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End of Life Care Medication Health Literacy Pertaining to Aging Adult Populations

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END OF LIFE CARE MEDICATION HEALTH

LITERACY PERTAINING TO AGING ADULT POPULATIONS

By Hanna Leschisin

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ABSTRACT

End of Life Care Medication Health Literacy Pertaining to Aging Adult Populations

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In recent years, an expansion of palliative care and hospice care programs has revolutionized how individuals approach death. The philosophies about these programs focus on patient autonomy, dignity, pain management, and improving quality of life, all which could benefit many individuals at the ends of their lives. To increase proper utilization of these programs, there needs to be a focus on increasing health literacy about end of life. Health Literacy is defined by H. Ishikawa and E. Yano as pertaining to the importance of using health information as a resource to allow greater patient participation in managing and making competent decisions in response to health concerns (2008). People at all stages of life need to be informed about their medical choices for better understanding and decision making through the transitions of life, but it is especially important in helping individuals to approach death.

This thesis will focus on the central theme of taking full advantage of end of life care through increasing health literacy. To make a meaningful impact on individuals with low health literacy at end of life, this thesis will focus on a precise application: medication use. Pharmaceutical use is notoriously complicated, but has the potential to help illustrate

the philosophies behind the End of Life Care programs and make dramatic improvements on reinforcing patient autonomy. The goal is to increase understanding about the medications prescribed to aging individuals who are enrolled in end of life care programs, which in turn would assist in serving this population in improving health care participation and outcomes. Medication use in aging adults enrolled in end of life care is a practical focus to increase health literacy.

Keywords: Hospice Care, Palliative Care, Medication Use, Heath Literacy,

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Ideally, advances and expansion in health care should reflect the needs of the population. One of the largest growing needs in the United States is improvement of health care accessibility, quality, and cost for the aging population. As the adult population ages, they will spend more time utilizing the health care system, necessitating their increased understanding about health care proceedings. Modern technology has expanded access to information, but elderly individuals still struggle to navigate the health care system and take ownership as health care consumers despite being most likely to use health care. This calls for an increase in health literacy for those aging adults.

In addition, many of these aging individuals look towards End of Life Care to bring them comfort in their final days. End of Life Care is a growing program created to ease the transition to death, but despite its many benefits to bring respite to patients, caregivers, and the health system, it carries a large drawback. This program encourages patient autonomy, which requires increased knowledge to be able to make informed decisions. Health literacy and End of Life Care intersect for those who wish to have autonomy in their final health care decisions, but are ill prepared to make them because of a lack of understanding. To improve the United States health care system, advances in health literacy for aging adults about End of Life Care will be critical.

To make a meaningful impact on individuals with low health literacy in End of Life Care, this thesis will focus on a precise application: medication use. By examining a list of typical medications prescribed for this population, End of Life Care Programs can be understood more fully. This paper is designed to increase understanding about medications prescribed to aging individuals who are enrolled in End of Life Care

Programs, which would serve this population in improving health care autonomy and outcomes.

Health Literacy

Health literacy is a concept defined by Ishikawa and Yano as pertaining to the importance of using health information as a resource to allow greater patient participation in managing and making competent decisions in response to health concerns (2008). It was first referred to in medical literature as "a constellation of skills, including the ability to perform basic reading and numerical tasks required to function in the health-care environment" (Ishikawa & Yano, 2008). Health literacy applies general literacy to the context of health care to make individuals owners of their health information. Traditionally, information possession in health interactions "creates a basic asymmetry in the patient-physician relationship, and a professional dominance is grounded in a stratified distribution of technical knowledge" (Ishikawa & Yano, 2008). Information is a sense of power, and can be the cause of poor communication between the patient and provider because of the lack of mutual participation.

Life is full of transitions as individuals age, and utilizing health care services also follows this model of change across the lifespan. This transition is difficult whether it be as a teenager going from pediatrics to adult medicine, or as an adult transitioning from general health to dying. Research on health care transitions realized the need for heightened information possession to navigate the health system successfully. Assessing the confidence of an individual in areas such as "I know my medical needs…I know my own medications, what they are for, and when I need to take them… I can explain to others how my customs and beliefs affect my health care decisions and medical treatment"

(Wood, Sawicki, Reiss, Livingood & Kraemer, 2014), can be key for determining health literacy. Health care is constantly ministering to a moving target of individuals in ever changing life stages, and areas with significant transitions require better health knowledge for participation.

Poor health literacy exacerbates poor health outcomes. This association has been observed demonstrating "limited literacy is associated with poor health status, even after controlling for potentially confounding-sociodemographic variables such as income, education, ethnicity, and other factors" (Ishikawa & Yano, 2008). This lack of information is associated with "less knowledge of disease management, poorer health status, less use of preventative services and a higher rate of hospitalization and emergency services use" (Ishikawa & Yano, 2008). These behaviors are costly to human life and the economy of health care.

End of Life Care

The United States health care system is plagued by chronic health conditions. Currently, the top causes of death include "disease of the heart, cancer, chronic lower respiratory diseases, cerebrovascular disease, and unintentional injury" (Yoon et. al., 2014). This is a significant impact on the system since "three-quarters of individuals who die in the United States do so from chronic illness" (Carlson, Morrison, Holford & Bradley, 2007). The increases in medical advancements have expanded the human lifespan and increased prevalence of chronic diseases in aging individuals.

Previously, health care in the United States focused on an aggressive, cure at all costs approach. This has failed to align with the preferences of many aging individuals so End of Life Care Programs have been expanded to provide care while maintaining dignity.

When an individual first considers End of Life Care, palliative care is often a first step. Palliative care "improves quality of life for patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification, and impeccable treatment of problems, including physical, psychosocial and spiritual challenges" (Minton et al., 2014). These services help individuals who realize death may be imminent to transition towards prioritizing relief *in lieu* of aggressive treatments. Palliative care often does not require a complete cessation of life-prolonging treatments, but rather gives individuals more resources for comfort care. As chronic diseases progress, palliative care would ideally transition to hospice care as the individual nears the end of life (Minton et al., 2014). The transition to hospice usually occurs when the individual has less than 6 months of projected life left, and all curative treatments are discontinued. Palliative care and hospice care are designed to work together to cover the dynamic needs of a dying individual.

End of Life Care Programs work to address common struggles for those who are dying. Examples of this include "inadequate pain and symptom management, caregiver burden and stress, limited communication, and overall dissatisfaction with care" (Carlson, Morrison, Holford & Bradley, 2007). These programs are designed to "reduce and manage distressing symptoms" (Isaacson & Lynch, 2017). Another large area of concern for aging adults is their ability to stay in their own homes. This flexible program can be implemented in a variety of settings, and an estimated 72% of those enrolled in hospice are still living at home (Carlson, Morrison, Holford & Bradley, 2007). This helps contribute to the fact that, "persons receiving hospice care are more likely to die in their own homes, have fewer hospitalizations and intensive care admissions and incur

significantly less health care expenditures in the last year of life when compared with those not receiving hospice" (Isaacson & Lynch, 2017). Dying is a difficult process and End of Life Care Programs are expertly designed to cater to individual preferences, concerns, and needs. Palliative care, hospice care and other advanced care planning "are rooted in the principle of patient autonomy and are at the core of a cogent, patient-oriented advance care planning model" (Minton et al., 2014). End of Life Care Programs are patient centered ways to address common concerns of dying individuals.

The needs of society continue to propel the popularity of End of Life Care Programs. Hospice care is one of the fastest growing End of Life Care Programs, and "between 2002 and 2009 the number of persons who received hospice care in the United States increased by 76%" (Dwyer, Lau, & Shega, 2015). This expansion is significant as "in 2011, an estimated 45% of all death in the United States occurred in hospice care" (Dwyer, Lau, & Shega, 2015). These services can help patients with a variety of abilities, and individuals enrolled in hospice are not required to have extensive health care needs. In fact, the "mean number of ADL (Activities of Daily Living) dependencies that the hospice provided assistance with was 3.5" (Carlson, Morrison, Holford & Bradley, 2007). With this influx of individuals utilizing this care, more resources should be made available to help patients understand End of Life Care.

Many of the resources provided by End of Life Care attempt to improve communication between the patient and provider. Palliative care and hospice have five key categories including, "nursing care, physician care, medication management, psychosocial care, and caregiver support" (Carlson, Morrison, Holford & Bradley, 2007). Of these resource categories, this thesis will focus in greater detail on medication management.

Medication Literacy

A key way of understanding the philosophy of End of Life Care Programs is through a closer look at medication use. The non-curative approach and priorities of increasing comfort and dignity for the patient are reflected in the medication choices. However, medicinal information can be daunting and difficult to understand for the average health care consumer. Medication literacy is pertinent to End of Life Care for many people who utilize these programs and suffer from numerous chronic illnesses, each of which is usually accompanied by several prescriptions. With compounding illnesses, comprehending the implications of medication use on the life of the patient is tricky.

Many of the medications used in End of Life Care can be predicted by looking at the common health diagnoses for those enrolled in End of Life Care. Primary diagnoses included: “cancer, debility unspecified, dementia, heart disease, and lung disease” (Dwyer, Lau, & Shega, 2015). Common symptoms that necessitated medication use include “pain, dyspnea, fatigue depression, anxiety, delirium, insomnia, constipation, nausea, and vomiting” (Dwyer, Lau, & Shega, 2015). Many in End of Life Care Programs juggle multiples of the pre-mentioned chronic illnesses and symptoms. Individuals with comorbidities likely will be taking multiple medications which may put them at “a high risk of polymedicine and adverse drug-drug interactions” (Dwyer, Lau, & Shega, 2015). The numbers of prescriptions per individual enrolled in End of Life Care was consistently high, with the “average number of medications taken was 10.2” (Dwyer, Lau, & Shega, 2015). The complicated nature of multiple prescriptions in a frequently evolving field requires careful attention and monitoring by health professionals, adding another level of difficulty to understanding medication use in End of Life Care.

This thesis will look into the types of medication most likely to be used in patients nearing the End of Life Care. The therapeutic drug classes most commonly prescribed for individuals in hospice and palliative care programs include analgesics, opioid narcotics, antiemetic/antivertigo drugs, anxiolytic/sedative/hypnotic drugs, anticonvulsants, laxatives, antihypertensive drugs, functional bowel disorder agents, antipsychotics, diuretics, bronchodilators, proton pump inhibitors, anticoagulants, antidepressants, antacids, and antibiotics (Figure 1) (Dwyer, Lau, & Shega, 2015). These drug classes will be examined in detail in the following paper, focusing on information useful for the public to be able to understand their prescriptions, and to understand how each drug plays into the philosophy and goals of hospice and palliative care programs.

Figure 1 (Dwyer, Lau, & Shega, 2015)

Table 2. Weighted Prevalence of Selected Therapeutic Drug Classes That Individuals in Hospice Aged 65 and Older Took in the Last Week of Life According to Primary Admission Diagnosis

Therapeutic Class	Total, n = 2,623 (561,300)	Cancer, n = 1,277 (256,800)	Dementia, n = 319 (83,800)	Debility, n = 358 (83,000)	Heart Disease, n = 416 (83,300)	Lung Disease, n = 253 (54,400)
	% (95% Confidence Interval)					
Analgesic	97.8 (96.8–98.4)	98.3 (97.1–99.0)	96.6 (92.8–98.4)	97.3 (93.9–98.9)	97.3 (94.4–98.7)	98.3 (96.2–99.3)
Opioid (narcotic)	91.9 (89.8–93.5)	95.4 (93.1–96.9)	82.8 (75.6–88.1)[f,i,j]	88.8 (82.6–93.0)[f]	91.8 (87.0–95.0)	93.9 (88.4–96.9)
Nonopioid	57.7 (53.5–61.8)	46.9 (41.2–52.8)[g,h,i,j]	71.8 (62.1–79.8)	65.9 (56.6–74.1)	66.0 (57.8–73.4)	62.0 (51.4–71.6)
Antiemetic and antivertigo	78.4 (74.8–81.6)	81.8 (76.9–85.8)	70.4 (62.0–77.6)	77.2 (68.9–83.7)	75.3 (67.4–81.8)	81.6 (72.4–88.2)
Anxiolytic, sedative, hypnotic	75.5 (72.1–78.6)	73.8 (68.4–78.6)	69.9 (61.8–76.9)	79.5 (71.9–85.5)	77.2 (69.5–83.4)	83.1 (73.5–89.7)
Anticonvulsant	70.5 (66.6–74.0)	68.0 (62.3–73.3)	69.9 (61.4–77.2)	74.4 (66.1–81.3)	73.0 (65.0–79.7)	72.9 (62.9–81.0)
Laxative	53.1 (48.6–57.6)	53.0 (47.2–58.7)	53.7 (44.5–62.7)	61.4 (51.8–70.1)	50.0 (40.6–59.3)	45.0 (34.6–55.9)
Antihypertensive	49.2 (45.5–52.8)	46.0 (41.0–51.2)[d]	42.1 (32.7–52.2)[d]	47.6 (38.0–57.4)[d]	64.7 (56.6–72.1)	53.3 (42.7–63.6)
Functional bowel disorder agent	44.2 (39.5–49.1)	43.8 (37.9–49.9)	47.3 (37.3–57.5)	44.1 (34.1–54.5)	41.2 (32.3–50.7)	46.5 (35.8–57.5)
Antipsychotic	37.7 (33.3–42.3)	41.2 (35.7–47.0)	43.6 (34.1–53.7)	34.6 (25.0–45.6)	34.9 (27.8–42.7)	20.8 (13.4–30.7)[a,b,c,d]
Diuretic	28.3 (25.1–31.7)	24.8 (20.7–29.5)[i]	—	24.1 (17.0–33.0)[j]	51.8 (43.0–60.4)	34.1 (24.7–44.9)[i]
Bronchodilator	27.3 (24.2–30.6)	25.2 (21.1–29.9)[j]	20.2 (13.6–28.9)[j]	24.4 (18.0–32.3)[j]	18.8 (13.7–25.1)[j]	65.1 (54.6–74.3)
Proton pump inhibitor	25.7 (22.5–29.1)	28.5 (23.7–33.8)	—	19.9 (13.7–28.1)[e]	27.6 (20.5–36.0)	35.4 (26.2–45.7)
Anticoagulant	25.2 (22.5–28.1)	20.5 (16.9–24.6)[c,d]	24.5 (16.8–34.2)	29.4 (22.2–37.7)	36.0 (28.2–44.6)	25.9 (17.1–37.2)
Antidepressant	24.0 (21.1–27.2)	19.6 (15.9–24.0)[g,h]	31.3 (22.7–41.4)	37.9 (29.2–47.4)	21.2 (15.2–28.7)[h]	16.5 (10.6–24.6)[g,h]
Antacid	18.6 (15.9–21.7)	14.5 (11.5–18.1)[g,h]	24.3 (17.7–32.4)	32.0 (23.0–42.5)	17.0 (11.7–24.1)[h]	—
Antibiotic	17.9 (15.3–20.8)	14.0 (10.5–18.4)	24.7 (17.1–34.2)	24.2 (17.1–32.9)	17.6 (12.4–24.5)	16.8 (10.5–25.7)

Significantly different from [a]cancer, [b]dementia, [c]debility, [d]heart disease, [e]lung disease estimate at $P < .05$.
Significantly different from [f]cancer, [g]dementia, [h]debility, [i]heart disease, [j]lung disease estimate at $P \leq .001$.
— = unreliable estimate because of small cell size.

