategies than themselves.³⁸⁵

C3. Detail ways to reduce pharmaceutical influence on clinical practice at the level of individual clinician and health care systems.

- Decline visits from pharmaceutical companies, and do not accept pharmaceutical detailing, lunch, swag or materials in your clinical practice.
- Replace pharmaceutical detailing with academic detailing (non-commercial-based educational outreach), which is evidence-based and effective.
- Replace pharmaceutical samples with Prescription Assistance Programs.
- Read financial disclosures of all authors of clinical guidelines and consider them in how they are applied to patients.
- Search ProPublica's Dollars for Docs program or CMS Open Payments data website, in order to see particular pharmaceutical companies' influence on referral clinicians' and your own care.
- [See Component #2 for the role of intellectual courage in reducing undue influence on clinical care.]

APPENDIX A

APPENDIX A: ARIZONA AND NATIONAL RESOURCES

There are a number of new resources for Arizona clinicians to aid in the teaching of this material and in implementing it into a clinical setting.

ARIZONA RESOURCES

Arizona Pain and Addiction Curriculum Homepage [azhealth.gov/curriculum]

 This page contains links to the Arizona Pain and Addiction Curriculum and the associated Arizona Pain and Addiction Faculty Guide. It also provides infographics about the process to create the curriculum, along with details and links regarding the initial Curriculum Summit.

Arizona OAR Line – Opioid Assistance and Referral Line [1-888-688-4222]

• This 24/7, real-time call line is answered by Arizona experts in order to provide consultation regarding complex patients with pain and opioid use disorder, recommendations on exit strategies and referrals to medication-assistant treatment.

Arizona Prescription Drug Monitoring Database [pharmacypmp.az.gov]

This is the Arizona Board of Pharmacy's Prescription Drug Monitoring Database. A.R.S. § 36-2606 requires each medical practitioner licensed under Title 32 (i.e. MD, DO, DDS, DMD, DPM, HMD, PA, NP, ND, and OD) and who possesses a DEA license to review the preceding 12 months of a patient's PMP record before prescribing an opioid analgesic or benzodiazepine controlled substance listed in schedule II, III or IV. Exceptions are described in A.R.S. § 36-2606. Medical residents may register using the hospital DEA number and appropriate suffix. Prescribers must register on the Arizona Board of Pharmacy website.

Arizona Opioid Prescribing Guidelines (2018) [azhealth.gov/opioidprescribing]

 A voluntary, consensus set of guidelines that promote patient safety and best practices if prescribing opioids for acute and chronic pain. The posted guidelines have clickable links and search functions. Bound printed copies of the guidelines can be ordered on the website.

Arizona Opioid Epidemic Homepage [azhealth.gov/opioid]

• This page hosts real time opioid data, naloxone standing orders, the information on the Arizona Opioid Epidemic Act, links to Licensing Rules, Laboratory Testing and Reporting.

NATIONAL RESOURCES

Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain [cdc.gov/drugoverdose/prescribing/guideline]

This set of guidelines was released in 2016 and served as a jumping point for the Arizona Opioid Prescribing Guidelines (2018).

VA/DoD Clinical Practice Guidelines: Management of Opioid Therapy for Chronic Pain [healthquality.va.gov/guidelines/pain/cot]

• This set of guidelines was released in 2017 and was helpful in accumulating the evidence toward moving toward the use against unnecessary opioids while still addressing a person's pain from a whole-person perspective.

Providers Clinical Support System (PCSS) [pcssnow.org]

• PCSS is a program funded by the Substance Abuse and Mental Health Services Administration (SAMHSA) that maintains an electronic repository of training materials and educational resources to support evidence-based treatment of opioid use disorder and chronic pain. Of note, PCSS provides medication-assisted treatment (MAT) training in several formats (including for nurse practitioners and physician assistants) at no cost.

VA/DoD Clinical Practice Guidelines: Management of Substance Use Disorder [healthquality.va.gov/guidelines/mh/sud]

• This set of guidelines was released in 2015 and is formatted as two algorithms and 36 evidence-based recommendations.

The ASAM National Practice Guidelines For the Use of Medications in the Treatment of Addiction Involving Opioid Use [https://www.asam.org/docs/default-source/practice-support/guidelines-and-consensus-docs/asam-national-practice-guideline-supplement.pdf]

• This practice guideline was published in 2015 and is meant to assist clinicians in diagnosing and treating opioid use disorder and in management opioid overdose. It leads with a summary of recommendations (Assessment Recommendations, Diagnosis Recommendations, Treatment Recommendations, Psychosocial treatment recommendations and Recommendations for Special Populations) before becoming more detailed in exact assessment and treatment.

APPENDIX B

APPENDIX B: CLINICAL TOOLS FOR PAIN AND ADDICTION

There are a number of clinical resources for providers treating patients with pain and/or addiction. The below list includes the Choosing Wisely campaign and VA Personal Health Inventory, which promote discussions of testing and treatment goals between patients and providers; the NIDA Quick Screen and TAPS, which are two user-friendly screening tests for risky substance use; and COWS and CIWA-Ar, the clinical withdrawal scale for opioids and alcohol, respectively.

Choosing Wisely Initiative [choosingwisely.org/]

This is an initiative that seeks to advance the discussions between patients and providers about unnecessary tests and procedures. There are nearly sixty pages of clinical recommendations from difference societies (ranging from the American College of Physicians to the American Dental Association). Relative to pain, it lists recommendations against the routine use of imaging for nonspecific, uncomplicated causes and against using irreversible interventions for non-cancer pain.

VA Personal Health Inventory [va.gov/PATIENTCENTEREDCARE/docs/Personal-Health-Inventory-final-508-WHFL.pdf]

In applying a socio-psycho-biological model of pain and addiction, this is a tool for patients that helps to explore what they want from their health and why. This 11-page workbook that asks patients to consider where they are and where they would like to be, and lists brief tools and techniques for self-care.

NIDA Quick Screen [drugabuse.gov/nmassist]

The NIDA Quick Screen is a screening tool that helps identify risky substance use (including opioid use) in their adult patients. It includes asking the patient how many times, within the past year, has he or she used any of the substances (alcohol, tobacco, prescription drugs, illegal drugs). If the patient says "Never" to all substances, the clinician should reinforce abstinence, and screening is complete. There are other recommendations if the patient says yes to Alcohol or Tobacco, but If the patient says "Yes" for use of illegal or prescription drugs for nonmedical reasons, the clinician should move onto a second eight-question screen.

Tobacco, Alcohol, Prescription medication, and other Substance use tool (TAPS) [drugabuse.gov/taps/#/]

This screening tool consists of a combined screening component (TAPS-1, a 4-item screen for tobacco, alcohol, illicit drugs and nonmedical use of prescription drugs) followed by a brief assessment (TAPS-2, brief substance-specific assessment questions to arrive at a risk level) for those that screen positive. Like the NIDA Quick Screen, it is combines screening and brief assessments for commonly used substances, eliminating the need for multiple screens, and may be either self-administered by the patient or as an interview by a health professional.

Clinical Opiate Withdrawal Scale (COWS)

[drugabuse.gov/sites/default/files/files/ClinicalOpiateWithdrawalScale.pdf]

This is an 11-item scale designed to be administered by a clinician in inpatient and outpatient settings to reproducibly rate common signs and symptoms of opioid withdrawal. The summed score for the complete scale can be used to help clinicians determine the stage or severity of withdrawal and monitoring the symptoms over time.

Clinical Institute Withdrawal Assessment for Alcohol Scale, Revised (CIWA-Ar) [umem.org/files/uploads/1104212257_CIWA-Ar.pdf]

This is an assessment for monitoring withdrawal symptoms that requires approximately five minutes to administer. The maximum scores is 67, and patients scoring less than 10 usually do not need additional medication to manage withdrawal.

APPENDIX C

APPENDIX C: RISK FACTORS FOR ADOLESCENT AND YOUNG ADULT SUBSTANCE USE

There have been multiple studies on the risk factors for drug use, particularly in youth. Likelihood of substance use escalates dramatically across adolescence, peaks in the person's twenties and descends thereafter. Early substance misuse, including alcohol misuse, is associated with a greater likelihood of developing a substance use disorder later in life.^{386 387 388} The following two tables adapt the material from the *Surgeon General's Report on Alcohol, Drugs, and Health*. Tables are formatted so the risk or protective factor is bolded with its definition italicized underneath.

