Examining Change in Symptoms of Depression, Anxiety, and Stress in Adults after Treatment of Chronic Cough: A Dissertation

Examining Change in Symptoms of Depression, Anxiety, and Stress in Adults After Treatment of Chronic Cough

A Dissertation Presented

by

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DEDICATION

This work is dedicated to the memory of:

KENNETH E. FLETCHER, Ph.D.
Associate Professor of Psychiatry
Associate Professor in the Graduate School of Nursing
Director, UMMS Behavioral Sciences Research Core

Ken --- friend, colleague, guru, and mentor who was called away by those above far too early

Ken, I finished! I know you are smiling, as I cross home plate!

Just as I sat beside you, for so many years analyzing the data, now you are beside me in spirit.

Thank you for your mentorship and inspiration!

Together we still share the joy of a job well done!

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Abstract

Background: Chronic cough is a common health problem with variable success rates to standardized treatment. Psychologic symptoms of depression, anxiety, and stress have been reported in association with chronic cough. The purpose of this study was to examine changes in the psychologic symptoms of depression, anxiety, and stress in adults with chronic cough 3 months after management using the ACCP cough treatment guidelines.

Methods: This study used a descriptive longitudinal observation design. The major tenets associated with the Theory of Unpleasant Symptoms were examined. Intervention fidelity to the study components was measured.

Results: A sample of 80 consecutive patients with chronic cough of greater than 8 weeks duration was recruited from one cough specialty clinic. Mean age of subjects was 58.54 years; 68.7% were female; 98.7% were white, and 97.5% were non-smokers. Mean cough duration was 85.99 months and mean cough severity was 6.11 (possible 0 –10; higher scores equal greater cough severity). Cough severity improved post treatment (n=65, M=2.32, (SE =.291), t (64) =7.98, p=.000); cough-specific quality-of-life also improved (n=65, M=9.17, (SE=1.30), t (64) =7.02, p=.000). Physiologic (urge-to-cough r=.360, ability to speak r=.469) and psychologic factors (depression r=.512, anxiety r=.507, stress r=.484) were significantly related to cough-specific quality-of-life and to cough severity (urge-to-cough r=.643, ability to speak r=.674 and depression r=.356, anxiety r=.419, stress r=.323) (all r, p=.01); social support and number of diagnoses were not related to either variable. Those experiencing greater financial strain had worse cough severity. Women, those experiencing financial strain, and those taking self-prescribed therapy had worse cough-specific quality-of-life. Intervention fidelity to the study plan was rated as high according to observation, participant receipt, and patient/physician

concordance. Qualitative review identified potential areas of variability with intervention fidelity.

Conclusions: By measuring the factors related to the major tenets of the Theory of Unpleasant Symptoms, this theory has helped to explain why those with chronic cough may have symptoms of depression, anxiety, and stress and why these symptoms improve as cough severity and cough-specific quality-of-life improve. Moreover, by measuring intervention fidelity, it may be possible to determine why cough guidelines may not be yielding consistently favorable results.

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CHAPTER 1

State of the Science

Introduction

Patients presenting with the symptom of cough comprise the most common reason for seeking medical attention in ambulatory settings in the United States (US) resulting in 29, 804, 000 visits (5%) of the overall 1,083,215,000 medical visits reported for all ages in 2007 (Hing, Hall, Ashman, & Xu, 2010) . While frequency data are lacking and definitions of chronic cough vary in the literature, chronic cough has been identified as one of the most common reasons for new patient visits to a pulmonary outpatient practice (Altman & Irwin, 2010; Irwin, Baumann, et al., 2006; Morice et al., 2007). Moreover, it has been suggested that if only two percent of annual cough-related visits were for chronic cough this would represent 2,166,430 people (Hing et al., 2010; Hsiao, Cherry, Beatty, & Rechtsteiner, 2010). Data exist that suggest why chronic cough is a major health problem. Patients with chronic cough have reported some of the problems associated with their cough as including: feeling that something is seriously wrong or worry (Everett, Kastelik, Thompson, & Morice, 2007; Irwin & Curley, 1991), anger (Everett et al., 2007; Kuzniar, Morgenthaler, Afessa, & Lim, 2007), ability to speak impaired (Kuzniar et al., 2007; Vernon, Leidy, Nacson, & Nelsen, 2009), exhaustion (Irwin & Curley, 1991; Kuzniar et al., 2007), self consciousness (Irwin & Curley, 1991; Vernon et al., 2009), inability to participate in usual social activities (Everett et al., 2007; Kuzniar et al., 2007) , frustration (Everett et al., 2007; Kuzniar et al., 2007), insomnia (Everett et al., 2007; Irwin & Curley, 1991; Vernon et al., 2009), need to change life-style or habits (Everett et al., 2007; Irwin & Curley, 1991; Kuzniar et al., 2007), hoarseness (Irwin & Curley, 1991; Kuzniar et al., 2007), fatigue (Everett et al., 2007), urinary incontinence (Everett et al., 2007; Irwin & Curley, 1991; Kuzniar

et al., 2007), and urge-to-cough (Vernon et al., 2009). Additionally, studies have demonstrated the adverse impact of cough on health related quality-of-life as well as significant improvement in the same when the symptom is successfully treated (Baiardini et al., 2005; S. S. Birring et al., 2003; C. T. French, Irwin, Fletcher, & Adams, 2002).

The Theory of Unpleasant Symptoms can be useful in understanding the role of the symptoms of depression, anxiety, and stress and the role of social support as they relate to the symptom of chronic cough and its impact on quality-of-life (Lenz, Pugh, Milligan, Gift, & Suppe, 1997). This theory proposes that physiologic, psychologic, and situational factors influence symptoms and that the symptoms influence quality-of-life. The theory also proposes that the presence of more than one symptom can result in each acting as a catalyst for the other (Lenz et al., 1997). No studies were found that address the role of both psychologic factors and social support as influencing chronic cough and its effects on cough-specific quality-of-life.

Studies using various measures of psychologic status have reported symptoms of depression (Dales, Spitzer, Schechter, & Suissa, 1989; Dicpinigaitis, Tso, & Banauch, 2006; McGarvey et al., 2006), and anxiety (Dales et al., 1989; McGarvey et al., 2006) as being present in association with chronic cough. The psychologic factor stress has also been reported in association with chronic cough (Lin, Chen, Hong, & Lin, 2010). The support of others or social support may be a situational factor that can influence the symptom of cough. Addressing social support may be useful in the case of chronic cough associated with symptoms of depression, anxiety and stress. Social support has been cited as being important in ameliorating the negative effects of psychologic factors on both mental and physical health (Broadhead, Gehlbach, deGruy, & Berton, 1989; Broadhead, Gehlbach, Gruy, & Berton, 1988).

The American College of Chest Physicians (ACCP) has published guidelines to assist healthcare providers in the diagnosis and management of cough (Irwin, Baumann, et al., 2006).

These guidelines provide three separate diagnosis and treatment algorithms that categorize cough based upon duration of the symptom (Irwin, Baumann, et al., 2006). The three categories of cough described in the ACCP guidelines include acute, subacute, and chronic duration (Irwin, Baumann, et al., 2006). The success rates reported in association with the use of the chronic cough diagnosis and management guidelines such as those provided by the ACCP have varied widely (Irwin, 2010). The use of intervention fidelity measures, such as a manual outlining the interventions to be employed and observer and participant checklists used to measure the adherent and competent delivery and receipt of the proposed management interventions (Bellg et al., 2004; Santacroce, Maccarelli, & Grey, 2004), have not been reported in studies of chronic cough. Thus, the wide variation in success rates reported in the treatment of chronic cough could be related, at least in part, to variability in intervention fidelity.

The purpose of this study was to describe changes in the symptoms of depression, anxiety, and stress in adults with chronic cough after management using the ACCP guidelines. The Theory of Unpleasant Symptoms (Lenz et al., 1997) was used to guide this study (see chapter 2 for details).

The specific aims of this study were to:

1. describe the change in psychologic factors represented by symptoms of depression, anxiety, and stress from baseline to 3 months post initiation of standardized treatment for chronic cough;
2. determine the relationship between baseline cough severity and cough-specific quality-of-life with baseline urinary incontinence, financial strain, employment; self prescribed remedy, gender, marital status, and education.
3. determine the influence of physiologic factors (ability to speak without coughing, urge- to-cough and number of diagnoses), situational factors (social support), and

psychologic factors (symptoms of depression, anxiety, and stress) on cough-specific quality-of-life and cough severity (global symptom/cough measure of timing, intensity, distress, and quality) at baseline and at 3 months post standardized treatment.

4. describe the process of measuring intervention fidelity in the application of the ACCP guidelines for managing cough using the Technology Model.

Several research hypotheses derived from the theory of unpleasant symptoms were tested to address the previous specific aims. These hypotheses included:

a. Treatment of chronic cough using the ACCP guidelines will result in improvement in cough severity and subsequently improvements in cough-specific quality-of-life. Collectively these improvements will result in improvements in psychological factors, physical factors, and situational factors.
b. Physiologic factors (ability to speak without coughing, urge- to-cough and number of diagnoses), situational factors (social support), and psychologic factors (symptoms of depression, anxiety, and stress) predict cough severity (timing, intensity, distress, and quality)
c. Cough severity (timing, intensity, distress and quality) predicts cough-specific quality-of-life and, collectively if improvements are found in cough severity and therefore in quality-of-life they will result in improvements in psychologic, physiologic, and situational factors.

Background and Significance

Chronic Cough: The Symptom

Cough is as a mechanism of defense that is important in keeping the airways clear of harmful substances or as a problematic symptom or self perceived indicator of ill health (Irwin, Baumann, et al., 2006). This study will focus on chronic cough as a symptom that can pose a substantial burden for patients. Resolution of the symptom of cough is important to patients. The amount of money spent on over-the-counter remedies for cough can be inferred to mirror the magnitude of the individual's self perceived need for relief from the adverse affects of cough. Expenses for over-the-counter remedies purchased by those with cough are estimated to be in excess of several billion dollars annually (Altman & Irwin, 2010; Everett et al., 2007; Morice, 2002).

Definitions of chronic cough, and the duration of time for cough to be considered chronic, vary in the literature. The definition of chronic cough used in this study is based upon symptom duration and it is that which has been proposed by the 2006 ACCP Guidelines (Irwin, Baumann, et al., 2006). These guidelines propose three categories of cough, acute, subacute, and chronic, using duration of the symptom of cough to most efficiently work through the multitude of potential diagnoses most commonly associated with each category (Altman & Irwin, 2010; Irwin, Baumann, et al., 2006). Acute cough, most likely being that which is related to the common cold, is described as having a duration of less than three weeks (Irwin, Baumann, et al., 2006; Morice et al., 2007; Pratter, 2006a). Subacute cough commonly occurs as part of the aftermath of an infection, such as cough secondary to an exacerbation of asthma due to the common cold, and is cough with a duration of 3 to 8 weeks (Irwin, Baumann, et al., 2006).

Chronic cough is defined as cough with a duration of greater than eight weeks that can be the result of any one or more of a wide variety of conditions (Irwin, Baumann, et al., 2006).

The cause of chronic cough can most often be determined using the well established internationally recognized ACCP guidelines for the diagnosis and management of cough (Irwin, 2010; Irwin, Baumann, et al., 2006). These guidelines are meant to inform provider decisions regarding patient care through recommendations that have been graded by a consensus panel based upon both the quality of the evidence and the benefit/harm ratio to those with chronic cough (Irwin, Baumann, et al., 2006). The ACCP guidelines use a systematic diagnostic protocol to identify the causes of cough and suggest empiric management interventions for the most common causes (Irwin, Baumann, et al., 2006).

The ACCP guidelines provide algorithms for acute, subacute and chronic cough by which the cause(s) of cough can be identified and cause focused treatment interventions can be employed (Pratter, Brightling, Boulet, & Irwin, 2006). See Figure 1.

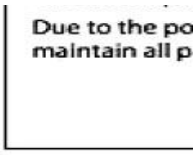

***Figure 1*. Chronic cough algorithm for the management of patients ≥ 15 years of age with cough lasting > 8 weeks. ACE-I = ACE inhibitor, BD = bronchodilator, LTRA = leukotriene receptor antagonist, PPI = proton pump inhibitor. Reproduced with permission from The American College of Chest Physicians from the "Diagnosis and Management of Cough Executive Summary, " by R.S. Irwin, M. H. Baumann, D.C. Bolser, L. P. Boulet, S.S. Braman, C.E. Brightling, et al., 2006, *Chest, 129*, p. 4S. Copyright 2006 by the American College of Chest Physicians.**

The algorithm for chronic cough (see Figure 1) systematically directs the clinician to the assessment of the most common causes with the guidelines suggesting focused empiric treatment for each cause identified (Pratter et al., 2006). If the initial chest radiograph is normal, or shows nothing more than stable inconsequential scarring, the patient is screened for exposure to environmental irritants such as cigarette smoking or use of an angiotensin converting enzyme inhibitor. After screening for and eliminating smoking and the use of angiotensin converting enzyme inhibitors, the management algorithm suggests initial empiric management interventions for the four most common causes of chronic cough: upper airway cough syndrome, asthma, non-asthmatic eosinophilic bronchitis, and gastroesophageal reflux disease (Pratter et al., 2006). If response to empiric intervention for the most common causes of chronic cough is inadequate the algorithm suggests further diagnostic and treatment interventions (Irwin, Baumann, et al., 2006).

The ACCP guidelines note the importance of the systematic approach to diagnosis and management of chronic cough. This approach is recognized as being important to sorting out the cause(s) of chronic cough, as often more than one cause is simultaneously in effect and the differential of potential diagnoses is extensive (Pratter et al., 2006). When the ACCP guidelines are employed with management interventions that are focused towards identifying and treating causes of chronic cough, success rates in managing chronic cough range from 54-100% (Irwin, Ownbey, Cagle, Baker, & Fraire, 2006; Pratter, 2006b, 2006c). Reasons for this wide variability in reported success rates, in studies that employ cough guidelines for the management of chronic cough, are not clear.

Initial management interventions for the four most common causes of chronic cough include the use of first generation antihistamine decongestants for *upper airway cough syndrome*; inhaled corticosteroids and bronchodilators and leukotriene receptor antagonists *for asthma*; inhaled corticosteroids for *non-asthmatic eosinophic bronchitis*, and the use of proton

pump inhibitors, diet and lifestyle changes, and on occasions, gastrointestinal prokinetic drugs for *gastroesophageal reflux disease* (Pratter et al., 2006). Resolution of cough or self report of evident improvement is noted to signify successful treatment of chronic cough (Pratter et al., 2006).

While patients with chronic cough are sometimes diagnosed as having habit cough or psychogenic cough, these diagnoses are sometimes incorrectly used as a default when the cause of chronic cough cannot be explained (Irwin, Glomb, & Chang, 2006). Cough management guidelines advise that the diagnosis of unexplained chronic cough only be used after failure of described diagnostic and treatment protocols with resulting reasoning that the cause of cough has not been successfully identified (Pratter, 2006c).

Both subjective and objective outcome assessment measures can be used in the evaluation of chronic cough. Subjective measures can include both visual analogue scales and cough-specific quality-of-life questionnaires (Irwin, 2006a). The Cough Quality of Life Questionnaire (subscale range Cronbach's alpha .62-.86; and total scale .92) (C. T. French et al., 2002) and the Leicester Cough Questionnaire (Cronbach's alpha .79-.85 subscales and total scale .92) (S. S. Birring et al., 2003) are currently the most commonly used instruments to evaluate cough-specific quality-of-life in adults with chronic cough. A variety of other single item numeric rating scales have been used to rate cough severity and/or frequency (Fletcher, French, Irwin, Corapi, & Norman, 2010; Smith, Owen, Earis, & Woodcock, 2006). Objective measures that may be helpful in artificially stimulating cough in an effort to quantify cough reflex sensitivity include both the inhaled citric acid and capsaicin cough challenges (Irwin, 2006a; Wright, Jackson, Thompson, & Morice, 2010). Computerized 24 hour cough counting has also been found to be useful for quantifying chronic cough (Irwin, 2006a).

Symptom Qualities

The symptom cough has been described as having different qualities. Findings from a cross sectional qualitative study of three focus groups *(N=22)* resulted in the recommendation that chronic cough severity be evaluated in terms of the qualities of frequency, intensity and disruption (Vernon et al., 2009). Qualitative findings from the three focus groups identified words such as hacking, deep, strong, harsh, intense, and barking used to describe the intensity of chronic cough (Vernon et al., 2009). With regards to frequency, participants noted that cough could be continuous or intermittent and their personal awareness of the cough could vary in that at times they were not aware of the symptom (Vernon et al., 2009). Additional findings from this study included chronic cough occurring during daytime activities or nighttime sleep as being disruptive to the life of those studied (Vernon et al., 2009).

Symptom Combinations

Multiple symptom combinations have been reported in association with chronic cough. Prospective questionnaire interviews in patients (*N*=108) seeking medical attention for chronic cough followed by thematic reduction of data resulted in identification of 18 reasons for seeking assistance (Irwin & Curley, 1991). Physical issues identified included exhaustion (57%), musculoskeletal pain (44%), hoarseness (43%), excessive perspiration (42%), urinary incontinence (39%), dizziness (38%), headache (32%), retching (21%), vomiting (18%), nausea (16%), anorexia (15%), and syncope (5%) (Irwin & Curley, 1991). Sleep disturbances associated with chronic cough were reported as insomnia (45%) (Irwin & Curley, 1991). In a similar study (*N*=136), symptoms associated with cough were noted to be a minor to major problem and included exhaustion (66%), fainting (16%), and sleep disturbances (78%) (Kuzniar et al., 2007). Postal survey results (*N*=856) seeking information related to chronic cough in the

United Kingdom found that in those who returned the survey (*N*=373) a number of physical complaints were reported and included breathlessness (55%), wheeze (37%), tired (72%), sore throat (45%), incontinence (55% in females, 5% in males), syncope (10%) dizziness (20%), and disturbed sleep (70%) (Everett et al., 2007). Qualitative focus groups have noted sleep disruption as a problem for those with chronic cough (Vernon et al., 2009).

