

Post-Acute Care Management of Patients with Angiostrongyliasis: A Guideline in Caring for
Patients Who Suffer Long Term Sequelae of Rat Lungworm Disease

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May 2020

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Abstract

Angiostrongyliasis, also known as rat lungworm disease (RLWD), is a parasitic infection caused by the nematode *Angiostrongylus cantonensis*. Anecdotal experience in Hawaii has shown that many patients diagnosed with RLWD develop chronic neurological sequelae which can last for years and possibly a lifetime (Hawaii's Joint Task Force, 2018). Currently, there is no available literature or guidelines on chronic care treatment of RLWD. Previous and current literature focuses on RLWD acute manifestation and treatments. Through a rigorous literature search and critical analysis of evidence-based information on possible treatment options of the chronic symptoms of RLWD, an evidence-based guideline was created. Ten Hawaii island primary care providers participated in a project aimed at educating providers on the guideline. The providers' knowledge level of RLWD chronic care management strategies was assessed before and after the guideline was presented to them. Data analysis showed increased knowledge in all participants. Ninety percent of participants stated that the guideline was significantly effective in increasing their knowledge about the long-term sequelae of RLWD. Limitations of the project included a small sample size and participants' limited practice experience. Primary care providers who are not familiar with RLWD or are new to the Hawaii community should familiarize themselves with the chronic health effects of RLWD, especially those practicing in endemic regions such as East Hawaii. This evidence-based guideline could serve as a basic introduction to the chronic care aspect of RLWD.

Keywords: rat lungworm disease, eosinophilic meningitis, angiostrongyliasis, *angiostrongylus cantonensis*

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Chapter 1: Statement of Problems, Project Aim and Objectives

Introduction

Angiostrongyliasis, also known as rat lungworm disease (RLWD), is a parasitic infection caused by a nematode called *Angiostrongylus cantonensis* (Centers for Disease Control and Prevention [CDC], 2017). The adult forms of *A. cantonensis* are found exclusively in rodents. The infected rats pass larvae of the parasite through their feces. Slugs and snails become infected after ingesting the larvae. Worms remain in its larvae stage in slugs and snails. The life cycle is complete when rats ingest the infected slugs and snails, where the larvae will then travel to the rat's lungs to mature into adult worms (CDC, 2017). Hence the name, rat lungworm. Once the parasite has entered the human body, it can have devastating effects on the central nervous system, often causing eosinophilic meningitis (Hammoud et al., 2017). Although cases of RLWD are prevalent among Southeast Asian countries, it has also surfaced in North America, including the United States (US) (York, Creecy, Lord, & Caire, 2015). The rising number of angiostrongyliasis cases warrant increased awareness among health care providers and the entire community, especially in Hawaii.

Although the disease is relatively new to the US, preliminary guidelines for diagnosis and treatment of RLWD were recently issued by the Hawaii Governor's Joint Task Force on RLWD (Department of Health [DOH], 2018). However, there is no literature regarding chronic care treatment of the disease. Many patients who have been diagnosed with this parasitic infection report long lasting health effects such as muscle weakness, paresthesia, and tremors which can last for years and possibly a lifetime. Many victims in Hawaii have permanent disabilities

resulting from angiostrongyliasis (Howe & Jarvi, 2017). Once discharged, patients with long term health effects should still receive ongoing medical attention and regular follow up care from their primary care providers to ensure a progressive recovery. For the purpose of this project, care management protocols for patients who are ready to be discharged from inpatient care into the care of a primary care provider will be explored.

Background and Significance

The rat lungworm, *A. cantonensis*, is a nematode that primarily infect rodents. Adult worms reproduce in the rat's pulmonary arteries. The eggs are then hatched into first stage larvae in the lungs. The larvae travel up to the trachea and are swallowed into the rat's digestive system where they are later released in the feces. The larvae in the feces are then often ingested by snails, slugs, freshwater crabs, prawns, land crabs, and frogs, which allow the larvae to develop further. These animals then become the intermediate host for the disease. Human infection, as accidental hosts, is acquired by ingesting raw or undercooked intermediate hosts or contaminated vegetables containing the infected larvae form of the worm. Once the parasite enters the human body, it can affect the central nervous system, resulting in clinical manifestations of eosinophilic meningitis which are characterized by a heightened level of eosinophils in the cerebrospinal fluid. Once the worm larvae reach the brain, they develop into the sub-adult stage and die. The movement of the worm in the brain and the body's immune response to the dying worms can cause severe, and sometimes permanent, neurological damage (Cowie, 2017).

This disease has been reported globally but is most common in southeast Asian countries and Pacific Basin. Cases have since surfaced in North America beginning in 1987 (Hammoud et al., 2017). In a press release by the Hawaii State Department of Health (2019), there were a total

of nine confirmed cases in Hawaii in 2018 and five confirmed cases statewide as of May 23, 2019. A study conducted by the University of Hawaii at Manoa revealed that semi-slugs are the most common vector for *A. cantonensis* in Hawaii, with the area of most prevalence being East Hawaii, specifically in the lower Puna District (Hollingsworth et al., 2007).

Anecdotal experience in Hawaii has shown that many patients diagnosed with RLWD develop chronic neurological sequelae (Hawaii's Joint Task Force, 2018). The long term sequelae of the disease has been shown to affect the victims' activities of daily living as well as financially with prolonged health care needs, some costing over \$1,000,000 in medical bills, plus added loss of income for the victim and their caregivers (Howe & Jarvi, 2017). Chronic health effects include severe weakness of the extremities, chronic pain, dysesthesias, insomnia, and recurrent headaches. These patients can benefit from long term multidisciplinary support including primary care, occupational therapy, physical therapy, social work support, and alternative/complementary medical care (Hawaii's Joint Task Force, 2018).

Attending Hilo Medical Center's (HMC) RLWD support group provided insights into the long-term sequelae that many patients continue to experience months and years after the initial infection. The 6th Annual International Workshop on *Angiostrongylus* and *Angiostrongyliasis* was held on January 5-8, 2020 in Hilo Hawaii. The workshop featured anecdotal experiences and perspectives from health care providers who have treated RLWD patients along with RLWD patients themselves. Chronic neuropathic pain was the most frequently reported symptom by patients who attended both the support group and the workshop. Other symptoms reported include sleep disturbances, fatigue, and muscle weakness. Many patients who have sought medical care for these symptoms reported that the treatments prescribed are not always effective, which in turn, causes increased depression and a sense of defeat. Health care providers in

attendance at the workshop also agreed that there is a limited amount of resources on management strategies for chronic symptoms of RLWD and that ongoing studies on this aspect of the disease is highly indicated.

Problem Statement

RLWD is a threat to public health, particularly to populations in Southeast Asia and the Pacific Basins (Hammoud et al., 2017). In the US, the state of Hawaii, and specifically the East Hawaii community is most at risk for development of this disease which can cause long-term devastating health effects (Howe & Jarvi, 2017). The literature shows that there is lack of adequate research and guidelines on the post-acute outpatient, long-term management of the disease (Hawaii Joint Task Force, 2018). Care management by primary care providers following acute inpatient hospital discharge is essential in ensuring a successful and progressive recovery, allowing each patient to achieve their optimum health.

Project Goal

The purpose of this pilot project was to develop care management guidelines for primary care providers to use in following up with patients who suffer from long term sequelae of RLWD. The guideline would provide various evidence-based management strategies based on common chronic symptoms that affect RLWD patients physically, behaviorally and socially. The evidence-based information can assist primary care providers in providing holistic, effective and quality care to patients affected by RLWD.

Aims and Objectives

Aim 1

Develop evidenced-based treatment guidelines for management of the post-acute care of patients diagnosed with RLWD.

Objective 1. Utilizing the search terms “rat lungworm disease,” “angiostrongyliasis,” and “eosinophilic meningitis,” and specific long-term symptoms reported by patients who are affected by RLWD, find and critically appraise evidence for effective post-acute care management of RLWD through various components of care including physical (medication, physical, occupational, and speech therapy), social and behavioral including mental health support.

Objective 2. Assess primary care providers’ baseline knowledge relative to management of post-acute, outpatient care of patients diagnosed with RLWD.

Objective 3. Synthesize findings into evidence-based guidelines for use in the outpatient primary care settings.

Objective 4. Assemble a panel of stakeholders including experts on the subject and primary care providers with experience in treating RLWD to evaluate the guideline and make revisions as indicated.

Aim 2

Provide education to primary care providers regarding evidence-based strategies for managing post-acute, follow-up outpatient care of patients with confirmed diagnosis of RLWD.

Objective 1. Implement an educational virtual presentation utilizing the evidence-based guidelines.

Objective 2. Evaluate the effectiveness of the virtual presentation and primary care provider participants’ perceptions of the potential usefulness of the evidence-based guidelines.

Chapter 2: Review of Literature and Theoretical Framework

Review of Literature

Clinical manifestations. Angiostrongyliasis infection in its acute phase can present as generalized malaise, loss of appetite, fever, headache, neck stiffness, paresthesia, abdominal pain, nausea, and vomiting (Wang, Lai, Zhu, Chen & Lun, 2008). In some cases, patients can develop a non-pruritic vesicular rash over their body which spreads rapidly over 48 hours and may be accompanied by cutaneous hypersensitivity, hypersomnolence, altered sensorium, decreased motor strength and severe foot drop. Visual disturbances, diplopia, muscle twitching, convulsion, atonic bladder and fecal incontinence and death has also been reported (Nalini et al., 2013). The case reporting by Kwon et al. (2013) also describes profuse night sweats, generalized myalgia of trunk and limbs, headache, altered mental status, anxiousness and left 6th cranial nerve palsy. In a case of pediatric RLWD, fever of unknown origin, decreased oral intake and irritability began on day three of illness. By day 11, the child's fever continued as she also began to develop lethargy and emesis (Hammoud et al., 2017).

Diagnostic criteria. Hawaii's Joint Task Force on RLWD (2018) recommended that presumptive diagnosis of angiostrongyliasis should be made based upon a triad of findings which include characteristic symptoms and signs, demonstration of eosinophilic meningitis upon lumbar puncture (LP), and exposure history including residence in or travel to an endemic area. In cases reported by Flerlage et al. (2017), Hammoud et al. (2017), Kwon et al. (2013) and Tseng et al. (2011), serum hematology panel demonstrated some degree of leukocytosis with elevation in eosinophil differential. In the case reported by Tseng et al. (2011), the patient's serum IgE was elevated, as was the creatine kinase, lactate dehydrogenase, and hepatic enzymes. Sonography, however, did not indicate hepatomegaly. All of the patients who received X-ray or

computer tomography had no significant findings. In addition, the cerebrospinal fluid (CSF) had a cloudy appearance, which was congruent with CSF results reported by Nalini et al. (2013) and Hammoud et al. (2017). In all three cases, the opening pressures of the LP were elevated and the CSF samples were confirmed to have contained glucose, elevated protein, and eosinophils. In the case reported by Flerlage et al. (2017) and Hammoud et al (2017), the CSF samples were sent to a CDC laboratory for further testing and both results had confirmed presence of *A. cantonensis* larvae in them.

In some cases, magnetic resonance imaging (MRI) was also obtained which in certain cases showed leptomeningeal enhancement, consistent with meningitis (Tseng et al., 2011). In other cases, the MRI revealed multiple scattered small punctate areas of signal change in both cerebral and white matter, corpus callosal lesions (Nalini, et al., 2013), scattered areas of restricted diffusion throughout the parenchyma, leptomeningeal enhancement, and multifocal nodular enhancement along the ventral portion of multiple spinal levels (Flerlage et al., 2017).

According to the Hawaii's Joint Task Force on RLWD (2018), early detection and presumptive diagnosis of angiostrongyliasis should be made when all three criteria are met: history of suggestive clinical signs and symptoms, evidence of eosinophilic meningitis upon LP characterized by CSF eosinophil level above 10 percent, and exposure history that includes recent travel history or residence in an endemic area. It is also important to note that eosinophil levels in the CSF may be low or undetectable in the early stage of infection. The LP should be repeated if RLWD is still suspected (Hawaii's Joint Task Force, 2018). In Hawaii, RLWD is a reportable disease by health care providers to the Hawaii State DOH. In suspected cases, CSF samples are sent to the DOH lab for further real-time polymerase chain reaction (RTi-PCR) testing. This test evaluates for the presence of *A. cantonensis* DNA and is a standard for disease

confirmation in Hawaii. It is important to note that it is not necessary to have RTi-PCR confirmation to begin treatment. A presumptive diagnosis is clinically valid and vital in starting treatment in order to prevent long-term sequelae (Hawaii's Joint Task Force, 2018).

Acute care treatment. High dose corticosteroid therapy via intravenous and oral routes for a minimum of 14 days has been shown to improve outcomes in non-comatose patients in limited studies and is becoming accepted as standard therapy for RLWD treatment (Hawaii's Joint Task Force, 2018). In a study in Thailand, patients who received oral prednisolone at a 60 mg/day dose reported less headache days and required less repeat LPs to reduce intracranial pressure (Chotmongkol, Sawanyawisuth & Thavornpitak, 2000). Intravenous dexamethasone therapy given at 24 mg/day in divided doses has also been associated with dramatic improvement in symptoms within 48 hours after administration. Intravenous dexamethasone was later converted to an oral tablet after two weeks in which the patient continued to have decreased overall symptoms (Nalini et al., 2013). The effects of corticosteroid therapy in RLDW was studied by using Evans Blue stain to measure the permeability of the blood brain barrier. Evans Blue is a widely used dye to study cellular membrane permeability and blood vessels because of its nontoxic property. Results showed that administration of dexamethasone for two weeks significantly decreased blood brain barrier permeability, therefore preventing *A. cantonensis* larvae from crossing into the brain (Tsai et al., 2015).

Furthermore, corticosteroids can also decrease inflammatory response to migrating and dying worms (Chotmongkul et al., 2000). In severe cases, however, patients experienced long term health and neurological effects which included tremor, diplopia, muscle weakness and ataxia despite the use of corticosteroids during the acute treatment period (Kwon et al., 2013). Tapering of corticosteroids is clinically recommended for courses longer than 14 days but

adjustment should be made according to a patient's clinical course and outcomes (Hawaii's Joint Task Force, 2018). Corticosteroids can induce hyperglycemia in patients with diabetes, thus, blood glucose should be monitored closely (Hawaii's Joint Task Force, 2018).

There is little evidence to suggest effectiveness of anthelmintic drugs in management of RLWD (Hawaii's Joint Task Force, 2018). However, studies have shown that the combination of corticosteroid and anthelmintic drugs can alleviate symptoms without any adverse side effects (Howe & Jarvi, 2017). This combination of treatment has been shown to provide the most relief for patients whose diagnosis was made early (Wang et al., 2008). The use of anthelmintic drugs is controversial in that it may elicit an inflammatory response due to dying worms, therefore, exacerbating neurological symptoms (Chotmongkol, Wongjitrat, Sawadpanit, & Sawanyawisuth, 2004). However, a study in Thailand concluded the use of albendazole is needed to eradicate the migrating worm and prevent axonal damage. Patients who received albendazole alone without corticosteroid demonstrated reduction in days of symptoms without any adverse effects (Kwon et al., 2013). Despite this evidence, until better safety data are available, Hawaii's Joint Task Force on RLWD recommends concurrent use of corticosteroid and anthelmintic drugs when treating angiostrongyliasis. When anthelmintic therapy is used, albendazole is the drug of choice due to its ability to reach high concentrations in the central nervous system. It can be given as an oral tablet form at 15 mg/kg/day in two divided doses for 14 days. The decision to use albendazole should be made on a case-by-case basis. Studies suggest that albendazole is less effective in the treatment of angiostrongyliasis when started after two weeks post-exposure. Therefore, albendazole should be given as soon as a presumptive diagnosis is made (Hawaii's Joint Task Force, 2018). In the setting of ocular angiostrongyliasis disease, treatment options include surgery or laser therapy (Sawanyawisuth & Sawanyawisuth, 2008).