TABLE 5: Risk Factors for Adolescent and Young Adult Substance Use

(Adapted from The Surgeon General's Report on Alcohol, Drugs and Health, 2016)¹²

SCHOOL FACTOR	Adolescent Substance Use	Young Adult Substance Use
Academic failure beginning in late elementary school (Poor grades in school)	RISK	RISK
Lack of commitment to school (When a young person no longer considers being a student meaningful or rewarding, or lack investment or commitment to school)	RISK	RISK
COMMUNITY FACTOR	Adolescent Substance Use	Young Adult Substance Use
Low cost of alcohol (Low alcohol sales tax, happy hour specials, and other price discounting)	RISK	RISK
High availability of substances (High number of alcohol outlets in a defined geographical area or per a sector of the population)	RISK	RISK
Community laws and norms favorable to substance use (Community reinforcement of norms suggesting alcohol and drug use is acceptable for youth, including low tax rates on alcohol or tobacco or community beer tasting events)	RISK	RISK
Media portrayal of alcohol use (Exposure to actors using alcohol in movies or television)	RISK	
Low neighborhood attachment (Low level of bonding to the neighborhood)	RISK	
Community disorganization (Living in neighborhoods with high population density, lack of natural surveillance of public places, physical deterioration, and high rates of adult crime)	RISK	
Low socioeconomic status (A parent's low socioeconomic status, as measured through a combination of education, income and occupation)	RISK	
INDIVIDUAL/PEER FACTOR	Adolescent Substance Use	Young Adult Substance Use
Early initiation of substance use (Engaging in alcohol or drug use at a young age)	RISK	RISK
Early and persistent problem behavior (Emotional distress, aggressiveness and "difficult" temperaments in adolescents)	RISK	
Rebelliousness (High tolerance for deviance and rebellious activities)	RISK	RISK
Favorable attitudes toward substance use (Positive feelings towards alcohol or drug use, low perception or risk)	RISK	RISK
Peer substance use (Friends and peers who engage in alcohol or drug use)	RISK	RISK
Genetic predictors (Genetic susceptibility to alcohol or drug use)	RISK	RISK
FAMILY FACTOR	Adolescent Substance Use	Young Adult Substance Use
Family management problems (Poor management practices, including parent's failure to set clear expectations for children's behavior, failure to supervise and monitor children, and excessively severe, harsh, or inconsistent punishment)	RISK	RISK
Family conflict (Conflict between parents or between parents and children, including abuse or neglect)	RISK	RISK
Favorable parental attitudes (Parental attitudes that are favorable to drug use and parental approval or drinking and drug use)	RISK	RISK
Family history of substance misuse (Persistent, progressive and generalized substance use, misuse, and use disorders by family members)	RISK	RISK

TABLE 6: Protective Factors for Adolescent and Young Adult Substance Use

(Adapted from The Surgeon General's Report on Alcohol, Drugs and Health, 2016)¹²

INDIVIDUAL FACTOR	Adolescent Substance Use	Young Adult Substance Use
Social, emotional, behavioral, cognitive and moral competence (Interpersonal skills that help youth integrate feelings, thinking, and actions to achieve specific social and interpersonal goals)	PROTECTIVE	PROTECTIVE
Self-efficacy (An individual's belief that they can modify, control, or abstain from substance use)	PROTECTIVE	PROTECTIVE
Spirituality (Belief in a higher being, or involvement in spiritual practices or religious activities)	PROTECTIVE	PROTECTIVE
Resiliency (An individual's capacity for adapting to change and stressful events in healthy and flexible ways)	PROTECTIVE	PROTECTIVE
FAMILY, SCHOOL, AND COMMUNITY FACTOR	Adolescent Substance Use	Young Adult Substance Use
Opportunities for positive social involvement (Developmentally appropriate opportunities to be meaningfully involved with the family, school, or community)	PROTECTIVE	PROTECTIVE
Recognition for positive behavior (Parents, teachers, peers and community members providing recognition for effort and accomplishments to motivate individuals to engage in positive behaviors in the future)	PROTECTIVE	PROTECTIVE
Bonding (Attachment and commitment to, and positive communication with, family, schools, and communities)	PROTECTIVE	PROTECTIVE
Marriage or committed relationship (Married or living with a partner in a committed relationship who does not misuse alcohol or drugs)		PROTECTIVE
Healthy beliefs and standards for behaviors (Family, school, and community norms that communicate clear and consistent expectations about not misusing alcohol and drugs)	PROTECTIVE	PROTECTIVE

APPENDIX D

This detailed clinical insert is for programs that teach the specifics of treatment for opioid use disorder. This material draws heavily from the Substance Abuse and Mental Health Services Administration (SAMHSA) Treatment Improvement Protocol (TIP) #63.³³

The World Health Organization's (WHO's) principles of good care for chronic diseases can guide care of a person with opioid use disorder.³⁸⁸

- Develop a treatment partnership with patients.
- Focus on patients' concerns and priorities.
- Support patient self-management of illness.
- Use the five A's at every visit (Assess, Advise, Agree, Assist, and Arrange).
- Organize proactive follow-up.
- Link patients to community resources/support.
- Work as a clinical team.
- Involve "expert patients," peer educators, and support staff in the health facility.
- Ensure continuity of care.

Pharmacotherapy for opioid use disorder is effective and should be offered to all patients with opioid use disorder.

- The main pharmacologic agents used for opioid use disorder include methadone (Methadose[®], Dolophine[®]), buprenorphine (Suboxone[®], Subutex[®], Zubsolv[®], Bunavail[®], Sublocade[™], Probuphine[®]), and extended-release naltrexone (Vivitrol[®]).
 - Methadone and buprenorphine are opioid *agonists*. They have the strongest evidence of effectiveness, and they work by binding to and activating the brain's opioid receptors. When used to treat individuals who are opioid tolerant, these medications result in reduced opioid withdrawal symptoms and cravings. Providers can monitor for any feelings of euphoria on these medications which may occur if initial dosing is too high, the patient is uniquely sensitive to medication, or if the individual is not opioid tolerant.
 - Naltrexone is an opioid antagonist. It works by blocking the activation of the brain's opioid receptors, thus preventing other opioids from producing rewarding effects.
- Pharmacotherapy for opioid use disorder can be referenced by several terms.
 - Medication-assisted treatment (MAT) refers to pharmacotherapy for opioid use disorder + counseling + monitoring for relapse.
 - Opioid agonist therapy (OAT) refers to a subset of pharmacotherapy for opioid use disorder (the opioid agonists, methadone and buprenorphine) and does not include others (the opioid antagonist, naltrexone).

There is strong evidence of the effectiveness of pharmacotherapy in treating opioid use disorder.

- Methadone and buprenorphine can reduce and eliminate withdrawal symptoms.
- Methadone, naltrexone and buprenorphine can blunt or block the effects of illicit opioids.
- Methadone, naltrexone and buprenorphine can reduce or eliminate cravings for opioids.
- Pharmacotherapy can reduce illicit use and dramatically increase treatment retention (compared to placebo, medicallysupervised withdrawal and no treatment).
- Methadone has been shown to reduce the risk of HIV and HCV infection, to lower rates or cellulitis, and to reduce criminal behavior.
- Methadone and buprenorphine can reduce opioid overdose deaths and all-cause mortality^{237, 389} (compared with no medication treatment or psychosocial treatment alone.)

- Pharmacotherapy for opioid use disorder should be continued as long as the patient benefits from it and wishes to continue (with the understanding that therapy may be indefinite). There are very high rates of relapse following tapering of pharmacotherapy for opioid use disorder, thus determining the duration of therapy should be a shared decision-making process.
 - One study found that only 13% of patients were able to taper off methadone with a successful outcome at 19 months.³⁹⁰
 - If a patient decides to discontinue use of buprenorphine or methadone, they should be followed closely and offered Injectable Extended-Release Naltrexone (XR-NTX) after 7-10 days of abstinence. A low threshold should be maintained for restarting treatment.
 - Patients discontinuing buprenorphine or methadone should be prescribed rescue naloxone for family, friends, and bystanders to administer in case of a relapse-related opioid overdose.
- The risks and benefits of using pharmacotherapy, versus no pharmacotherapy, should be discussed with patients.
 - Psychosocial therapies given alone, without pharmacotherapy, have poorer results. For example, one study demonstrated a 0% retention in treatment at one year after cognitive behavioral therapy alone.²³⁴
 - For patients who prefer to avoid medications that activate the opioid receptors, Injectable Extended-Release Naltrexone (XR-NTX) may be an appropriate option. Informed consent should inform patients that XR-NTX is associated with a higher risk of relapse and lower retention in treatment during the required 7-10 days of abstinence prior to initiation, compared to buprenorphine.
 - For patients who prefer to avoid medications altogether, it is important that they understand the risks associated with nonpharmacologic treatment approaches, compared to use of evidence-based medications.

Methadone and buprenorphine are on the World Health Organization's list of essential medications.

Pharmacotherapy for opioid use disorder continues to be underused.

After discussing the use of pharmacotherapy with persons with opioid use disorder, individualized decisions should be made regarding referral for counseling and psychosocial support.