Weighted Prevalence of Therapeutic Drug Classes that Older Adults in Hospice took in the last Week of Life. Therapeutic Drug Classes do correspond to the primary admission diagnosis, but also reveal misunderstandings about the role of medication in hospice End of Life Care Programs.

Analgesic & Opioid Narcotics

Analgesics and opioid narcotics manage pain. Pain is a common complaint particularly for patients affected by chronic disease. While many attempts are made to avoid pain, pain can be useful to aid in diagnosing disease because pain is an indication of possible dysfunction. However, it is critical to treat pain whenever possible as this is "one of the most important duties of a doctor" (Ritter, Lewis, Mant, & Ferro, 2008). In a culture where addiction to pain medication is a public health concern, it is important to be aware of proper indicators for prescribing such medications.

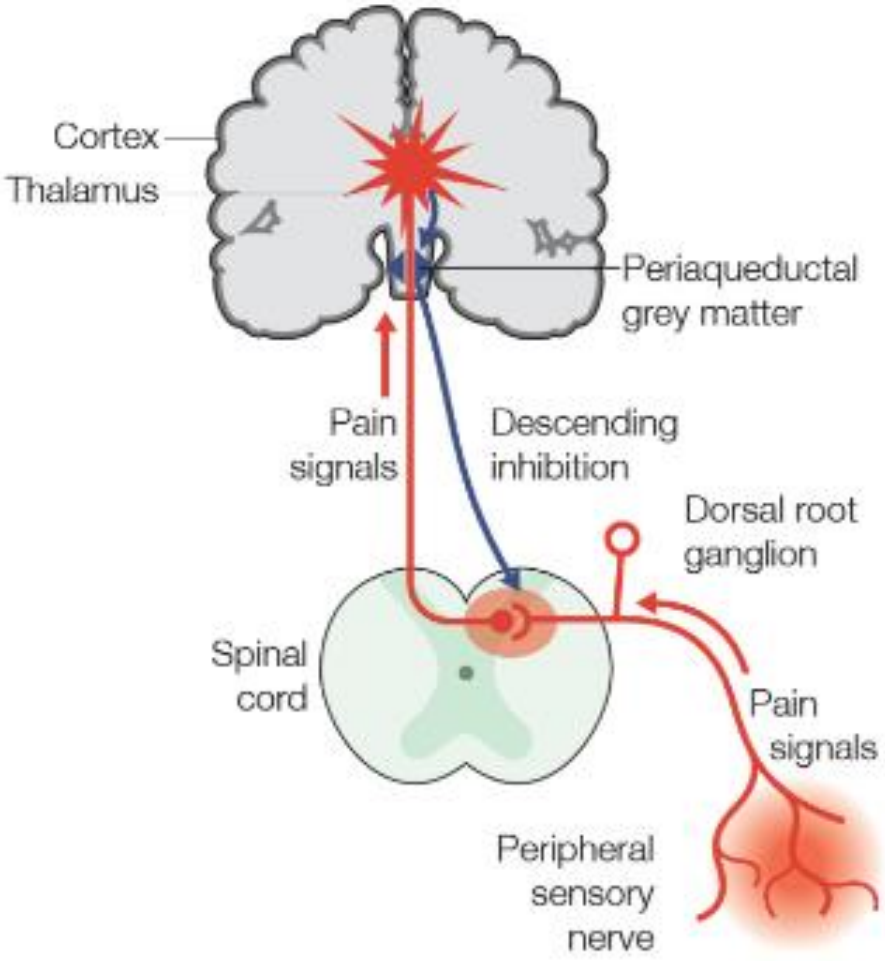
Pain is a sensation initiated within the nervous system by a stimulus, and can be demonstrated pictorially as seen in Figure 2. Nociception, the harmful stimulus associated with the sensation of pain, sends signals down several types of afferent nerve fibers, including "slowly conducting non-myelinated C-fibers that are activated by stimuli of various kinds and fine myelinated fibers that conduct more rapidly but respond to similar stimuli" (Ritter, Lewis, Mant, & Ferro, 2008). These afferents pass their signal along in a synapse within the "dorsal horn of grey matter in the spinal cord in laminae I, V and II" (Ritter, Lewis, Mant, & Ferro, 2008). The laminae I and V "cross over and project to the contralateral thalamus" (Ritter, Lewis, Mant, & Ferro, 2008). Nociception stimuli send a signal down a cascade, stimulating laminae and the thalamus.

In addition to the nociception stimuli in the laminae and thalamus, nociception endings can also be stimulated in the periphery. This is "predominantly chemically mediated" (Ritter, Lewis, Mant, & Ferro, 2008). Injured tissue releases "bradykinin, prostaglandins and various neurotransmitters (e.g. 5-hydroxytryptamine, 5HT) and metabolites (e.g. lactate) or ions (e.g. K)" which all can stimulate these peripheral endings (Ritter, Lewis,

Mant, & Ferro, 2008). Primary nociception fibers can also be stimulated by glutamate, ATP, and neuropeptides (Ritter, Lewis, Mant, & Ferro, 2008). Pain can be stimulated in the periphery through the presence of key chemical components responsible for stimulating the end of nociception fibers.

Luckily, the painful nociception stimuli can be blocked. *Substantia gelatinosa* projections and a similar mechanism in the thalamus can block the signal in the laminae (Ritter, Lewis, Mant, & Ferro, 2008). Another important component to inhibiting nociception signals is the periaqueductal grey (PAG) matter area in the midbrain. When electrical current stimulates this PAG region, analgesia is the result (Ritter, Lewis, Mant, & Ferro, 2008). The PAG region is connected to the medulla and the dorsal horn of the cord, "connecting with the interneurons involved in nociception" (Ritter, Lewis, Mant, & Ferro, 2008). Understanding the components that inhibit nociception stimuli are key to pain management.

Figure 2 (Ritter, Lewis, Mant, & Ferro, 2008)



Pain is a signal that travels throughout the nervous system, eventually entering the brain. Inhibition descends from the periaqueductal grey matter, causing pain relief. This signal is stimulated in the periphery, and subsequent afferent and efferent signals communicate pain and relief.

The diagnosis of pain and understanding its cause can be complex. While the sensation of pain is real, pain often doesn't present in physical manifestations illustrating the magnitude and diffuse nature of pain throughout an area. For elderly individuals, children, those with intellectual disabilities, and the nonverbal, communicating the symptom of pain may be difficult. For this reason, a pain scale is often used so patients can match their sensations to pictures that portray "gradations of pain" (Iserson, 2016). While this remains a subjective measure, it does provide a rough qualitative value. Based on the reported value, the subsequent approach to managing pain should vary. Preferably, pain management will be performed "by the mouth", using oral medications to allow the individual more freedom in maintaining normalcy (Iserson, 2016). It is recommended to use a "treatment pain ladder", a treatment strategy that "starts with the weakest medications and progressively increases the strength of the medication" (Iserson, 2016). This progressive system is well suited to increase dosage as needed, while attending to not overwhelming the patient's system. Another approach to treatment is to design dosage scheduled "by the clock", keeping the level of the pain medication consistent via a "fixed schedule to avoid getting the pain" (Iserson, 2016). These approaches strive to help address pain concerns and patient comfort, while avoiding toxicities.

Pain medications are drugs used to relieve discomfort associated with disease, injury, or surgery. Because the pain process is complex, there are many types of pain drugs that provide relief by acting through a variety of physiological mechanisms. Based on the strength of the drug in question, they can be classified into two categories. Pain medications can be over-the-counter, meaning they are available to all individuals, or prescription, making those who have access to them more limited. For our uses, we will

classify pain medication into 8 categories. These include nonsteroidal anti-inflammatory drugs, corticosteroids, acetaminophen, opioids, muscle relaxants, anxiolytics, antidepressants, and anticonvulsants. Pain management is a secondary effect for anxiolytics, antidepressants, and anticonvulsants so greater understanding of these classes can be found in their respective sections.

NSAID is an acronym to describe a nonsteroidal anti-inflammatory drug. These drugs affect "substances in the body that can cause inflammation, pain, and fever", working directly at the source of pain (Morelli, 2016). Most common over the counter NSAIDs include Aspirin and Ibuprofen. Aspirin inhibits "prostaglandin biosynthesis, irreversibly acetylating a serine residue in the active site of cyclo-oxygenase (COX)" (Ritter, Lewis, Mant, & Ferro, 2008). COX has two isoforms, of which the first is a constitutive enzyme that is "present in platelets and other cells under basal conditions" (Ritter, Lewis, Mant, & Ferro, 2008). Aspirin acetylates COX-1 at the active site, which leads to the disruption of the normal binding of COX-1 with arachidonic acid and causing inhibition of thromboxane and prostaglandin formation (Ritter, Lewis, Mant, & Ferro, 2008). This slows the basal rate of aggregation and prostaglandin production. Ibuprofen and Aspirin are similarly potent as acetaminophen but have additional anti-inflammatory properties making them useful in managing certain types of pain.

Corticosteroids and muscle relaxants are less common pain management drugs utilized in the elderly population. In contrast to the goal of administering pain medication orally, corticosteroids are most commonly administered by injection. This is due to the "powerful anti-inflammatory effects" they can provide for musculoskeletal injuries

(Morelli, 2016). However, an oral intake method can also be useful for arthritis (Morelli, 2016). Similarly, muscle relaxants tend to work on musculoskeletal pain. Their mechanism sedates the central nervous system, which releases subsequent pain from tension (Morelli, 2016). Because of their decreased commonality for End of Life Care patients, specific mechanisms for anti-inflammatory and relaxant effects will not be discussed further.

The next major classification is acetaminophen, or paracetamol. These medications are useful in increasing the tolerable threshold of pain, but have "little effect on inflammation" and "no effect on platelet aggregation" in contrast with NSAIDs (Morelli, 2016), Like other classes, paracetamol "inhibits prostaglandin biosynthesis under some circumstances" (Ritter, Lewis, Mant, & Ferro, 2008). Acetaminophen is a useful alternative to NSAIDs to produce similar effects for pain control, but is best suited for acute pain.

Opioids, or narcotics, tend to be utilized to combat chronic pain because of their potency. They are a "gold standard for treating moderate to severe pain", but because of their strength carry a high risk of abuse and tend to be closely regulated (Iserson, 2016). This leads to a "consistent underutilization in patients who require strong analgesics for chronic painful conditions" (DeBattista, 2017). In addition to their potency, these drugs are especially useful in chronic pain because there is no ceiling effect. The ceiling effect means that "continuous dose escalation does not provide concomitant escalation in pain relief", a limitation of other medications (Morelli, 2016). These medications work at modifying pain messages within the brain, as well as with "the inhibitory gates in the

dorsal horn and thalamus" (Ritter, Lewis, Mant, & Ferro, 2008). Opioids can also "alter the central appreciation of pain" (Ritter, Lewis, Mant, & Ferro, 2008). Most of the potent effects of narcotics are due to morphine and codeine combined with a vasodilator termed papaverine (Ritter, Lewis, Mant, & Ferro, 2008). Opioid narcotics are potent and well suited to chronic pain management.

Pain medications, while useful in maintaining comfort, do not come without risks because of the influence they have on other body systems. Morphine metabolites accumulate in the kidneys, and for individuals with kidney failure can lead to "narcosis and ventilatory depression lasting several days" (Butterworth, Mackley, & Wasinick, 2013). Overdosing and taking pain medications with other drugs such as alcohol can also lead to liver damage (Morelli, 2016). Another concern is "chest wall rigidity severe enough to prevent adequate bag-and-mask ventilation" for individuals administered large doses of opioids rapidly (Butterworth, Mackley, & Wasinick, 2013). In these ways, pain management can have a profound impact on other body systems.

In addition to large system effects, pain medications have many other side effects. Opioids when taken over a prolonged period can lead to increased pain in an opioid-induced hyperalgesia, in which "patients become more sensitive to painful stimuli" (Butterworth, Mackley, & Wasinick, 2013). Opioids have also been associated with "euphoria, dysphoria, agitation, seizures, hallucinations, lowered blood pressure and heart rate, muscular rigidity and contractions, nausea and vomiting, non-allergic itching, pupil constriction, sexual dysfunction, and urinary retention" (Morelli, J., 2016). In addition, tolerance is a large concern, in which increased dosages over a prolonged time will have

a decreased effect. The effects of pain medication may extend beyond simple pain management.

One of End of Life Care's greatest priorities is comfort, which is most commonly interpreted as proper pain management. While making pain medication more accessible and prescribing adequate dosages should be a priority, there are complications to consider when using these medications with the elderly population. One of the largest concerns deals with the changes in pharmacokinetics with age. While all drugs are subjected to differing rates of effect and metabolic rate in the elderly, using too strong pain medications can have dire consequences. Older individuals are "markedly more sensitive to the respiratory effects of these agents because of age-related changes in respiratory function" (DeBattista, 2017). This can decrease respiratory drive, so increased dosage of particularly strong narcotics should be monitored closely. While dosing pain medication in general and especially narcotics, health professionals should take measures to avoid dependence and addiction. However, in an elderly patient, long-term concerns about drug abuse are minimal and it is far more important to provide them comfort than limit their access to these medications. This makes proper pain management an efficacious component of End of Life Care, necessitating the appropriate use of analgesics and narcotics.