Finally, repeat LP can help improve persistent headache by reducing intracranial pressure (Howe & Jarvi, 2017). Analgesics such as acetaminophen are often used to alleviate headache. Non-steroidal anti-inflammatory (NSAIDs) use should be avoided due to its associated risk of gastrointestinal bleeding, especially when used with high dose steroids. Opioids should be used cautiously, if at all, because it may cause confusion and increased fall risk along with high potential for abuse or dependence (Hawaii's Joint Task Force, 2018).

Chronic Care Treatment

For the purpose of this project, chronic care treatment was considered to begin when the patient is discharged from the hospital. To date, there are no known specific guidelines regarding management strategies of long-term health effects of RLWD and strategies to manage these sequelae (Hawaii's Joint Task Force, 2018). Patients who experience limb weakness, difficulty ambulating, dysesthesia, and inability to perform executive function should receive multidisciplinary support which include physical, occupational, and speech therapy and social work supports (Hawaii's Joint Task Force, 2018). Various management strategies for RLWD chronic symptoms have been studied such as acupuncture, vitamin therapies, and natural anti-inflammatories. However, there have been no guidelines developed to date for other long-term sequelae. Below is a review of evidence-based strategies for management of long-term sequelae which include chronic neuropathic pain, supplements/vitamin therapy, depression, post-traumatic stress disorder, insomnia, sleep disturbances, benefits of social support and importance of case management.

Physical Chronic Care

Pharmacological treatments of chronic neuropathic pain. Chronic neuropathic pain is one of the long-term sequelae of RLWD (Hawaii's Joint Task Force, 2018). It is important to

distinguish chronic neuropathic pain from chronic nociceptive pain in order to select an appropriate treatment option (Mersky & Bogduk, 1994). The treatment of chronic neuropathic pain can be categorized as follows: pharmacologic, physical medicine, behavioral medicine, neuromodulation and interventional. Literature suggests that optimal patient outcomes often result when multiple approaches are utilized through a multidisciplinary care team. For most patients, initial pharmacological treatment involves the use of antidepressants or calcium channel alpha 2-delta ligands (gabapentin and pregabalin) (Driscoll, & Kerns, 2016).

Gabapentin has been primarily studied and was found to be an effective treatment for postherpetic neuralgia and painful diabetic neuropathy. It is amongst the drugs approved by the U.S. Food and Drug Administration (FDA) for the treatment of neuropathic pain (Dobecki, Schoket, & Wallace, 2006). Gabapentin may reduce pain associated with polyneuropathy and is generally well tolerated (Pop-Busui et al., 2017). Gabapentin should be initiated at a low dose with gradual increases until pain relief or dose limiting adverse effects occur, or to a maximum of 3600 mg per day in three divided doses. It was also noted that an adequate trial of treatment for gabapentin can require up to two months or more (Wiffen et al., 2017). In another clinical trial, gabapentin provided the most effective neuropathic pain control when it was given at 1200 mg daily for the treatment of postherpetic neuralgia and painful diabetic neuropathy. Evidence to support its use for other types of neuropathic pain is very limited (Wiffen et al., 2017). In a consensus statement issued by the Canadian Pain Society, gabapentin was still recommended as a first-line agent, along with pregabalin, for the treatment of chronic neuropathic pain (Moulin et al., 2014).

Pregabalin is an analogue of gabapentin, with the same mechanism of action, but it has higher affinity for the presynaptic calcium channel (Moulin et al., 2014). Its effectiveness was

evaluated in randomized clinical trials with results suggesting that compared with placebo, pregabalin treatment at total daily doses of 150, 300, and 600 mg resulted in significant reduction in painful neuropathy. At higher doses, there were dose-related increases in effectiveness but also an increase in adverse effects. The most common adverse effects were dizziness, somnolence, and peripheral edema (Freeman, Durso-Decruz, & Emir, 2008). A systematic review and published guideline for pain management in peripheral neuropathy by the American Academy of Neurology suggests pregabalin (300 to 600 mg daily) was regarded as more effective than gabapentin (Bril et al., 2016). Pregabalin is typically started at 25 to 75 mg once daily or in two to three divided doses. It can be titrated upwards based on response and tolerability in increments of up to 75 mg every week to 150 mg two times a day or 100 mg three times a day. A total daily dose of 300 mg is the maximum dose approved by the FDA for diabetes-associated neuropathic pain, although some patients may require 450 mg per day (Pop-Busui et al., 2017). In addition, the FDA has recently approved pregabalin for the management of neuropathic pain associated with diabetes, post herpetic neuralgia, fibromyalgia, and other neuropathic pain associated with spinal cord injury (FDA, 2019).

Tricyclic antidepressants (TCA) and serotonin norepinephrine reuptake inhibitors (SNRIs) both possess analgesic properties while the evidence of effectiveness of selective serotonin reuptake inhibitors (SSRIs) is weaker (Saart & Wiffen, 2010). The mechanism of action of TCAs is uncertain, but it is theorized that its analgesic effects are associated with their actions as serotonin and norepinephrine reuptake inhibitors. Consistent with this theory is the observation that TCAs with the greatest effect upon serotonin seem to have the greatest analgesic effect (Salerno, Browning, & Jackson, 2002). None of the current TCAs on the market are approved for pain management. However, they are widely used in the treatment of chronic pain,

with or without coexisting depression. In various randomized trials, amitriptyline and desipramine were equally effective at treating chronic painful neuropathic pain and were superior to fluoxetine or placebo (Max et al., 1992). At average effective dosage, it may take up to six to eight weeks for an adequate trial of treatment with TCA, although, onset of analgesic effects may be seen after one week of administration and typically at lower doses than typically needed for the treatment of depression (Dworkin et al., 2007; Finnerup et al., 2005). The American Academy of Neurology (AAN) (2016) categorized amitriptyline as a Level B recommendation, suggesting that it has moderate evidence and should be considered for the treatment of painful neuropathy. Recommended dosing for amitriptyline is 25 to 100 mg daily. Some experts prefer nortriptyline as a first-line agent because it has fewer anticholinergic side effects than amitriptyline (Kaur et al., 2011). TCAs are contraindicated in patients with cardiac disease, particularly conduction disturbances. Therefore, obtaining a pretreatment electrocardiogram is recommended. Consulting with a patient's cardiologist should be considered (Aiyer, Barkin, & Bhatia, 2017).

SNRIs such as venlafaxine have demonstrated significant pain relief in the management of painful diabetic neuropathy, mixed polyneuropathy, and chemotherapy-induced peripheral neuropathy in multiple randomized controlled trials (Moulin et al, 2014). Venlafaxine in particular has shown efficacy in randomized controlled trials involving painful diabetic neuropathy and mixed painful polyneuropathy at doses of 150 mg to 225 mg daily (Moulin et al., 2014). This was also confirmed in a systematic review of randomized controlled trials, which concluded that effectiveness of venlafaxine extended release formulation was only achieved at higher doses of 150 to 225 mg, but not at the lower dose of 75 mg daily (Boyle et al., 2012). In addition, the AAN (2016) suggests that venlafaxine may be added to gabapentin for better

response. Reported adverse effects of venlafaxine include nausea, somnolence, blood pressure and cardiac rhythm changes. Duloxetine, a dual serotonin and norepinephrine reuptake inhibitor, has been shown to be effective in the treatment of chemotherapy-induced peripheral neuropathy, diabetic neuropathy, fibromyalgia and in 2010 it was also approved by the FDA for treatment of musculoskeletal discomfort (Ormset, Scholz & Boomershine, 2001). In various clinical trials, patients reported improvement in their neuropathic pain as early as the first week of treatment and continued for the duration of the studies (Boyle et al., 2012; Kaur et al., 2011; Majdinasab, Kaveyani, & Azizi, 2019). The AAN (2016) recommended dosage of duloxetine is 60 to 120 mg per day, however, 120 mg daily dosing was not as well tolerated as 60 mg daily (Lunn, Hughes, & Wiffen, 2014). The most common adverse effects relating to duloxetine include nausea, somnolence, dizziness, decreased appetite and constipation. Patients are encouraged to take the drug on a full stomach to lessen the gastrointestinal side effects. Duloxetine should not be combined with other serotonin or norepinephrine uptake inhibitors (Lunn, Hughes, & Wiffen, 2014).

Multiple evidence-based sources including the AAN (2016) suggest utilizing opioids as second-line analgesics. They may be considered earlier in treatment or in selected patients whose pain is severe and intractable or in episodic exacerbations of severe pain (Bril et al., 2016). Literature suggests starting off with tramadol because it is a weak opioid agonist and also mimics some properties of TCAs in that it inhibits reuptake of norepinephrine and serotonin (Moulin et al., 2014). In randomized control trials, tramadol has shown significant benefits for the treatment of diabetic neuropathy and mixed polyneuropathic syndromes. In two small randomized trials, tramadol at an average dose of 210 mg/day was more effective than placebo in relieving pain (Cohen, Shinkazh, Frank, Israel, & Fellner, 2015). This is congruent with the

dosage recommendation by the AAN (2016). Tramadol should be used with caution in patients who are taking SSRIs due to increased risk of confusion and serotonin syndrome (Moulin et al., 2014). In several trials, oxycodone was studied and found to be more effective in neuropathic pain control than placebo. However, these trials were limited by its small size and short-term follow-up (Gaskell, Derry, Stannard, & Moore, 2016). In a clinical trial that studied the effectiveness of dextromethorphan in painful diabetic neuropathy, it was found that dextromethorphan relieved pain moderately and improved quality of life by 16% compared to placebo (Bril et al., 2016). The AAN (2016) rates opioid use for the treatment of neuropathic pain a level B recommendation with moderate evidence to support its effectiveness. However, data is insufficient to recommend one agent over the other. In a cohort study of patients prescribed long-term use of opioid for nonmalignant pain, the use of higher doses was associated with increased risk of opioid overdose. Therefore, opioid use is not recommended for ongoing management of neuropathic pain because of the potential for tolerance, addiction, and overdose (Busse et al., 2018).

In a meta-analysis of clinical trials involving use of NSAIDs for neuropathic pain, trial results show that there was no difference between NSAIDs and placebo in terms of pain or adverse events (Moore, Chi, Wiffen, Derry, & Rice, 2015). In another study of 251 participants with chronic low back pain with a neuropathic component or postherpetic neuralgia, there was no indication of any significant pain reduction with NSAIDs. Therefore, Moore et. al. (2015) concluded that there is insufficient evidence to support or refute the suggestion that oral NSAIDs have any efficacy in any neuropathic pain condition. The absence of any reliable evidence of oral NSAID efficacy is a challenge to their continued widespread use (Moore et. al., 2015).

Many evidence-based studies, however, recommend combinations of analgesics such as NSAIDs, acetaminophen, topical agents, and muscle relaxants as adjunct therapy to the above-mentioned pharmacological agents. The AAN (2016) categorized topical capsaicin and topical isosorbide dinitrate as a category B recommendation in treating painful neuropathy. Capsaicin is a naturally occurring component of hot peppers that can be utilized as a topical analgesic. The AAN (2016) recommends capsaicin 0.075% topically four times daily to the site of neuropathy. Adverse effects of capsaicin include burning, stinging, and erythema to application sites. This may lead to patient intolerance of this medication, especially in warm to hot weather (Bril et al., 2016). In a placebo-controlled pilot study of isosorbide dinitrate topical spray in patients with painful diabetic polyneuropathy, patients reported overall reduction of neuropathic pain in the control group (Snyder, Gibbs, & Lindsay, 2016). There is insufficient evidence to support use of topical lidocaine patch to treat neuropathic pain based on evidence from several controlled studies (AAN, 2016). However, it may be considered in patients who have well localized neuropathic pain as either monotherapy or likely more effectively as an adjunct to systemic medication (Baron et al., 2016). In patients who experience painful muscle spasm, antispasmodics such as cyclobenzaprine, baclofen, and carisoprodol can be useful in treating this symptom. However, their effectiveness is likely due to the result of sedation rather than muscle relaxation (Chou, Peterson, & Helfand, 2004). These medications should be used cautiously, especially when combined with other central nervous system depressant medications. Antispasmodic therapy is not supported by the AAN (2016).

Several cannabis-based products have been suggested as treatment for chronic pain, including neuropathic pain. However, evidence to suggest this treatment is conflicting. Recent randomized controlled trials evaluating medical cannabis for the treatment of neuropathic pain

found evidence to support the efficacy of low-dose, vaporized and oral mucosa delivery in reducing neuropathic pain. However, the trials were limited by their short duration, therefore, unable to determine the long-term effects of medical cannabis use (Lee, Grovey, Furnish & Wallace, 2018). Another study published in Cochrane review concluded that cannabis-based medications were better than placebo for the treatment of moderate neuropathic pain relief and psychological distress (Mucke, Phillips, Radbruch, Petzke, & Hauser, 2018). However, more participants did not feel that cannabis-based products improved their quality of life and reported adverse effects of sleepiness, dizziness, and mental problems with cannabis-based products compared with placebo. Therefore, the study concluded that the potential benefits of cannabis-based products in chronic neuropathic pain might be outweighed by its potential short- and long-term adverse effects (Mucke et al., 2018).

Naltrexone is a mu-opioid receptor antagonist that was approved by the FDA in 1984 for the treatment of opioid addiction and requires daily dosage of 50 to 100mg daily (Younger, Parkitny & McLain, 2014). Low dose naltrexone (LDN) refers to a dosage that is approximately 1/10th of the typical dose used to treat opioid addiction or 4.5 mg daily. At the low dosage level, naltrexone exhibits paradoxical properties, including analgesia and anti-inflammatory actions, which have not been reported at larger dosages (Younger, Parkitny & McLain, 2014). While LDN has been researched and used clinically for immune modulations, there have been many clinical trials that support its use for treating chronic pain syndromes such as fibromyalgia and complex regional pain syndrome (Kim & West, 2019). Many studies have found evidence to suggest that LDN plays a role in reducing the inflammatory state in the central nervous system, resulting in decreased pain (Kim & West, 2019). In a clinical trial that studied the use of LDN on fibromyalgia, 32% of patients who were given LDN reported significant improvement in pain

and improved quality of life compared to only 11% of placebo. In addition, baseline labs were collected on all patients which included erythrocyte sedimentation rate (ESR). At the conclusion of the study, it was noted that fibromyalgia patients with greater ESR at baseline had a greater response rate to the use of LDN for pain. This suggests that the effects of LDN may include the reduction of inflammation (Kim & West, 2019). It is proposed that LDN may best act as a glial cell antagonist thereby preventing their activation and subsequent inflammatory cascades. This mechanism may explain why and how LDN may function to not only treat autoimmune conditions but also mitigate pain response. Complex Regional Pain Syndrome (CRPS) is of a similar presentation to fibromyalgia although is unique in its intensity and duration (Kim & West, 2019). There are three, primary proposed physiological causes in the development of CRPS; these include inflammatory cascades, vasomotor dysfunction and central nervous system pathology. Although there are no clinical trials to date on the use of LDN for the treatment of CRPS, a 2013 case study describes its positive effect on a 17-year-old female with the diagnosis of intractable CRPS. The patient presented with a chief complaint of chronic left lower extremity pain rated 8/10 on a pain scale, unrelieved by gabapentin, ibuprofen, nortriptyline, transdermal clonidine, and trazodone. After four weeks of LDN administration at 1.5 mg daily alongside trazodone, the patient reported pain reduction to 1/10 on a pain scale. The patient continued on a 1.5 mg daily dose of LDN for the next year without any reported adverse side effects (Kim & West, 2019).