- Legislation from the Drug Addiction Treatment Act of 2000 (DATA-2000) requires clinicians who are prescribing pharmacotherapy for opioid use disorder to be able to refer patients to counseling. The actual referral is not mandatory.³⁸
- Many patients benefit from referral to mental health services or specialized addiction counseling and recovery support services, but it has not been found to be universally beneficial when compared to well-conducted medication management.
 - For patients taking buprenorphine randomized trials have found no extra benefit of adding adjunctive counseling to well-conducted medical management visits delivered by the physician prescribing buprenorphine (although medical management in trials is likely much more intensive than usual care and includes prescribing, assessing for cravings and encouraging support group attendance, motivational interviewing, and relapse prevention counseling).³⁹¹
 - This finding does not apply to all groups: patients with psychiatric comorbidities do benefit from additional therapy.³⁹²
 - This finding does not apply to all psychosocial treatments: e.g. contingency management (offering rewards for abstinence) shows benefit.^{393 394 395}
 - For patients in methadone maintenance programs, the addition of counseling and psychosocial services to methadone pharmacotherapy may result in improved outcomes including decreased illicit opioid use.³⁹⁶ The optimal frequency, of counseling, however, is unknown.³⁹⁷
 - Pharmacologic treatment should not be withheld for the sole reason of patients declining to participate in counseling or other structured psychosocial interventions.
- Common psychosocial support may include one or more of the following during treatment of opioid use disorder:
 - · Supportive counseling by prescriber and support staff (e.g. RNs) in medical management visits
 - · Individual counseling through a mental health provider
 - Mutual support groups (Alcoholics Anonymous, Narcotics Anonymous, Heroin Anonymous, SMART Recovery, Refuge Recovery)
 - Family therapy
 - Standard outpatient program 1 day per week group counseling
 - Intensive outpatient program (IOP) 3 days per week group counseling
 - Partial hospitalization 5 days per week group counseling
 - Residential treatment

The pharmacologic treatment of opioid use disorder is unique due to the additional provider and location requirements dictated by federal law. With the creation of the federal DATA-waiver, providers can now use buprenorphine for opioid use disorder outside of a federally-licensed opioid treatment program, which has significantly increased this medication's accessibility.

- [See TABLE 7 for Comparison of the Medication Administration for Opioid Use Disorder.]
- Note: Federal law prohibits the use of opioid agonists for the treatment of opioid "dependence", with the following exceptions: 1) use of methadone and buprenorphine within federally licensed opioid treatment programs (OTP, often referred to as "methadone maintenance clinics") and 2) use of buprenorphine outside of an OTP by providers with a DATA-waiver.
 - Criteria for DATA-waiver eligibility are briefly listed in *Component #1* and #2, and are comprehensively listed on the SAMHSA DATA-waiver website.³⁹⁸

TABLE 7: COMPARISON OF THE MEDICATION ADMINISTRATION FOR OPIOID USE DISORDER ADAPTED FROM TIP 63 (SAMHSA)³⁸

	BUPRENORPHINE (opioid agonist)
SUMMARY STATEMENT	Buprenorphine has a strong evidence base for its effectiveness. A DATA-waiver is required in order to prescribe or administer it in a standard outpatient clinical setting, which allows for more flexible patient follow up. Patients can be seen daily or weekly. Treatment is not cost-prohibitive.
APPROPRIATE PATIENTS	Typically for patients with OUD who are physiologically dependent on opioids
OUTCOMES	Higher retention in treatment (compared to treatment without medication; compared to treatment with placebo or naltrexone) Effective suppression of illicit opioid use Lower overdose mortality
DRUG SCHEDULES AND PROVIDER REQUIREMENTS	Schedule III Narcotic DEA license required DATA-waiver required
TREATMENT LOCATION AND FREQUENCY	 Office/clinic option*: Begins daily to weekly, then is tailored to patient's needs (requires DATA-waiver) OTP option*: Can treat with buprenorphine 6-7 days/week initially; take- homes are allowed without the time-in-treatment requirements of methadone
WHO CAN PRESCRIBE, ORDER + DISPENSE	Physicians, NPs and PAs ^{**} possessing a federal DATA-waiver can prescribe and dispense; community pharmacies or an OTP can also dispense
TREATMENT FORMULATION	Sublingual/buccal; implant and injectable by specially trained provider and only for stabilized patients
MISUSE/DIVERSION POTENTIAL	Low in OTP and in other observed dose settings, moderate for take-home doses; risk can be mitigated by providing take-homes to stable patients and a diversion plan
ACTION AT THE MU RECEPTOR	Partial agonist at mu receptor; high affinity for mu receptor (blocks and displaces other opioids); slow dissociation from mu receptor
HALF LIFE	24-46 hours
RISK OF RESPIRATORY DEPRESSION	Very rare
WITHDRAWAL RISK AND SYMPTOMS	Risk of precipitated withdrawal if started too prematurely after recent use of other opioids Withdrawal symptoms on discontinuation
SIDE EFFECTS	Constipation, vomiting, headache, sweating, insomnia, sedation blurred vision
MONITORING	Comparatively minimal respiratory suppression and no respiratory arrest when used as prescribed
DRUG-DRUG INTERACTIONS	Phenytoin Atazanavir Rifampin Caution when patient also taking sedative hypnotics

*Exceptions:38

If administering an opioid for <3 days to patient in acute opioid withdrawal while preparing for ongoing care.
 If administering opioid medications in a hospital to maintain or detoxify a patient as an adjunct to medical or surgical treatment of conditions other than addiction.

**NPs and PAs should check with their state to determine whether prescribing buprenorphine and/or naltrexone is within their allowable scope of practice. In Arizona, NP and PAs can prescribe buprenorphine and naltrexone.

METHADONE (opioid agonist)	NALTREXONE (opioid antagonist)	
Methadone has a strong evidence base for its efficiency, but it requires administration in a federally certified opioid treatment program. It requires patients to be seen daily initially. It may be the best treatment option for patients with high degree of complexity who require a structured treatment setting. Treatment is not cost-prohibitive.	Naltrexone is rarely the first choice for treatment, as it has less evidence of effectiveness and requires patients to be abstinent for 7-10 days prior to initiation (corresponding to a high level of drop out). Oral naltrexone is not recommended, due to poor adherence. Injectable naltrexone can be an option used when patients request a non-opioid treatment only. It is more expensive than the other two options.	
Typically for patients with OUD who are physiologically dependent on opioids and who meet federal criteria for OTP admission	Typically for patients with OUD who are abstinent from short-acting opioids for 7 days and long-acting opioids for 10-14 days	
Higher retention in treatment (compared to treatment without OUD	Oral naltrexone shows no better retention in treatment (compared to no medication) and is not recommended	
medication and treatment with placebo) Effective suppression of illicit opioid use	<i>XR-NTX</i> *** (injectable) shows a lower retention in treatment compared to buprenorphine (due to patients dropping out prior to the required 7-10 day abstinence period) but a higher retention in treatment compared with treatment with placebo or no medication	
Lower overdose mortality	Effective suppression of illicit opioid use	
	Unknown effect on overdose mortality	
Schedule II Narcotic DEA license required DATA-waiver not required	Unscheduled DEA license not required DATA-waiver not required	
	Office (alinia: Varias from weakly to monthly	
OTP required: * Begins 6-7 days/week; take-homes allowed based on	Office/clinic: Varies from weekly to monthly. Due to the requirement of requiring abstinence x 7-14 days for naltrexone initiation,	
time-in-treatment and patient progress	inpatient/residential treatment programs are an ideal setting for this medication.	
OTP physicians order the medication; OTP nurses and pharmacists administer and dispense it	Physicians, NPs and PAs**	
Oral	Oral or long-acting injectable (Due to concerns for non-adherence, relapse, and subsequent overdose, use of oral naltrexone is generally limited to patients who are highly motivated, legally mandated to receive treatment, or when observed dosing is possible.)	
Low in OTPs with directly observed therapy; moderate for take-home doses; risk can be mitigated by a diversion control plan	None	
Full opioid agonist; weak affinity for the mu receptor, can be displaced by partial agonists and antagonists	Antagonist; competitive binding at mu receptor; high affinity for mu receptor (blocks and displaces other opioids)	
15-60 hours	Oral – 4 hours IM – 5-10 days	
Rare, although higher than buprenorphine; may be elevated during first 2 weeks of treatment or in combination with other sedating substances	None	
No risk of precipitated withdrawal when starting medication	Severe risk of withdrawal if period of abstinence is inadequate before starting medication.	
Withdrawal symptoms of discontinuation (higher than for buprenorphine)	No withdrawal symptoms on discontinuation	
Constipation, vomiting, sweating, dizziness, sedation	Difficulty sleeping, anxiety, nausea, vomiting, low energy, joint and muscle pain, headache, liver enzyme elevation. (For XR-NTX: injection site pain, nasopharyngitis, insomnia, toothache)	
QTc prolongation, EKG monitoring is performed according to risk for developing ventricular arrhythmias ³⁹⁹	Naltrexone tablet is associated with poor daily adherence; XR monthly injection has	
Significant respiratory suppression and potential respiratory arrest in overdose	better compliance	
Decreases methadone Increases methadone concentrations: concentrations:		
Pentazocine Ciprofloxacin Eluvoyamine		
Phenytoin Fluvoxamine Carbamazepine Drugs that inhibit 2D6,	Patients who are currently taking opioid medication	
Rifampin 3A4, 2B6 (some SSRIs) Efavirenz		
Nevirapine CAUTION with QT prolongating drugs CAUTION with QT prolongating drugs CAUTION when patient taking sedative hypnotics		
Opiate withdrawal syndrome possible		

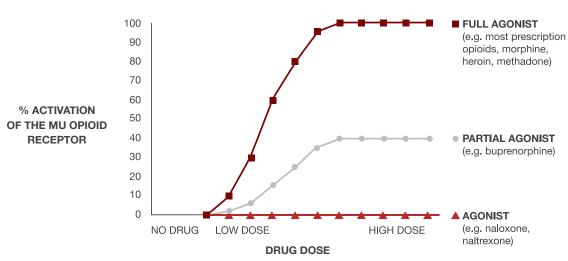
*Exceptions:38

If administering an opioid for ≤3 days to patient in acute opioid withdrawal while preparing for ongoing care.
 If administering opioid medications in a hospital to maintain or detoxify a patient as an adjunct to medical or surgical treatment of conditions other than addiction.