Cross sectional descriptive studies have identified urinary incontinence to be an important reason for seeking medical attention for chronic cough *N* =108, 39% (Irwin & Curley, 1991); *N*=136, 43% (Kuzniar et al., 2007). In a study of gender differences (*N*=154; *n*=116, female 38 male) using a 28 item cough-specific quality-of-life questionnaire woman scored significantly higher than men on only one item and that item was urinary incontinence $t(29) = -2.48$; $p = .021$ (C. T. French, Fletcher, & Irwin, 2004).

Physiologic Factors

Cough Anatomy and Physiology

Cough is a visceral reflex (Canning, 2006, 2007) that results in a respiratory maneuver involving inspiration, followed by expiration against a closed glottis that then opens allowing an expulsion of air producing the characteristic sound recognized as cough (McCool, 2006). The cough reflex is thought to be regulated by mechanisms that are both non voluntary and voluntary (Canning, 2007). Stimuli for cough can include inhalation of some type of matter, inflammation and inflammatory mediators originating in the airway and mechanical stimuli from extra pulmonary sources such as the ear and esophagus (Canning, 2006).

The cough reflex is initiated with the afferent neural pathways bringing the cough stimulus to the central nervous system and efferent pathways responsible for respiratory muscle action that are involved in cough (Canning, 2006). It has been proposed that cough is generated

via these afferent vagal neural pathways, bringing the stimulus for cough to the brain stem and cerebral cortex, with the spinal cord also playing a role in the process (Canning, Mori, & Mazzone, 2006; Mazzone, 2004). Efferent impulses are then generated from the brain stem and cerebral cortex resulting in the respiratory muscular effort producing cough (Canning, 2006; Mazzone, 2004). Cognition and conscious action are thought to potentially play some role in the voluntary generation of cough at the level of the cerebral cortex (Davenport, 2009).

Urge-to-Cough

The urge-to-cough has been described as a respiratory sensation that precedes cough (Davenport, Vovk, Duke, Bolser, & Robertson, 2009). The urge-to-cough is thought to be the result of the translation of stimuli to neural responses that are interpreted and responded to at the level of the cerebral cortex by the motor action of cough (Davenport, 2009; Mazzone, 2004). Additionally, urge-to-cough describes an internal signal that may be related in the clinical situation as a sensation in the throat or lungs that is perceived as the need to cough, resulting in the physical action of cough (Woodcock, Young, & Smith, 2010). Qualitative focus groups have identified patients as relating a tickle in the throat that ultimately leads to cough (Vernon et al., 2009).

It has been proposed that some voluntary control of cough is possibly related to the translation of the urge-to-cough to the motor action of cough (Canning, 2007). In a study evaluating urge-to-cough and cough motor response modulation by the central effects of nicotine, 20 smoking and non smoking subjects rated their urge-to-cough or intensity of their need to cough after nicotine administration (Davenport et al., 2009). In this study urge-to-cough scores were significantly lower ($p<.05$) in smokers at higher concentrations of capsaicin after nicotine administration (Davenport et al., 2009). Results of this study suggest that central neural

response to nicotine is associated with a modulation of perceptual and motor cough response to a known cough stimulus (Davenport et al., 2009). In an effort to evaluate the usefulness of mindfulness stress reduction training as an intervention used in an effort to reduce urge-to-cough on inhaling citric acid and to reduce cough and cough reflex sensitivity, two sequential trials were conducted (Young et al., 2009). The trials included one with healthy subjects (N=30) and one with those with chronic cough *(*N=30) and each trial randomized subjects to no intervention, mindfulness, and to voluntary cough suppression (Young et al., 2009). Mindfulness reduced cough sensitivity in healthy controls (p=0.043) but not in those with chronic cough; both groups were able to voluntarily suppress cough in response to citric acid inhalation (healthy p=0.002; cough p=0.02), and there were no significant changes in urge-to-cough (Young et al., 2009).

Medical Conditions Causing Cough

Chronic cough can be a symptom resulting from one or more condition(s) (Pratter, 2006b). It is widely accepted that the most common causes of chronic cough include upper airway cough syndrome, asthma, non-asthmatic eosinophilic bronchitis, and gastroesophageal reflux disease (Irwin, Baumann, et al., 2006; Pratter, 2006b). These most common causes, along with cigarette smoking and use of angiotensin converting enzyme medications, explain the greatest majority of cases of chronic cough (Pratter, 2006b). A wide range of other causes are responsible for 6 percent or less of chronic cough (Madison & Irwin, 2010). Conditions of varying severity such as bronchogenic carcinoma, bronchiectasis, pharyngeal dysfunction, interstitial lung disease, heart failure, tuberculosis, and psychogenic issues are some of the other causes of chronic cough (Madison & Irwin, 2010). In at least twenty five percent of cases, more than one cause of chronic cough can concurrently be identified (Irwin, Curley, & French, 1990). It can be inferred that treatment complexity increases for both the patient and the provider when

more than one diagnosis is concurrently in operation. It can also be inferred that when treatment complexity increases adherence to treatment may be more difficult to achieve.

Physical Complications of Cough

Chronic cough can also result in the development of a multitude of physical complications resulting in secondary diagnoses (Irwin, 2006b). The physical trauma from the physical action of cough can induce an inflammatory state in the airways (Irwin, Ownbey, et al., 2006). Complications of cough can vary in severity affecting multiple body systems including cardiovascular, gastrointestinal, genitourinary, musculoskeletal, neurological, ophthalmologic, and integumentary systems (Irwin, 2006b). Complications resulting from cough can be those that are bothersome, but not life threatening, such as subconjunctival hemorrhage or urinary incontinence (Irwin, 2006b). In contrast, case reports of complications of cough include those that can be potentially life threatening such as diaphragmatic rupture (Chaar, Attanasio, & Detterbeck, 2008; Daniel, Naidu, & Khalil-Marzouk, 2008; Kallay et al., 2000), the development of stress cardiomyopathy (Butman, 2010; Dahdouh et al., 2011), and myocardial infarction (Butman, 2010). Chronic cough, thought to occur as a manifestation of pulmonary infection or inflammation, has been reported in association with an overall increase for myocardial infarction (non productive chronic cough OR 1.8; 95% CI 1.1-2.8 and productive chronic cough OR 1.6; 95% CI 1.1-2.4) (Haider et al., 1999).

Cough Related Problems with Speaking

Cough related problems with speaking have been noted in multiple descriptive cross sectional studies of those with chronic cough (Everett et al., 2007; C. T. French et al., 2004; Kuzniar et al., 2007). One study of those with chronic cough (*N*=53) reported speaking as a trigger for cough in 71% of participants (Vertigan & Gibson, 2011). Problems with speaking

that have been identified include: cough affecting the voice 67% (Everett et al., 2007), hoarseness 43% (Irwin & Curley, 1991), 53% (Kuzniar et al., 2007) and trouble speaking 63% (Kuzniar et al., 2007). Impairment in vocal quality has been described as a problem in as many as 40% of those with chronic cough (Gibson & Vertigan, 2009). In a study of cough triggers in those with chronic cough unresponsive to medical management (*N*=53), triggers that are not known to stimulate cough receptors included abnormal sensation in the throat (85%), talking (71%), and talking on the telephone (56%) (Vertigan & Gibson, 2011). Qualitative focus groups specifically identified coughing as affecting voice quality while speaking (Vernon et al., 2009)

Psychologic Factors

Depression and Anxiety in the General Population

Based upon the frequency of anxiety and depression in the population at large, it stands to reason that many of those who are seeking care for chronic cough may concurrently suffer from one or both of these problems with its associated manifestations. Depression is differentiated from anxiety in that it is one of multiple mood disorders and a disorder characterized by extreme and sustained sadness (American Psychological Association, 2010b; Task Force on DSM-IV, 2000). DSM-IV criteria for a Major Depressive Disorder, that has a lifetime risk of 10-25% in females and 5-12% for males in community samples, include the presence of one or more Major Depressive Episodes (Task Force on DSM-IV, 2000). A Major Depressive Episode is characterized by at least two weeks of depressed mood or loss of interest accompanied by at least four other specified symptoms that may include psychomotor agitation or retardation or fatigue and is also associated with impairment in usual life activities (Task Force on DSM-IV, 2000). Major Depressive Disorder needs to be differentiated from issues associated with normal life loss and from Mood Disorder Due to a General Medical Condition (Task Force on DSM-IV, 2000).

Similar to Generalized Anxiety Disorder, Mood Disorder Due to a General Medical Condition is that in which the physiologic consequences of a medical condition are felt to be the cause of the symptoms (Task Force on DSM-IV, 2000). For the purposes of this study, depression was defined as a state characterized by symptoms of dysphoria, hopelessness, devaluation of life, self-depreciation, lack of interest or involvement, anhedonia, and inertia (P. F. Lovibond & S. H. Lovibond, 1995).

While there are a number of major anxiety disorders, anxiety is identified in general as a psychologic condition characterized by the symptoms of excessive and sustained fear and worry (American Psychological Association, 2010a). Generalized Anxiety Disorder, one of the more common anxiety disorders with a reported lifetime prevalence of 5% in a community sample, is that where symptoms occur on more days than not and are sustained over a period of at least 6 months (Task Force on DSM-IV, 2000). To meet the criteria established by the Diagnostic and Statistical Manual of Mental Disorders – IV (DSM-IV) of a Generalized Anxiety Disorder, the fear and worry described must also be accompanied 3 or more other specific symptoms such as restlessness, irritability, and muscle tension (Task Force on DSM-IV, 2000). Generalized Anxiety disorder is differentiated from Anxiety Disorder Due to a General Medical Condition when the physiologic consequences of a medical condition are felt to be the cause of the symptoms (Task Force on DSM-IV, 2000). Generalized Anxiety Disorder is also to be differentiated form Somatoform Disorders where anxiety and worry are associated with physical symptoms that could suggest a medical problem but are not fully explained by the medical problem (Task Force on DSM-IV, 2000). For the purposes of this paper, anxiety was defined as a state characterized by symptoms of autonomic arousal, skeletal muscle effects, situational anxiety, and subjective experience of anxious effect (P. F. Lovibond & S. H. Lovibond, 1995).

The term stress as used in this study refers to a state of nervous tension characterized by symptoms of difficulty relaxing, nervous arousal, being easily upset or agitated, irritable or overreactive and impatience (P. F. Lovibond & S. H. Lovibond, 1995). This definition of stress has been proposed as being akin to the state of Generalized Anxiety Disorder (Lovibond, 1998).

While anxiety and depression exist as separate and distinct conditions, they also share a component of general affective distress and a potential overlap in symptomatology such as occurs with restlessness, fatigue, problems with concentration, and insomnia (Clark & Watson, 1991; Task Force on DSM-IV, 2000). Mixed Anxiety-Depressive Disorder has been identified as having a primary care prevalence rate of 1.3 - 2% and is a description used to identify a clinically significant combination of the symptoms described and more in association with a persistent dysphoric mood of at least one months' duration (Task Force on DSM-IV, 2000). While research criteria for establishing the presence of Mixed Anxiety-Depressive Disorder are defined, individuals who meet the criteria are formally identified using a DSM-IV diagnosis of Anxiety Disorder Not Otherwise Specified (Task Force on DSM-IV, 2000). Additionally, depression and anxiety have been related to elevated levels of the pro-inflammatory marker pleiotropic cytokine interleukin-6 (Morozink, Friedman, Coe, & Ryff, 2010) opening speculation as to their role in chronic cough.

Depression and Anxiety and Chronic Cough in the General Population

The symptom chronic cough has been reported in association with multiple psychologic factors such as depression, anxiety, and stress. Epidemiologic population cohort studies have associated the presence of depression and anxiety or their symptomatology with chronic cough (Adams, Appleton, Wilson, Taylor, & Ruffin, 2009; Dales et al., 1989). An Australian adult longitudinal population cohort of those without identified lung disease (n=3,355) found 18.2% of

those studied at baseline to complain of chronic cough (Adams et al., 2009). Using the General Health Questionnaire (CHQ)-28 anxiety and depression domains in the same (*n*=3,355) population, 23.6% were classified as having anxiety and insomnia and 34.4% severe depression (Adams et al., 2009). In this study, overall severe and mild GHQ-28 scores in those who were complaining of chronic cough at baseline improved when cough was reported as resolved (24.8% to 16.9%; $p<0.01$ vs. never coughed) (Adams et al., 2009). Secondary analyses of a Canadian population cohort of never smokers, with no reported respiratory disease and normal spirometry (*n*=600; age 14-55; 63% female, 37% male) were derived from a large (*N*=3,628) population based health survey (Dales et al., 1989). Using the Psychiatric Symptom Index (PSI) and the American Thoracic Society Respiratory Symptom Questionnaire, associations were found between chronic cough and PSI subscales (anxiety symptoms OR 1.64; 95% CI 1.16-2.30; $p<0.05$; depression symptoms OR 1.39; 95% CI 1.06-1.82; $p<0.05$) (Dales et al., 1989).

Psychologic Complaints in Chronic Cough

Multiple cross sectional descriptive studies have identified psychological complaints as being related to chronic cough. Psychologic complaints identified (*N*=108) in a study of reasons patients seek medical attention for chronic cough were reported as including issues such as feeling that something is wrong (98%), self-consciousness (55%), fear of cancer (33%), fear of AIDS or tuberculosis (28%) (Irwin & Curley, 1991). A questionnaire included in a packet mailed to individuals requesting chronic cough information offered during a radio broadcast was returned by 43% (*N* = 856; *n* = 373) of those surveyed (Everett et al., 2007). Respondents reported multiple psychologic complaints and were characterized as follows: (*n*=373; *M* = 65.3, *SD*=12) years of age; 73% female; 41% ex-smokers; 8% current smokers; median duration of cough 6.5 years; 66% no prior respiratory disease). Psychological findings included anger or

frustration (83%), not feeling in control of their body (76%), worry about health (69%), depressed (55%), upset (80%) and worried about what others think (76%) secondary to chronic cough (Everett et al., 2007). Similarly, in a study of those seeking medical assistance for cough (*N*=136), patient complaints included feeling frustrated, irritable or angry (79%) and anxiety about an underlying problem (66%) (Kuzniar et al., 2007). A focus group study of participants with chronic cough (*N*=22) related feelings of being annoyed, frustrated, irritated and worried because of cough (Vernon et al., 2009).

Anxiety in Chronic Cough

Multiple studies have noted the presence of anxiety in those with chronic cough. The prevalence of psychologic factors associated with chronic cough was explored in patients without prior psychiatric disease (McGarvey et al., 2006). In this study, a single visit survey (*N*=57; *n*=47 female; *M* = 47.5 (14.3) years of age; cough duration *M*=69.2 (78.5) months) identified subgroups of those with explained (*n*=42) and unexplained chronic cough (*n*=15) (McGarvey et al., 2006). With patients being matched for cough severity by use of a visual analogue scale, State Trait Anxiety Inventory scores identified 72% of patients as having low state anxiety and 28% as having moderate state anxiety (McGarvey et al., 2006). Trait anxiety levels were identified as moderate in 44.2% and high in 3.8% of patients (McGarvey et al., 2006). Scores using the Hospital Anxiety and Depression Scale identified 21% of all patients as having borderline anxiety and 12.3% as having clinically important anxiety symptoms (McGarvey et al., 2006). Independent t-test comparing the means of all those with cough to healthy populations (*M*=32.8, *SD* =8.3) found Trait anxiety to be significantly higher among those with cough (*M* = 38.9, SD = 11.3; $p<.001$). Significantly higher scores (*N*=57) were found for phobic anxiety ($t = 2.32$; $p<.05$), obsession ($t = 1.71$; $p<.05$), and somatization ($t =3.9$;

$p<.001$) (McGarvey et al., 2006). Trait anxiety was significantly higher in treatment non-responders compared to treatment responders (M=36.3, SD=9.53 vs. M=30.92, SD=8.20; p = 0.027).

In an effort to determine whether affective state driven by the withdrawal of the anxiolytic nicotine would modulate cough in 20 smoking adults and matched controls, subjects inhaled capsaicin before and after nicotine or placebo gum (Davenport et al., 2009). Withdrawal from smoking for 12 hours in smoking subjects resulted in an increase in urge-to-cough ratings, number of coughs, and trait anxiety scores while administration of nicotine gum resulted in a reduction in the same measures and the placebo gum had no effect (Davenport et al., 2009). In the smokers, nicotine gum decreased trait anxiety scores measured using the State Trait Inventory (M=36.3$\pm$3 to 34.3$\pm$3; p=.03) (Davenport et al., 2009).