Although LDN is still an experimental therapy for chronic pain, it has demonstrated significant benefits to patients in many clinical trials (Younger, Parkitny & McLain, 2014). Its advantages also include low reported incidence of adverse side effects such as ulcers, renal insufficiency, interference with warfarin or other common medications, increased risk of heart

attack, or other common side effects that are commonly associated with NSAIDs. Furthermore, there were also no reported withdrawal symptoms when LDN was stopped or discontinued. The most common side effect reported by patients in a clinical trial was increased vivid dreams, which was seen in 37 % of participants, but decreased over time. It is unclear what mechanism may drive increased vividness of dreams. Individuals generally self-report increased effectiveness of sleep, so it is unlikely that the vivid dreams represent an adverse disruption of normal sleep patterns (Younger, Parkitny & McLain, 2014). While not observed in research studies, some physicians have anecdotally reported anxiety and tachycardia as adverse reactions to LDN. As an opioid antagonist, naltrexone in general does not provide any euphoric effects and has no reported dependence, tolerance, misuse or abuse potential (Younger, Parkitny & McLain, 2014). Unfortunately, there is lack of adequate data to support long term use of LDN. While inhibition of immune system parameters could theoretically raise the risk of infections or cancer due to decreased immunosurveillance, there have been no reports of such a side effect at any dosage of naltrexone (Younger, Parkitny & McLain, 2014). In addition, due to its non-mainstream, experimental use of LDN, it may not be covered by insurance plans. Although generic forms of naltrexone are available at a monthly out of pocket cost of approximately 35 dollars per month, there may be patients who will find this additional monthly cost prohibitively expensive (Younger, Parkitny & McLain, 2014).

Nonpharmacological treatments of chronic neuropathic pain. Non-pharmacological therapies for pain reduction encompass many modalities from physical interventions (such as physical therapy, acupuncture, massage, etc.) and psychological interventions such as cognitive behavioral therapy, psychotherapy, and patient education (Park & Hughes, 2012). There is evidence that combination therapies are more effective than any single approach. Therefore, a

multidisciplinary program is often more successful for patients with chronic pain of more diverse etiologies (Scascighini, Toma, Dober-Spielmann, & Sprott, 2008).

Electrical nerve stimulation. Electrical nerve stimulation has been shown to significantly reduce neuropathic pain. Possible action mechanisms of electrotherapy have been suggested to include local release of neurotransmitters such as serotonin, raised levels of ATP, release of endorphin and its own anti-inflammatory effects. Dorsal column activation is another mechanism of electrotherapy (Akyuz & Kenis, 2013). Transcutaneous electrical nerve stimulation (TENS) is one of the best modalities that has been shown to be effective in the treatment of neuropathic pain. It is suggested that TENS activates central mechanisms to provide analgesia. At low frequency, TENS activates the mu-opioid receptors in the spinal cord and brain stem while high frequency TENS produces its effect via the delta-opioid receptors (Akyuz & Kenis, 2013). The AAN (2016) classifies TENS as a category B recommendation, probably effective for reducing pain from polyneuropathy (Bril et al., 2016). Compared with sham treatments, TENS was effective in reducing chronic neuropathic pain by 45%. Patients also reported improved sleep. In one case study, the combination of TENS and amitriptyline was more effective than amitriptyline alone (Bril et al., 2016). However, in a Cochrane review publication of randomized controlled trials, although some patients reported neuropathic pain reduction from TENS, the quality of the evidence to support its use was low. Therefore, the authors could not confidently recommend TENS therapy as a treatment for chronic neuropathic pain (Gibson, Wand, & O'Connell, 2017).

Acupuncture. The effects of acupuncture on chronic pain have been studied in many trials for its clinical implication in the treatment of acute pain, chronic pain, fibromyalgia, and depression (Ahn, 2019). The most thoroughly studied application of acupuncture is for pain relief. According to studies conducted on the mechanism of action of acupuncture by multiple

researchers, a common theme was that acupuncture stimulates neurotransmitter effects such as release of endorphin at both the spinal and supraspinal levels (Han & Terenius, 1982). In many studies, the effect of acupuncture versus sham acupuncture in reduction of chronic pain were similar, suggesting that there is little difference in its effects on pain. It is likely that acupuncture moderates pain through a strong placebo effect (Madsen, Gøtzsche, & Hróbjartsson, 2009). However, patients continued to report that treatment benefits of acupuncture persisted over time. Another study of acupuncture versus control resulted in 90 % of patients reporting continued benefits of acupuncture up to one year after the end of treatment (Vickers et al., 2018). Treatment effects of acupuncture persist over time and cannot be explained solely by placebo effects. Major clinical implications from study conclusions suggest that patients with chronic pain may consider acupuncture as a treatment option. Referral for a course of acupuncture treatment is a reasonable option to be made by clinicians (Macpherson et al., 2017).

Behavioral therapy. Cognitive-Behavioral Therapy (CBT) is the most commonly used form of behavioral medicine approach for patients with chronic pain. CBT is widely used because it is structured, goal directed, problem focused, and time limited (Sturgeon, 2014). Patients learn cognitive training to help them understand their own response to pain. In particular, patients learn to monitor situational factors that can affect or trigger their pain and what they experience emotionally, behaviorally, and physical when they feel pain. In randomized controlled trials of patients with chronic widespread pain who participated in CBT, 72 % reported improvement in pain after six months (McBeth et al., 2012). In another meta-analysis of 23 studies of over 3,000 patients with chronic low back pain, CBT was found to be superior than usual care, waitlist control and guideline-based treatment in both short and long-term pain and reduction of disability (Richmond et al., 2015). Further research has also shown

that CBT may be more effective in women than in men (Lim et al., 2018). A trial by Lim et al. (2018) found evidence that females showed higher levels of empathy in response to affective issues and reported greater affective pain than males. This result suggests that the effectiveness of CBT is affected by the patient's level of empathy and implies that females may benefit more from the CBT intervention than men (Lim et al., 2018). Lastly, CBT is also endorsed by the U.S. Department of Veterans Affairs (VA), who have implemented national initiatives to disseminate evidence-based psychotherapy for various mental and behavioral conditions including chronic pain syndrome (Murphy et al., 2014).

Exercise and rehabilitation therapy. Neuropathy pain can affect any nerves in many body systems. In addition to pain, patients may also experience muscle weakness and poor coordination, poor reflexes, joint pain, or inability to feel temperature differences. Thus, exercise routines are major adjuvants to medical and pharmacological treatment for peripheral neuropathy. There is evidence of benefits such as functional increase in macro and microvascular beds, improved endothelial function, decreased vasoconstriction and increased blood flow, increased muscle strength, and increased cardio-respiratory resistance (Souza, Carqueja, & Baptista, 2016).

The main aims of rehabilitation are to decrease pain and amount of medication, improve dysfunction, increase quality of life and physical activity, and bring the patient's self-esteem back (Akyuz & Kenis, 2013). Strength training exercises help build muscle to improve both strength and function, which in turn can help with balance and coordination. In a neuropathic pain study of mice that were inflicted with a peripheral nerve injury in their sciatic nerve; the study concluded that after 25 days of exercises in water and swimming, the mice exhibited decreased in edema, inflammation, and peripheral neuropathic pain (Kuphal, Fibuch, & Taylor,

2007). This is supported by a recent study that showed how regular aerobic exercise increases anti-inflammatory cytokines such as interleukin 4, and the expression of M1 and M2 macrophages, which secrete anti-inflammatory cytokines at the site of injury. These effects on cytokines and macrophages promote nerve healing and analgesia in animal models of neuropathic pain (Chimenti, Frey-Law, & Sluka, 2018). In people with diabetic neuropathy, a decrease in pain was associated with increased growth of epidermal nerve fibers after a regular exercise program. Therefore, a regular exercise routine can be considered a disease modifying treatment in chronic neuropathic pain by promoting healing of injured tissues and nerves (Chimenti, Frey-Law, & Sluka, 2018). Exercise has also been shown to improve learning, memory and cognitive ability in patients with chronic neuropathic pain. In an animal study, voluntary exercise reduced depressive behaviors with concomitant increases in brain-derived neurotrophic factor and opioid receptor expression in the hippocampus (Chimenti, Frey-Law, & Sluka, 2018). Pain catastrophizing also decreases with exercise, thus reducing negative psychological factor associated pain, and improves cognitive and social factors (Chimenti, Frey-Law, & Sluka, 2018).

Occupational therapy can also be instrumental in helping a patient cope with the functional, vocational, and social impact of peripheral neuropathy. Occupational therapy can help to improve sensory-motor skills that can be crucial in regaining ability to perform executive functions such as safely and independently performing self-care activities, changing positions, and paying attention to their surroundings (Foundation for PN, 2019).

Supplements and vitamin therapy. There are many claims regarding supplements and certain indications for vitamins that have no scientific validation. However, in a case of a patient who was diagnosed with RLWD who received a vitamin infusion after being discharged from the

hospital, vitamin therapy may have contributed to the improvement of his overall physical symptoms (Howe, 2013). The article stated that the patient received two alternating intravenous infusions of phosphatidylcholine/glutathione mixture; while the other consisted of high doses of vitamin C plus B vitamins and trace minerals, sometimes referred to as a Myers Cocktail after its creator, Dr. John Myers, of Johns Hopkins University. Both infusions were prescribed by a licensed doctor (Howe, 2013). Within 14 days of starting vitamin therapy, the patient's left eye began to straighten and he experienced markedly improved vision and mental clarity. The patient's physical therapists also noticed improvements in his ataxia and ability to recognize left from right. Within three weeks of vitamin therapy, the patient was able to ambulate without two canes for support and had improved sleep and bowel/bladder functions. His use of prescription medications stopped within six months of being released from the hospital. According to Howe (2013), the patient continued to take supplements four years after being discharged from the hospital. The supplements he consistently took included fish oil, curcumin, vitamins B-1 and B-12, acetyl l-carnitine and 5HTP.

Mental Health Chronic Care

Depression and post-traumatic stress disorder. The relationship between depression and chronic illness have long been studied and the increased risk of depression in the presence of a chronic illness is recognized by the National Institute of Mental Health (2019). Although RLWD is not considered a chronic disease, it can leave devastating long-term health effects in many patients. Illness-related stress and anxiety can trigger symptoms of depression (National Institute of Mental Health, 2019). Research suggests that people who have depression and other chronic medical illness tend to have more severe symptoms of both (National Institute of Mental Health, 2019). Depression has also been linked to chronic pain. One possible explanation is the

overlap between pain- and depression-induced neuroplasticity changes (Sheng, Liu, Wang, Cui, & Zhang, 2019). It is not uncommon for patients who suffer from post-traumatic stress disorder (PTSD) to also suffer from major depressive disorder (MDD). The diagnostic criteria for diagnosing MDD and PTSD according to the diagnostic and statistical manual of mental disorder (DSM-5) have many overlapping features (Flory & Yehuda, 2015). Patients with PTSD and MDD report higher levels of distress and role impairment in life. In addition, they also exhibit higher impairment in neurocognitive functioning and are at greater risk for suicide than patients who suffer MDD or PTSD alone (Flory & Yehuda, 2015).

Depression. Depression can often be difficult to diagnose since patients can present with a variety of symptoms, such as mood, cognitive, neurovegetative, and somatic symptoms (Tylee & Gandhi, 2005). Because the optimal interval of screening has not been established, the U.S. Preventive Services Task Force (USPSTF) recommends screening all patients during routine visits and further evaluating those who score above a specified threshold (Siu & USPSTF, 2016). Screening should be completed with adequate follow-up systems in place to ensure correct diagnosis, treatment and appropriate follow-up. Adequate follow-up system refers to supporting clinical staff such as health care providers, behavioral health therapists, case managers, and care support staff that may assist in providing referral, symptom monitoring, assess medication adherence and create self-management plans. Depressions screening tools with sensitivity for primary care use include the Patient Health Questionnaire (PHQ)-9 (88%) (Levis, Benedetti, Thomas, & DEPRESSD Collaboration, 2019), PHQ-2 (83%) (Manea et al., 2016), and Beck Depression Inventory for Primary Care (97%) (Steer, Cavalieri, Leonard, & Beck, 1999).

Post-traumatic stress disorder. PTSD has also been shown in many studies to have strong associations with serious physical illness. Analysis of data from a nationally

representative epidemiological study found that 6.5 % of PTSD diagnosed in 2017 was due to a medical illness, especially in patients who have survived intensive care unit hospitalizations (Sommer, Mota, Edmonson, & El-Gabalawy, 2018). PTSD is characterized by intrusive thoughts, nightmares, and flashbacks of past traumatic events. It can also manifest as behaviors of avoidance of reminders of trauma, hypervigilance, and sleep disturbance (Sareen, 2019). Primary care patients who present with new onset symptoms of anxiety, fear, or insomnia should be evaluated for history of trauma and PTSD. In a systematic review of available PTSD screening tools, two screening instruments including the four-item PTSD screening tool for primary care (PC-PTSD-5) and the PTSD Checklist (PCL-5), demonstrated the best performance (Spoont et al., 2015). The PC-PTSD-5 has sensitivity of 69% and specificity of 92% while the PCL-5 has sensitivity of 70% and a specificity of 90% (Spoont et al., 2015). In addition, the PCL-5 can also be used to monitor the severity of a patient's symptoms over time (Blevins, Weathers, Davis, Witte, & Domino, 2015).

The diagnosis of PTSD is made after persistence of symptoms for at least four weeks following trauma. Treatment for PTSD should be initiated shortly after the patient has a positive screening (Ursano et al., 2004). The treatment choice of PTSD between psychotherapy versus pharmacotherapy should be evaluated carefully. New guidelines suggest that first-line treatment should include psychotherapy such as trauma-focused psychotherapy, CBT, or eye movement desensitization and reprocessing. Psychotherapies should be performed by clinicians who have received appropriate training (Stein, 2019a). Pharmacotherapy is a reasonable alternative treatment for patients who prefer medication or when psychotherapy is not available. The therapeutic goals of pharmacotherapy are to reduce intrusive thoughts, phobic avoidance, hyperarousal, hypervigilance, irritability, anger, and depression. According to multiple

guidelines, the first-line in pharmacological treatment of PTSD are serotonin reuptake inhibitors. Multiple randomized trials have found that patients with PTSD experience less symptoms when treated with an SSRI compared to placebo (Davidson et al., 2006). Alpha-adrenergic receptor blockers such as prazosin have been shown to reduce overall PTSD symptoms such as nightmares and sleep disturbances in some PTSD patients (Khachatryan, Groll, Booij, Sepehry, & Schutz, 2016). Other classes of medications that have been studied and used in the treatment of PTSD with varied results include benzodiazepines, tricyclic antidepressants, beta-adrenergic receptor blockers, anticonvulsants, and cannabis (Stein, 2019b).

Insomnia and sleep disturbances. Chronic insomnia is categorized by three or more occurrences per week that persist for at least three months (American Academy of Sleep Medicine, 2014). Some patients may be able to recall an initial stressful event that triggered insomnia, while others report suffering chronic insomnia without an identifiable stressor. A waxing and waning course related to psychological stressors and medical comorbidities are common and usually vary from night to night (American Academy of Sleep Medicine, 2014). Sleep disturbances are common amongst patients who suffer from PTSD. It can have many negative sequelae including worsening perception of level of stress, depression, and suicidal ideation. Commonly reported sleep disturbances in patients with PTSD include nightmares, anxiety provoking dreams, frequent awakenings, difficulty falling asleep and staying asleep (Tomas, 2014). Insomnia and sleep disturbances can last long after the initial trauma or trigger has been removed (Tomas, 2014). The diagnosis of insomnia and sleep disturbances are both established by history and patient report (Schutte-Rodin, Broch, Buysse, Dorsey, & Sateia, 2008). A sleep history should provide a detailed description of the sleep problems such as number awakenings, duration of awakenings, sleep times, length, etc. in a 24-hour period and

over one week. It should also include any sleep disturbances and symptoms of disturbed sleep (Schutte-Rodin et al., 2008).