Buprenorphine is a first-line, evidence-based treatment for opioid use disorder. Its unique pharmacologic profile determines prescribing and administration considerations in a physician's office.⁴⁰³

- Buprenorphine is a partial opioid receptor agonist which activates the mu opioid receptor less than 50% of its maximum capacity and has a ceiling effect (past a certain point, higher doses will not further activate the opioid receptor). [See FIGURE 1: Intrinsic Mu Receptor Activity of Opioids and OUD Medications.]
 - Because of the partial agonist activity and ceiling effect, buprenorphine is much less likely than methadone or other opioids to cause respiratory depression and overdose death. (Note: most cases of buprenorphine-related fatalities occur with parenteral use of buprenorphine or concurrent use of other sedatives such as benzodiazepines and alcohol).
- Buprenorphine has a high affinity (i.e. it binds tightly) to the mu opioid receptor.
 - Because buprenorphine has a high receptor affinity and is a partial agonist, it has the potential to cause precipitated withdrawal.
 - Spontaneous opioid withdrawal is a characteristic syndrome [See GLOSSARY, Opioid withdrawal] that occurs when an individual who is physically dependent on opioids abruptly discontinues or rapidly reduces the opioid dose. As the agonist spontaneously dissociates from the opioid receptor, opioid receptor activation decreases.
 - Precipitated opioid withdrawal is the sudden onset of the opioid withdrawal syndrome that results from a sudden reduction in mu opioid receptor activation caused by the presence of substances that displace and bind to the opioid receptor and have lower agonist effects (either opioid antagonist or partial opioid agonist).

FIGURE 1. COMPARISON OF OPIOID RECEPTOR ACTIVITY WITH OPIOIDS AND OUD MEDICATIONS ADAPTED FROM TIP 63 (SAMHSA)³⁸



COMPARISON OF OPIOID RECEPTOR ACTIVITY WITH OPIOIDS AND OUD MEDICATIONS

The ability of medications to cause precipitated withdrawal can be explained through an analogy of a car.

- A full opioid agonist which fully activates the opioid receptor is like a car able to go 100 mph.
- A partial opioid agonist which is only able to activate the opioid receptor at approximately 40% is like a driver's education car that cannot exceed 40 mph despite pushing the gas pedal all the way down.
- Thus, starting buprenorphine at the same time that a person is taking a full agonist is like suddenly transitioning a car at 100 mph to one that cannot exceed 40 mph. This abrupt deceleration is experienced as precipitated withdrawal. If instead a car is going 100 mph and you release the gas pedal and coast down to 30mph (i.e. allowing 12-24 hours after a short-acting opioid), switching to a car that is able to go 40 mph (i.e. starting buprenorphine) will not precipitate withdrawal and will be able to relieve withdrawal symptoms that may be present.
- If naltrexone (antagonist) is administered at the same time that a person is taking a full agonist, it is like you're slamming on the brakes while going 100 mph (abruptly decelerating from 100 mph to 0 mph).

- The pharmacology of buprenorphine affects its dosing and medication interactions.
 - Sublingual is the most common route, due to buprenorphine's poor oral bioavailability. Alternative parenteral formations (depot injection and implantable) are available and are more costly than generic sublingual tablets and other branded sublingual formulations.
 - Peak plasma time for the sublingual preparation of buprenorphine is 120 minutes.
 - Buprenorphine has a long elimination half-life (24-96 hours), and slow dissociation translates to a prolonged therapeutic effect. It can be dosed less frequently than daily.
 - Buprenorphine is metabolized in the liver by the cytochrome P450 3A4 enzyme system,^{404, 405} so CYP 3A4 inhibitors/ inducers can affect metabolism. [See TABLE 8: Medication Management for Patients with Respiratory or Hepatic Impairment]
 - Overall, there are few clinically relevant drug-drug interactions, especially compared to methadone.
 - Case reports of serotonin syndrome have been reported when buprenorphine is taken with other serotonergic agents.
 - Clinicians must monitor the response to buprenorphine in patients with HIV who are taking nonnucleoside reverse transcriptase inhibitors and atazanavir/ritonavir.
 - ▶ Rifampin may reduce buprenorphine concentrations.
 - [See TABLE 7: Comparison of the Medication Administration for Opioid Use Disorder.]
- The combined use of buprenorphine with CNS depressants (e.g. alcohol and benzodiazepines) should be avoided.
 - Considerations with alcohol: Alcohol use disorder is associated with higher rates of relapse to opioid use. There is some evidence however, that treatment with buprenorphine can help decrease craving for alcohol, ethanol intake and the Addiction Severity Index subscale of alcohol use score.^{406, 407}
 - Considerations with benzodiazepines: Most fatal poisonings involving buprenorphine also involve the presence of benzodiazepines.
 - The FDA created a boxed warning for the combined use of opioid medications with benzodiazepines or other CNS Depressants (e.g. alcohol).⁴⁰⁸
 - However in 2017, the FDA recommended that buprenorphine and methadone should not be withheld from patients taking benzodiazepines or other CNS depressants.⁴⁰⁹ The combined use of these drugs increases the risk of serious side effects but the harm caused by untreated opioid addiction can outweigh these risks. As such, careful medical management by clinicians can reduce these risks.
- There is a combination formulation as buprenorphine-naloxone (Suboxone[®], Bunavail[®], Zubsolv[®]) that acts as an abuse deterrent. Naloxone has negligible oral/sublingual bioavailability, but it becomes active if the medication is crushed and dissolved for intranasal or IV misuse. Because of this, the combination product is preferred for most outpatient buprenorphine prescriptions (except in the case of pregnancy for which the buprenorphine only sublingual product, Subutex[®], is preferred.)
- The main contraindication for buprenorphine use is an allergy to buprenorphine or naloxone (for combination products), and there are a few precautions:
 - Respiratory depression and overdose are uncommon but can occur, particularly with IV use of buprenorphine combined with alcohol, benzodiazepine or other sedatives.
 - Overdose can also occur in opioid-naïve individuals, but it is less common than with use of other opioids.
 - Unintentional pediatric exposure can be life threatening.
 - Cases of hepatitis and liver failure have been reported, but usually in presence of pre-existing liver disease.
- The side effects of buprenorphine can include constipation, nausea/vomiting, excessive sweating, sedation, insomnia, headache and dizziness. Patients should be cautioned against driving and the use of heavy machinery until they are sure they do not have psychomotor impairments (e.g. sedation, which is most likely seen during induction and early dose stabilization.)

- Diversion can occur with buprenorphine.
 - Buprenorphine has IV misuse potential. Most estimates suggest that, per dose, tablets are more likely to be diverted than films, and mono-product tablets are more likely to be diverted than combined buprenorphine/naloxone. Combination use is therefore the standard of care.
 - Compared with the diversion of other full opioid agonists, diversion of buprenorphine is rare, making up a small proportion of all diverted medications and is usually diverted for the purpose of self-treatment of opioid withdrawal.⁴¹⁰
 - Universal use of risk mitigation strategies should be used to minimize diversion: frequent monitoring with office visits, urine drug tests and monitoring of the prescription drug monitoring program.

TABLE 8: MEDICATION MANAGEMENT FOR PATIENTS WITH RESPIRATORY OR HEPATIC IMPAIRMENT ADAPTED FROM TIP 63 (SAMHSA)³⁸

CONTRAINDICATION/CAUTION	CONSIDERATIONS FOR THE USE OF BUPRENORPHINE FOR TREATMENT OF OPIOID USE DISORDER
Compromised respiratory function [e.g. chronic obstructive pulmonary disease, decreased respiratory reserve, hypoxia, hypercapnia, pre-existing respiratory depression]	Prescribe cautiously and monitor closely. Warn patients about risks of using benzodiazepines or other depressants while taking buprenorphine. Support patients in attempts to discontinue tobacco use.
Hepatic impairment Buprenorphine and naloxone are extensively metabolized by the liver. Moderate-severe impairment results in decreased clearance, increased overall exposure to both medications, and higher risk of buprenorphine toxicity and precipitated withdrawal from naloxone. These effects have not been observed in patients with mild hepatic impairment.	Mild impairment(Child-Pugh score of 5-6): No dose adjustment needed.Moderate impairment(Child-Pugh score 7-9)*: Combination products are not recommended as they may precipitate withdrawal.Severe impairment(Child-Pugh score 10-15)*: Combination products should not be used. For monoproduct, consider halving the starting and titration doses used in patients with normal liver function; monitor for signs and symptoms of toxicity or overdose caused by increased buprenorphine levels.

*Moderate to severe impairment results in much more reduced clearance of naloxone than of buprenorphine. Moderate impairment doubled or tripled exposure for both medications. In severe impairment, buprenorphine exposure was also two to three times higher; naloxone exposure increased more than tenfold.

Before starting buprenorphine treatment for opioid use disorder, a standardized assessment must take place.