In an effort to evaluate mindfulness, stress reduction training as an intervention for chronic cough, healthy subjects (N=30) were compared to those with chronic cough *(*N=30) and each subject was randomized to receive no intervention, mindfulness, or to voluntary cough suppression (Young et al., 2009). Anxiety was measured in this study using the State Trait Anxiety Inventory. No significant change was found post intervention in either state (p=0.23) or trait anxiety (p=0.78) for either group (Young et al., 2009). Those with chronic cough, in comparison to a working population, were found to have high trait anxiety levels (males M=36.60, SD=16.21 vs. M=34.89, SD=9.19 and females M=40.50, SD=11.00 vs. M=34.79, SD=9.22) but below average state anxiety scores (M=30.50, SD=10.30 vs. M=35.72, SD=10.40 and females M=34.15, SD=8.83 vs. M=35.20, SD=10.61) (Young et al., 2009).

Depression in Chronic Cough

Several studies have assessed the presence of depression in chronic cough. The Hospital Anxiety and Depression Scale was used to identify depression in those with chronic cough *(N=57)* finding 10.5% as having borderline depressive symptoms and 5.3% as having clinically important depression symptoms (48%) (McGarvey et al., 2006). Significantly higher depression scores were found in those with chronic cough (t =2.54; p<.05) compared to published healthy controls (McGarvey et al., 2006). The prevalence of depressive symptoms among patients with chronic cough was also investigated using a non-randomized prospective intervention trial (Dicpinigaitis et al., 2006). At baseline (N = 100), 53% scored positively for significant depressive symptomatology and risk for depression (CES-D M = 18.3, SD =13.2) (Dicpinigaitis et al., 2006). Both cough and depression scores significantly improved in those who completed the post intervention testing (n=81; CES-D; M = 7.4, SD=10.4); cough z = 7.34; Wilcoxon signed –ranks test p<.001; and depression z = 7.14; Wilcoxon signed-ranks test; p<.001) (Dicpinigaitis et al., 2006). Findings also included improvement in cough and depression as being moderately correlated (r =.323; p =.003) (Dicpinigaitis et al., 2006).

Stress in Chronic Cough

Stress has also been reported in association with chronic cough. In young healthy individuals *(N=47), g*reater numbers of common health complaints including cough have been reported (Lovell, Moss, & Wetherell, 2011). In this study, those with higher levels of self perceived stress were found to have hypersecretion of cortisol when compared to those with lower levels of stress (Lovell et al., 2011). In a study of bank call center workers (N=289) in Taiwan, multivariate logistic regression demonstrated that when compared to those reporting low stress, workers reporting high stress had significantly greater complaints of chronic cough with

phlegm (OR=2.13, 95% CI = 1.02-4.44) (Lin et al., 2010). This study was limited in that smoking status of the subjects was not reported (Lin et al., 2010).

In a study of cough triggers in those with chronic cough unresponsive to medical management (*N*=53), reports of stress as a trigger were compared with Hospital Anxiety and Depression Scale (HADS) scores (Vertigan & Gibson, 2011). Subjects reporting stress had higher anxiety and depression scores (anxiety p=0.002; depression p= 0.020) than those not reporting stress; yet, all scores were in the normal range (Vertigan & Gibson, 2011). Anxiety and depression scores were similar in this study when comparing those reporting stress as a trigger for cough to those who did not report stress as a trigger (M=8.6, *SD*=4.1); vs. *M*=8.1, *SD*=2.9) and no significant correlations were found between urge-to-cough and either anxiety (r=0.036, p=.0.780) or depression (r=0.019, p=0.881) (Vertigan & Gibson, 2011).

Situational Factors

Demographic Variables

Situational factors such as gender, age, work, ability to socialize in public situations, time of day, and number of physician visits have been reported in association with chronic cough. Gender has been identified as an issue in chronic cough with more woman seeking assistance for chronic cough than men (C. T. French et al., 2004; Kelsall, Decalmer, McGuinness, Woodcock, & Smith, 2009). Additionally, the cough reflex has been found to be more sensitive to provocative challenge in woman using both capsaicin (p = 0.0007) and citric acid (p=0.032) when compared to men (Kastelik et al., 2002). In a study of sex differences and predictors of objective cough frequency (*N*=100; n =65 females, n=35 males), woman coughed more than men (*M*=16.6 vs. 9.5; p=0.01). Linear regression showed 38.6% of the variation in cough frequency was predicted by sex (p=0.01) and age (p<0.001) (Kelsall et al., 2009). In a study of

gender differences in health related quality-of-life in patients complaining of chronic cough, women reported more adversely affected cough-specific quality-of-life when compared to men (*n=116* female; *n*=38 male; *M*= 67.1 vs. 59.7; *p* =0.002). In the same study, it was noted that men and women scored differently in the various subscales with urinary incontinence being greater in women and the item demonstrating the most significant difference ($p<0.001$) (C. T. French et al., 2004).

A prospective self report survey (*N*=146, *n*=136) used to identify factors that patients identify as a major problem secondary to cough include lifestyle/leisure (38%), frequent physician visit/testing (41%), interference with social gatherings (35%), other peoples' reactions (32%), expense for medications (21%), spouse moving out of the bedroom (13%), and being absent from work (11%) (Kuzniar et al., 2007). A questionnaire mailed to those requesting information (*N*=853; *n*=373 returned) offered during a radio broadcast revealed multiple negative affects related to chronic cough (Everett et al., 2007). Negative effects reported in this study, as related to chronic cough, included altering behaviors involving cinema or bingo (39%), eating out (34%), visiting family and friends (19%), affecting phone calls (81%) and hobbies (45%) (Everett et al., 2007). While only 45% of those responding were employed, 53% noted that cough affected their employment (Everett et al., 2007).

Focus groups have been used to assess the severity of chronic cough from the participants perspective (Vernon et al., 2009). Participants in three focus groups (*N* = 22) composed of those with chronic cough identified the adverse impact of chronic cough as related to situations specific to work, ability to socialize in public, and sleep (Vernon et al., 2009).

Qualitative review of videos of those seeking assistance for cough (*N*=33) using sociolinguistic analysis put cough in the perspective of a non-verbal behavior involved in the process of complex communication between the patient and physician (Bailey, 2008). This

analysis was described as based upon language that is dependent upon the social context and the concepts of social accountability and maintenance of face (Bailey, 2008). Cough was found to be dependent upon the social situation rather than cough as a direct physical complaint (Bailey, 2008). Cough was noted to be used by the patient to animate symptoms during explanation to further elucidate a problem when the patient and the general practitioner did not agree on the importance of what was being presented by the patient (Bailey, 2008). Cough was proposed as a communicative resource, a non verbal behavior used in physician patient communication as well as a manifestation of respiratory disease (Bailey, 2008). Similarly, qualitative interviews (*N*=30) revealed that those who perceived cough as abnormal, causing worry, and interfering with social roles were more likely to seek medical assistance (Cornford, 1998).

Social Support

Definitions of social support vary, yet it is generally accepted that greater levels of social support are associated with better physical and psychological health (Broadhead et al., 1983; Powers, Goodger, & Byles, 2004). Social support, a concept with many definitions (Finfgeld-Connett, 2005; Langford, Bowsher, Maloney, & Lillis, 1997; Williams, Barclay, & Schmied, 2004), can be viewed as a buffer of the effects of stress on psychologic and physical health, or as a determinate or outcome of health (Broadhead et al., 1983). It has been proposed that high levels of social support are important to psychologic health and that the impact of stress has greater adverse effects when social support is low (Broadhead et al., 1983; Landerman, George, Campbell, & Blazer, 1989).

Social support can be defined as a multidimensional construct composed of the social network, social interactions, self perceived or subjective social support, and instrumental or tangible service support (George, Blazer, Hughes, & Fowler, 1989; Landerman et al., 1989).

Social support can also refer to social transactions such as a confident relationship where important issues are shared, affective support or positive emotional expression, affirmation or expressions of agreement or praise, and/or aid or direct tangible cognitive or physical assistance (Broadhead et al., 1988; Broadhead et al., 1983). The term instrumental support or aid has been used to describe a dimension of social support that is more specific to those in need of support from outside the home and is not necessarily related to populations that are not in need of outside services (Koenig et al., 1993).

Social support can be measured by evaluating the qualitative or functional aspects of supportive relationships and/or by the quantitative or structural aspects of supportive relationships such as size of the social network (Broadhead et al., 1989; Broadhead et al., 1988). Qualitative aspects of supportive relationships can include emotional, appraisal, informational, and instrumental dimensions of support (Broadhead et al., 1989). In contrast, quantitative support relates to issues such as size and frequency of social networks (Broadhead et al., 1989). When assessing the impact of social support on health outcomes, qualitative or functional dimensions of social support rather than the quantitative dimensions have been identified as being most important (Broadhead et al., 1988; Broadhead et al., 1983). Emotional support, as an aspect of the qualitative or functional aspects of social support, has been cited as the most important predictor of the impact of social support on health outcomes (Broadhead et al., 1989; Broadhead et al., 1988). This study will limit its focus to the dimensions of social support related to relationships where important issues are shared and support related self perceive positive emotional expression from others (Broadhead et al., 1989; Broadhead et al., 1988)

Performance and Consequences

Health Related and Cough-Specific Quality-of-Life

Health related quality-of-life refers to a construct that includes subjective collective evaluations of multiple domains representing aspects of life whose quality may be impacted by health issues such the symptom experience (Centers for Disease Control and Prevention, 2011; U.S. Department of Health and Human Service, 2010). Domains identified as part of health related quality-of-life vary, most often including mental, physical, and social functions (U.S. Department of Health and Human Service, 2010), as well as occupational and somatic sensations (Schipper, Clinch, & Olweny, 1996). The patient's perception of symptoms, the way they affect individual ability to function, and the way the resulting distress from symptoms is communicated have been cited as contributing to the overall illness experience (Schipper et al., 1996). It has also been noted that physiological and psychological states are often interdependent as demonstrated by the case of stress and hypertension (Schipper et al., 1996). The measurement of health related quality-of-life can be important in understanding the burden of disease and progress towards reducing this burden (Centers for Disease Control and Prevention, 2011).

Cough-specific quality-of-life is a useful outcome measure for identifying the impact of chronic cough on patients' lives and for assessing response to treatment (S. S. Birring et al., 2003; C. T. French et al., 2002). Chronic cough has been described as having a negative effect on overall and on the physical, psychological, and social domains of quality-of-life (S. S. Birring et al., 2003; C. T. French et al., 2002). In a study of patients presenting to an adult respiratory clinic for treatment of cough, those successfully treated (N=9) have reported overall improvements in the individual domains of cough-specific quality-of-life (S. Birring et al., 2007). Improvements in all domains of quality-of-life measured in this study included: physical

(effect size 1.00), psychological (effect size 1.75), and social (effect size 0.84) domains (S. Birring et al., 2007). Similarly, in a study of those presenting to a cough specialty clinic, successfully treated patients (N=24) reported significant improvements ($p \leq 0.001$) in mean score for each domain of cough-specific quality-of-life (C. T. French et al., 2002). Domains measured included physical complaints M= 63.33, SD=13.69 to M=30.50, SD=5.80, psychosocial issues M=21.19, SD=5.75 to M= 9.67, SD=1.97, functional abilities M=13.79, SD=3.48 to M=5.54, SD=1.28, emotional well-being M=7.59, SD=1.69 to M=3.54, SD=1.18, extreme physical complaints M=8.13, SD=2.77 to M=4.29, SD=0.91, and personal safety fears M=6.38, SD=2.12 to M=4.21, SD=0.83 (C. T. French et al., 2002).

Adverse effects on total quality-of-life scores (N=9; t-test not reported; p<.007; N=24; t=-10.73; $p \leq .001$) have significantly improved with successful treatment of chronic cough (S. S. Birring et al., 2003; C. T. French et al., 2002). Additionally, multiple studies have noted interference with lifestyle as a problem for those with chronic cough (N =373, 64%; N =108, 45%; N =136, 81%) (Everett et al., 2007; Irwin & Curley, 1991; Kuzniar et al., 2007). The burden of chronic cough on patients can be inferred based upon data that demonstrate that the health related quality-of-life scores in patients with chronic cough are of similar severity when compared to those of patients with severe disabling dyspnea due to chronic obstructive pulmonary disease (C. L. French, Irwin, Curley, & Krikorian, 1998).

Intervention Fidelity and the Reliability and Validity of Study Outcomes

Intervention Fidelity

While intervention fidelity measures that specifically address the adherent and competent delivery of proposed management interventions by the interventionist (Santacroce et al., 2004) appear to be important, intervention fidelity has not been reported in studies of chronic cough.

Intervention fidelity is important to ensuring the reliability and validity of an intervention's effects on the outcomes (Bellg et al., 2004; Santacroce et al., 2004). The lack of clearly identified intervention fidelity measures has resulted in difficulty in assessing reliability and validity issues that may play a role in variations in outcomes of studies using specified management strategies (Bellg et al., 2004; Santacroce et al., 2004). The Technology Model for ensuring intervention fidelity that focuses on the use of a manual, training and supervision of those who deliver the intervention, and monitoring of the processes has been found to be useful in research (Santacroce et al., 2004). Measuring subject receipt of information is an additional component of intervention fidelity that has been shown to be important in reducing statistical error and therefore unexplained variation when formulating study conclusions (Santacroce et al., 2004). Use of the Technology Model for managing and monitoring intervention fidelity was important to the reliability and both the internal and external validity of the conclusions of this study.

Summary

A focused review of the literature in the area of research associated with the impact of chronic cough on patients and the concurrent presence of psychologic factors has been provided. This review has demonstrated support for the serious impact of the symptom as experienced by patient with chronic cough. This review also demonstrates the concurrent presence of psychologic factors such as the symptoms of depression, anxiety, and stress in those with chronic cough. Social support has been cited as being associated with better physical and psychological health. Intervention fidelity has been shown to be important to the reliability and validity of research findings.

The strength of the evidence supporting the presence of the symptoms associated with the psychologic factors of depression, anxiety, and stress in those with chronic cough vary. No study could be found that directly assesses social support or intervention fidelity in those with chronic cough. Epidemiologic studies provide evidence for an association of the psychologic factors of depression, anxiety, and stress with chronic cough in the population at large. Qualitative, descriptive, and quasi-experimental studies provide evidence for the association of these psychologic factors in those seeking medical care for chronic cough. The strength of the evidence related to the psychologic factors associated with chronic cough severity and performance outcomes has been limited by studies that are primarily descriptive and cross sectional, use of small size samples, and by study designs that are not randomized, controlled, and interventional. No studies were identified that concurrently assess longitudinal changes in the symptoms of depression, anxiety, and stress in those whose chronic cough is both defined and treated based upon the diagnostic and management interventions recommended by the ACCP guidelines.

This study provides information related to longitudinal changes in symptoms of depression, anxiety, and stress in those with chronic cough treated using the ACCP guidelines. Additionally, this study provides information regarding the longitudinal influence of psychologic, physiologic factors, and the situational factor of social support associated with chronic cough. Finally, a process for measuring intervention fidelity in the application of the ACCP guidelines has been described.

CHAPTER 2

Theoretical Framework

The purpose of this prospective study was to describe changes in the psychologic symptoms of depression, anxiety, and stress in adults with chronic cough after standardized management intervention using the ACCP guidelines. Additionally, this study describes the influence of physiologic factors (ability to speak without coughing, urge-to-cough, and number of diagnoses), situational factors (social support), and psychologic factors (symptoms of depression, anxiety, and stress) on cough severity (timing, distress, intensity, and quality) and cough-specific quality-of-life following standardized treatment. The Theory of Unpleasant Symptoms (Lenz et al., 1997) was used as a guide to assess and describe the concepts addressed in this study.

Theory Overview

The Theory of Unpleasant Symptoms, first described in 1995 by Lenz, Suppe, Gift, Pugh, and Milligan, was proposed as a middle range theory developed to help guide research and practice in the area of symptoms across multiple populations (Lenz, Suppe, Gift, Pugh, & Milligan, 1995). This theory was devised in an effort to improve the understanding of the experience of a symptom and to provide information that would be helpful in identifying preventive and/or management interventions for patients experiencing the adverse impact of symptoms (Lenz & Pugh, 2008; Lenz et al., 1997; Lenz et al., 1995). The theory was revised in 1997 in response to further recognition of the complexity and interactive nature of the patient experience of one or more simultaneously experienced symptoms (Lenz & Pugh, 2008; Lenz et al., 1997). The theory implies that managing one symptom contributes to the management of others (A. Gift, 2009). See Figure 2.

