Nutritional Concerns in Substance Use Disorders

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Chapter 1: Introduction

In the autumn quarter of 2020, a seminar class was offered discussing the presentation and treatment considerations for substance use disorders for students in the School of Medicine at the University of Washington. A group of six students and the professor, Dr. Jared Klein, organized guest speakers to cover a range of topics including the nutritional impacts of substance use. This capstone project was created to present the nutritional impacts, related medical complications and potential nutrition support for substance use disorders. While there are many substance use disorders with nutrition complications, this presentation specifically addressed opioid and alcohol use disorders as these were the disorders defined as the topics of interest for the seminar.

The primary purpose of this presentation was to inform students of the physical and social mechanisms causing malnutrition, micronutrient deficiencies and hormonal and microbiome disruptions in substance use disorder patients. These nutrition related impacts have the potential to precipitate acute and chronic diseases which require treatment and even delay recovery from unrelated injuries if nutrition impacts are not addressed in clinical settings. Substance use disorders and addiction treatment still carry a stigma in the United States, and treatment for these disorders is often separate from other medical care. This means that in recovery and addiction treatment centers, practitioners may not be aware of or have the ability to treat the chronic disorders that arise for these patients. As future practitioners, even in settings not focused on addiction treatment, knowledge of the nutrition impacts and implications would allow these practitioners to provide better, more comprehensive care including making referrals to social work and nutrition professionals when warranted.

The secondary purpose of this presentation is to broaden the scope of the nutrition-related substance use disorder impacts beyond the immediate clinical definition to include the larger socio-ecologic context. The multitude of barriers faced by individuals with substance use disorders extend beyond barriers to recovery and can include homelessness, incarceration, structural racism, past trauma and other mental health disorders. By recognizing these potential barriers and being aware of the larger contexts that influence patients, practitioners will be more likely to see the root causes of the substance use and provide more person-centered care. Additionally, they can be advocates for larger social and public health changes that can benefit their patients.

The final purpose of this presentation is to determine and present to what extent nutrition and dietitians can benefit patient care. Currently, dietitians are not often included in the treatment of

substance use disorders, but like other mental health disorders like eating disorders, there is potential for nutrition support to benefit these patients. As future practitioners, if these students recognize the value that a dietitian and nutrition support can offer, they will be more likely to invite this care on to the treatment team.

The content of this capstone project and the presentation for the seminar class was gathered by interviewing six substance use disorder professionals and by conducting an extensive literature search. The information was summarized and highlighted in the presentation given remotely on the evening of December 1, 2020.

Chapter 2: Lesson Plan

Target Audience: Student population description

The students in this seminar were from within the school of medicine. This likely included medical students, nursing students and pharmacy students, but it may have also included any students enrolled in the graduate health science programs. Students in the medical program are mostly from Washington state or the 5-state WWAMI region.[1] Data from students matriculating in 2019 show that students range in age from 19 to 45, and 13% of the students are from communities that are underrepresented in medicine.[1] 21% of the students self-identify as disadvantaged, and 12% are from rural communities.[1]

Needs Assessment

MED 569 Addiction Medicine class

The course description stated "Themes relevant to treatment of substance-using patients. Designed to build curiosity and increase familiarity with individual and societal factors that impact such patients, including various forms of bias and discrimination. Students develop and practice skills in order to become competent future providers for drug-using patients."[2] The focus of the class was largely about alcohol and opiate substance use disorders, but may have also included some considerations about methamphetamines.[3] The learning objective given for the specific nutrition session is "Recognize the consequences of common nutritional deficiencies seen in people with alcohol use disorder, opiate use disorder, and other use disorders."[4]

In addition to the stated objective from the organizers, it was also important to address the intersection of specific disorders such as eating disorders or mental health disorders with substance use and to address specific nutrition interventions for these disorders.

As these students are all at a graduate or professional program level in medical fields, the content and vocabulary used in the lesson could be advanced and could contain some general medical terminology. As adult learners, it was important to both engage the students through activities, questions or case-studies as applicable and to create a learning environment that can connect with all different styles of learning despite being delivered in a seminar with about 30 students over a video conferencing application.

Student-specific needs

Medical Students

The curriculum in the UW Medical School Program includes a 6 week section which includes nutrition and a section on psychiatry during the foundation coursework.[5] In addition to the standard coursework, students may choose a "pathway" for electives to prepare them to work in specific fields.[6] These pathways may include work with populations vulnerable to substance use.[6] Information on the nutritional impacts of substance use disorders may better prepare these students to effectively serve these populations.

For medical licensing, there is a section of the exam on behavioral health, however, no specific section exists on substance use disorders or nutrition.[7] However, after becoming an MD, professionals may pursue specialist credentials in Psychiatry, Emergency Room, Pediatrics or Preventative Medicine.[8] All of these specialties require specific training in substance use treatment and prevention, and knowledge of the nutritional impacts may be beneficial.

Nursing students

Degree tracks in nursing graduate programs are very diverse. Of the primary core classes, there are no specific classes on nutrition or on substance use disorders.[9] There is a degree, Psychiatric Mental Health Nurse Practitioner, which may be most applicable to the topics presented. License requirements for nurses include two specific topics which are pertinent to substance abuse, Health Promotion and Maintenance and Psychosocial Integrity.[10] In these topic areas, nurses are required to assess patients for high risk health behaviors and chronic psychosocial issues, educate clients about these issues and intervene as required for the health of the patient. Knowledge of the complex nutritional issues surrounding substance abuse would aid these students in this particular knowledge area.

Pharmacy students

The curriculum for the Pharmacy degree does not include specific classes on nutrition or substance use disorders; however, there are classes on ethics and regulations which likely include substance addiction awareness and regulations.[11] Like the medical license, there are no specific requirements around substance use disorder training for pharmacists, but there is a psychiatric pharmacist specialty license which may require this training.[12] Aside from specific drug-food interactions, pharmacy students may not have much knowledge or perhaps need for knowledge of the nutritional impacts of substance use.

Behavioral goals

To facilitate and direct the development of the lesson plan and the learning goals and objectives, the following behavioral change goals were created. These goals address the overall desired outcomes of the lesson plan. The first behavioral goal was directly addressed in the evaluation of the presentation.

1. Students will consider the impacts and importance of nutrition in their assessment and treatment of substance use disorder patients.
2. Students will be encouraged to pursue specialties in substance use disorders and related fields and work collaboratively in those disciplines.

Theoretical Model and Determinants: Social Cognitive Theory

Theoretical models aid in lesson design by giving a framework on which behavioral goals can be more successfully achieved. These models allow for assessment of what drives behavior change and what barriers need to be overcome. In the social cognitive theory, personal beliefs, current behaviors and environmental factors are thought to influence each other to produce or hinder the intended behavioral change. The individual factors, called determinants, are defined in Table 1 below. In this assessment, these determinants were considered from both how the students may perceive determinants in relation to themselves and how they perceive it may change their own future practice.

Table 1: Theoretical model and determinants

Ideas from interviews/needs assessment	**Determinant**
• Eating well to minimize blood sugar spikes can help people in recovery feel better and make progress • With effective evidence-based treatments, patients can do very well in recovery • Treatment and recovery can mitigate symptoms of depression and anxiety • Working collaboratively with many professions improves outcomes	Outcome Expectations: what an individual believes will happen to them if they make the behavior change

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• Working in addiction recovery can be very rewarding because the patient can turn their life around • Addiction recovery work allows the provider to work with the patient over an extended period and learn their story	Expectancies: the value that an individual places on the outcome expectations
• Addiction changes eating behaviors, often driving patients toward sugar • Addicts lack hunger and satiety cues • Substance use symptoms can mimic psychiatric disorders which may lead to inaccurate diagnoses • It is easy for both addicts and providers to feel hopeless • Patients with housing or food insecurity have less access to resources for treatment and nutritious food • Stigma and stereotypes may lead to assumptions about underserved populations or those with mental illness • Constipation is a significant problem for opioid users and during recovery • Patients may have inaccurate perceptions about treatments causing or worsening symptoms like poor dental health, weight gain and constipation • Lab results for micronutrient levels are too expensive and take too long • Boredom can trigger relapse	Barriers: perceived and actual challenges to making a behavior change
• Many patients are successful in recovery • Doctors need to give patients a sense of hope because it is easy for both doctor and patient to feel hopeless	Self-efficacy: individual's confidence in the ability to perform the behavior
• A multivitamin and supplements can address deficiencies and help start the healing process in the brain • "I don't spend time on [nutrition] other than… the weight [gain]." • Patients need to have their malnutrition and food insecurity risk considered during treatment instead of just withdrawal	Behavioral Capability: knowledge and skills needed to perform the behavior

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management • Sugar and caffeine may increase or mitigate cravings • Eating disorders may precede and even promote substance use and relapse if not addressed • Nutrition education may not be emphasized in medical programs or connected to mental health disorders	
• Nutrition education and cooking classes help patients eat better and can address boredom • Drop-in centers with free food can help mitigate financial disparities for patients • If both eating disorders and substance abuse disorders aren't treated concurrently, risk of relapse is very high	Observational learning/ Modeling: learning by observing the behavior and its consequences

Learning Goals and Objectives

1. Goal: Students will learn to recognize the consequences of common nutritional deficiencies in people with substance use disorder
    a. Objective: Describe common deficiencies of AUD and OUD and potential causes or impacts
    b. Objective: Describe changes in hormones which impact eating behaviors and health (links to insulin regulation/hyperglycemia and to hunger and satiety cues)
    c. Objective: Describe effects of AUD, OUD and methamphetamines on the GI tract and dental health and the barriers to eating that arise from these effects
2. Goal: Students will be able to identify potential nutritional treatments and interventions to assist patients in recovery from substance use disorder
    a. Objective: Discuss eating disorders as a comorbidity and potential barrier to recovery
    b. Objective: Describe common treatments currently used for constipation and deficiencies
    c. Objective: Discuss the controversy of using sugar/fat/caffeine as an addiction replacements (harm reduction vs. promoting relapse)
    d. Objective: Describe cooking and nutrition education in recovery programs
3. Goal: Students will be able to identify social and systemic issues surrounding substance use disorders which impact nutrition both in the onset and the recovery of substance use disorders

a. Objective: Discuss home and food insecurity as a barrier to eating well during recovery
b. Objective: Discuss disproportionate impact of food accessibility for low-SES and homeless communities
c. Objective: Describe the cycle of substance use and incarceration in the context of structural discrimination, lack of treatment resources and poor nutrition availability in prisons

Lesson Plan

Table 2: Presentation outline

Time Allotted	Topic/Content/Activity	Notes
Intro		
1 minute	Overview of topic	
2 minutes	Poll Everywhere activity	This is part 1 of the evaluation designed to show a before and after snapshot of student opinions regarding nutrition and substance abuse
Mechanisms of Malnutrition and Deficiency		

15 minutes	Content Delivery
	• Energy-protein malnutrition
	• Disruptions to the GI system
	• Deficiencies and nutrition disturbances
	  ○ Emergencies
	  ○ Other chronic disorders
	• Hormonal changes affecting nutrition
	• Changes in eating behaviors
	• Body composition
		Overview of changes and disruptions to nutrition with a focus on what disease states (diabetes, osteoporosis, malnutrition) may result from these disruptions

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Nutrition Treatment Options		

15 minutes	Content Delivery
	• Addressing malnutrition and related conditions
	• Addiction replacement: Using sugar and salt
	• Effectiveness of education initiatives
	• Importance and challenges of nutritious diet in SUD
	  ○ Barriers related to homelessness and food insecurity
	  ○ Barriers related to incarceration and mental health
	  ○ Connections to eating disorders and mental health
		There aren't many nutrition-specific treatment studies that show effectiveness. Focus on some of the variable results from studies and controversies (use sugar or don't)
		
		Spend some time reviewing important barriers and challenges which have public health implications in addition to nutrition implications.

10 minutes	Activity: Poll Everywhere with Group Discussion • Where do you fall in the debate of harm reduction vs. blood sugar control?	Use a clickable image for students to place themselves on a range from one to the other. Ask for a few students to explain how or why they made that choice.
Conclusion		
2 minutes	Summary and wrap up	Show addiction and nutrition in context of all the factors that affect them (including systemic and social problems). Final idea: make system level changes so that making the healthy decision is the easy decision
10 minutes	Questions	

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Evaluation		
2 minutes	Poll Everywhere	This is part 2 of the evaluation designed to show a before and after snapshot of student opinions regarding nutrition and substance abuse

Total time anticipated: 57 minutes

Resources/Visuals

The PowerPoint presentation is the only visual used in this presentation (see Appendix C). Poll Everywhere is used for the evaluation of the lesson and for an interactive group discussion (see Chapter 6).

