MEDICATIONS ALS PATIENTS TAKE IN THE LAST SIX MONTHS OF LIFE

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For my Mom

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Amyotrophic lateral sclerosis (ALS), an incurable neuromuscular disease, causes progressive paralysis resulting in respiratory failure and ultimately death. Although there are only 30,000 people nationwide living with ALS, this population is of significant public health concern as those afflicted with ALS suffer from progressive symptoms of disability, making them a particularly vulnerable population in need of public health advocacy for improved access to medications and care. As the symptoms of disability become increasing acute in the final months of life, achieving the best quality of life possible is of paramount importance. To achieve this, a number of medications exist to both treat the direct and indirect symptoms of ALS.

The purpose of this thesis is to examine barriers terminal ALS patients experience in accessing medications, medication trends as ALS patients near death, and the effect of medications on quality of life for ALS patients in the terminal phase of the disease. Literature pertaining to the terminal phase of ALS was reviewed and an analysis of secondary data was performed. The data analyzed for this thesis was from the National Institute of Mental Health grant funded Living with ALS study, which collected medication data in the preceding months before death from terminal ALS patients. For the purposes of this analysis, patient medications were categorized into four domains: *ALS treatment* medications, *palliative* medications, *mood* medications, and *other* medications. The correlation between the medication domains and

sociodemographic and quality of life indicators were investigated. Changes in medications over time were also investigated.

Results of the analysis revealed that those with higher incomes and educational attainment were taking significantly fewer *palliative* medications. Additionally, those on Medicaid were on significantly fewer *other* medications. Finally, across all medication domains, medication use declined significantly as patients approached imminent death. These findings suggest that the medications used to treat the symptoms of ALS do little to improve symptoms and even less to improve quality of life. Future research recommendations include exploring patients' motivations for discontinuing medications, improving symptom management medications, and improving ALS patients' access to both pharmacological and non-pharmacological interventions to improve overall quality of life.

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1.0 INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a neuromuscular disease that causes progressive paralysis resulting in respiratory failure and ultimately death. The central focus of care for this fatal and incurable disease is improved quality-of-life, which is achieved through pharmacological and non-pharmacological interventions. The purpose of this thesis is to examine barriers terminal ALS patients experience in accessing medications, medication trends as ALS patients near death, and the effect of medications on quality of life for ALS patients in the terminal phase of the disease. If patient comfort and improved quality of life are the essential priorities of ALS care, what medications do patients continue, stop or initiate as they are faced with progressive disease in the last six months of life? To answer this question, this thesis will examine literature pertaining to the terminal phase of ALS and report the findings of a secondary data analysis. The data to be analyzed for this thesis is from the National Institute of Mental Health grant-funded, Living with ALS study. The Living with ALS study was performed at the Eleanor and Lou Gehrig MDA/ALS Research Center at Columbia University and other surrounding clinics in New York from January 2000 to June 2004.

Although ALS affects only 30,000 people nationwide, this population is of significant public health concern. Those afflicted with ALS suffer from progressive symptoms of disability, making them a particularly vulnerable population, quite literally without a voice of their own. Pubic health professionals are charged not only with protecting the health of the public at large

but are also charged with assuring that our most vulnerable populations receive the healthcare services they need. ALS patients and their families are a population in need of public health advocacy for improved end-of-life care. By investigating terminal ALS patients' access to medications, insights on how to improve barriers to access of care can be identified and better end-of-life care achieved.

2.0 BACKGROUND

2.1.1 Amyotrophic Lateral Sclerosis (ALS)

Amyotrophic Lateral Sclerosis (ALS), also known as Lou Gehrig's disease, is the most common motor neuron disease. This fatal, incurable, neurodegenerative disorder is characterized by the death of motor neurons in the brain and spinal cord, causing symptoms of progressive paralysis of skeletal muscles, muscle atrophy, and hyperreflexia.[1] The initiating factor that causes neuron death is not fully understood. It is believed however, that altered mitochondrial function,[2] oxidative damage,[3]and a glutamate reuptake malfunction[4] may all contribute to the demise of the neuron. As the disease progresses, patients experience increased muscle weakness across all body regions, leading to the inability to walk, feed and toilet themselves, speak, and swallow. Eventual death is most commonly caused by respiratory failure due to thoracic and upper cervical spine involvement.[5]

Worldwide the incidence rate of ALS is 0.86 to 2.4 per 100,000 with an elevated incidence of ALS among men. The onset of symptoms usually occurs in mid to later life with a peak age of onset at 65-74 years of age.[6] Murray,[7] in a review of more than 20 studies, found the duration of disease, from symptom onset to death, ranged from a mean of 26.6 months to a mean of 47 months with a median survival of approximately three years.

2.1.2 Direct and Indirect Symptoms of ALS

As ALS progresses, patients are faced with numerous symptoms that are indirectly and directly caused by ALS. Symptoms directly caused by ALS include weakness and muscle atrophy, fasciculations and muscle cramps, spasticity, dysarthria (the inability to communicate), dysphagia (difficulty swallowing), sialorrhea (excessive salivation or drooling), dyspnea (shortness of breath), and involuntary emotional expression disorder. Indirect symptoms include anxiety, depression, sleep disturbances and insomnia, constipation, and musculoskeletal pain. [1]

2.1.3 The Terminal Phase of ALS

ALS, although considered a fatal condition, is unlike many other incurable illnesses in that the progression of disease may take years before death occurs. Even as the ALS patient exhibits signs and symptoms of progressive debilitation, it is often difficult to predict life expectancy.[8] As patients near the terminal phase of the disease nutritional impairment and respiratory difficulties become more acute. To determine the terminal phase of the disease (a life expectancy of six months or less) a number of predictive factors exist. Medicare deems an ALS patient to have a life expectancy of six months or less if he/she meets one of the following criteria: (1) Patient must demonstrate critically impaired breathing (a forced vital capacity (FVC) of less than 30%, significant dyspnea at rest, oxygen needed at rest, and patient refusal of invasive ventilation); (2) Patient must demonstrate both rapid progression of ALS and crucial nutritional impairment; or (3) Patient must demonstrate both rapid progression of ALS and life-threatening complications. [9]

In contrast Del Bene et al.,[10] determined that a revised set of criteria would provide a more accurate measure in predicting a six-month survival. In their revised criteria, patients with a

FVC of 30% without other inclusive criteria would be considered to be in the terminal phase of the disease. In addition those patients with a FVC of less than 60% with steady decline of the FVC over the preceding two-three months and who also manifested at least two other respiratory indicators, or one respiratory and one nutritional indicator, were also deemed to be in the terminal phase of the disease.

