AN INTEGRATIVE REVIEW OF THE USE OF GABAPENTIN IN TREATMENT-SEEKING ADULTS WITH ALCOHOL USE DISORDER IN AN OUTPATIENT SETTING

by

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DEDICATION

This project is dedicated to my loving parents, my brilliant husband, and my three beautiful children. Thank you all for moving so courageously through life with me. It would not have been possible to complete this project without your love, support, and encouraging faces. Words cannot express the love and gratitude I have for all of you.

TABLE OF CONTENTS

TABLE OF CONTENTS CONTINUED

GLOSSARY

Addiction: A primary, chronic disease of brain reward, motivation, memory, and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social, and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors. (American Society of Addiction Medicine, 2011, p. 1).

Alcohol Use Disorder (AUD): A problematic pattern of alcohol use occurring within a 12-month period leading to clinically significant impairment of distress as manifested by at least two of the following (American Psychiatric Association [APA], 2013, p. 490):

1) Alcohol is often taken in larger amounts or over a longer period than was intended.
2) There is a persistent desire or unsuccessful efforts to cut down or control alcohol use.
3) A great deal of time is spent in activities necessary to obtain alcohol or recover from its effects.
4) Craving or a strong desire or urge to use alcohol.
5) Recurrent alcohol use resulting in failure to fulfill major role obligations at work, school, or home.
6) Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol.
7) Important social, occupational, or recreational activities given up or reduced because of alcohol use.
8) Recurrent alcohol use in situations in which it is physically hazardous.
9) Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol.
10) Tolerance, as defined by either of the following:
    a. A need for markedly increased amounts of alcohol to achieve intoxication or desired effect.
    b. A markedly diminished effect with continued use of the same amount of alcohol.
11) Withdrawal as manifested by either of the following:
    a. The characteristic withdrawal syndrome of alcohol.
    b. Alcohol is taken to relieve symptoms.

Alcohol Withdrawal: The presence of two or more of the following characteristic symptoms of withdrawal syndrome that develop within several hours to a few days after the cessation of (or reduction in) heavy and prolonged alcohol use (APA, 2013, p. 500):

1. Automimic hyperactivity
2. Increased hand tremor
3. Insomnia
4. Nausea or vomiting
5. Transient visual, tactile, or auditory hallucinations or illusions
6. Psychomotor agitation
7. Anxiety
8. Generalized tonic-clonic seizures

Alcohol Withdrawal Syndrome (AWS): Represents a clinical condition characterized by symptoms of autonomic hyperactivity such as agitation, tremors, irritability, anxiety, hyperreflexia, confusion, hypertension, tachycardia, fever, and diaphoresis. Mild to moderate forms are characterized by tremors, nausea, anxiety, and depression (Mirijello et al., 2015).

Addiction Treatment: The use of any planned, intentional intervention in the health, behavior, personal and/or family life of an individual suffering from alcoholism or from another drug addiction, and which is designed to enable the affected individual to achieve and maintain sobriety, physical, spiritual, and mental health, and maximum functional ability (National Institute on Drug Abuse, 2018).

Binge Drinking: Defined as having five or more alcoholic drinks on one occasion for men, and four or more alcoholic drinks on one occasion for women (National Institute on Alcohol Abuse and Alcoholism, n.d.).

Protracted Abstinence: Altered emotional processing that persists longer than six weeks of abstinence from alcohol due to subtle neuroadaptations caused from alcohol dependence. Symptoms of protracted abstinence include craving, negative affect, anxiety, depression, and sleep disturbances (Mason et al., 2014).

ABSTRACT

Background: Alcohol use disorders (AUD) and alcohol consumption are complex public health issues that involve multiple comorbidities and significant healthcare costs. In the United States, one-third of adults will be diagnosed with an AUD within their lifetime and over 59.5 million Americans are at risk for an AUD due to reported binge drinking. The State of Montana has one of the highest AUD statistics in the country costing Montanans millions of dollars managing AUD-related physical and psychological illnesses. Despite the high rate of AUDs in Montana, the State has very few inpatient treatment facilities for Medicaid recipients to address alcohol abuse and addiction, causing significant lag time to enter alcohol-abuse inpatient treatment. Gabapentin, an anticonvulsant, has recent evidence for use as a medication to aid in mild to moderate alcohol withdrawal symptoms, remedy symptoms of protracted abstinence, and help treatment-seeking individuals remain abstinent until inpatient alcohol addiction services are available.

Objective: The purpose of this integrative literature review was to identify current knowledge related to the use of gabapentin in an outpatient setting for treatment-seeking adult patients (18–65 years) with an AUD, for preventing the symptoms of mild to moderate alcohol withdrawal syndrome, for treatment of symptoms related to protracted abstinence, and for assisting the individual to abstain from alcohol until initiation of inpatient substance-abuse treatment.

Method: This topic was explored using an integrative literature review. Research articles were identified using the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Library, PubMed, PsycINFO, and Medline, from January 2014–December 2019. A review of abstracts using inclusion and exclusion criteria was conducted to determine relevant studies.

Conclusion: The integrative review revealed limited evidence for the use of gabapentin to decrease symptoms of mild to moderate alcohol withdrawal and protracted abstinence in treatment-seeking adults on an outpatient basis. Heterogeneity of sample populations, interventions, and study aims should be addressed in future research studies.

CHAPTER ONE

INTRODUCTION

Alcohol use disorders (AUD) and alcohol consumption are complex public health issues with multiple comorbidities and significant healthcare costs. In the United States (US), one-third of adults will be diagnosed with an AUD over their lifetime and over 59.5 million Americans are at risk for an AUD due to reported binge drinking, or consuming greater than five alcoholic beverages in one sitting (Substance Abuse and Mental Health Services [SAMHSA], 2012; National Institute on Alcohol Abuse and Alcoholism [NIAAA], 2018). The State of Montana has frequently been listed in the top five states with the highest AUD prevalence in the country, as well as the greatest number of adults in the United States who binge drink (SAMHSA, 2015; NIAAA, 2015). In 2014, the most recent year for which data are available, the annual alcohol consumption amount in Montana per capita among those aged 21 years and older was 3.5 gallons. By comparison, the 2014 US rate of alcohol consumption amount per capita among those aged 21 years and older was 2.6 gallons (NIAAA, 2015). Additionally, the Centers for Disease Control and Prevention (CDC) and Montana Department of Public Health and Human Services (MDPHHS) estimate that there were 475 alcohol-attributable deaths in Montana from 2012 to 2016, for an overall alcohol-attributable death rate of 42.3 per 100,000, the highest rate in the country (CDC, 2019; MDPHHS, 2016).

The data for residents in Montana related to alcohol use are significant. In 2011, nearly 40% of Montana residents reported drinking five or more alcoholic beverages in

one sitting in the past 30 days (MPDHHS, 2019). In 2013, the Office of Epidemiology and Scientific Support concluded 41.5% of Montana inpatient hospital admissions were binge drinkers. More recently, 2015 data from the CDC show that 21.3% of Montana residents aged 18 years and older binge drink on a regular basis (CDC, 2015). Furthermore, the 2015 Behavioral Health Barometer for Montana determined about 7.0 %, or over 60,000 Montanans, 12 years of age or older have an AUD (SAMHSA, 2015). With Montana's high incidence of alcohol abuse, it is understandable that a great number of patients will present with an AUD in all types of healthcare settings with requirement for both medical and behavioral services.

Binge drinking and AUD cost Montanans millions of dollars annually from losses in workplace productivity, costs related to law enforcement and criminal justice expenses, motor vehicle accidents, and from treating AUD-related comorbid physical and psychological illnesses (CDC, 2014). In 2017, over $42 million dollars were charged by Montana hospitals for alcohol-related hospitalizations and emergency department visits (Montana Hospital Discharge Data System, 2017). In 2013, the annual cost in Montana due to excessive alcohol consumption was approximately $800 million (CDC, 2014).

Problem

In the United States, the Affordable Care Act (ACA) and Medicaid expansion increased coverage for adults with incomes up to 138% of the federal poverty level (FPL) (Norris, 2018). Benefits extended to cover Medicaid beneficiaries include mental health and substance-abuse services to meet the requirements of the Mental Health Parity and

Addiction Equity Act (MHPAEA) (Centers for Medicare and Medicaid Services, 2016). Due to the Montana acceptance of Federal Medicaid expansion in 2016, there is a high likelihood that individuals with an AUD will also be recipients of Medicaid, requiring treatment facilities to be State-approved.

Although Medicaid expansion has increased access to treatment for individuals with an AUD, entry into a State-approved treatment facility is precarious. Montanan adults with an AUD, who utilize Medicaid as a source of payment for inpatient treatment services, require a diagnosis and referral for a chemical-dependency (CD) evaluation prior to seeking entry into a Montana treatment center. A CD evaluation must be performed by an appropriately licensed mental health professional including licensed addiction counselors (LAC) and those who hold a professional license with a substance-use-disorder (SUD) scope. The individual conducting the chemical-dependency evaluation must document how the client meets criteria for a SUD, as well as confirm that the individual meets SUD criteria, and admit to a treatment facility on an annual basis (MDPHHS, 2018). As of 2017, LACs were not eligible for direct reimbursement from the State's Medicaid plan unless they were deemed a State Approved Chemical Dependency Program. "For LACs (individual or otherwise) seeking to bill Medicaid, the individual must apply and become a State Approved Chemical Dependency Program" (MDPHHS, 2017b, p. 2). Due to this stipulation, in addition to a state statute requiring state-approved facilities to prove they are not duplicating services, Montana had just 32 State-approved licensed CD evaluators in 2017 (Loveland, 2017).

Additionally, despite the high rate of reported AUDs in Montana, the known costs to the State due to excess alcohol consumption and the fact that many individuals with an AUD are Medicaid recipients, the State of Montana has very few State-approved inpatient treatment facilities to address alcohol abuse and addiction. Once a CD evaluation has been completed and the client is approved for treatment, individuals utilizing Medicaid to treat an AUD can find just four State-approved inpatient treatment facilities in Montana (Loveland, 2017), further limiting access to inpatient treatment services.