A self-evaluation screening tool can be utilized to determine the severity of insomnia. A Pittsburgh Sleep Quality Index (PSQI) score of 5 or higher indicates significant sleep disturbance (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Chronic pain has also been associated with sleep disturbances. Chronic pain can affect quality of sleep, duration of sleep, and overall quality of life (Anderson, Araujo, Frang & Tufik, 2018). All patients should undergo a thorough examination to confirm or exclude other factors contributing to insomnia and sleep disturbances such as medical comorbidities, certain medications, and substance use. Conditions such as depression, anxiety are highly comorbid with insomnia, thus patients should be screened as part of the routine evaluation (Bonnet & Arand, 2019).

Nonpharmacological modalities to treat insomnia includes sleep hygiene, stimulus control, image rehearsal therapy (IRT), cognitive behavioral therapy for insomnia (CBTI), prolonged exposure (PE), and eye movement desensitization (EMDR) (Tomas, 2014). Cognitive behavioral therapy (CBT) is considered the first line for treating PTSD-related insomnia and sleep disturbances. IRT has also demonstrated effectiveness in reducing the intensity of chronic nightmares and negative emotions that are related to nightmares (Tomas, 2014). Pharmacological intervention should be considered second line or as an adjunct therapy in patients who do not respond to non-pharmacological modalities (Tomas, 2014). Short term use of a medication in combination with CBT is a reasonable alternative to CBT or medication alone in patients with severe symptoms, however, this combination modality has weak supporting evidence (Morin et al., 2009). In a randomized trial of patients who underwent CBT plus zolpidem versus CBT alone for six weeks, both groups had decreased sleep onset latency and decreased wake time

when compared to placebo. However, there were no significant differences in the remission rate when the two groups were compared with each other (Morin et al., 2009). When pharmacotherapy is utilized in the treatment of insomnia and sleep disturbances, selection of medication should be made with considerations to co-morbidities, side effect profiles, interaction with other medications, and cost. Many classes of medications are approved for the treatment of insomnia such as benzodiazepines, melatonin agonists, hypnotics, and doxepin. While these medications have shown multiple studies to be more effective than placebo, its adverse effects such as hypotension, dizziness, syncopal, and psychological addiction may outweigh the benefits (Buscemi et al., 2007). One medication that has shown the most evidence supporting its use in PTSD-related insomnia and sleep disturbances is prazosin (Tomas, 2014). The dosage that was studied in various trials ranged from 1 to 10 mg per day, taken 30 to 60 minutes prior to bedtime (Khachatryan et al., 2016). Prazosin should be avoided in patients with unstable angina, heart failure, arrhythmias or orthostatic hypotension (Tomas, 2014).

Social Chronic Care

Support groups. Support groups can bring together people who are going through or have gone through similar experiences. It also provides opportunity for people to share personal experiences and feelings, coping strategies, or first-hand information about a specific topic (Mayo, 2019). Support groups also enable individuals to freely express their emotions and be heard in an atmosphere of acceptance, understanding, and encouragement. Many people find that helping others in a support group helps to strengthen and empower themselves (Winchester Health, 2019). For many people, attending a support group can fill a gap between medical treatment and the need for emotional support that a “doctor-patient” or family and peer relationships cannot fulfill (Winchester Health, 2019). According to Delisle, Gumuchian, &

Kloda, (2016), benefits of participating in a support group may include feeling less lonely, isolated or judged, as well as reducing distress, depression, anxiety and fatigue. In a study published in the Mayo Clinic Proceedings that investigated the correlation between patient's psychosocial comorbidities and the effectiveness of the treatment of neuropathic pain, it was found that psychosocial support increases the efficacy of neuropathic pain treatment (Turk, Audette, Levy, Mackey, & Stanos, 2010). In addition, support groups can sometimes include guest speakers from various professions that could offer expert advice and assistance such as a healthcare provider, nurse, social worker or licensed mental health care provider (Mo & Coulson, 2014). Although online peer-to-peer support groups are also available, their benefits have been studied with varying results. Patients should take precautions if they choose to participate in an online support group as anonymity could lead to inappropriate or disrespectful comments or behaviors. In addition, participating online may result in further isolation from others (Embuldeniva et al,2013).

Case management. Case managers (CM) are considered an advanced role in nursing and they also play an integral part in providing comprehensive patient care. Case management is an important practice in nursing that aims to coordinate patient-centered care while reducing health care costs and ensuring quality of life (Joo & Huber, 2014). Under the Affordable Care Act, using registered nurses for population health management is increasing because of the complexity of care coordination. CMs have been shown to be effective in many aspects of chronic illness care. They can assist in coordinating multidisciplinary care, patient education, promote self-management support, and advocate for the patients and their families (Joo & Huber, 2014). In a study by Hudon, Chouinard, Diadiou, Lambert, & Bouliane (2015), CMs played an effective role in reducing unnecessary frequent uses of health care services. Because CMs

responded to the complex needs of a vulnerable patient population, they built a trusting relationship. Therefore, many patients preferred to contact their nurse CM rather than their primary care provider or proceeding to the emergency department (Hudon et al., 2015). Many patients were satisfied with the advocacy role of nurse CMs. Patients felt that their needs were heard and taken into consideration, allowing them to be actively involved in developing their own individualized plan of care. In addition, patients also reported that they felt less frustrated with their health care provider and more comfortable seeking care (Hudon et al., 2015).

Despite many benefits of primary case management, there are two limitations that prevent some patients from taking advantage of this service (Bravata, 2016). The first challenge is communicating the needs and benefits of CM to patients. The second challenge is the inadequate access and at times, increased out of pocket expense for the patient. Even though the cost may be minimal, for many patients on fixed incomes, this can become an obstacle (Bravata, 2016). According to the Center for Medicare and Medicaid Services (CMS) (2019), targeted case management services are provided to only specific classes of individuals. According to the Hawaii Medical Services Association (HMSA) (2017), the largest insurance provider in Hawaii, some of the conditions that warrant CM include but are not limited to serious and or chronic long-term illness such as progressive neurological conditions, and long-term needs for home healthcare services.

Community social services. The State of Hawaii Department of Human Services provides many assistance programs to qualified individuals in the community. Patients with RLWD who are considered medically disabled and on limited incomes may benefit from services such as Supplement Nutrition Assistance Program (SNAP), Aid to the Aged, Blind, and

Disabled (AABD), transportation services, and other available services. Patients are able to contact the Public Assistance Information Line at 1-855-643-1643 for more information.

Summary

Through extensive literature review and research, it was concluded that there are currently no available guidelines for post-acute care management of RLWD patients experiencing long term sequelae. Much of the current research is focused on management of the acute phase and prevention of RLWD. This lack of available information and current research on post-acute care management was also repeatedly mentioned in the Hawaii Joint Task Force on RLWD's preliminary guideline of acute RLWD. However, there is evidence-based literature to support management strategies of common and lasting physical, mental/behavioral and social symptoms and complications caused by RLWD. The available information can be synthesized into comprehensive guidelines to assist health care providers in managing care of RLWD patients with long term sequelae.

Conceptual and Theoretical Frameworks

Conceptual framework. The main components of this practice inquiry project involve development of guidelines for post-acute comprehensive care that addresses the physical, mental, and social health of RLWD patients suffering from long term sequelae. This could be achieved through multidisciplinary care through various entities. Due to lack of current guidelines for chronic care management of RLWD patients, a conceptual framework (Figure 1.) was formulated to clearly depict different aspects of health that should be addressed when caring for RLWD patients with long term sequelae.

Concept definitions. In the below map, the RLWD patient includes post-acute patients who are suffering from long term sequelae including physical, mental, and social health

sequelae. These patients should receive necessary physical health care treatments which may include pharmacologic interventions, rehabilitation, and/or complementary therapies (Howe & Jarvi, 2017). Referral to other medical specialists should also be considered (Hawaii’s Joint Task Force, 2018). RLWD patients should also receive appropriate mental/behavioral health care including screening to determine their need to meet with a behavioral health therapist and referrals to attend support groups in order to exchange stories, information, and suggestions (Hawaii’s Joint Task Force, 2018). Health care providers should also consider the benefits of involving community social workers and case managers who can further assist patients with other available community resources relative to finance such as supplemental nutrition assistance program (SNAP), transportation assistance, and prescription delivery services to benefit RLWD patients.

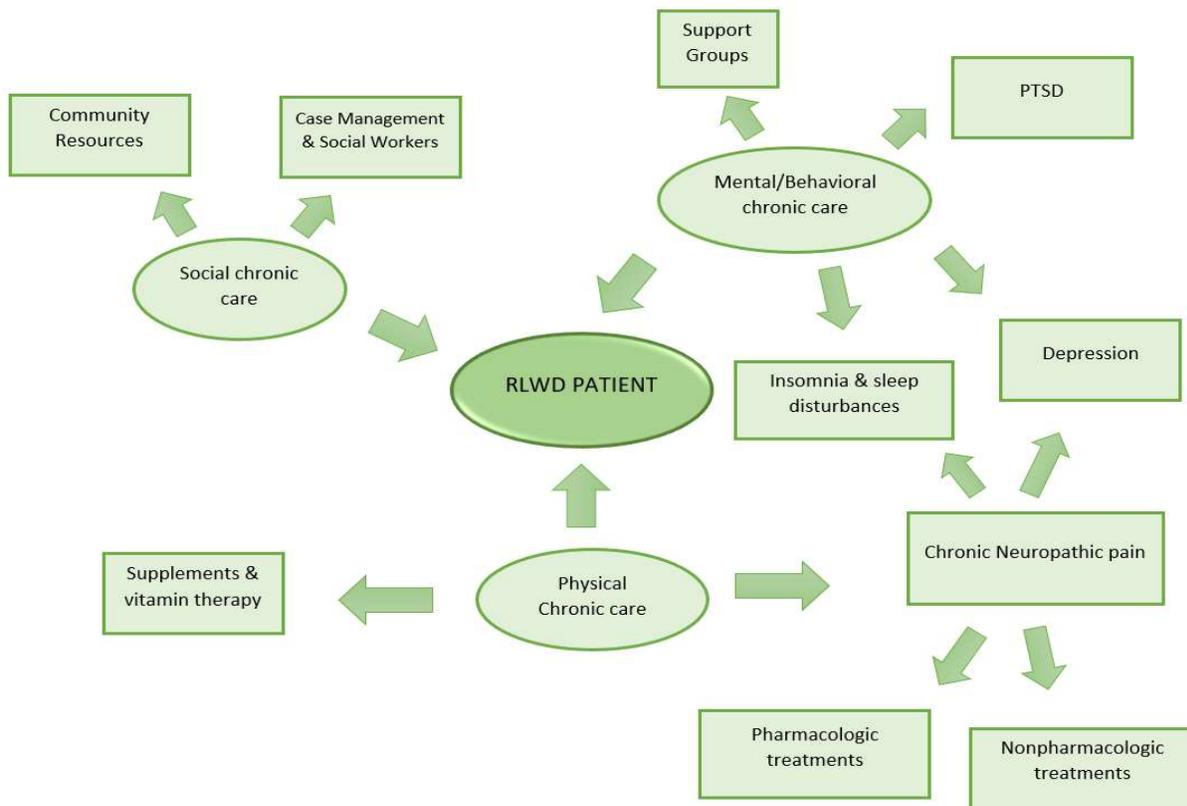


Figure 1. Post-Acute Care of RLWD Patients with Long Term Sequelae

Theoretical framework. The Adult Learning Theory proposed by Malcolm Knowles (1984) was used as the theoretical framework for this evidence-based project. Knowles' theory of andragogy identified five assumptions about adult learners: self-concept, past learning experience, readiness to learn, orientation to learning, and motivation to learning. The self-concept assumption proposed that because adults are at a matured developmental stage, they are able to take part in directing their own learning. Past learning experience refers to the array of experiences that become an increasing resource of learning. Readiness to learn involves an assumption that as a person matures, their readiness to learn becomes oriented increasingly to the developmental tasks of their social roles. In other words, as adult learners move into different social roles in life (employee, parent, spouse, etc.), their readiness to learn becomes oriented towards those specific roles. Orientation to learning involves how a learner's perspective evolves as they mature from subject-centered learning toward practical, problem-centered learning. Lastly, as a person matures, their motivation to learn becomes internal (Smith, 2002), which means that they recognize the need for improvements and become internally motivated to pursue the necessary steps/education to achieve it.

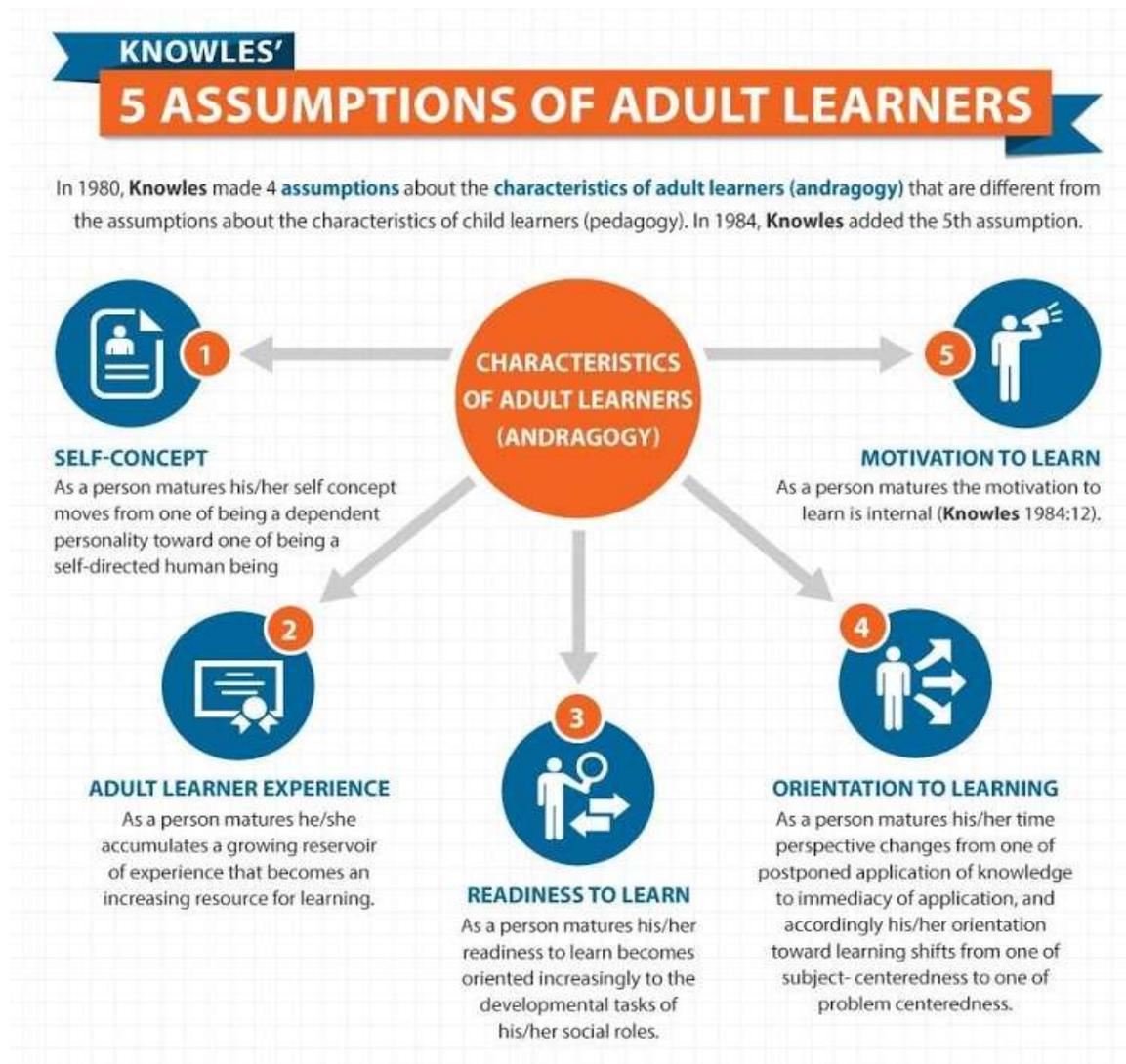


Figure 2. Malcolm Knowles' Assumptions of Adult Learners (eLearning Industry, 2014)

According to Knowles (1975), there are four principles that apply to adult learning: (1) Adults need to be involved in the planning and evaluating of their instruction; (2) Experiences, including mistakes, provide the basis of learning activities; (3) Adults are most interested in learning subjects that have immediate relevance to their career or personal life; (4) Adult learning is problem-centered, rather than content-oriented (Knowles, 1975).