Accurate guidelines for the terminal phase of ALS are imperative in providing appropriate end-of-life care. Hospice, which is most often covered by Medicare and other privates insurances, aims to provide improved quality of life and quality of death through assessment, symptom management, spiritual and psychological counseling, and improved access to services, medical equipment, and medications. To be eligible for these hospice services, the patient's life expectancy must be six months or less. As such, end-of-life indicators must accurately reflect the course of the disease for hospice to be beneficial for the dying ALS patient. Numerous researchers in the field have advocated the revised Del Bene et al. end-of-life hospice measures. An ALS Peer Workgroup that was charged with investigating end-of-life care reported:

> Medicare and other insurers lack correct information regarding markers for end of life in ALS. Current hospice referral guidelines are not relevant to ALS, and hospice intake forms do not ask questions that accurately reflect the patient's condition. Medicare Criteria for admission to hospice are too restrictive for ALS patients, thus patients with ALS are referred to hospice too late to benefit from the supportive services that hospice offers.[11]

2.2 PHARMACOLOGICAL TREATMENT AND SYMPTOM MANAGEMENT

From diagnosis through the terminal phase of ALS, maximizing quality of life is the central focus of care. In order to maintain and when possible improve quality of life, a number of

pharmacological interventions are available to assist in the treatment of symptoms. Although no curative treatment exists, the glutamate antagonist riluzole[12] has been approved by the FDA for prolonging the life of ALS patients. In a 2007 review the Cochrane Collaboration concluded:

> Riluzole 100mg daily probably prolongs median survival by two to three months in patients with probable and definite amyotrophic lateral sclerosis with symptoms less than five years, forced vital capacity greater than 60%, and age less than 75 years. [13]

Unfortunately riluzole, the only FDA approved medication to treat ALS, minimally extends life, and research has yet to determine if there is any effect on quality of life or functionality. In an effort to treat ALS and prolong life, there are a number of additional medications frequently taken by ALS patients. Although many of these medications have been in clinical trial, none is FDA approved for the treatment of ALS. These medications include creatine,[14] a supplement to assist in mitochondrial function, antioxidants,[15] to aid in the repair of oxidative damage, and gabapentin,[16] a glutamate-blocking agent.

Moreover, a number of other pharmacological interventions exist to ease symptoms directly and indirectly associated with ALS and provide increased comfort for the ALS patient. Antidepressants, anxiolytics, analgesics, skeletal muscle relaxants, anticholinergics, laxatives, and sedatives are all commonly used to treat disease-specific symptoms.

2.2.1 Medication Trends: The ALS CARE Database

As ALS progresses, the treatment regimen prescribed by clinicians has been shown to vary greatly depending on the continent, country, and even city where the patient receives care.[17] Due to the lack of randomized control trials directly investigating symptom management and available evidence-based standards, the management of ALS symptoms has largely relied on clinician experience and anecdotal reports from patients and experts within the field.[18, 19]

In an effort to provide an optimal standard of care for patients with ALS, the ALS Patient CARE Database was established in 1996.[20] The ALS CARE Database aims to identify ALS treatment trends, establish research needs, and provide insight for improved practice by collecting data from patients, caregivers and neurologists. All neurologists across North America, regardless of practice setting, are invited to provide patient data. Data are collected and entered by the neurology practice at the patient's baseline visit and at subsequent visits at 6, 12, 18, and 24 months.[18] With more than 5600 ALS patients enrolled across North America, the ALS CARE Database has been able to capture significant data, especially pertaining to disease-specific medication trends. The proportion of patients taking common ALS medications such as riluzole, creatine, gabapentin, high dose vitamins, antioxidants, and other non-traditional medications are summarized in Table 1. Additionally, Table 1 summarizes the proportion of enrolled ALS patients medicated for the treatment of sialorrhea, depression, emotional lability, and pain. Content included in Table 1 is based on the Miller et al.[18] findings.

Table 1: Results from the ALS Care Database: Pharmacological Interventions

Medication	% of patients†
riluzole	52%
creatine	39%
gabapentin	14%
high dose vitamins or antioxidants	48%
non-traditional	15%

Symptom	% of patients medicated for symptom
sialorrhea	25%††
depression	34%†††
emotional lability	44%††††
pain (terminal phase)	80%†

†Source did not indicate whether the percentage of patients was an average over the total number of years the ALS CARE Database has been in existence or if the percentage was an average for a particular year.
†† The number of patients taking medications for sialorrhea ranged from a low of 12% in 1999 to high of 25% in 2002.
†††Percentage of patients treated with antidepressants in 2003.
†††† Percentage of patients treated for emotional lability ranged from a low of 29% in the period prior to 1999 to a high of 44% in the period following 1999.

Furthermore, the ALS CARE Database found that pharmacological interventions used for the treatment of depression, constipation, spasticity, cramps, insomnia, and sialorrhea were generally reported by patients to be effective. Unfortunately, the large majority of patients were not on any symptomatic therapies.

Although the ALS CARE Database has undoubtedly made a significant impact on how clinicians practice, it does have a number of limitations. One significant limitation is that disease-specific medications are reported by the physician rather than the caregiver or patient, who may be more appropriate to report what medications the patient is actually taking. Another significant challenge, particularly pertaining to gathering end-of-life data, is obtaining continued follow-up data from patients. Patient data are to be collected and entered at baseline, 6, 12, 18 and 24 months. However, the number of patients with data at each of these milestones drops rapidly from 1838 to 1334, 736 and 682 respectively.[18] Patient death certainly accounts for some of the missing data, but the number of patients lost to follow-up is another significant factor to consider.

2.3 THE TERMINAL PHASE OF ALS: AVAILABLE RESEARCH AND RECOMMENDATIONS FOR CARE

2.3.1 Available Research

Although the ALS CARE Database has been able to provide significant insight into medication trends and population-based data, little has been published about ALS-specific pharmacological

interventions in the terminal phase of the disease. In an effort to gain insights about the terminal phase, Mandler et al.[21] used data from the ALS CARE Database to explore whether or not ALS patients experience a "good death." The ALS CARE Database collected end-of-life data on 1014 ALS patients and found that 90.8% were considered to have died "peacefully." A peaceful death was defined as "occurring under the least amount of distress and often related to progressive carbon dioxide narcosis, with little pain or dyspnea, as witnessed and reported by the relative or caregiver present during the end-of-life period." Interestingly, results of the CARE database also revealed that low income and not dying at home correlated with the experience of not dying peacefully.

While results of the ALS CARE Database indicate that most ALS patients have a peaceful death, conflicting reports exist. In a study performed by Ganzini et al.,[22] the investigators explored the final month of life of ALS patients and discovered that one-third of caregivers were dissatisfied with some aspect of symptom management. In the last month of life, 56% of patients experienced dyspnea either frequently, almost all the time, or constantly and 48% experienced discomfort other than pain either frequently, almost all the time, or constantly. With such a high caregiver dissatisfaction and severe discomfort and dyspnea among patients, it appears that ALS patients in the terminal phase of the disease could benefit from more aggressive treatment of symptoms.