Interestingly, access to inpatient addiction services for persons using Medicaid has been further limited by the Medicaid Institutions for Mental Diseases exclusion (Medicaid IMD) implemented in 1965. The Medicaid IMD exclusion prohibits the use of federal Medicaid financing for substance-abuse treatment facilities with more than 16 beds (Legal Action Center, 2016). This exclusion rule was initially put in place to ensure states would have primary responsibility over funding for inpatient psychiatric/substance-abuse services. However, for states who rely heavily on federal funding, like the State of Montana, the Medicaid IMD exclusion limits treatment opportunities and leads to health disparities for treatment-seeking individuals with Medicaid (Kiernan, 2018). In 2018, Montana ranked ninth out of 50 on the list of the most federally dependent states (Kiernan, 2018), perhaps accounting for the limited number of inpatient addiction facilities available to its constituents.

Due to the limitations put on chemical-dependency evaluators and inadequate inpatient treatment facility options, the average length of time individuals with an AUD

who utilize Medicaid wait for an inpatient bed in a substance-abuse treatment facility ranges from 60 days to one year (Loveland, 2017). When a treatment-seeking individual is motivated to stop consuming alcohol, without an option to initiate treatment, they may attempt to forgo using alcohol on their own. Without proper treatment, there is a significant risk for the individual to develop alcohol withdrawal syndrome (AWS), a life-threatening outcome resulting from decreased alcohol consumption in an alcohol-dependent person. Nearly 50% of individuals with an AUD will experience some degree of AWS when alcohol consumption is reduced (Schuckit, 2014). During abstinence from alcohol use in the alcohol-dependent patient, the brain undergoes multiple neurological changes making it difficult for the patient to remain sober while they wait for inpatient treatment. Alternatively, if the patient has recently undergone detoxification and attempts to wait for treatment, the patient may experience symptoms of protracted abstinence affecting the patient's ability to maintain abstinence from alcohol. Protracted abstinence is the term used for the multiple symptoms individuals with an AUD experience when they detoxify and abstain from alcohol. Symptoms include high anxiety, depression, and insomnia, and may account for the large number of individuals who return to alcohol consumption to ease these ongoing symptoms (Mason, 2017).

The ongoing complications between government resources, including the Medicaid IMD exclusion, limited treatment facilities, risk for alcohol withdrawal, protracted abstinence symptoms, and other barriers to treatment such as patient denial and stigma of alcoholism, may provide reason for the paucity of individuals receiving treatment in Montana. In 2015, a single-day count in Montana State-approved addiction

treatment facilities revealed just 3347 of the 60,000 individuals with an AUD receiving treatment for alcohol abuse (Loveland, 2017).

Considering the difficulty individuals with an AUD have in obtaining proper withdrawal support and addiction treatment coupled with the dangers of AWS, it is important to explore alternate approaches to help treatment-seeking individuals with an AUD remain abstinent from alcohol, in control of their addiction, and decrease withdrawal symptoms while they wait for inpatient treatment. One solution to help individuals seeking treatment for alcohol abuse is to determine new ways to support, educate, and treat individuals with an AUD on an outpatient basis. Recent evidence supports the use of gabapentin in the treatment of an AUD to lessen anxiety from protracted abstinence, aid in mild to moderate alcohol-withdrawal symptoms, and help the treatment-seeking individual with an AUD remain abstinent until inpatient alcohol addiction treatment is made possible.

Purpose

The objective of this integrative review was to identify whether the use of gabapentin is safe and effective for use on an outpatient basis to prevent relapse of alcohol abuse and reduce symptoms of withdrawal and protracted abstinence in treatment-seeking individuals with an AUD.

Theoretical Concept

The role of an advanced practice registered nurse (APRN) serving the client with alcohol addiction in a state with low availability of addiction services includes canvassing client's access to resources, directing the client toward evidence-based treatment, and promoting informed and shared decision making between the APRN and client. One way to accomplish these efforts is through the philosophical assumptions supporting Imogene King's Theory of Goal Attainment.

King's Theory of Goal Attainment, introduced in 1967, is a middle-range, prescriptive nursing theory based on a client-centered approach. King's theory supports and values the nurse-client relationship, emphasizes the importance of a therapeutic rapport, and reinforces the benefit of interpreting relevant health information for clients to promote trust and understanding. According to King, the patient is a social being with three distinct fundamental needs: the need for health information, the need for care that seeks to prevent illness, and the need for nurturing when the individual is unable to help him or herself (King, 1992). King explains health as the understanding and connecting of life experiences as well as the consideration of how an individual may adjust to stressors in both an internal and external environment. King believes in the validity of a therapeutic nurse-client relationship to allow for optimal communication through the giving and receiving of information (p. 21). This transaction offers the client the opportunity to make informed decisions about their disease, ensure understanding of the options for their plan of care, and promotes the development of shared patient goals to promote goal obtainment.

King's Theory of Goal Attainment guides the APRN to develop concepts and organize knowledge for their clients. Consisting of three ever changing and interacting models, King's theory facilitates the client's learning about self, the interaction of self with other individuals and groups, and society when the individual interacts with the environment (King, 1992, p. 20).

King's interacting systems assist the nurse practitioner and client to create a shared plan of care through the organization of concepts and knowledge about the individual (personal system), the individual's interaction with groups (interpersonal system), and society (social system). The related concepts for the personal systems include perception, self, growth, development, body image, space, and time. The concepts of the interpersonal system include interaction, communications, transaction, role, and stress. The concepts for the social system include organization, authority, power, status, and decision-making. Among these three systems, King reports the conceptual framework of the interpersonal system had the greatest influence on the development of her theory.

> Although personal systems and social systems influence quality of care, the major elements in a theory of goal attainment are discovered in the interpersonal systems in which two people, who are usually strangers, come together in a health care organization to help and to be helped to maintain a state of health that permits functioning in roles (King, 1981, p. 142).

King's theory provides a foundation for the APRN to assist the patient with alcoholism. Using the concept of King's theory, the APRN assists the client to organize knowledge, recognize resources for support, and identify treatment options for the client with an AUD. The three intertwining concepts developed by King may be used by the

APRN as the underpinning of education needed to assist addicted individuals to recognize and make use of their personal resources, identify community resources, initiate new or unused resources and, recognize areas within the patient's own environment that may be optimized.

CHAPTER TWO

LITERATURE REVIEW

Background

Alcohol abuse is the fourth-leading cause of preventable death, killing an estimated 88,000 Americans a year, and is a common problem that should be adequately screened for by clinicians in all types of settings (NIAAA, 2018). For adults aged 18 years or older, the US Preventative Services Task Force (USPSTF) (2013) concludes with moderate certainty that there is a moderate net benefit to screening for alcohol misuse and brief behavioral counseling interventions in the primary care setting.

Screening, brief intervention, and referral to treatment (SBIRT) is an evidence-based pathway used to identify, reduce, and prevent problematic use, abuse, and dependence on alcohol and illicit drugs (SAMHSA-HRSA Center, n.d.). The construction of the SBIRT model was prompted by an Institute of Medicine (IOM) recommendation calling for community-based screening for health-risk behaviors including substance use.

There is also evidence suggesting benefit for the primary care provider to screen for alcohol consumption when comorbidity with alcohol is diagnosed (Rehm et al., 2016). Binge drinking and excessive alcohol intake affect tissue and organ systems, promote skeletal fragility, and cause damage to tissues such as the brain, liver, and heart, resulting in medical comorbidities frequently accompanying alcohol consumption. Medical comorbidities in the individual with an AUD include cancer of the digestive system and breast, gastrointestinal issues, adverse cardiovascular effects, diabetes,

insomnia, liver issues, renal impairments, depression and anxiety disorders, and hormonal imbalances (Chakravorty et al., 2013; Rehm et al., 2015; Lavinghousez, 2018). Although the influence from alcohol-related harm are numerous and ever evolving, there is a distinct relationship between average daily alcohol consumption and lifetime risk of disease caused by alcohol consumption (Rehm, Guiraud, Poulnais, & Shield, 2018). Evidence suggests individuals without somatic comorbidities may also be identified through systematic screening for an AUD with evidence-based screening tools (Rehm et al., 2016).

Following screening for an AUD, assessing co-occurring conditions, educating the client regarding the risks of excess alcohol consumption, and developing shared goals for treatment, a comprehensive and person-centered treatment plan should include evidence-based pharmacological treatments (The American Psychiatric Association [APA], 2018). In the US, there are three FDA-approved medications for use in the client with an AUD on an outpatient basis. They include disulfiram, a medication that causes intentional adverse effects when used with alcohol; naltrexone, an opiate antagonist available in both an oral form and a monthly intramuscular injection; and acamprosate, a glutamate modulator.

In the 1950s, the focus of medication development for AUDs was to block the motivation to seek alcohol in the binge/intoxication stage (Mason, 2017; Miller, Feillin, Rosenthal, & Saitz, 2019). Alcohol sensitizing agents, such as disulfiram, were designed to decrease alcohol seeking motivation in the client with an AUD by altering the way the body responds to alcohol consumption. Rather than experiencing euphoria with alcohol

ingestion, the client medicated with disulfiram experiences a self-limited, toxic response lasting approximately 30 minutes (Miller, Feillin, Rosenthal, & Saitz, 2019). This toxic response results from the interaction between disulfiram and ethanol and may involve the intended reaction of warmness, flushing of the skin, increased heart rate, heart palpitations, dyspnea, nausea, vomiting, and hypotension requiring stringent external monitoring (Micromedex, 2017; Miller, Feillin, Rosenthal, & Saitz, 2019). Clients treated with disulfiram require monthly monitoring of liver enzymes during the first three months of treatment and subsequent quarterly monitoring to detect hepatotoxicity (p. 784). Disulfiram should not be used with clients who do not consider abstinence the end goal of treatment and is contraindicated in patients who are consuming alcohol or products containing alcohol (APA, 2018). Moreover, several case reports have identified disulfiram as an agent that may induce psychosis among susceptible individuals such as those with low levels of amine and monoamine oxidase and those with a family history of schizophrenia (Mohapatra & Rath, 2017; de Melo, Lopes, & Alves, 2014). Due to the potential for adverse side effects, monitoring of liver enzymes, and the necessity of supervised administration, clinicians do not readily prescribe disulfiram for persons with an AUD (Williams et al., 2017).