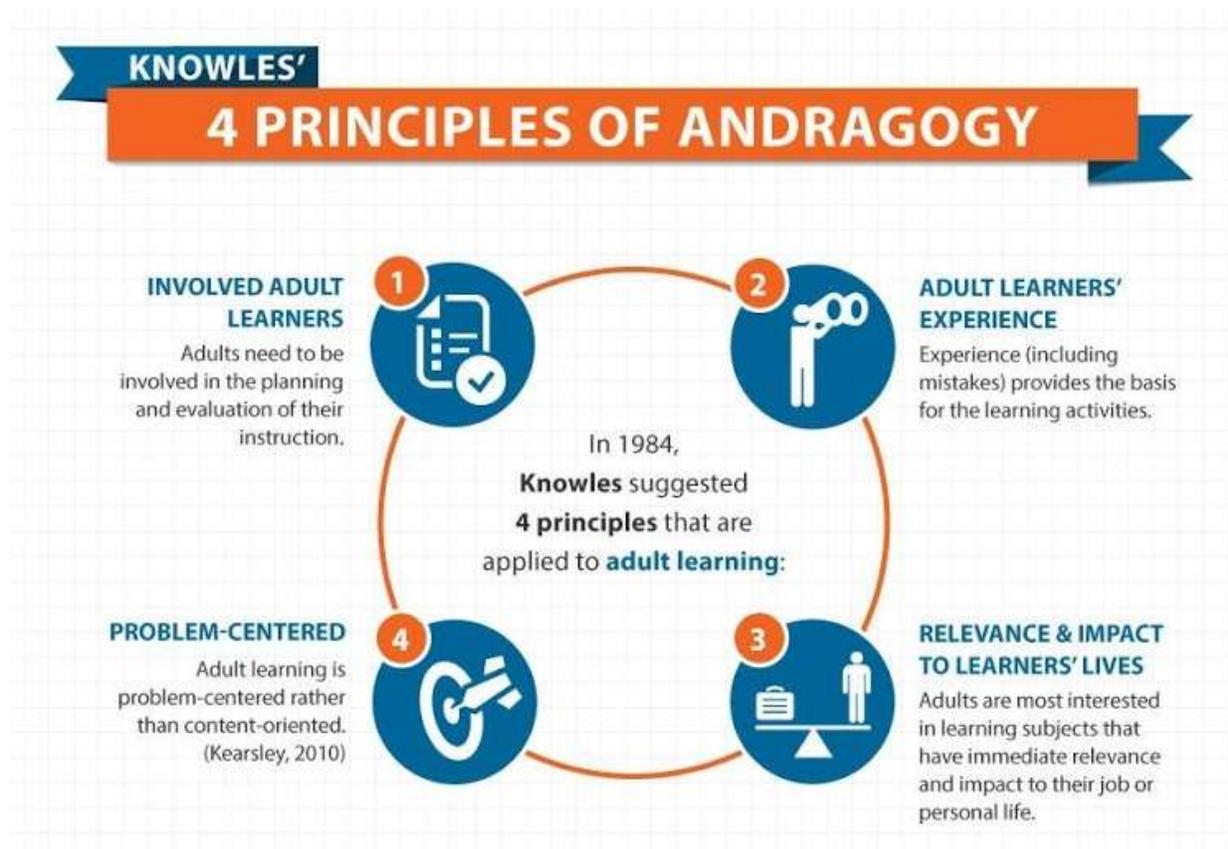


Figure 3. Malcolm Knowles' 4 principles of andragogy (eLearning Industry, 2014)

In relation to this project, mature adult learners used their past experiences including as health care providers, combined with their social role as primary care providers to internally motivate themselves to acquire new evidence-based knowledge that can directly improve their practice as well as their patient outcomes. Participants were able to select the education delivery method of their learning style and preference, either by virtual presentation and/or as printed material. By providing a baseline knowledge pre-test, adult learners would recognize the areas of post-acute care management of RLWD that they needed to improve on and aimed to increase their knowledge through the provided education. Their new level of knowledge on post-acute care management of RLWD was measured again by a post-test. By providing various evidence-based treatment options and rationales, each primary care provider participant was able to use

self-directed learning and reasoning to select treatment options that are most appropriate for their patient population. Participants were also involved in evaluating their learning by completing a post-project survey, which assessed the overall usefulness of the information presented and the methods in which the information was delivered.

Chapter 3: Project Design and Evaluation Plan

Project Design Overview

Baseline knowledge amongst primary care providers in the East Hawaii region on the topic of chronic care management of RLWD patients was assessed via a pre-test (see Appendix A). The evidence-based information obtained through extensive research on the subject was synthesized into evidence-based guidelines for post-acute, outpatient care management of patients with confirmed diagnosis of RLWD. The guidelines were then shared with participating primary care providers in the format of an educational voice-over PowerPoint presentation. Primary care providers' knowledge level of the topic was then reassessed with a post-test (see Appendix A). The effectiveness of the educational presentation as well as primary care providers' perception of the usefulness of the evidenced-based guidelines were also assessed through a post project survey (see Appendix C) at the conclusion of the project.

Recruitment flyers (see Appendix B) which briefly explained the project scope and risks versus benefits were distributed to various East Hawaii primary care offices. All participant information including those obtained from pre-tests, post-tests, and post project surveys were kept anonymous. Upon conclusion of the project, results of the project were shared with participants who were interested.

Setting

Only primary care providers in the East Hawaii region were given the opportunity to participate in the project. The East Hawaii region includes a total of four districts; Puna, South Hilo, North Hilo, and Hamakua (County of Hawaii, 2019). Recruitment flyers were distributed to the Hawaii Island Family Health Center and other private primary care offices. Participants were able to access the educational presentation electronically from their preferred location via a USB flash drive.

Participants

A convenience sample of 10 primary care providers actively practicing in the East Hawaii region were included in this project. These participants were recruited by the recruitment flyer (see Appendix B) and in person at Hawaii Island Family Health Center. An informed consent (see Appendix E) was provided to each participant interested in participating.

Inclusion criteria. Participants needed to be at least 18 years of age and a primary health care provider practicing on Hawaii Island or completed residency training in primary care. Participants had to possess either an MD, DO, APRN, or PA license. Participants needed to have a reliable computer with internet access if they chose to receive study material electronically.

Exclusion criteria. Health care providers other than a MD, DO, NP, or PA and who had not received training in primary care were excluded.

Methodology

Goal. The purpose of this pilot project was to develop care management guidelines for primary care providers to use in following up with patients who suffer from long term sequelae of RLWD. The guidelines would provide various evidence-based management strategies based on the common chronic symptoms that affect RLWD patients physically, behaviorally and

socially. The evidence-based information would assist primary care providers in providing holistic, effective and quality care to patients affected by RLWD.

Aim 1. Develop an evidenced-based treatment guideline for management of the post-acute care of patients diagnosed with RLWD.

Objective 1. Utilizing the search terms “rat lungworm disease,” “angiostromyiasis,” and “eosinophilic meningitis,” and specific long-term symptoms reported by patients who are affected by RLWD, find and critically appraise evidence for effective post-acute care management of RLWD through various components of care including physical (medication, physical, occupational, and speech therapy), social and behavioral including mental health support.

Methods. Performed rigorous literature search and review of possible treatment options based on specific symptoms RLWD patients continue to experience after they have been discharged from acute care treatment such as neuropathic pain, insomnia, PTSD, and depression.

Objective 2. Assess primary care providers’ baseline knowledge of post-acute, outpatient care management strategies of patients diagnosed with RLWD.

Methods. An assessment of primary care providers’ baseline knowledge of post-acute, outpatient care management of patients diagnosed with RLWD were performed via a pre-test (see Appendix A). The pre-test consisted of questions that explore primary care providers’ baseline knowledge about chronic care management of long-term symptoms reported by patients diagnosed with RLWD, including but not limited to various treatment modalities of chronic neuropathic pain, depression, PTSD, and insomnia.

Objective 3. Synthesize findings into evidence-based guidelines for use in the outpatient primary care settings.

Methods. Findings were synthesized into a detailed literature review that provided potential treatment options which can be utilized in the outpatient primary care setting. Information gathered through research on the subject (Objective 1) combined with data collected from the pre-test (Objective 2) were then synthesized into an educational, voice-over PowerPoint presentation aimed at offering potential treatment and management strategies of RLWD patients with long-term sequelae. A disclaimer was included that providers should evaluate these guidelines and literature sources for appropriateness in their own individualized patient care practice.

Objective 4. Assemble a panel of stakeholders including experts on the subject to evaluate the guidelines and make revisions as indicated.

Methods. Experts on the topic of RLWD were presented with the educational presentation (Objective 3) for their review. Necessary changes were made to the education presentation based on recommendations received from experts' review.

Aim 2. Provide education to primary care providers regarding best practices for managing post-acute, follow-up outpatient care of patients with confirmed diagnosis of RLWD.

Objective 1. Implement the educational virtual presentation of the evidence-based guidelines with primary care provider participants.

Methods. A voice-over education PowerPoint presentation (Aim 1, Objective 3) was distributed to primary care provider participants via email or USB flash drive, whichever method they preferred. Participants were allotted up to four weeks to view the presentation as many times as they chose. In addition to the presentation, participants were also provided with the literature review of the various strategies of post-acute care management of RLWD patients

including physical (medication, physical, occupational, and speech therapy), social and behavioral including mental health support.

Objective 2. Evaluate the effectiveness of the virtual presentation and primary care provider participants' perceptions of the potential usefulness of the evidence-based guidelines.

Methods. After each participant completed reviewing the educational presentation, they were asked to complete an anonymous post-test and post-presentation survey (see Appendix A & C). The post test was aimed at assessing the amount of knowledge about chronic care management of RLWD acquired through the presentation. The survey was aimed at evaluating the participants' perceptions of the presentation as well as its potential usefulness and likelihood of adopting these care management strategies when caring for RLWD patients with long-term sequelae in an outpatient setting. Participants were given a hard copy of the test and survey to complete after they have viewed the presentation. Personal identifiers were not included on the post-test and survey. Participants contacted the study coordinator for pick up once they completed filling out both post-test and post-project surveys.

Data Collection and Analysis Methods

Data analysis in this pilot project included assessing the baseline knowledge level of primary care provider participants in East Hawaii in regards to RLWD and the effectiveness of the educational project intervention in increasing participant knowledge on the topic of caring for RLWD patients with long-term sequelae in an outpatient setting. Quantitative data gathered included the total number of participants who successfully viewed the entire educational presentation and the pre/post test scores (see Appendix A). Qualitative data was collected through a post-survey (see Appendix C) that aimed to assess participants' perception of the presentation and their professional opinion on the potential usefulness of the evidence-based

information provided. The pre/post tests were scored manually with numbers of correct answers out of a total possible 31 points. The post-survey included open ended questions (see Appendix C) that were aimed at better understanding the potential utility of the RLWD chronic management strategies for primary care providers. The analysis of the post-project survey results was accomplished through categorizing data that occurred most frequently in the Likert scale questions and qualitative analysis of the open-ended answers for common themes. Descriptive statistical analysis was used for the post project survey demographic variables such as education level, type of professional license, and years of experience in primary care practice. See results below.

Protection of Human Subjects

Approval from the University of Hawaii Internal Review Board was granted to the project as an exempt application (see Appendix F). Persons meeting all project inclusion criteria and who wished to participate were provided with an informed consent prior to completing the anonymous pre-test (see Appendix A). Participants were not required to provide any personal information other than a valid email address if they elected to receive the Pre/Post tests, post survey and PowerPoint presentation via email. All data from the project was stored on a password protected computer. The study coordinator was solely responsible for distribution, collection, scoring and analyzing the results of tests and surveys. Hard copies of tests and surveys were kept in a separate file in a locked cabinet that only the study coordinator and principal investigator had access to. Other agencies that had legal permission had the right to review the project records. The University of Hawai'i Human Studies Program has the right to review records for this project. All of the participants were informed of the purpose and procedures of the project. Informed consent was reviewed and given to each participant to

ensure understanding of the project and participant rights, and to address confidentiality of the project information (see Appendix E).

Study Personnel

The principal investigator of this project was Project Committee Chair, Dr. Patricia Hensley, DNP, FNP-BC. Dr. Hensley, along with the study coordinator, Chayata Otsuka, BSN, RN, collaborated on this project and implemented the project in its entirety. Otsuka is a Doctor of Nursing Practice candidate at the University of Hawaii at Hilo and worked with and under the guidance and supervision of the Practice Inquiry Project Committee. Otsuka is a registered nurse and has been working within a health care system on Hawaii Island since 2016. She has cared for multiple patients affected by RLWD. She has received appropriate training on Human Subject Research and is certified through the CITI Program (see Appendix D). Otsuka was responsible for recruiting, enrolling and consenting participants for the project. With reviews and guidance from the expert stakeholders on the project, Otsuka created the educational virtual presentation of the comprehensive guidelines. In addition, she also facilitated the evaluation process and analyzed project results.

Project Budget

The projected budget for this project was \$1,210.00. This amount was broken down into seven categories as follows: recruitment flyers, consent forms, surveys, travel costs, miscellaneous supplies, virtual presentation production, and handout materials. The detailed breakdown and cost justification for each category are listed below.

Resource	Qty	Projected Cost	Funding Source	Justification
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Recruitment flyers	50 pages	\$50.00	Hilo Medical Center Medical Staff Scholarship	Production, design, printing hard copies of recruitment flyers.
Pre/Post Test production	40 copies	\$40.00	Hilo Medical Center Medical Staff Scholarship	Production, design, printing hard copies of consent forms.
Surveys	20 copies	\$20.00	Hilo Medical Center Medical Staff Scholarship	Production, design, printing hard copies of surveys. Possibly other costs relating to online survey modalities.
Travel costs	N/A	\$300.00	Hilo Medical Center Medical Staff Scholarship	Cost of travel to various areas of East Hawaii for recruitment, observations, data collection and collaborating with participants
Misc. supplies	N/A	\$200.00	Hilo Medical Center Medical Staff Scholarship	Miscellaneous supplies to be used throughout project such as stationary, pens, paper, toner, etc.
Virtual presentation	N/A	\$400.00	Hilo Medical Center Medical Staff Scholarship	Equipment and software to create a virtual presentation of the guideline for ease of access for participants.
Handout material	20 copies	\$200.00	Hilo Medical Center Medical Staff Scholarship	Production, design, and printing of the evidence-based guideline to be distributed to various health care providers.
	Total	\$1,210.00		

Project Timeline

The recruitment process was projected to begin on January 15, 2020. At this time, participants who expressed interest in participating in the project were given informed consent for their records and provided their intent to participate by completing the pre-test. Completing the extensive literature review was projected to be complete by December 7, 2019. The

evidence-based information obtained was synthesized into an educational, voice-over PowerPoint presentation by January 10, 2020. The presentation was then submitted to a panel of experts on the topic for their review and input. The experts' recommendations and comments were reviewed and necessary changes made to the PowerPoint by January 31, 2020 at which time distribution of the presentation to participants began. The participants had until February 29, 2020 to view the presentation and complete and return the post-test and the presentation evaluation survey to the study coordinator. A detailed project timetable is provided below.