Assessment

Because of the online seminar format of the class, the presentation will be evaluated by a before and after survey using a 5-point Leikert scale. The statement “Nutrition support in substance use disorders improves outcomes” is meant to assess the degree to which other professions see nutrition as useful and important in this particular disease state. The goal is to show an increase in the number of students who view nutrition as supportive in treatment. This does not necessarily specifically address the stated goals and objectives, but if those goals are met, then an increase in perceived nutrition relevance would be expected.

Chapter 3: Methods

Interviews

Interview subjects were recruited through several different means. Successful contact methods included:

- Substance recovery centers were searched for via the internet with a focus on local centers. These centers were contacted via online contact forms or email.
- A request for interviews with subject matter experts was posted on the AND's Behavior Health Nutrition dietetic practice group forum
- Dr. Averill emailed professional contacts in clinical and interdisciplinary groups

The interviews were conducted using a semi-structured set of questions (see Appendix A). These questions were developed based on information found in several reviews of nutrition problems within substance use disorders and were adjusted slightly to reflect the different work experience and qualifications of each interviewee. However, the interviews were conducted as a conversation, and the question set was adapted during the interview based on the responses of the interviewee. Regardless of question structure or order, all topics were covered with each interviewee. The interviewees were as follows:

- Quincy Jefferson, SUDP, Director of Quality Control at Lakeside-Milam Recovery Center
- Sherry Fixelle, RD, Dietitian at Ocean Recovery Treatment Center
- Kristie Drenckpohl, RN, Harborview Opioid Outpatient Treatment Center
- Dr. James Darnton, MD, Evergreen Treatment Center and Harborview
- Charlotte Sanders, MSW, Youth Clinic Manager for Homeless Youth Program (past employment)
- Kelly Heshelman, RD, Harborview ICU and Behavioral Health Floor

The interviews were recorded and roughly transcribed (some parts were reworded for clarity). The transcripts were coded based on the question topics and are summarized into themes. Interview subjects were provided with the reviews used to develop the questions after the interview.

Potential Sources of Bias in Interviews

Three of the six interviewees were connected to a single contact at CHSIE. Additionally, three of the six interviewees work at Harborview. These similarities in workplace and interdisciplinary contacts may result in similar viewpoints and may not be representative of all people working in substance use disorder treatment.

Cold contacting professionals did not result in a high rate of response. It is possible that those who did respond were more likely to have considered the implications of nutrition in treatment of substance use disorders than those who did not respond. This difference may be reflected in their observations.

As not all interviewees were dietitians or professionals who might be experienced with considering the nutritional implications, many questions were asked about situations which may influence nutrition or ability to eat (ie food security, dental health, constipation). These questions are more leading and less open-ended and may have influenced the response. Additionally, the response may be associated in analysis with a nutrition complication which was not intended by the interviewee.

Literature Review

The literature review was conducted using the following PICOT and search terms:

P: Any person diagnosed with an addiction to alcohol or opioids
I: Nutrition effects of substance use (for consequences), nutrition treatments to mitigate complications of addiction or assist in recovery (for interventions)
C: Non-addicted persons or recovered SUD
O: Nutrition improvements, reduced addiction (for interventions); prevalence of deficiencies (for consequences)
T: Before, during or after treatment (long-term complications included)

Search terms: “nutrition opioid addiction” “diet opioid addiction” “nutrition alcohol addiction” “diet alcohol addiction” “nutrition amphetamines addiction” “diet amphetamines addiction” “opioid alcohol insulin” “alcohol opioid ghrelin” “alcohol opioid microbiome” “eating disorder substance addiction”
Search databases: SCOPUS, PubMed

Additionally, some references were sourced from reviews or recommended by interviewees. Each reference was reviewed for relevance, and an annotated bibliography of the most relevant sources was compiled for mentor review. The notes from all relevant sources were combined into a single outline and used to write the literature review and prepare the PowerPoint presentation.

Chapter 4: SUD Population Description and Nutrition Issues

In the United States, substance use disorders (SUD) were present in approximately 20.3 million (7.4%) individuals over 12 in 2018.[13] The majority of these disorders were alcohol use disorders (AUD) with an estimated 14.8 million people (5.4% of the total population).[13] Of illicit drugs, marijuana was the most common SUD followed by prescription pain relievers. Heroin had the fewest estimated SUDs, however, when combined with prescription pain reliever disorders, the opiate use disorders are found in approximately 2.0 million people (0.7% of the total population).[13] The economic cost of these disorders is enormous with AUDs accounting for $249 billion (2010 data) and prescription OUDs accounting for $78.5 billion (2013 data) each year.[14] Despite the cost and extent of the problem, SUD treatment facilities are still separated from other health care[15] with a prevailing notion that SUDs are the result of social and moral failings instead of a treatable chronic disease.[16]

No segment of the population is immune from SUDs. There are however some trends in the population. In hospital admission records, females have much lower overall prevalence of SUDs and odds of having SUDs than males.[17,18] In overall prevalence, SUDs are more common in people aged 18-44, however this may vary by type of substance.[17] For AUD with no second SUD, the prevalence is higher in older adults.[17] Most other substances are more common in younger age brackets with the exception of smoked cocaine (crack) which peaks at age 44.[17] When looking at epidemiologic analyses of hospital records, the data support generational preferences in substance use. Individuals currently in the 35-64 age bracket have the highest odds of an AUD while those in the 26-49 age bracket have greater odds for SUDs involving cocaine and amphetamines. OUD and cannabis use disorders have the highest odds in the 18-25 age bracket.[18] It is important to remember, however, that all these data coming from hospital records miss segments of the population who do not use medical services. This fact may affect the odds and prevalence overall.

When looking at the SUD population by racial identity, the highest overall numbers of SUDs are among those identifying as white.[17] However, this is a reflection perhaps of the overall demographic makeup of the United States. National drug use surveys during the 2000s among adolescents indicate that Native American adolescents have the highest incidence of SUDs followed by those who identify as multiracial and then those who identify as white.[19,20] In these data sets, African American, Hispanic and Asian adolescents had significantly lower prevalences of SUDs,[20] however the data also shows that African American and Hispanic adolescents are significantly less likely to receive treatment for SUDs

than their white counterparts.[20] Despite lower prevalence, this may still indicate greater risk and consequences for those groups. These trends do not necessarily hold true in adult patients. In a study looking at adult patients in treatment centers, African American patients had higher odds for all SUDs compared to white individuals except for opiates[18] which has a higher incidence among white individuals.[21]

In considering the data on adolescents, it should be noted that it does not include people who are currently incarcerated.[19,20] This is important since studies examining race, substance use and criminal involvement have shown that race is a significant predictor for drug-related arrests in adolescents.[22] Despite white adolescents having the same or higher drug use and drug selling activity,[22,23] African American adolescents were more likely to be charged with sales and possession.[23] Additionally, although there were a fewer number of convictions, African American adolescents were more likely to be given jail time and to have longer sentences than white adolescents.[23] As one study author comments, there is a significant disparity in how society in the United States has responded to SUD epidemics associated with different racial communities.[23] According to Alana Rosenberg et al, the opioid epidemic associated with white communities was met with rehabilitation initiatives while the crack cocaine epidemic associated with African American communities was met with the war on drugs.[23] These contrasting responses further reinforce the barrier that people of color face in seeking treatment and demonstrate the more significant consequences of SUDs for these groups overall.

In the SUD population, there are high rates of homelessness, mental health disorders and incarceration compared to the general population, especially when these conditions occur simultaneously. While not considered the cause of homelessness,[24] rates of substance use in the homeless population are very high with estimates as high as two thirds having a lifetime prevalence of an SUD and one third having a current SUD.[25] Given that the estimated homeless population was approximately 1.4 million in the United States in 2017,[26] these estimates place the total SUD in a year for this population at about 420,000 out of the estimated yearly 20.3 million SUDs. Substance use can likely contribute to initiation and continuance of homelessness for many individuals, especially as many housing programs require treatment[24,27] and as there are fewer treatment options for homeless SUD individuals who are not motivated to quit.[25] Over time, overdoses and SUD have become a major cause of mortality in homeless populations accounting for approximately one third of deaths in homeless adults under the age of 45.[28] In this particular study, 80% of the overdose deaths were due to opioids[28] which may indicate a different prevalence of various drugs among the homeless population compared

to the general SUD population. Authors of another study found that intravenous drug use is more common in homeless women compared to housed women.[29]

Like homelessness, substance use is more common in individuals with a mental health illness.[13] It is estimated from the 2018 National Survey on Drug Use and Health that 9.2 million people (3.7% of the total population) have a mental illness and at least one SUD.[13] The National Institute on Drug Abuse estimates that 25% of people with a severe mental illness also have an SUD and approximately half of people with a mental illness will have an SUD sometime in their life. [15] This high co-prevalence is likely due to the fact that both disorders promote the onset of and worsen the other condition.[15] There are also common risk factors for the disorders including genetic and epigenetic vulnerability and environmental stress and trauma.[15] Additionally, both mental illness and homelessness increase the risk of arrest.[25,30] It is estimated that 75% of prisoners with a mental illness have an SUD compared to 55% of prisoners without a mental illness, and those with a mental illness were twice as likely to be homeless prior to arrest.[30] In contrast to the general SUD population in which drug dependence is much lower than alcohol dependence, 61% of prisoners with comorbid mental illnesses and SUDs are dependent on drugs and 51% are dependent on alcohol.[30]

A mental health condition of specific interest to nutrition is eating disorders. Conditional prevalence of comorbid eating disorders and substance use disorders can be high depending on how the study population is defined. In the eating disorder population, lifetime prevalence of SUDs were estimated to be 22% (95% CI 16.7-28.0) in a meta-analysis with the highest prevalences being in white females with binge-purge disorders.[31] In SUD populations, the rates of eating disorders are much lower. In a mixed-gender group with substance use disorders, researchers in Canada found a prevalence of approximately 7.5% for both anorexia and bulimia in women and 2.6% for anorexia and 1.5% for bulimia in men.[32] Of these results, only anorexia was found to be significantly higher prevalence ($p<0.0005$) in both genders than the general Canadian population.[32] It should be noted that the authors only included diagnosed eating disorders in their study as opposed to disordered eating symptoms. In a study of women with SUDs in Australia, the authors reported at least 2 disordered eating symptoms using a validated in 60% of the subjects with 32% of the subjects reporting a history of an eating disorder.[33] The authors of this study did not compare this prevalence to the general population or a control group. Yet another study in women with AUD and nicotine use disorder (NUD) found that the relative risk of an eating disorder for subjects with both AUD and NUD compared to those with neither SUD was between 2.59 (95% CI 1.24 – 5.43) for purge disorder and 3.17 (95% CI 1.35 – 7.44) for anorexia.[34] The vast range

of eating disorder estimates in the SUD population indicates several ideas. First, this mental health condition is clearly more prevalent in the SUD population than the general population, but the variations in gender makeup and definitions of eating disorders between studies make it difficult to understand the extent and severity of this co-morbidity. Second, subclinical eating disorders (as evidence by disordered eating symptoms) are likely more prevalent in the SUD population than is recognized.[32,33] This may be particularly true as many disordered eating patterns have been normalized in society at large and because underweight in SUD individuals could be attributed to malnutrition from substance use or food insecurity.

Food insecurity in drug users is estimated to be 30-70%.[35] In a study of injection drug users in Canada, 50% were found to be marginally housed with 54.5% reporting daily to weekly food insecurity due to lack of money and 60.4% reporting food insecurity related to reduced quantity and quality of food.[35] The authors studying this population found that the injection drug users they surveyed were 2.5 to 6 times more likely to experience food insecurity than the general Canadian population.[35] In another study of female SUD individuals positive for HIV, the authors reported these women had multiple nutritional hazards including routinely eating from dumpsters and skipped meals.[29] The authors additionally found through qualitative interviews that one important factor in the promotion of these hazards was lack of personal resources and neighborhood food availability.[29] Interestingly, in this sample of women, injection drug use was much higher among the homeless women than among the housed women.[29] Most estimates of food insecurity have been for injection drug-using individuals as opposed to the SUD population at large, and these results[29] in addition to those indicating that the primary cause of overdoses in the homeless is due to opioids[28] may indicate that injection drug users are at a higher risk for food insecurity than other SUD subpopulations.

It is estimated that 80% of heroin users first misused prescription opioids and that 8-12% of people prescribed opioid pain relievers develop an OUD.[36] Researchers have found that there are correlations between SUDs and other chronic conditions. Not only does the prevalence of SUDs increase with the number of chronic conditions,[18] but having a chronic disease is associated with an increased odds of having an SUD.[21] While these studies are cross-sectional and cannot indicate causality, one scenario explaining this correlation is the high number of opioid prescriptions given for chronic pain. The CDC reports that while opioid prescription rates are dropping with improved practices, more than 17% of Americans had an opioid prescription filled in 2017.[37] This rate of exposure to opioids could very well be an initiating factor in the opioid epidemic. An alternative scenario, however, is that opioid and other

substance abuse could be promoting development of chronic diseases instead of arising as the result of medication use for pain. The nutritional consequences of SUDs and the diseases they facilitate have severe and potentially long-lasting impacts which promote acute and chronic illness.