Moreover, it has been argued that ALS patients who desire physician-assisted suicide or who would consider hastening their death also lack effective and appropriate end-of-life care. In a study by Albert et al.,[23] 43.4% of terminal phase ALS patients thought about ending their life, 18.9% expressed a desire to die, and 5.7% took actions to hasten their deaths. In a similar study by Ganzini et al.,[24] 56% of ALS patients indicated that they would consider assisted suicide and

of those who consider assisted suicide, 78% would request a lethal prescription from a physician if it were legal. In response to these studies, Carter et al.[25] reported: "…the stunningly high percentage of ALS patients who would consider [ending their lives] strongly implies that the quality of care in advanced ALS is inadequate."

2.3.2 Recommendations from the AAN Practice Parameters

In 1999 the Quality Standards Subcommittee (QSS) of the American Academy of Neurology (AAN) published practice parameters for the care of ALS patients.[26] The practice parameters set forth by the AAN were based on an extensive review of evidence-based research and strived to provide best practice standards for the management of ALS and identify areas in which further research is needed. The AAN reported:

> The practice parameters presented here comprise the first recommendations for the management of ALS based on a prescribed review and analysis of the peer-reviewed literature. These practice parameters were developed to improve the care and the quality of life of people with ALS by providing a rational basis for managing the disease. [26]

Since their publication in 1999, the practice parameters have led to significant changes in how clinicians manage the progression of ALS, and as a result there has been an increase in the number of both pharmacological and non-pharmacological interventions prescribed for patients.[27]

The task force charged with developing the practice parameters investigated five areas of care, one of which was "advanced directives and palliative care." The AAN reported: "As ALS progresses, the goal of patient care changes from maximizing function to providing effective and compassionate palliative care." In a collaborative review of evidence-based literature, the following four questions were investigated:

- Is pain common in the terminal phase of ALS?
- Can terminal dyspnea be relieved by therapeutic intervention?
- Does hospice care improve quality of life in the terminal phase?
- Do advance directives improve quality of life in the terminal phase of ALS?

After a review of the literature, the AAN reported 40-73% of ALS patients experience pain in the later stages. Immobility was described as the most likely source of discomfort, causing pressure on the skin and joints as well as muscle cramping and stiff joints. The AAN recommended the use of non-narcotic analgesics, anti-inflammatory drugs, and antispasticity agents for initial treatment of pain. In patients who are unresponsive to these, the liberal use of opioids is recommended following the World Health Organization's guidelines for pain management for cancer patients.

Two of the most common and unpleasant symptoms of the terminal phase of ALS are dyspnea and anxiety. The AAN reported approximately 50% of patients with ALS experience dyspnea from respiratory muscle weakness, and anxiety caused by dyspnea is a common symptom among ALS patients suffering from respiratory insufficiency. Dyspnea relief, however, was rated as "good" by 81% of hospice patients with ALS when opioids were used. The AAN set forth recommendations that included the use of short-acting anxiolytics for anxiety and the use of opioids and supplementary oxygen as needed.

The role of hospice was also explored by the AAN. While a number of studies have been conducted on the use of hospice care, consensus has not been reached as to its effectiveness. Uncontrolled studies have shown that hospice care provides improved pain management and peaceful deaths. The AAN recommends that clinicians consider hospice referrals in the terminal

phase of ALS but also emphasize that there continue to be research gaps as to the effect of hospice care on quality of life and inpatient versus homecare hospice services.

Finally, the AAN found no evidence that advance directives improve quality of life for any disease. Moreover, the evidence the AAN reviewed showed that advance directives did not substantially enhance physician-patient communication or aid in patient healthcare decision-making among seriously ill cancer patients. Despite this, the AAN still recommends their use. Studies have shown that physicians and patients would like to utilize directives more effectively. The AAN suggests this can be done by initiating discussion of advance directives early in the course of the disease and by creating therapy-specific treatment guidelines rather than broad generalities. As ALS progresses, often this population's preference for care can change. Thus, the AAN recommends updating advance directives every six months to accurately reflect patient desires.

2.3.3 Recommendations from an ALS Peer Workgroup

Promoting Excellence in End-of-Life Care is a national program sponsored by the Robert Wood Johnson (RWJ) Foundation. The RWJ Foundation aims to improve care of the dying and has recognized ALS patients as a special population in need. In an effort to address end-of-life care, an ALS Peer Workgroup was established to work collaboratively with the ALS Association. The Workgroup was convened to explore current palliative practice during the terminal phase of ALS and make recommendations for improvement. The findings of this ALS Peer Workgroup were published in 2005.[11]

The ALS Workgroup confirmed that there are very few studies that specifically investigate and identify optimal treatment of the dying ALS patient. The Workgroup also

acknowledged that due to the lack of evidence-based research on the terminal ALS patient, the Practice Parameters set for by the AAN for palliative care have been largely influenced by cancer research. Due to lack of evidence, the Workgroup's major contribution has been identifying the gaps in research and making recommendations for improved prospective studies.

Moreover, the Workgroup recognized that beyond symptom management and psychological care, ALS patients face considerable barriers to both accessing care and securing the financial means necessary for the cost of care. The Workgroup set forth a number of policy recommendations for the improved care of the dying ALS patient. These recommendations included developing a comprehensive reimbursement program to cover the cost of hospitalizations, medications, physical therapy, assistive devices, and homecare. In addition, they strongly supported the revision of hospice and Medicare guidelines to more accurately reflect end-of-life indicators to better benefit the patient.

2.3.4 Implications for Future Research

As evidenced by the findings of the AAN Practice Parameters and the RWJ Foundation ALS Peer Workgroup, very few studies exist that specifically investigate and identify best practice standards based on findings about terminal ALS patients. Although the ALS CARE Database and AAN Practice Parameters have made significant strides in providing evidence-based care as ALS progresses, much research is still needed to refine standards of care for the terminal phase of this disease.

Additionally, to date there have been no published data on medication trends in the terminal phase of the disease, nor has there been any research on medication trends in which the patients and/or their caregivers reported medication use. Patient and/or Caregiver reported

medications could potentially reflect more accurately what the ALS patient takes on a day-to-day basis. Furthermore, although efficacy of individual medications has been determined, no research has been completed on terminal ALS patients' medication choices. Although clinicians can suggest best practice standards to their patients, individual choice and patients' rights to refuse medications should be considered. For an array of reasons including unpleasant side effects, cost, and no demonstrated personal benefits, patients and physicians may not comply with the recommendations set forth by the AAN practice parameters. More research is needed to identify what medication choices terminal patients make so that improved interventions for both quality of life and quality of death can be developed.