Medications designed to directly reduce alcohol consumption and decrease cravings are also available to the clinician to treat the client with an AUD. Naltrexone and acamprosate are two medications designed to reduce alcohol consumption, improve treatment adherence, and aid in the prevention of relapse to heavy drinking (Miller et al., 2019; APA, 2018). Naltrexone, an opiate antagonist, is contraindicated within seven days

of opioid use, and buprenorphine or methadone within 14 days (APA, 2018; Micromedex, 2017). Naltrexone has a reported mild side effect profile including transient nausea, headache, dizziness, lightheadedness, and weakness (Miller et al., 2019; Micromedex, 2017). However, like disulfiram, oral naltrexone is hepatotoxic, should not be administered during the alcohol withdrawal period, and requires monitoring of liver-function tests at baseline, one month, six months, and annually (APA, 2018). Despite evidence for use in clients with an AUD, only 3% of patients with an AUD received a prescription for naltrexone, and less than 10% of those treated with naltrexone received the long-acting injectable naltrexone (Iheanacho et al., 2013; Marienfeld et al., 2014).

Acamprosate, like naltrexone, was designed to reduce alcohol consumption, improve treatment adherence, and aid in the prevention of relapse to heavy drinking. Evidence suggests acamprosate works by increasing gamma-aminobutyric acid (GABA) neurotransmission with a possible righting effect on glutamate, an excitatory amino acid neurotransmission (Myrick, Saxon, & Jaffe, 2019). Alcohol consumption creates an imbalance between glutamate and GABA when alcohol enhances inhibition at GABA synapses, increasing GABA release (Stahl, 2013). Alcohol also prevents the release of glutamate by acting on presynaptic metabotropic glutamate receptors and presynaptic voltage-sensitive calcium channels (p. 555). Acamprosate promotes abstinence by balancing the dysregulated GABA and glutamate systems. In treatment for alcohol-use disorders, acamprosate has been found to be slightly more effective in promoting abstinence and naltrexone slightly more effective in reducing heavy drinking and craving **(**Maisel, Blodgett, Wilbourne, Humphreys, & Finney, 2013; Myrick, Saxon, & Jaffe,

2019). Although contraindicated in renal failure, acamprosate may be used in clients with liver disease as it is not hepatotoxic and is excreted unchanged in the urine (Haber & Fryer, 2019). Perney & Lehert (2018) report acamprosate may also be useful to decrease insomnia in patients with alcohol dependence. Both acamprosate and naltrexone have better abstinence-outcome profiles compared to placebo when detoxification and abstinence from alcohol occur prior to medication administration (Myrick, Saxon, & Jaffe, 2019).

Data from the Veterans Health Administration (VA) show low rates of pharmacotherapy for AUDs suggesting clients with an AUD often receive medications to treat psychiatric and medical complications, but only 7–11% receive medications to treat an AUD (Rubinsky, Chen, Batki, Williams, & Harris, 2015). Barriers to prescribing FDA-approved, evidence-based AUD medications include: provider lack of knowledge/training, lack of optimism regarding both prescribing and managing AUD medications, and belief that patients are better served with specialty addiction treatment due to known adverse side effects and needed monitoring (Williams et al., 2017).

While the current FDA-approved medications have evidence behind them to increase motivation among abstinent individuals to avoid alcohol consumption (disulfiram), decrease craving for alcohol (acamprosate and naltrexone), and reduce number of heavy drinking days and total alcohol consumption (naltrexone), none of these medications are effective for mild to moderate withdrawal symptoms on an outpatient basis nor may be used to decrease symptoms of protractive abstinence. Reversing the motivational dysregulations associated with withdrawal from an AUD, including negative

affect, anxiety, sleeplessness, and preoccupation/anticipation stages during protracted abstinence, is important to prevent relapse of alcohol consumption (Mason, 2017).

Early identification of an AUD, recognition of the limitations and paucity of current FDA-approved medications for an AUD, and finding alternatives to inadequate treatment options align with the Institute for Healthcare Improvement's (IHI) Triple Aim (IHI, 2019). The goals of the Triple Aim are supported via an outpatient medication regimen for treatment-seeking individuals and optimize our current healthcare system performance by:

- improving the patient experience of care (including quality and satisfaction);
- improving the health of populations; and
- reducing the per capita cost of healthcare (IHI, 2019, para. 1).

As clinicians, we may aid treatment-seeking patients with an AUD on an outpatient basis in rural, urban, and suburban areas via an evidence-based medication regimen to prevent withdrawal symptoms, provide relief for protracted abstinence, and support the client's abstinence until an inpatient treatment option is available. Gabapentin is a medication with a seemingly low-risk profile that may play a useful role in establishing an outpatient-based treatment plan of care for treatment-seeking individuals suffering from an AUD.

CHAPTER THREE

METHODS

An integrative review of the literature as outlined by Whittemore and Knafl (2005) was conducted to explore evidence for the use of gabapentin in the outpatient treatment of an AUD. An integrative review is the broadest type of research review. The integrative approach allows for the inclusion of diverse methodologies, e.g., randomized controlled trials, observational studies, qualitative research, theoretical literature, expert opinion from clinical experts, and other types of evidence to increase knowledge regarding a specific phenomenon (Souza, Silva, & Carvalho, 2010; Whitmore & Knafl, 2005). The integrative review is beneficial for addressing emerging topics, enables the incorporation of many different perspectives, and allows for the opportunity to examine numerous types and levels of evidence (experimental, non-experimental, qualitative, and expert-opinion) to gain comprehensive understanding of the problem and direct practice (Whittemore & Knafl, 2005).

Problem Identification

In the first phase of this nursing project, the clinical problem was identified, the purpose of the integrative review was determined, and variables of interest were distinguished. The graduate student's experience assisting patients with alcohol detoxification in an acute psychiatric setting provided background for problem recognition. The identified problem was a lack of immediate inpatient treatment for

treatment-seeking individuals with an AUD. The purpose for utilizing an integrative literature review for this project was to identify current knowledge related to the use of gabapentin in treatment-seeking adults (18–65 years) with an AUD to (a) prevent symptoms of mild-to-moderate alcohol withdrawal syndrome in an outpatient setting, (b) lessen anxiety from protracted abstinence, and (c) help the individual remain abstinent until inpatient treatment is possible.

Literature Search Strategy

Whittemore and Knafl (2005) report a well-defined search strategy is essential to promote rigor and reduce errors such as incomplete and/or biased results. Grey literature, clinical practice guidelines, expert-opinion, and research articles were identified through the Montana State University library site using the following computerized databases: Cumulative Index to Nursing and Allied Health Literature (CINAHL), PubMed, PsycINFO, Medline, and *Cochrane* from January 2014–December 2019.

The primary key term used was "gabapentin." In five separate searches, the key term "gabapentin" was combined using the Boolean operator AND with the terms: alcohol use disorder, protracted abstinence, alcohol withdrawal syndrome, alcohol withdrawal symptoms, alcohol dependence, and outpatient treatment. Saturation was deemed to have occurred once the same articles, authors, themes, and patterns were observed and relevant evidence was no longer discoverable. Analysis of the reference lists from retrieved articles and sources was performed in order to determine any

additional relevant primary resources followed by a manual search of the identified citations.

Inclusion and Exclusion Criteria

Inclusion criteria for the integrative review were English language, peer-reviewed, human study population, journal articles, and empirical reports published between January 2014 and December 2019. The abstracts of the articles were evaluated for the following inclusion data: (a) the abstract described the use of gabapentin for an AUD, and/or (b) the abstract described the use of gabapentin to aid in alcohol withdrawal symptoms, and/or (c) the role of gabapentin was discussed to aid in abstinence from alcohol use. Literature from all countries was also included when meeting the inclusion data.

Publications were excluded for the following reasons: (a) not meeting eligibility criteria, (b) if research studies had not been completed, (c) if the research exclusively combined gabapentin with another medication for the treatment of AUDs and withdrawal, (d) if the research included gabapentin use in combination with another medication that would not be safely administered in an outpatient setting, and (e) if the patient population included patients younger than 18 years of age and over 65 years of age. Literature reviews were also not included if the studies reviewed were comprised of research studies prior to 2014.

Data Evaluation

The literature search resulted in empirical studies. No theoretical articles or abstract principles were discovered in the integrative-review search process. Empirical reports were comprised of meta-analyses, randomized-controlled trials, systematic reviews, observational studies, and retrospective chart reviews. The initial review of literature involved a screening of titles and abstracts for duplications as well as an appraisal of the article title and abstract against the inclusion and exclusion criteria. In cases where either the title or abstract were not satisfactory to make an initial selection, the entire article was reviewed. The following set of guiding questions was used to further eliminate irrelevant articles: (1) Can gabapentin be used to aid in mild to moderate alcohol withdrawal symptoms? (2) Is gabapentin effective to help the treatment-seeking individual with an AUD remain abstinent? (3) Can gabapentin lessen anxiety from protracted abstinence?

The final sample of articles was read in entirety and evaluated for scientific rigor, sample size, ability to be generalized to the population with an AUD, and relevance to the research question via a framework posited by Melnyk and Fineout-Overholt (2015) (see Appendix A). Articles were not excluded based on the quality of the data; however, quality was considered when drawing conclusions about implications for practice. Studies with little rigor and low relevance had less impact in the course of the data-analysis stage (Whittemore & Knafl, 2005).

Data Synthesis and Analysis

Per Whittemore & Knafl (2005), the steps of data analysis (data reduction, data display, data comparison, and obtaining conclusion) were used to derive common themes and patterns. Data synthesis included combining information into an evaluation table to determine citation, purpose of the study, sample, design, measured outcomes, and study findings (see Appendix B). When themes were identified, the results of the studies were further analyzed to determine conclusions, identify any existing conflicts, and to build a logical chain of evidence to contribute to the knowledge of the use of gabapentin for individuals with an AUD. Both analysis and synthesis of data extracted from the articles were carried out in a descriptive fashion, allowing for reflection, tallying, describing, and categorizing data to gain knowledge of the topic addressed in the integrative review.