Chapter 5: Literature Review and Interviews

Literature Review

Substance use disorders (SUDs) are characterized by a myriad of metabolic and nutritional disturbances ranging from micronutrient deficiencies to hormonal disregulation and microbiome dysbiosis. While many of the mechanisms thought to cause for these problems are different, the outcomes can be similar in various substance use disorders as can the nutritional approach to treatment. Because of ethical considerations, much of the data generated in this field is limited to observational studies, surveys and pre-clinical experimental trials. Additionally, it is difficult to control for all of the demographic factors and comorbidities found in the SUD population, particularly as some sub-populations may have significant variations from the overall population. As a result, there are contradictions in study findings and a relative paucity of treatment approaches to address nutritional disturbances.

Malnutrition

The main nutrition problem for individuals with severe SUDs stems from primary malnutrition. This can occur for many reasons. Progressed SUD individuals may replace calories from food with the substance [38–42] or consume fewer calories and protein because of reduced access to the proper quantity/quality of food.[38–40,43] Reports in alcohol use disorder (AUD) populations estimate that advanced cases can replace as much as 60% of calories with alcohol[44] while, in a survey of 195 drug users recruited from the streets in Norway, 64% of the respondents reported limited access to food leading to reduced calorie consumption.[43] A separate survey of 285 injection drug users in Australia reported that 79% of respondents ate less than 3 meals a day with 16% reporting often eating no food in a given day.[45] Individuals with drug use disorders may fast from both food and water to intensify the experience when on a binge.[35,40] In a survey of 144 injection drug users in Canada, 57.6% of the respondents reported this type of fasting.[35] Those with opiate use disorder (OUD) may also experience reduced appetite and changed taste for food due to the effect of the drug of the gastrointestinal system which leads to drastically reduced food intake.[39–41,46]

In addition to reduced energy and protein consumption, many SUD patients also have micronutrient deficiencies leading to secondary malnutrition. This can result from this primary malnutrition in that reduced calories also leads to reduced micronutrient intake, but it can also result from changes in food preferences and damage to the gastrointestinal system. Both AUD and OUD

surveys report changes in type of food intake indicative of preference for both sweet[38,42,47,48] and salty[49] foods. Both salty and sweet foods are thought to trigger the dopaminergic reward system in similar ways to substance use and reinforce the disorder.[48–50] These preferences contribute to micronutrient deficiencies in that these foods are often low in fiber and micronutrients and can replace foods with more protein and fat leading to a nutritionally unbalanced diet even if the energy intake is not reduced.[41,51] In a survey of drug users, the authors reported from a 24 hour dietary recall that 30% of the total calories consumed were from added sugar, 60% of the calories consumed came from carbohydrates and poly-unsaturated fat intake was 5-10% of the total calories.[43] Paradoxically, even though this population was consuming calories sufficient only for bed rest, the majority of BMIs of the respondents were at or above the recommended range.[43] This type of primary and secondary malnutrition from an unbalanced diet does not necessarily present in underweight,[39] and may therefore be more difficult for clinicians to recognize.

Deficiencies and Consequences: Alcohol

One of the differences between AUD and OUD is the etiology of changes in the gastrointestinal system leading to micronutrient deficiencies. In AUD, the ethanol can directly damage the gastrointestinal tissue or cause changes in gene expression which reduce absorption.[38,39,42] The damage to the tissue in the small intestine can be severe, and it has been compared to damage in untreated Celiac's disease.[38] This damage not only reduces absorption, but it can lead to a range of problems including delayed gastric emptying, changes in intestinal transit time, dysbiosis and small intestinal bacterial overgrowth, intestinal inflammation and even lactose intolerance.[38,39,52] Changes in gastric emptying and intestinal transit time, specifically, have been noted to be variable depending on the concentration and frequency of alcohol use, but either effect is thought to impact the ability of the gastrointestinal system to absorb nutrients.[52] Liver damage from alcohol can also impair the absorption and the ability to use the nutrients that are absorbed.[38] Documented deficiencies in AUD include thiamine,[38,39,42] riboflavin,[39,42] niacin,[39] pyridoxine,[38,39,42] folic acid,[38,39,42,53,54] vitamin B12,[38,39,53,54] vitamin A[38,39,42,44,55], vitamin C,[39,42,47] vitamin D, [38,39,56,57] vitamin E,[39,58] vitamin K,[39,59] magnesium, [39,57,60–62] selenium,[39,58] zinc,[39,42,44,60] choline,[42] potassium,[47] sodium,[63] and calcium.[60] See table 3 on page 28 for a summary of deficiencies. It is important to note that rates of these deficiencies are often low in the AUD population and may not even cause a clinical presentation of deficiency. However, several of these may contribute to life-threatening emergencies or other chronic illnesses, and sub-clinical deficiencies may still have functional impact.

One well known consequence of thiamine depletion is Wernicke-Korsakoff encephalopathy. Often described as two consecutive diseases, Wernicke-Korsakoff is a progressive cognitive dysfunction characterized by confusion, eye involvement and confabulation.[16,38,63] The syndrome constitutes an emergency particularly because delay in treatment may cause irreversible cognitive damage, and for this reason, many hospitals have policies to treat with thiamine injections and glucose if Wernicke-Korsakoff is suspected.[63] Thiamine deficiency is affected by magnesium deficiency, however, since magnesium is a cofactor in thiamine reactions.[38,39,64] Failure to also administer magnesium when the patient is deficient could result in failure of the thiamine treatment.[64]

This is particularly important as hypomagnesaemia is one of the most common electrolyte disturbances in alcoholics with prevalence ranging from 13% in an outpatient clinic in Denmark[57] to 48% in a hospital in Australia.[61] Hypomagnesaemia is, in itself, a medical emergency leading to muscle weakness, irregular heartbeat with increased QT intervals and overactive reflexes,[63] and low serum magnesium has been linked to cognitive deficits independently of thiamine levels in a population of mostly Aboriginal patients in Australia.[61] This disturbance is easily corrected with administration of magnesium.[63] However, it is important to note that there are many potential causes of hypomagnesaemia aside from reduced intake and absorption, and several of these causes may interact with other deficiencies or metabolic disturbances.[62,63] The most influential of these centers around vitamin D and calcium levels and the parathyroid gland.

Vitamin D levels are the main determinant of calcium absorption from the intestine.[60] When serum calcium levels fall, the parathyroid gland secretes parathyroid hormone which increases serum calcium at the expense of bone and increases active vitamin D and therefore calcium absorption.[65] In vitamin D deficiency, calcium remains low due to reduced absorption which not only causes demineralization of bone but can also result in greater excretion of magnesium in the kidney.[60,65,66] Parathyroid hormone increases the amount of calcium reabsorbed in the kidney, but magnesium and calcium compete for the same transporter in the thick ascending limb of the loop of Henle which may account for the increased excretion of magnesium when calcium levels are low.[67,68] In alcoholics, the incidence of vitamin D deficiencies varies but is generally high. One study in Spain found 40% of alcoholic patients had insufficient vitamin D while 20% were deficient.[56] Another study in Norway found 28% insufficiency and 36% deficiency.[57] It has been suggested from research that the primary factor behind these deficiencies are reduced intake of vitamin D and reduced sun exposure[60] which may account for the greater prevalence of deficiency in Norway compared to Spain. While vitamin D

deficiency and the related low serum calcium can cause hypomagnesaemia, reverse causation is also possible. Low levels of magnesium can trap calcium inside cells,[65] and magnesium is a cofactor in vitamin D activation.[69] In both cases, hypomagnesaemia contributes to vitamin D deficiency and hypocalcaemia. The interplay of calcium, vitamin D and magnesium highlight the complexity of metabolic systems and the fact that the disturbance of any one nutrient can disrupt a number of essential functions.

Evidence of malfunctions in this system is not only seen in specific deficiencies but also in prevalence of osteoporosis and reduced bone density. Researchers consistently show that about 50% of alcoholic patients exhibit bone density loss with increased prevalence of osteopenia and osteoporosis compared to the general population.[60] There are other factors aside from vitamin D levels which may promote the bone loss. One of these is acidosis and related acid/base balance disorders.[60] Metabolic acidosis may result from the increased parathyroid hormone levels which decrease the amount of bicarbonate reabsorbed in the kidneys,[66] and this increased acidity has been shown to be correlated with osteopenia.[60] Interestingly, research has shown that hyperparathyroidism is transient in AUD instead of persistent[60] which may mean that this effect is inconsistent in patients.

Sodium is another electrolyte which is reduced in AUD and may lead to life-threatening situations if the levels fall too low. Like magnesium, there are several different causes of hyponatremia such as hypovolemia[63] which may be related to dehydration and vomiting during acute intoxication[70] and syndrome of inappropriate antidiuretic hormone secretion[63] which may be triggered during alcohol consumption or withdrawal.[71] Another potential cause is beer potomania which is caused by consuming large volumes of a hypotonic solution, usually beer.[63] The kidneys are unable to excrete water at a high enough rate to match consumption and all the serum factors are diluted as a result.[63] Because symptoms are often similar to other aspects of AUD including intoxication and withdrawal and because the cause of the hyponatremia can change the treatment, it is important to not only recognize the disease but also to treat the condition correctly.[63] When salt concentrations are corrected too quickly, patients are at risk for osmotic demyelination syndrome which causes neurological damage.[63,72]

Emergencies also arise from the primary malnutrition seen in advanced AUD patients. In cases where there is heavy alcohol intake and malnutrition, AUD individuals may develop ketoacidosis.[66,73] Patients with malnutrition have low glycogen stores from being in a fasted state, but the addition of alcohol consumption promotes use of fatty acids for energy.[63,73] Alcohol oxidation to acetate produces excess NADH which inhibits gluconeogenesis and keeps available glucose low.[63,74] Alcohol also impacts hormone systems and increases catecholamines which promote a catabolic state by inhibiting insulin

and promoting glucagon and lipolysis.[63] All of these factors promote formation of ketones which can cause acidosis.[44,63] Additionally, NADH and acetate excesses can promote lactic acid formation which contributes to overall acidosis.[74]

A chronic problem that results from protein malnutrition in AUD is alcoholic myopathy.[39] AUD individuals may be in a state of negative nitrogen balance not only from primary malnutrition, but also from impaired storage and absorption and increased excretion and protein turnover.[44] Alcohol itself can alter the expression and functioning of many enzymes which decrease protein synthesis and increase degradation.[75] The end result of this is a loss of lean tissue[39] with weakness, swelling and pain which can lead to kidney injury via rhabdomyolysis in acute cases.[75] Additionally, myopathy and loss of muscle mass is linked to oxidative stress and chronic inflammation.[75] Alcohol oxidation and the products of those reactions have been known to increase free radicals and the risk of lipid peroxidation.[42,58,75] Given that the antioxidant nutrients selenium, vitamin E and vitamin C may be reduced due to malnutrition,[39,42,58] these increased levels of reactive oxygen species are able to promote inflammation and injure tissues.

Inflammation could also promote anemia in alcoholics when iron stores are low.[38,39] Interestingly, iron status can be low or high in AUD.[38,39] In a study of AUD patients compared to social drinkers, the prevalence of reduced iron or functional iron deficiency was found to be about 10% while excess iron and iron overload was found in 9% of participants.[54] In a large national survey, the authors found that iron status increased with increased daily drinks and that any alcohol consumption reduced risk of anemia by 42% compared to the group who had no alcohol consumption.[76] They also found a significantly increased risk of iron overload in the group who consumed more than 2 drinks per day.[76] A second large survey in Australia found similar correlations between drinks per day and iron status confirming these results.[77] It seems that alcohol promotes higher levels of iron, but low iron status and iron deficiency anemia may result from AUD complications such as gastritis, esophagitis and mallory-weiss tears which lead to blood loss or from alcoholic fatty liver disease.[76]

Individuals with AUD are also at risk of megaloblastic anemia due to reduced B12 and folate levels.[54,78] Reported prevalence of folate and B12 deficiency in one observational study were found to be significantly higher than controls at 8.5% and 28.3%, respectively,[53] however reported rates of insufficient serum folate have ranged as high as 33-80%.[78] Folate and B12 are essential in methionine cycling and in purine and pyramidine synthesis.[65] When these processes are halted by deficiency in either folate or B12, it reduces the effects of methylation, cell differentiation and cell division which

leads to a reduced number of large red blood cells.[65] The other effect of reduced folate and B12 is elevated levels of homocysteine since folate and B12 are essential for methylation of homocysteine to make methionine.[65,79] In addition to low folate and B12, it is thought that acetaldehyde itself can inhibit methylation.[79] Although somewhat contested, high levels of homocysteine are associated with mental health disturbances and are considered neurotoxic.[79–81] Homocysteine has been shown in pre-clinical trials to increase the permeability of the blood brain barrier,[80] to create reactive oxygen species[79,81] and to damage the dopaminergic reward system.[79,81] In human studies, elevated homocysteine is associated with increased mood and anxiety disorders and increased alcohol craving.[79] These results provide a biologic connection for the increased rates of mental health disorders in SUD populations, and they also point to mechanisms which perpetuate the cycle of addiction.[79]

Deficiencies and Consequences: Opioids

In OUD, micronutrient deficiencies are more connected to the physical effects of the opioids which lead to reduced appetite than to tissue damage as in AUD. There are opioid receptors in many tissues throughout the gastrointestinal system, and when these are triggered inappropriately by exogenous opioids, it causes disregulation in the enteric nervous system.[38–40,82] This interaction reduces and changes motility in the gastrointestinal tract which delays gastric emptying and slows transit time.[38–40,83] Exogenous opioids also disrupt secretion of electrolytes and water and increase fluid absorption.[82] All of these effects lead to intense constipation,[38–40,82] gastroesophageal reflux and bloating.[82] The secondary complications of these changes include bowel obstruction, nausea and vomiting[82] which reduces appetite and promotes malnutrition. These stagnant conditions also create an opportunity for bacterial overgrowth which can change the microbiome and cause a buildup of endotoxins.[38] It is in this environment that inflammation and toxins can damage the epithelium of the intestine and reduce absorption to some degree.[38] This compounds the deficiencies caused by anorexia.