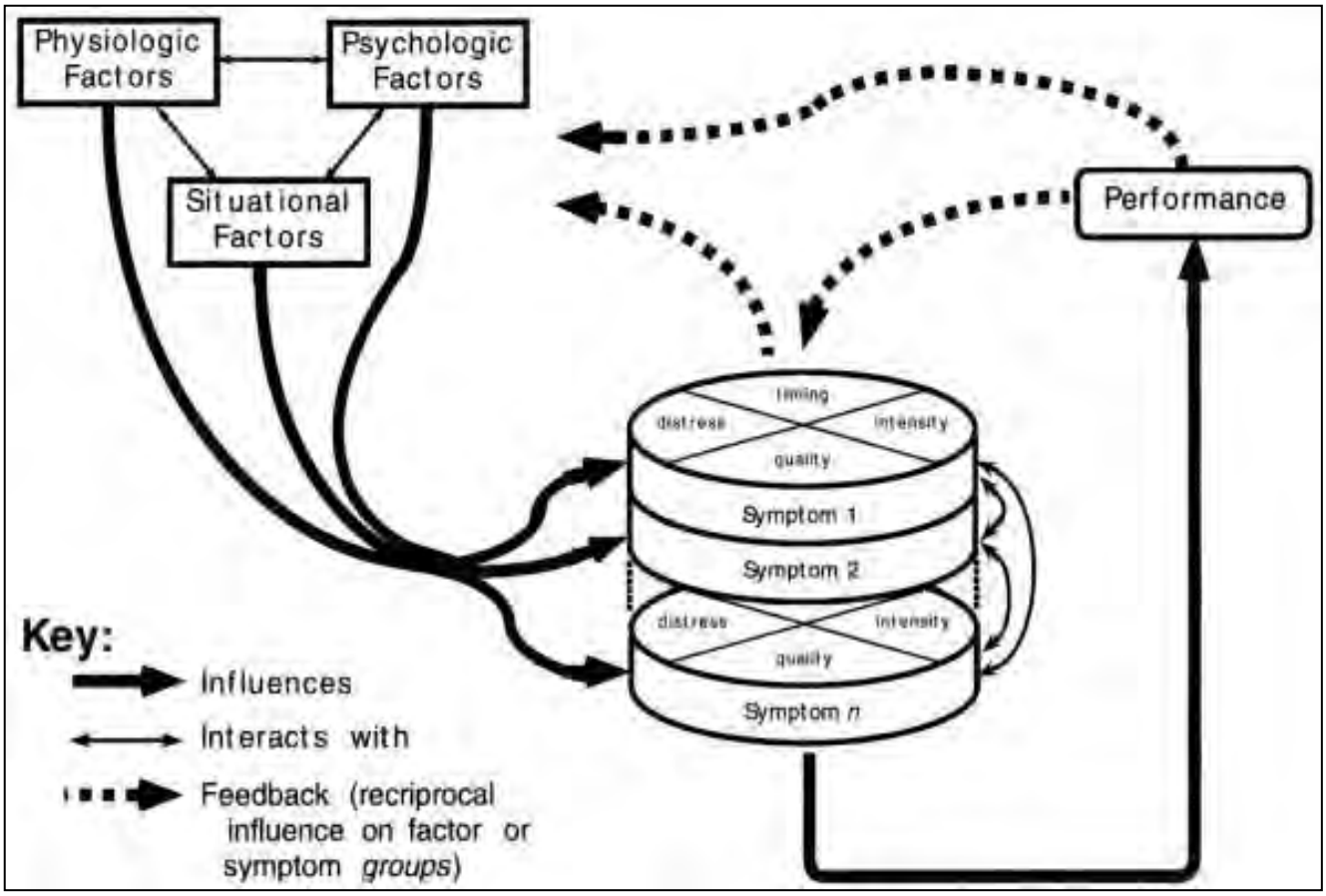

Figure 2. **Schematic representation of the Theory of Unpleasant Symptoms. Reproduced with the permission of Wolters Kluwer Health from "The Middle-Range Theory of unpleasant symptoms: An update," by E.R Lenz, L.C. Pugh, R.A. Milligan, A. Gift, and F Suppe, (1997), *Advances in Nursing Science, 19,* p. 14-27. Copyright 2008 by Aspen Publishers, Incorporated. See text for an in-depth description of how each component of this figure relate to each other and the theory.**

Assumptions and Antecedents of the Theory

According to Lenz and colleagues (1997), the Theory of Unpleasant Symptoms includes the following assumptions:

a) Symptoms are multidimensional and include: timing, intensity, quality, and distress (Lenz et al., 1997);

b) Symptoms are experienced alone or more commonly in combination with other symptoms (Lenz et al., 1997) and the relationship is multiplicative rather than additive (A. Gift, 2009);

c) The simultaneous presence of more than one symptom results in each symptom catalyzing the other (Lenz et al., 1997);

d) Physiologic, psychologic, and situational factors, all of which can interact with one another, influence the multidimensional symptom(s) experience (Lenz et al., 1997);

e) Consequences of the symptom experience include both functional and cognitive performance (Lenz et al., 1997);

f) There is a reciprocal relationship between both consequences of the symptom experience and the symptom experience itself and the influencing factors (Lenz et al., 1997).

The Theory of Unpleasant symptoms has been described as possessing antecedent factors or events that precipitate the symptom experience and its consequences or the results of the experience. These antecedent factors include the physiologic, psychological and situational influencing factors (Brant, Beck, & Miaskowski, 2010; A. Gift, 2009). Physiologic factors are antecedents that can affect the severity of the symptom (A. Gift, 2009). Physiologic factors can include comorbidities, stages of disease, and other physical finding (A. Gift, 2009). Psychologic factors such as mood, affective response and meaning ascribed to a symptom and situational factors related to the physical and social environment also act as antecedents influencing the symptom experience (A. Gift, 2009). Demographic factors such as marital status, age, sex, race, and culture as well as social support, employment and access to healthcare have been described as additional situational factors (A. Gift, 2009). When more than one symptom occurs at a time, they too may act as antecedents, influencing the symptom experience (A. Gift, 2009). A critique

of models and theories of symptom management noted that the antecedents and outcomes associated with the Theory of Unpleasant Symptoms need further refinement and, as such, may be open to interpretation (Brant et al., 2010).

Concepts of the Theory

The Theory of Unpleasant Symptoms is composed of 3 primary concepts (Lenz & Pugh, 2008; Lenz et al., 1997). Figure 2 provides a visual overview of the theory. These concepts include the symptom itself, with all of its dimensionality, influencing factors, or factors that can influence the symptom experience, and performance or the outcome of the symptom experience (Lenz et al., 1997). Influencing factors include the 3 categories of physiologic, psychologic and situational factors (Lenz & Pugh, 2008; Lenz et al., 1997). These 3 factors are described as influencing the predisposition to or manifestation of a symptom(s) and the symptom experience (Lenz & Pugh, 2008). The symptom experience includes the multidimensional subjective experience of the symptom or symptoms as influenced by physiologic, psychologic, or situational factors (Lenz & Pugh, 2008). The symptom experience affects the individual's performance that can encompass cognitive, physical, and social functioning. (Lenz & Pugh, 2008). These performance outcomes can feedback as modifiers affecting the symptom experience or the influencing factors (Lenz & Pugh, 2008).

Conceptual Definitions

Symptom(s) are the central focus and concept in the Theory of Unpleasant Symptoms (Lenz & Pugh, 2008; Lenz et al., 1997). Symptoms are defined as "the perceived indictors of change in normal functioning as experienced by patients" (Lenz & Pugh, 2008, p. 164). This theory notes that often more than one symptom is experienced at a time with each symptom conceptualized as a multidimensional experience (Lenz et al., 1997). Dimensions addressed by

this theory and common to many symptoms, include intensity, timing, distress, and quality (Lenz et al., 1997). The *intensity* dimension refers to the severity, amount, degree or strength of the symptom experienced (Lenz & Pugh, 2008; Lenz et al., 1997). The *timing* dimension refers to variable frequency or duration of the symptom or a combination of both (Lenz et al., 1997). Timing can also refer to a relationship of a symptom to an event (A. Gift, 2009). The *distress* dimension refers to the how much the person is bothered by the symptom (Lenz et al., 1997) or their reaction to the sensation (A. Gift, 2009). The *quality* dimension of a symptom refers to what it feels like to have the symptom or the unique way that the individual experiences the symptom and it includes descriptors used by the individual to describe the symptom (Lenz & Pugh, 2008; Lenz et al., 1997). The quality dimension has also been described as including the location of the symptom or the reaction to an intervention (A. Gift, 2009).

Influencing factors include three categories that can individually or collectively influence how the symptom(s) with all of its dimensions is experienced (Lenz & Pugh, 2008; Lenz et al., 1997). Influencing factors include physiologic, psychologic, and situational factors (Lenz et al., 1997). *Physiologic factors* that can influence symptoms are described by the Theory of Unpleasant Symptoms as including the interrelated components of normally functioning bodily systems, energy level, and the existence of pathology (Lenz et al., 1997). These factors have been further described as also including genetic and treatment related variables (Lenz & Pugh, 2008). *Psychological factors* are described as affective (mood) mental or cognitive states that may influence the meaning and or experience of a symptom (Lenz et al., 1997). Psychologic state prior to, during, or in response to the experience of the symptom has been noted to influence the symptom (Lenz & Pugh, 2008). Uncertainty regarding knowledge of the meaning of a symptom is a cognitive factor that can also influence the symptom experience (Lenz & Pugh, 2008). *Situational factors* are described by the Theory of Unpleasant Symptoms as social

or physical environmental factors that may influence the meaning or experience of a symptom (Lenz et al., 1997). *Situational factors* include the social and/or physical environment such as cultural, financial resources, lifestyle, healthcare access, employment, and/or social support (Lenz & Pugh, 2008; Lenz et al., 1997).

Performance outcomes are described by this theory as the consequences or the effect of the symptom experience (Lenz et al., 1997). This theory proposes that effects of the symptom experience can affect functional performance (physical activity, social activities, and role performance) and/or cognitive (thinking, problem solving) outcomes (Lenz et al., 1997). It has been suggested by the developer of the theory that current evidence may warrant the addition of quality-of-life and or affective outcomes to the performance outcomes of this theory (Lenz & Pugh, 2008).

Utility of the Theory of Unpleasant Symptoms in Research

The Theory of Unpleasant Symptoms is a useful middle range theory for guiding nursing research. This middle range theory is useful because it highlights aspects of the phenomenon associated with the symptom experience thereby providing a structure for the study of the experience (Lenz et al., 1997). Additionally, this theory allows for the prediction of patient responses that can be useful in the development of interventions (Lenz & Pugh, 2008; Lenz et al., 1997). The concepts associated with this theory are measureable (A. Gift, 2009; Lenz et al., 1997). The dimensions and interactive nature of one or more symptoms can be assessed allowing for a greater explanation of the complexity of the experience so that interventions can be developed to minimize the negative aspects and maximize the positive aspects of the experience. Physiologic, psychologic, and situational factors that influence the symptom experience can be assessed and this information can be used to guide the development of

interventions in an effort to enhance performance outcomes (Lenz et al., 1997). The symptom experience directly influences performance outcomes that can be measured as functional or cognitive status. This theory has been described as needing refinement in multiple areas with one area being that of performance outcomes (Lenz & Pugh, 2008). It has been suggested that quality-of-life with its affective aspects may be a more inclusive measure of performance than functioning alone and that this issue needs further exploration (Lenz & Pugh, 2008).

Review of Research Using the Theory of Unpleasant Symptoms

Numerous studies have examined the utility of the Theory of Unpleasant Symptoms to understand the patient's experience of unpleasant symptoms (Corwin, Brownstead, Barton, Heckard, & Morin, 2005; A. G. Gift & Shepard, 1999; Jurgens et al., 2009; Liu, 2006; McCann & Boore, 2000; Reishtein, 2005; Rychnovsky, 2007; Woods, Kozachik, & Hall, 2010). It has been noted that multiple studies of symptoms across the literature support the premises of the Theory of Unpleasant Symptoms linking symptoms and performance even though the theory was not used to guide the study (Lenz et al., 1997).

Fatigue in postpartum woman has been studied by several investigators using the Theory of Unpleasant Symptoms (Corwin et al., 2005; Rychnovsky, 2007). Using a prospective longitudinal descriptive design, Rychnovsky evaluated 109 (N=155) military women who completed the surveys at three different postpartum time periods (Rychnovsky, 2007). Some findings of this study included both significant positive and negative correlations with various physiologic, psychologic, and situational factors (Rychnovsky, 2007). Depression was positively correlated with fatigue at all time periods (r =.516; r = .557; r =.477; p <.05) (Rychnovsky, 2007). Moderate to high levels of fatigue were reported at all data collection points with almost half of the women reporting moderate fatigue at the time of return to work;

maternal anxiety during hospitalization explained 6 percent of the variance and maternal anxiety at 2 weeks explained 20 percent of the variance in fatigue at 6 weeks (Rychnovsky, 2007). These findings demonstrate the complexity of the fatigue experienced by postpartum military women (Rychnovsky, 2007).

Similarly, other investigators used a correlational longitudinal study design to assess the role of postpartum fatigue in the development of postpartum depression using hypotheses generated via the Theory of Unpleasant Symptoms (Corwin et al., 2005). Forty-two women were enrolled before 36 weeks of pregnancy and followed at multiple time points (Corwin et al., 2005). Fatigue and stress experienced over time accounted for a progressively increasing amount of the variance from 36 weeks gestation to 28 days postpartum in depressive symptoms (fatigue: day 7 = 29%; day 14 =49%; day 28 = 59% and stress day 7 = 45%; day 14 =57%; day 28 = 77%) (Corwin et al., 2005). Those who reported higher levels of fatigue (M=11.93, SEM= 1.67) on day 14 also scored significantly higher for symptomatic depression on day 28 in contrast to those reporting below average fatigue (M=4.94, SEM= .92; $t(29) = -3.84$; $p = .001$) (Corwin et al., 2005). This finding lead the authors to conclude that fatigue significantly contributes to postpartum depression (Corwin et al., 2005). This study was noted to support the premises of the Theory of Unpleasant Symptoms in that fatigue was identified as a significant contributor to postpartum depression (Corwin et al., 2005).

The Theory of Unpleasant Symptoms has been helpful in the study of symptoms associated with chronic obstructive pulmonary disease. Using a measure of three of the four dimensions described by the Theory of Unpleasant Symptoms for fatigue and for dyspnea, Gift evaluated predictors of fatigue in 48 female and 56 male outpatients with chronic obstructive pulmonary disease (A. G. Gift & Shepard, 1999). Findings of the prospective cross sectional analyses included dyspnea and physical symptoms explaining 42% of the variance in predicting

fatigue in both sexes and 67% for women alone (A. G. Gift & Shepard, 1999). Dyspnea and physical symptoms were found to have a greater impact than the objective physiologic severity measures (A. G. Gift & Shepard, 1999). Additionally, these symptoms were found to have a greater impact for predicting fatigue than did symptoms that emulated psychologic status (A. G. Gift & Shepard, 1999). These finding imply that dyspnea and physical symptoms are more useful predictors of fatigue than disease severity or psychologic symptoms (A. G. Gift & Shepard, 1999). Based on these findings, the authors suggest that in this population interventions directed at dyspnea and physical symptoms may more useful for reducing fatigue than those for altering psychologic symptoms or physical status (A. G. Gift & Shepard, 1999).

Using the Theory of Unpleasant Symptoms, Reishtein prospectively evaluated 77 males and 23 females with chronic obstructive pulmonary disease (Reishtein, 2005) to determine the effect of dyspnea, fatigue and sleep difficulty on functional performance. In this study, dyspnea correlated with fatigue (r = .43; p =<.001), sleep difficulty (r = .39; p =<.001), dyspnea (r = -.54; p =<.001), and fatigue r = -.24; p=<.01). Despite these finding, sleep difficulty was not correlated with functional performance (Reishtein, 2005). Dyspnea alone was found to significantly explain the variance (adding 19% for a total of 44%; p<.001 to the 25% explained by age and oxygen use) in functional performance (Reishtein, 2005). Findings guided by the Theory of Unpleasant Symptoms resulted in the suggestion that focusing on the symptom dyspnea might be the best way to improve both symptoms in general and functional outcomes (Reishtein, 2005).

The symptom of fatigue has also been studied in those who require hemodialysis using the Theory of Unpleasant Symptoms (Liu, 2006; McCann & Boore, 2000). Several studies have specifically assessed fatigue and its relationships to physiologic, psychologic, and situational factors (Liu, 2006; McCann & Boore, 2000). Prospective cross sectional analyses of 119

Taiwanese hemodialysis patients demonstrated multiple findings that included the psychologic variable of depression, and the situational variable of age were significant predictors of fatigue explaining 62% of the variance when using a fatigue assessment scale as the dependent variable (Liu, 2006). When using a depression assessment scale as the outcome, depression and the physiologic variable of urea reduction ratio explained 48% of the total variance (Liu, 2006). In this study, unemployed subjects (situational factor) reported higher levels of the fatigue (differences in fatigue score by employment t =4.33; p<.01) than did employed subjects (Liu, 2006). It was noted that patients at risk for experiencing problematic fatigue can be identified and interventions could be employed to promote positive outcomes (Liu, 2006). In a similar study, prospective cross sectional analysis of questionnaire data returned via the mail by 39 of 50 hemodialysis patients (25 male; 14 female) surveyed was analyzed to examine fatigue and its relationship to physiologic, psychologic and situational variables (McCann & Boore, 2000). Some of the findings from this study included fatigue being associated with the physiologic factors of sleep problems (r = .476; p=<.01), poor physical health (r = -.775; p =<.01) and the psychologic factors of depression *(*r = .647; p =<.01) but not with the physiologic factors of biochemical or situational factors (role function, employment status and others) (McCann & Boore, 2000). The authors suggested that complex interactions occur at the level of physiologic and psychologic factors that may influence the fatigue experienced (McCann & Boore, 2000).

Using hypotheses generated from an adapted version of the Theory of Unpleasant Symptoms, Woods and associates studied 157 abused women (N=162) analyzing the contributions of situational, psychological, and physiological factors on subjective sleep quality (Woods et al., 2010). Findings suggested that the psychologic factor of posttraumatic stress disorder (ß=.33, p= <.01) and the physiologic factor of stress related physical health symptoms (ß=.22, p= <.01) mediated the effect of partner violence on sleep quality (Woods et al., 2010).