When organizing the data, it was determined that all reports included in the final sample discussed the use of gabapentin for individuals with alcohol use disorder. Although interventions between studies varied related to GBP dose, its use as an adjunct or primary medication, sample population, and setting, there were similarities in outcomes.

CHAPTER FOUR

RESULTS

Search terms applied to the PubMed, Cochrane, PsycInfo, Medline, and CINAHL databases generated 564 results. After excluding duplicates and off-topic titles, 51 articles remained. The abstracts of the remaining articles were manually screened for inclusion and exclusion criteria and those 51 articles were reduced to 34. Of those 34 articles, 10 studies satisfied inclusion and exclusion criteria after conducting a full-text review (see Figure 2).

The final 10 studies were used to determine the current state of knowledge related to the use of GBP for treatment-seeking individuals with an AUD. Study methods of the articles included in the review consist of two meta-analyses, one systematic review, two randomized controlled trials, two retrospective chart reviews, and one observational study. Two literature reviews of empirical evidence were also included in the final study results of the integrative-review evaluation, as was a clinical guideline addressing the use of anticonvulsants for individuals with an AUD.

Description of Studies

Sample

Each study represented in the integrative review includes a sample population diagnosed with an AUD. However, the severity of the AUD within each sample population was either not factored into the research results, was unreported, or not

measured (Ahmed et al., 2019a; Ahmed et al., 2019b; Chompookham, et al., 2018; Kranzler, Feinn, Morris, & Hartwell, 2019; Leung et al., 2018; Mason et al., 2014). Variations among the level of the AUD within each sample population may be one cause for the differences in effect results among studies included within this review. Of the nine-studies meeting inclusion and exclusion criteria, only one listed the severity of the AUD among its sample population (Levine et al., 2019).

Under the American Psychiatric Association (APA) Diagnostic and Statistical Manual of Mental Disorders, DSM-5 (2013), any individual meeting two of the 11 criteria for an AUD during the same 12-month period may receive a diagnosis of an AUD. However, the addition of a mild, moderate, or severe specifier is key as it indicates the number of criteria and denotes severity (p. 491). The AUD "mild" specifier includes the presence of two to three symptoms; "moderate" includes the presence of four to five symptoms; and "severe" AUD includes the presence of six or more symptoms (p. 491). Without the determination of the level of severity for individuals with an AUD, it is difficult at best to determine whether the conclusions made regarding the effect of GBP on abstinence, withdrawal, and protracted abstinence are valid. Determining the level of severity in the AUD within sample populations promotes congruency, increases generalization, and boosts strength of evidence.

Additionally, sample populations differed among studies related to the level of alcohol being consumed while studied. Researchers included individuals who received GBP while still consuming alcohol (Chompookham et al., 2018; Kranzler, Feinn, Morris, & Hartwell, 2019; Rentsch et al., 2019), while in withdrawal (mild, moderate, and

severe) (Ahmed, et al., 2019a; Ahmed et al., 2019b; Leung et al., 2018; Leung et al., 2015; Levine et al., 2019; Mason, Quello, & Shadan, 2018), and after detoxification from alcohol (Mason, et al., 2014).

Interventions/Dosage

The dosages of GBP between the final studies were not similar. Each study incorporated a unique GBP dosing schedule for individuals with an AUD. In the meta-analyses and systematic reviews analyzed for this integrative review, the GBP dose used in the sample populations were diverse and dependent on the studies analyzed for the reviews (Ahmed et al., 2019a; Ahmed et al., 2019b, Kranzler, Feinn, Morris, & Hartwell, 2019). The remaining studies contained varying dosing schedules including 300 mg of GBP per day (Chompookham et al., 2018), 900 mg three times per day (Leung et al., 2018), 1800 mg per day with an 800 mg loading dose (Levine et al., 2019), less than or greater than 1500 mg per day (Rentsch et al., 2019), and a fixed dose of either 900 mg or 1800 mg of immediate release GBP (Mason et al., 2014).

Study interventions were also not similar. One meta-analysis included a study using GBP enacarbil extended-release medication as equivalent to the immediate-release GBP formulation without allowance for the difference in the way each medication is metabolized (Kranzler, Feinn, Morris, & Hartwell, 2019). Gabapentin enacarbil extended release is a prodrug requiring the intake of food to enhance absorption. A prodrug requiring food consumed in adequate amounts for medication absorption would not be beneficial in individuals with an AUD as alcohol consumption and its metabolism hinders the absorption of essential nutrients (e.g., carbohydrates, proteins, and vitamins) and

alters digestion (National Institute on Alcohol Abuse and Alcoholism, 2000). Therefore, any drug requiring food for absorption is not an optimal medication for those with an AUD. Additionally, both meta-analyses included studies involving use of GBP as an adjunct, as well as a primary agent (Ahmed et al., 2019a; Kranzler, Feinn, Morris, & Hartwell, 2019), further skewing study results.

Social Group Representation

The sex and race of participants within the studies were either not noted or vastly underrepresented. For many diseases and disorders, the proportion of female participants researched does not match the gender breakdown of real-world patients. According to the 2018 National Survey on Drug Use and Health (NSDUH), 14.4 million adults aged 18 and older have been diagnosed with an AUD in the United States. Of these 14.4 million individuals, 9.2 million are male and 5.3 million are female (SAMSA, 2019). Therefore, to generalize study results for both female and male individuals, researchers must consider the inclusion of women for approximately 1/3 of their AUD sample population. The characteristic of sex within study sample populations was either not determined (Ahmed et al., 2019a; Ahmed et al., 2019b; Kranzler, Feinn, Morris, & Hartwell, 2019; Leung , Hall-Flavin, Nelson, Schmidt, & Schak, 2015; Mason et al., 2014) or greatly overrepresented males (Chompookham, 2018; Leung et al., 2018; Levine et al., 2019; Rentsch, et al., 2019). The highest representation among studies for females with an AUD was 27% of the sample population (Leung et al., 2018) with 2% representing the least representation for women among studies (Rentsch et al., 2019).

Including women in the sample population and specifying race in research studies are important to ensure generalization of study results and to promote equality when determining the effectiveness of an intervention. Although excessive alcohol consumption begins at a later age in females, their progression of alcohol consumption is quicker from the first consumption until the onset of dependence due to a number of vulnerabilities specific to females (Del Carmen Míguez, & Permuy, 2017). Women have a greater vulnerability to the effects of an AUD than men and must be represented in the sample population when this disease is researched. An insufficient sample number of women was included in the research studies to generalize study results to this vulnerable population.

Outcomes

Withdrawal

The results of this integrative review suggest evidence for the use of GBP to aid with the symptoms of mild-to-moderate withdrawal in treatment-seeking individuals. Authors of five of the articles report evidence for the use of GBP in this manner for withdrawal (Ahmed et al., 2019a; Ahmed et al., 2019b, Kranzler, Feinn, Morris, & Hartwell, 2019; Levine et al., 2019; Mason et al., 2014; Rentsch et al., 2018). An observational study provides evidence for statistically significant changes in AUDIT-C scores among alcohol-dependent clients exposed to >1500mg/d of GBP without consideration to motivation for treatment (Rentsch, et al., 2019).

Abstinence

According to a randomized controlled trial, GBP significantly improved rates of abstinence (placebo: 4.1%; gabapentin 900 mg: 11.1%; gabapentin 1800 mg: 17.0%) and heavy drinking (placebo: 22%; 900 mg: 29.6%; 1800 mg: 44.7%) (Mason et al., 2014). Two meta-analyses and a systematic review that include the Mason et al. (2014) study echo this result (Ahmed et al., 2019a; Ahmed et al., 2019b; Kranzler, Feinn, Morris, & Hartwell, 2019). At lower GBP doses (300 mg–900 mg), the percentage of heavy drinking days were reduced, but overall alcohol consumption was not affected (Chompookham et al., 2018).

Protracted Abstinence

Protracted abstinence or the altered emotional processing may persist for months or years after abstinence from alcohol due to subtle neuroadaptations caused from alcohol dependence (Rich & Martin, 2014). Symptoms of protracted abstinence include craving, negative affect, anxiety, depression, and sleep disturbances (Mason et al., 2014). The benefit of GBP for protracted abstinence may be observed in three studies determining effectiveness for GBP related to craving, insomnia, depression, and anxiety (Ahmed et al., 2019a; Ahmed et al., 2019b; Mason et al., 2014). Two studies provided a favorable linear-dose effect and suggest preliminary support for the use of GBP to reduce craving in treatment-seeking individuals who were detoxed from alcohol prior to administration (Ahmed et al., 2019, & Mason et al., 2014). Although the type of anxiety disorder was not specific to the anxiety caused from protracted abstinence, one study discussed the benefit of GBP for treatment of multiple types of anxiety (Ahmed, 2019b).

Outpatient Population

Only one research study utilized GBP for use in an outpatient population (Mason et al., 2014). However, this study was conducted at an outpatient research facility (Mason et al., 2014) and may not be generalizable to patients being treated as outpatient clients in an office setting.

Summary of Analysis of the Literature

The information contained in these studies provides evidence for the use of GBP to reduce mild-to-moderate withdrawal symptoms for individuals with an AUD (Ahmed et al., 2019a; Ahmed et al., 2019b; Leung et al., 2018; Leung et al., 2016; Levine et al., 2019; & Rentsch et al., 2018). There is also evidence to suggest GBP is effective for decreasing ongoing alcohol consumption by reducing alcohol craving and number of days of heavy drinking (Ahmed et al., 2019a; Ahmed et al., 2019b; Chompookham, et al., 2018; Kranzler, Feinn, Morris, & Hartwell, 2019; Mason et al., 2014). However, the nature of an AUD as a heterogenic disorder contributes to the heterogeneity within and between studies complicating the importance of the study results included in this integrative review.