Documented deficiencies in OUD include thiamine,[84] riboflavin,[84] niacin,[84] B6,[84] folate,[84] B12,[84] vitamin A,[38,39,41] vitamin C,[38,39,41,43] vitamin D,[43] vitamin E,[38,39,41] vitamin K,[41,85] calcium,[41,85] magnesium[41] and selenium.[86] See table 3 on page 28 for a summary of deficiencies. While many of these deficiencies have a low prevalence, some studies found high levels of deficiency in vitamins B6 and folate at around 40% of subjects[84] and in vitamins C and D at 50% and 70% of subjects, respectively.[43] It is worth noting that subjects tested in the study which revealed high levels of vitamin C and D insufficiency were compared to recommended ranges and not a comparison group with the same demographic profiles.[43] Interestingly, while many authors testing for deficiencies comment on the possibility of these

deficiencies impacting chronic health conditions, few report the prevalence of those conditions in OUD. Certainly, it would be reasonable to assume that low folate and B6 levels would disrupt methylation affecting anemia or that low calcium and vitamin D would increase risk of osteoporosis as in AUD, but the full body effects of the opioids may be more impactful than the low vitamin levels.

Risk of osteoporosis has been noted in opioid users.[85,87,88] Instead of being attributed to vitamin D levels, however, this risk has been connected to opioid effects on the hypothalamus which regulates the pituitary gland and, from there, both the gonadal and adrenal hormones.[85,87,88] These hormonal changes are linked to increased risk of bone density loss.[85,87,88] It is also thought that osteoblasts may have opioid receptors which exogenous opioids can trigger thereby reducing activity.[85,88] In this case, the low vitamin levels, while certainly not helping, may actually be somewhat irrelevant since the mechanism to rebuild the bone is not functioning.

One interesting marker often reduced in OUD is cholesterol. Low cholesterol in current addicts is often noted in research[43,85,89] with one survey of addicts in Norway estimating the prevalence at 35%.[43] Another study found that addicts in recovery had a significant increase in cholesterol compared to those with current OUD.[85] This change in cholesterol was attributed not only to disturbances in lipid metabolism but also malnutrition and reduced fat intake.[85] This low cholesterol is important in that it has implications for mental health problems and has been shown to be associated with not only increased rates of relapse but also increased rates of suicide.[90] In a study of cocaine users, addicts in recovery who had significantly lower levels of cholesterol had faster and higher rates of relapse compared to addicts with higher levels of cholesterol.[90] While it is not clear why this association exists, theories revolve around cholesterol as a biomarker for omega-3 polyunsaturated fat intake and around the ability of tryptophan to cross the blood brain barrier.[90] As omega-3 fats are connected to brain health and reduced inflammation[91] and tryptophan is the precursor for many neurotransmitters,[65] these theories connecting cholesterol to mental health seem plausible even if unproven. Regardless of the use of cholesterol as a marker, reduced essential fatty acid and amino acid intake would both impair mental health and may promote or mimic the mental health disorders noted in the SUD population.[40] Efforts to improve the nutritional status of an individual with OUD during treatment or active addiction could potentially diminish these mental health conditions and make recovery from the OUD more achievable.

While not a true deficiency, a side effect of opioid use which significantly affects nutrition is dry mouth or xerostomia.[40] Xerostomia leads to dental problems and tooth decay which not only affects food choices but also the ability to eat without pain.[40] In a survey of injection drug users, approximately

68% reported severe dental problems and 40% reported difficulty in maintaining personal hygiene such as dental care.[45] These challenges make it more attractive to eat soft foods and consume liquids, many of which are nutritionally poor and high in sugar or simply eat less overall.[40] This contributes to both primary and secondary malnutrition in OUD.

Table 3: Summary of documented anomalies

Alcohol Use Disorder	Opioid Use Disorder
Deficient Vitamins Thiamine (B1) Riboflavin (B2) Niacin (B3) Pyridoxine (B6) Folic acid (B9) Vitamin B12 Choline Vitamin A Vitamin C Vitamin D Vitamin E Vitamin K **Deficient Minerals** Calcium Iron Magnesium Selenium Zinc **Elevated Nutrients and Markers** Iron Copper (serum) Homocysteine	**Deficient Vitamins** Thiamine (B1) Riboflavin (B2) Niacin (B3) Pyridoxine (B6) Folic Acid (B9) Vitamin B12 Vitamin A Vitamin C Vitamin E Vitamin K **Deficient Minerals** Calcium Magnesium Selenium Zinc **Decreased Macronutrients and Other Markers** Cholesterol Essential Fatty Acids Amino Acids

Hormonal changes, body composition and glycemic control: Alcohol

Alcohol consumption and addiction can significant hormonal effects in the body, but the most pertinent to food consumption, body composition and glycemic control are leptin, ghrelin and insulin. Both ghrelin and leptin have shown varying effects in research. Leptin is a hormone made in white adipose tissue that coordinates both food intake and body weight.[92] Research on leptin's role in AUD is unclear with results showing increases, decreases or even no change in subjects.[92] Despite this, AUD individuals often have lower BMI and fat mass.[39,93] As in the discussion of alcoholic ketoacidosis, there

are many biochemical processes that push alcohol users toward a catabolic state with increased lipolysis and free fatty acids and reduced lipogenesis[39] including changes in redox states,[74] increases in glucocorticoids,[94,95] and reduced insulin levels.[96] Despite a general consensus and documented reductions in fat mass, there is still some debate about this process with some authors presenting data of lower lipolysis rates in alcoholics.[95]

Ghrelin is a hormone which is produced in response to fasting and lower levels of blood glucose,[97] and it is thought to regulate appetite and food intake to maintain energy homeostasis.[97,98] Ghrelin interacts with the hypothalamus to stimulate food intake, but it is also associated with increased activity in dopaminergic neurons.[97,98] This activity stimulates the reward center in the brain in similar patterns to drug and alcohol intake.[97,98] This stimulation in food and substance intake is thought to be so similar that hunger cues may be mistaken for substance cravings and thus ghrelin may perpetuate substance-seeking behavior.[97,98] Studies show that ghrelin increases prior to consumption of alcohol and is reduced after consumption, and preclinical trials demonstrate that artificially raising ghrelin levels increases the amount of alcohol consumed in a sitting.[97,98] However, these results are more related to acute alcohol consumption behavior. In chronic alcohol consumption and AUD, both human and preclinical trials serum ghrelin levels have been mostly reported as reduced overall with significant increases during abstinence which may promote relapse.[93,97] In contrast, recent experimental data in rats has shown increased levels of ghrelin in both fasting and fed states in chronic alcohol use.[96] Some of this discrepancy may be attributed to differences in testing methods (fasting vs. fed states for testing),[97] but one author presenting a human observational study notes that decreased serum levels of ghrelin may be influenced by the extent of malnutrition in the subject.[93]

Insulin production is drastically changed in AUD, and chronic alcohol use been found to be a risk factor for development of type 2 diabetes mellitus.[92] Alcohol itself can damage the pancreas, causing inflammation in acinar cells and damaging the β-cells.[92] Data from studies in rats indicates that while insulin production in not changed, the insulin is not released from the β-cells.[96,99] This may be linked to ghrelin levels as *in vitro* studies have shown that high levels of ghrelin impair the membrane potential of β-cells which would affect the ability of the cell to secrete insulin.[96] Alcohol is also thought to induce insulin resistance as research indicates that alcohol is associated with decreased insulin-stimulated glucose uptake and glucose intolerance.[44,92,99] Some of this change may be related to adiponectin. Adiponectin is secreted from adipose tissue and is thought to be involved in glucose homeostasis.[92] In AUD, adiponectin has been found to be decreased, and, in rats, low adiponectin is associated with

insulin resistance and macrophage infiltration into adipose tissue.[92] Interestingly, AUD individuals are at risk of both hyperglycemia and hypoglycemia events. In context of developing insulin resistance and reduced insulin secretion, the danger is hyperglycemia, especially with changes in eating behavior to prefer simple sugars and low fiber foods. However, impairments to gluconeogenesis and reduced glycogen stores from fasting may create a risk for hypoglycemia.[44,63,99] Hypoglycemia is not often seen clinically[63] while glucose intolerance and inhibited insulin secretion is observed more often.[95] These studies are largely done in pre-clinical and non-diabetic populations. For individuals with pre-existing type 1 or type 2 diabetes mellitus (T1DM or T2DM), the metabolic changes cause by AUD and the changes in eating behaviors have the potential to exacerbate glucose control problems to dangerous levels much more quickly.

Hormonal changes, body composition and glycemic control: Opioids

As is the case with deficiencies, some similar hormone effects are seen in OUD and AUD, but the mechanisms appear to be different. Additionally, there is less research in the effects of opioids. It is presumed that since endogenous opioids are involved the reward response that exogenous opioids also have an effect, but there are very few completed studies examining the impact of opioids on serum ghrelin levels.[97] In a preclinical study, researchers showed that experimentally increasing ghrelin levels increases the amount of heroin that rats can self-administer.[97] While this amount of evidence is not enough to draw conclusions about the relationship of ghrelin and opioids, it suggests a hypothesis that increased levels of ghrelin may augment opioid seeking behavior.

Research in leptin levels during OUD has indicated that leptin levels decrease with opioid use.[100,101] In a trial with opioid-naïve subjects, 30 days of daily morphine administration showed a trend of decreasing leptin levels.[101] This trend was not significant compared to controls,[101] but this is may be a result of the relatively short duration of administration. When considering leptin levels in active OUD cases, subjects displayed hypoleptinemia.[100] This condition is normally associated with decreased adiposity and malnutrition, but in this study, the leptin levels were not correlated to BMI.[100] As high levels of leptin signal satiety, chronically low levels in active OUD might indicate increased food and drug cravings. When researchers followed the active OUD through opioid replacement with methadone over a period of one year, they found that leptin levels normalized.[100] Interestingly, adipocyte derived hormones, adiponectin and resistin began and remained different from controls through methadone maintenance.[100] Both adiponectin and resistin are associated with glucose homeostasis, and the OUD patients displayed abnormally low adiponectin and high resistin.[100] This particular pattern is sometimes

found in insulin resistance which suggests that while leptin-related body fat and satiety cues may return to normal, the risk of insulin resistance and related disorders remains through at least a year of recovery.[100] It is important to note that methadone itself is an opioid which is often used to help patients recover from OUD, so the continuing effects on adiponectin and resistin seen in this study may not be the same in individuals who use other methods or even other pharmaceuticals in recovery.