- A clinical History and Physical, including pertinent medical, psychiatric and substance use history, must be done.
 - For opioid use disorder, this also includes checking urine drug screens and confirmatory tests, the prescription drug monitoring database and obtaining informed consent.
 - [See Component #4 for assessing a person with opioid use disorder.]
- If possible, the clinician should obtain liver function tests, but does not need to wait for the results before starting buprenorphine treatment. Patients with chronic liver disease, including hepatitis C virus, appear to tolerate buprenorphine well if transaminase levels are less than five times the normal level. Risks and benefits should be discussed with the patient if their enzymes are at or above five times normal levels [See TABLE 8: Buprenorphine for Patients with Respiratory or Hepatic Impairment.]
- The clinician should consider the patient's suitability for pharmacologic therapy, such as adherence with treatment requirements, psychosocial circumstances of the patient, other medications that may interact with buprenorphine, on-call coverage resources at the office, other treatment programs for more intensive levels of service if needed.
 - Patients with other concurrent substance use disorders may benefit from completion of more intensive treatment (e.g. intensive outpatient programs or residential treatment) before being ready for outpatient treatment with buprenorphine. Buprenorphine is a treatment for opioid use disorder, not other substance use disorders, although sometimes reductions may occur indirectly as a result of participating in monitored treatment. In particular, clinicians should be aware that if a patient is at risk for withdrawal seizures from alcohol of sedative-hypnotic use, buprenorphine will not prevent or control seizures.
- NOTE: Careful consideration should be made with patients on methadone maintenance therapy (MMT) who wish to transition to buprenorphine. The relative benefits of transitioning should be discussed between the patient, methadone clinic provider/ counselor, and the buprenorphine provider with a shared decision-making process.
 - Benefits of transitioning to buprenorphine may include a more favorable safety profile, potentially less stigma, and better geographic accessibility.
 - Patients should discuss with their MMT prescriber. If there is a mutual team decision to transition to buprenorphine, the MMT prescriber should generally work to taper to 30-40 mg/day of methadone and stay on that dose for at least one week prior to starting buprenorphine. Because a methadone taper may increase the risk of the patient returning to non-prescribed opioid use, the team should employ careful follow-up and an individualized approach.
 - At least 36-48 hours should have passed since the last dose of methadone prior to starting buprenorphine and start with a lower dose (e.g. 2 mg) and titrate up more slowly.

Buprenorphine treatment takes place in three phase: A) INDUCTION, B) STABILIZATION, and C) MAINTENANCE.

- A) THE INDUCTION PHASE is the initiation of buprenorphine treatment, usually with medical monitoring. It can occur in the office or at home.⁴¹¹ (Note: Home induction should only be used when the provider has experience in using buprenorphine and the patient understands withdrawal symptoms and dosing instructions, and adequate communication with the provider is possible.)
 - The primary goal of the induction phase is to initiate buprenorphine while avoiding precipitated withdrawal and other potential adverse medication effects (e.g. sedation) while also retaining the patient in treatment by achieving a timely reduction in opioid withdrawal symptoms and cravings.
 - Because buprenorphine only partially activates opioid receptors and binds tightly to the opioid receptor, starting
 buprenorphine in patients who are physically dependent on opioids and still have opioids in their system can result in
 precipitated withdrawal. Three main factors determine the likelihood that buprenorphine will cause precipitated withdrawal
 are: 1) the degree of physical dependence 2) the time since the patient's last dose of opioids and 3) the starting dose of
 buprenorphine.

- For patients with a significant degree of physical dependence, buprenorphine should only be started when patients are exhibiting at least mild-moderate opioid withdrawal (e.g. COWS ≥ 8) and after an adequate time since the last opioid dose as follows:
 - 12-24 hours after a short-acting opioid (i.e., oxycodone, heroin, fentanyl, morphine)
 - 24 hours after long-acting opioid (i.e., extended release morphine or oxycodone)
 - 36-48 hours after longer-acting opioid (i.e., methadone, fentanyl patch)
- For patients with a lower degree of physical dependence (e.g. patients using lower doses of prescription opioids) induction may be appropriate with mild or minimal opioid withdrawal symptoms if adequate time from the last opioid dose has elapsed (see above time frames).
- The reason not to be overly cautious and delay the initial dose is that delaying too long and starting too low of a dose may result in the patient remaining in opioid withdrawal and dropping out of treatment.
- Special note on transitioning from methadone maintenance therapy (MMT): Prior to starting buprenorphine, evaluate that the patient is in moderate withdrawal by using scales such

as COWS scale. Given risk of precipitated withdrawal, advise patient of risk of precipitated withdrawal and consider doing induction in clinic.

If performed at the right time, buprenorphine induction remains one of the most satisfying procedures for patients and providers.⁴¹¹

- The induction schedule for buprenorphine is the following:
 - DAY 1: The initial dose should be 2-4 mg of SL

buprenorphine. Allow three to ten minutes for the product to completely dissolve under the tongue. Acidic drinks such as coffee or fruit juice should be avoided prior to administration. Patients should be re-evaluated after about two hours, and an additional 2-4 mg of buprenorphine can be given if withdrawal symptoms are still present and there is no sedation.

- The FDA label recommends a maximum of 8 mg buprenorphine/naloxone on Day 1. [See TABLE 9: Adjusting the Buprenorphine Dose].
- NOTE: For situations where the provider is initiating buprenorphine in a patient who is not currently physically dependent (e.g. has been abstinent for several months but is now experiencing opioid cravings, patient exiting criminal justice system or abstinence-based treatment programs), the provider can start at lower doses of buprenorphine (e.g. 1 mg) and titrate up more slowly.
- If precipitated withdrawal occurs, there are two potential treatment options: 1) increase the buprenorphine dose with the goal of providing enough mu opioid receptor agonist effect from the buprenorphine to suppress the symptoms of precipitated withdrawal and 2) stop the induction and provide non-opioid withdrawal support medications and have the patient return the next day for induction. Option #1 is generally preferred as Option #2 carries the risk of the patient not returning for care.
- **DAY 2:** Initial dosing depends on how the patient is feeling the morning of Day 2.
 - If the patient is feeling well on the morning of the Day 2 (i.e. has no withdrawal symptoms or cravings), then the total dose from Day 1 should be taken as a single dose on the morning of Day 2.
 - If the patient is feeling continued symptoms of opioid withdrawal or opioid cravings, then the total dose from Day 1 can be increased by 2-4 mg and taken as a single dose on the morning of Day 2.
 - If the patient is still feeling continued symptoms of opioid withdrawal or opioid cravings later in the day on Day 2, then an additional 2-4mg can be taken.
 - Split doses can be considered on a case-by-case basis if patients experience symptoms of withdrawal later in the day/evening or have comorbid chronic pain conditions.
 - The FDA label recommends a maximum of 16mg on Day 2. [See TABLE 9: Adjusting the Buprenorphine Dose].
 - Telephone follow-up with the patient on Day 2 or 3 can be helpful to guide the induction dosing.
- **DAY 3-7:** Over the next few days, the dosing should start to stabilize.
 - On the morning of Day 3, the total dose from Day 2 should be taken as a single dose.
 - On subsequent days, if the patient experiences continued withdrawal symptoms or cravings and has not reached 16mg/d, the dose can be increased in 2-4 mg increments each day until withdrawal symptoms and cravings are suppressed or a target dose of 16mg/d is reached (see below). As long as no side effects are present, the total daily dose from the prior day is taken as a single daily dose on the morning of the following day.
- See TABLE 10: Sample Buprenorphine Induction Schedule]

TABLE 9: ADJUSTING THE BUPRENORPHINE DOSE ADAPTED FROM TIP 63 (SAMHSA)³⁸

BACKGROUND

When considering the appropriateness of a certain dose of buprenorphine, first:

- · Evaluate if patient is taking doses correctly; resolve if he/she is not.
- Evaluate if patient is taking medications that may interfere with buprenorphine metabolism; resolve if he/she is not.

Be aware of the following pharmacological properties of buprenorphine:

- It takes 5-7 days after a dose change to reach steady state plasma concentrations.
- When taking \geq 16 mg/day, mu-opioid receptors are approximately 80-95% occupied.

When evaluating for craving or withdrawal symptoms, be aware that:

- Craving can be a conditioned response and may not decrease with dose increases if patients spend time with people who use opioids in their presence.
- A psychosocial problem may be contributing to cravings or psychological symptoms of withdrawal (e.g. depression, anxiety, PTSD or chaotic life situation). Addressing these conditions and situations is key to whole-person management.