Antiemetic & Antivertigo

Antiemetic and Antivertigo drugs are used to promote comfort in End of Life Care patients by combating the effects of nausea, vomiting, and dizziness. Nausea is described as a "subjective sensation of 'queasiness' which typically precedes vomiting" (DynaMed Plus, 2017). This phenomenon can lead to other physical effects such as "sweating,

bradycardia, pallor and profuse salivary secretion" (Ritter, Lewis, Mant, & Ferro, 2008). Vomiting is best described as a "forceful evacuation of gastric contents in retrograde fashion from stomach up to and out of mouth" (DynaMed Plus, 2017). Vertigo typically causes dizziness described as "false sense of motion and possibly a spinning sensation" that can also cause sweating, pallor, nausea, and vomiting (DynaMed Plus, 2017). Antiemetic and antivertigo drugs are key to decreasing the number of negative symptoms for End of Life Care patients.

Nausea and vomiting can be attributed to many different conditions, which makes determining the cause of nausea and vomiting complex. For those in End of Life Care, nausea and vomiting could be linked to chronic gastrointestinal diseases, adverse reactions to medications, psychiatric disturbances, or pain. To determine causation, questions should examine: "timing of vomiting in relationship to meals, new onset vs. recurrence, current gastrointestinal symptoms in family members or close contacts, head injury or other trauma, urine output, weight loss, prescription or nonprescription medications, travel and use of illicit drugs or alcohol" (DynaMed Plus, 2017). Vertigo typically is a result of disturbances in the vestibular system, or in the inner ear (DynaMed Plus, 2017). Despite the importance of decreasing nausea, vomiting, and vertigo for patient comfort, determining causation is often difficult.

The mechanics of vomiting can have useful clues to better understand how antiemetic drugs work. Vomiting is a somatic function, "preceded by rhythmic muscular contractions of the 'respiratory' muscles of the abdomen" (Ritter, Lewis, Mant, & Ferro, 2008). This process is coordinated by a so called 'vomiting center', found close to the cardiovascular and respiratory centers of the medulla oblongata of the brain (Ritter,

Lewis, Mant, & Ferro, 2008). This brain area can be activated by the "phrenic nerve, the visceral efferent of the vagus to the stomach and esophagus, and the spinal nerves to the abdominal musculature" (Ritter, Lewis, Mant, & Ferro, 2008). The chemoreceptor trigger zone (CTZ), a group of neurons in the vomiting center, is activated by stimuli such as "radiation, bacterial toxins and uremia" as well as by the neurotransmitter dopamine (Ritter, Lewis, Mant, & Ferro, 2008). For vomiting caused by the vestibular organs such as in vertigo, the CTZ is stimulated indirectly (Ritter, Lewis, Mant, & Ferro, 2008). Vomiting is a complex process mediated by stimulation of the brain.

Antiemetic drugs can fall into several major categories. These include the following: serotonin 5-HT3-receptor antagonists, corticosteroids, neurokinin receptor antagonists, dopamine antagonists, antihistamines and anticholinergics, and cannabinoids. Each class will be described in further detail below.

Three antiemetic drug classes tend to be prescribed together for a specific group of patients. Serotonin 5-HT3- receptor antagonists benefit from synergistic effects from combined use with corticosteroids and neurokinin receptor antagonists to prevent "chemotherapy- and radiation-induced emesis", proving most useful for those undergoing cancer treatment (McQuaid, 2017). The second use of these drugs is to prevent "post-operative nausea and vomiting" (Ritter, Lewis, Mant, & Ferro, 2008). Currently, the site of action for these drugs is not well described (Ritter, Lewis, Mant, & Ferro, 2008). Since these drugs are most useful in cancer treatment, and those pursuing End of Life Care typically forgo curative treatments, the frequent use of these drugs in End of Life Care patients is unlikely.

Dopamine antagonists are drugs that cause multiple types of effects. These drugs cause dopaminergic blockade, which is useful for both a sedative antipsychotic effect as well as an antiemetic (McQuaid, 2017). As previously mentioned, dopamine is considered a key activator of the CTZ area of the brain, so suppression of this neurotransmitter decreases activation. One dopamine antagonist, Metoclopramide, has several effects that decrease vomiting. These include raising the threshold of the CTZ, decreasing sensitivity of the "visceral nerves that carry impulses from the gut to the emetic center" and increasing "the amount of acetylcholine released at post-ganglionic terminals" (Ritter, Lewis, Mant, & Ferro, 2008). However, since more effective and safer antiemetics are available, the use of this drug for its antiemetic properties is less common to avoid antidopaminergic side effects like depression and extrapyramidal reactions (McQuaid, 2017). Dopamine antagonists will be discussed in greater detail in the section relating to antipsychotics.

Antihistamines are drugs commonly used in allergic reactions, but are also considered the antiemetic of choice for disorders affecting the inner ear. The inner ear if disrupted can cause a labyrinth disorder, which often presents as motion sickness, vertigo, or migraines (McQuaid, 2017). Antihistamines also have "anticholinergic actions, and these contribute to their anti-emetic effect" (Ritter, Lewis, Mant, & Ferro, 2008). Multiple drugs can have antiemetic properties, along with their abilities to treat other symptoms.

The last group of antiemetic drugs, cannabinoids, carry additional legality concerns. Cannabinoids such as marijuana have been widely used as "an appetite stimulant and antiemetic" (McQuaid, 2017). The use of these drugs is currently illegal in most of the United States, which limits their uses in a medical environment. However, an important active ingredient in marijuana, pure delta9-tetrahydrocannabinol (THC), is commonly

available by prescription and can be used to treat nausea (McQuaid, 2017). Using cannabinoids as an antiemetic has been associated with central nervous system side effects (McQuaid, 2017). Cannabinoid antiemetics have a restricted use because of side effects and legality concerns.

Nausea, vomiting, and dizziness may be significant factors affecting the comfort of patients nearing end of life. Nausea and vomiting are common in the general population, and are involved in "4 million emergency department visits annually in United States" (DynaMed Plus, 2017). If not properly addressed, excessive vomiting can lead to dehydration, hypovolemia, aspiration pneumonia, metabolic abnormalities, or emetogenic esophageal rupture (DynaMed Plus, 2017). These resultant effects of uncontrolled vomiting only increase discomfort and risk of poor health outcomes in individuals with other chronic diseases. For the elderly population, dizziness caused by vertigo can be hazardous to maneuvering in their environment, and could put patients at risk for falls. For End of Life Care patients, control of these symptoms can improve overall quality of life and help avoid further complications, making access to antiemetic and antivertigo drugs appropriate for these patients.

Anticonvulsants

Anticonvulsants, or antiepileptics, are the therapeutic drug class designed to treat seizures. A seizure is best described as abnormal electrical brain activity causing "a paroxysmal discharge of cerebral neurons associated with a clinical event apparent to an observer, or as an abnormal sensation perceived by the patient" (Ritter, Lewis, Mant, & Ferro, 2008). Seizures can be classified based on the cause of the abnormal activity. Provoked seizures occur "immediately or within 7 days of acute insult of electrolyte

imbalance, medication or medication withdrawal, ingestion of toxin, encephalitis, central nervous system lesion, or overexertion" (DynaMed Plus, 2017). Unprovoked seizures do not have apparent acute causes but may have a temporally remote cause (DynaMed Plus, 2017). Epilepsy is a brain disease seizure disorder categorized by two or more unprovoked seizures in more than 24-hours (DynaMed Plus, 2017). Anticonvulsants are used to treat a variety of seizures regardless of cause.

Seizures are not common, but are alarming when they occur. Seizures account for "1%-2% of emergency room visits in United States" (DynaMed Plus, 2017). It is estimated that 5-10% of individuals have a seizure during their life and the incidence of seizures in those over 60 years of age is 0.1% (DynaMed Plus, 2017). Risk of an individual having a seizure for the first time is age dependent, since younger and older persons are more susceptible to this occurrence. Other risk factors include cardiac surgery and use of medications such as "anesthetic agents, antipsychotics, antidepressants, theophylline, tramadol, antibiotics, amphotericin B, antivirals, chemotherapeutic agents, and immunosuppressive agents" (DynaMed Plus, 2017). In addition, risk increases if the patient is withdrawing from medications such as "anticonvulsant therapy, baclofen, barbiturates, benzodiazepine, opiates, and zolpidem" (DynaMed Plus, 2017). Many risk factors predict the likelihood of experiencing a seizure.

The primary cause of a seizure is often not well known, and understanding the pathophysiology of anticonvulsant drugs can also be complex. Drugs commonly used to treat seizures include carbamazepine, sodium valproate, phenytoin, phenobarbital, benzodiazepines, vigabatrin, lamotrigine, gabapentin, topiramate, tiagabine, and ethosuximide. For the most part, these drugs are not well understood or described.

The most common anticonvulsant used is Benzodiazepine. This drug is commonly cited for “initial treatment for cessation of acute seizures” (DynaMed Plus, 2017). It functions to “selectively block repetitive discharges at concentrations below those that block normal impulse conduction” and “prolong the inactivated state of the sodium channel and reduce the likelihood of repetitive action potentials” (Ritter, Lewis, Mant, & Ferro, 2008). Gamma-aminobutyric acid (GABA), acts as “an inhibitory neurotransmitter by opening chloride channels that lead to hyperpolarization and suppression of epileptic discharges” (Ritter, Lewis, Mant, & Ferro, 2008). The receptor-channel complexes that GABA binds to also has recognition and binding sites for “benzodiazepine and barbiturate which can potentiate GABA anti-epileptic activity” (Ritter, Lewis, Mant, & Ferro, 2008). Because of these actions in stabilizing nerve cells, “some anticonvulsant drugs also relieve the pain of neuropathies”, giving them a secondary use (Morelli, 2016). There are many therapeutic drug classes used for anticonvulsant treatment, but most are not well described in terms of physiological effects.

While it is common for drugs to cause side effects, anticonvulsants are prone to significantly common occurrences of adverse reactions. To illustrate this point, two of the drug class interactions and side effects will be discussed. Carbamazepine carries with it a 50% chance of side effects in patients with plasma concentrations greater than 8.5mg/L such as “sedation, ataxia, giddiness, nystagmus, diplopia, blurred vision and slurred speech” (Ritter, Lewis, Mant, & Ferro, 2008). This drug is also prone to several adverse drug interactions with monoamine oxidase inhibitors and has been known to increase the rate of “metabolism of warfarin, theophylline and the oral contraceptive” (Ritter, Lewis, Mant, & Ferro, 2008). Sodium valproate carries similar risks, warning of symptoms

including “tremor, nausea, vomiting and abdominal pain, enhancement of sedatives (including alcohol), hair loss, thrombocytopenia, teratogenic effects (neural-tube defects and hypospadias), hepatic necrosis, and acute pancreatitis (another rare complication)” (Ritter, Lewis, Mant, & Ferro, 2008). Anticonvulsants may be the choice drug class for treating seizure disorders, but adverse reactions may be common.

The use of anticonvulsants in End of Life Care may be appropriate, but carries significant risk. Seizures are disturbing symptoms, and their onset in patients may be detrimental to mental health and social interactions. Psychosocial health is a key component to End of Life Care Programs, and being able to address and alleviate these concerns by controlling seizures pharmaceutically may be necessary. Elderly patients are susceptible to the incidence of a seizure, as described earlier, which makes increasing availability of anticonvulsants a priority. However, the use of anticonvulsants in those experiencing negative drug interactions and adverse effects should be closely examined to determine if the discomfort is worth the therapeutic benefits of decreasing the likelihood of seizures. If the anticonvulsant prescribed has known drug interactions with other essential medications, choosing another pharmaceutical or forgoing treatment may be necessary. Also considering discontinuing use of seizure-causing medications may be more appropriate than adding an anticonvulsant to a patient’s medication regime. The use of anticonvulsants in End of Life Care may be best assessed on the individual level.

Laxative & Functional Bowel Disorder agent

Laxatives and functional bowel disorder agents both work to combat digestive tract symptoms. Laxatives treat constipation, a condition that is described as “fewer than three bowel movements per week with stools that are generally hard, dry, small and painful to

pass" (Buck, 2011). Clinicians should "exclude both local and systemic disease which may be responsible for the symptoms" before diagnoising constipation (Ritter, Lewis, Mant, & Ferro, 2008). Functional bowel disorder agents treat digestive tract maladies such as "irritable bowel syndrome, functional bloating, functional constipation, and functional diarrhea" (Häuser, Layer, Henningsen, & Kruis, 2012). Functional bowel disorders are diagnosed using a "typical constellation of symptoms (chronic abdominal pain, bloating, constipation, diarrhea, and stool irregularity) and the absence of pathological findings that would adequately explain them" (Häuser, Layer, Henningsen, & Kruis, 2012). Laxatives and functional bowel disorder agents are used to treat digestive tract symptoms.

The causes of digestive system complaints may be complex. Constipation may result from "reduced food, fluid intake and mobility" or from "partial bowel obstruction or tumour-related hypercalcaemia" (Sykes, 1998). Functional bowel disorder symptoms may be physical, mental, or functional in nature. One such functional bowel disorder, irritable bowel syndrome, has symptoms that "fluctuate over years, and may be exacerbated by stress", and "can be complicated by depression and anxiety" (DynaMed Plus, 2017). Digestive disorders are associated with both lifestyle choices and physical and mental health.