Problems of heterogeneity include differing study aims, methods, settings, and diversity among sample characteristics. Diversity in sample characteristics among studies includes the utilization of GBP in individuals experiencing mild-to-moderate withdrawal versus individuals suffering from acute and severe withdrawal, administering GBP to

detoxed individuals versus varying levels of intoxication, and the unknown quality of the individuals' AUD severity.

Heterogeneity among studies also includes differences in study purpose, interventions, and desired effects. Moreover, treatment settings among studies are disparate including inpatient treatment centers, hospital settings, research settings, and VA treatment facilities. Additionally, a troubling result observed among research included in the review is the fact that study results are not generalizable to women with an AUD due to their insufficient inclusion.

Due to the limited number of well-designed studies for the use of GBP with alcohol-dependent individuals, diversity of interventions, sample population, and unspecified AUD severity, more rigorous research is needed to determine the effectiveness of GBP on abstinence and protracted abstinence. Larger studies with diverse populations of alcohol dependency, increased homogeneity among sample sizes, doses, severity of the AUD, and similar study purpose are needed to further extend findings. Despite significant heterogeneity and the list of limitations among studies, clinical guidelines recommend utilizing gabapentin when the patient does not respond to FDA-approved medications, if the client is intolerant of the FDA-approved medications, and if the client prefers GBP over FDA-approved medications (Reus, et al., 2018).

CHAPTER FIVE

DISCUSSION

Alcohol use disorder is a complex disorder that can be classified as mild, moderate, or severe. Individuals within the same AUD-severity category may experience differing types of aliment, symptom severity, and degrees of withdrawal. Individuals with an AUD also experience varying degrees of mental health, medical comorbidities, family and community support, and personal beliefs. Due to the heterogeneity of an AUD, it is important to fully consider the individual's unique experience with the AUD to determine the risk and/or benefit for the use of GBP as an off-label medication for abstinence, alcohol withdrawal symptoms, and protracted abstinence. Consideration of the above factors contributes to the success of medications for treatment.

The purpose of this integrative literature review was to identify current knowledge related to the use of gabapentin in an outpatient setting for treatment-seeking adult patients (18–65 years) with an AUD, for preventing the symptoms of mild-to-moderate alcohol withdrawal syndrome, for treatment of symptoms related to protractive abstinence, and for assisting the individual to abstain from alcohol on an outpatient basis until initiation of inpatient substance-abuse treatment. It was conducted with the idea that an outpatient gabapentin-medication treatment may contribute to the individual's management of an AUD, reduce the chances for alcohol consumption and/or relapse, and decrease the danger of AWS for patients awaiting inpatient treatment. Although no studies reviewed demonstrated significant evidence for the use of gabapentin in

treatment-seeking clients with moderate-to-severe AWS on an outpatient basis, there is evidence for its use in mild-to-moderate AWS and to aid in decreasing days of heavy drinking and cravings. Overall, results of this integrative review demonstrate limited research with low-to-moderate quality of evidence surrounding the use of gabapentin for supporting treatment-seeking patients with AWS, abstinence, and protracted abstinence symptoms.

Strengths

The strengths of this integrative review involve the utilization of five separate digital databases to discover research articles pertaining to the use of GBP for individuals with an AUD. Of the ten studies included in the review, two were meta-analyses and one was a systematic review of randomized-controlled trials offering high levels of evidence. Two randomized controlled trials were included in this review, with both offering a sample population greater than n=100. Additionally, research included in the integrative review was conducted in the last five years. The strength of each research study is found in Appendix B.

Limitations

There are limitations to this integrative review. The nature of an integrative review is to include multiple methodologies to increase knowledge regarding a specific phenomenon (Souza, Silva, & Carvalho, 2010; Whittemore & Knafl, 2005). However, when combining diverse methodologies, the issues of rigor, inaccuracy, and bias may

result (Whittemore, 2005). This graduate student's limited experience in conducting an integrative review may have led to biases when integrating and synthesizing data found in the remaining articles. Additionally, the process of selecting key search words and the author's decision to utilize specific electronic databases may have limited the full selection of articles pertaining to the subject. Further, the absolute process of an integrative review is not explicit as there are no evidence-based reporting guidelines developed at this time. Therefore, rigor may be low related to the conclusions drawn about the outcomes of the studies included in this integrative review.

Implications for Practice

Identifying and treating an AUD in Montana is an important endeavor. Due to the fast-paced nature of outpatient appointments, limited patient-provider interaction, and lack of knowledge related to treatment options for AUDs, many Montanans with an AUD are underdiagnosed and significantly undertreated.

Currently, benzodiazepines serve as the standard of care for the treatment of AWS by targeting GABA-A receptors (Ahmed et al., 2019a). Gabapentin does not directly interact with GABA-A receptors and is not indicated for use in individuals with severe AWS (Leung et al., 2018). Individuals with severe AWS should be admitted to an inpatient facility and monitored for delirium tremens and seizures (Sachdeva, Choudhary, and Chandra, 2015). Additionally, although most studies reviewed in this review considered the use of GBP with an inpatient population, clinicians will continue to see AUDs in all healthcare settings and among their outpatient patients. Implications for

practice include ensuring individuals are adequately screened for an AUD in all types of healthcare settings, assessed for support, and educated about the possibilities for using FDA-approved medications, as well as novel medications like GBP, to reduce mild-to-moderate AWS when attempting to limit consumption.

Overall, GBP is a medication that reduces heavy drinking (Chompookham et al., 2018; Kranzler et al., 2019; Mason et al., 2014), may aid with protracted abstinence (Ahmed et al., 2019b; Mason et al., 2014), and is beneficial for mild-to-moderate withdrawal (Ahmed et al., 2019a; Ahmed et al., 2019b, Kranzler, Feinn, Morris, & Hartwell, 2019; Levine et al., 2019; Mason et al., 2014; Rentsch et al., 2018). It is metabolized unchanged in the kidneys making it beneficial for those with comorbid liver disease and may be used in clients with kidney disease (Mason et al., 2014). The reduction of heavy drinking is valuable to the alcohol-dependent client seeking treatment, as any reduction in alcohol consumption contributes to limiting the progression of comorbid disease.

Implications for Research

Efficacy for the current FDA-approved medications to treat an AUD is limited (Kranzler & Soyka, 2018; Litten et al., 2016; Lyon, 2017; Winslow et al., 2016). Therefore, it is important to continue to research safe and effective medication options for clients with an AUD to provide a sufficient number of medication options to meet the unique needs of the alcohol-dependent patient. Research on the use of the medication, gabapentin, for the alcohol-dependent client is important, particularly with considerations

regarding sample homogeneity and distinction by severity of an AUD. Further, there is a need to focus research on women with an AUD as their experience with the disease is unique to their male counterparts. Ongoing research is needed for medications that treat AUDs safely and effectively on an outpatient basis. Inclusion of studies with outpatient clients meets the reality of need for individuals with an AUD as inpatient addiction services are generally limited.

Summary

In Montana, AUDs continue to cost individuals and society millions of dollars each year through workplace productivity loss, law enforcement and criminal justice expense, motor vehicle accidents, and treatment of the AUD-related comorbid physical and psychological illnesses (CDC, 2018). Inpatient substance-abuse facilities in Montana are limited with even fewer inpatient treatment options available to clients utilizing Medicaid. With Montana's high incidence of alcohol abuse, it is likely a great number of clients with an AUD will present in all types of Montanan healthcare settings. The high incidence of alcohol abuse coupled with insufficient inpatient treatment options requires the clinician to consider individualized outpatient treatment plans to support treatment-seeking individuals with an AUD.

Additionally, the debilitating nature of AUDs coupled with the complexities of circumnavigating modern-day healthcare options necessitates the clinician to use a systems approach. King's Theory of Goal Attainment assists the clinician to plan for and organize care and treatment options for the individual with an AUD. King's theory

supports and values the nurse-client relationship, emphasizes the importance of a therapeutic rapport, and reinforces the benefit of interpreting relevant health information for clients to promote trust and understanding. Using concepts included in King's theory, the clinician organizes knowledge for the client, assists the client to recognize resources for support, promotes shared decision-making, and provide education related to available treatment options. The organization of healthcare knowledge, including the use of novel research for the treatment of an AUD, is essential to provide support and hope for clients with an AUD.

Ideally, clinicians care for individuals with an AUD via a patient-centered approach by first identifying the AUD as an issue, determining community and individual support, educating the client related to the health risks involved with ongoing alcohol consumption, and by providing all options for beneficial medication to bridge the gap for treatment-seeking individuals waiting for inpatient treatment. The use of medication on an outpatient basis for treatment-seeking clients with an AUD provides support for treatment-seeking individuals with an AUD in anticipation of inpatient treatment. The use of gabapentin may be effective for assisting the treatment-seeking individual with abstinence by reducing the number of heavy-drinking days, cravings, sleeplessness related to protracted abstinence, and aid with mild-to-moderate alcohol withdrawal.

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APPENDICES

APPENDIX A

RAPID CRITICAL APPRAISAL TOOLS

Rapid Critical Appraisal of Case-Control Studies

1. Are the results of the study valid?

a. How were the cases obtained?	Yes	No	Unknown
b. Were appropriate controls selected?	Yes	No	Unknown
c. Were data collection methods the same for the cases and controls?	Yes	No	Unknown

2. What are the results?

a. Is an estimate of effect given (do the numbers add up?)	Yes	No	Unknown
b. Are the multiple comparisons of data?	Yes	No	Unknown
c. Is there any possibility of bias or confounding?	Yes	No	Unknown

3. Will the results help me in caring for my patients?

a. Were the study patients similar to my own?	Yes	No	Unknown
b. How do the results compare with previous studies?			
c. What are my patients/family's values and expectations for the outcome?			