Aim & Objective	Task (s)	Completion Date
Aim 1 Objective 1	Research and literature review	December 7, 2019
Aim 1 Objective 2	Begin recruitment and pre-test	January 15, 2020
Aim 1 Objective 3	Synthesize findings into PowerPoint	January 10, 2020
Aim 1 Objective 4	Submit for expert reviews	January 10, 2020
Aim 2 Objective 1	Implement educational presentation	January 31, 2020
Aim 2 Objective 2	Collect all post-test and surveys	February 29, 2020

Chapter 4: Results

In this chapter, objective project results and analysis of project results will be discussed. The results of the aims and objectives are summarized with the appropriate data analysis.

Results

Aim 1. Develop an evidenced-based treatment guideline for management of the post-acute care of patients diagnosed with RLWD.

Objective 1. Utilizing the search terms “rat lungworm disease,” “angiostrongyliasis,” and “eosinophilic meningitis,” find and critically appraise evidence for effective post-acute care

management of RLWD through various components of care including physical (medication, physical, and occupational therapy), social and behavioral including mental health support.

Literature including case studies on the disease produced through the database search were critically appraised and examined thoroughly. Findings from the literature review are described under the literature review section above.

Objective 2. Assess primary care providers' baseline knowledge relative to management of post-acute, outpatient care of patients diagnosed with RLWD.

Out of the total 10 primary care providers who participated in the study, four out of 10 (40%) were advanced practice registered nurses (APRN), specifically three family nurse practitioners (FNP) and one adult-gerontology nurse practitioner (AGNP). The remaining six out of 10 participants (60%) were family medicine trained primary care providers. All three of the FNPs completed the doctor of nursing practice degree while the AGNP completed a master of science in nursing. Of note, the AGNP had also been practicing in the pain management specialty for the past two years in addition to their experience as a primary care provider. Out of the 10 participants, five of the physicians (50%) were medical residents practicing at Hawaii Island Family Health Center (HIFHC). See further demographic results under Aim 2 below.

All 10 participants were given the same pre-test (see Appendix A) to complete. There was no time limit, as long as participants completed the pre-test prior to viewing the presentation. All 10 participants completed the pre-test with scores ranging from 19 to 27 points, with a mean of 22.1 points out of 31 (71.3 %) total points possible (see Figure 4 below).

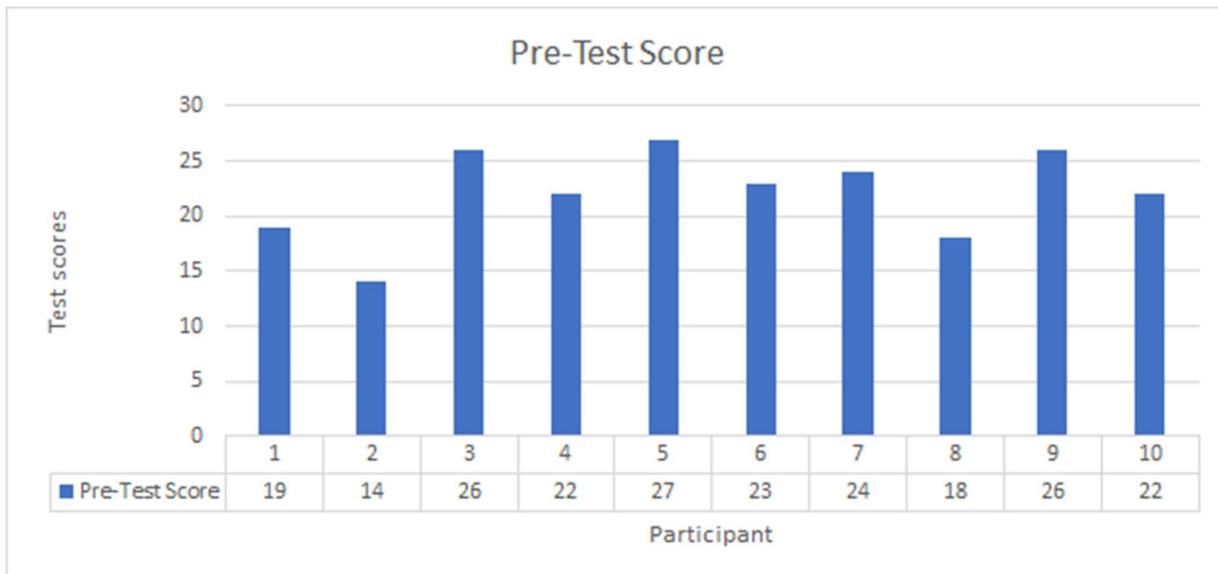


Figure 4. Pre-test scores

Objective 3. Synthesize findings into evidence-based guidelines for use in the outpatient primary care settings.

Evidence-based information obtained through the extensive literature review was synthesized into a RLWD treatment guideline that was categorized as follows 1) Physical chronic care 2) Mental health chronic care, and 3) Social chronic care. The physical chronic care section focused mainly on the management strategies of chronic neuropathic pain. Since literature suggests that optimal patient outcomes often result when multiple approaches are utilized through a multidisciplinary care team (Driscoll, & Kerns, 2016), many treatment modalities, pharmacological and non-pharmacological, were included in this section. As described in detail in the literature review, pharmacological treatments included GABA-receptor agonists, TCAs, SSRIs, SNRIs, low dose naltrexone, antispasmodics, cannabinoid products, and opiates while the nonpharmacological treatment options discussed included CBT, TENS, and rehabilitation therapy. Much of the information obtained for this section came from the AAN's (2016) treatment guideline for neuropathic pain, therefore, almost all of the treatment options

discussed in this section of the ROL are accompanied by the AAN's categorical grade based on evidence of effectiveness, with grade A being most effective. Furthermore, medication dosage recommendations were provided based on results of randomized controlled trials reported in the literature. A separate section on vitamin and supplement therapy was included in the guideline. Information in this section was obtained primarily through a literature search as well as an informal interview of a local naturopathic medicine physician who had been treating many RLWD patients for many years.

The mental health chronic care section of the guideline included evidence-based screening and treatment options for psychological and behavioral diagnoses common amongst those that suffer from chronic illnesses including chronic pain. Such common diagnoses include depression, PTSD, and sleep disturbances which can occur as long-term sequelae of RLWD (Hawaii's Joint Task Force, 2018). Various evidence-based psychotherapy and pharmacotherapeutic modalities were included (Blevins, Weathers, Davis, Witte, & Domino, 2015; Davidson et al., 2006; Flory & Yehuda, 2015; Khachatryan et al., 2016; Levis, Benedetti, Thomas, & DEPRESSD Collaboration, 2019; Manea et al., 2016; Mersky & Bogduk, 1994; Morin et al., 2009; National Institute of Mental Health, 2019; Sheng et al., 2019; Siu & USPSTF, 2016; Spont et al., 2015; Steer, Cavalieri, Leonard, & Beck, 1999; Stein, 2019b; Tomas, 2014; Tylee & Gandhi, 2005). The social chronic care section contained information on evidence-based indications and benefits of support groups, CM, and available local community resources (Bravata, 2016; Embuldeniya et al., 2013; Hudon et al., 2015; Joo & Huber, 2014; Mo & Coulson, 2014; Turk et al., 2010; Winchester Health, 2019).

Objective 4. Assemble a panel of stakeholders including experts on the subject and primary care providers with experience in treating RLWD to evaluate the guideline and make revisions as indicated.

The expert reviewer of the project was the Chief Medical Officer (CMO) of HMC. The HMC CMO has treated many cases of RLWD in the state and has been heavily involved in developing diagnosis and acute care treatment protocols (Hilo Medical Center, 2020). The HMC CMO reviewed the guideline and the PowerPoint presentation that was implemented in the project as part of Aim 2. He provided comments for revisions and additional foci of the disease that should be included and further researched. He also provided recommendations for future studies that would tremendously benefit RLWD patients with long-term sequelae.

Other expert stakeholders on this project included the HIFHC's medical director who also reviewed the guideline and presentation and provided comments and suggestions for improvement. The HIFHC's medical director published an article titled "In Suspected Eosinophilic Meningitis Cases, Ask About Recent History of Travel to Hawaii" in the *Consultant* medical journal along with the HMC CMO (Walker, Holmes & Martell, 2018).

Aim 2. Provide education to primary care providers regarding evidence-based strategies for managing post-acute, follow-up outpatient care of patients with confirmed diagnosis of RLWD.

Objective 1. Implement an educational virtual presentation utilizing the evidence-based guidelines.

A voice-over PowerPoint presentation was created using evidence-based information from the ROL guideline. The presentation consisted of 33 voiced over slides and one slide listing references used in the presentation. The presentation was pre-loaded onto USB flash

drives and given to each participant along with the project instructions, ROL guideline, post-test, and post project evaluation survey in a sealed manila envelope. Study packets that were given to medical residents were marked with a letter R on the back of the envelope. Participants had the option of dropping off the completed and sealed packets to the medical unit at HMC or having them picked up from their place of employment by the student investigator.

Objective 2. Evaluate the effectiveness of the virtual presentation and primary care provider participants' perceptions of the potential usefulness of the evidence-based guidelines.

Quantitative Findings

As part of the project instructions, participants were directed to complete a post-test and a project evaluation survey after they viewed the entire presentation. All 10 participants (100%) answered "yes" to having viewed the entire presentation and completing the post-test and post project evaluations. The post test scores ranged from 25 to 30 points, with a mean score of 27.6 out of possible 31 (89%) points. Each participant showed improvement in their post-test score compared to their respective pre-test scores (see Figure 5 below). Using the Wilcoxon signed rank test, results showed improvement from pre-test baseline knowledge scores (mean = 22.1 out of 31 points possible or 71.3%) to post-test knowledge scores (mean = 27.6 out of 31 points possible or 89%) with an average gain of 5.5 points (17.7%) (see Figure 6 below).

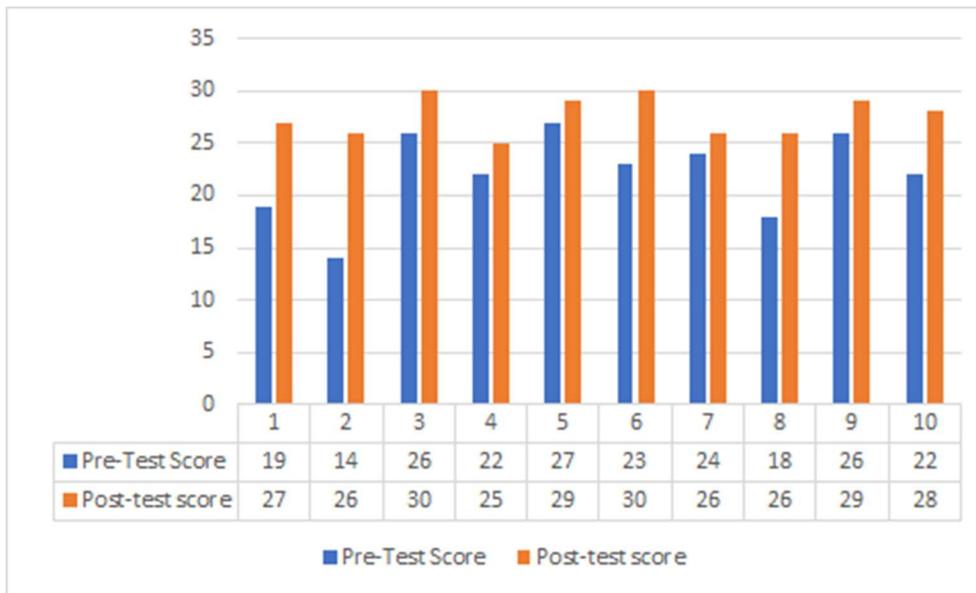


Figure 5. Post-test scores with overall improvement compared to pre-test scores



Figure 6. Wilcoxon signed rank test results of knowledge gained – mean scores.

The evaluation of the presentation and its potential usefulness in practice were achieved through a post-presentation survey (see Appendix C). In addition to demographic information, this survey consisted of four sections: 1) General, 2) Time, 3) Method and Application, and 4) Practice Implications. Specific questions and results are described next below.

Q1. What is your highest education level?

Q2. What is your professional license type?

Nine out of ten participants (90%) reported that they completed doctorate degrees while one participant (10%) completed a masters degree as their highest education level. Four participants held APRN licenses (40%), one participant held a Doctor of Osteopathic Medicine (DO) license (10%) and five participants (50%) held Doctor of Medicine (MD) licenses (see Figure 7 below).

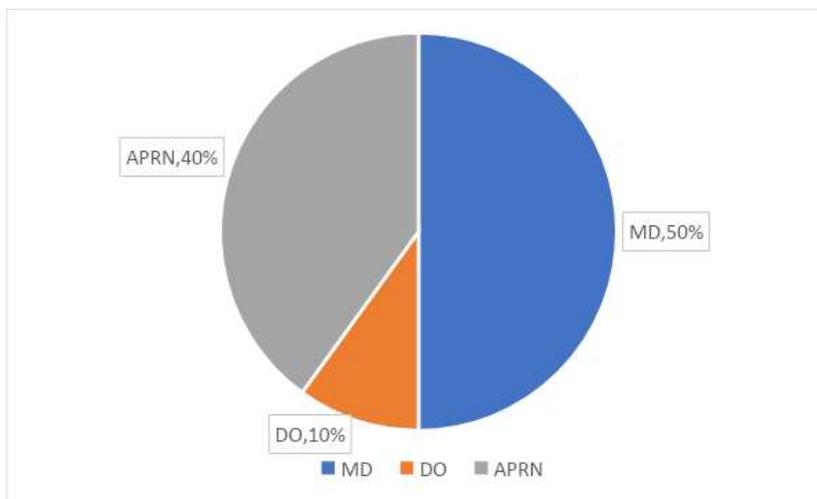


Figure 7. Q2. What is your professional license type?

Q3. Experience in primary care (number of years)?

Seven participants (70%) reported that they had 0 to 3 years of experience in primary care. All of the medical residents fell into this category. Two participants (20%) reported having 4 to 10 years in primary care, while one participant (10%) reported having over 20 years of experience in primary care (see Figure 8 below).

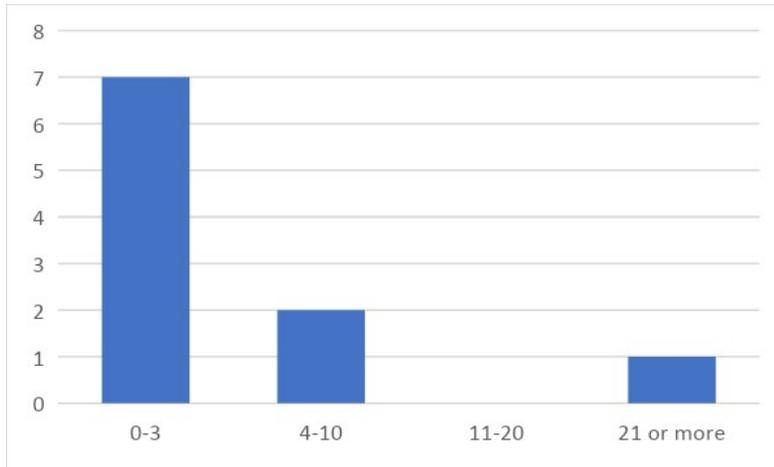


Figure 8: Experience in primary care (number of years)?

Q4. Have you cared for patient(s) with RLWD?