Individuals using opioids are not only at risk for insulin resistance as seen in the effects of adiponectin and resistin but also for the development of a diabetes-like hyperglycemia. Endogenous opioids play a role in regulating insulin production as β-cells have μ-opioid receptors which means that exogenous opioids can have a direct effect on those cells.[48,101] Additionally, μ-opioid receptors in the hypothalamus also play a role in regulating insulin secretion.[101,102] This relationship may be dependent on the dose, however, as pre-clinical studies in the hypothalamic μ-opioid receptor stimulation show that high doses of an opioids inhibit insulin production while lower doses stimulate insulin production.[102] This reduction in insulin levels was seen in the study of opioid-naïve subjects given a morphine for 30 days.[101] Subjects receiving the morphine showed a significant decrease of 42.8% in insulin levels from baseline.[101] At the same time, opioids have been shown to enhance gluconeogenesis and inhibit glycolosis through action on the glycolytic enzymes.[48,50] This increases the levels of blood glucose, and taken together with the drastic decrease in insulin, could lead to hyperglycemia and a diabetes mellitus like disease state.[50,94,101] This conclusion is supported by the increased prevalence of metabolic syndrome seen in OUD individuals during recovery[50] and by increased levels of glycosylated hemoglobin among individuals with OUD not seeking treatment.[43,103] In a study comparing the diagnoses of metabolic syndrome between individuals on methadone and buprenorphine, researchers found that both groups have much higher prevalence than the general public at 56% and 34%, respectively.[50] For both individuals with and without pre-existing diabetes mellitus, the use of opioids has a clear effect on the ability to control glucose levels. In a study following individuals with concurrent OUD and T2DM over 2 years, the individuals who were on a buprenorphine and naloxone substitution therapy saw decreased levels of glycosylated hemoglobin compared to those not participating in the therapy.[103] In a non-diabetic population of heroin users in Norway, glycosylated hemoglobin was above the recommended levels in 12% of male and 20% of female subjects.[43] While this does not indicate that opioids cause diabetes mellitus, it shows that blood glucose levels over time can be elevated in OUD potentially leading to many of the same long-term effects as uncontrolled diabetes mellitus.

Despite the strong evidence that opioids promote hyperglycemic states, case reports of hypoglycemia have also been described. These cases are observed most often in individuals who recently began taking opioids[104,105] or in cases of overdose.[105] In one case, the hypoglycemia was thought to be related to adrenal insufficiency caused by an opioid Tramadol.[104] This led to an impairment of gluconeogenesis and two episodes of hypoglycemia during fasting.[104] In the other case report, an overdose of tramadol caused excess secretion of insulin which led to hypoglycemia.[105] These reports are contradictory to the research showing decreases in insulin production. This may be due to the complexity of endogenous opioid system effects, variations in reactions to the opioids between individuals or because these cases are related to tramadol use instead of other opioids. Tramadol is a synthetic opioid,[106] and most reports of hypoglycemia have been with either tramadol or with methadone[105] which is also synthetic.[107] It could be that variations between individuals or the side effects of synthetic versus natural exogenous opioids account for this apparent contradiction.

All of these hormone effects are not only reflected in the glucose homeostasis, though, but also in the body composition of individuals with OUD. While research from Sweden shows that the entire range of BMI from underweight to overweight is represented in the extreme cases of OUD, other regions of the world have generally reported lower BMI[39,108] and higher fat free mass.[39] These changes indicate an altered metabolism since the BMI does not necessarily reflect the caloric intake,[39] especially given the simple sugar and high carbohydrate food preference observed in many OUD cases. The mechanism regulating this discordance between BMI and calories consumed as well as the higher levels of fat free mass is not clear. However, *in vitro* research using adipocytes has shown that endogenous opioids, β-endorphins, are involved in lipolysis and that naloxone, an opioid antagonist, can stop the effect.[109] While not direct evidence of changes in body composition in OUD, this study supports a hypothesis that exogenous opioids could also stimulate higher rates of lipolysis and lead to lower fat mass. It is interesting to note that the study in Sweden which showed higher BMIs overall than other surveys noted that the subjects all displayed signs of proper hygiene and relative food security.[108] This is not necessarily the case in other countries with fewer social supports. Increased food insecurity and malnutrition for a significant proportion of OUD individuals might also account for higher rates of fat free mass and lower BMIs.

Microbiome effects: alcohol and opioids

Through the various effects on the gastrointestinal system, both alcohol and opioids cause dysbiosis. In AUD, dysbiosis is apparent in approximately 31% of individuals.[110,111] This is evidenced not

only by decreased diversity in the microbiome but also in changes in the metabolites produced.[110] Additional research shows that alcohol itself can disrupt the epithelial barrier of the intestine through oxidative stress which causes damage to tight junctions.[110,112] The end result is intestinal permeability which allows bacterial antigens and bacteria to cross the barrier into the blood stream.[110] Importantly, these leaks into the bloodstream are associated with chronic inflammation[110,112] and symptoms of anxiety and depression.[110] As many AUD individuals experience anxiety during withdrawal which may promote relapse, this is an important problem to address.

Opioid use is also associated with changes in microbiome composition, but the added change in intestinal motility and decrease in bile acid production also promotes overgrowth of bacteria.[41,110] This overgrowth may include opportunistic pathogens which produce toxins. In a large cross-sectional study from hospital records, researchers found that patients using opioid painkillers had an increased risk of developing *Clostridium difficile* infections with an odds ratio of 8.3 compared to patients not taking opioids.[113] Unlike alcohol which directly damages the epithelium, opioids can damage the epithelium by interactions with the microbiome itself.[114] Research shows that opioids can interact with bacterial receptors on *Pseudomonas aeruginosa* increasing the virulence and shifting the bacteria to a phenotype capable of reducing the mucosal layer of the intestinal epithelium and allowing for damage to the epithelium and tight junctions.[114,115] This again allows for bacteria, antigens and toxins to cross the epithelial barrier and increases the risk of sepsis and septic shock.[110,114–118] This isn't limited to opportunistic pathogens, though. Research in mice indicates that opioid dependence made them more susceptible to an oral challenge of *Salmonella* Typhimurium.[115] Given reports of injection drug users resorting to taking food from the trash,[29] this is a very real health threat to these individuals. Additional data indicates that even withdrawal from opioids has an effect. In mice suffering from opioid withdrawal, researchers found evidence of immune suppression and increased risk of septic shock.[115]

Nutrition Treatment for SUD

SUD disorders have both elements of chronic and acute diseases. During detoxification and withdrawal or in case of an overdose, patients will experience severe, short-lived symptoms which must be addressed. In these early, acute stages, malnutrition, muscle wasting and deficiencies are the primary target of intervention.[16,119] Multivitamins and frequent interval feedings are recommended with enteral feeding if the consequences of the disorder are severe.[119] As many of the patients with protein malnutrition may be losing muscle mass, protein intake should be between 1.2-1.5 grams per kilogram bodyweight per day to prevent further muscle loss.[119] Many hospitals or detoxification centers will

already have protocols established to meet these acute effects, however, because the malnutrition may be extreme and take time to fully correct, other treatment centers should also consider these guidelines.[16]

In longer-term care or less severe malnutrition, there are disagreements in the best approach toward nutrition. One approach is to use foods that trigger the dopaminergic reward system to help individuals in recovery resist the temptation of using the substance. This approach has been promoted by Alcoholics Anonymous with apparent success for decades.[16] In a study following AUD individuals after detoxification over 6 months, authors found that patients who were abstinent for one month consumed three times more chocolate than those who were not abstinent in that month.[120] Additionally, of the 25% of patients who drastically increased chocolate consumption from their baseline consumption before detoxification, 84% remained abstinent at one month compared to 60% of patients who decreased or maintained chocolate consumption.[120] This association did not hold for other types of sweets,[120] however. The authors conclude that for some subgroup of the AUD population, chocolate specifically may be a protective factor against relapse.[120] It is interesting that chocolate had an effect compared to candies that are primarily sugar. Chocolate is a complex food with many bioactive molecules with mood modulating effects, and this result particularly may point to the importance of this complex mixture over other sweets in recovery.

Critics of this approach believe that this creates more problems than it addresses. One potential problem is that these individuals may substitute a new addiction to sweet, salty or snack-type foods for the original substance. There have not been many quality studies addressing symptom substitution, as this problem is often called.[121] Authors of one randomized control trial tested if indulging in sweets, eating a balanced diet including sweets or avoiding sweets entirely affected the long-term abstinence in subjects with ALD.[122] Despite higher abstinence in the avoidance group at 83% compared to about 55% in the indulging and balanced groups, there was too much loss-to-follow up in the subject population to make the results significant.[122]

Another critique of encouraging individuals in recovery to indulge in sweet and salty cravings is that, as discussed previously, many SUD individuals may have trouble with glycemic control as a result of the substance use or chronic low blood sugar from malnutrition. These critics maintain that drastic swings in blood glucose from simple carbohydrates will result in the individual feeling physically worse with higher levels of depression and anxiety.[16] These feelings presumably will make substance use seem more attractive and result in relapse.[16] This leads to a second approach to nutrition during recovery,

nutritional discipline.[16] This approach as given by Dr. James Milam details frequent meals and snacks with an emphasis on fruits and vegetables, whole grains, nuts, seeds, milk and meat.[16] Caffeine and refined carbohydrates are avoided because of the blood glucose spike and subsequent crash.[16]

This nutritional discipline approach logically follows from research in SUDs. Both AUD and OUD have been shown to have higher rates of metabolic syndrome and glycemic control problems than the average population.[48,50,92,99,101] Both hyperglycemia and hypoglycemia can cause a host of uncomfortable symptoms like fatigue, headache and confusion[123] which can be similar to some symptoms of withdrawal.[16] Studies have also shown that caffeine can affect insulin sensitivity causing acute increases in blood glucose and insulin and acute decreases in insulin sensitivity.[124–126] The overall effects of this are not clear in the case of SUD recovery as these studies were not conducted in this specific population. Additionally, authors of a population level study show that chronic use of caffeinated drinks have an inverse relationship with type 2 diabetes mellitus,[127] but it is possible that caffeine use during a specific period of recovery may further impair glycemic control and promote relapse.

Another benefit of the nutritional discipline diet could be increased omega-3 polyunsaturated fatty acid intake. In a study in mice, authors simulated an addiction to opioids with two periods of extinction equivalent to approximately three years of OUD with periods of abstinence.[128] Compared to OUD mice on a regular diet, OUD mice receiving a supplement of omega-3 showed reduced anxiety during the periods of extinction and reduced opioid-seeking behavior during the second extinction period.[128] These results indicate that higher levels of omega-3 may reduce relapse and promote abstinence.[128] They may also indicate that reduced anxiety during abstinence may promote relapse.[128]

It is important to point out that despite the theoretical connections and pre-clinical data, the nutritional discipline diet has not been tested for effectiveness in promoting recovery, reducing blood glucose swings or decreasing anxiety in human SUD populations. Additionally, depending on the substance and extent of withdrawal symptoms, patients may not be receptive to changing their diet to foods which they do not prefer. In a survey of OUD patients both during and after various recovery or substitution programs, respondents reported that during the initial detoxification, food was not a priority because they felt poorly.[129] Patients with dental problems due to less access to dental services and hygiene opportunities or because of xerostomia may not be able to consume fresh fruits and vegetables very easily which would make it difficult to adhere to the diet.[40]

Although a specific diet intervention has not been tested, some nutrition and exercise education programs have. In the survey of OUD patients during and after recovery programs, several of the participants identified cooking as having therapeutic benefit.[129] They reported that it promoted creativity, satisfaction and self esteem while also creating opportunities to be social.[129] These reports open up the possibility that nutrition and cooking can promote recovery not only through actual intake but also though the social and mental benefits. Two education interventions show success and failure of this type of initiative.

In the first intervention, authors created a targeted six week intervention in six urban residential treatment programs.[130] The intervention included active nutrition education, challenges with rewards and food policy changes in the treatment center to approach the problem of poor diet from multiple social-ecological levels.[130] The overall goal of the program was to improve dietary habits and physical measures of BMI and waist circumference compared to a previous six week control period.[130] While there was a small reduction in waist circumference, the test period was too short to see difference is physical measures.[130] Diet quality, however, was improved with a 42% increase in fruit and vegetable consumption and a reduced intake of sweets and desserts.[130] While the authors make no claims about improving SUD recovery, they do conclude that education interventions in this setting can be successful.[130]

In the second intervention, researchers had much higher aims. Participants entering recovery programs were enrolled in an intensive six week education program with diet and exercise counseling, motivational interviewing and diet education with the aim of reducing rates of relapse.[131] While this program was based on a successful smoking cessation program and theoretical models,[132] this intervention was associated with worse mental and physical quality of life at a 12 month follow-up and fewer substance-free days.[131] This result was very surprising to the authors as it indicates that not only that the intervention did not improve the outcome but also that it seemed to make it worse.[131] The authors theorized that it is possible that the intervention group struggled more because of negative feelings of guilt and failure coming from an intense and possibly judgmental program.[131]

Comparing these two studies reveals a couple points. First is that tone of the program is important. The first intervention had active learning with positive reinforcements while the second intervention may have unintentionally promoted negative feelings of shame and judgment. In this particular population which already struggles with social and familial tensions and with mental health problems, the tone of an intervention could be very impactful. The second point is that using dietary

interventions specifically for improvement in recovery rates is not a supported application. Nutrition education may well help recovery in certain subgroups of the population, but the research at this point does not show that it has universal impact. This also further detracts from the idea that a nutritional discipline approach to recovery as promoted by Dr. Milam is the best approach and instead points to use of strategies from Health at Every Size (HAES)[133] and Eating Competence[134] to improve nutritional status. These programs, like the active learning study, create positive associations with foods and promote mindfulness about body cues which, especially as recovery progresses, can improve an individual's food habits.