Rapid Critical Appraisal of Qualitative Evidence

1. Are the results of the study valid (i.e. trustworthy and credible?)

a. How were study participants chosen?			
b. How were accuracy and completeness of data assured?			
c. How plausible/believable are the results?	Yes	No	Unknown
i. Are implications of the research stated?	Yes	No	Unknown
(1)May new insights increase sensitivity to other's needs?	Yes	No	Unknown
(2) May understandings enhance situational competence?	Yes	No	Unknown
d. What is the effect on the reader?	Yes	No	Unknown
(1) Are results plausible and believable?	Yes	No	Unknown
(2) Is the reader imaginatively drawn into the experience?	Yes	No	Unknown

2. What were the results?

a. Does the research approach fit the purpose of the study?	Ye	N	Unknow

	s	o	n
	Ye	N	Unknow
i. How does the researcher identify the study approach?	s	o	n
(1) Are language and concepts consistent with the approach?	Ye s	N o	Unknow n
(2) Are data collection and analysis techniques appropriate?	Ye s	N o	Unknow n
	Ye	N	Unknow
ii. Is the significance/importance of the study explicit?	s	o	n
(1) Does review of the literature support a need for the study?	Ye s	N o	Unknow n
(2) What is the study's potential contribution?			
iii. Is the sampling strategy clear and guided by study needs?	Ye s	N o	Unknow n
(1) Does the researcher control selection of the sample?	Ye s	N o	Unknow n
(2) Doe sample composition and size reflect study needs?	Ye s	N o	Unknow n
	Ye	N	Unknow
b. Is the phenomenon (human experience) clearly identified?	s	o	n
	Ye	N	Unknow
i. Are the data collection procedures clear?	s	o	n
(1) Are sources and means of verifying data explicit?	Ye s	N o	Unknow n
	Ye	N	Unknow
(2) Are researcher roles and activities explained?	s	o	n
	Ye	N	Unknow
ii. Are data analysis procedures described?	s	o	n
(1) Does analysis guide direction of sampling and when it ends?	Ye s	N o	Unknow n
	Ye	N	Unknow
(2) Are data management processes described?	s	o	n
	Ye	N	Unknow
c. What are the reported results (description or interpretation)?	s	o	n
i. How are specific findings presented?			
(1) Is presentation logical, consistent, and easy to follow?	Ye s	N o	Unknow n
(2) Does quotes fit the findings they are intended to illustrate?	Ye s	N o	Unknow n
ii. How are overall results presented?			
(1) Are meanings derived from data described in context?	Ye s	N o	Unknow n
(2) Does the writing effectively promote understanding?	Ye s	N o	Unknow n

3. Will the results help me in caring for my patients?

a. Are the results relevant to persons in similar situations?	Yes	No	Unknown
b. Are the results relevant to patient values and/or circumstances?	Yes	No	Unknown
c. How may the results be applied in clinical practice?			

Rapid Critical Appraisal of Randomized Clinical Trials (RCTs)

1. Are the results of the study valid?

a. Were the subjects randomly assigned to the experimental and control groups?	Yes	No	Unknown
b. Was random assignment concealed from the individuals who were first enrolling subjects into the study?	Yes	No	Unknown
c. Were the subjects and providers blind to the study group?	Yes	No	Unknown
d. Were reasons given to explain why subjects did not complete the study?	Yes	No	Unknown
e. Were follow-up assessments conducted long enough to full study the effects of the intervention?	Yes	No	Unknown
f. Were the subjects analyzed in the group to which they were randomly assigned?	Yes	No	Unknown
g. Was the control group appropriate?	Yes	No	Unknown
h. Were the instruments used to measure the outcomes valid and reliable?	Yes	No	Unknown
i. Were the subjects in each of the groups similar on demographic and baseline clinical variables?	Yes	No	Unknown

2. What are the results?

a. How large is the intervention or treatment effect? (NNT, NNH, effect size, level of significance)?

b. How precise is the intervention or treatment (CI)?

3. Will the results help me in caring for my patients?

a. Were all clinically important outcomes measured?	Yes	No	Unknown
b. What are the risks and benefits of the treatment?			
c. Is the treatment feasible in my clinical setting?	Yes	No	Unknown

d. What are my patients/family's values and expectations for the outcome that is trying to be prevented and the treatment itself? _____

Rapid Critical Appraisal of Systematic Reviews of Clinical Interventions/Treatments

1. Are the results of this review valid?

a. Are the studies contained in the review randomized controlled trials? Yes No Unknown

b. Does the review include a detailed descriptions of the search strategy to find all relevant studies? Yes No Unknown

c. Does the review describe how validity of the individual studies was assessed (e.g. methodological quality, including the use of random assignment to study groups and complete follow-up of the subjects? Yes No Unknown

d. Were the results consistent across studies? Yes No Unknown

e. Were individual patient data or aggregate data used in the analysis? Yes No Unknown

2. What were the results?

a. How large is the intervention or treatment effect (OR, RR, effect size, level of significance)? _____

b. How precise is the intervention or treatment (CI)? _____

3. Will the results assist me in caring for my patients?

a. Are my patients similar to the ones included in the review? Yes No Unknown

b. Is it feasible to implement the findings in my practice setting? Yes No Unknown

c. Were all clinically important outcomes considered, including risks and benefits of treatment? Yes No Unknown

d. What is my clinical assessment of the patient and are there any contraindications or circumstances that would inhibit me from implementing the treatment? Yes No Unknown

e. What are my patient's and his or her family's preferences and values about the treatment that is under consideration? Yes No Unknown

Rapid Critical Appraisal of Cohort Studies

1. Are the results of the study valid?

a. Was there a representative and well defined sample of patients at a similar point in the course of the disease? Yes No Unknown

b. Was follow up sufficiently long and complete? Yes No Unknown

c. Were objective and unbiased outcome criteria used? Yes No Unknown

d. Did the analysis adjust for important prognostic risk factors and confounding variables? Yes No Unknown

2. What are the results?

a. What is the magnitude of the relationship between predictors (i.e. prognostic indicators and targeted outcome)? _____

b. How likely is the outcome event(s) in a specified period of time? _____

c. How precise are the study estimates? _____

3. Will the results help me in caring for my patients?

a. Were the study patients similar to my own? Yes No Unknown

b. Will the results lead directly to selecting or avoiding therapy? Yes No Unknown

c. Are the results useful for reassuring or counseling patients? Yes No Unknown

APPENDIX B

EVALUATION TABLES

THE USE OF GABAPENTIN IN TREATMENT SEEKING ADULTS WITH ALCOHOL USE DISORDER IN AN OUTPATIENT SETTING

An Integrative Review of the Evidence

January 2014-December 2019

#	Title	Citation	Study Methods	Study Purpose/Results	Conclusions / Recommendations / Nursing Implications	Quality of the Evidence
1	Effectiveness of gabapentin reducing cravings and withdrawal in alcohol use disorder: A meta-analytic review.	Ahmed S., Stanciu, C.N., Kotapati PV, Ahmed, R, Bhivandkar, S., Khan, A.M., Afridi, A., Qureshi, M., Esang, M. (2019). *The Primary Care Companion for CNS Disorder, 21*(4). pii: 19r02465. doi: 10.4088/PCC.19r02465.	A meta-analysis of 10 studies to determine the effect of GBN on alcohol withdrawal and cravings in participants with an AUD dx. The sex of the sample populations was not considered r/t the efficacy of GBP in the treatment of the AUD. **Dependent variable:** • Cravings • Withdrawal **Independent variable:** • GBP (used as a primary medication and as an adjunct medication, GBP dose is dependent on study) **Statistical Analysis:** Random Effects Model Pretest-posttest SMD	**Purpose:** To synthesize previous findings and examine the overall effect of GBN on alcohol withdrawal and craving. **Results:** Statistically significant effect sizes found for craving and withdrawal in the meta-analysis of single-group pretest-posttest outcome changes with **high level of heterogeneity.** Literature suggests GBP is effective as an adjunct medication rather than for us as monotherapy.	**Conclusions:** • Improving withdrawal symptoms may decrease ongoing alcohol consumption. • Preliminary support exists for the use of GBP for treating alcohol craving and withdrawal. • GBP is not hepatically metabolized. • GBP is well tolerated. • Blood draws not required like carbamazepine and divalproex. • Unlike FDA approved acamprosate, GBP may be used in clients with renal function < 20mg/dL. • GBP improves sleep issues, a symptom of protractive abstinence. **Recommendations:** Results suggest preliminary data for the use of GBP in treating alcohol craving and withdrawal. More well-designed studies are needed with more rigorous methodology **Nursing Implications:** Ensure the client with an AUD is informed of their options for medications and support when seeking treatment for an AUD.	**Evidence Level:** 1 **Strengths:** A meta-analysis of peer reviewed literature **Limitations:** Using pre-post SMDs should be avoided in meta-analyses as they may result in biased outcomes (Cuijpers,Weitz, Cristea, Twisk (2017). High level of heterogeneity within chosen studies due to population sample, GBP dose, and the use of adjunctive medication. Some studies included GBP use as an adjunct; others used GBP as a primary agent Severity of AUD unknown between study samples. Low external validity.

#	Title	Citation	Study Methods	Study Purpose/Results	Conclusions / Recommendations / Nursing Implications	Quality of the Evidence
2	Use of gabapentin in the treatment of substance use and psychiatric disorders: A systematic review	Ahmed, S., Bachu, R., Kotapati, P., Adnan, M., Ahmed, R., Farooq, U., Saeed, H., Khan, A. M., Zubair, A., Qamar, I., Begum, G. (2019b). *Front Psychiatry, 10*(228). doi: 10.3389/fpsyt.2019.00228.	A systematic review: n=54 articles related to the effect of gabapentin on various psychiatric and substance abuse disorders. The sex of the sample populations was not considered r/t the efficacy of GBP in the treatment of the AUD. **Dependent variables:** • Abstinence • Heavy drinking • Anxiety • Other psychiatric disorders **Independent variables:** • GBP (dose dependent on study) • placebo **Statistical Analysis:** Review performed and reported according to PRISMA guidelines.	**Purpose:** To determine the efficacy of gabapentin for treatment of substance abuse and psychiatric disorders. **Results:** Gabapentin may be effective in alcohol withdrawal and dependence when used as an adjunct medication. More rigorous and larger clinical trials are required. Literature suggests GBP is effective as an adjunct medication rather than monotherapy.	**Conclusions:** GBP at 1200-3200mg may be used as an adjunctive medication or as monotherapy in the treatment of AWS regardless of severity at presentation. • GBP 1200-3200 mg/day effective for alcohol withdrawal symptoms, cravings, sleeplessness, depression, and for maintaining abstinence. • 1800 mg/day significantly improved the rate of abstinence and prevent heavy drinking **Recommendations:** Use in outpatient setting for treatment seeking clients with an AUD may be considered r/t reported effectiveness for improving rates of abstinence and reducing heavy drinking. GBP is not hepatically metabolized making it a safer option to some FDA approved medications for an AUD. **Nursing Implications:** Ensure adequate screening to diagnose an AUD. Educate treatment-seeking clients about options for support through medication and therapy.	**Evidence Level:** 1 **Strengths:** A systematic review of peer reviewed literature **Limitations:** Only 2 databases (Pubmed and Ovid MEDLINE were included r/t PRISMA guidelines. Selected search terms may have missed relevant studies. Qualitative comparison versus in-depth meta-analysis. Studies included GBP used as an adjunct while others used GBP as a primary agent Not generalizable due to small # of primary studies Insufficient evidence to determine quality of studies used in this systematic review.