WHEN TO INCREASE THE BUPRENORPHINE DOSE [usually in 2-4mg increments]

· If patients are taking doses correctly and withdrawal symptoms/cravings do not resolve with aforementioned interventions

OR

· If patients still have opioid withdrawal, opioid craving, or good effects (feeling "high") from using illicit opioids

WHEN TO DECREASE THE BUPRENORPHINE DOSE

 If there is evidence of dose toxicity (typically sedation or rarely clearly linked clinically relevant increases in liver function tests)

WHEN TO HOLD/STOP THE BUPRENORPHINE DOSE

· If there is acute alcohol or benzodiazepine intoxication

TABLE 10: SAMPLE BUPRENORPHINE INDUCTION SCHEDULE

DAY 1 (DAY OF INDUCTION)	DAY 2	DAY 3-7
0100 - Last use of a short-acting opioid (e.g. heroin, oxycodone)	0600 – Patient feeling well (minimal withdrawal/cravings) and takes the total from day 1 all in one morning dose - 8 mg buprenorphine SL	0600 – Patient feeling well (no withdrawal/ cravings) and takes the total from day 2 all in one morning dose - 12 mg buprenorphine SL
1300 – Patient in withdrawal and COWS>8, takes first dose 4 mg buprenorphine SL	1800 – Patient notes withdrawal symptoms again and takes additional 4 mg buprenorphine SL	
1500 – Patient still in withdrawal and takes additional 4 mg buprenorphine SL		

- B) THE STABILIZATION PHASE occurs when there are minimal or no symptoms of opioid withdrawal, craving, and medication side effects and euphoria is prevented if non-prescribed opioids are used. Stabilization generally occurs with SL buprenorphine doses of 8-16mg/d and is typically reached within the first 1-2 months.
 - Generally, the patient will be seen on a weekly basis by the buprenorphine team for the first 4 weeks.
 - Clinical visit checklists (https://www.accessdata.fda.gov/drugsatfda_docs/rems/BTOD_2017-01-23_Appropriate_Use_ Checklist.pdf) can facilitate visits during the stabilization and maintenance phases.
 - Once the major symptoms of opioid withdrawal and cravings have been suppressed and a dose of 8-16mg/d of SL buprenorphine has been reached, a period of approximately 5-7 days can be allowed for a specific daily dose to reach pharmacokinetic steady state, and for the patient to experience the full effect of that specific dose.
 - If a patient experiences sedation during the titration process, the clinician should stop and re-evaluate. It is highly advised to confirm the accuracy of opioid substance history and to inquire about other sedating substances. One can consider decreasing the dose or using a slower titration. Discontinuation of induction and use of alternative options could be considered if the patients is not responding to lower dose or slower titration.
 - While most patients can be stabilized at SL buprenorphine doses between 8-16mg/d, occasionally doses up to 24mg/d are needed to achieve stabilization.
 - Rarely, doses up to 32mg/d can be used, however there is only limited evidence that doses above 24mg/d improve outcomes⁴¹² while these higher doses may increase the risk of diversion.
 - Quote from TIP 63³⁸: "Be cautious when increasing doses above 24/6 mg buprenorphine/naloxone per day. Nearly all patients stabilize on daily doses of 4/1 mg buprenorphine/naloxone to 24/6 mg buprenorphine/ naloxone. Very limited data show additional benefits of doses higher than the FDA label's recommended maximum of 24/6 mg buprenorphine/naloxone. Carefully document clinical justification for higher doses and always have a diversion control plan in place. Doses above 24/6 mg buprenorphine/naloxone a day may unintentionally heighten diversion risk. Patients not responding to high doses of buprenorphine at the upper limit approved by FDA should be considered for methadone treatment."
- C) THE MAINTENANCE PHASE occurs when a patient is doing well on a stable dose of buprenorphine. This phase can last indefinitely and should be continued as long as the patient is benefiting from treatment with buprenorphine and wishes to continue.
 - An effective maintenance dose is the lowest dose that is not associated with withdrawal or side effects, minimizes craving, and blocks effects if non-prescribed opioids are used.
 - Buprenorphine maintenance doses typically range from 4-24 mg/day and should be individualized. The target dose is 16mg/d at which dose 80-95% mu receptors appear to be occupied.⁴¹³ Treatment retention appears to increase with increasing buprenorphine dose⁴¹² and doses at or above 16 mg/day appear to be associated with better suppression of illicit opioid use⁴¹⁴ compared to lower doses. The US FDA recommends a maximum dose of 24 mg per day and there is limited evidence of additional clinical benefit at higher doses. If patients continue to use illicit opioids at doses of 16mg/d or below, higher doses can be considered with the recognition that higher doses may increase the risk of diversion. See above quote from TIP 63 regarding guidance for dosing above 24 mg/day.
 - Basic counseling should continue, including supporting the patient's overall recovery process and relapse prevention strategies. Referrals can be individualized if more intensive psychosocial support is indicated.

Special consideration is needed in the case of pregnancy. Methadone has been the standard of care, but newer studies show buprenorphine to be similar to methadone and may result in less neonatal opioid withdrawal syndrome (NOWS, a specific form of NAS).⁴¹⁵

- Since opioid withdrawal is potentially harmful for the fetus (and the fetus experiences symptoms prior to the mother), the aim is to prevent opioid withdrawal and provide stability to the mother.
- The standard of care for opioid use disorder during pregnancy is methadone or buprenorphine. The relapse to opioid use is high, so neonatal abstinence syndrome is *not* more common for women on methadone or buprenorphine versus no medication-assisted treatment.⁴¹⁶
 - Buprenorphine monotherapy is traditionally used during pregnancy and patients are transitioned to the buprenorphine combo-therapy postpartum. The rationale has been that the combo-product may cause more harm to the fetus because of the possibility of precipitated opioid withdrawal. There is limited experience using the combo-product in pregnancy with studies showing efficacy and safety.⁴¹⁷

- Methadone and buprenorphine have not been shown to be teratogenic.
- Methadone and buprenorphine decrease drug use and obstetrical complications, as well as increase prenatal care, birth weight, and gestational age at the time of delivery.
 - Pregnant women with substance use disorder and who receive integrated addiction medicine services during the prenatal period have similar rates of obstetrical complications compared to the general population.
- Neonatal opioid withdrawal syndrome (NOWS) is a known consequence of MAT in pregnancy. It is a manageable condition and dose of maternal MAT does not increase the incidence of NOWS.
- After the pregnancy, breastfeeding should be encouraged unless there are other contraindications. Methadone and buprenorphine are excreted in very low levels in breast milk. Breastfeeding decreases withdrawal symptoms in the neonate, the requirement for medication in the neonate, and length of hospital stay for neonates with NOWS. ^{418 419 420}

Special consideration is needed in the case of anticipated or unanticipated pain while taking buprenorphine for opioid use disorder.⁴²¹

- Managing moderate to severe acute pain while undergoing treatment for opioid use disorder requires knowledge of the unique pharmacology of buprenorphine and close collaboration with surgical or other specialists who are involved with the care of the patient with acute pain.
 - For less severe pain, non-pharmacologic and non-opioid pharmacotherapy can be used with no changes to the dosing of buprenorphine.
 - For moderate pain requiring lower-intensity opioid analgesia, the buprenorphine dose can be split into 3-4 divided doses during the day, with or without a temporary increase in the total daily dose.
 - For severe pain requiring higher-intensity opioid analgesia, the following options can be considered:
 - > OPTION 1: Continue buprenorphine and add full mu agonist medications (most opioids used for pain).
 - Due to the partial blockade cause by buprenorphine, it is common to require higher doses of opioid analgesics at shorter intervals than would be used for a similar situation in an opioid-naïve patient.
 - Short-acting opioid analgesics could be used for the same duration anticipated by the type of injury or procedure for opioid-naïve patients. Recommendations for opioid prescribing for common surgical procedures in opioid naïve patients can be found at https://opioidprescribing.info/.
 - The Stanford protocol describes a perioperative approach to patients on buprenorphine.422
 - **OPTION 2:** Stop buprenorphine and initiate full mu agonist medications.
 - Stopping buprenorphine should not be routinely recommended and may increase the risk for withdrawal, relapse, and more difficult pain control in the setting of acute pain. Due to cross tolerance, higher doses of opioid analgesics at shorter intervals will likely be required than for a similar situation in an opioid naïve patient.
- For most types of chronic non-terminal pain, focus on optimizing non-pharmacologic and non-opioid pharmacotherapy.
- Methadone maintenance may provide enhanced opioid analgesia in the short term for situations such as end-of-life pain or cancer pain. Alternatively, cessation of pharmacotherapy and initiation of a full mu agonist may be considered when higher intensity opioid analgesia is required for end of life or cancer-related pain.

Office policies and procedures should exist to support the providers and patients in treating opioid use disorders.

- Standard policies should exist about obtaining informed consent, monitoring practices, having regular visits, regular and random urine drug testing, checking the prescription drug monitoring database and patient education.
- If dispensing buprenorphine onsite, policies and procedures should also address processes for maintaining medication security and storage.
 - The following records must be maintained for two years inventories (including amounts of buprenorphine received and amounting dispensed), reports of theft or loss, destruction of controlled drugs, and records of dispensing.⁴²³
- Regular and random urine drug screening should be a standard clinic policy.
 - EIA can be performed as point-of-care.
 - Gas/Liquid chromatography mass (GC/MS) spectroscopy tests can be used to confirm false positive and false negative test results. Legal, parenting, and critical clinical decisions should be made based off confirmatory testing (GC/MS) when the patient's history doesn't match an immunoassay (EIA) screening test.
 - A major limitation of immunoassays is cross-reactivity with other drugs and medications leading to lower specificity. The manufacturers of these screening tests publish common structures that may cross-react with the test causing false positives in the package insert.
 - [See TABLE 11: Expected detection times for drugs of abuse]

TABLE 11: WINDOWS OF DETECTION FOR DRUGS OF ABUSE ADAPTED FROM ASAM'S APPROPRIATE USE OF DRUG TESTING IN CLINICAL ADDICTION MEDICINE (2017)⁴²⁴

DRUG	DETECTION TIME IN URINE
Amphetamine or Methamphetamine	1-3 days
Barbiturates	Short-acting barbiturates: 1-4 days Long-acting barbiturates: 30 days
Cocaine metabolite benzoylecgonine	1-3 days
Ethyl glucuronide (alcohol metabolite)	2-6 days
Heroin	Heroin metabolizes to 6-monoacetylmorphine (6-MAM) which is specific to heroin, is only present for about 6 hours and therefore of limited clinical utility. 6-MAM is subsequently metabolized to morphine which has a window of detection of 1-3 days in the urine and will result in a positive result on an opiate immunoassay screen.
Marijuana*	Occasional Use: 1-3 days Chronic Use: 30 days
Methadone	2-10 days
Morphine	1-3 days
Phenycycline (PCP)	Occasional Use: 2-7 days Chronic Use: 30 days

*Passive exposure to marijuana will not produce false positive urine drug screen.