3.0 PURPOSE, RESEARCH QUESTIONS, AND HYPOTHESES

3.1.1 Purpose

As identified by the literature, a major knowledge gap exists as to what medications terminal ALS patients take over the last six months of life. In an effort to gain further insight about medications use in the terminal phase of ALS, this thesis will analyze secondary data from the National Institute of Mental Health grant-funded study performed at the Eleanor and Lou Gehrig MDA/ALS Research Center at Columbia University and other surrounding clinics in New York from January 2000 to June 2004. This Living with ALS study collected data on disease management and mental health indicators from terminal ALS patients and their caregivers. Included in this secondary data are the medications the terminal ALS patients took while enrolled in the study, as reported by their caregiver.

The purpose of this analysis is to identify what medications terminal ALS patients take in the last six months of life, what trends emerge, how hospice services and economic and educational status of the patient and caregiver affect access to medications, and how medications affect quality of life.

3.1.2 Research Questions

The specific research questions investigated in this thesis include:

1. What medications are ALS patients taking during the last six months of life?
2. What changes in medications occur over the last six months of life?
3. Is there a relationship between economic and educational status of the patient/caregiver and medications taken?
4. Does the utilization of hospice services increase the number of palliative medications taken by a participant?
5. What relationship exists between medications taken by patients and quality of life?

3.1.3 Hypotheses

1. I anticipate the medications taken by patients in the Living with ALS study will mimic the results already obtained by the ALS CARE Database, as there is little evidence and few practice parameters to guide physicians in the terminal phase of ALS. I expect that care in the last six months does not dramatically change until death is imminent. Only a minority of patients in the Living with ALS study will have prescriptions for palliative medications, ALS treatment medications, or mood medications.

2. As patients near death, I expect the number of chronic medications and ALS treatment medications taken by patients will significantly decline. However, I also expect that as the patient approaches imminent death the number of palliative and mood medications will increase.

3. I anticipate disparities in access to medications; namely, that those with higher education status and increased monetary means will be on more medications, as they may be more likely to seek out additional treatments.

4. I predict that the utilization of hospice services will increase the number of palliative and mood medications. Typically, having hospice services increases the number of symptom

assessments by clinicians and nurses, which may increase the number of palliative medications they prescribe. Additionally, hospice services that are covered by Medicare or other private insurances provide substantial financial assistance to cover medication costs that are disease-specific.

5. I anticipate an increased quality of life with the use of palliative medications and mood medications. Medications available to patients are completely palliative and are given in hopes of increasing quality of life. As such, those patients taking palliative or mood medications should have increased quality of life indicators.

4.0 STUDY DESIGN OF THE SECONDARY DATA SOURCE

The secondary data source, the Living with ALS study, explored the ways in which ALS affects patients and their families. Specifically, this study aimed to gain insights from patients and their primary caregiver about how they managed ALS, how ALS has affected their mood, what services patients utilize, and what plans patients made as they lived with ALS. Approval for this study was obtained through the Institutional Review Boards of Columbia-Presbyterian Medical Center and the New York State Psychiatric Institute. Described below are the eligibility criteria for patients and their caregivers, the procedure for collecting data, and the measures used in this study.

4.1.1 Participant Eligibility

Interviews were conducted with ALS patients who demonstrated advanced disease and who had a life expectancy of approximately six months. The indicator used to predict life expectancy was a forced vital capacity of <50%. As previously discussed in this thesis, this value has been related to anticipated death within six months.[10] Eligible patients had to be English speaking, able to communicate "yes" or "no" responses, have a non-paid caregiver who agreed to participate in the interviews, and live within a three-hour drive of the medical center conducting the research. Individuals were excluded from the study if they met criteria for dementia or were

on mechanical ventilation at the time of enrollment. Approximately 94% of participants were enrolled from the Eleanor and Lou Gehrig MDA/ALS Research Center at Columbia University. An additional 6% of participants were enrolled through various other clinics and hospices in the area.

4.1.2 Procedure

Clinicians at both the ALS center and other clinics identified potential participants based on the inclusion and exclusion criteria stated above. The purpose and procedure of the study were explained by the clinician, and if patients and caregivers expressed an interest in participating, clinicians obtained consent to forward their contact information to the principal investigator. The principal investigator then called the potential participants to provide a more in-depth explanation of the study, to review the consent form, and to answer any additional questions. Once a verbal consent had been obtained, trained interviewers scheduled visits at a time and place that would be convenient for the patient and caregiver. The majority of interviews were conducted in the homes of the participants.

On the first interview, the research team obtained written consent and administered the first interview. Patients and caregivers were interviewed separately. Follow-up interviews were conducted monthly until the patient met a study endpoint of either tracheostomy or death. For those patients who chose to have a tracheostomy, the interview schedule was changed to every three months following tracheostomy. One additional interview was conducted with the caregiver after the death of the patient.

4.1.3 Measures

Because the patients in this study demonstrated advanced disease with a high likelihood of death within six months, a variety of information was requested of the caregiver rather than the patient. Information about demographics for the patient and caregiver, patient medications, and services utilized were included in the caregiver interviews only. In addition, caregivers were asked a series of four questions to establish the patient's overall status. These questions assessed concentration, memory, emotional lability and ability to follow a plot when reading or watching TV.

To measure the progression of the disease, the patient and caregiver were asked to complete the ALS Functional Rating Scale (ALSFRS).[28] The ALSFRS is a validated instrument used to measure the progression of disability. The four domains of the questionnaire include gross motor skills, fine motor skills, bulbar function, and respiratory status. Each of the 12 items of the questionnaire was rated on a four-point scale. When the sum of the tallied scores is calculated, those with lower scores have a greater amount of disability and have increased difficulty with swallowing and breathing.

Depression was assessed using the Beck Depression Inventory-Revised (BDI-II).[29] The BDI-II is a 21-question self-report survey that assesses the presence or absence of depressive symptoms. The sum of the scores ranges from 0-63. Scores indicate one of four outcomes: absence of depression (0-9), mild symptoms (10-16), moderate symptoms (17-29), and severe symptoms (30+). Utilization of the BDI-II was incorporated into the study for its high validity in identifying likely depressed and non-depressed individuals.

In addition, patients completed the 15-item Quality-of-Life Enjoyment and Satisfaction Questionnaire.[30] This instrument assessed quality of life by exploring the patients' sense of fulfillment and contentment with their daily experiences, overall well being, and life satisfaction.