Q5. Prior to viewing the presentation, how would you rate your pre-existing knowledge on the topic?

Six participants (60%) stated that they had cared for patient(s) with RLWD and four participants (40%) answered “no” to having cared for patients with RLWD. Nine of the 10 participants (90%) rated their pre-existing knowledge of the topic as “somewhat familiar” while one participant (10%) rated themselves “novice.”

Q6. Did you view the entire RLWD chronic care presentation?

Q7. If no, please describe why you were not able to complete

Q8. How long did you take to view the presentation?

All ten participants (100%) responded that they viewed the entire presentation, making Q7 irrelevant. Four participants (40%) stated that they viewed the presentation in less than one hour, five participants (50%) spent between one to two hours, and one participant (10%) spent

over three hours to view the presentation. Data analysis did not reveal a relationship between time spent viewing the presentation and post-test scores.

Q9. On a scale of 1 to 5 where 1 is “Very difficult” and 5 is “Very easy,” was the presentation easily accessible?

Q10. On a scale of 1 to 5 where 1 is “Not effective” and 5 is “Very effective,” was this presentation effective in increasing your knowledge about chronic care management of RLWD patients?

Q11. On a scale of 1 to 5 where 1 is “Not at all” and 5 is “Significant,” how would you rate the usefulness of the knowledge gained from this presentation?

Q12. On a scale of 1 to 5 where 1 is “Not at all” and 5 is “Very interested,” how much did the presentation facilitate your interest in caring for RLWD patients?

In the third section of the survey entitled , “Method” and “Application”, all four questions were presented in the form of a Likert scale. All ten participants (100%) responded that the presentation was “very easy” to access. Nine participants (90%) responded that the presentation was “Very effective” in increasing their knowledge about chronic care management of patients with RLWD and one participant (10%) responded that the presentation was “somewhat effective.” Nine participants (90%) reported the usefulness of the knowledge gained from the presentation as “significant” while one participant (10%) rated it “somewhat useful.” Lastly, all ten participants agreed that the presentation either “very much” (70%) or “somewhat” (30%) facilitated their interest in caring for RLWD patients. Data analysis showed that there was no relationship identified between the years of experience in primary care and these post-test measures. See Figure 9 below.

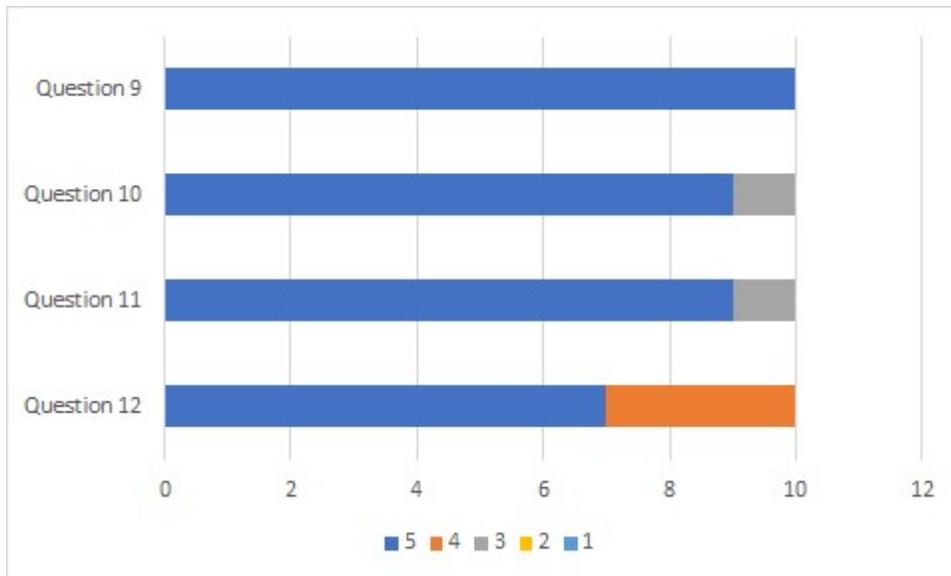


Figure 9. Tabulated Likert scale answers to questions 9 to 12

Q13. Did you learn new information about the management strategies of RLWD patients with long-term sequelae that you did not know about before?

All ten participants (100%) agreed that they learned new information about the management strategies of RLWD patients with long-term sequelae that they did not know about before.

Q16. How likely are you to implement these strategies in your medical practice?

Seven participants (70%) responded that they would “definitely” implement the treatment strategies they learned from the presentation in their medical practice when treating patients with long-term sequelae of RLWD. One participant (10%) reported that they are “very likely” to implement, and two participants (20%) felt they “maybe” would implement the learned strategies. None of the participants (0%) reported that they are not likely to implement these strategies. See Figure 10 below.

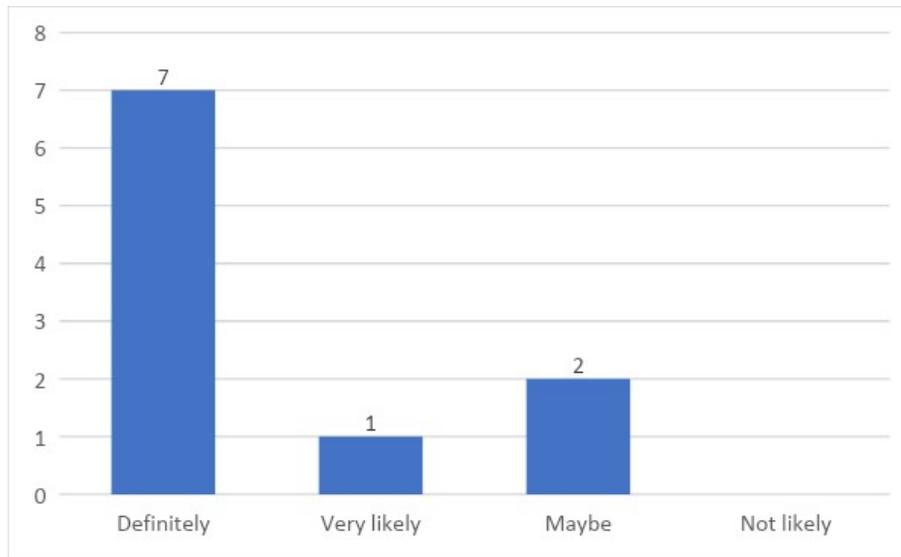


Figure 10. Tabulated results from Q16. How likely are you to implement these strategies in your medical practice?

Q17. Would you recommend this presentation to others who wish to learn about chronic care management strategies of RLWD patients?

Nine participants (90%) answered “yes” when asked if they would recommend this presentation to others who wish to learn more about chronic care management strategies of RLWD patients. One participant (10%) stated that they would not recommend this presentation to “other healthcare providers because the information was too basic for medical education level.” See Figure 11 below.

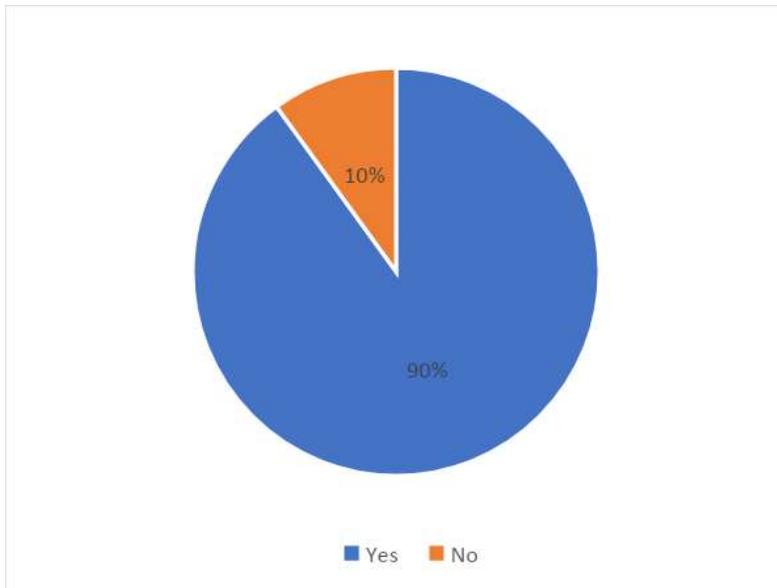


Figure 11. Q17. Would you recommend this presentation to others who wish to learn about chronic care management strategies of RLWD patients?

Q19. After viewing the presentation, how would you rate your current level of knowledge on the topic?

Two participants (20%) rated their knowledge level of the topic “somewhat familiar,” while the majority of participants (70%) rated their knowledge level as “very familiar.” Only one participant (10%) rated their knowledge level of the topic as “expert.” Figure 12 below shows comparisons between the participants' self-rated knowledge level of the topic prior to viewing the presentation and their self-rated knowledge level after viewing the entire presentation.

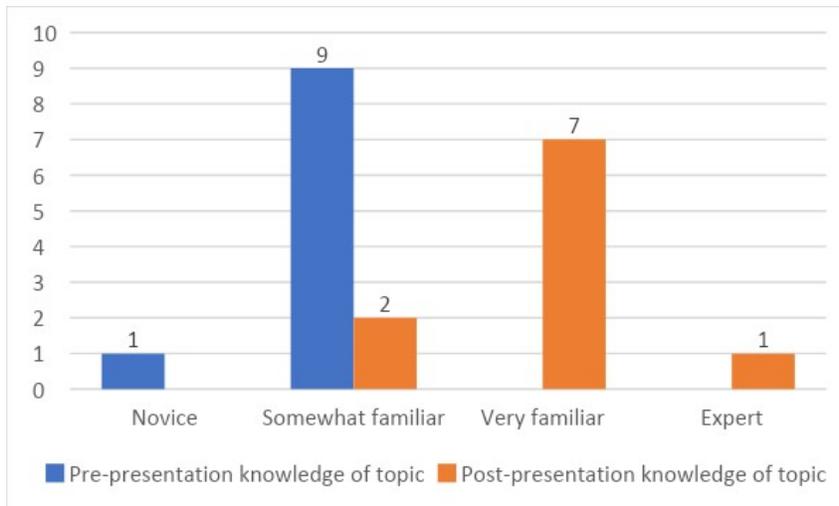


Figure 12. Bar graph comparing pre vs. post presentation knowledge of the topic

Qualitative Findings

Question 14 of the post survey asked participants which topics from the presentation they found to be most useful. Two participants (20%) felt that the information about the various types of long-term sequelae that RLWD patients might suffer from and the possible treatment options for the various sequelae suffered were the most useful. Eight participants (80%) found the various treatment modalities presented for chronic neuropathic pain to be most useful. Out of the eight participants who found treatment modalities for chronic neuropathic pain to be most useful, five participants (62.5%) found non-pharmacological interventions most useful, two participants (25%) found pharmacological interventions most useful, and one participant (12.5%) felt that the most useful topic was the use of low-dose naltrexone specifically.

Question 15 asked participants *Which topic of the presentation did you find least useful?* Nine participants (90%) answered this question with either “none” or N/A,” while one participant (10%) felt that they found treatment modalities discussed in the presentation that are not readily available in Hilo to be the least interesting and least useful topics, although the participant did not state which treatment modalities those were. However, according to the

experts consulted in reviewing the guidelines and presentation, all treatment modalities are indeed readily available on Hawaii Island.

Q17. If you did not find the information helpful, please provide future topic(s) about RLWD you would like to learn about.

Eight participants either responded “N/A” to this question or left the answer area blank. One participant stated that they would like to learn more about the initial work-up and acute phase treatment of RLWD. This answer is somewhat irrelevant since the purpose of the presentation was aimed at educating primary care providers about the long-term sequelae of RLWD and various management strategies for these chronic symptoms as there are no current evidence-based guidelines on this specific topic. Another participant stated that they would like to learn more about specific case studies of local RLWD patients and specific treatments that have been attempted locally along with its results. Indeed, since there are little publications on the topic of chronic care management of RLWD, case studies on evidence-based chronic management strategies of RLWD and treatment results would be beneficial for all health care providers. The lack of such available studies only solidifies the fact that this is a neglected aspect of RLWD care and that further research and studies are indicated.

Q20. Please provide other feedback or comments

Again, eight participants either answered “N/A” or left the answer area blank. One participant commented that the presentation contained “good and useful information” while another participant commented “well done presentation, very useful information.”

Chapter 5: Recommendations and Conclusions

Discussion of Results

The purpose of this project was to develop care management guidelines for primary care providers to use in caring for patients who suffer from long-term sequelae of RLWD. The evidence-based information will assist primary care providers in providing holistic, effective and quality care to patients affected by RLWD. A literature search and needs assessment performed revealed that this is currently a neglected aspect of care for this particular disease. In piloting this project, results showed that participating primary care providers gained knowledge about the long-term sequelae of the disease and various evidence-based management strategies that are available. All participants (100%) reported that they learned new information about chronic care management of RLWD. Nine out of ten participants (90%) felt that the information provided was significantly useful and would recommend the guidelines to others who wish to learn about chronic care management strategies of RLWD. Furthermore, eight primary care provider participants reported that they would either “definitely” (70%) or “very likely” (10%) implement these treatment strategies in their medical practice. Chronic neuropathic pain and possible treatments was the most useful topic of the presentation as reported by 8 out of 10 participants (80%).

These findings are not surprising considering the lack of literature covering the topic of long-term sequelae of RLWD. According to extensive research performed on the topic of RLWD, much of the literature available only focuses on the early diagnosis and acute treatment of the disease. Primary care providers who are interested in the chronic aspect of the disease would not be able to find an evidence-based treatment guideline like those available for other chronic diseases such as hypertension and diabetes. Another possible explanation for the project

findings could be that many of the participants have limited medical practice experience in general. Some of the participants are also new to the State of Hawaii, and most have not taken care of RLWD patients who experience chronic sequelae. Thus, any information regarding RLWD would be considered useful. Regardless, we feel strongly that because 90% of participants felt that the information provided was significantly useful and would recommend the guidelines to others, the guideline would tremendously help improve patient outcomes and further spread the awareness about the chronic aspect of RLWD.

Impact of Results on Practice

The results showed that participating primary care providers, both with and without experience in caring for patients with RLWD, learned new information regarding chronic care management of long-term sequelae of RLWD. The presentation of the evidence-based information would provide knowledge to other primary care providers in the Hawaii communities where RLWD is prevalent, especially in the East Hawaii region. If more primary care providers are aware of the long-term health effects of RLWD and strategies to manage them, patients who suffer from these sequelae would have improved overall health outcomes as well as optimal recovery.

Strengths and Limitations

One of the major strengths identified in this project was the increased level of knowledge gain for all participating primary care providers and their recognition that there are patients who suffer from the long-term health effects of RLWD. The evidence-based guidelines provided various treatment strategies, pharmacological interventions and non-pharmacological interventions, to specific chronic symptoms experienced by RLWD survivors. The guideline also provided alternative therapies such as vitamin and natural supplements, which many RLWD

survivors may prefer over other medications. Participants felt that the presentation was easy to follow and contained useful information that many of them would implement in their medical practice.

A limitation of this project included the small sample size. This could be the result of the lack of incentives to participate in the project and the limited timeframe for participant recruitment prior to project implementation. In addition, many of the participants are primary care providers who have less than three years of practice experience. Although the evidence-based information included in the presentation were treatment specific to the symptoms of the long-term sequelae of RLWD, many of the participants had not cared for RLWD patients directly or long enough to provide substantial evidence to determine that these should become part of the standard practice for this disease. Had participants had more years of practice experience, perhaps they would have indicated learning less and/or finding the guidelines less useful.