- Brief supportive counseling should be offered during medical visits including:
 - · Encouragement and support of the patient's recovery process
 - Assistance with trigger identification and relapse prevention
 - ▶ Empathetic listening and motivational interviewing [See Component #7].
 - Referral as needed for treatment of medical or mental health comorbidities, more intensive counseling, case management, or community resources
- Visit frequency: start with weekly visits and extend to every two weeks and then monthly as patient demonstrates stability. Therapeutic contingencies can be used (through increasing the frequency and intensity of treatments) for a pattern of nonadherence to treatment plans.
- Diversion control policies should be established in the clinic and discussed with patients before prescribing buprenorphine.
 - Patient education including clarification of clinic expectations, safety monitoring, and discussion of safe storage.
 - · Safety monitoring including urine drug tests, prescription drug monitoring program queries, medication counts
 - · Provision of limited medication supply until patient demonstrates stability
 - Prescription of adequate but not excessive doses. Most patients respond to doses ≤ 24mg/day. Providers should carefully evaluate requests for higher doses and monitor, assess, and document adherence regularly.
- Per DATA 2000, documentation needs to include full identifying information for the patient, full sig for the prescription, and both DEA and DATA-waiver numbers of the provider. This becomes less of an issue with e-prescriptions, which are now required here in Arizona.
 - A complete history and physical exam [See Component #4: Evaluation of Opioid Use Disorder]
 - Initial diagnosis (opioid use disorder, if present) and treatment plan
 - · Prior treatments/treatment outcomes for opioid use disorder
 - · Ongoing assessment, monitoring, response to treatment
 - Lab results including urine drug tests, prescription drug monitoring program queries, medication counts
 - Adherence to plan
 - Psychosocial treatments
 - · A log must be kept of patients who are treated with buprenorphine must be kept.
 - Medical records must be kept according to state and federal requirements.
 - The Drug Enforcement Agency (DEA) is authorized by the Controlled Substances Act and 21 CFR 1316.03 to enter registered locations and conduct periodic inspections to ensure compliance with recordkeeping security and other requirements of the Controlled Substances Act.
 - These inspections are not intended to be punitive and are low key, as they are ensuring that prescribers who are registered with the DEA comply with the patient limits that they are waivered to treat, recordkeeping and security. Having a log of patient's treated with buprenorphine provides confirmation that the buprenorphine prescriber is adhering to patient limits.

Treatment of opioid use disorder with buprenorphine lies within the scope of primary care and several other outpatient specialties and can be very clinically impactful and professionally rewarding. It requires comfort with opioid use disorder (a prevalent chronic disease in the United States), reflection on any personal and professional stigma, getting a DATA-waiver, and establishment of office procedures.

- For further review on opioid use disorder, see Components #1-5.
- For reflection on self and systems stigma, see *Components* #7 and #10.
- For requirements for a DATA-waiver, see SAMHSA or contact the Arizona Medical or Osteopathic Boards.
- For familiarity with buprenorphine, see Appendix D and SAMHSA TIP 63.

For further information about the other pharmacotherapies for opioid use disorder, see TIP 63.³⁸

ACTIVE THERAPY FOR PAIN: Treatment done by the patient, includes self-care activities that promote physical, mental, social and spiritual activities; generally grouped into movement therapies and psychological therapies

ACUTE PAIN: Pain lasting less than 90 days

ADDICTION: A primary, chronic disease of brain reward, motivation, learning, memory and related circuits with socio-psycho-biological components and manifestations; characterized by inability to consistently abstain, impairment in behavior control, cravings, diminished recognition of significant problems with one's behaviors and interpersonal relationships and a dysfunctional emotional response

ADVERSE CHILDHOOD EXPERIENCES (ACE): Stressful or traumatic events, including abuse and neglect; may also include household dysfunction such as witnessing domestic violence of growing up with family members who have substance use disorders

BIOMEDICAL MODEL OF PAIN: An older conceptual framework that has shaped the clinical approach to pain; identifies a 1:1 correlation between physical pathology of pain (i.e. the structural pathology paradigm); establishes the role of the patient as a passive victim of an identifiable disease and doctor as responsible for pain relief

BIOPSYCHOSOCIAL MODEL OF PAIN: An updated conceptual framework to the Biomedical Model; views pain as a dynamic interaction among and within the biological, psychological and social factors unique to each individual

BUPRENORPHINE: A schedule III partial opioid agonist that is FDA-approved for the treatment of opioid dependence, with sublingual, subdermal implant, and extended release subcutaneous injection formulations available; sublingual formulations available as a monoproduct and a combination product with naloxone to reduce misuse; able to be prescribed for opioid use disorder by DATA-waivered clinicians; parenteral injection and patch formulations are FDA-approved for the treatment of pain

CATASTROPHIZING: Pain-specific pattern of cognition and emotional distress characterized by the triad of amplification, rumination and helplessness

CENTRAL SENSITIZATION: Process in which the central nervous system amplifies the processing of pain, such that the central nervous system response to peripheral nociceptors is hyperexcitable and augmented; associated with the development and maintenance of chronic pain

CHEMICAL COPING: Use of medication in nonprescribed or inappropriate ways to manage psychological or other distress, and does not include the craving and behavioral issues indicative of addiction

CHRONIC PAIN: Pain persisting longer than 3-6 months and beyond the normal tissue healing time

COMPASSION: A complex multidimensional construct that is thought to include (1) an awareness of suffering (cognitive component), (2) sympathetic concern related to being emotionally moved by suffering (affective component), (3) a wish to see the relief of that suffering (intentional component), and (4) a responsiveness or readiness to help relieve that suffering (motivational/action component)⁴²⁵

COMPREHENSIVE ADDICTION AND RECOVERY ACT (CARA): A federal bill that addresses the full continuum of addiction care from primary prevention to recovery, including expanded access to addiction treatment and overdose reversal medications; includes language to allow allows nurse practitioners and physician assistants to use buprenorphine to treat opioid use disorder

COMPULSIVITY: Repetitive behaviors in the face of adverse consequences and repetitive behaviors that are inappropriate to a particular situation.

DRUG ADDICTION TREATMENT ACT OF 2000 (DATA-2000): A federal bill that enables qualified physicians, nurse practitioners, and physician assistants to prescribe and/or dispense schedule III-V narcotic medications for the maintenance or detoxification treatment of narcotic dependence in any clinical setting; includes a limit of number of patients per physician

DEATHS OF DESPAIR: Deaths from "diseases of despair" (drug abuse, alcoholism, suicide), seen in analyses to have increased in areas of economic distress and cumulative disadvantage and contributed to a decreased life expectancy in middle-aged white males in the United States; coined by Deaton and Case⁶¹

DETOXIFICATION: Older term referring to medically-supervised withdrawal, also known as the treatment of acute opioid withdrawal

DRUG ADDICTION TREATMENT ACT OF 2000 (DATA-2000): A federal bill that enables qualified physicians, nurse practitioners, and physician assistants to prescribe and/or dispense schedule III-V narcotic medications for the maintenance or detoxification treatment of narcotic dependence in any clinical setting; includes a limit of number of patients per physician

EMPATHY: The capacity to understand what another person is experiencing from within the other person's frame of reference, i.e. the capacity to place oneself in another's shoes

FEAR AVOIDANCE: Avoidance of activities due to anticipation and fear of increased pain or reinjury

ILLNESS BEHAVIORS: Ways that individuals respond to bodily symptoms, monitor internal states, define and interpret symptoms, make attributions, take remedial actions and utilize sources of care

INFORMATION MASTERY: Application of evidence-based concepts and techniques to the daily practice of medical care

INTELLECTUAL VIRTUES: Qualities of mind that promote intellectual thriving and critical thinking; include: intellectual curiosity (drive to seek out answers and to question one's own knowledge, intellectual humility (ability to question one's own knowledge), intellectual courage (the ability to do the right thing in the face of personal and professional resistance) and intellectual creativity (the ability to "look outside the box" for solutions)

INTERDISCIPLINARY CARE: Healthcare team approach that involves multiple clinicians from different disciplines who share a common treatment model; team members develop coordinated treatment plans together, in daily communication and regularly scheduled meetings

INTERPROFESSIONAL CARE: Healthcare team approach that involves multiple clinicians from different disciplines who share a common treatment model and a strong interest for collaboration between diverse disciplines; high degree of care integration

MEDICALIZATION: The process by which common human problems become defined and treated as medical problems