Extrapolating further, it is also important to point out that one approach to diet in SUD treatment will not fit everyone. For individuals with co-morbid disorders such as eating disorders, this is particularly true. Strict dietary guidelines may promote disordered eating behaviors. In the survey of OUD patients during and after recovery programs, many respondents, particularly women, reported increasing anxiety associated with weight gain and perceived ability to control appetite.[129] Anecdotally, some treatment providers also report that eating disorder symptoms may increase as the SUD is treated,[32] especially when just the SUD is treated.[135] In a retrospective study of an eating disorder cohort, authors report that recovery from the eating disorder is associated with a significantly lower odds of having an SUD.[136] While not a cohesive body of evidence, these reports indicate that there is danger for many individuals in creating a one-size fits all approach to nutrition in recovery. It is important to treat each individual with respect to their unique situation.

Nutrition in SUD treatment is important both in the acute and chronic phases of recovery. Addressing the malnutrition and severe micronutrient deficiencies are the first primary treatment and are relatively universal depending on the severity of the SUD. In the long-term recovery, though, there are many factors that need to be considered in addressing treatment of individuals. Treatment providers should be aware of the multifaceted nature of SUDs and the complications and co-morbidities that can surface during use and treatment. For interested individuals, nutrition education and cooking classes can offer benefits both physically and mentally, but as in all long-term treatments, these are not beneficial for everyone. Practitioners working with SUD patients should assess the protocols and practices in place in order to identify the best patient centered approaches to SUD treatment. Additional qualitative or mixed method research is essential to improving the quality of care and the quality of life for individuals with SUD.

Interview Themes and Summaries

Socioeconomic Status/ Housing and Food Security

It was very clear from the interviews that while people experiencing housing and food insecurity may be over-represented in the SUD population, this is a disorder that affects individuals from every socio-economic class. Several professionals suggested that substance use disorder is likely rooted in trauma, and one person thought that the factors that promote housing and food insecurity and even the process of becoming unstably housed may contribute to the trauma which makes a person more vulnerable to substance abuse. Regardless of SES and amount of disposable income, people who have SUD are more likely to prioritize procuring the substance over other needs such as food which may lead to malnutrition prior to beginning recovery.

The notable connection between SUD and SES, however, is really access to recovery and nutrition resources. One person noted that their for-profit, inpatient program was at the lower end of average cost at approximately $10,000 for treatment. For patients with personal or family financial resources, this program which provides regular, balanced meals is available. For patients without financial resources to absorb that cost, the options are more limited. Particularly for outpatient, non-profit clinics, patients may be able to get treatment and medication, but nutrient dense food may not be readily available to them. This impact is even more extreme during the COVID-19 pandemic as many of the services or opportunities to get food may be even more limited due to financial cutbacks or quarantine closures.

Comorbidities Tied to SUD

Every professional interviewed reported a high concordance of substance use disorder with other mental health disorders. Two people noted, however, that some of these disorders are a product of the substance use itself and may be resolved during recovery. The interviewees noted that symptoms of substance use or withdrawal like tiredness may be influential in promoting mental health disorders in addition to possible neurotransmitter disruptions.

Despite noting the high concordance of substance use disorders and mental health disorders, five out of six interviewees noted only a few cases of eating disorders in patients with substance use. One RD noted particularly that while many patients may have anorexia and malnutrition, the vast majority eat very well while in her care. The sixth interviewee had the exact opposite experience. Her experience was that the majority of patients with substance use disorders also have an eating disorder,

and, in her opinion, the eating disorder also likely preceded the substance use as the first response to trauma. She now specializes as an RD in a clinic that treats both disorders simultaneously, and she believes that without treating both disorders, the risk of relapse is very high.

Most interviewees also noted that the majority of patients used multiple substances. The one exception was a person who observed that her impression was that people with alcohol use disorder often only abused alcohol. However, other people interviewed did not observe the same phenomenon.

Nutritional Complications of SUD and Treatment

General malnutrition was the primary nutrition complication of substance use disorder noted by the interviewees. One inpatient program and the Harborview ICU handled this problem by providing nutritious food and giving the patients a multivitamin. For the ICU where the patients were recovering from overdoses, more aggressive treatments including thiamin would be administered if warranted by patient presentation. Testing for specific deficiencies is too slow and too expensive for the majority of cases. Professionals interviewed from outpatient programs did not report providing multivitamins or other nutrition treatment; however, several programs offered free workshops for patients on healthy eating or cooking. Other programs had resources to connect patients with social services or help them sign up for programs like Fresh Bucks.

All interviewees noted significant complications from opioid use that could affect the patient's ability to eat. These include gastrointestinal symptoms, particularly constipation, and dental issues. Treatment of the constipation included both dietary changes and pharmaceutical treatments as applicable with extreme cases requiring even more aggressive measures.

Addiction replacement is the transference of craving from the abused substance to something else. Literature suggests that the common replacements are fatty or sugary foods or other substances like coffee. When asked, many interviewees noted a high consumption of sugar among patients, but opinions were divided as to whether this was bad or good. One person noted that his inpatient program did not allow caffeine in the building, and they provided low-sugar, nutrient dense food for the patients because the founder of the program believed that caffeine and sugary foods increased the likelihood of relapse. On the opposite side, two interviewees saw the addiction replacement as "harm reduction." One commented that the greatest risk to the patient was death from an overdose and that this should be the primary focus. Other problems that arose from this eating pattern could be dealt with at a later point.

One interviewee particularly addressed diabetes within the SUD population. While she most often associated a higher rate of diabetes with patients with alcohol use disorder and with those having a larger BMI, she also linked the potential of diabetes to increased sugar and fat consumption.

Weight gain was also frequently noted among patients in recovery. For the professionals interviewed, it was unclear if the weight gain was truly associated with the medication as is often the case for other psychiatric prescriptions or if this weight change was the result of better self-care and more regular meals. However, several people mentioned that the weight gain may be a source of concern for the patients with one interviewee reporting that patients have asked about changing dosing or medications due to increases in weight. This interviewee also reported that patients may associate other problems like the dental decay with the medications and treatment as opposed to the substance use or lack of self-care.

Important Ideas to Share with Students

Each interviewee noted something unique which they felt was important for future medical professionals to know. Some ideas had commonalities. One idea is that taking a holistic viewpoint of each patient is important. This encompasses not only symptoms and recovery management but also the nutrition problems and the entire scope of societal problems that promote substance use disorders.

Another common idea is that approach is important. This patient population is complex and may have many negative experiences with authorities and with the medical system. This population needs providers who are non-judgmental and can use good motivational interviewing skills. They also need an interdisciplinary team that can assess and support them on many different levels.

Finally, working with this population is challenging, but it can be very rewarding.

Chapter 6: Dissemination and Evaluation

The information gathered through the literature review and the interviews with professionals was delivered to the MED 569 class in a lecture format on December 1, 2020. Due to the COVID-19 pandemic, the class was held remotely and in real time using video conferencing technology. The visual presented to assist in the lecture was a PowerPoint (see Appendix). The PollEverywhere application was used for a before and after survey to evaluate the presentation and to facilitate a dialogue during the presentation.

In the pre-presentation survey of students (Figure 1), it is evident that there was already a tendency to agree with the evaluation statement. Out of the 31 respondents, only 1 responded with a neutral opinion. All other respondents either agreed (n=11) or strongly agreed (n=19) with the statement from the outset.

The after survey (Figure 2) does show an increase in the number of students who strongly agreed with the statement (n=26). This is a 37% increase from the initial survey. Additionally, the individual who responded with a neutral opinion either did not respond or changed opinion to a more positive one. It is notable, however, that there were only 29 respondents in the second survey (loss of 6.5%). It is unclear why there were fewer respondents in the second survey. Regardless, there was still an increase in the number of students strongly agreeing with the statement.

While the survey was anonymous, the presentation of the question in real time with the presenter watching may have influenced the results to be more positive than they would have been otherwise.

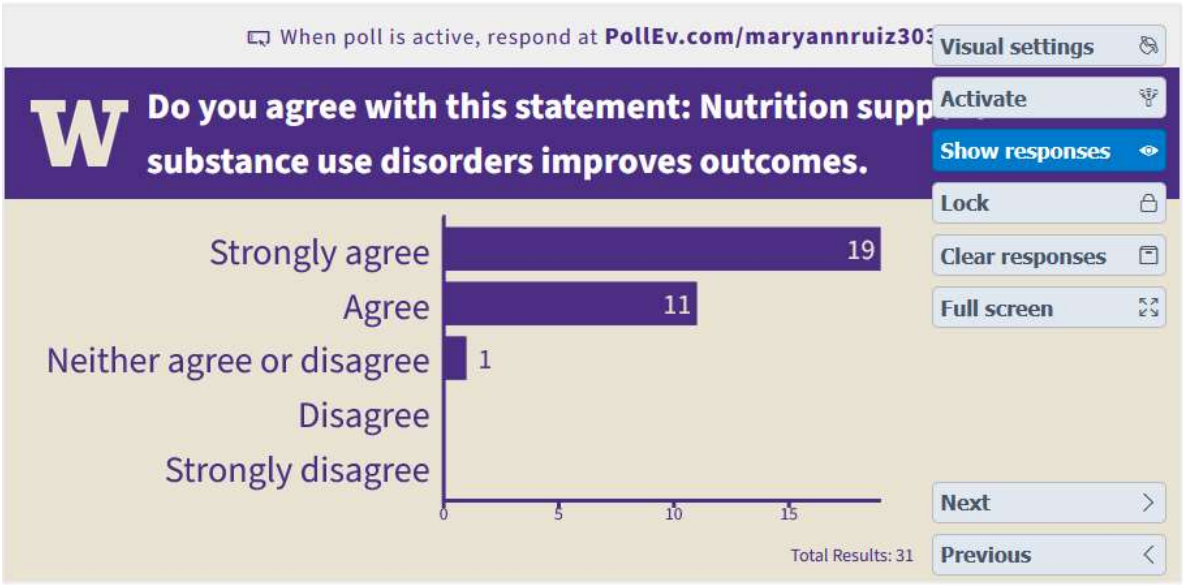


Figure 1: Survey results at the beginning of the presentation

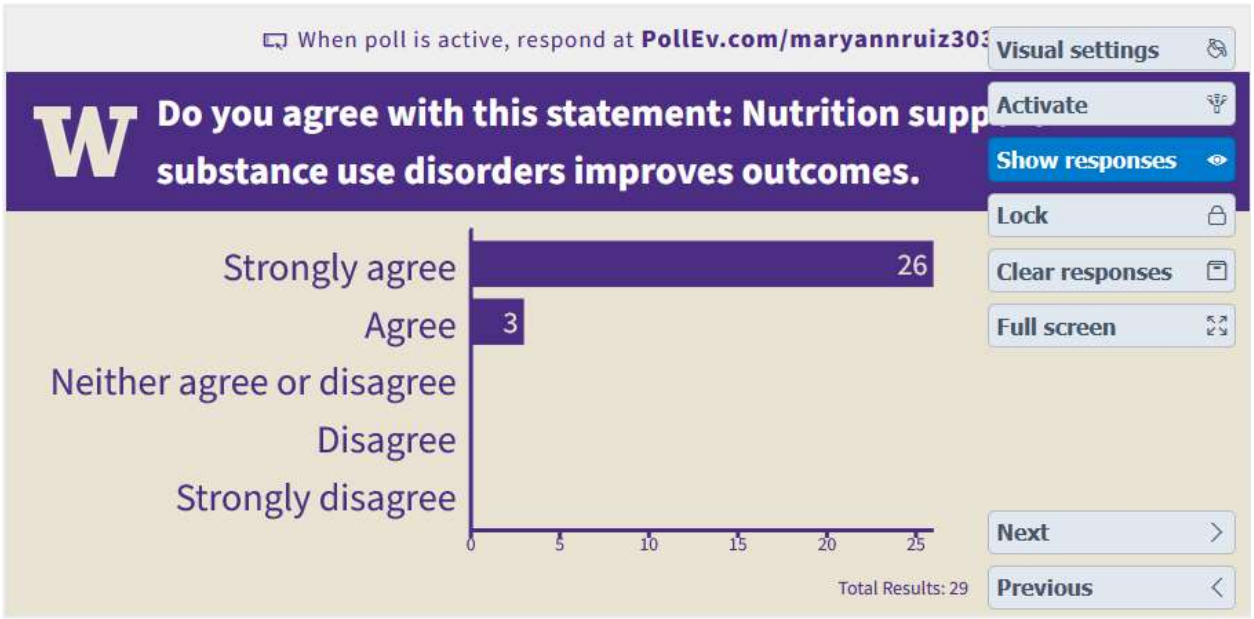


Figure 2: Survey results at the end of the presentation

Chapter 7: Summary and Future Directions

Role of Nutrition in Substance Use Disorders

Alcohol and opioid use disorders (AUD and OUD) cause a host of nutritional and metabolic abnormalities. Some of these abnormalities arise from behavioral choices or social circumstances. Energy and protein malnutrition may arise from prioritizing the substance purchase or experience over eating a meal, or it may be a result of food or housing insecurity. Micronutrient deficiencies can occur as a result of malnutrition, but in alcohol and opioid use, these may also stem from tissue damage in the gastrointestinal tract, uncoordinated motility or dysbiosis. All of these factors contribute to the primary problems of malnutrition and deficiencies, but they also contribute to secondary conditions like electrolyte imbalances and osteoporosis.