Variability in sleep quality was not significantly related to depression or the demographic variables in this study (Woods et al., 2010). Physiologic, psychologic, and situational factors were found to be responsible for 32% of the variance in global sleep quality (Woods et al., 2010). This theory was also employed to develop hypotheses used to study the relationships of mood disturbances, symptom experience, and attentional function in female breast cancer patients (Lee, 2005). This cross sectional correlational design study of 125 female Korean patients receiving chemotherapy for treatment of breast cancer found mood disturbance (r= -.46, p < .01) and symptom experience (r= -.20, p < .05) negatively correlated with attentional function as a measure of cognition (Lee, 2005). Symptom experience was found to be a moderator, but not a mediator, between mood disturbance and attentional function (unstandardized regression coefficient b = -.081, t= -5.23 (SE=.015), p < .05), but only when symptoms were at a medium level rather than a low or high level (Lee, 2005). The author suggests that interventions directed towards moderating the influence of mood disturbance on attention function may only be useful when symptoms are at a moderate level (Lee, 2005)

The Theory of Unpleasant Symptoms has been used to study symptoms in those hospitalized with heart failure (Jurgens et al., 2009). Findings from this secondary analysis of data from a heart failure registry (N=687) noted three symptom clusters that included acute volume overload, chronic volume overload, and emotional distress (Jurgens et al., 2009). The acute volume overload symptom cluster that included shortness of breath, fatigue, and sleep problems explained the greatest variance (45.7%) on living as desired (Jurgens et al., 2009). Patients put different emphasis on different symptoms depending on whether the symptoms were acute or chronic demonstrating the utility of the Theory of Unpleasant Symptoms in understanding the multidimensional nature of symptoms as including more the physical sensation of the symptoms (Jurgens et al., 2009).

Conclusion

The Theory of Unpleasant Symptoms provides a useful structure for this study as it highlights aspects of phenomena associated with the primary focus of the theory, that is the symptom(s), thereby allowing for examination of the experience of those with chronic cough (Lenz et al., 1997). The dimensionality and interaction of one or more symptoms as described by this theory was useful in describing changes in the symptoms of depression, anxiety, and stress in adults with the symptom of chronic cough before and after management using the ACCP guidelines. This theory provided a guide for the physiologic, psychologic, and situational factors that influence the experience of chronic cough.

This study fit well with this theory that allowed for describing the relationship of factors that were identified as physiologic factors (ability to speak without coughing, urge-to-cough, and number of diagnoses), situational factors (social support), and psychologic factors (symptoms of depression, anxiety, and stress) and the experience of chronic cough. The theory provided a plan for the assessment of performance outcomes as a result of the experience of chronic cough. This study advances the field by further exploring the role of the antecedent influencing factors for the symptom experience and the use of cough-specific quality-of-life as a performance outcome for the Theory of Unpleasant Symptoms. Finally, this theory allowed for the prediction of patient responses to chronic cough that can be useful in the development of interventions (Lenz & Pugh, 2008; Lenz et al., 1997).

Operational Definitions

In this study, concepts are operationalized in the following manner:

1. *Physiologic Factors* are influencing factors that include number of cough-related diagnoses attributed to a patient by a cough clinic physician. Physiologic factors will also include self

reported urge-to-cough and ability to speak being bothered by cough based upon intensity, timing, distress, and quality measured using Punum Ladder type of visual analogue scales.

2. *Psychologic factors* are influencing factors that include symptoms of depression, anxiety and stress measured using the Depression, Anxiety, and Stress Scale 21 (P. F. Lovibond & S. H. Lovibond, 1995).
3. *Situational factors* are influencing factors that include social support or the support of others or social relationships measured using the Duke-UNC Functional Social Support Scale (Broadhead et al., 1988)
4. *Symptom(s)* are the self reported experience of chronic cough measured by a based upon intensity, timing, distress, and quality as measured using a Punum Ladder.
5. *Performance outcomes* are cough-specific quality-of-life as measured by the Cough Quality of Life Questionnaire (C. T. French et al., 2002).

CHAPTER 3

Methods

Research Design

This was a descriptive longitudinal observation study designed to examine changes over time in the psychologic symptoms of depression, anxiety, and stress in adults with chronic cough before and after management using the ACCP guidelines. Factors examined for their potential influence on chronic cough were derived from the Theory of Unpleasant Symptoms. These factors included: physiologic factors (ability to speak without being bothered by cough, urge- to-cough and number of diagnoses), situational factors (social support), and psychologic factors (symptoms of depression, anxiety, and stress). Findings revealed through quantitative analysis were used to provide further understanding of factors that may influence chronic cough. Finally, intervention fidelity to the study components was monitored and a process for measuring intervention fidelity in the application of the ACCP guidelines for treating cough using the Technology Model has been described. These findings were used to help understand the role of fidelity to the ACCP guidelines as can be applied to future studies of the management of chronic cough.

Sample

The sample for this study was composed of a consecutive sample of patients recruited from a specialty cough clinic located at UMass Memorial Medical Center. Patients were recruited from the spring of 2013, until a sample of 80 study participants were enrolled.

A power analysis was conducted for the analyses planned to address specific aims #1 and #3. Power analysis based on specific aim # 1 using a one-group paired t-test design and mean difference of .5, alpha = .05 and 80% power resulted in the recommendation for 56

subjects. A linear regression analysis was conducted to address the power analysis for specific aim #3, using 7 predictors, an anticipated effect size (r^2) of .3, alpha = .05, and 80% power, also resulting in the recommendation for 56 subjects. To provide for a liberal 25 percent drop-out rate, 80 subjects were recruited. This cough clinic draws patients from a wide geographic area and cares for approximately 2-4 new chronic cough patients each week. Specific aim #4 was descriptive only and therefore did not require a power analysis.

In an effort to improve subject interest and retention, subjects were informed that all names of those completing the study would be placed in hat for a drawing at the conclusion of all subjects three month data collection. One study participant received a Kindle Reader based upon the drawing.

Inclusion and Exclusion Criteria

Subjects were eligible for this study if they met the following inclusion criteria: (1) were age 18 years or older; (2) had a self reported cough of greater than eight weeks duration; (3) were able to read and speak English; and (4) had the ability to give written informed consent. Subjects were excluded if they: (1) were pregnant; (2) had a cognitive disability that renders them unable to provide written informed consent; and/or (3) were prisoners. The principal investigator documented the number of participants who declined to participate and the number excluded based on the exclusion criteria and the reason(s) for non-participation.

Setting

This study was conducted at UMass Memorial Medical Center (UMMMC), an academic medical center and clinical partner of the University of Massachusetts Medical School. The specific site for the study was the internationally recognized cough specialty clinic located within the Lung and Allergy Center on the University Campus, in Worcester, Massachusetts. The

cough clinic fully embraces the use of the American College of Chest Physicians' Diagnosis *and Management of Cough: American College of Chest Physicians (ACCP) Evidence Based Clinical Practice Guidelines* (Irwin, Baumann, et al., 2006). This site and practice were chosen as it attracts a continuous population of new patients with a chief complaint of chronic cough. The cough clinic attracts referrals from primary care physicians, pulmonologists, otolaryngologists, and gastroenterologists from Massachusetts and from across the US, Canada, and beyond. The cough clinic is staffed by four board certified pulmonary and critical care physicians who are experts in the use of the ACCP guidelines. The director of the cough clinic serves as the chair of the ACCP Cough Guideline Committee. The principal investigator serves as a member of both the ACCP Cough Guideline Committee and its Executive Committee.

Procedures

The principal investigator (PI) works as a clinical care coordinator and nurse practitioner for the cough clinic, and as such, plays a role in the triage of patients into the cough clinic. The patient scheduling coordinator, for the cough specialty clinic, provided the principal investigator with the names, medical record numbers, and phone numbers of new patients who called to book a visit in the cough specialty clinic (a HIPAA waiver was obtained). The principal investigator called all of these patients on the telephone prior to their appointment in the cough specialty clinic and offered them the opportunity to participate in this study. The investigator asked patients who did not want to participate if they would be willing to share the reason why they chose not to participate. A flow diagram was used to document the number and status of participants during each phase of data collection.

For those patients who met study eligibility criteria and who were interested in participation, an appointment to obtain both written informed consent and initial data was

scheduled. Patients were advised that the initial consent and data collection process would take approximately one to two hours. This allowed plenty of time for questions during the consent process. This appointment was conducted in a private setting and on a day deemed acceptable by the potential research participant. The consent form was reviewed with potential participants. The consent form noted that the purpose of the study was to examine factors including symptoms of depression, anxiety, and stress, cough severity, their number of medical problems, their ability to speak being bothered by cough, urge-to-cough, and how the support provided by others may influence chronic cough and its effects on quality-of-life. Participants were informed that we would also be measuring fidelity to the study and their receipt of the interventions. It was noted that the results would be used to better understand chronic cough and to generate recommendations for future interventions. Potential participants were allowed time for questions. A copy of the signed consent form was provided to those willing to participate. Data collection was conducted in five phases. See Figure 3.

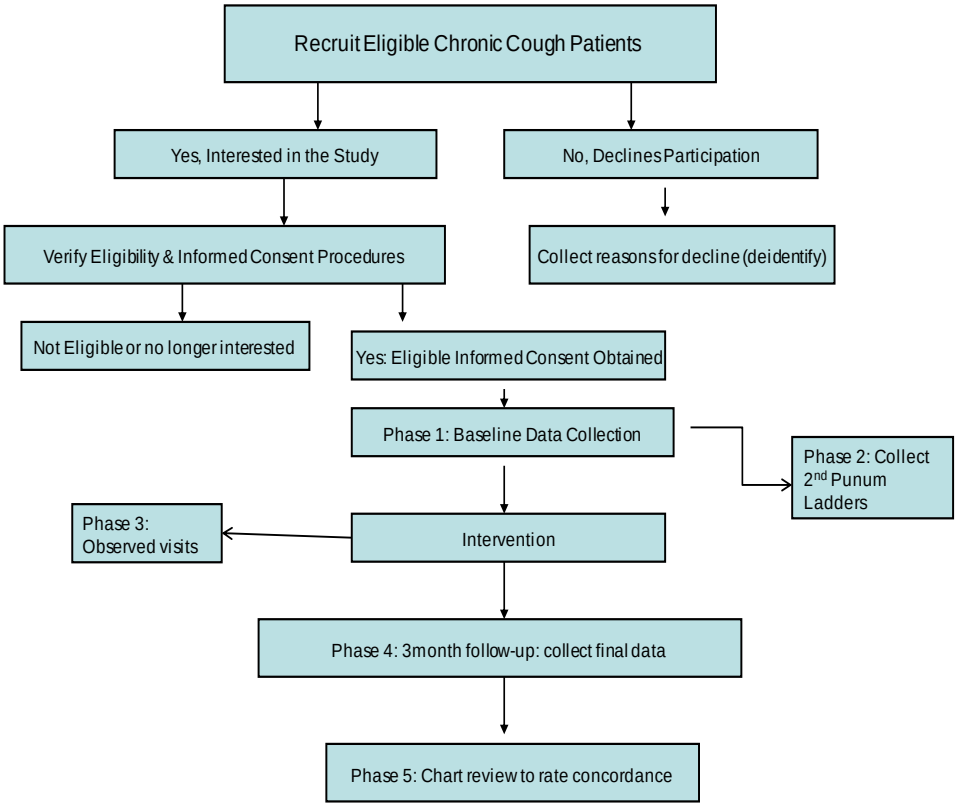

Figure 3. **Flow diagram of the participants' progress thorough the study**

Phase One Data Collection

Initial data collection began after completion of the consent process. Research participants were asked to complete a short sociodemographic questionnaire, the Cough Quality of Life Questionnaire (CQLQ), separate Punum Ladders for rating both urge-to-cough (whether or not cough was produced), ability to speak being bothered by cough, and cough severity based upon rating of timing, distress, intensity, and quality (Lenz et al., 1997), the Depression, Anxiety, Stress Scale (DASS-21), SF12v2, and the Duke Functional Social Support Scale using paper and pen self report questionnaires.

Phase Two Data Collection

To examine test-re-test reliability for the Punum Ladder measure, research participants returning on separate days 24-48 hours apart prior to their initial visit with the physician were asked if they would be willing to complete the three Punum Ladders on two separate occasions. The second Punum Ladders were completed within 48 hours of the first and prior to physician appointment in the cough specialty clinic.

Phase Three Data Collection

To establish intervention fidelity to the study components 12 patient physician cough clinic visits were scheduled to be observed by the principal investigator. Fidelity in the application of the ACCP guidelines was measured by the principal investigator using an intervention fidelity checklist adapted specifically for this study.

Phase Four Data Collection

Follow-up data collection was completed 3 months after the initial physician visit and post initiation of the intervention. Data collected included all prior questionnaires, minus the sociodemographic survey and included the addition of a subject intervention receipt questionnaire. Subjects were contacted via phone and reminded that it is time for the three month data collection. If research participants did not return to the clinic for in person data collection, they were mailed the questionnaires and a prestamped self-addressed envelope. If questionnaires were not returned, the principal investigator contacted patients via telephone to see if they received the reminder. Additional, reminders consisting of a postal letter, or a phone call, were conducted up to twice within 4 weeks and then the data were considered "missed" at 4 months.

Phase Five Data Collection

The electronic medical record was reviewed after the 3 month data collection was completed to collect the following: medications that are known to cause cough, antihistamines,

bronchodilators, and decongestants, diagnoses, and diagnostic and therapeutic interventions prescribed. See Appendix H for data extraction sheet. Additionally, during the 3 month post data collection review, the electronic medical record was reviewed to evaluate concordance between what was prescribed and participant receipt within the context of the individual situation. The principal investigator determined and rated the degree of concordance between these two sources of information using a single variable.

Measures

Sociodemographic Questionnaire

Data collected using a sociodemographic questionnaire was used to characterize the population. Demographic variables included age (in years), duration of cough, gender, marital status, educational level (in years), self-reported race and ethnicity, financial strain (Gold et al., 2001) employment status, use of self prescribed medications, herbal or other home remedies and were collected using a self report survey administered at the initiation of the study. See Appendix A. Subjects were given the opportunity to respond to an open ended question at the end of the survey asking them to provide any additional information about their chronic cough. The investigator collected baseline medications and diagnoses from the electronic medical record at the 3 month post data collection period.

Cough Quality of Life Questionnaire

Consequences of chronic cough were measured using the Cough Quality of Life Questionnaire (CQLQ). The CQLQ is a 28-item self report cough-specific quality-of-life questionnaire developed for use with patients complaining of acute or chronic cough. This questionnaire does not include a referent time period, patients are asked to rate the impact of

cough on the items for their current state. See Appendix B. The CQLQ takes six to eight minutes to complete (C. T. French et al., 2002). Each item is scored on a four point Likert type scale (1-4): strongly disagree (1), disagree (2), agree (3), or strongly agree (4). Scores are determined by summing the individual item scores. The lowest possible total overall score of 28 indicates no adverse effects on quality-of-life because of cough. The highest possible total score of 112 is indicative of the most adverse effects of cough on quality-of-life. The CQLQ consists of six subscales that assess the following domains: physical complaints, psychosocial issues, functional abilities, emotional well-being, extreme physical complaints, and personal safety fears. Internal consistency reliability has been demonstrated using data from both those with acute and chronic cough (*N*=184), with Cronbach alphas ranging from .62-.86 for the subscales and .92 for the total CQLQ score (C. T. French et al., 2002). Test-retest reliability (chronic coughers *n*=154; 38 male and 116 female) demonstrated excellent reliability (total CQLQ r=.89; p <.001 and subscales ranged from r= .75-.92; p<.001) (C. T. French et al., 2002). Construct validity was supported in a study with a sample of 24 chronic coughers who demonstrated significant improvement in post treatment CQLQ scores when cough was self reported as no longer being a problem (pretreatment scores for total CQLQ mean 63.33, *SD* = 13.69 versus 30.50; *SD* = 5.80; paired *t* = - 10.73; *p* <.001) (C. T. French et al., 2002). Using prospective measures, the minimal important difference has been reported as 21.89 for change CQLQ quality-of-life (Fletcher et al., 2010).

Punum Ladders

Separate Punum Ladders were used to rate the physiologic factors of ability to speak without coughing, and urge-to-cough. Cough severity was also measured using a Punum ladder. All Punum Ladders asked that the dimensions of timing, intensity, distress and quality (Lenz et

al., 1997) of be taken into account when rating the issue and that the rating take the past 7 days into account (Fletcher et al., 2010). The Punum Ladder is a self report scale that uses three anchoring cues: faces (0 smiling to 10 tearful), words (0 no problem to 10 worst possible problem; in the case of cough severity the word problem was replaced with cough), and numbered steps on a ladder (bottom rung no problem to top rung worst problem) and scores range from 0-10 with higher scores indicating more dysfunction (Fletcher et al., 2010). See Appendix C. Administration time is approximated at one minute per ladder.

Depression Anxiety and Stress Scales

Background: The clinical overlap of general affective distress and symptomatology associated with anxiety and depression has made quantitative measurement specific to the differentiation of these two disorders complex (Clark & Watson, 1991; Henry & Crawford, 2005). In an effort to resolve this problem, a tripartite model of anxiety and depression has been proposed (Clark & Watson, 1991). The structure of this model includes a "general distress factor and specific factors for anxiety and depression" (Clark & Watson, 1991, p. 316). The tripartite model also proposed that the anxiety component of the model is differentiated from the depression component in that anxiety alone is marked by physiologic hyperarousal whereas depression alone is marked by the absence of positive affect or anhedonia (Clark & Watson, 1991). The model proposes that in addition to sharing common symptoms, those with both anxiety and depression share a general state of affective distress or highly negative affect supporting the presence of mixed anxiety and depression (Clark & Watson, 1991).