#	Title	Citation	Study Methods	Study Purpose/Results	Conclusions / Recommendations / Nursing Implications	Quality of the Evidence
3	A randomized trial of low-dose gabapentin for post hospitalization relapse prevention in a Thai clinical sample of alcohol dependence.	Chompookham, P., Rukngan, W., Nilaban, S., Suwanmajo, S., Yoosom, P., & Kalayasiri, R. (2018). Psychiatry Research, 270, 34-40. doi: http://dx.doi.org.proxybz.lib.montana.edu/10.1016/j.psychres.2018.09.002	Randomized Clinical Trial of n=112 Thai individuals hospitalized at an inpatient drug abuse treatment center with alcohol dependence and very high alcohol consumption n=44 male (86%) n=7 female (13%) 70% dropout rate. Average ethanol intake/day prior to treatment 300 g/day **Dependent variable:** • Alcohol consumption • Percentage of heavy drinking days • Number of drinking days **Independent variable:** at least 300mg of gabapentin PO per day or placebo **Statistical Analysis:** Poisson repeated measures model Generalized Estimating Equations Chi-square statistics	**Purpose:** To investigate the effects of gabapentin on alcohol consumption. **Results:** Support for the use of gabapentin to reduce the frequency of drinking days and heavy drinking days per week. GBP group showed a lower percentage of heavy drinking days per week than placebo ($p<0.005$); did not affect the overall alcohol consumption in alcohol dependent individuals. GEE analysis showed treatment by time interaction on lowering drinking days/week ($p< 0.05$). Heavy alcohol drinking defined as < 60g of ethanol/day for males and <40 g/day for females+	**Conclusions:** GBN reduces number of drinking days and heavy drinking in treatment seeking individuals with an AUD without significant side effects. 12 weeks GBN administration **Recommendations:** GBN may be used safely to reduce heavy alcohol drinking upon discharge from an inpatient hospital, substance abuse treatment center, or any facility where the individual has been treated for alcohol withdrawal during their stay. **Nursing Implications:** Education r/t the benefit of medications for reducing alcohol consumption should be considered for patients treated for alcohol withdrawal to help reduce relapse and reduce serious effects of alcohol on patient's health, career, family, and society.	**Evidence Level:** 2 **Strengths:** A randomization and large sample size; blinded study. Patients had all been part of alcohol dependency program prior to study…actively seeking treatment. Same as my treatment population. **Limitations:** Subjects received silymarin (420 mg daily, q8h). lorazepam (1mg daily q6 h), and thiamine (100mg intramuscularly qDay x 7 days) prior to study initiation. Pt's were fully detoxed. 70% dropout rate 50mg trazadone qHS administered during study

#	Title	Citation	Study Methods	Study Purpose/Results	Conclusions / Recommendations / Nursing Implications	Quality of the Evidence
4	A meta-analysis of the efficacy of gabapentin for treating alcohol use disorder.	Kranzler, H. R., Feinn, R., Morris, P., & Hartwell, E. E. (2019). *Addiction, 114*, 1547-1555. doi:http://dx.doi.org.proxybz.lib.montana.edu/10.1111/add.14655	Meta-analysis of placebo controlled randomized controlled trials (7 RCTS) involving subjects >18 yo with AUD The sex of the sample populations was not considered efficacy of GBP in the treatment of the AUD **Dependent variables:** • Abstinence • Relapse to HD • # of drinks/day • % abstinent day • % HD days • GGT concentration • **Independent variable:** • GBP or placebo (dose dependent on the study) **Statistical Analysis:** • Meta-analysis conducted using the PRISMA guidelines. • Cochrane Risk of Bias Tool • Risk ratio • Hedges' *g* (0.2 =small effect; 0.5=medium effect and 0.8= large effect) • **Random effects model** • *Q* statistic • Forest plots • Bivariate meta-regression	**Purpose:** To determine the effect of GBN on multiple alcohol consumption outcomes. **Results:** GBP found to be efficacious for reducing the frequency of HD only. (after testing effect size, study completion rate, GBN dose, and study duration)	**Conclusions:** Optimal GB dosage has yet to be defined and it is unclear which individuals with an AUD may be most responsive to administration of this medication. **Recommendations:** More studies needed to confirm the treatment effects of GBP. The ER formulation requires biotransformation which can be reduced by alcohol, leading to decreased absorption. Optimal GBP dosage has yet to be defined and it is unclear which individuals with an AUD may be most responsive to administration of this medication. **Nursing Implications:** Ensure clients are adequately screened for an AUD and educate treatment seeking clients related to available FDA approved options for an AUD and alternatives like gabapentin. Understand mechanisms of heterogeneity of an AUD to advance personalized treatment**.**	**Evidence Level:** 1 **Strengths:** Meta-analysis of placebo controlled RCTs. *Q* statistic used to test for heterogeneity. Excluded studies that combined GBP with another medication for treatment of an AUD **Limitations:** Study subjects with an AUD diagnosis irrespective of severity. Studies were excluded that focused on treating alcohol withdrawal or insomnia. Study used a fixed-effects analysis finding smaller effects for outcomes when studies are weighted against their sample size. Small number of placebo controlled RCTs available for this meta-analysis; limited statistical power. The largest study in this meta-analysis used an ER-prodrug (gabapentin encarbil) instead of the immediate-release formulation. Evidence for significant heterogeneity of effect sizes existed for 4/6 outcome measures and moderate heterogeneity for the other 2.

#	Title	Citation	Study Methods	Study Purpose/Results	Conclusions / Recommendations / Nursing Implications	Quality of the Evidence
5	Use of a gabapentin protocol for the management of alcohol withdrawal: A preliminary experience expanding from the consultation-liaison psychiatry service.	Leung, J.G., Rakocevic, D.B., Allen, N.D., Handler, E.M., Perossa, B.A., Borreggine, K.L., Stark, A.L., Betcher, H.K., Hosker, D.K., Minton, B.A., Braus, B.R., Dierkhising, R.A., Philbrick, K.L. (2018). *Psychosomatics, 59*(5), 496-505. doi: 10.1016/j.psym.2018.03.002	A retrospective chart review of patients with an AUD (n=77) at Mayo Clinic who experienced alcohol withdrawal management via a gabapentin protocol/ secondary outcomes derived by comparing matched cohort of patients who rec'd benzos n=56 males (73%) n=21 females (27%) **Dependent variable:** • length of stay • symptoms of AWS **Independent variable:** • GBP taper protocol (900mg TID) **Statistical Analysis:** • paired *t*-test • McNemar's test	**Purpose:** To detect safety concerns with the use of a GBN protocol for alcohol withdrawal syndrome. **Results:** no patients managed via gabapentin protocol during the study period required transfer to a higher level of care or a documented seizure from withdrawal.	**Conclusions:** When GBP is appropriately dosed, it appears to be a safe and effective alternative for the management of mild to moderate AWS. Effect on length of stay similar to those who rec'd BZN for AWS. **Recommendations:** Dosing strategies of GBN warrant further investigation for clients with mild to moderate AWS. **Nursing Implications:** Ensure clients are adequately screened for an AUD and educate treatment seeking clients related to options for medication to assist with mild-to-moderate AWS	**Evidence Level:** 4 **Strengths:** Seizure activity measured in withdrawal. Utilizes a GBP order set. **Limitations:** Benefit from continued GBN, medication adherence, or adverse events were not appreciated given the design of the study. Retrospective chart review with low sample population. Possible selection bias, as clinicians may have selected patients at less risk for serious AWS sequalae Concurrent use of valproate may have occurred. BZN use prior to initiation of GBP protocol occurred in some of the patient population.

#	Title	Citation	Study Methods	Study Purpose/Results	Conclusions / Recommendations / Nursing Implications	Quality of the Evidence
6	The role of gabapentin in the management of alcohol withdrawal and dependence.	Leung JG, Hall-Flavin D, Nelson S, Schmidt KA, Schak KM. (2015). *Annals of Pharmacotherapy, 49(*8), 897-906. doi: 10.1177/1060028015585849.	A literature search including 10 publications n=5 utilizing GBP in alcohol withdrawal and n=5 utilizing GBP in alcohol dependence The sex of the sample populations was not considered r/t the efficacy of GBP in the treatment of the AUD **Dependent variable:** Alcohol dependence Alcohol withdrawal **Independent variable:** GBP	**Purpose:** To assess current evidence for the use of GBP in alcohol withdrawal and alcohol dependence **Results:** Evidence suggests GBP may be used with individuals in mild AWS. Future studies should be larger, include more diverse populations, and directly compare GBP with FDA approved agents for AUDs.	**Conclusions:** GBP may be considered for mild to moderate alcohol withdrawal when barriers prevent the use of traditional agents. Limited data suggests GBP improves sleep, mood, and anxiety **Recommendations:** Consider concomitant gabapentin administration while administering CIWA and withdrawal protocol in patients with moderate to severe AWS. **Nursing Implications:** Ensure clients are adequately screened for an AUD and educate treatment seeking clients related to options for medication to assist with mild-to-moderate AWS	**Evidence Level:** 5 **Strengths:** Comprehensive literature search. Compiles literature related to alcohol dependence and alcohol without repetition. Identifies gaps in the literature. **Limitations:** Included studies utilizing GBP in combination with other agents. GBP dosing is varied between studies.