Visual Analogue Scales (VAS) examined patient and caregiver moods and attitudes. The VAS incorporated questions with scales ranging from 1-10 with "1" being the least intensity and "10" being the greatest intensity. When necessary, these visual scales were held by the interviewer for the patient to read. Patients than rated each of the questions through head nodding, eye movement and other established gestures. The VAS was incorporated into the study to ensure that those patients nearing death, who wanted to continue to contribute to the Living with ALS study, would be able to participate with the least amount of effort and required communication. The patient VAS included questions regarding degree of pain, energy, suffering, depression, anger, optimism, weariness, control over ALS, desire to live, and interest in hastening death.

Of note, throughout the interview, research team members ensured that those patients with communication disabilities were able to complete survey tools through augmentative communication devices, eye movements, and/or other established gestures.

5.0 ANALYSIS OF SECONDARY DATA

5.1.1 Determining Medication Categories and Domains

Medication information was collected from caregivers at the first interview and at each subsequent interview. In order to analyze medication data for this thesis, all reported medications were categorized by drug purposes, which included:

- treatment of ALS
- pain
- muscle cramping & spasticity
- pulmonary dysfunction
- sialorrhea
- bowel irregularities
- sleep disorders
- oral mouth care
- nausea
- allergies
- osteoporosis
- gout
- other
- anxiety
- agitation
- depression
- other mood disorder
- cardiovascular disease
- diabetes
- gastroesophageal reflux disease (GERD)
- arthritis
- seizures
- infection (antibiotics & steroids)
- hypothyroidism
- genitourinary disorders
- unknown

These 26 drug categories were than further collapsed into four medication domains. The domains consisted of: (1) *ALS treatment* medication; (2) *palliative* medications; (3) *mood* medications, and (4) *other* medications. Table 2 contains a summary of medication domains and their subcategories. *ALS treatment* medications consisted of medications specifically designed to slow the progression of the disease and included riluzole, high-dose vitamins, gabapentin, antioxidants, creatine, and clinical trial medications.

Table 2: Medication domains and their subcategories

ALS Treatment	Palliative	Mood	Other
ALS treatment	pain muscle cramping & spasticity pulmonary dysfunction bowel irregularities sleep disorders oral mouth care nausea	anxiety agitation depression other mood disorders	cardiovascular disease diabetes GERD arthritis seizures infection hypothyroidism allergies osteoporosis gout genitourinary disorders other unknown

Palliative medications were classified as pharmacological therapies aimed at treating common symptoms of ALS such as pain, sialorrhea, respiratory insufficiency, constipation, muscle spasms, cramping, and insomnia. Medications in this category included morphine, glycopyrrolate, baclofen, and scopolamine.

The practice parameters set forth by the AAN recommend the use of amitriptyline to treat both sialorrhea and emotional lability.[26] As such, although amitriptyline is both an antidepressant and anxiolytic, it was included in the *palliative* domain for its use in controlling direct symptoms of ALS. Gastroesophageal reflux disease (GERD), a less common indirect symptom, may occur in patients with ALS due to diaphragmatic weakness involving the lower esophageal sphincter.[31] Unlike proton pump inhibitors whose mechanism of action is to decrease acid production, Metoclopramide acts by increasing muscle tone of the lower esophagus sphincter. Due to its mechanism of action, dual uses for GERD and nausea, and frequent use for those patients who have percutaneous endoscopic gastrostomy (PEG) tubes, metoclopramide was added to the *palliative* domain. Proton pump inhibitors used to treat GERD were added to the *other* domain, as ALS does not cause an increase in acid production.

Those medications aimed at treating depression, anxiety, and agitation were included in the *mood* domain. Medications included alprazolam, buspirone, bupropion, paroxetine, and sertraline. Included in the *other* domain were medications to treat chronic conditions and co-morbidities. Medications to treat cardiovascular disease, diabetes, osteoporosis, hypothyroidism, gout, chronic gastrointestinal and genitourinary issues, and other unknown medications were included as subcategories in this domain. Medications included atrovastatin, atenolol, quinapril, levothyroxine, warfarin, metformin, insulin, and tamsulosin. Additionally, the *other* domain included a subcategory of "other unknown;" these medications were unidentifiably misspelled by the either the caregiver or interviewer.

Caregivers in the Living with ALS study did not describe specific medication doses or why patients were taking particular medications. As a result, those medications that could be used for multiple purposes were categorized by best clinical judgment based on the available standards of care for ALS patients and review of patient interview data. The medications were categorized by myself (a Registered Nurse) and then reviewed by the principal investigator and a neurologist. In one particular instance, HIV medications were moved to the *ALS treatment* domain as suggested by the principal investigator. The PI reported that the patient taking these medications did not have HIV but rather was trialing the medications for the purpose of treating ALS. See Appendix A for a complete list of medications and their subcategories.

5.1.2 Statistical Methods

The percentage of patients in each medication domain was defined as all patients who took at least one drug in a particular domain.

The correlation between the medication domains and age, household income, educational attainment, Medicaid status, and hospice were investigated for significance using the Chi-square test.

The correlation between medication domains and patient answers on the Visual Analogue Scale, the Beck Depression Inventory–Revised, and the Quality of Life Enjoyment and Satisfaction Questionnaire was investigated for significance using the Independent Samples T-test and Levene's test. The Independent Samples T-test and Levene's test were used to compare the mean scores of patient answers to the QOL indicators and their use or non-use of medications in each of the four medication domains.

To investigate the changes in medication across the last six months of life, the percentages of patients taking any medications in each of the four medication domains at their first interview was compared to the percentage of patients taking any medications in that domain at their last interview. The Wilcoxon Signed Ranks test was used to test for significance.

6.0 RESULTS

6.1.1 Patient Sociodemographics

A total of 78 patients and their caregivers were interviewed for this study. The gender split among patients was 60% male 40% female. Fifty-five percent of patients had an educational attainment of some college or greater. Fifty-three percent of household incomes were greater than $60,000. Sixteen percent of patients were receiving Medicaid and 36% were on hospice. See Table 3 for a list of demographics.

Table 3: Patient sociodemographics

Patient Demographics	n (%)
Age	
<62 years old	38 (49)
>=62 years old	40 (51)
Gender	
Male	47 (60)
Female	31 (40)
Education	
No College	35 (45)
>= Some College	43 (55)
Household Income	
<60,000	36 (47)
>60,000	40 (53)
Medicaid Recipient	
Yes	12 (16)
No	65 (84)
Hospice Recipient	
Yes	27 (36)
No	48 (64)

6.1.2 Baseline Medication Use

At the first interview 32% of patients were on an *ALS treatment* medication, 47% were on a *palliative* medication, 33% were on a *mood* medication and 31% were on an *other* medication. One third of patients were on zero medications and only 6% were taking medications from all four domains. Table 4 summarizes the percentage of patients in each of the four medication domains.