Measure: Psychological influencing factors of symptoms of depression, anxiety, and stress were measured using the Depression Anxiety Stress Scales (DASS-21), a 21 item self report questionnaire (Antony, Bieling, Cox, Enns, & Swinson, 1998).

Subjects reply to each question by rating the degree to which the statement applies over the past week using a four point (0-3) Likert type scale with higher scores indicating a greater degree of severity of anxiety, depression, and stress. Administration time for the DASS-21 is approximately five minutes.

The DASS-21 (21 item) was derived from the DASS (42 item) (Antony et al., 1998). The DASS-21 was chosen for this study despite the fact that it has slightly lower reported reliability than the DASS (.94, .87, and .91. for the DASS-21 versus .97, .92, .95 for the DASS) (Antony et al., 1998) because it has good psychometric properties, is shorter and will therefore impose less burden on the participants (Antony et al., 1998). The DASS-21 was also chosen for it similarities to the tripartite model proposed by Clark and Watson (Antony et al., 1998; P. F. Lovibond & S. H. Lovibond, 1995). The DASS was designed to define separate core symptoms of depression, anxiety, and stress that would allow for differentiation between the conditions (S. H. Lovibond & P. F. Lovibond, 1995). The DASS anxiety scale (7 items) is reflective of the symptoms associated with various Anxiety Disorder defined by DSM-IV (Brown, Chorpita, Korotitsch, & Barlow, 1997). The developers of the DASS describe anxiety as involving long term anticipation of adverse events such as those that are of major significance to self esteem (S. H. Lovibond & P. F. Lovibond, 1995). Anxiety is more likely to occur in those with a low threshold for fear (S. H. Lovibond & P. F. Lovibond, 1995). The DASS anxiety scale additionally addresses situational anxiety (S. H. Lovibond & P. F. Lovibond, 1995). The DASS depression scale (*N*=7 items) is reflective of the DSM-IV criteria for Mood Disorders (S. H. Lovibond & P. F. Lovibond, 1995). The developers of the DASS describe depression as more than a state characterized by sadness, in that it is a state of loss of self esteem or incentive associated with a low self perceived probability of achieving significant life goals (S. H. Lovibond & P. F. Lovibond, 1995). The third component identified by the DASS is the stress

scale (7 item), which in contrast to the tripartite model, is not derived of commonalities of symptoms, but is correlated with common causes of anxiety and depression (S. H. Lovibond & P. F. Lovibond, 1995). The stress scale reflects symptoms associated with over arousal or tension reflecting ongoing difficulty in meeting life demands (P. F. Lovibond & S. H. Lovibond, 1995). Despite being correlated with the other scales, the DASS stress scale is factorially distinct from the other scales (S. H. Lovibond & P. F. Lovibond, 1995). The stress scale is proposed to potentially be helpful in exploring "links between environmental demands and emotional and physical disturbances" (P. F. Lovibond & S. H. Lovibond, 1995, p. 343) .

The DASS was not designed as a tool to be used in categorizing a diagnosis (S. H. Lovibond & P. F. Lovibond, 1995). The focus of the DASS-21 is the dimension of severity of the symptom and the risk of more extreme symptoms rather than categorizing symptoms using a single cut off score (S. H. Lovibond & P. F. Lovibond, 1995). Lovibond noted that stress can precipitate symptoms of anxiety and depression and that it has a clear connection with anxiety (P. F. Lovibond & S. H. Lovibond, 1995). Cut off scores are available to augment an understanding of the degree of severity to symptoms in relation to populations. It is recommended that during statistical analyses, the scores of the DASS-21 be doubled for interpretation as this most closely represents the original DASS (S. H. Lovibond & P. F. Lovibond, 1995). The 7 subscales are rated 0 -3 did not apply to me at all to applied to me very much, or most of the time. Subjects are asked to respond based upon the past week. Scores are determined by summing the individual item scores for each scale and multiplying them by 2, with subscale scores ranging from 0-42. The total scale score ranges from 0-126.

SF-12v2

The Quality Metric's SF-12v2® Health Survey was used in this study as a measure of concurrent validity for the CQLQ. The SF-12v2 is a commonly used self-report measure of functional health and well being developed as a shorter alternative to the SF-36v2® (QualityMetric, 2012). This questionnaire uses 3 and 5 point response options and it takes 2-3 minutes to be completed. This version of the questionnaire is composed of 12 items that address eight domains with one to two questions per domain and two overall summary outcomes that address a physical and mental health component summary score as well as eight domain scores (J. E. Ware, Kosinski, Turner-Bowker, & Gandek, 2002). Domains include physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health (J. E. Ware et al., 2002). The acute recall version of the questionnaire used in this study was based on a one week recall period. Test-retest reliability for the physical component summary was 0.89 and 0.76 for the mental component summary for a US population (J. Ware, Kosinski, & Keller, 1996). The lowest possible scores reflect poor quality-of-life and highest reflect excellent quality-of-life. Scoring was completed using the program provided by Quality Metrics.

During its early development, results obtained with this questionnaire were shown to closely mirror the statistical outcomes of the 36 item version from which it was derived (J. Ware et al., 1996). Earlier work demonstrated correlations between the SF12 and the SF36 ranging from 0.94 to 0.96 for the physical component summary and 0.94 to 0.97 for the mental health component summary (Gandek et al., 1998). Reliability coefficients for the physical component summary score were 0.89 and 0.86 for the mental component summary score and the eight domains ranged from 0.73 to 0.87 (J. E. Ware et al., 2002). Only one study was found comparing any version of the SF with a cough questionnaire. In a study of those with COPD (N=54) weak

to moderate correlations (r=0.04 to 0.41) were found between similar components of the SF-36 and the Leicester Cough Questionnaire (Berkhof et al., 2012).

Duke-UNC Functional Social Support Questionnaire

The situational factor of social support was measured using the Duke-UNC Functional Social Support Questionnaire (FSSQ). The 8 item FSSQ was derived by factor and item remainder analysis derived from a 14 item social support questionnaire (Broadhead et al., 1988). Psychometric testing of the 8 item FSSQ was performed with 401 subjects from a family medicine clinic; it demonstrated good reliability (test-retest r=.50-.77; p = .05) (Broadhead et al., 1988). The 8 item FSSQ is a self report questionnaire that uses a 5 category Likert type response format (ranging from 1 =as much as 5= I would like to much less than I would like) (Broadhead et al., 1989; Broadhead et al., 1988). This questionnaire does not offer a referent time period. The total score is the sum of the individual scores. Higher scores are indicative of greater social support. Five minutes or less should be all that is required for completion of this questionnaire.

The FSSQ measures two dimensions of social support that include confidant and affective support (Broadhead et al., 1989; Broadhead et al., 1988). The confidant support scale includes five items and the affective support scale includes three items (Broadhead et al., 1989; Broadhead et al., 1988). Confidant support relates to chances to talk about important issues, useful advice, and invitations to participate in activities (Broadhead et al., 1989). The affective support scale relates to others who provide caring and affection as well as help when bed ridden (Broadhead et al., 1989). Cronbach's alpha of .88 for the total 8 item scale using the 5 response options has been reported in a study of HIV infected woman (N=101) and their adjustment to chronic illness (Bova, 2001) and .87 in a study of quality-of-life in ovarian cancer survivors (N=132) (Champion et al., 2007).

Intervention Fidelity

A process for measuring intervention fidelity to the study components was developed using the ACCP guidelines (Irwin, Baumann, et al., 2006). Intervention fidelity was evaluated based upon the Technology Model (Santacroce et al., 2004). We developed a detailed intervention manual to help guide the interventionist in the application of the ACCP guidelines. The intervention that was the focus of this study was the application of the 2006 American College of Chest Physicians' *Diagnosis and Management of Cough: American College of Chest Physicians (ACCP) Evidence Based Clinical Practice Guidelines (Irwin, Baumann, et al., 2006)*.

Development of an Intervention Manual

An intervention manual was developed to serve as the baseline for the delivery of care for the diagnosis and management of chronic cough. The purpose of the manual was to provide a basis for review to help ensure fidelity to the study components has been maintained as outlined in the manual. The manual contents were derived from the 2006 American College of Chest Physician Guidelines for the Diagnosis and Management of Cough. The algorithm for the management of chronic cough, a component of the 2006 guidelines, was used as the focus for the development of the clinical components of the manual. The care outlined in the manual is the accepted standard of practice in the Cough Clinic at the UMass Memorial Medical Center. Clinical components of the manual included core diagnostic and management elements associated with the 4 most common causes of chronic cough and beyond and process elements that address issues relative to baseline cough evaluation and follow-up. The intervention manual is included in this paper as Appendix D.

The PI reviewed the manual with the 4 physicians providing care in the cough clinic prior to the onset of the study. This review was conducted to establish agreement that the manual

outlined the care that the Cough Clinic physicians deliver, to those with cough of greater than 8 weeks duration on a routine basis. This care was in accordance with the 2006 ACCP Guidelines for the Diagnosis and Management of Cough. The care outlined in the manual included baseline measurement of cough severity and follow-up visits scheduled at 4-6 weeks. All 4 physicians agreed that the manual accurately outlined the care they deliver and they agreed to randomly undergo assigned observations of their patient care evaluation and management visits by the primary nurse investigator.

The PI monitored the intervention delivery by direct observation of 15% of the visits (approximately 12 visits over the course of the study). All research participants attended a face to face cough specialty clinic new patient visit. Follow-up medical care was delivered in person or via phone call (when travel was not feasible) as is also the standard in the cough specialty clinic. It was expected that follow-up will occur in 4-6 weeks so at least one follow-up contact should occur during the three month follow-up period. Research participant care was managed by a physician and augmented by nurses, nurse practitioners, and nutritionists as is standard in this clinic.

The intervention fidelity process focuses on monitoring for the prescribed behaviors by the physician that demonstrate adherence and competence in the delivery of treatment of identified causes of cough (Irwin, Baumann, et al., 2006). The process also seeks to measure participant receipt of the interventions prescribed and concordance between what is prescribed and what is received. Specifically, the intervention fidelity process assessed for evidence of prescribed focused and/or empiric treatment of:

1) upper airway cough syndrome with first generation antihistamine/decongestants;
2) asthma with inhaled corticosteroids and bronchodilators, and/or leukotriene receptor antagonists;

3) non-asthmatic eosinophilic bronchitis with inhaled corticosteroids; and

4) gastroesophageal reflux with diet, lifestyle recommendations, acid suppression medications, and prokinetic therapy if needed at each visit (Irwin, Baumann, et al., 2006).

Intervention adherence was defined as prescribing identified diagnostic interventions and focused and/or empiric therapy for identified causes of cough and avoiding proscribed recommendations (Santacroce et al., 2004). Competence in intervention delivery was defined as probing for patient understanding of and adherence with prescribed therapy, maintaining partially effective therapy, stepping up ineffective therapy, and ordering further evaluation when therapy has been maximized and cough has not resolved. This study included three different measures of intervention fidelity.

Measures of Intervention Fidelity

Intervention fidelity was measured in three ways:

1. Direct observation of interventionist and research participant cough clinic visits was conducted by the PI for a planned total of 12 random observations over the course of data collection. Random numbers were generated using SPSS to generate a list of 56 numbers. The first 12 random numbers taken from this list were to be used to identify the research subjects whose visits will be observed. The list was maintained for use in the event of research subject drop out.

   The PI unobtrusively sat in on patient visits with interventionists who volunteered to have their visits monitored to assess intervention delivery. The observation goals were the measurement of the application of the ACCP cough management guidelines within the context of the patient visit. Adherence to and dose of intervention delivery and competence

were measured using an Intervention Fidelity Monitoring Checklist. This form was adapted from a form previously developed for use in a pediatric intervention study (Bova & Sullivan-Bolyai). This form also listed the most common diagnoses and treatments for chronic cough and provided space to write in others. The rater was asked to check diagnoses and treatments for chronic cough that were addressed during the visit This 7 item rating form addresses 7 processes of care delivery associated with the use of the cough guidelines. The form uses a 4 point scale (0-3) point scale. The scale includes 0- none; 1= low level of intervention fidelity (2 or less of the 4 most common causes addressed); 2 moderate level of intervention fidelity (3 or more of the 4 most common causes addressed); 3=high level of intervention fidelity (all 4 of the most common causes addressed). Scores may range from 0 (lowest fidelity) to 21 (highest fidelity). See Appendix E.

2. Patient self report of receipt of the information related to the guideline interventions prescribed was measured using an Intervention Fidelity Questionnaire for Monitoring Patient Receipt Evaluation. This form was adapted from a form previously developed for use in a pediatric intervention study (Bova & Sullivan-Bolyai). This form also lists the most common diagnoses and treatments for chronic cough and leaves space to write in others. Subjects are asked to check off their conditions that the physician advised them were causing cough and the treatments advised to control the cough. This evaluation uses a 3 point scale (0=not covered, not given any information; 1= covered somewhat, would have liked more information; and 2=covered completely, given all the information I needed) for subjects to rate 7 processes of care delivery associated with the use of the cough guidelines. Scores may range from 0 to 14 (highest fidelity). An additional 8th question (not part of the scale), asks the subject how closely they have followed the cough specialists' recommendations and is rated on a 0-3 scale (0=none of the time, 1 = some of the time, 2= most of the time, 3= all of

the time). The rating scales are followed by 3 open ended questions asking for comments on why they did not follow recommendations, other treatments prescribed, and anything else that may have changed since they began treatment. These data were collected for all patients at the three month post initiation of intervention time point. See Appendix F.

3. Concordance with patient self report of receipt and interventionist prescribed care was established by electronic medical record (EMR) review (Allscripts EMR). The PI rated the degree to which the research subjects' self reported receipt corresponded with documented causes of chronic cough and prescribed interventions. Concordance was rated and reported as a single and separate variable. A data concordance rating scale (see Appendix G) was used to rate the degree to which concordance found using a 0-3 point scale (0- not at all congruent; 1= somewhat congruent (2 or less of the 4 most common causes congruent); 2 Almost all (3 or more of the 4 most common causes congruent); 3=complete congruence (all 4 of the most common causes congruent). Scores range from 0 (lowest concordance) to 3 (highest concordance). The rating scale was adapted to the number of established diagnoses for each subject. This form was adapted from a form previously developed for use in a pediatric intervention study (Bova & Sullivan-Bolyai).

Data Collection

The PI collected all self-report data via questionnaires. Subjects were asked to complete all questionnaires by themselves in a private setting at baseline and at three months post initiation of the ACCP guidelines. Questionnaires were mailed to any subjects not returning in person for follow-up visits. Upon receipt of questionnaires, the investigator reviewed them for completeness. Attempts were made to reduce missing data by advising subjects who failed to complete an item that it was noticed that they had not completed an item and asking if they

would like the opportunity to do so or by calling the patient on the phone immediately upon receiving the questionnaire and doing the same.

Data collection specific to observation of intervention fidelity was randomly assigned and collected as outlined under the section titled Measures of Intervention Fidelity.

Data Management

Data were stored on a University of Massachusetts secure research drive. Each participant was assigned a unique research identification number. A log identifying patients by name and unique identification number as well as any paper and pencil questionnaires was kept in a separate locked cabinet in the investigator's office. Only the principal investigator had have access to the locked cabinet. Deidentified data were kept on a password protected drive at the University of Massachusetts Medical School that was backed up nightly. Data collected during observation of visits and that generated by medical record review were deidentified and stored under the research participants deidentified study code. Data were uploaded to IBM® SPSS® Statistics 21 for analysis.

Data Analyses

Data were evaluated for missing values. As the questionnaires were checked for missing data immediately upon completion and the investigator queried the subject as to whether they would like to complete the item. Descriptive statistics (frequencies, means, standard deviations, and percentages) were calculated for all study variables as appropriate to the level of data. For continuous variables, mean, median, skewness, standard error of the mean, standard deviation, and histograms were calculated. Frequencies were run on all categorical variables. All continuous variables were checked for normal distribution. Internal consistency reliability was evaluated using Cronbach'alpha for all multi-item scales.

Data collected using the sociodemographic survey was described using descriptive statistics and measures of central tendency to characterize the population. Physiologic factors were characterized by number of diagnoses, focusing on those related to cough, ability to speak being bothered by cough, and urge-to-cough. The situational factor of social support was described using results obtained from the FSSQ and the psychologic factors were described using data from the DASS-21. To further support validity for the CQLQ, Pearson Correlations were conducted to establish concurrent validity for the CQLQ and the SF12v2 using total scores of the CQLQ and the two primary SF12v2 scores. Test-retest reliability for the cough severity, ability to speak being bothered by cough, and urge to cough Punum Ladders was conducted using Pearson Correlations for 2 administrations of each of the Punum Ladders collected 24-48 hours apart. Data were coded for method of collection, in person or via postal mail. A flow chart was developed to track number of participants and their status.

For specific aim #1: describe the change in psychologic factors, symptoms of depression, anxiety, and stress from baseline to 3 months post standardized treatment for chronic cough the DASS-21 were collected at both time points. Descriptive statistics were used to compute the DASS total score and the DASS depression, anxiety, and stress subscale scores. Using Fisher's measure of skewness these scores were found to be significantly skewed at baseline (range 3.06 to 6.36). The non parametric statistical test, Related Samples Wilcoxon Signed Rank Test was computed to evaluate change between baseline and the 3 month post treatment for chronic cough data. To determine change in the situational factor of social support similar analyses were conducted for the FSSQ total score (skew range -2.21 to -2.56). To determine whether or not there were differences in psychologic factors related to medications used the non parametric Mann Whitney U was employed.