#	Title	Citation	Study Methods	Study Purpose/Results	Conclusions / Recommendations / Nursing Implications	Quality of the Evidence
7	High-dose gabapentin for the treatment of severe alcohol withdrawal syndrome: A retrospective cohort analysis.	Levine, A.R., Carrasquillo, L., Mueller, J., Nounou, M.I., Naut, E.R., Ibrahim, D. (2019). Pharmacotherapy, 39(9):881-888. doi: 10.1002/phar.2309.	A retrospective cohort analysis conducted in a large academic center with adults diagnosed with **severe** AWS diagnosis presenting to the emergency department between January 2015 and April 2018. n=50 control group (40 males (80%); 10 (20%) females) n=50 treatment group (40 males (80%); 10 (20%) females) **Dependent variable:** • Alcohol withdrawal symptoms • Length of stay • BZN administration **Independent variable:** • High dose GBP (1800mg/day) including 800mg loading dose **Statistical Analysis:** Pearson χ^2 tests *t*-tests Regression model IBM SPSS Statistics version 22.0 IBM SPSS Statistics version 7	**Purpose:** To evaluate the impact of a high-dose gabapentin protocol on concomitant benzodiazepine use, alcohol withdrawal symptoms, and hospital length of stay in patients hospitalized with AWS. **Results:** A high dose GBN (1800mg/day) regimen was well tolerated without risk of over sedation compared to the control group. Length of stay, concurrent BZN use, and withdrawal symptoms were reduced.	**Conclusions:** A high dose GBN (1800mg/day) regimen may be effective as part of moderate to severe AWS. **Recommendations:** Consider concomitant gabapentin administration while administering CIWA and withdrawal protocol in patients with moderate to severe AWS. **Nursing Implications:** Ensure default withdrawal systems are in place when considering the addition of gabapentin to a withdrawal protocol. Continue to monitor for delirium tremens and seizure.	**Evidence Level:** 3 **Strengths:** specifies level of AUD severity. Generalizable to adults with an AUD presenting to ED **Limitations:** Concurrent BZN use with GBP *as needed*.

#	Title	Citation	Study Methods	Study Purpose/Results	Conclusions / Recommendations / Nursing Implications	Quality of the Evidence
8	Gabapentin for the treatment of alcohol use disorder.	Mason, B.J., Quello, S., Shadan, F. (2018). *Expert Opinion on Investigational Drugs, 27*(1):113-124. doi: 10.1080/13543784.2018.1417383.	Literature Review of n=11 studies **Dependent variables:** • Drinking • Craving • Mood • Sleeplessness **Independent variable:** GBP	**Purpose:** To summarize literature for the use of GBP for alcohol withdrawal **Results:** Literature suggests GBP is safe and efficacious treatment for an AUD with benefits for sleeplessness	**Conclusions:** GBP is safe and efficacious for an AUD with benefit for craving and sleeplessness r/t alcohol use. Not metabolized in the liver. **Recommendations:** Consider GBP in treatment seeking individuals to reduce heavy drinking and improve sleeplessness. **Nursing Implications:** GBP is a familiar medication used by primary care physicians with evidence of its use with abstinence and protracted abstinence.	**Evidence Level:** 5 **Strengths:** Comprehensive literature search. Compiles literature related to alcohol dependence and alcohol without repetition. Identifies gaps in the literature. **Limitations:** Small number of studies included. Only 2 studies include a sample population n>100. No pivotal trials Single-site studies 6 studies older than 2009

#	Title	Citation	Study Methods	Study Purpose/Results	Conclusions / Recommendations / Nursing Implications	Quality of the Evidence
9	Gabapentin treatment for alcohol dependence: A randomized clinical trial.	Mason, B.J., Quello, S., Goodell, V., Shadan, F., Kyle, M., Begovic, A. (2014). *JAMA Internal Medicine, 174*(1), 70-7. doi: 10.1001/jamainternmed.2013.11950.	A 12-week, double-blind, placebo-controlled, randomized dose-ranging trial of 150 men and women over 18 yo with an AUD conducted 2004-2010 at a single outpatient clinical research facility. The sex of the sample population was not considered in baseline characteristics. rate of study completion= 85/150 **Dependent variable:** • Abstinence • Heavy drinking • Mood • Sleep • Craving **Independent variable:** • 0, 900, 1800mg/day and concomitant manual-guided counseling **Statistical Analysis:** χ^2 ANOVA 2-tailed tests Extended Mantel-Haenszel χ^2 test for linear association MIXED TEST subcommand for Linear Trend Contrasts and Multiple Event Models PASW 17.0 software	**Purpose:** To provide a more definitive evaluation of the efficacy and safety of gabapentin at the highest (1800mg) and lowest (900mg/d) FDA-approved doses with recently abstinent (at least 3 days) individuals with an AUD. **Results:** GBP showed favorable linear dose effects on cravings, mood, sleep, and increased rates of abstinence. Favorable safety profile,	**Conclusions:** In detoxed and treatment seeking individuals, GBP (1800mg/day dose) may be effective for the treatment of alcohol dependence and protracted abstinence. **Recommendations:** Larger studies with more diverse populations of individuals with an AUD are needed to extend findings. **Nursing Implications:** GBP is a familiar medication used by primary care physicians with evidence of its use with abstinence and protracted abstinence.	**Evidence Level:** 2 **Strengths:** Same as my population: outpatient and treatment seeking. **Limitations:** Medication was included with manual-guided counseling. Significant drop out rate Result is from a single-site study and may not be generalizable to all treatment settings. *Individuals were detoxed prior to study and treatment seeking.*

#	Title	Citation	Study Methods	Study Purpose/Results	Conclusions / Recommendations / Nursing Implications	Quality of the Evidence
10	Association between gabapentin receipt for any indication and alcohol use disorders identification test-consumption scores among clinical subpopulations with and without alcohol use disorder.	Rentsch, C.T., Fiellin, D.A., Bryant, K.J., Justice, A.C., Tate, J.P. (2019). *Alcoholism: Clinical and Experimental Research, 43*(3):522-530. doi: 10.1111/acer.13953.	Observational Study/Propensity-score matched analysis n= 562 GBP exposed patients with an AUD who were prescribed GBP for >180 days for a medical indication between 2009-2015 in the Veterans Ageing Cohort Study (VACS) matched by propensity score to n=562 unexposed patients with an AUD n=1101 males (98%) n=23 females (2%) **Dependent variable:** • Alcohol use • AUDIT-c scores **Independent variable:** • with/without an AUD • > or < 1500 mg GBP/day **Statistical Analysis:** AUDIT-C scores; multivariable differences-in- difference linear regression models; chi square tests; sensitivity analysis *all statistical analyses performed using SAS version 9.4	**Purpose:** To determine the impact of gabapentin on changes of alcohol use among patients receiving gabapentin for common medical conditions, with reported alcohol consumption and whether or not effects differed with the AUD history, level of alcohol consumption, and prescribed daily dose of gabapentin. **Results:** Statistically significant changes in AUDIT-C scores among clients with AUD exposed to >1500mg/d gabapentin	**Conclusions:** Gabapentin influences AUDIT-c scores among clients with an AUD exposed to >1500mg gabapentin/day without consideration to motivation for treatment. • real-world data with observed effect of drinking outcomes with >1500mg/day gabapentin administration. • client stability observed with >1500mg/day prescribed at >180 consecutive days. • Statistically significant decrease in reported alcohol consumption • findings observed in the absence of substance abuse counseling and treatment. **Recommendations:** Use in outpatient setting for treatment seeking clients with an AUD should be considered r/t tolerability of gabapentin, improved AUDIT-c scores, and familiarity of medication among primary care providers. **Nursing Implications:** Ensure clients are adequately screened for an AUD and educate treatment seeking clients unable to get into alcohol abuse treatment related to options for medication and therapy.	**Evidence Level:** 4 **Strengths:** Well-designed observational studies have been shown to provide results similar to randomized controlled trials, challenging the belief that observational studies are second-rate (Song & Chung, 2010). **Limitations:** Restricted to US veterans utilizing VA healthcare system; does not generalized to all outpatient clients. Sample overrepresented, black, middle-age veterans.

Synthesis Table			
Study	Design	Sample	Outcome
Ahmed et al., 2019a	Meta-analysis	n=10 studies	cravings, withdrawal
Ahmed et al., 2019b	Systematic Review	n=54 studies	cravings, withdrawal, sleeplessness, depression
Chompookham et al., 2018	RCT	n=112 individuals	#of drinking days; #of heavy drinking days
Kranzler, 2019	Meta-analysis	n=10 studies	#of heavy drinking days
Leung et al., 2018	Retrospective chart review	n=77 charts	withdrawal
Leung et al., 2016	Literature review	n=10 studies	withdrawal
Levine et al., 2019	Retrospective chart review	n=100 individuals	withdrawal
Mason et al., 2014	RCT	n=150 individuals	cravings, mood, sleeplessness abstinence, # of heavy drinking days
Mason et al., 2018	Literature review	n=11 studies	sleeplessness
Rentsch et al., 2018	Observational Study	n=1124 individuals	withdrawal

DATABASE SEARCH RESULTS TABLE

Key Search Terms (2009-2019)	Search Results					
Gabapentin AND	Cochrane	PubMed	Psych Info	Medline	Total	Relevant Articles
alcohol use disorder	1	63	39	53	156	51
protracted abstinence	1	1	2	2	6	
alcohol withdrawal syndrome	12	21	22	12	67	
alcohol withdrawal symptoms	13	27	23	5	68	
alcohol dependence	2	45	44	38	129	
outpatient treatment	0	27	39	72	138	
	29	184	169	182	**564**	

Flow Diagram Depicting Article Selection