Table 4: Percentage of patients in each of the four medication domains

Medication Domain	Patients – n (%)
ALS Treatment	25 (32)
Palliative/Symptom Management	37 (47)
Mood	26 (33)
Other	31 (40)

6.1.3 Relationship Between Sociodemographic Status and Medication Domains

The age of the patient was found to have no significant correlation to whether or not he/she was taking an *ALS Treatment* medication, *palliative* medication, *mood* medication or *other* medication. Increased educational attainment was correlated with taking significantly *fewer palliative* medications (p= 0.001) but no correlation existed between educational attainment and *ALS treatment* medications, *mood* medications or *other* medications. Those patients with household incomes of greater that $61,000, which accounted for 55% of patients enrolled, were also less likely to be taking a *palliative* medication (p=0.003) but again, no correlation existed between income and the remaining three medication domains.

Those patients who received Medicaid were significantly less likely to be on a drug in the *other* medication domain (p=0.014). Patients who utilized hospice services were no more likely to be on *ALS treatment* medications, *palliative* medications, *mood* medications or *other* medications than those patients not receiving hospice care. The correlation between patient demographics and medication domains are summarized in Table 5.

Table 5: Proportion of Patients with prescribed medications by sociodemographic status

	ALS Meds – n (%)			Pall. Meds – n (%)			Mood Meds – n (%)			Other Meds – n (%)		
	Taking	Not Taking	p	Taking	Not Taking	p	Taking	Not Taking	p	Taking	Not Taking	p
Age												
<62 years old	11 (29)	27 (71)		15 (40)	23(61)		12 (32)	26 (68)		12 (32)	26 (68)	
≥62 years oid	14 (35)	(26 (65)		22 (55)	18 (45)		14 (35)	26 (65)		19 (48)	21 (53)	
Education												
No College	13 (37)	22 (63)		24 (69)	11 (31)	.001	14 (40)	21 (60)		17 (49)	18 (51)	
≥ Some College	12 (28)	31 (72)		13 (30)	30 (70)		12 (28)	31 (72)		14 (33)	29 (67)	
Income												
<$60,000	12 (33)	24 (67)		24 (67)	12 (33)	.003	12 (33)	24 (67)		14 (39)	22 (61)	
≥$60,000	13 (33)	27 (68)		13 (33)	27 (68)		14 (35)	26 (65)		15 (38)	25 (63)	
Medicaid Recipient												
Yes	2 (17)	10 (83)		6 (50)	6 (50)		4 (33)	8 (67)		1 (8)	11(92)	.014
No	23 (35)	42 (65)		31 (48)	34 (52)		22 (34)	43 (66)		30 (46)	35(54)	
Hospice Recipient												
Yes	9 (33)	18 (67)		16 (59)	11(41)		10 (37)	17 (63)		15 (56)	12 (44)	.061
No	16 (33)	32 (67)		21 (44)	27 (56)		16 (33)	32 (67)		16 (33)	32 (67)	

6.1.4 Relationship Between Quality of Life and Medication Domains

When examining the correlation between medication domains and quality of life indicators no significant relationships emerged. Quality-of-life (QOL) indicators included the visual analogue scale (VAS), the Beck Depression Inventory-Revised (BDI-II), and the Quality-of-Life Enjoyment and Satisfaction Questionnaire. The QOL questions used from the VAS included:

- What degree of pain you are feeling today?
- How much are you suffering today?
- How depressed are you today?
- Are you interested in hastening your death?
- How weary are you from ALS?
- How much do you want to live?

Across all four medication domains, VAS scores of pain, suffering, depression, desire to hasten death, weariness and wish to live were not significantly impacted by the use or non-use of any of the medications.

Similarly, the total BDI-II score was not associated with the use of medications in each of the four domains. The mean total BDI-II score of patients taking a medication in each of the four domains did not differ significantly from the mean score of those patients not taking medication.

Moreover, the Quality-of-Life Enjoyment and Satisfaction Questionnaire mean scores did not reveal any significant correlation between medication use and improved quality of life. The specific QOL indicator question used from the Quality-of-Life Enjoyment and Satisfaction Questionnaire was the following: "How would you rate your overall life satisfaction and contentment during the past week?" Again, as with all previous QOL indicators, patients' mean scores did not differ significantly based on use or non-use of medications in each of the four domains.

6.1.5 Medication Trends

Finally, medication changes were investigated. Medications at first and lat interviews were compared. On average, patients' last interviews were conducted within a month of their death. Previous research has shown that those ALS patients who opt for tracheostomy and long-term mechanical ventilation (LTMV) differ substantially from those ALS patients who do not choose LTMV in that LTMV patients report increased optimism and an increased desire to live.[23,32] As such, those patients meeting a study endpoint of tracheostomy and death were analyzed separately. Twelve out of seventy-eight patients opted for tracheostomy. Non-tracheostomy

patients exhibited *highly* significant declines in the number of medications taken across all four medication domains. Tracheostomy patients had no significant changes in medications, and but rather remained on medications or increased medications up to the last assessment before tracheostomy. Table 6 summarizes the medication changes for both non-tracheostomy and tracheostomy patients.

Table 6: Medication Trends–A comparison of domains at first and last interview

Non-Tracheostomy Patients	ALS Meds	Pall. Meds	Mood Meds	Other Meds
First Visit	36%	54%	34%	43%
Last Visit	5%	9%	7%	5%
Wilcoxon Signed Ranks	.000	.000	.002	.000

Tracheostomy Patients	ALS Meds	Pall. Meds	Mood Meds	Other Meds
First Visit	20%	10%	50%	50%
Last Visit	30%	20%	50%	50%
Wilcoxon Signed Ranks	ns	ns	ns	ns

(ns = not significant)

7.0 DISCUSSION

7.1.1 Sociodemographics and Relationship to Medication Domains

It was hypothesized that patients with higher incomes would be on a greater number of medications, due to their financial means to access such drugs. Those patients with increased incomes and increased educational attainment however, were prescribed significantly fewer *palliative* medications. These findings are similar to that of a study conducted in Denmark that investigated prescription and non-prescription drug use based on sociodemographic indicators.[33] The study found that as income decreases, prescription drug use increases even when health status was controlled for. The authors of the study suggested that those with lower incomes, because they have access to free or reduced cost services, consult physicians more frequently and are provided with more medications whereas those with higher incomes, who do not have access to free services, deal with health problems independently.

For the patients in the Living with ALS study, higher socioeconomic status may have made patients ineligible for a number of financial assistance programs yet their incomes may have been too little to adequately afford medications. Moreover, those with increased educational attainment may have an increased awareness of effectiveness of palliative medications and choose not to take a number of the palliative medications due to the lack of clinical evidence indicating efficacy or a lack of personal benefit.

The health disparities that exist for our nation's poor were evident in this cohort of ALS patients. Those on Medicaid were on significantly fewer *other* medications indicating that although they were on medications to treat and manage their ALS, they were on very few if any *other* medications to treat chronic conditions like diabetes or cardiovascular disease.