MEDICATION-ASSISTED TREATMENT (MAT): Use of medications, in combination with counseling and behavioral therapies, to provide a whole-person approach to the treatment of substance use disorders

METHADONE: An schedule II full mu opioid agonist usually taken in oral form; an option for pharmacotherapy for opioid use disorder within a federally licensed Opioid Treatment Program

MULTIDISCIPLINARY CARE: Healthcare team approach that involves multiple clinicians from different disciplines; often co-located but clinicians work from different treatment models and do not gather to coordinate a patient's treatment plan

NARCOTIC: Originally used to refer to any drug that induced narcosis or sleep; Has become associated with opioids and is often used in a legal context to refer to substances with abuse or addictive potential

NALOXONE: An opioid antagonist approved by the Food and Drug Administration (FDA) to reverse an overdose by opioids by blocking opioid receptor sites, reversing the toxic effects of the overdose; poor oral bioavailability

NALTREXONE: An opioid antagonist available in oral and extended release intramuscular injection forms. Oral formulation is FDA approved for treatment alcohol dependence and extended release intramuscular injection formulation is FDA approved for treatment of alcohol and opioid dependence

NEONATAL ABSTINENCE SYNDROME: A withdrawal syndrome experienced by a neonate following repeated intrauterine drug exposure

NEONATAL OPIOID WITHDRAWAL SYNDROME (NOWS): A specific form of Neonatal Abstinence Syndrome in which a neonate experiences an opioid withdrawal syndrome following repeated intrauterine opioid exposure

NEUROPLASTICITY: The process of change in the brain that occurs among, between, and within neurons throughout life; changes can be adaptive and developmental or maladaptive and pathological

NOCICEPTION: Nerve activity that results from detection of stimuli capable of causing tissue damage

OPIOID: All natural, synthetic, and semisynthetic substances that have effects similar to morphine

OPIOID EPIDEMIC: The rapid and large increase in the number of people dying from an opioid overdose

OPIOID AGONIST TREATMENT: Medications for opioid use disorder that have either full or partial agonist properties at the mu opioid receptor (current FDA approved opioid agonist medications for opioid use disorder include methadone and buprenorphine)

OPIOID EXIT STRATEGY: Individualized treatment plan to minimize opioid-related adverse events to patients on long-term opioid therapy; includes a variety to approaches to transition away from use of long-term opioid therapy for pain

OPIOID TREATMENT PROGRAM (OTP): Federally licensed and regulated programs where methadone and buprenorphine can be prescribed and dispensed for opioid use disorder; methadone for the treatment of opioid use disorder can only be ordered, administered and dispensed in this type of program

OPIOID USE DISORDER: Problematic pattern of opioid use leading to clinically significant impairment or distress as manifested by at least two of symptoms listed in the DSM-5 criteria; typically remembered by the 3Cs (Loss of Control, Craving and Use despite Negative Consequences)

OPIOID WITHDRAWAL: Characteristic syndrome manifested by dysphoric mood, nausea or vomiting, pain, lacrimation or rhinorrhea, pupillary dilation, piloerection, sweating, diarrhea, yawning, anxiety, and insomnia; can occur after an abrupt discontinuation or a sudden decrease in the dose of opioids after long-term use (spontaneous withdrawal) or after administration of an opioid antagonist or partial agonist (precipitated withdrawal); very uncomfortable and distressing but rarely a medical emergency (except in pregnant women and neonates)

PAIN: A mutually recognizable somatic experience that reflects a person's apprehension of threat to their bodily or existential integrity (2018 proposed update to the 1976 IASP definition)²; a multidimensional experience with social, cognitive, emotional, physical, and existential components

PAIN BEHAVIOR: A type of illness behavior; includes a broad range of behaviors that people display to communicate to others that they are experiencing pain, distress or suffering

PAIN CHRONIFICATION: The process of acute pain transitioning to chronic pain

PAIN-RELATED DISABILITY: A reduction in social, physical, cognitive, or recreational functioning due to pain

PARTNERING: Collaborative relationship between patient and clinician that serves to foster a strong therapeutic alliance

PASSIVE THERAPY FOR PAIN: Treatment done to the patient by the medical team; common biomedical passive therapies include medication, injections, invasive procedures and surgery; low-risk passive therapies (e.g. acupuncture, chiropractic, massage) and passive physical modalities (e.g. heat, ultrasound) may be useful as "bridging therapies" to facilitate adoption of active therapies

PERSON-CENTERED LANGUAGE: Language that implicitly affirms the intrinsic value, dignity and self-efficacy of each person, fostering self-management and supporting recovery

PATIENT-REPORTED OUTCOMES (PROS): Reports of a patient's health, quality of life of functional status associated with health care or treatment that are directly reported by the patient and that are important to the patient

PERIPHERAL SENSITIZATION: The increased sensitivity and hyperexcitability of peripheral nociceptors such that they can be activated by lower than normal noxious stimuli, non-noxious stimuli, and even in the absence of stimuli; can occur after injury or tissue damage

PHARMACOTHERAPY FOR OPIOID USE DISORDER: Medications used to treat opioid use disorder

PHYSICAL DEPENDENCE: A state of physiological adaptation that is manifested by a drug-class specific withdrawal syndrome (with effects that are typically opposite of the acute drug effects) that occurs after prolonged drug use and can be produced by abrupt cessation, rapid dose reduction, and/or administration of an antagonist

PICO: Acronym that stands for Patient, Problem or Population / Intervention / Comparison, Control or Comparator / Outcome; format to help define a clinical question

POEMS (PATIENT ORIENTED EVIDENCE THAT MATTERS): Framework that guides clinicians toward highly relevant medical evidence; consists of looking at outcomes that are important to patients and that has potential to change one's clinical practice

PROMIS® (PATIENT-REPORTED OUTCOMES MEASUREMENT INFORMATION SYSTEM): A set of person-centered measures that evaluates and monitors physical, mental and social health in adults and children; developed and evaluated with support from National Institutes of Health

PROTECTIVE FACTORS: Characteristics associated with a lower likelihood of negative outcomes or that reduce a risk factor's impact

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RED FLAGS: Findings that may indicate serious pathology and when combined with the full clinical picture, may prompt further investigation.

RESILIENCE: Sustainability of purpose in the face of stress and challenge, and recovery from adversity^{424 426}; components include recovery, sustainability and growth

REWARD SYSTEM: A collection of brain structures and neural pathways that are responsible for rewarding behaviors

RISK FACTORS: Characteristics at the biological, psychological, family community or cultural level that precede and are associated with a higher likelihood of negative outcomes

SAMHSA (SUBSTANCE ABUSE AND MENTAL HEALTH SERVICES ADMINISTRATION): The agency within the U.S. Department of Health and Human Services that leads public health efforts to advance the behavioral health of the nation; mission is to reduce the impact of substance abuse and mental illness on America's communities

SBIRT: Acronym that refers to Screening, Brief Intervention and Referral to Treatment; a comprehensive, integrated approach to the delivery or early intervention and treatment services

SELF-COMPASSION: Compassion for one-self that involves self-kindness, recognition of common humanity, and mindfulness¹⁰¹

SELF-EFFICACY: Belief in one's own capacity to implement specific behaviors (i.e. the belief that you can self-manage)

SELF-MANAGEMENT: Ability to manage the symptoms, treatment, physical and psychosocial consequences and lifestyle changes inherent in living with a chronic condition

SINGLE-DISCIPLINE CARE: Medical care provided by a provider of one discipline without involvement or integration with other disciplines

SOCIAL DETERMINANTS OF HEALTH: Conditions in which people are born, grow, work, live and age, and the wider set of forces and systems shaping the condition of daily life

SOCIO-PSYCHO-BIOLOGICAL MODEL OF PAIN: The newest conceptual framework that shapes the clinical approach to pain; represents a paradigm shift to an integrated whole-person and whole-system focus on person-centered outcomes, such as function and quality of life; places person with pain at the center of the care team

STIGMA: The prejudicial attribution of negative qualities to an individual based on his/her social identity in an undesirable social category

SUBSTANCE USE DISORDER: A disorder that includes a cluster of cognitive, behavioral and physiological symptoms indicating that the individual continues using the substance despite significant substance-related problems; diagnosis based on a pathological pattern of behaviors related to use of the substance; diagnostic criteria fits within the following groupings: impaired control, social impairment, risky use and pharmacological criteria.

TAPS SCREENING TOOL: A two-step screen for problematic use of Tobacco, Alcohol, Prescription Medication and other Substance Use developed with support from National Institute on Drug Abuse

THERAPEUTIC ALLIANCE: Includes the collaborative nature of the relationship, the affective bond between the patient and provider, and the patients' and providers' ability to agree of treatment goals and tasks

TOLERANCE: Alteration of the body's responsiveness to alcohol or a drug such that higher doses are required to produce the same effect achieved during initial use or use of the same amount of a substance results in a diminished effect

WELLNESS BEHAVIORS: Behaviors that are incompatible with the expression of pain and support health and wellbeing

WHOLE-PERSON CARE: Assessment and treatment of each individual as an entire person rather than as separate symptoms, diagnoses or body party; involves the coordination of health, behavioral health and social services in a patient-centered manner with the goals of improved health outcomes

YELLOW FLAGS: Psychosocial risk factors for the development of pain chronification and pain-related disability

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VERSION 2/Grey Edition