AUD and OUD are also linked to changes in hormone regulation and body composition. The most important hormone that is affected is insulin. In both disorders, insulin availability is reduced leading to chronic hyperglycemia and a diabetes mellitus-like state. Additionally, changes in the metabolic regulation or biochemical milieu of the body promote increased blood sugar, increased lipolysis and increased protein degradation. These changes have been connected to increase fatty deposits in the liver and increased risk of metabolic syndrome.

Value of Interdisciplinary Education

While there is very little evidence and research to show that direct nutrition intervention is beneficial in recovery from AUD and OUD, it is clear that nutrition plays a role in the resulting acute and chronic conditions associated with these disorders and with the social and behavioral factors that promote them in the first place. Current academic programs for medical, nursing and dental students at the University of Washington include very little time and attention to nutrition and metabolism, so while students are aware that nutrition is important, they have little background in more advanced nutrition problems such as those posed by substance use disorders. Interdisciplinary education and coordination are essential to filling in these gaps and providing informed patient care. Due to time constraints in medical school, this cannot be as in depth as is warranted for holistic patient care, however. This places future and current dietitians in a unique position as nutrition experts to assist in treating these patients beyond the initial malnutrition or micronutrient deficiency.

Future Needs and Directions

- Education in the nutrition effects of substance use should be included in medical school curriculum for interested students in order to familiarize them with the extent of nutritional and metabolic derangements that may present in a patient.
- More extensive training in substance use disorders should be developed and made available to nutrition professionals in graduate or continuing education programs. This specialty area would be valuable in public health planning and clinics as well as in inpatient and outpatient recovery centers as a referral service.
- Interdisciplinary workgroups including nutrition and social work are needed to create protocols that address both the immediate clinical problems that arise from substance use disorders as well as the more systemic social and behavioral factors in patient lives that contribute to substance use. These workgroups are important for creating protocols and for updating them with the most recent research.
- More research is needed in nutrition care for substance use disorders. Research to this point has been inconclusive due to poor study design or lack of trauma informed care. In order to determine the benefit of dietetic advice and nutrition interventions, more systematic and larger studies are needed. These studies will elucidate the extent to which dietitians are needed in direct patient recovery care and the necessary context for delivering that education or intervention.

Appendix

Appendix A: Interview Question Guide

Interviews were conducted as a conversation, and while all topics were covered with each interviewee, the order and exact wording of the questions were different for each interview.

1. Can you tell me a little about your background working in substance abuse as an [profession]?
    a. How did you get into addiction medicine?
2. Can you tell me a little bit about the programs at your facility?
    a. What is the structure of the inpatient and outpatient programs?
        i. % outpatient vs. inpatient
        ii. What type of services/treatments are offered to patients in the program?
    b. Patient demographics
        i. I have read some conflicting reports on the conjunction of socioeconomic status and SUD. In your experience, is it common for them to come from situations with housing or food insecurity?
        ii. What are the most common substance use disorders you have treated? (alcohol, opioid or other)
        iii. Are co-morbidities common, and how do you treat them?
            1. Multiple addictions
            2. Eating disorders-
            3. Mental health- How often is that seen in conjunction with SUD? I have read some theories that some of the mental health disorders are misdiagnosed based on the SUD and on nutrient deficiencies. Do you think that is true based on your experience?
3. As I mentioned earlier, I am particularly interested in the nutritional complications of SUD.
    a. Do you check for nutritional deficiencies at [your facility] when patients check in?
        i. I have read some conflicting data about weight for SUD patients. Is it common for patients to be underweight?
        ii. Do symptoms from drug use or recovery impair the patient's ability to eat during recovery?
            1. Constipation, nausea
        iii. I have read that dental disease can be a problem for some SUD patients. Is that a problem you have had to address? Does that cause additional problems related to eating for those patients?
    b. Do you see nutrition problems arise during recovery?
        i. I have read about sweet or fatty foods used as an addiction replacement. Do you attempt to prevent or address either of those during the early stages?
        ii. As a corollary, I have read that many patients gain a lot of weight during recovery. Is that a concern for you as staff or for the patients?
    c. As you recall, I will be presenting this information to future doctors, nurses and pharmacists. What do you think these students should know about SUD and addictions?
        i. If you were to work with these students as professionals in the future, what would you want them to know? What skills would you want them to have?

Appendix B: Question and Evidence Table

Research questions were analyzed for quality of evidence supporting the conclusions. Evidence grades include the following: Grade I: Good, Grade II: Fair, Grade III: Limited, Grade IV: Expert opinion only, and Grade V: Not assignable. Refer to http://www.andevidencelibrary.com/ for a complete list of evidence analysis citations.

Evidence Analysis Library Question	Conclusion and Evidence Grade
Nutrition Effects from Alcohol and Opioid Use Disorders	
#1: What are the primary macro and micronutrient deficiencies that arise from alcohol and opioid use disorders?	• Based on cross-sectional survey and interviews, energy and protein malnutrition are significant problems in more advanced cases of alcohol and opioid use disorder. • Many researchers report significant micronutrient deficiencies in alcohol and opioid use disorders, although there are far more studies on deficiencies in alcohol use. See Table 3 (page 29) for a complete list of documented micronutrient abnormalities. These studies are all cross-sectional in nature and most are relatively small and do not have a specific comparison group. While reported incidence does vary, the results from various reports are in alignment overall. **Grade II - Fair**
#2: What physiological and behavior changes lead to these deficiencies?	• Cross-sectional surveys of opioid use disordered individuals indicate significant dental problems. Constipation has been reported in comprehensive reviews for both disorders. • Authors of several cross-sectional studies report altered nutrient intake with increased sugar and decreased micronutrient, protein and fiber intake. Data from both cross-sectional and preclinical randomized control trials suggest changes in food preference which increase sweet and salty food intake. **Grade II - Fair**
#3: What are effects of alcohol and opioid use disorders on metabolism and body composition?	• Authors of one case control study and those of several systematic pathophysiology reviews show increased lipolysis in alcohol use disorder resulting from alcohol metabolism and reduced protein and carbohydrate intake. This phenomenon leads to alcohol ketoacidosis which was first described in 1971. • As reported in a systematic review, authors of preclinical studies and a few case control studies report increased protein turnover with an overall catabolic effect. Authors of numerous in vitro studies have described many changes in gene regulation involved in the disorder. The resulting alcoholic myopathy has been found in medical reports since the 1890s. **Grade I – Good** • Authors of three systematic reviews report increased

Continued on the next page

	gluconeogenesis and reduced glycolysis in opiate use. Authors of one *in vitro* study found increased lipolysis in adipocytes with administration of opioids. This supports reports of increased fat free mass in opiate use disorders in cross-sectional studies. **Grade III - Limited**
#4: What are effects of alcohol and opioid use disorders on hormonal regulation related to nutrition?	• Authors of several cross-sectional studies, preclinical randomized control trials and one small human randomized control trial (opioids) show significant decreases in insulin and increases in blood glucose and hemoglobin A1c in alcohol and opiate use disorders. **Grade I - Good** • In a small randomized control trial and a case control study, opioids were found to decrease leptin. Leptin was also found in the case control study to be uncorrelated to BMI in contrast to the controls. **Grade II - Fair** • In cross-sectional and pre-clinical randomized control trials, alcohol has been found to influence ghrelin and therefore feelings of hunger/craving. The results from these studies are contradictory, however, with some studies reporting increased ghrelin and some decreased ghrelin with consistent alcohol consumption. **Grade III - Limited**
#5: What changes occur in the microbiome as a result of alcohol and opioid use disorders?	• Authors of from two cohort studies and several systematic review show changes in the microbiome as a result of chronic alcohol use. Data from one of the cohort studies also demonstrates increased intestinal permeability in alcohol use disorder subjects. • In a cross-sectional study, authors found an increased incidence of *C. difficile* infection in patients prescribed opiates. Authors of five pre-clinical randomized control trials all found that opiates increased intestinal permeability and sepsis in mice or rats. Authors from one of these studies additionally found that opiates can increase the pathogenicity of opportunistic bacteria. **Grade II - Fair**
Nutrition-Based Treatment Strategies	
#6: Is nutrition support beneficial in recovery from alcohol and opioid use disorders?	• Cross-sectional studies demonstrate significant potential micronutrient deficiencies. Some of these like thiamin and magnesium have been linked to severe disorders like Wernike-Korsakoff Encephalopathy in previous research and in one cross-sectional study. Current guidelines and testing costs only indicate provision of a multivitamin. There are no studies on more extensive nutrition support. • Disturbances in insulin production and glucose tolerance have been demonstrated in alcohol and opiate use

Continued on the next page

	disorder, but no research has been done to indicate that diet counseling for these individuals is beneficial. **Grade V – Not Assignable**
#7: Can nutrition education assist in recovery from alcohol and opioid use disorders?	• Data from one randomized control trial show no benefit to intensive diet and lifestyle counseling in addiction recovery. Researchers from one randomized control trial report that diet education with positive reinforcement may improve diet quality. Analysis from structured interviews indicate that some individuals find cooking education beneficial in maintaining recovery from a substance use disorder. • Data from one cohort study indicates that chocolate but not other sweets has been shown to be beneficial in recovery programs for a subset of individuals. Data from a small, randomized control trial with significant design flaws and retention problems shows no difference in recovery between groups following diets with different sugar levels. **Grade III - Limited**
Other Factors in Alcohol and Opioid Use Disorders	
#8: To what extent do eating disorders and substance use disorders coincide?	• Very few studies have been published on eating disorders within the population of substance use disorders. While cross-sectional studies do show an increase in diagnosed eating disorders compared to the baseline population statistics, there is a wide variation due to the study designs. A few expert opinions support these studies. **Grade III - Limited**

Appendix C: Presentation slides

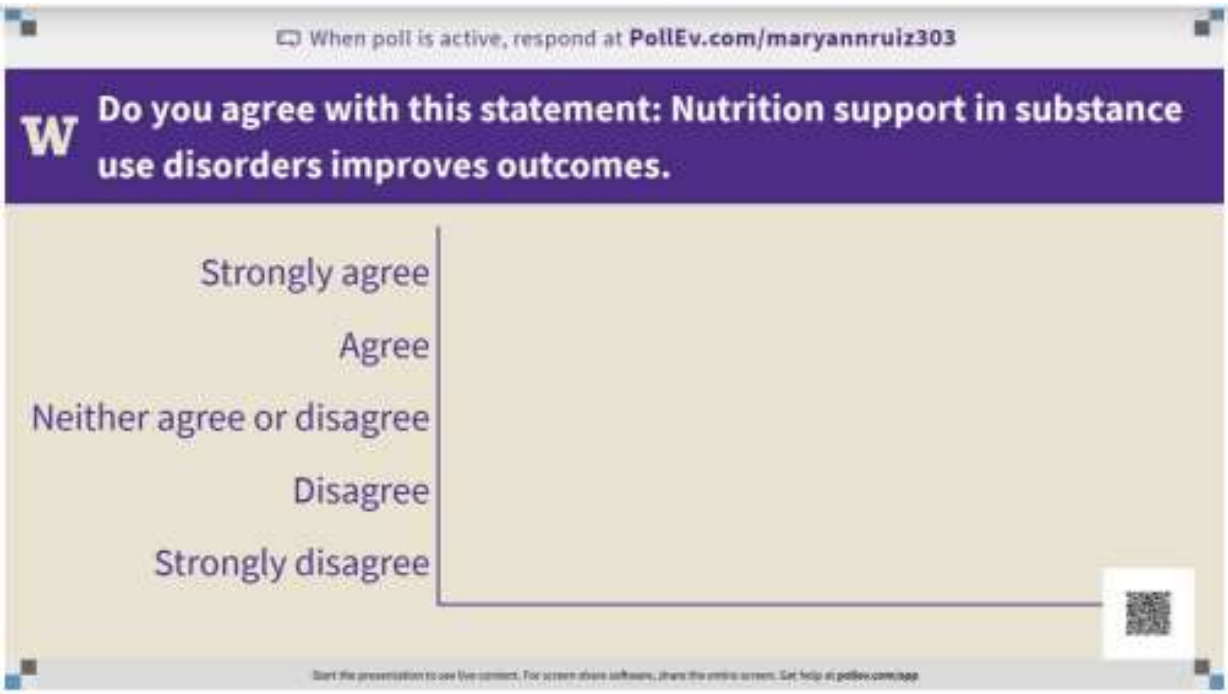
Nutritional Concerns in Substance Use Disorders

Maryann Ruiz, Dietetic Intern, Graduating Summer 2021
Faculty Mentor: Michelle Averill PhD RDN

UNIVERSITY of WASHINGTON

Topics

- Substance use effects on food consumption
- Associated deficiencies
- Short and long-term consequences of SUDs
- Nutrition's role in recovery



Methods

- **Interviews with SUD professionals**
  - **MD, MSW, RN, 2 RDN, SUDP**
  - **Qualitative analysis**
- **Literature review**
  - **Guided by interview themes**
- **Class objectives**

Primary Nutrition Problems

Malnutrition

What is Malnutrition?