Surprisingly, hospice patients were not prescribed any more *palliative* or *mood* medications than those patients not on hospice. Having hospice services increases the number of clinical assessments by nurses and clinicians in the home, which I believed would result in an increase in medications prescribed. However, hospice and non-hospice patients were on similar numbers of medications, indicating that hospice patients did not have an advantage for obtaining medications.

Although results of this analysis indicate that those patients on hospice have no greater advantage to obtaining medications, a number of influencing factors must be considered. Patients who are referred to hospice too late may not have significant changes in their medication regimens, making them appear similar to their non-hospice counterparts. Moreover, as the literature has demonstrated, no evidence-based studies have confirmed best practice standards for the terminal ALS patient. Without concrete guidelines, the progressive and terminal phases of the disease may not differ significantly in their medication regimens.

To better assess the influence of hospice on access to medications, further research and policy changes are needed. First and foremost, hospice guidelines must be revised to accurately reflect the terminal stage of ALS before the effects of hospice can be determined. For this to happen, public health officials must work together with clinicians, patients, families, and other ALS patient advocacy groups to change Medicare and private health insurance criteria for end-

of-life care for hospice ALS patients. Additionally, further research is needed to determine effective treatment regimens for terminal ALS patients.

7.1.2 Relationship of QOL Indicators and Medication Domains

According to the World Health Organization:

> Palliative care is an approach that improves the quality of life of 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 assessment and treatment of pain and other problems, physical, psychosocial and spiritual. [34] (emphasis mine)

Disappointingly, the use of medications in any of the four medications domains was not significantly related to the quality-of-life indicators used in this study. A plausible explanation could be attributed to the fact that the medications, especially those in the *palliative* and *mood* domains, did not provide effective symptom relief. At present, the vast majority of drugs available are those intended to treat symptoms and ultimately increase the quality-of-life of the patient. However, it appears that they fall far short of delivering improved quality-of-life. Many of the medications prescribed to treat the symptoms of ALS have significant side effects and many have few personal benefits, both of which certainly contribute to patient non-adherence to recommended treatment regimens. Creatine, antioxidants, and gabapentin, all medications frequently taken by ALS patients, have shown no clinical evidence of increasing survival or slowing the progression of the disease.[35-37] Furthermore Riluzole, the only FDA approved medication for the treatment of ALS, has been found to extend life by only two months. An additional two months of life, especially when self-dignity and quality-of-life will almost certainly be greatly compromised, is hardly comforting to patients and their families.

The utmost priority of ALS research is finding and developing a cure. Unfortunately this breakthrough has yet to occur. However, as researchers diligently investigate causes and cures, we must also investigate and develop new symptom management medications that have fewer side effects and more patient benefits. In addition we must find and provide other interventions to assist ALS patients and families successful maintain quality of life. Pharmacological interventions used by patients in the Living with ALS study had no effect on the patient's quality of life and many of the drugs were discontinued as death approached. As we attempt to improve our pharmacological interventions, non-pharmacological interventions should be provided and made accessible. The AAN indicated that the pain experienced by ALS patients during the later stages of the disease was most likely due to immobility. The use of physical therapy, massage, and acupuncture could potentially greatly reduce discomfort experienced by ALS patients. More research on the effectiveness of these alternative treatments could help to influence clinicians to prescribe these interventions more readily. However, very few (if any) insurance companies pay for these non-pharmacological interventions, adding to the cost of care for patients and their families that has already been estimated at thousands to hundreds of thousands of dollars each year.[38] By actively pursuing policy changes and educating third-party payers of the value of these non-pharmacological interventions, public health professional can advocate for improved care of the dying.

7.1.3 Medication Trends

Non-tracheostomy and tracheostomy patients differed considerably in medication trends from first to last interview. Only 10% of eventual tracheostomy patients were on a *palliative* medication at the first visit, as compared to the rest of the cohort, in which 54% of patients were

on a *palliative* medication at first visit. Another interesting difference was in their use of *ALS treatment* medications. From first to last interview, tracheostomy patients, although not statistically significant, increased their use of *ALS treatment* medications from 20% to 30% whereas non-tracheostomy patients decreased their use of *ALS treatment* medications from 36% to 5% (p=0.000). These striking differences could be attributed to the tracheostomy patients' desire to live and extend life. Patients undergo tracheostomies to extend life; hence it is no surprise that they are taking fewer *palliative* medications and more *ALS treatment*.

Across all four medication domains, non-tracheostomy patients stopped taking medications as they approached their last month of life. It was hypothesized that palliative and mood medications would increase as ALS patients approached death. However, the analysis for this thesis revealed that ALS patients significantly decreased their use of medications in both of these domains. A number of plausible explanations could account for this significant decline in the number of medications taken. First and foremost, as ALS progresses, swallowing becomes increasingly difficult, making it correspondingly difficult to take oral medications. Secondly, although a number of alternative routes could be prescribed, patients may opt to forego any medications due to lack of personal benefit. As symptoms become increasing more severe, medications previously used may no longer be effective, therefore patients stop taking medications. Finally, physicians may not be adequately prescribing medications to meet the needs of ALS patients who are approaching the actively dying stage of the disease; consequently there was no increase in the *palliative* or *mood* medications prescribed.

The lack of quality-of-life, increased difficulty swallowing, and lack of evidenced based standards to guide physicians in the care of terminal ALS patients most likely contribute to the significant decline in medications taken from first interview to last interview. As has already

been discussed, improved symptom management medications could greatly affect the medication usage of patients. Additionally more research is needed to investigate and determine best practice standards for the terminal ALS patient. Finally, physician-patient communication must be open and honest. Physicians should provide accurate information about the expected benefits and side effects of medications to help patients make informed medication decisions.

As hypothesized, the number of *ALS treatment* and *other* medications decreased from first interview to last interview. Interestingly, 5% of patients were still taking a medication in the domain *other*. It could be argued that medications to treat chronic conditions such as hyperlipidemia, osteoporosis and even diabetes are unnecessary in the terminal phase of any disease. Additionally, no drug is without side effects, and these should be considered especially if they have the potential to make the terminal phase of the disease more uncomfortable. Physicians and patients should openly discuss medication regimens as the patient transitions to the terminal phase of the disease, to ensure that the patient is taking the most effective and most appropriate pharmacological treatments.

7.1.4 Limitations

There are a number of limitations to the Living with ALS study and the results of this analysis. The study had a small sample size with a relatively low participation rate (63%). In addition, because patients were primarily from one ALS Center, they may not be representative. Moreover, data on why patients were taking particular medications was incomplete and why patients discontinued medications was not within the scope of this study. Because of a number of these limitations, medications were classified into domains, based on best clinical judgment. Findings of this thesis should be considered tentative rather than established.