For the specific aim #2: determine the relationship between baseline cough severity and cough-specific quality-of-life with baseline urinary incontinence, financial strain, employment; self prescribed remedy use, gender, marital status and education various statistical tests were conducted. Due to skewed data, Spearman's Rho Correlations were conducted for the continuous variables of cough severity and cough-specific quality-of-life and urinary incontinence, cough duration, and age. Independent t-tests were used to determine the differences in the continuous variables cough severity and cough-specific quality-of-life and the categorical sociodemographic variables of financial strain (no financial strain or at least some financial strain), employment (employed or not employed), self prescribed remedy use (yes used or no not used), gender (male or female), marital status (married or not), and education (less than college or college or more).

For specific aim #3: describe the influence of physiologic factors (urge-to-cough, number of diagnoses, ability to speak without coughing), situational factors (social support) and psychologic factors (symptoms of depression, anxiety, and stress) on cough-specific quality-of-life and cough severity (global symptom measure of timing, intensity, distress, and quality) at baseline and at 3 months post standardized treatment various statistical tests were conducted. Due to skewed data unadjusted associations were assessed for using Spearman's Rho correlation for all variables first at baseline. Subsequently, Spearman's Rho correlations were conducted seeking relationships between baseline cough severity and cough-specific quality-of-life and 3 month post treatment scores for physiologic, situational and psychologic variables. Analysis of Variance (ANOVA) was then used to assess for unadjusted association for the categorical variables of self prescribed remedies, gender, employment, marital status, education, and financial strain and baseline cough severity and cough-specific quality-of-life. The assumptions of one-way ANOVA were met in that: the continuous dependent variables were normally

distributed; the groups were independent of each other. and homogeneity of variance was present (Munro, 2005).

Hypothesis #1. To evaluate the associated hypothesis, that treatment of chronic cough using the ACCP guidelines will result in improvement in cough severity with subsequently improvements in cough-specific quality-of-life various statistical tests were conducted. Sequential paired t-tests were used for normally distributed data and the non-parametric Related Wilcoxon Signed Rank test for skewed data.

Hypothesis #2. To evaluate whether physiologic factors (ability to speak without coughing, urge- to-cough and number of diagnoses), situational factors (social support), and psychologic factors (symptoms of depression, anxiety, and stress) predict cough severity (timing, intensity, distress, and quality) Spearman's Rho correlations were conducted,

Hypothesis #3. Cough severity (timing, intensity, distress and quality) predicts cough-specific quality-of-life, that collectively if improvements are found in cough severity and quality-of-life they will result in improvements in psychological factors, physical factors, and situational factors Spearman's Rho correlations were conducted.

For specific aim #4: describe a process of measuring intervention fidelity in the application of the ACCP guidelines using the Technology Model; a manual was developed to guide the interventionist and the monitoring process related to the intervention delivery. Existing scales were described earlier in this chapter and used in monitoring intervention delivery, receipt, and concordance of understanding by the clinician and participant receipt of the intervention. Descriptive statistics were used to describe the dose, adherence and competence of intervention delivery, participant receipt, and concordance of documented intervention delivery and participant receipt to the ACCP guideline-based intervention.

Human Subject Considerations

Approval was received from the Human Subjects Committee of the Institutional Review Board (IRB) at the University of Massachusetts Medical School prior to conducting this study (Docket # H: 00000732). Participants were identified for recruitment based upon obtaining a HIPAA IRB Waiver of Authorization. Research participants were told the purpose of the study and were advised that participation is voluntary and that responses will be kept confidential. Coercion was avoided by sending participants the consent in advance or explaining the study to them over the phone in advance, so that they had the chance to contemplate the study and to develop their response to the invitation to participate. Participants were also advised of their rights regarding withdrawal from the study at any time and that refusal to participate will not affect their care in any way. Each participant was asked to sign an IRB approved informed consent that fully explains study procedures as well as an "Authorization to Disclose Protected Health Information for Research Purposes" consent form (to allow for review of their medical record). A copy of the consent form complete with contact information for the PI was given to participants who were verbally advised to contact the investigator if problems related to the study arose.

No physical risks were expected. Some participants may have experienced some emotional distress at being asked to complete questionnaires describing their experiences. We anticipated that this risk would be minimal. Participants were advised that the questionnaire results will not be available real time and that after completion of the questionnaires the PI would ask if they have any serious concerns related to what they shared in the questionnaires, noting that the investigator was willing to help them decide if they or the investigator should contact their primary care physician.

There were no direct benefits for participants of this study. This study may help others in the future by helping to expand knowledge in the area of chronic cough in an effort to further research to help others.

Potential Difficulties

Potential difficulties were related to enrollment. Difficulties could have occurred if an inadequate number of participants were available. If enrollment was inadequate, the addition of another site could have been considered. While there were no problems with enrollment, it was quickly realized that there would be a problem with drop-outs, and an extra 10 subjects were added with IRB approval.

CHAPTER 4

Results

This chapter describes the results of this study that used the Theory of Unpleasant Symptoms (Lenz et al, 1997) to examine changes in psychologic factors, physiologic factors, and situational factors in adults after management of chronic cough using the standard treatments outlined in the 2006 ACCP Guidelines. This chapter also presents an analysis of intervention fidelity related to the application of the 2006 ACCP Cough Guidelines in this study population.

The sociodemographic variables associated with this study are described for the baseline period and 3 months post treatment. These data are followed by study results that are presented and categorized according to the study's 4 specific aims and the 3 associated hypotheses.

Sociodemographic Variables

During the recruitment period, February 7th 20013 through June 27th 2013, 111 consecutive patients seeking care for cough of greater than 8 weeks duration were offered the opportunity to participate in this study. Fifteen patients refused participation and therefore were not screened for study participation. Ninety-six subjects were screened with 16 not meeting inclusion criteria. Reasons for not meeting inclusion criteria included, medical conditions resulting in impaired cognition due to developmental disorders (n = 3); cough resolved prior to the scheduled Cough Clinic appointment (n = 2); pregnancy (n = 3); and non English speaking (n = 8). Of the initial 111 patients seeking care for chronic cough, 80 were enrolled as study subjects (see Figure 4). Seventy-eight (97.5%) of the 80 baseline questionnaires were collected in person with the other 2 being completed and returned via mail prior to the initial visit. At 3 months, 65 questionnaires were collected, 9 in person and 56 by mail.

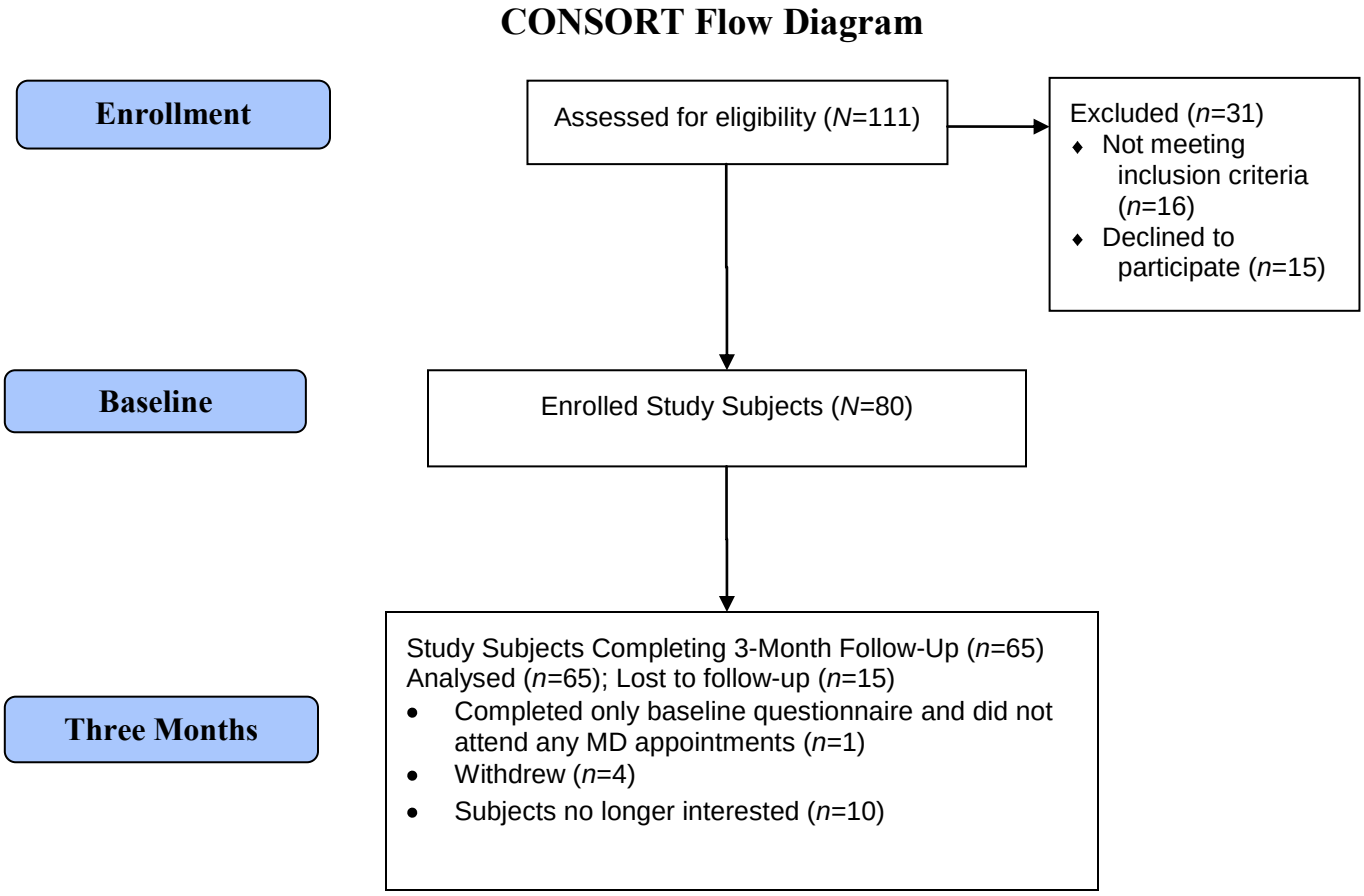

Figure 4. **Consort diagram summarizing the flow of study subjects from screening for eligibility through 3 months post initial treatment.**

Table 1 and Table 2 summarize the categorical and continuous sociodemographic data respectively for study subjects. Initially enrolled subjects (*N*=80) were predominately middle aged, mean age was 58.54 (*SD*=11.10) years; the majority were female (68.7%) and white (98.7%). Those enrolled were predominately non-smokers (97.5%) and most (75%) used self prescribed remedies for cough. More than half were married (66.2%), employed (63.7%) and had at least a college education (68.7%). The majority of subjects (73.7%) were financially stable reporting little to no financial strain.

Most subjects had a chronic cough for years with the mean cough duration being 85.99 (*SD*=123.67) months. Mean cough severity rated on a scale of 0-10 (zero no cough and 10 worst possible cough) was 6.11 (*SD*=2.22).

Table 1

Baseline Demographic Data for Categorical Variables for Those Initially Enrolled (N=80)

Variable	*n*	*(%)*
Female Gender	55	(68.7)
Male Gender	25	(31.3)
Smokers*	2	(2.5)
Marital status		
Single	8	(10.0)
Married	53	(66.2)
Widowed	6	(7.5)
Divorced	12	(15.0)
Significant other	1	(1.3)
Employed	51	(63.7)
Highest Level of Education		
Less than high school	1	(1.3)
High school	24	(30.0)
College	35	(43.7)
Graduate school	20	(25.0)
How Hard is it to Pay for Basics		
Don't know	1	(1.3)
Refused	3	(3.8)
Very hard	2	(2.5)
Somewhat hard	15	(18.7)
Not very hard at all	59	(73.7)
Race		
White	79	(98.7)
American Indian	1	(1.3)
Ethnicity		
Hispanic or Latino	4	(5.0)
Not Hispanic or Latino	76	(95.0)
Self Prescribed Remedy	60	(75)

Note. *n*=77 for smokers due to missing data for 3 subjects

Table 2

Baseline Demographic Data for Continuous Variables for Those Initially Enrolled (N=80)

Variable	*M*	*Mdn*	*(SD)*	*Range*
Age in years	58.54	61.0	(11.10)	24-79
Cough duration in months	85.99	24.0	(123.67)	2.5-600
Cough severity (0-10)	6.11	6.0	(2.22)	1-10*

Note. *Range possible of scores is 0-10 with no cough =0 and worst possible cough = 10. *M*= mean; *Mdn*= median; *SD*=standard deviation.

The baseline influencing factor clinical characteristics of the study subjects initially enrolled (*N*=80) are shown in Table 3. These data are categorized using the physiologic, psychologic, and situational influencing factors, as described by the Theory of Unpleasant Symptoms.

Table 3

Baseline Influencing Factor Clinical Characteristics (N=80)

Clinical Characteristic	*M*	*Mdn*	*(SD)*	*Range*
Physiologic Factors				
Urge-to-cough	5.91	6.00	2.40	1-10*
Ability to speak bothered	5.21	5.00	2.97	0-10*
Number of diagnoses (Presumptive)	2.28	2.00	0.81	1-5
Psychologic Factors				
DASS total score	26.65	22.00	21.33	0-106
DASS anxiety	8.60	6.00	8.13	0-40
DASS stress	11.45	10.00	9.01	0-38
DASS depression	6.60	4.00	7.06	0-28
Situational Factors				
FSSQ social support	33.42	34.00	6.00	16-40

Note. *Urge-to-cough and ability to speak (possible range 0-10; higher scores = worse symptoms); DASS = Depression, Anxiety, and Stress Scale 21 (subscale possible range 0-42; higher scores = worse symptoms); Duke-UNC Functional Social Support Questionnaire = FSSQ (possible range 8-40; lower scores = less support than they would like). *M*= mean; *Mdn*= median; *SD*=standard deviation.

Sixty five subjects completed the 3 month data collection. These 65 were similar in clinical and sociodemograpahic characteristics when compared to those initially enrolled (*N*=

80). Independent t-tests revealed that these 65 subjects did not significantly differ from the 15 who did not complete the 3 months data collection by baseline cough severity, urge-to-cough, or ability to speak being bothered by cough. Chi Square analyses demonstrated that these 2 groups did not significantly differ by use of self-prescribed remedies, gender, marital status, financial strain (how hard is it to pay for basics like food, housing, medical care, and heating), employment or education. Differences by race and ethnicity could not be evaluated due to the small number of racial and ethnic minorities in this sample.

Causes of Chronic Cough

Table 4 summarizes the frequency of number of cough-related diagnoses at the 3 month time period. Table 5 describes the frequency of the type of diagnoses present in this sample. Diagnoses were collected via electronic medical record review for 75 of 80 subjects (5 subjects withdrew prior to record review). The majority of subjects (75%) had 2 or 3 simultaneous diagnoses and the most frequent diagnoses were GERD, UACS, and asthma.

Table 4

Multiplicity of Cough-Related Diagnoses (N=80)

Number of Diagnoses	*Number*	*(%)*
One	12	(15.0)
Two	34	(42.5)
Three	26	(32.5)
Four	2	(2.5)
Five	1	(1.3)
Missing	5	(6.2)*

Note. *5 subjects of those initially enrolled (*N*=80) withdrew before the electronic medical record was reviewed.

Lung Nodules were not considered cough-related diagnoses but were revealed as part of the cough evaluation in 10 subjects (12.5%).

Table 5

Frequency of Presumptive Cough-Related Diagnoses Baseline (N=80)

Individual Presumptive Diagnosis	*n*	*(%)*
GERD	69	(86.3)
UACS	58	(72.5)
Asthma	22	(27.5)
Drug Induced	4	(5.0)
Bronchiectasis	3	(3.8)
Post Infectious	3	(3.8)
NAEB	2	(2.5)
COPD	2	(2.5)
Laryngeal Sensory Neuropathy	2	(2.5)
CHF	1	(1.3)
Bronchiolitis	1	(1.3)
Infiltrate	1	(1.3)
Supprative Airway Infection	1	(1.3)
Vocal Cord Dysfunction	1	(1.3)
Interstitial Lung Disease	1	(1.3)

Note. *Note.* UACS= upper airway cough syndrome; GERD = gastroesophageal reflux disease; NAEB= non-asthmatic esosinophilic bronchitis, COPD= chronic obstructive pulmonary disease; CHF= congestive heart failure.

Reliability and Validity of Measures

Seventeen subjects agreed to complete the test-retest component of the study. The 3 Punum Ladders were completed on 2 separate occasions within 48 hours. Test-retest reliability for the 3 Punum Ladders demonstrated significant correlations of .8 or more as shown in Table 6.

Table 6

24-48 Hour Test-Retest Reliability using Pearson Correlations for Punum Ladders (n=17)

	Cough Severity	Urge-to-Cough	Ability to Speak
Cough Severity	.801**		
Urge-to-Cough		.902**	
Ability to Speak			.892**

Note. **Significant at the 0.01 level (2 tailed).

Internal consistency reliability of all multi-item scales used in the study was assessed at both baseline and at 3 months post treatment for chronic cough (see Table 7). Data are reported

for total scale scores for the CQLQ, DASS, and FSSQ. Subscale scores are reported for the DASS Anxiety, Stress and Depression subscales and the SF12v2 Physical and Mental Component subscales for both time periods in Table 7. All scales were found to have good to excellent reliability (range = .77-.94) at both baseline and 3 months post treatment.