Inadequate intake of protein and/or energy over a period of time

- Weight loss: 10%+ in 6 months
- Low BMI: <18.5
- Loss of muscle mass, reduced grip strength
- Reduced food intake: <75% energy for more than 3 months

Factors in Malnutrition: Low food priority

- **Financial**
  - Sæland et al: limited food access in 64% drug users
  - Laslett et al: 79% injection drug users <3 meals a day
- **Enhanced substance effects**
  - Strike et al: Over 50% injection drug users fasted
- **Replaced calories**
  - AUD: Up to 60% calories from alcohol

Factors in Malnutrition: Physical Effects

- **Nausea and constipation: reduced appetite**
- **Liver Disease and complications: nausea, early satiety, changes in taste**
- **Dental disease: xerostomia**
  - Laslett et al: 68% injection drug users reported severe dental problems
  - Pain/difficulty eating leads to changes in food consumption
  - Sæland et al: 30% of total calories from added sugar

Secondary Nutrition Problems

Micronutrient Deficiencies

Documented Abnormalities

Deficient Vitamins		Deficient Minerals
Thiamine (B1) Riboflavin (B2) Niacin (B3) Pyridoxine (B6) Folic acid (B9) Vitamin B12 Choline*	Vitamin A Vitamin C Vitamin D* Vitamin E Vitamin K	Calcium Iron* Magnesium Selenium Zinc

*Documented in AUD only

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Causes of Secondary Malnutrition: Alcohol

- **Changes in motility**
  - **Gastric emptying**
  - **Intestinal transit time**
- **Direct Damage to the GI tissue**
  - **Reduced absorption**
  - **Inflammation**
- **Reduced enzyme function**

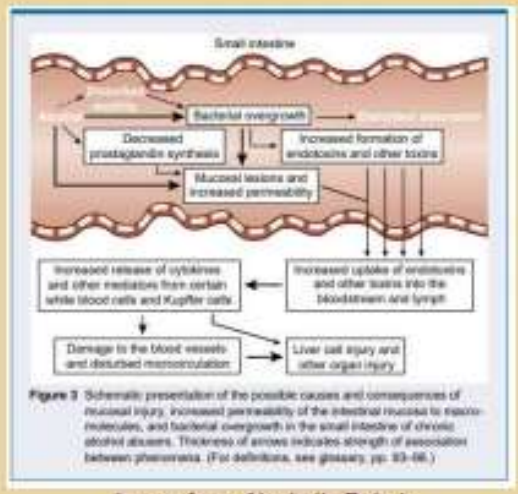

Image from *Alcohol's Role in Gastrointestinal Disorders*, Bode and Bode

Alcohol can increase iron and homocysteine

Links to iron overload
&
Neural impacts

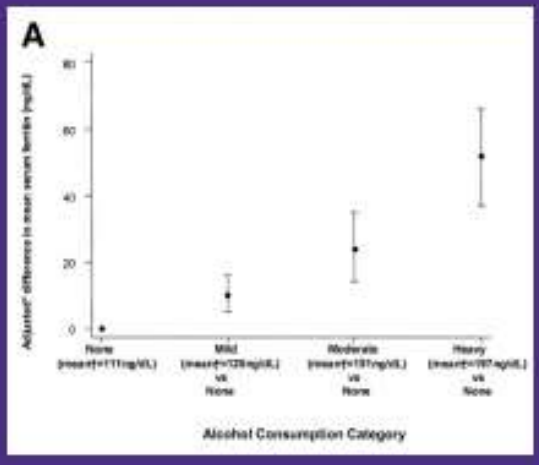

Image from Ioannou et al 2004

Causes of Secondary Malnutrition: Opiates

- **Trigger natural opiate receptors**
  - **Motility disrupted**
  - **Intestinal secretions reduced: fluid, bile acid**
  - **Constipation**
  - **Xerostomia**
- **Increased bacterial toxins and pathogenicity**
  - **GI damage leading to reduced absorption**
  - **Mora et al.: 8.3 higher odds of *C. difficile* when taking opiate painkillers**

Microbiome Effects

Damage, Inflammation and Risk of Sepsis

Alcohol

- Dysbiosis - 30% of cases
- SIBO
- Reduced diversity
- Bacterial translocation

Opiates

- Overgrowth *C. difficile*
- Increased virulence of opportunistic pathogens
- Reduced protective mucosal layer
- Bacterial translocation

Body composition: alcohol

- Lower BMI
- Reduced fat mass
  - Increased lipolysis
  - Reduced lipogenesis
  - Increases in free fatty acids
- Reduced lean muscle mass
  - Decreased protein intake and impaired absorption
  - Increased protein excretion and turnover

Body composition: opiates

- Range of BMI
  - Higher BMI in Norway with more social support
  - Other countries report more lower BMI
- Reduced fat mass
  - Altered metabolism
  - Rajs et al: Increased lipolysis *in vitro*

BMI is not always the best assessment of nutrition status

A case for looking past weight

- High calorie, low nutrient dietary pattern leads to micronutrient deficiencies
- Altered metabolism and loss of lean body mass can lead to health problems
- Normal weight and overweight can mask these

Important to consider intake and body composition

Hormones: alcohol

- **Ghrelin and the Reward system**
  - Similar reaction to hunger and craving
  - Link to preference for sweet and salty foods
  - Possible increases and decreases
- **Insulin and glucose regulation**
  - Damage to pancreas
  - Rasineni et al: Insulin not released
- **Adiponectin**
  - Increases may promote insulin resistance

Hormones: opiates

- **Opioids trigger reward system**
  - **Independent of hormones**
  - **May augment opioid seeking**
- **Leptin**
  - **Decreased levels - reduced satiety**
  - **Not correlated to BMI**
- **Insulin and glucose control**
  - **High opioid doses inhibit insulin production**
  - **Enhanced gluconeogenesis, inhibited glycolysis**

Risk of Diabetes Mellitus

- **Alcohol use is an independent risk factor for T2DM**
- Opiates
  - Tillbrook et al: Elevated HbA1c in heroin users
  - Mueller et al: Subjects taking morphine had 42% decrease in insulin
  - Elman et al: 56% MetS diagnosis for patients on methadone treatment
- Symptoms can be similar to withdrawal

Nutrition-related Clinical Emergencies

Mostly seen in AUD

- **Malnutrition**
  - Refeeding syndrome
- **Hypomagnesaemia**
  - Most common: up to 48% AUD
- **Wernicke-Korsakoff**
  - Thiamine
- **Ketoacidosis**
  - Fasted state + higher lipolysis
- **Hyponatremia**
  - Many causes

Chronic Disorders

- **Osteoporosis**
  - **Rico et al: bone loss in 50% AUD**
  - **Vitamin D and Calcium**
  - **Hormonal Changes- gonadal and adrenal**
- **Alcoholic myopathy**
  - **Rhabdomyolysis leads to kidney injury**
  - **Oxidative stress and chronic inflammation**
- **Hyperglycemia/Diabetes Mellitus and AFLD**

Nutrition in Recovery

Nutrition Goals in Recovery

- **Early recovery**
  - **Sufficient calories and protein**
  - **Multivitamin**
- **Help patients eat a varied diet**
  - **Micronutrients, omega-3 FA, fiber**
- **Barriers to better diet**
  - **Withdrawal symptoms**
  - **Preferences for salt and sugar persist**
  - **Concern for addiction substitution**

Controversies in Recovery

Use Sugar

- Promoted and used successfully by AA
- Stickel et al: chocolate promoted abstinence at one month

Avoid Sugar

- Substitute SUD for another addiction (food)
- More problems with glycemic control
- Krahn et al: Increased abstinence in group avoiding sugar (not significant)

Controversies in Recovery

Use Sugar

I see that as harm reduction. What's the greatest risk here? It's death from the substance use... So, whatever could possibly be used the ward off that or to prevent it, that's a good solution...

Charlotte Sanders MSW

Avoid Sugar

What becomes really important in treatment for substance abuse is a steady state of blood sugar to prevent mood changes, to decrease the reliance on caffeine, breakfast as the most important meal of the day...

Sherry Fixelle RD

Nutrition Education

- **Cooking and nutrition education can therapeutic**
  - **Promotes creativity, satisfaction and self-esteem**
  - **Promotes social ties and builds community**
- **Approach is important**
  - **Hovhannisyan et al: Intensive education and counseling intervention**
    - **Worse quality of life; more relapse**
  - **Cowan and Devine: Active nutrition education with rewards and institutional food policy changes**
    - **42% increase in fruit and vegetable consumption**

There is a lot of stigma out there, and it may take a little extra work to make the patient feel comfortable... and make sure that patient can feel hope. Just like a lot of providers if they aren't seeing people successful in treatment may feel hopeless, a lot of patients may feel that way, too.

James Darnton, MD

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Recovery barriers

- **Homelessness and food insecurity**
  - **Estimates ⅓ have current SUD**
  - **Low availability of nutritious food**
- **Imprisonment**
  - **2006 DOJ: 55% of prisoners have SUD**
  - **Prison Voice Washington: WA state prisons do not meet government standards**
- **Comorbidities**
  - **Mental health: 25% with Severe Mental Illness have SUD**
  - **Eating disorders**

Eating Disorders & SUD

The drug of choice for these kids who are anxious and have attachment disorders is food... But eventually,... it doesn't quiet the "ism" part of the disorders which is in your head. And so they find drugs or alcohol...

Sherry Fixelle, RD

- Prevalence of comorbidity higher than the general population
  - Bahji et al: Prevalence of diagnosed AN 3.9% (Canada)
  - Higher in women than men
- Disordered eating vs eating disorder
  - Robinson et al: 60% of female subjects had disordered eating
  - Disordered eating patterns normalized in society at large
  - Underweight more easily attributed to other factors
- Anecdotal reports of ED resurfacing during SUD recovery

Putting it in context

Complex nature of SUDs requires multilevel interventions

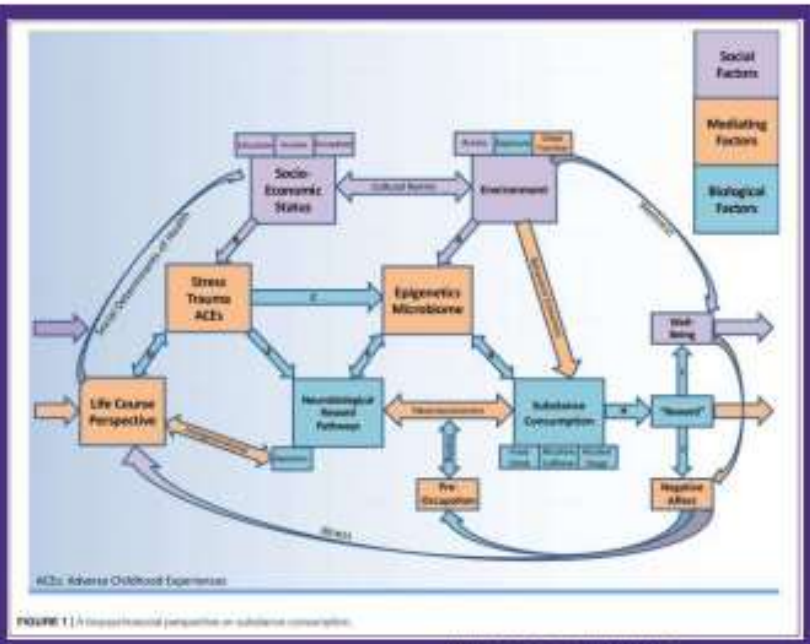

Figure from "A Biopsychosocial Overview of the Opioid Crisis: Considering Nutrition and Gastrointestinal Health" by David Wiss RDN

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When poll is active, respond at **PollEv.com/maryannruiz303**

Do you agree with this statement: Nutrition support in substance use disorders improves outcomes.

Start the presentation to see live content. For screen share software, share the entire screen. Get help at pollev.com/app

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Questions?

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