8.0 CONCLUSIONS

The results of this secondary analysis clearly demonstrate that terminal ALS patients stop taking medications. A number of factors could influence this decline and include inability to swallow medications, lack of improved quality of life, and lack of effective symptom management. To better understand this decline in medication usage, more research is needed, particularly investigating patient motivations for compliance with medication regimes, such as side effects, lack of personal benefit, and barriers to taking or obtaining medications. Neither the guidelines nor the research needs set forth by the AAN or the ALS Peer Workgroup address how patient choice influences compliance with medication recommendations. To better meet the needs of ALS patients, realistic benefits and side effects of medications should be discussed with patients to assist them in making decisions about medication use. Physicians should continue to offer patients whatever pharmacological interventions are available, but it must be considered that patient choice has significant ramifications for adherence.

In addition, continued research is needed to investigate and develop improved symptom management medications. Furthermore, additional research specifically investigating ALS patients in the terminal phase of the disease is needed to provide evidenced-based standards of care.

As pharmacological research continues to find ways to treat ALS and ultimately find a cure, we must also provide additional non-pharmacological interventions to improve quality of

life and quality of death. By investigating the effectiveness of non-pharmacological interventions, improved practice could be provided to the dying. Terminal ALS patients are a vulnerable population that require advocacy on the part of public health officials. Through actively pursing policy changes, hospice criteria could be altered, and improved healthcare reimbursement systems could assist terminal ALS patients in accessing medications and services.

APPENDIX: LIVING WITH ALS STUDY: PATIENT MEDICATIONS LISTED BY SUBCATAGORIES AND DOMAINS

Items written in red are the direct misspellings from the data source.

ALSTX	ALSPALL	MOOD	OTHER
Rilutek *Rilutec* *Rilytek* *Rilutex*	**PAIN**	**ANXIETY/ AGITATION**	**CARDIOVASCULAR**
	Roxanol (Morphine, Morphine Sulfate) *Roxenol,* *Roxarol,* *Roxinol,* *Roxamol* *Roenol* *MSO4*	Ativan (Lorazepam) *Lorazrpran* *Atavan* *Adavan* *Lorazapam* *Lorazepan* *Adavent* *Avodant*	Prinzide *Privizide*
Creatine	Duragesic (Fentanyl Patch) *Duragenic Patch* *Fentinol*	Alprazolam (Xanax) *Alprazolane* *Alprolazam* *Alprazolane*	Potassium
Sanofi, Sandofi "Clinical Trial"	Oxycodone (Roxicet)	Buspirone (Buspar) *Busporin*	Enalapril *Enslapril*
Co-Q10 Co-Enzyme Q10 Co-Qio	Darvon (Darvocet)	Clonidine *Klonopin*	Atenolol *Atendol*
Indinavir (Cirxivan) *Indivor* *Crixivar*	Ibuprofen *Ibuprophine*	Stelazine (Schizophrenia or unresponsive anxiety) "Side	Accupril *Acupril*

		effects of coughing"?	
Viracept *Virocept*	Tylenol #3	Chlorpromazine (CPZ): Schizophrenia; hiccups, nausea, anticholinergic	Cardura *Cadua* *Cadvra*
Cyclophilin Receptor Antagonist *HIV co Claiml*	Aleve (Naproxen)	Zyprexa	Toprol *Toperal*
Minocycline	Tylenol	Haldol	Cozaar
	MUSCLE CRAMPING/ SPASTICITY	Diazepam (Valium)	Avapro
	Baclofen *Baclophen* *Blaclofen*		
	Soma	**DEPRESSION**	Lipitor
		Wellbutrin (Bupropion)	
	Zanaflex (Tizanidine) Tizandine Tizaridne *Zana Flex*	Celexa	Coumadin
	Quinine Sulfate (Used for leg cramps has some components of Skeletal muscle relaxants)	Paxil	Norvasc
	PULMONARY DYSFUNCTION	Prozac *Prosac*	Zocor
	Hycodan *Hycodian*		
	Guaifenex (Humibid, Guaifenesin-LA)	Zoloft	Pletal

	Humabid *Guaifensin- LA*		
	Atrovent (Ipratropium Bromide)	Doxepin (Sinequan)	Digoxin (Lanoxin)
	Albuterol	Serzone	Lopressor
	DuoNeb	Effexor	Tiazac *Tiazar*
	Pulmozyme (Pulmozine)	Fluoxetine	Lasix *Lasex*
	Mucomyst (Acetylcysteine)	**OTHER**	Vasotec
		Anafranil	
	Saline Solution	Ritalin	Triamterene
	SIALORRHEA		**ARTHRITIS**
	Scopolamine (Transderm Scope) *Scopolanin* *Scopolaine* *Scopolame*		Vioxx *Viox*
	Sal-Tropine *Saltropine*		Celebrex *Celbrex*
	Secretion		**DIABETES**
			Glyburide
	Elavil (Amitriptyline) *Amitryphytine*		Insulin
	Robinul *Robinvl* *Robinole* *Robinmul* *Robinol* *Robinal*		Metformin *Mefformine*
	BOWEL IRREGULARITIES		Glucotrol (Glipizide)
	Cephulac (Lactolose)		
	Stool Softner		Humalin
	Senna *Semma*		Glucophage *Glucaphage*

			Glucophase
	Docusate Sodium (Colace) *Ducuate Sodium*		**GERD** Prevacid *Prevasid* *Previcid* *Prevacia*
	Ducolax		Protonix
	SLEEP DISORDER Restoril		Pepcid
	Ambien		**GENITOURINARY DISORDERS** Ditropan XL
	Trazadone		Flomax
	ORAL MOUTH CARE Oral Mouth Gel		**SEIZURES** Dilantin
	GERD/NAUSEA Metoclopramide (Reglan)		"Medication for seizures"
			ALLERGIES

			Allegra
			Nasonex *Nasenix*
			INFECTION
			Predisone* long term steroid use
			Vibramycin* (Doxycycline) *Vibromicin* *Vibromycin*
			Cipro*
			"AntiBiotic"
			OSTEOPOROSIS Evista

			HYPOTHYROIDISM
			Synthroid
			GOUT
			Allopurenol
			OTHER
			Benadryl
			Dexatrim
			Marijuana
			Neurontin (non-diabetic patient)
			Chinese Herbs
			Mepron used for treatment of PCP (per patient tx of Lyme disease)
			Cephlin (maybe ceftin?) (for tx of Lyme Disease per patient)
			OTHER/ UNKNOWN
			Riloter
			Vceferin IV* (antibx per patient)
			Serna
			Selerium
			Suppositories
			Inviveol
			Compro
			Amsxaulll
			Preipro
			tep
			Supplements
			Bodofin
			Rosepherme
			Supplementary

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