Constipation and functional bowel disorders may benefit from preventative measures and non pharmaceutical interventions. Patients should be advised to "eat regularly, drink adequate noncaffeinated fluids, limit insoluble fiber intake, and increase physical activity" (DynaMed Plus, 2017). Elimination diets may be useful in ruling out food insensitivities. Patients with functional bowel disorders could benefit from peppermint oil

to “relax intestinal smooth muscle” (Ritter, Lewis, Mant, & Ferro, 2008). Cognitive therapy may be used to reduce physiological impacts (DynaMed Plus, 2017). Resorting to pharmaceutical measures such as laxatives should only be used “if straining at stool will cause damage, in hepatocellular failure to reduce formation and/or absorption of neurotoxins produced in the bowel, and occasionally in drug-induced constipation” (Ritter, Lewis, Mant, & Ferro, 2008). Non-pharmaceutical interactions should be considered first in the management of digestive tract symptoms, unless the symptoms become detrimental to patient health.

Laxatives can be classified as “bulkforming, chemical stimulant, hyperosmotic, softeners, or lubricants” (Buck, 2011). Bulk forming laxatives work by “increasing the amount of fiber in the diet to increase the bulk of the stools and decrease the bowel transit time” (Ritter, Lewis, Mant, & Ferro, 2008). Fiber is useful because it absorbs water and binds organic molecules, which encourages healthy stool formation by stimulating the large bowel (Ritter, Lewis, Mant, & Ferro, 2008). Chemical stimulants can be used as suppositories for an immediate rectal stimulant, or for long term control (Ritter, Lewis, Mant, & Ferro, 2008). Osmotic agents may work by “retaining fluid in the bowel by virtue of the osmotic activity of their unabsorbed ions” which would increase bulk and stimulate peristalsis (Ritter, Lewis, Mant, & Ferro, 2008). The magnesium found in these agents may also have a more indirect effect via cholecystokinin, a hormone that stimulates release of bile and pancreatic enzymes that encourages digestive system function. Finally, softeners and laxatives “act by softening or lubricating the feces” as well as “stimulating purgatives by inhibiting intestinal electrolyte transport” (Ritter,

Lewis, Mant, & Ferro, 2008). Laxatives promote the digestive system's function to move stool through the system, which relieves constipation.

Treatment of functional bowel disorder may use many medications depending on the symptoms in the patient. An emerging idea is that functional bowel disorder may result from dysbiosis, which implies that the "community of microorganisms living in an environment, is unbalanced, that the composition of the different bacterial genera living there regularly is disturbed, that some or many bacteria are missing and others may become more prevalent or dominant (Enck, 2017). This may encourage the use of probiotics for treatment. Laxatives, antispasmodics, loperamide and 5-HT3 antagonists (anti-diahrrea), and rifaximin (anti-bloating) may be prescribed to control specific symptoms (DynaMed Plus, 2017). In addition to utilizing drugs designed for the digestive tract, psychotropic antidepressant medications like serotonin reuptake inhibitors may be useful in decreasing patient stress (Häuser, Layer, Henningsen, & Kruis, 2012). Functional bowel disorder treatment may require the use of multiple lifestyle and pharmaceutical interventions.

Laxatives and functional bowel disorder agents are beneficial in enhancing patient comfort and quality of life. Chronic or prolonged constipation can "result in impaction and predispose the patient to perforation, sepsis, and death if left untreated" (Buck, 2011). Functional bowel disorders "neither cause organic damage nor shorten life expectancy" but can interfere with everday activities and cause physical discomfort and social embarassment (Häuser, Layer, Henningsen, & Kruis, 2012). While the symptoms treated by laxative and functional bowel disorder agents are not often life threatening, having adequate control is linked to patient satisfaction.

While negative drug interactions associated with laxatives and functional bowel disorder agents are less common, the symptoms in these disorders can be a result of medication use. Opioids and analgesics are notorious for increasing the likelihood of constipation. Laxatives were deemed necessary for "87% of patients taking oral strong opioids, 74% of those on weak opioids and 64% of those not receiving opioid analgesia" (Sykes, 1998). This suggests that opioids are responsible for about 25% of the constipation for those hospice patients with cancer diagnoses (Sykes, 1998). Pain medication use can significantly increase the likelihood of taking a laxative, and increase the dosage required to control symptoms. Opioids affect "the gastrointestinal tract and paraspinal nerve plexi to decrease peristalsis and intestinal secretions resulting in dry stools" (Strassels, Maxwell, & Iyer, 2010). While opioids may be critical to proper pain management, they also may cause increased use of digestive tract related medications. In addition, "antacids, iron supplements, and herbs such as soy-based supplements, flaxseed, and lavender also increase the likelihood of constipation" (Buck, 2011). While these medications may be important to a patient's care, they are associated with an increased likelihood of constipation.

In End of Life Care, laxatives and functional bowel disorder agents play a signficant role. Around 33% of hospice patients nearing end of life may experience constipation upon admission to inpatient hospice, and 71% of hospice patients did experience constipation during their care (Strassels, Maxwell, & Iyer, 2010). In addition to being prevalent, constipation during the last 2-5 months of life was considered to "cause quite a bit or very much distress for 44.4% of participants" (Strassels, Maxwell, & Iyer, 2010). End of Life Care patients are likely to experience constipation because of the large prevalence of pain

relieving medication and the lack of mobility. The use of medication to control these symptoms is well warranted for this population. In addition it is important to understand the need to "set realistic goals for treatment because functional disorders are rarely fully curable" (Häuser, Layer, Henningsen, & Kruis, 2012). Since these medications are used primarily to manage symptoms instead of curing illnesses, they are appropriate for End of Life Care patients, and should be encouraged because of their potiential to increase patient satisfaction.

Antihypertensive & Diuretic

Antihypertensive drugs are used to prevent hypertension, or high blood pressure. Medical professionals have created guidelines to indicate healthy blood pressure values. Currently, guidelines indicate that a target systolic blood pressure should be less than 130 mmHg, and a diastolic blood pressure should be less than 80 mmHg (DynaMed Plus, 2017). Diastolic and systolic relate to pressures at specific points in the heart's pumping cycle. Guidelines may be used to determine an individual's need of antihypertensive drugs to treat blood pressure.

There are many factors that determine an individual's blood pressure. In the arteries, "blood pressure is determined by cardiac output, peripheral vascular resistance and large artery compliance" (Ritter, Lewis, Mant, & Ferro, 2008). These values describe the quantity of blood pumped, the contribution of the blood vessel to slowing blood flow, and ability of the vessels to adjust to changes in pressure. Difficulty in regulation of blood pressure is more likely to affect the elderly population because of age-related changes to the vascular system. "With ageing, elastic fibers in the aorta and conduit arteries are replaced by less compliant collagen causing arterial stiffening and systolic hypertension"

(Ritter, Lewis, Mant, & Ferro, 2008). This may contribute to the high number of elderly End of Life Care patients who are currently taking anti-hypertensives.

The medications used to treat hypertension remain a complicated intervention. Several categories of antihypertensives are on the market currently, each which approaches the problem of anti-hypertension by unique pathways. These drugs can be categorized as the following: "A angiotensin-converting enzyme inhibitors (ACEI) and angiotensin AT1 receptor antagonists (sartans); B beta-adrenoceptor antagonists; C calcium channel antagonists; D diuretics" (Ritter, Lewis, Mant, & Ferro, 2008). In the interest of End of Life Care, drugs from classes C and D are most relevant because they are the preferential treatment since "older people often have a low plasma renin" which implies that the angiotensin inhibitors would not help them (Ritter, Lewis, Mant, & Ferro, 2008). Each of these categories will be discussed briefly to explain basic pathways of each drug.

To better understand the workings of antihypertensive drugs, basic understanding of the renin-angiotensin aldosterone system is required. Renin is an enzyme secreted into the blood by specialized cells in the kidneys, that is stimulated by decreased blood flow caused by "loss of sodium and water. Renin causes the conversion of angiotensinogen released by the liver into the blood into angiotensin 1, which is subsequently modified by angiotensin converting enzyme (ACE) found in blood vessels throughout the body to create angiotensin II. ACE also "inactivates bradykinin – a vasodilator peptide" (Ritter, Lewis, Mant, & Ferro, 2008). Angiotensin II acts on receptors in the adrenal gland to stimulate the secretion of aldosterone, which stimulates salt and water reabsorption by the kidneys, and the constriction of small arteries (arterioles), which causes an increase in blood pressure. This step-like system has long term effects. Activation of the renin–

angiotensin–aldosterone system influences “vascular tone and electrolyte balance” (Ritter, Lewis, Mant, & Ferro, 2008). This creates an overall chronic usage effect resulting in which “total peripheral vascular resistance falls slowly” (Ritter, Lewis, Mant, & Ferro, 2008). The renin-angiotensin aldosterone system is key to understanding the regulation of blood pressure.

Angiotensin-converting enzyme inhibitors (ACEI) and angiotensin AT1 receptor antagonists (sartans) are prevalent in pharmaceutical treatment of hypertension. These drugs block the actions of ACE resulting in vasodilation, or relaxation of blood vessel smooth muscle that leads to decreased blood pressure. The pharmacology of sartans works similarly to ACEI to decrease effectiveness of the potent vasoconstrictor angiotensin II. The difference between the two is that sartans “do not inhibit the degradation of bradykinin” (Ritter, Lewis, Mant, & Ferro, 2008). The A class of antihypertensive drugs work to combat the molecular creation of angiotensin II to prevent vasoconstriction.

Beta-adrenoceptor antagonists, or beta blockers are a less preferred method of lowering blood pressure. These drugs “reduce cardiac output, inhibit renin secretion and some reducing sympathetic outflow from the central nervous system (CNS)” (Ritter, Lewis, Mant, & Ferro, 2008). These drugs are unique by comparison to other antihypertensives because they work to modify the heart’s cardiac output and decrease the impact of the sympathetic nervous system. The sympathetic nervous system typically responds quickly to fight or flight situations with changes in cardiovascular demand to “providing background α receptor mediated vasoconstrictor tone and β receptor-mediated cardiac stimulation” (Ritter, Lewis, Mant, & Ferro, 2008). This class of antihypertensives works

directly on the heart through decreasing cardiac output (heart rate times stroke volume) and sympathetic activation by stimulating Beta 1 receptors on the pacemaker cells of the sino-atrial node that set the heart rate, and mediating blood pressure control by decreasing the stimulation of Beta 1 receptors that lead to renin secretion.

Calcium channel antagonists are blood pressure medications that work on the molecular level to block calcium channels in cardiac and smooth muscle. The effects of these drugs inhibit calcium influx through L type voltage dependent channels (Ritter, Lewis, Mant, & Ferro, 2008). Entry of calcium ions into these muscle cells is coupled to the release of stored calcium inside the cells. Higher levels of calcium inside muscle cells leads to longer and stronger contractions of those muscles. The overall effects of decreased calcium ion influx decrease the strength of contraction of cardiac muscle cells and "relax arteriolar smooth muscle, reduce peripheral vascular resistance and lower arterial blood pressure" (Ritter, Lewis, Mant, & Ferro, 2008). Thus, calcium channel antagonists work on the cellular level in muscle cells to affect blood pressure in a unique way compared to other antihypertensive drugs.

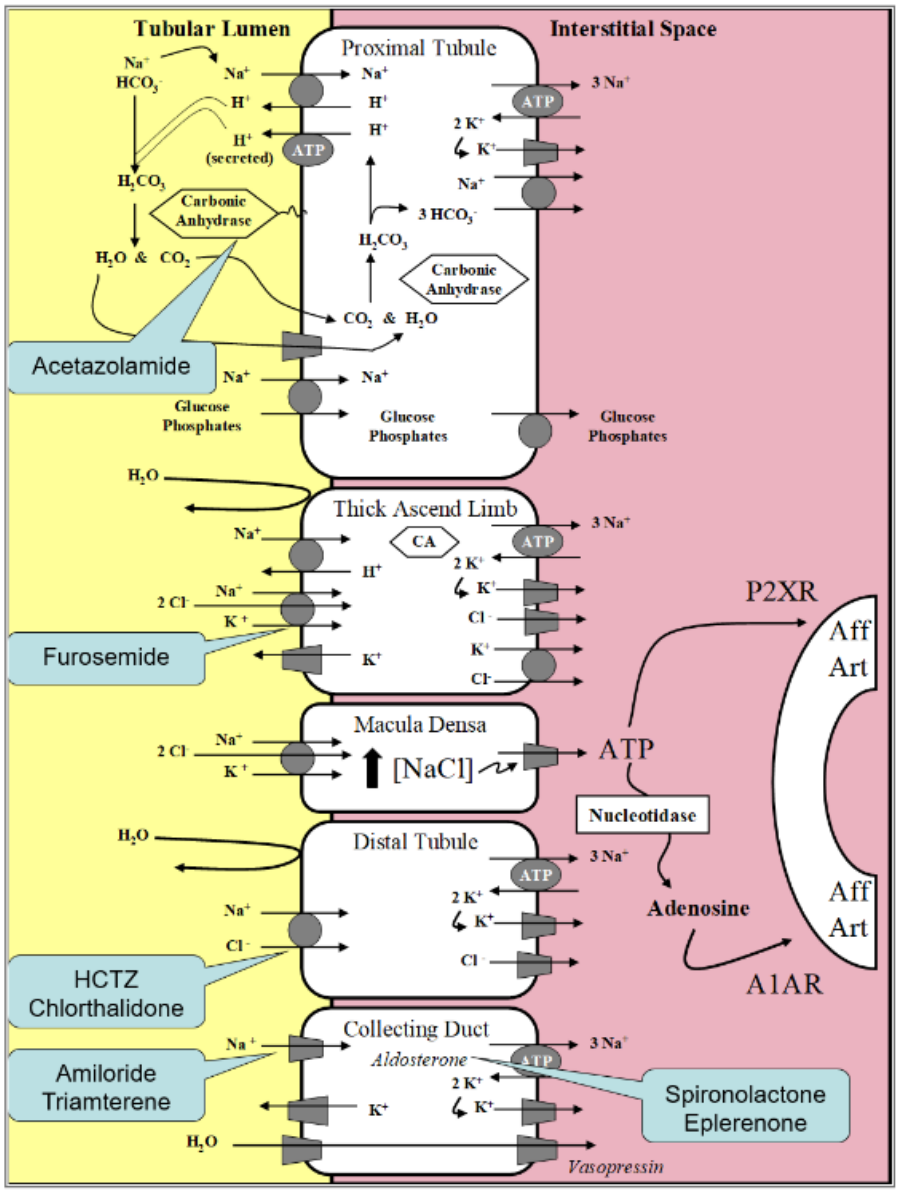
Diuretics focus on the renal system's contribution to blood pressure by maintaining body fluid balance. The renal system controls the volume of fluid intravascularly which it regulates through excreting or retaining water and salt (Ritter, Lewis, Mant, & Ferro, 2008). There are three main classes of diuretics: loop, thiazide, and potassium sparing (Sherwood, 2001). These subgroups of antihypertensives are discussed below.