Dissemination Plans

Results of the project should be shared at future RLWD support group meetings and/or future conferences about RLWD. Publishing the results of this project would also bring more attention to the chronic care aspect of RLWD, which has been neglected. The evidence-based guidelines created in this pilot project could be implemented in the management of RLWD patients who could be monitored to determine the benefits and response to each of the treatment options discussed. As new information emerges about effective treatments of RLWD chronic symptoms, the guidelines shall keep expanding. This will in turn result in improved health outcomes of RLWD patients. Collaborating with other researchers and experts who are

interested in this aspect of the disease could further the research and ultimately improve the health outcomes of RLWD patients.

Future Implications for Practice

Many organizations and health care provider experts in the community have contributed to the project, either by providing support, insights, comments, and reviews of the guidelines or by allowing recruitment of participants. Current literature on RLWD mainly focus on the acute manifestations and treatments of the disease. Long-term sequelae of RLWD is evident by many patients who suffer from it, yet, research and literature on this is very limited. Further study on the management of long-term sequelae of RLWD would improve the quality of life for RLWD patients as well as their caregivers. It is also important that primary care providers who are not familiar with RLWD or are new to our Hawaii community familiarize themselves with the chronic health effects of RLWD, especially those who are practicing in endemic regions such as East Hawaii including in the lower Puna District. The evidence-based guidelines and presentation could serve as a basic introduction to the chronic care aspect of RLWD.

Conclusion

RLWD can be a devastating disease to both patients and caregivers. The disease not only affects patients during the acute phase, but anecdotal experience in Hawaii has shown that many patients also develop residual chronic symptoms that can last many years. The long term sequelae of the disease has been shown to affect the victims' activities of daily living as well as financially with prolonged health care needs, plus added loss of income for the victim and their caregivers (Howe & Jarvi, 2017). The evidence-based information and the implementation of the educational presentation amongst primary care providers in the community showed it was beneficial in helping primary care providers learn more about the long-term health effects of the

disease and that many different strategies can be used to manage and provide holistic, effective, quality care to patients affected by RLWD.

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Appendix A

Post-Acute Care Management of Patients with Angiostrongyliasis: A Guideline in Caring for Patients Who Suffer Long Term Sequelae of Rat Lungworm Disease (RLWD)

Pre/Post Test

Disclaimer: By completing this test, you have consented to participate in this Practice Inquiry Project on a voluntary basis. You may withdraw from the project at any time without penalty. This is a confidential and anonymous assessment.

1. What is the maximum daily dose of gabapentin for the treatment of chronic neuropathic pain?
 - a. 9000 mg in four divided doses
 - b. 3200 mg in three divided doses
 - c. 3600 mg in three divided doses
 - d. 2400 mg in three divided doses
2. True or False: Research has shown that virtual participation in a support group has demonstrated superior benefits compared to an in-person group due to less possibility of bullying?
 - a. True
 - b. False
3. Limitations that may prevent patients from utilizing primary care case management include (select all that apply):
 - a. Transportation to case manager's office
 - b. Understanding the benefits of case management
 - c. Fear of losing privacy in their own home
 - d. Possible out of pocket cost
 - e. Inadequate resources of case managers in the community
4. The following symptoms are manifestation of what condition: hyperarousal, hypervigilant, anger, phobic avoidance, intrusive thoughts?
 - a. Bipolar disorder
 - b. Major depressive disorder

- c. Substance use disorder
 - d. Post-traumatic stress disorder
5. True or False: Research shows that there is no relationship between major depressive disorder, post-traumatic stress disorder, and chronic pain?
- a. True
 - b. False
6. Possible long-term sequelae of RLWD includes (select all that apply):
- a. Depression
 - b. Chronic neuropathic pain
 - c. Early onset dementia
 - d. Tremor
 - e. Muscle weakness
 - f. Diplopia
 - g. Speech difficulty
7. Which depression screening tools are recommended for use in the outpatient primary care setting, therefore, should be used to assess RLWD patients? (select all that apply)
- a. Patient health questionnaires 9 (PHQ-9)
 - b. Beck Depression Inventory
 - c. Alcohol use disorders identification (AUDIT)
 - d. Screening, brief intervention and referral to treatment (SBIRT)
8. According to evidence-based studies, which medications have been shown to be effective for the treatment of chronic neuropathic pain? (select all that apply)
- a. Gabapentin
 - b. Pregabalin
 - c. Amitriptyline

- d. Venlafaxine
9. Which non-pharmacologic interventions have been utilized effectively in the treatment of chronic neuropathic pain? (select all that apply)
- a. Cognitive behavioral therapy (CBT)
 - b. Sleep therapy
 - c. Transcutaneous electrical nerve stimulation (TENS)
 - d. Acupuncture
10. Which screening instrument is used to *screen and monitor* the severity of a patient's post-traumatic stress disorder (PTSD) over time?
- a. Primary care PTSD Screen for DSM-5 (PC-PTSD-5)
 - b. Post-traumatic stress Check List for DSM-5 (PCL-5)
 - c. Patient health questionnaire (PHQ-9)
 - d. Trauma screening questionnaires (TSQ)
11. According to the United States Preventive Services Task Force (USPTF), what is the recommended interval for depression screening?
- a. At every well women's visit
 - b. Screen all patients during routine visits
 - c. When there are presenting signs and symptoms
 - d. Every 6 months
12. According to research, what is the first-line treatment of insomnia and sleep disturbances?
- a. Sleep hygiene and Cognitive Behavioral Therapy (CBT)
 - b. Prazosin
 - c. Combination therapy of CBT and Prazosin
 - d. Benzodiazepines
 - e. Melatonin agonists

13. True or False. Hilo Medical Center holds a Rat Lungworm support group every second Wednesday of each month?
- a. True
 - b. False
14. True or False. Case management services are generally covered by insurance regardless of what chronic condition a patient is diagnosed with.
- a. True
 - b. False

Appendix B

The University of Hawaii at Hilo is conducting a project:

Post-Acute Care Management of Rat Lungworm Disease (RLWD) Patients with Long-Term Sequelae

Are you a primary care provider practicing in East Hawaii areas? If the answer is **YES...**

Doctor of Nursing Practice student Chayata Otsuka, BSN, CMSRN would like to invite you to participate in a practice inquiry project.

The purpose of this pilot project is to provide evidence-based chronic care management strategies for patients with RLWD in an outpatient setting. These strategies will address various care components such as physical, mental/behavioral, and social health. The potential usefulness of the information provided and the likelihood of adopting such practices in your care will also be evaluated.

Background. RLWD is a threat to public health, particularly to the populations in Southeast Asia and the Pacific Basins. In the US, the state of Hawaii, and specifically the East Hawaii community is most at risk for development of this disease which can cause long-term devastating health effects. The literature shows that there is a gap in post-acute outpatient care guidelines for the long-term management of the disease. Care management by primary care providers following acute inpatient hospital discharge is essential in ensuring a successful and progressive recovery, allowing each patient to achieve their optimum health.

Project Description. You will be asked to take an anonymous survey to assess your basic knowledge about RLWD. This should not take more than 10 minutes to complete. After the survey, you will be asked to view a virtual presentation of the evidence-based chronic care management strategies of patients with RLWD (a hard copy will also be provided) and then complete a post-test and a project evaluation. This process should take no longer than 60 minutes. A summary of the guidelines will be provided to you along with survey results upon completion of the study.

Risk and Benefits of participating. There is little to no risk in participating in this project. There will be no direct benefit to you for participating in this project, however, findings from this project may help to improve knowledge of the current literature evidence of chronic care of RLWD patients. Should you feel uncomfortable at any time during this project, you may take a break or ultimately withdraw from the project altogether without penalty.

Questions. If you have any questions about this project, please email me at chayataw@hawaii.edu or via phone at 808-854-1343. My advisor, and the principle investigator Dr. Patricia Hensley, can also be contacted at 808-932-7067 and hensleyp@hawaii.edu. You may contact the UH Human Studies Program at 808-956-5007 or uhirb@hawaii.edu to discuss problems, concerns and questions; obtain information; or offer input with an informed individual who is unaffiliated with the specific research protocol. Please visit <http://go.hawaii.edu/jRd> for more information on your rights as a research participant.

Appendix C

Post-Acute Care Management of Patients with Angiostrongyliasis: A Guideline in Caring for Patients Who Suffer Long Term Sequelae of Rat Lungworm Disease (RLWD)Post-Presentation Survey**Section 1: General information**

1. What is your highest education level?
 - a. Master's degree
 - b. Doctorate degree

2. What is your professional license type?
 - a. MD
 - b. DO
 - c. APRN
 - d. PA

3. Experience in primary care (number of years)?
 - a. 0-3 Years
 - b. 4-10 years
 - c. 11-20 years
 - d. 21 or more years

4. Have you cared for a patient with rat lung worm disease (RLWD)?
 - a. Yes
 - b. No

5. Prior to viewing the presentation, how would you rate your pre-existing knowledge on the topic?
 - a. Novice
 - b. Somewhat familiar

- c. Very familiar
- d. Expert

Section 2: Time

- 6. Did you view the entire RLWD chronic care presentation?
 - a. Yes
 - b. No

- 7. If no, please describe why you were not able to complete_____

- 8. How long did you take to view the presentation?
 - a. Less than 1 hour
 - b. 1-2 hours
 - c. More than 3 hours

Section 3: Method & Application

- 9. Was the presentation easily accessible?

1	2	3	4	5
Very		Somewhat		Very
Difficult		Difficult		Easy

- 10. On a scale of 1 to 5 where 1 is “Not effective” and 5 is “Very effective,” was this presentation effective in increasing your knowledge about chronic care management of RLWD patients?

1	2	3	4	5
Not		Somewhat		Very

Effective

Effective

Effective

11. On a scale of 1 to 5 where 1 is “Not at all” and 5 is “Significant,” how would you rate the usefulness of the knowledge gained from this presentation?

1

2

3

4

5

Not

Somewhat

Significant

At all

useful

12. On a scale of 1 to 5 where 1 is “Not at all” and 5 is “Very interested,” how much did the presentation facilitate your interest in caring for RLWD patients?

1

2

3

4

5

Not

Somewhat

Very

Interested

Interested

Interested

Section 4: Practice Implications

13. Did you learn new information about the management strategies of RLWD patients with long-term sequelae that you did not know about before?

a. Yes

b. No

14. Which topic of the presentation did you find most useful? _____

15. Which topic of the presentation did you find least useful? _____

16. How likely are you to implement these strategies in your medical practice?

- a. Definitely
- b. Very likely
- c. Maybe
- d. Not likely

17. If you did not find the information helpful, please provide future topic(s) about RLWD you would like to learn about _____

18. Would you recommend this presentation to others who wish to learn about chronic care management strategies of RLWD patients?

- a. Yes
- b. No

19. After viewing the presentation, how would you rate your current level of knowledge on the topic?

- a. Novice
- b. Somewhat familiar
- c. Very familiar
- d. Expert

20. Please provide other feedback or comments _____

Appendix D



Completion Date 22-Mar-2019
Expiration Date 21-Mar-2022
Record ID 31013395

This is to certify that:

Chayata Wongpojanee

Has completed the following CITI Program course:

Human Subjects Research (HSR) (Curriculum Group)
Exempt Researchers and Key Personnel (Course Learner Group)
1 - Basic Course (Stage)

Under requirements set by:

University of Hawaii



Verify at www.citiprogram.org/verify/?wff54df45-7d41-438e-b0c4-779b87700e9d-31013395

Appendix E

University of Hawaii at Hilo Consent to Participate in a Research Project
Patricia Hensley, Principal Investigator

Project title: Post-Acute Care Management of Patients with Angiostrongyliasis: A Guideline in Caring for Patients Who Suffer Long Term Sequelae of Rat Lungworm Disease (RLWD)

Aloha! My name is Chayata W. Otsuka, BSN, RN, CMSRN. I am a graduate student at the University of Hawaii at Hilo in the Doctorate of Nursing Program. As part of the requirements for earning my graduate degree, I am conducting a practice inquiry project. One of the purposes of my project is to assess primary care provider's knowledge about RLWD and their opinion on the potential usefulness of evidence-based guidelines that I have created for post-acute care of RLWD patients suffering from long term sequelae.

Project Description. You will be asked to take an anonymous survey to assess your basic knowledge about RLWD. This should not take more than 10 minutes to complete. After the survey, you will view a virtual presentation of the guidelines (a hard copy will also be provided) and complete a post survey to assess your opinion of the potential usefulness of the guidelines. This process should take not take longer than 30 minutes.

Taking part in this study is your choice. Your participation is completely voluntary. You may stop participating at any time. If you stop being in the project, there will be no penalty or loss to you.

Risk and Benefits of participating. There is little to no risk in participating in this project. There will be no direct benefit to you for participating in this project, however, findings from this project may help to improve patient outcomes. Should you feel uncomfortable at anytime during this project, you may take a break or ultimately withdraw from the project altogether.

Privacy and Confidentiality. I will not ask you for any personal information, such as your name and address. All data from the project will be stored on a password protected computer. Hard copies of surveys will be kept in a separate file in a locked cabinet that only myself and the principle investigator will have access to. Other agencies that have legal permission have the right to review research records. The University of Hawai'i Human Studies Program has the right to review records for this project.

Questions. If you have any questions about this project, please email me at chayataw@hawaii.edu or via phone at 808.854.1343. My advisor, and the principle investigator Dr. Patricia Hensley, can also be contacted at 808.932.7054 and hensleyp@hawaii.edu. You may contact the UH Human Studies Program at 808.956.5007 or uhirb@hawaii.edu. to discuss problems, concerns and questions; obtain information; or offer input with an informed individual who is unaffiliated with the specific project. Please visit <http://go.hawaii.edu/jRd> for more information on your rights as a project participant.

Please feel free to keep a copy of this document for your records and reference.

Appendix F



UNIVERSITY
of HAWAII®
MĀNOA

Office of Research Compliance
Human Studies Program

DATE: January 06, 2020
TO: Hensley, Patricia, DNP, University of Hawaii at Hilo, School of Nursing
 D'Haem, Rebecca, University of Hawaii at Hilo, School of Nursing, Otsuka, Chayata,
 DNP, University of Hawaii at Hilo, School of Nursing
FROM: Rivera, Victoria, Dir, Ofc of Rsch Compliance, Biomedical IRB
PROTOCOL TITLE: Post-Acute Care Management of Patients with Angiostrongyliasis: A Guideline in Caring
 for Patients Who Suffer Long Term Sequelae of Rat Lungworm Disease
FUNDING SOURCE:
PROTOCOL NUMBER: 2019-00897
APPROVAL DATE: January 06, 2020

NOTICE OF APPROVAL FOR HUMAN RESEARCH

This letter is your record of the Human Studies Program approval of this study as exempt.

On January 06, 2020, the University of Hawaii (UH) Human Studies Program approved this study as exempt from federal regulations pertaining to the protection of human research participants. The authority for the exemption applicable to your study is documented in the Code of Federal Regulations at 45 CFR 46.101(b) 3.

Exempt studies are subject to the ethical principles articulated in The Belmont Report, found at the OHRP Website www.hhs.gov/ohrp/humansubjects/guidance/belmont.html.

Exempt studies do not require regular continuing review by the Human Studies Program. However, if you propose to modify your study, you must receive approval from the Human Studies Program prior to implementing any changes. You can submit your proposed changes via the UH eProtocol application. The Human Studies Program may review the exempt status at that time and request an application for approval as non-exempt research.

In order to protect the confidentiality of research participants, we encourage you to destroy private information which can be linked to the identities of individuals as soon as it is reasonable to do so. Signed consent forms, as applicable to your study, should be maintained for at least the duration of your project.

This approval does not expire. However, please notify the Human Studies Program when your study is complete. Upon notification, we will close our files pertaining to your study.

If you have any questions relating to the protection of human research participants, please contact the Human Studies Program by phone at 956-5007 or email uhirb@hawaii.edu. We wish you success in carrying out your research project.

UH Human Studies Program, Office of Research Compliance
 Office of the Vice President for Research and Innovation, University of Hawai'i, System
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