Loop and Thiazide diuretics work in similar ways to control blood pressure. Loop diuretics target the "sodium-potassium-chloride cotransporter in the thick ascending limb" of the loop of Henle (Figure 3). (Sherwood, 2001). This has a significant effect on

the amount of sodium, because it is responsible for reabsorbing about 25% of the sodium load (Sherwood, 2001). This inhibition causes increased water loss, called diuresis, and increased sodium loss, called natriuresis (Sherwood, 2001). Thiazide diuretics are a commonly used class which affect sodium-potassium-chloride cotransporters. This drug works in the distal tubule (see Figure 3), affecting transporter responsible for 5% of the sodium reabsorption (Sherwood, 2001). In comparison, this class targets an area with less reabsorption capability than the loop diuretics, but still is often sufficient to address the therapeutic needs of an individual.

The third class of diuretics, potassium-sparing, work in a unique way in comparison to the other diuretics. Their target is to antagonize the effects of aldosterone in the distal tubule, causing more sodium and water to "pass into the collecting duct and be excreted in the urine" (Sherwood, 2001). A primary pharmaceutical way of controlling volume of intravascular fluid is through regulation of water and salt balance using diuretics using the standard mantra that water follows salt.

Figure 3 (Kost, n.d.)



The digestive system uses many different transporters to move a variety of ions and cellular products between the tubular lumen and the interstitial space. In each component of the digestive system, the movement of ions are different changes between these areas, which is reflected in the physiological targets of different antidiuretic medications.

Proper blood pressure regulation is key for positive long term cardiovascular health. This danger can be overlooked, for blood pressures above the recommended range may be asymptomatic (Ritter, Lewis, Mant, & Ferro, 2008). However, uncontrolled blood pressure may contribute to an increased risk of mortality. Many adverse outcomes are affected by blood pressure, for "systemic arterial hypertension is one of the strongest known modifiable risk factors for ischemic heart disease, stroke, renal failure and heart failure" (Ritter, Lewis, Mant, & Ferro, 2008). The anti-hypertensive drugs have proven to be effective for treatment through meta-analysis research that indicated that "the reduction in diastolic blood pressure achieved by drug treatment reduced the risk of stroke by the full extent predicted, and reduced the risk of coronary disease by about 50% of the maximum predicted, within approximately 2.5 years" (Ritter, Lewis, Mant, & Ferro, 2008). Attending to blood pressure guidelines may require use of multiple types of pharmaceutical interventions for the same individual to avoid greater long-term risk of death.

Using antihypertensives increases risk of drug interactions. One such adverse effect is caused by the co-usage of anti-hypertensives with a popular drug class: NSAIDs. (See Analgesic for description of NSAIDs). NSAID use decreases the efficiency of antihypertensives, decreasing the therapeutic value of the medication because of its effect on inhibiting creation of prostaglandins that act as vasodilators and natriuretics in the kidney (Ritter, Lewis, Mant, & Ferro, 2008). Another drug interaction exists for those taking potassium supplements or potassium-sparing diuretics. Hyperkalemia, an increased level of potassium in the blood, could hazardously affect those with renal

impairment in the individuals taking these medications (Ritter, Lewis, Mant, & Ferro, 2008). Using antihypertensives may limit usage of pain relief medications and have negative consequences for those with kidney impairments, which may complicate their medication use for End of Life Care patients.

In End of Life Care patients, antihypertensive drug treatment may not be appropriate for multiple reasons. Firstly, use may limit ability to use NSAID pain relief as previously discussed, which contrasts with the emphasis of End of Life Care Programs on comfort and pain regulation. Secondly, options are available to use non-pharmaceutical interventions like salt restriction, which may be less effective but carry the weight of fewer interactions and risks of side effects (Ritter, Lewis, Mant, & Ferro, 2008). Thirdly, chronic use carries risk of side effects. In some antihypertensive classes such as ACEI, a dry cough may affect up to 30% of patients (Ritter, Lewis, Mant, & Ferro, 2008). While a cough is not life threatening, it doesn't contribute to making the patient more comfortable. Finally, hypertension is often asymptomatic and as previously mentioned antihypertensives hold the greatest benefit with long term usage. For individuals with less than 6 months to live, a decreased risk of death for long-term interventions makes anti-hypertensive control less a priority. For these reasons, decreasing antihypertensive use in End of Life Care patients may be better suited to the goals of care.

Antipsychotics & Antidepressants

Antipsychotics and antidepressants are used to treat psychological and physiological symptoms. Antipsychotics may treat the following: "bipolar disorders, schizophrenia, and major depressive disorder, acute agitation, irritability in patients with autism spectrum disorder, alcohol withdrawal, Tourette syndrome, and nausea and vomiting" (DynaMed

Plus, 2017). Antidepressants are commonly used to treat depressive disorders such as "depression, postpartum depression, seasonal affective disorder, depression associated with bipolar disorder, dysthymia, premenstrual dysphoric disorder" (DynaMed Plus, 2017). It has been found that the only clinically relevant improvements in depressive symptoms is found in the most severe cases, but antidepressants are protective in lowering the risk of relapse (DynaMed Plus, 2017). They also have been found to be helpful for anxiety disorder like "generalized anxiety disorder, obsessive compulsive disorder, panic disorder, post-traumatic stress disorder, and social anxiety disorder" (DynaMed Plus, 2017). Antidepressants are licensed to treat "bulimia, fibromyalgia, smoking cessation, diabetic peripheral neuropathy, chronic musculoskeletal pain, enuresis, and Parkinson disease" (DynaMed Plus, 2017). Antidepressants are presumed to "reduce pain transmission through the spinal cord" which justifies their use in pain management (Morelli, 2016). A wide range of emotional and physical symptoms have been found to benefit from treatment with antipsychotics and antidepressants.

In addition to the FDA approved uses, antidepressants have been found helpful to treat non-approved disorders. These off label uses include "migraine prophylaxis, post-therapeutic neuralgia, attention deficit hyperactivity disorder in adults, irritable bowel syndrome, premature ejaculation, vasomotor symptoms (hot flashes) associated with menopause or breast cancer treatment" (DynaMed Plus, 2017). A wide variety of disorders have been FDA approved for antidepressant use, but many other conditions may be relieved with these medications.

Antipsychotics are categorized based on generations. The first-generation antipsychotics achieve "dopamine D_2 neuroreceptor blockade" (DynaMed Plus, 2017). These drugs bind "more tightly than dopamine itself to the D_2 receptor, and dissociate from it slowly" (DynaMed Plus, 2017). The second generation tends to "bind more loosely than dopamine to the D_2 receptor, with higher dissociation constants than those for dopamine" (DynaMed Plus, 2017). The third-generation effectiveness is due to either "D_2 partial agonism or D_2 functional selectivity" (DynaMed Plus, 2017). All antipsychotics produce changes at both the structural and molecular levels of the pain including "production of neurotrophic factors, attenuation of glutamate excitotoxicity, oxidative stress, and apoptosis, enhancement of neurogenesis and connectivity" (DynaMed Plus, 2017). Hormones such as dopamine and serotonin are both key to the effectiveness of antipsychotics.

Types of antidepressants include selective serotonin reuptake inhibitors (SSRIs), Serotonin norepinephrine reuptake inhibitors (SNRIs), Tricyclics and tetracyclics, and Monoamine oxidase inhibitors (MAOIs). SSRIs impact the amount of serotonin in the system by targeting the serotonin transporter. Serotonin is a neurotransmitter associated with "sleep, mood, cognition, pain, hunger, and even aggressive behaviors" (Hicklin, 2016). Serotonin transporters move Na^+ and Cl^- into the cell when serotonin is bound extracellularly, and release serotonin inside the cell with "binding of intracellular K^+" (DeBattista, 2017). SSRIs "slow this recycling process" of re-uptake of serotonin into the original cell after its "release into the gaps between neurons" (Hicklin, 2016). This allosteric inhibitor makes "serotonin accessible to other neurons" and blocks about 80%

of the transporter's activity (Hicklin, T., 2016) (DeBattista, 2017). SSRIs are the most common antidepressants used.

Tricyclics and Serotonin norepinephrine reuptake inhibitors (SNRIs) work similarly to SSRIs. SNRIs and Tricyclics have similar functions of binding serotonin and norepinephrine transporters (DeBattista, 2017). Norepinephrine is a neurotransmitter released by neurons of the sympathetic nervous system associated with changes in metabolism and blood pressure in response to fight or flight situations and its transporter is similar in structure to the serotonin transporter (DeBattista, 2017). Tricyclics also have affinities for other receptors, but SNRIs tend to be specific to serotonin and norepinephrine (DeBattista, 2017). Tetracyclics, however, can affect a variety of different receptors. Some tetracyclics like Bupropion are "modest to moderate inhibitors of norepinephrine and dopamine reuptake" and are known to cause a "presynaptic release of catecholamines" (DeBattista, 2017). Amoxapine and maprotiline inhibit both norepinephrine and serotonin transporters, while vilazodone is "a potent serotonin reuptake inhibitor" (DeBattista, 2017). SSRIs, SNRIs, tricyclics and tetracyclics all target neurotransmitter transporters.

Monoamine oxidase inhibitors (MAOIs) are an older class of antidepressants that are used more sparingly in current clinical practices. MAOIs can be categorized by "their specificity for MAO-A or -B and whether their effects are reversible or irreversible" (DeBattista, 2017). These drugs work by "mitigating the actions of monoamine oxidase in the neuron and increasing monoamine content" (DeBattista, 2017). Monoamine

oxidase is an enzyme that causes oxidative deamination of monoamines and breaks down norepinephrine. MAO-A is present in “both dopamine and norepinephrine neurons” with primary substrates of “norepinephrine, epinephrine, and serotonin” (DeBattista, 2017). MAO-B is found in “serotonergic and histaminergic neurons” and acts on “dopamine, tyramine, phenylethylamine, and benzylamine” (DeBattista, 2017). Depending on the MAOI the drug targets and the metabolites used, there can be a “substantial CNS-stimulating effect” from these medications (DeBattista, 2017). MAOIs differ from other antidepressants by targeting monoamine oxidase.

While antipsychotics and antidepressants are used to treat a wide variety of disorders, they carry many adverse side effects. First generation antipsychotics are associated with “akathisia, dystonic reactions, tardive dyskinesia, and hyperprolactinemia” (DynaMed Plus, 2017). Second and third generation antipsychotics are known for their adverse metabolic effects (DynaMed Plus, 2017). Both first and second-generation antipsychotics can cause “arrhythmias, sudden cardiac death, sedation, orthostatic hypotension, sexual dysfunction, hyperprolactinemia, hypersalivation and choking, and impulse-control problems” in addition to increasing the “risk of mortality when used for treatment of behavioral disorders in elderly with dementia” (DynaMed Plus, 2017). SSRIs and SNRIs are both associated with “nausea, vomiting, diarrhea, agitation, insomnia, anxiety, akathisia, restless leg syndrome, sexual side effects, serotonin syndrome, increased risk for upper gastrointestinal bleeding, osteopenia, falls, fractures, weight gain, dizziness, lethargy, headache, flu-like symptoms, panic attacks, numbness and hyponatremia” (DynaMed Plus, 2017). SNRIs can also cause “tachycardia, dry mouth, diaphoresis,

constipation, increased pulse, dilated pupils, excessive sweating, and increased blood pressure" (DynaMed Plus, 2017). Tricyclic use is associated with "cardiovascular disease, arrhythmias, orthostatic hypotension, dry mouth, blurred vision, constipation, urinary hesitancy, confusion, sexual dysfunction, memory and concentration impairment, sedation, fractures, weight gain, and falls" (DynaMed Plus, 2017). MAOIs increase risk of "hypertensive crisis, orthostatic hypertension, serotonin syndrome, weight gain, anorgasmia, decreased libido, erectile or ejaculatory dysfunction, and neurologic effects (headache, insomnia, sedation, myoclonus, paresthesia, peripheral neuropathy)" (DynaMed Plus, 2017). Many adverse reactions and increased risk of life threatening conditions are associated with these medications.

For End of Life Care patients, use of antidepressants and antipsychotics may be instrumental to controlling rates of psychiatric disorders. This age group is notorious for underdiagnosed and undertreated instances of depression (Katzung, 2017). This is estimated as such since the "suicide rate in the over-65 age group is twice the national average" (Katzung, 2017). This may be a result of incorrect diagnosis of symptoms (apathy, flat affect, and social withdrawal) as indicative of senile dementia (Katzung, 2017). For those in hospice care, prevalence of depression is the lowest of any other long-term care service, and hospice patients receive more support from mental health professionals and counseling (Center for Disease Control and Prevention, 2013). End of Life Care prioritizes comfort, and proper management of psychiatric disturbances like depression is a high priority for these patients.

However, antipsychotics and antidepressants in the elderly have a long history of misuse and adverse effects. Antipsychotics are useful to treat symptoms from "delirium, dementia, agitation, combativeness, and a paranoid syndrome that occurs in some geriatric patients" (Katzung, 2017). These drugs are not able to produce full control of these symptoms, and often dosages are increased unnecessarily to futile attempts to reach full control (Katzung, 2017). There is "no evidence that these drugs have any beneficial effects in Alzheimer's dementia", so providers should take care to prescribe antipsychotics appropriately (Katzung, 2017). Patients receiving antipsychotic therapy should be attentive to the appropriateness of the prescription to their diagnoses to prevent the use of these medications as chemical restraints. Elderly are also "more likely to experience adverse effects" of antidepressant use (Katzung, 2017). Great care should be taken with their antipsychotic and antidepressant prescriptions for effectiveness and proper dosing in End of Life Care patients.

Anxiolytics & Hypnotics

Anxiolytics and hypnotics produce sedation. Anxiolytics reduce anxiety, while hypnotic sedatives produce "drowsiness and encourage the onset and maintenance of a state of sleep" and are commonly used to treat insomnia (Trevor, 2018). Anxiolytics can also be useful for pain management in a threefold way: "they reduce anxiety, they relax muscles, and they help patients cope with discomfort" (Morelli, 2016). The difference between the two drugs has been described as rather arbitrary. In some instances, they may be interchangeable since "drugs that induce sleep also reduce anxiety, and as most anxiolytic drugs are sedative, will assist sleep when given at night" (Ritter, Lewis, Mant, & Ferro,

2008). In fact, the increased sedative effect for hypnotics can be achieved by "increasing the dose" of anxiolytics (Trevor, 2018). One can differentiate between the two using half-life length, since a short half-life causes less of a "hangover effect" for those utilizing the medication for a hypnotic, and a longer half-life with "a longer duration of action is generally desirable" for anxiolytics (Ritter, Lewis, Mant, & Ferro, 2008). Differences between anxiolytics and hypnotics are subtle since both are used to produce a calming effect.

Anxiety can be a normal and healthy reaction to fear. Anxiolytics are prescribed when anxiety is in response to both threatening and non-threatening events, as with generalized anxiety disorder. This chronic condition is characterized by "unfocused, excessive worry and stress associated with clinically significant distress and functional impairment, often accompanied by insomnia, restlessness, muscle tension, and concentration problems" (DynaMed Plus, 2017). This unhealthy level of anxiety can cause panic attacks with "severe autonomic symptoms (e.g. chest pain, dyspnea and palpitations)" (Ritter, Lewis, Mant, & Ferro, 2008). However, pharmaceutical interventions should not be the first course of therapy. Many patients may see improvements with "cognitive therapy, relaxation techniques and simple psychotherapy without drugs" (Ritter, Lewis, Mant, & Ferro, 2008). Controlling patient anxiety manages both psychological and physiological symptoms.

The causes of insomnia can be varied. They include "pain, dyspnea, frequency of micturition, full bladder and/or loaded colon in the elderly, drugs, depression, and anxiety" (Ritter, Lewis, Mant, & Ferro, 2008). These causes require treating in their own

right. Withdrawal of "caffeine, nicotine, alcohol, and benzodiazepines" can disrupt sleep, while "amphetamines, certain antidepressants and ecstasy drugs can cause nightmares" (Ritter, Lewis, Mant, & Ferro, 2008). Dependence on hypnotics may result in chronic insomnia since when use is discontinued an excess of REM sleep can cause troublesome sleep symptoms which increases the temptation to "restart medication to suppress the withdrawal phenomena, resulting in a vicious cycle" (Ritter, Lewis, Mant, & Ferro, 2008). Before seeking hypnotics, other possible causes of sleep disturbances should be explored.

Sedative effects produced by anxiolytics and hypnotics is the result of central nervous system (CNS) depression. When prescribing these medications, the degree of CNS depression should "be the minimum consistent with therapeutic efficacy", and hypnotics will "involve more pronounced depression of the CNS" (Trevor, 2018). Dosage of sedative drugs determine the extent of symptom relief for the patient. Anxiolytics and hypnotics drug classes include Benzodiazepines and Nonbenzodiazepine hypnotic sedatives like clomethiazole, zopiclone, zolpidem and zaleplon, buspirone, and barbiturates (DynaMed Plus, 2017). Benzodiazepines, the drugs of choice, are both anxiolytic as well as anticonvulsant (Ritter, Lewis, Mant, & Ferro, 2008). The pharmacological functions of these drugs were discussed in greater detail in the discussion of anticonvulsants.

Nonbenzodiazepine hypnotic sedatives are newer and more specific drugs. These sedatives produce fewer anxiolytic effects but do "cause central nervous system depression and enhance inhibitory effects of GABA by interaction at benzodiazepine

recognition site on GABA receptor" (DynaMed Plus, 2017). There is less potential abuse than with benzodiazepines, and "generally do not cause withdrawal or tolerance" (DynaMed Plus, 2017). Clomethiazole is particularly useful in the elderly because "its short action reduces the risk of severe hangover, ataxia and confusion the next day" (Ritter, Lewis, Mant, & Ferro, 2008). Zopiclone, zolpidem and zaleplon "enhance GABA activity by binding to the GABA–chloride channel complex at the benzodiazepine-binding site" despite their lack of shared structural features with benzodiazepines (Ritter, Lewis, Mant, & Ferro, 2008). Buspirone is a "5HT1A receptor partial agonist", with slower therapeutic effects (Ritter, Lewis, Mant, & Ferro, 2008). With the development of the newer non-benzodiazepines, "therapeutic uses of barbiturates as hypnotics and anxiolytics are obsolete" because of the dangers and limitations (Ritter, Lewis, Mant, & Ferro, 2008). Newer non-benzodiazepines are useful for producing a specific and less risky drug effect to manage insomnia.

Many other drugs are commonly used to also manage symptoms of anxiety and insomnia. Second line treatments for anxiety and insomnia include "antidepressants, especially in patients with comorbid depression and/or anxiety", which can be used independently or in combination with other hypnotic sedatives especially to prevent panic attacks (DynaMed Plus, 2017). β-Blockers can be used for extreme physiological panic attack responses like palpitations or tremors. Anti-epilepsy drugs or atypical antipsychotics may also be prescribed for those seeking relief from insomnia (DynaMed Plus, 2017). Monoamine oxidase inhibitors treat "anxiety with depression, phobic anxiety, and recurrent panic attacks" (Ritter, Lewis, Mant, & Ferro, 2008). While several drug classes

are designed specifically for their sedative properties, other types of medications produce similar effects.

Sedatives can carry significant risk of tolerance and dependence. Combining multiple sedative drugs should be done with caution to prevent incorrect dosages. If doses are increased beyond a therapeutic value "sedative-hypnotics may depress respiratory and vasomotor centers in the medulla, leading to coma and death" (Trevor, 2018). These drugs can cause adverse effects like "morning sedation, anterograde amnesia, anxiety, impaired balance or motor incoordination, ataxia, dizziness, and parasomnias" (DynaMed Plus, 2017). Benzodiazepines are associated with "increased risk of falls, hip fractures, and mobility problems in older adults" (DynaMed Plus, 2017). Sedative medications carry many possible side effects that result from incorrect dosing.

For the elderly population, anxiolytics and hypnotic sedative use may be common. Lack of sleep is one of the most common complaints about aging, and "dissatisfaction with sleep reportedly occurs in 35% of adults and is most frequent in women aged over 65 years" (Ritter, Lewis, Mant, & Ferro, 2008). Relief from anxiety and poor sleep can significantly increase comfort as one approaches death. Long term use is not advisable, but for those with limited time these medications may provide adequate symptom relief. The key to anxiolytic and hypnotic use in End of Life Care is management of adverse medication effects. Older adults are at an increased risk of falling, so side effects of impaired motor coordination and balance can make these medications particularly dangerous for this population. Maintaining a proper dosage may be increasingly difficult for dementia patients and other elderly individuals who experience changes in their drug

metabolism rates as they age. It is estimated that the "half-lives of many benzodiazepines and barbiturates increase by 50–150% between ages 30 and 70" (Katzung, 2017). Since these changes occur more frequently the older an individual gets, correct dosing can be difficult with these changes in metabolism affecting half-life. Anxiolytics and hypnotics may be useful in the management of comfort, their use should be closely monitored to maintain a healthy level of sedation for End of Life Care patients.

Bronchodilators

Bronchodilators are medications used to expand small airways to make breathing easier. The most common use is to treat asthma. Bronchodilators may also be used to treat Chronic Obstructive Pulmonary Disease (COPD) with chronic bronchitis symptoms. COPD and asthma share a characteristic struggle to breathe, and bronchodilators are used to "relax airways, opening airways, and reduce air trapping" (Alberson et. al., 2013). Asthma is considered a "variable disease that presents at any age and when treatment is optimized or between the triggering of exacerbations a person with asthma should be relatively symptom free" (Scullion & Holmes, 2010). Asthma is also described as wheezing, coughing and breathlessness due to "fluctuating airways obstruction, with diurnal variation and nocturnal exacerbations" (Ritter, Lewis, Mant, & Ferro, 2008). These symptoms are a result of "constriction of bronchial smooth muscle, edema of the mucosa lining the small bronchi, and plugging of the bronchial lumen with viscous mucus and inflammatory cells (Ritter, Lewis, Mant, & Ferro, 2008). COPD can include both chronic bronchitis and emphysema components and is strongly associated with patients who are "older, with a smoking history and has irreversible damage giving daily symptoms that worsen during exacerbations" (Scullion & Holmes, 2010). It has been

described as a “progressive decline in expiratory airflow with consequent static lung hyperinflation and a fall in lung diffusion capacity” (Alberson et. al., 2013). This struggle to force air out of the lungs decreases the lung capacity to exchange air, resulting in air trapping at the end of exhalation. Bronchodilators expand small airways, but do not provide therapeutic relief from mucus blockages sometimes present in COPD patients. Bronchodilators are used in the treatment of pulmonary disease such as COPD and asthma by expanding airways. Physiologically, bronchodilation is initiated during the fight or flight response of the sympathetic nervous system by stimulation of beta-2 receptors on small airway smooth muscle cells to increase oxygen levels in the body. In contrast, the parasympathetic nervous system initiates bronchoconstriction by the action of acetylcholine on muscarinic receptors when the body is in a rest and digest mode.

Bronchodilators counteract bronchoconstriction. Bronchoconstriction can be caused by reversible airway obstruction, increased parasympathetic activation, or via “a membrane-bound G-protein which when stimulated leads to a fall in cAMP and increased intracellular calcium” (Ritter, Lewis, Mant, & Ferro, 2008). Bronchodilators include “short- and long-acting beta-2 agonists (SABAs and LABAs), and long-acting muscarinic antagonists (LAMAs)” (DynaMed Plus, 2017). These drugs have a global effect on many body systems and cause bronchodilation.

Beta-2 agonists treat bronchospasm by targeting β2-adrenoceptors. This causes an “increase cyclic adenosine monophosphate (cAMP) by stimulating adenylyl cyclase via stimulatory G-proteins” (Ritter, Lewis, Mant, & Ferro, 2008). Cyclic AMP is an enzyme responsible for phosphorylating a cascade of enzymes and reactions, causing “relaxation

of smooth muscle including bronchial, uterine and vascular" (Ritter, Lewis, Mant, & Ferro, 2008). The difference between the Beta-agonists is the amount of time to see a therapeutic benefit. Long acting agonists have slow onset of bronchodilation, which can take up to 15–30 minutes" (Ritter, Lewis, Mant, & Ferro, 2008). Beta-agonists use second messengers like cAMP to cause bronchodilation and differ in speed of effectiveness.

Antimuscarinic drugs work at a similar molecular level as Beta-2 agonists. These drugs "block muscarinic receptors in the airways" (Ritter, Lewis, Mant, & Ferro, 2008). Bronchoconstriction can result from "acetylcholine on the muscarinic (M2, M3) receptors in the bronchi" (Ritter, Lewis, Mant, & Ferro, 2008). Antimuscarinic drugs work by blocking muscarinic receptors that are responsible for the constriction of airways.

Like other medication interventions, prescription bronchodilators do not come without risk. Common adverse reactions include: "acute urinary retention, acute glaucoma when nebulized doses are given via a face mask, and paradoxical bronchoconstriction due to sensitivity to benzalkonium chloride, which is the preservative in the nebulizer solution" (Ritter, Lewis, Mant, & Ferro, 2008). The effects have also been known to cause "dysrhythmias and symptoms of palpitations (Ritter, Lewis, Mant, & Ferro, 2008). Depending on the specificity of beta-blockers to physiologic types of beta receptors in the body, these drugs also can cause effects such as the following: "inhibition of release of inflammatory mediators, increased mucociliary clearance, increase in heart rate, force of myocardial contraction, and speed of impulse conduction, muscle tremor, vasodilatation in muscle, metabolic effects like hypokalemia, raised free fatty acid concentrations;

hyperglycemia, and desensitization." (Ritter, Lewis, Mant, & Ferro, 2008). While these effects may seem benign, they can cause serious concerns for those with comorbidities. In addition, these drugs have a bitter taste, which is a factor that compromises proper compliance (Ritter, Lewis, Mant, & Ferro, 2008). These affects may seem mild, but can cause discomfort and dangerous global effects for patients who are prescribed bronchodilators.

Bronchodilators are a common drug in End of Life Care patients because of the increasing prevalence of the chronic diseases they treat. COPD has become the "third leading cause of death in the USA and ranks as a major cause of morbidity" (Alberson et. al., 2013), but bronchodilators use for COPD is not curative in nature. It has been indicated that "no bronchodilator has shown an improvement in the mortality of COPD patients" (Alberson et. al., 2013), and rather is used primarily to address patients' struggles to breathe. The major reason for this lack of relief is that the emphysema aspect of COPD destroys airways in the lungs causing them to collapse on exhalation so there is little help from bronchodilation due to lack of smooth muscle. This has resulted in the belief that "earlier use of palliative care should be considered when traditional pharmacotherapy fails to achieve outcome measures and before consideration of end-of-life issues" (Alberson et. al., 2013). While risk factors and comorbidities continue to be a concern with utilizing bronchodilators, the use of them throughout palliative and hospice care seems to be appropriate if the patient is receiving positive relief from usage. Bronchodilators should only be used in End of Life Care Asthmatic and COPD patients if the airway expansion provides symptom relief that is superior to the adverse effect of the medication and is not intended for curative results.

Proton Pump Inhibitor & Antacid

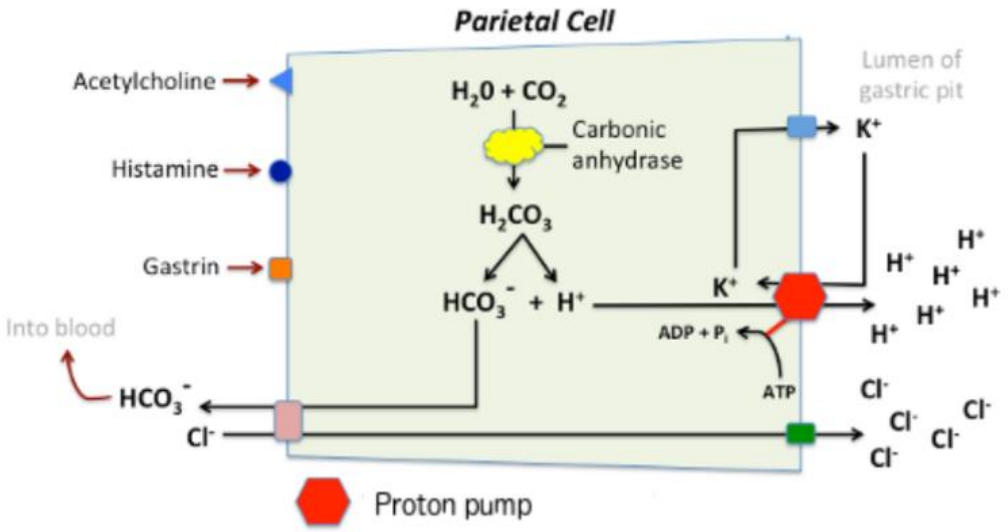
Proton pump inhibitors and antacids reduce acidity of stomach contents. While the mechanism of each drug is unique, both are useful in treating conditions relating to gastric acid such as gastroesophageal reflux disease, reflux esophagitis, and peptic ulcerations (Ritter, Lewis, Mant, & Ferro, 2008). Proton-pump inhibitors are also used "in combination with antibacterial drugs to eradicate H. pylori" (Ritter, Lewis, Mant, & Ferro, 2008). Gastric acid pH can be managed using proton pump inhibitors, antacids, and H_2 receptor antagonists, but since H_2 receptor antagonists are not included in the list of common drugs prescribed at end of life, its mechanisms will be excluded from this discussion.

While proton pump inhibitors and antacids manipulate gastric acid artificially, this process occurs normally. Gastric acid secretion is a physiological process used to help digest protein, absorb vitamins and minerals like iron, calcium, magnesium, and vitamin B_{12}, and kill bacteria (Del Valle, 2014). Acid secretion occurs by "basal or stimulated conditions" (Del Valle, 2014). Basal acid production operates in "a circadian pattern" via cholinergic input from the vagus nerve and histaminergic input from local sources (Del Valle, 2014). Stimulated gastric acid stages occur in response to signals. The cephalic phase stimulates the vagus nerve by the "sight, smell, and taste of food" (Del Valle, 2014). The gastric phase is driven by "amino acids and amines that directly stimulate the G cell to release gastrin, which in turn activates the parietal cell" when food enters the stomach or the stomach wall is distended (Del Valle, 2014). The last (intestinal) phase is "mediated by luminal distention and nutrient assimilation" as food enters the intestine

(Del Valle, 2014). These natural processes produce a steady supply of gastric acid to begin digestion of the appropriate food components.

Gastric Acid is hydrochloric acid (HCl) found in the stomach. The pH of this acid can be mediated by several ionic exchanges that manipulate the presence of hydrogen and chloride. This process is illustrated in Figure 4. The acid secreting pump, H^+/K^+-ATPase generates a "large concentration of H^+" by "transferring H^+ ions from parietal cell cytoplasm to the secretory canaliculi in exchange for K^+" (Del Valle, 2014). This abundance of H^+ makes the acid more acidic, and increasing amounts of acid are produced as hydrogen combines with chloride. Chloride is transferred to the parietal cell from the blood, then travels into the lumen of the stomach by being "secreted against both a concentration and electric gradient" (Bowen, 2017). This movement of chloride into the lumen is achieved by conductance channels" (Bowen, 2017). Maintenance of gastric acid pH occurs naturally through ion transport.

Figure 4 (Bowen, 2017)



The parietal cell is a primary source of hydrogen in the lumen of the gastric pit. It facilitates buffering reactions that produce this hydrogen balance in the presence of the necessary ligands, and then pumps it out using active transport.

Thus, the parasympathetic nervous system neurotransmitter acetylcholine, the regulator of physiological function in the gut histamine, and the hormone gastrin all stimulate the production of stomach acid. There are also pathways that inhibit gastric acid production. Acid production is inhibited directly when parietal cell receptors bind the following ligands: "prostaglandins, somatostatin, and epidermal growth factor" (Del Valle, 2014). However, the combined presence of histamine and gastrin inhibits gastric acid secretion. Histamine binds to the H_2 receptors, which activates adenylate cyclase and causes an "increase in cyclic adenosine monophosphate (AMP)" (Del Valle, 2014). When gastrin receptors are activated, the "protein kinase C/phosphoinositide signaling pathway" is

activated (Del Valle, 2014). The combination of increased cyclic AMP and increased protein kinase C/phosphoinositide signals creates "downstream kinase cascades that control the acid-secreting pump, H^+, K^+-ATPase" (Del Valle, 2014). The effect of cyclic AMP and the protein kinase C signals prevents the pump from producing H^+ ions, which makes the gastric acid more basic. Histamine also binds to the "H_3 receptor on D-cells, which inhibits somatostatin release in response to HCl" (Del Valle, 2014). Central and peripheral neural factors via the vagus nerve also balance acid secretion (Del Valle, 2014). Natural pathways inhibit gastric acid secretion via ions or neural impulses.

Another component of this system is pepsin. Pepsin secreted by gastric chief cells mediates proteolysis of protein into "di- and tripeptides and amino acids before absorption" (Del Valle, 2014). This proteolytic enzyme comes from pepsinogen, its "inactive precursor" (Del Valle, 2014). Pepsin requires a pH less than 2 for activity, and the "acid environment within the stomach leads to cleavage of the inactive precursor to pepsin and provides the low pH required" (Del Valle, 2014). Pepsinogen release is stimulated by many of the "secretagogues that stimulate acid secretion" (Del Valle, 2014) like acetylcholine, histamine, and gastrin (above). Antacids "inactivate pepsin by raising the gastric pH above 4–5" (Ritter, Lewis, Mant, & Ferro, 2008). Pepsin and acid secretion occur by similar mechanisms even though they originate in different gastric cells, so medications that inhibit one typically inhibit the other.

Antacids control the pH of gastric acid. Drug classes of antacids include sodium bicarbonates, calcium carbonates, magnesium salts and aluminum hydroxide. Antacids cause chemical reactions that buffer and neutralize hydrochloric acid and release byproducts such as carbon dioxide and water (DynaMed Plus, 2017). Aluminum

hydroxide forms an “insoluble colloid in the presence of acid and line the gastric mucosa to provide a physical and chemical barrier” (Ritter, Lewis, Mant, & Ferro, 2008). Thus, antacids increase pH of the acidic environments in the stomach.

Proton pump inhibitors target transporters that produce gastric acid. These inhibitors block the “H+/K+-adenosine triphosphatase enzyme system of the gastric parietal cell” (Ritter, Lewis, Mant, & Ferro, 2008). These drugs interfere by covalent binding with hydrogen–potassium ATPase, preventing the transport of H+ into the gastrointestinal lumen (McDonagh, Carson, & Thakurta, 2009). There are “six oral proton pump inhibitors currently available: omeprazole, rabeprazole, esomeprazole, lansoprazole, dexlansoprazole, and pantoprazole” (McQuaid, 2017). All proton pump inhibitors have “minor differences in their pharmacology”, which makes them “equally efficacious” (McQuaid, 2017). The six classes of proton pump inhibitors work similarly to prevent the movement of ions into the gastrointestinal system and increase pH.

Drug interactions associated with proton pump inhibitors and antacids tend to be minimal. Proton pump inhibitors should not be taken concurrently with clopidogrel (Plavix), because this is “associated with increased risk of major adverse cardiac events” (DynaMed Plus, 2017). In addition, “omeprazole has potential drug interactions with caffeine, clomipramine, theophylline, cimetidine and rifampin” (DynaMed Plus, 2017). Antacids may be less effective and cause adverse reactions when they are taken with calcium and magnesium containing products, or with acidic medications (DynaMed Plus, 2017). In comparison with other drugs, proton pump inhibitors and antacids have fewer drug interactions, making them at lower risk for poly-medicine interactions.

For End of Life Care patients, managing gastric acid pH may be advantageous. Proton pump inhibitors are "remarkably safe for short-term therapy" but should not be used long term because decreases in "vitamin B_{12}, iron, magnesium, and calcium absorption" are possible (McQuaid, 2017). Disruption of normal gastric acid pH is not typically life threatening, but does produce many uncomfortable symptoms like heartburn, dyspepsia (indigestion), and gastritis (inflammation and irritation of the stomach lining) (DynaMed Plus, 2017). End of Life Care practices do prioritize controlling uncomfortable symptoms. Elderly patients are also at increased risk of non-steroidal anti-inflammatory drug (NSAID)-induced peptic ulcerations. These ulcers are a result of overusing NSAID medications for pain relief (Ritter, Lewis, Mant, & Ferro, 2008). While proper pain management is important in End of Life Care, the resultant ulcers can provide more discomfort for the patient. In some cases, a "proton pump inhibitor should be considered as prophylaxis against upper gastrointestinal complications" (Ritter, Lewis, Mant, & Ferro, 2008). Proton pump inhibitors and antacids may provide relief from undesirable symptoms and ulcers, which is a useful contribution to End of Life Care.

Anticoagulants

Anticoagulants, commonly known as blood thinners, are drugs that manipulate coagulation, or clotting, of blood. They are primarily used to treat deep vein thrombosis and pulmonary embolism. Deep vein thrombosis is a condition where blood flow in a deep vein is blocked by a blood clot (DynaMed Plus, 2017). Pulmonary embolism is a "mechanical obstruction of one or more branches of the pulmonary vasculature, usually due to a blood clot" (DynaMed Plus, 2017). Blood clots can cause stroke, myocardial infarction (heart attack), or deep vein thrombosis that may lead to pulmonary embolisms.

Clotting is a natural response to control bleeding, but can also be detrimental if blood flow is impeded. Interfering with blood clotting carries significant risk of hemorrhage, especially "within first 30 days in elderly patients with atrial fibrillation" (DynaMed Plus, 2017). Anticoagulants are used to decrease the activation of the clotting cascade in patients that would cause blockage of blood flow to vital organs.

Anticoagulants can be classified as Vitamin K antagonists, Heparins, Factor Xa inhibitors, and Direct thrombin inhibitors (DynaMed Plus, 2017). Vitamin K antagonists, such as warfarin, cause anticoagulation indirectly. This effect is produced by the drug "interfering with synthesis of vitamin K-dependent clotting factors, including factor II (thrombin), factor VII, factor IX, and factor X" (DynaMed Plus, 2017). Functional clotting factors "contain residues of γ-carboxyglutamic acid formed by carboxylation of a glutamate residue in the peptide chain of the precursor" (Ritter, Lewis, Mant, & Ferro, 2008). Vitamin K accomplishes carboxylation as a cofactor by cycling through several forms (epoxide, quinone and hydroquinone) (Ritter, Lewis, Mant, & Ferro, 2008). Warfarin is similar in structure to Vitamin K, so it can "inhibit vitamin K epoxide reductase", which interrupts the cycle and prevents the production of the clotting factors (Ritter, Lewis, Mant, & Ferro, 2008). The similarity of warfarin to Vitamin K prevent carboxylation necessary for clotting factor production.

Use of warfarin in patients requires frequent blood work. For long-term control of coagulation, an international normalized ratio, or INR is measured via blood samples to measure how long it takes blood to clot (Ritter, Lewis, Mant, & Ferro, 2008). For most patients, the therapeutic range for INR is 2-3 (DynaMed Plus, 2017). This ideal therapeutic range can differ between patients depending on other comorbidities and

medical history. Initially, INR may be checked daily until therapeutic levels are achieved, and then may be checked weekly or monthly (Ritter, Lewis, Mant, & Ferro, 2008). Warfarin requires high patient compliance to measure INR values.

The second class of anticoagulants, heparins, also affect the normal coagulation cascade reactions. When the drug is combined with its cofactor, antithrombin III, "thrombosis is blocked through inactivation of Factor X" (DynaMed Plus, 2017). Antithrombin III naturally inhibits serine proteases such as thrombin, which has a significant effect on enzyme cascade reactions (Ritter, Lewis, Mant, & Ferro, 2008). Interrupting a cascade step also "prevents fibrin formation from fibrinogen" (DynaMed Plus, 2017). Heparins are classified on weight and the specific target factor: for example, "Low-molecular-weight heparins preferentially inhibit factor Xa" (Ritter, Lewis, Mant, & Ferro, 2008). These specific factor Xa inhibitors are considered a separate class of anticoagulants and include both low molecular weight heparins as well as synthetic pentasaccharides like Fondaparinux (Ritter, Lewis, Mant, & Ferro, 2008). Fondaparinux requires less extensive coagulation monitoring, which may be beneficial to noncompliant patients (DynaMed Plus, 2017). Many anticoagulants work to block the coagulation enzyme cascade, but targeting a key factor, Xa, is common.

Direct thrombin inhibitors are more specific than other anticoagulants. Instead of targeting antithrombin III, these drugs directly "inhibit clot-associated thrombin" (Ritter, Lewis, Mant, & Ferro, 2008). This type of anticoagulant is now synthesized artificially, but can be found naturally in leeches (Ritter, Lewis, Mant, & Ferro, 2008). These drugs are more predictable and are closely tied to plasma concentration (Ritter, Lewis, Mant, &

Ferro, 2008). While less common, direct thrombin inhibitors mount a specific and direct anticoagulant effect.

Anticoagulation should not be initiated without careful consideration of risk factors and drug interactions. Anticoagulants should not be used in those with active bleeding, blood dyscrasias, recent surgical histories, open wounds, active ulcers, aneurysms, cerebrovascular hemorrhages, pericarditis and pericardial effusions, diagnosis or therapeutic procedures with potential for bleeding, or uncontrolled hypertension (DynaMed Plus, 2017). In addition, conditions like pregnancy, bacterial endocarditis, and major regional or lumbar block anesthesia are contraindications for anticoagulation (DynaMed Plus, 2017). Anticoagulant control may be affected by age, sex, race, diet, "lower weight, liver, cardiac, and renal disease" (DynaMed Plus, 2017). Regular INR blood work may be critical, so patients must be dependably compliant. This means patients who are senile, are alcoholics, have psychological disturbances or are uncooperative should not be prescribed anticoagulants (DynaMed Plus, 2017). Anticoagulants carry a great risk of uncontrollable bleeding, and many patients are poor candidates for this intervention.

In addition to the contraindications for anticoagulant use, there are many drug interactions to consider. The following drugs should be avoided while on anticoagulants: "alcohol, amiodarone, barbiturates, disulfiram, estrogen-containing oral contraceptives, metronidazole, phenylbutazone, erythromycin, salicylates and urokinase" (DynaMed Plus, 2017). The response to anticoagulants also is affected by use of antiplatelets, other

anticoagulants, antifungals, and antibiotics (DynaMed Plus, 2017). Anticoagulants have a great potential to prevent life altering blood clots, but prescribing them as a course of treatment requires time to examine risk factors and potential drug interactions.

For those nearing end of life, use of anticoagulants may be complicated. Deep vein thrombosis may be more common in the elderly with risk factors like "recent surgery or trauma and hospitalization with prolonged bed rest (DynaMed Plus, 2017). Pulmonary embolism risk factors include those with a history of an embolism, as well as "surgery, cancer, immobilization, trauma, and obesity" (DynaMed Plus, 2017). If untreated, complications such as "arrhythmia, chronic thromboembolic pulmonary hypertension, and cor pulmonale (increased pulmonary vascular pressure and right heart disease resulting from lung disease) which may lead to obstructive shock" may arise in patients with pulmonary embolisms (DynaMed Plus, 2017). The elderly in End of Life Care are at increased risk for life threatening outcomes from deep vein thrombosis and pulmonary embolisms.

Despite the increased risk and poor outlook without anticoagulation treatment regimes, prescribing these medications may not be appropriate. If those at end of life have "impaired nutritional intake or require frequent alterations in medication (they) are at high risk of adverse consequences of warfarin and such patients may be better managed by stopping anticoagulation" (Parsons, Hughes, Passmore, & Lapane, 2010). The poly-medication interactions are likely, which further complicates pharmaceutical management care. For patients with mild to severe cognitive impairments and limited

mobility, the work of maintaining an ideal level of anticoagulation may be more stressful than beneficial. High health literacy requirements, may make anticoagulation a poor choice for End of Life Care patients.

Antibiotics

Antibiotics are drugs used to treat microbial infections. Antibiotics can be used to treat a wide range of infections not limited to respiratory, skin and soft tissue, abdominal, urinary tract, and sexually transmitted diseases. Antibiotic intervention is commonplace, resulting in the view that it is "usual care and not an 'aggressive' treatment" (Pautex et al., 2013). Infections occur in greater number for those with weakened immune systems who are unable to fight off infection, and as a result many individuals in End of Life Care may be prescribed courses of antibiotics.

Antibiotic drugs can be classified into several major classes: "quinolones, co-trimoxazole, aminoglycosides, glycopeptides and lipopeptides, metronidazole, oxazolidinones, clindamycin, macrolides, beta-lactams" (DynaMed Plus, 2017). Each class of antibiotics mounts microbial defense in a unique way, which contributes to the niche usage of specific drugs depending on the infection in question.

Quinolones work by preventing microbial cell reproduction. DNA replication is targeted by binding "enzyme-DNA complexes via interactions with DNA gyrase, type II topoisomerases, and topoisomerase IV" (DynaMed Plus, 2017). When the drug is bound to the replication machinery, replication stops. In addition, this binding leads to double strand breaks in the DNA, causing degradation of the replication transcripts (DynaMed Plus, 2017). Quinolones attack bacteria at their transcription machinery.

Co-trimoxazole, or trimethoprim-sulfamethoxazole (TMP-SMX), works by blocking cellular products needed for bacterial growth. This drug combines two agents to "inhibit the synthesis of folic acid and block bacterial growth" (DynaMed Plus, 2017). The first agent, sulfamethoxazole, "inhibits production of dihydrofolate from para-aminobenzoic acid (PABA)" while the second, trimethoprim, "inhibits reduction of dihydrofolate tetrahydrofolate" (DynaMed Plus, 2017). This results in lowered production of folic acid, leaving fewer cellular products for bacterial growth.

Antibiotics can also work by targeting protein synthesis. Aminoglycosides and tetracyclines "bind to proteins of the 30S subunit of bacterial ribosomes causing misreading of the genetic code" (DynaMed Plus, 2017). In addition, tetracyclines can cause another deleterious effect for bacteria for they "inhibit the elongation phase of RNA synthesis" (DynaMed Plus, 2017). Similarly, oxazolidinones and macrolides "binds to the 50S ribosomal subunit of susceptible bacteria" (DynaMed Plus, 2017). This bactericidal activity prevents ribosomes from making proteins from chains of amino acids. Protein synthesis is key to cellular growth, preventing the bacterial infection from spreading. Targeting ribosomes disrupts protein synthesis in bacteria.

Glycopeptides and lipopeptides target bacteria by attacking cellular membranes. This disruption of cell integrity can be accomplished in several ways. One approach is to "inhibit cell wall synthesis by binding to the D-Ala-D-Ala residues of peptidoglycan precursors in the cytoplasmic membrane" (DynaMed Plus, 2017). Another is using calcium ion pathways to form "membrane-spanning pores, leading to potassium efflux and cell death" (DynaMed Plus, 2017). Finally, these drugs can inhibit transpeptidation

and transglycosylation (DynaMed Plus, 2017). Beta-lactams also disrupt membrane integrity by binding "penicillin-binding proteins (PBPs) and block formation of cross-linkages in peptidoglycan" (DynaMed Plus, 2017). Fewer cross linkages weaken the integrity of the cell, especially in cell division, which can lead to cell death. Destroying bacterial cellular membranes is an effective way to produce cell death in bacterial infections.

Metronidazole works by increasing the presence of damaging products in bacterial cells. Activation of this drug causes "reduction of the nitro group" which results in subsequent production of free radicals (DynaMed Plus, 2017). Reduction is a chemical reaction that creates a product with great potential to damage bacteria, especially bacterial DNA, that leads to cellular death (DynaMed Plus, 2017). Metronidazole drugs utilize the damaging power of free-radicals.

Clindamycin also works by targeting protein synthesis. This drug "reversibly binds 23S rRNA nucleotides from the 50S subunit of bacterial ribosomes", causing a lack of initiation of protein synthesis because of the binding interaction (DynaMed Plus, 2017). In addition, this drug "inhibits toxin production by group A Streptococcus and *Staphylococcus aureus*", resulting in a less damaging effect for the organism infected (DynaMed Plus, 2017). Clindamycin works similarly to other antibiotics to target protein synthesis, but also has other effects reducing the toxic effect of the infection in the organism.

Antibiotic usage is not without risk. Quinolones like fluoroquinolones have the potential for negative drug interactions with warfarin. This is because the drugs act by "inhibiting

warfarin elimination, reducing the number of vitamin K-producing bacteria in the gut, and displacing warfarin from protein-binding sites" (DynaMed Plus, 2017). Warfarin is known as a blood thinner, the importance of which is discussed in further detail in the anticoagulant section. Potential side effects of use include ototoxicity, hypersensitivity reactions, nephrotoxicity, and lactic acidosis (DynaMed Plus, 2017). While antibiotics are key to fighting infection, they may have negative effects for individuals with other co-morbidities and weakened immune systems.

As individuals approach end of life, infections are more likely to affect their health outcomes. Infection in those with advanced chronic diseases have a high incidence of resulting in death, causing an increased antibiotic usage as individuals' overall health deteriorates (Pautex et al., 2013). For patients suffering from cancers, infection occurs more often because of "local factors due to a tumor, deficiencies in host defense mechanisms secondary to cancer and/or antitumor treatment, and the presence of invasive devices" (Pautex et al., 2013). In long term care settings antibiotic use runs rampant with annual prevalence of antibiotic prescriptions for 47 to 79% of the population (Fleming, Bradley, Cullinan, & Byrne, 2015). The prevalence of infection in the elderly and those in End of Life Care has contributed to increased antibiotic usage in this population.

Antibiotic use may be growing, but it lacks significant data indicating it is always the patient's best option. Studies into the necessity of antibiotic interventions revealed that "as many as 25–75% of antibiotic prescriptions in long term care facilities are inappropriate in terms of their indication, dose or duration of therapy" (Fleming, Bradley, Cullinan, & Byrne, 2015). Inappropriate antibiotic use can result in unhelpful outcomes

for patients. In a study of 41 patients who were prescribed antibiotics, only 62% indicated that the use of the antibiotics was helpful while 19% reported the drug intervention to be unhelpful (Pautex et al., 2013). More studies examining case-specific antibiotic use has determined that "antibiotic therapy and hospitalization have repeatedly failed to demonstrably improve the survival or reduce the discomfort of terminally ill demented people with pneumonia" (Pengo et al., 2017). This evidence may indicate benefits from decreasing antibiotic prescriptions in End of Life Care.

Heavy antibiotic use in End of Life Care patients may be inappropriate for many reasons. Increasing the number of drugs in an individual's system increases the likelihood of adverse drug interactions and toxicities. These unnecessary prescriptions can also lend a heavy burden on health care costs, without a high increase on quality and quantity of life (Pautex et al., 2013). There is evidence that drug interventions can increase patient stress "due to the way of administration of the treatment" (Pautex et al., 2013). Finally, overuse of antibiotics carries an "increased risk of subsequent antimicrobial resistance that not only affects the patients who are receiving treatment, but also presents a public health concern" (Pautex et al., 2013). For these reasons, antibiotic overuse prevention could be key for End of Life Care patients.

For many medical professionals, antibiotic use may not be considered an aggressive treatment approach, which contributes to their widespread use. Many antibiotic prescriptions are given because "it is often easier to prescribe antibiotic therapy than to withhold the treatment", in addition to feeling responsible to offer some treatment course for "possible infection even among patients in whom other aggressive therapies would

generally not be appropriate" (Pautex et al., 2013). Studies indicate that even when dementia patients were given life expectancies of "1–6 months, 79% of (medical professionals) agreed with Antibiotic Therapy" (Pengo et al., 2017). In the same study when life expectancy dropped to "less than 1 month, a large proportion (61%) of respondents still agreed with antibiotic therapy" (Pengo et al., 2017). When researchers tried to predict provider's response about recommending antibiotics on terminal dementia patients, "having received training in bioethics was the strongest correlate of the opinion that antibiotic therapy should not be continued when a patient's life expectancy dropped to less than 1 month" (Pengo et al., 2017). The atmosphere of the current U.S. health system, termed the cure at all cost approach, may contribute to these prevailing opinions about the necessity of antibiotic use in End of Life Care, and education of professionals about bioethics may help increase appropriate prescriptions.

Conclusion

In conclusion, understanding the intricacies of medication use during End of Life Care is exceedingly complex. Many different classes of medications are utilized in this patient population, but how efficacious each one is remains to be well explained in available literature. This information is also exceedingly difficult for the patient population to access and understand, which places a barrier to care for a patient enrolled in a patient centered program such as palliative and hospice care. End of Life Care is a quickly expanding opportunity to promote comfort and address patient concerns, and with its increasing prevalence, measures should be taken to understand how pharmacology plays a role in these situations.

While this literature review is not exhaustive, it does attempt to provide some recommendation of use based on medication use, pharmacological function, adverse effects, and specific concerns for elderly patients. Analgesics and Opioid Narcotics should be more accessible to these patients, with care to be attentive to dosing. Antiemetics and Antivertigo drugs are useful in management of particularly uncomfortable symptoms, and should be utilized more frequently. Anticonvulsants have great potential to align with goals of treatment, but should be closely monitored to ensure therapeutic benefits outweigh adverse effects. Laxatives and functional bowel agent use is most often in response to pain management, so should be used to promote comfort and further use of analgesics and narcotics. Antihypertensives and diuretics treat conditions characterized by their long term negative effects, and are notorious for adverse effects and therefore are a poor choice for End of Life Care patients. Antipsychotics and antidepressants should only be used if appropriateness is well established and all other avenues to address the psychological concern are explored and fail to produce the desired mood. Anxiolytics and hypnotics may be appropriate especially for sleep concerns but should be closely monitored for dosage and physical safety. Bronchodilators use in chronic disease is not curative in nature but rather addresses symptoms, making it a useful choice in End of Life Care pharmacology. Proton pump inhibitors and antacids are useful for short term relief and symptom management with few adverse effects, making their use acceptable. Anticoagulants are a poor choice in this patient population because of the extent of intervention, extensive health literacy demands, and adverse effects and drug interactions. Antibiotics have limited use in End of Life Care patients because of the

lack of significant data proving the indication and motivations are in the best interests of the patient.

That being said, this study aims to produce a generalized statement about the proper use of medications. In every case, patient and provider should openly discuss the goals of treatment and consider if the recommendation of pharmaceuticals is meeting those expectations. Pharmaceutical utilization is complicated, and the cost of promoting better patient outcomes in End of Life Care may be more extensive time invested in health literacy. These recommendations should act as guidelines to equip the patient to better participate in their health care process to achieve the goals they desired by enrolling in End of Life Care programs.

Additional Project Details:

In the spirit of making intentional efforts to increase health literacy in the elderly population, I chose to make my information accessible in a web based format that could be viewed widely. While this thesis was purposely directed in collecting information about medications in End of Life Care and consolidating them into one central location, it wasn't able to determine the best way to communicate this information to the general public. However, based on understanding of information distribution, making a web site seemed like an option with potential to be able to increase access to this population for this population and their families. The website is written at or below an eighth grade reading level, making it more easily understood by a wider variety of individuals.

The website is structured with a home page that explains the intention of this information and the best way to navigate the site. It includes links to the full paper and the complete reference list, inviting individuals interested to be able to come to a deeper understanding. It breaks each medicine into an individual page, which allows patients to only read about medications that pertain to their care.

URL: https://reflectiverosie.wixsite.com/endoflifemedication

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