Table 7

Scale Reliability Analyses Baseline and 3 Months

Number of items /Scale	Cronbach's Alpha Baseline (*N*=80)	Cronbach's Alpha 3 Months (*n*=65)
28 Item CQLQ	0.92	0.94
21 Item DASS	0.92	0.92
7 item DASS Anxiety	0.79	0.77
7 item DASS Stress	0.86	0.88
7 item DASS Depression	0.85	0.88
6 Item SF12v2 Mental Component	0.82	0.85
6 Item SF12v2 Physical Component	0.85	0.88
8 Item FSSQ	0.89	0.91

Note: DASS = Depression, Anxiety, and Stress Scale. CQLQ= Cough Quality of Life Questionnaire. FSSQ = Duke-UNC Functional Social Support Questionnaire.

To establish concurrent validity for the CQLQ, the baseline CQLQ total score was correlated with the baseline SF12v2 Physical Component Summary and the Mental Component Summary scores. Using Fisher's Measure of Skewness the SF12v2 scores, the physical component summary was found to be significantly skewed ranging from -2.79 to -3.58. The non parametric Spearman's Rho Correlations demonstrated significant and moderate negative relationships between the CQLQ total score (lower scores indicate better quality-of-life) and both the Physical and Mental Component Summary scores of the SF12v2 (higher scores indicate better quality-of-life) (see Table 8).

Table 8

Spearman's Rho Correlations Between Baseline and 3 Month Cough-Specific Quality-of-Life and SF12v2 Physical Component Summary and Mental Health Component Summary

	Cough-Specific Quality-of-Life	
	Baseline	3 Months
Baseline SF12v2		
Physical Component Summary	-.482**	
Mental Health Component Summary	-.325**	
3 Months SF12v2		
Physical Component Summary		-.518**
Mental Health Component Summary		-.415**

Note. ** Significant at the 0.01 level (2-tailed)

Specific aim #1: DASS scores were evaluated to determine if there was a change in psychologic factors (symptoms of depression, anxiety, and stress) from baseline to 3 months post standardized treatment for chronic cough. Mean signed rank scores were significantly reduced, reflecting improvement in psychologic symptom scores, for the DASS total score (p = .000), depression (p= .005), anxiety (p= .000), and stress (p= .000) subscales. Baseline scores and 3 month post treatment scores for symptoms of depression, stress, and anxiety were on the lower end of the scale as reflected in Table 9. Mann-Whitney U demonstrated no significant difference in any of the psychologic symptom scores based on the use or non-use of bronchodilators, antihistamines, or decongestants at baseline or 3 months post treatment.

Table 9

Baseline and 3 Month Mean Scores for Psychologic Factors

	M(SD) Baseline (*N*=80) *Mdn*		*M(SD)* 3 Months (*n*=65) *Mdn*	
Psychologic Factors				
DASS total	26.65 (21.33)	22.00	18.46 (18.54)	12.00
DASS depression	6.60 (7.06)	4.00	4.77 (6.67)	2.00
DASS anxiety	8.60 (8.13)	6.00	5.72 (6.40)	2.00
DASS stress	11.45 (9.01)	9.01	7.97 (8.36)	6.00

Note: Lower scores reflect improvement for all scales. Total score range = 0-126; subscale range = 0-42. *M*(*SD*)= mean (standard deviation), *Mdn*=median.

The situational factor, represented by the FSSQ social support total score, was statistically assessed in the same manner as the psychologic factors as they too were found to be significantly skewed at baseline (-2.56). No significant change was identified between baseline and 3 months post treatment values for social support (p=.087).

Of the initial 80 subjects, 53 (66.3%) reported taking antidepressant medications and 6 (7.5%) reported taking an anxiolytic drug. Mann Whitney U Test revealed significant differences, with those taking antidepressants scoring higher than those who were not taking them, for the DASS total score (p=.008), anxiety subscale score (p=.007), and the depression subscale score (p=.024), but not for the stress subscale score. Three months post treatment, the same analyses revealed that for the 52 subject where these data were available 17 (32.56%) reported taking antidepressants. Of these, there were significant differences with those taking antidepressants scoring higher vs. those who were not for the DASS 3 month post treatment total score (p=.044) and stress subscale score (p=.031). No significant differences were found in any DASS scores for those taking anxiolytic medications vs. those not taking them at baseline (n=6) or at 3 months post treatment (n=5). Paired t-tests found that those taking antidepressants at baseline (M=68.73, SD=8.74) had significantly worse cough-specific quality-of-life scores compared to those not taking them (M=61.55, SD=15.26) (M=-7.18, SEM=.2.80, t(65.45) = -2.56, p=.013) and no significant difference in cough severity scores at baseline. At 3 months post treatment, paired t-tests demonstrated no significant difference in either cough severity or cough-specific quality-of-life for those taking vs. those not taking antidepressants. Additionally, using the Mann Whitney U Test, no significant difference was found at baseline in FSSQ social support scores for those taking vs. those not taking antidepressants.

Hypothesis #1. To evaluate the associated hypothesis, that treatment of chronic cough using the ACCP guidelines will result in improvement in cough severity and cough-specific quality-of-

life, paired t-tests conducted revealed significant improvement in cough severity 3 post months post treatment (*M*=2.32, (*SEM* =.291), *t*(64) =7.98, *p*=.000). Second, cough-specific quality-of-life, measured using the CQLQ, significantly improved (*M*=9.17, (*SEM*=1.30), *t*(64) =7.02, *p*=.000). See Table 10 for baseline and 3 month mean scores

Additionally, physiologic factors, represented by urge-to-cough and ability to speak being bothered by cough, measured using Punum Ladders, were assessed for change at 3 months. Scores were significantly improved for urge-to-cough (*M*=1.85, (*SEM*=0.29), *t*(64) =6.38, *p*=.000) and ability to speak being bothered by cough (*M*=2.15, (*SEM*=0.29), *t*(64) =7.38, *p*=.000) at 3 months.

Table 10

Paired T-test of Baseline and 3 Month Mean Scores for Symptom, Physiologic Factors and Cough-Specific Quality-of-Life

	M(*SD*) Baseline	*M*(*SD*) 3 Months	*p*
Symptom			
Cough severity	6.11 (2.20)	3.78 (2.73)	.000
Physiologic Factors			
Urge-to-cough	5.77 (2.45)	3.92 (2.75)	.000
Ability to speak	4.94 (2.99)	2.78 (2.59)	.000
Cough-specific quality-of-life			
CQLQ Total Score	63.68(13.97)	54.50(14.37)	.000

Note: Lower scores reflect improvement for all scales. CQLQ= Cough Quality of Life Questionnaire (range 28-112). Range for all physiologic factors and symptom 0-10. *M*(*SD*)= mean (standard deviation)

The Related Samples Wilcoxon Signed Rank Test mean signed rank scores, evaluating change from baseline to 3 months, for SF12v2 Physical Component and the Mental Component Summary scores were significantly increased. Table 11 contains the SF12v2 Physical and Mental Component Summary and individual Mental Component variable baseline and 3 month post treatment mean scores. This increase reflects improvement in quality-of-life for the

Physical Component Summary (p=.001). The minor increase in the Mental Health Component score was not significant (p=.209).

Table 11

Baseline and 3 Months Post Treatment SF12v2 Physical and Mental Health Component Summary Scores and Mental Health Variable Scores

	M(*SEM*) Baseline	*M*(*SEM*) 3 Months
SF12v2		
Physical Components Summary	45.80(1.11)	48.64(1.17)
Mental Components Summary	49.22(0.97)	49.72(1.07)
Accomplished less	4.16(0.11)	4.12(0.13)
Less careful	4.38(0.10)	4.40(0.11)
Peaceful	2.79(0.11)	2.72(0.11)*
Depressed/downhearted	4.28(0.09)	4.34(0.10)
Social time	4.06(0.11)	4.46(0.11)
Energy	3.09(0.11)	2.98(0.12)*

Note: * = reverse scored item where higher scores mean worse quality-of-life, for all others higher scores indicate better quality-of-life. *M*(*SEM*) =mean (standard error of the mean).

Specific aim #2: To determine the relationship between baseline cough severity, cough-specific quality-of-life, urinary incontinence, financial strain, employment, self prescribed medications, gender, marital status and education various statistical tests were conducted. Spearman's Rho correlations (see Table 12) found urinary incontinence to be weakly (r = .231) related to cough severity, while a strong correlation (r=.612) was found with urinary incontinence and cough-specific quality-of-life. Cough duration and age were not found to be related to cough severity or cough-specific quality-of-life.

To better understand the relationship of urinary incontinence to cough-specific quality-of-life an independent t-test was conducted. As expected, there was a significant difference by gender, with woman (M = 2.44, SD = 1.03) having worse urinary incontinence than males (M=1.40, SD =.707), (M= -1.04, SEM=.198, t(65.64) = -5.22, p=.000).

Table 12

Spearman's Rho Correlations for Baseline Cough Severity and Selected Continuous Baseline Variables (N=80)

	Baseline	
	Cough-Specific Quality-of-Life	Cough Severity
Urinary Incontinence	.612**	.231*
Cough Duration	.122	.048
Age	.012	.124

Note. *Significant at the 0.05 level (2-tailed). ** Significant at the 0.01 level (2-tailed).

No significant difference in cough severity scores was detected by gender (p=0.17), marital status (p=0.53), highest level of education achieved (p=0.12), use of self prescribed remedies (p = .06), or employment status (p = .36). However, subjects who experienced some financial strain (M = 6.95, SD = 1.85) had significantly higher cough severity scores compared with those who had no financial strain (M = 5.81, SD =2.27), (M=1.14 SEM=.553, t(78) = 2.06, p = .043).

Additionally, there was no significant difference in cough-specific quality-of-life scores by marital status (p=.50), highest level of education achieved (p= .10), and employment (p=.85). Again, those subjects who experienced some financial strain had worse scores (M = 69.05, SD =9.95) compared to those who had no financial strain (M = 62.03, SD =14.60), t(78) =2.035, p=.045). Moreover, females were found to have worse cough-specific quality-of-life scores (M = 67.27, SD =12.61) than males (M = 56.40, SD =13.68), t(78) =-3.48, p=.001). Also, those who used self prescribed remedies also has worse cough-specific quality-of-life scores (M = 66.90, SD =13.35) than those who did not use them (M = 54.80, SD =11.21), t(78) =-3.64, p=.000).

Specific aim #3: To determine the influence of physiologic factors (ability to speak without coughing, urge- to-cough and number of diagnoses), situational factors (social support), and psychologic factors (symptoms of depression, anxiety, and stress) on cough-specific quality-

of-life and cough severity (global symptom/cough measure of timing, intensity, distress, and quality) at baseline and at 3 months post standardized treatment various statistical tests were conducted.

These statistical analyses also addressed **hypothesis # 2**, that the physiologic factors (ability to speak without coughing, urge- to-cough and number of diagnoses), situational factors (social support), and psychologic factors (symptoms of depression, anxiety, and stress) predict cough severity (timing, intensity, distress, and quality); and **hypothesis #3** that cough severity (timing, intensity, distress and quality) predicts cough-specific quality-of-life, that collectively if improvements are found in cough severity and cough-specific quality-of-life they will result in improvements in psychological factors, physical factors, and situational factors.

Table 13 demonstrates that the baseline and 3 month post treatment scores for the physiologic and psychologic factors were significantly related to baseline cough-specific quality-of-life and baseline cough severity. However, the situational factor of social support was not related to either variable at baseline or at 3 months post treatment. Additionally, not shown in this table, the symptom of baseline cough severity was found to be significantly related to cough-specific quality-of-life at baseline (r=.450, p=.01). Also, not shown in this table, baseline urge-to-cough was found to be significantly related to all psychologic factors (r= 315 to .405; p >=.01) as was ability to speak being bothered by cough (r= 259; p =.05 to 398; p =.01). At 3 months post treatment, the physiologic factor of number of diagnoses was not found to be related to cough severity or cough-specific quality-of-life.

Table 13

Spearman's Rho Correlations Between Baseline and 3 Month Post Treatment Physiologic, Situational and Psychologic Factors and Baseline Cough-Specific Quality-of-Life and Cough Severity

	Cough-Specific Quality-of-Life	Cough Severity
Baseline Physiologic		
Urge-to-cough	.360**	.643**
Ability to speak	.469**	.674**
# of diagnoses		
Baseline Situational		
FSSQ social support	-.126	-.085
Baseline Psychologic		
DASS total	.572**	.414**
DASS anxiety	.507**	.419**
DASS stress	.484**	.323**
DASS depression	.512**	.356**
3 Month Physiologic Factors		
Urge-to-cough	.291*	.501**
Ability to speak	.261*	.524**
# of Diagnoses	.136	.036
3 Month Situational Factors		
FSSQ total score	-.106	-.162
3 Month Psychologic Factors		
DASS total	**.**435**	.487**
DASS anxiety	.356**	.486**
DASS stress	.431**	.414**
DASS depression	.377**	.413**

Note. *Significant at the 0.05 level (2-tailed). ** Significant at the 0.01 level (2-tailed).

Additionally, using ANOVA to compare the effect of the unadjusted associations between the continuous dependent variable cough severity and the independent categorical variables of self prescribed therapy, gender, employment marital status, and education (see Table 14) no significant associations were found. When adjusting for financial strain, a significant association was found (p = .043), with those experiencing financial strain having higher or worse cough severity scores than those who are not experiencing financial strain.

Table 14

ANOVA Comparing Effects of Independent Sociodemographic Categorical Variables (N=80) on Cough Severity at Baseline

	Cough Severity	
	M (*SEM*)	*p*
Self Prescribed Therapy	-1.083 (.564)	.058
Gender	-.745 (.533)	.166
Employment	.473 (.517)	.364
Marital Status	-.333 (.527)	.529
Education	.825 (.531)	.124
Financial Strain	1.139 (.553)	.043*

Note. *Significant at the 0.05 level. Subjects were 97.8% white therefore associations were not assessed for race or ethnicity. *M*(*SEM*) =mean (standard error of the mean).

Similar analyses were conducted for the continuous dependent variable cough-specific quality-of-life. Results suggested that women, those experiencing financial strain and subjects taking self-prescribed therapy had worse cough-specific quality-of-life (see Table 15).

Table 15

ANOVA Comparing Effects of Independent Sociodemographic Categorical Variables on Cough-Specific Quality-of-Life (N=80) at Baseline

	Cough-Specific Quality-of-Life	
	M (*SEM*)	*p*
Self Prescribed Therapy	-12.100 (3.322)	.000*
Gender	-10.873 (3.123)	.001*
Employment	-.615 (3.236)	.850
Marital Status	-2.201(3.281)	.504
Education	5.476(3.299)	.101
Financial Strain	7.014(3.446)	.045*

Note. *Significant at the 0.05 level. Subjects were 97.8% white, therefore associations were not assessed for race or ethnicity. *M*(*SEM*) =mean (standard error of the mean).

Specific aim #4: A process for measuring intervention fidelity in the application of the ACCP guidelines for treating cough using the Technology Model was described in Chapter 3. Intervention fidelity was measured using (a) direct observations of care delivery of 15% of encounters using an observer checklist with, (b) completion of an intervention receipt form by all

subjects, and (3) review of the electronic medical record for concordance of subject and physician agreement of diagnoses and care. The visits for direct observation were selected by random assignment using a random numbers list generated by SPSS 21. Of the 12 planned observations only 11 were completed as 1 follow-up subject did not return for care. This 11 included the replacement of an additional subject who did not return for care by selecting the next random number. The observations included 6 initial evaluations and 5 follow-up visits.

Table 16 provides the checklist that the PI observer used to rate intervention fidelity during the observed visits. The level of intervention fidelity to the study plan was observed during all observed visits was very high with regards to the application of the core diagnostic and management elements of the 2006 ACCP guidelines. Using a 7 item checklist subject-physician fidelity to the implementation of the guidelines was very high with a mean score of 20.9 (*SD*=.09), with the possible range being 0-14 and 14 representing the highest fidelity.

Table 16

Direct Observation of Intervention Fidelity Monitoring 7 item Observation Checklist (n=11)

Variable	0 *n (%)*	1 *n (%)*	2 *n (%)*	3 *n (%)*
1. Was treatment prescribed according to the guideline?				11 (100)
2. Did the physician probe for patient understanding?			1(9.1)	10 (90.9)
3. Did the physician probe for patient response (including cough severity at baseline) and compliance?				11 (100)
4. Did the physician maintain treatment if indicated?				11 (100)
5. Did the physician step-up treatment if indicated?				11 (100)
6. Did the physician order further testing if indicated?				11 (100)
7. Was follow up arranged?				11 (100)

Note. IF= Intervention fidelity. 0=none; 1=low level of IF (addressed 2 or less); 2= moderate level of IF addressed 3; 3 high level of IF addressed all 4. Range 0-21 (21= highest fidelity).

Results related to the electronic medical record review revealed that the cough severity rating was only documented for 22 (27.5%) of 80 initial subjects (see Table 17). Moreover, Table 17 demonstrates that only 43 (53.8%) of the initial 80 subjects had a follow-up visit booked within 4-6 weeks.

Table 17

Dose: Visits booked (N=80)

Variable	First Visit *n (%)*	Second Visit *n (%)*
No visit booked	2 (2.5)	7 (8.8)
4-6 weeks	43 (53.8)	18 (22.5)
2-3 months	22 (27.5)	16 (20.0)
4-6 months	7 (8.8)	10 (12.5)
More than 6 months		2 (2.5)
Booked 3 months moved to 4 weeks	1 (1.3)	
Did not return	5 (6.3)*	24 (30.0)*
No visit booked, called for sick visit	2 (2.5)	
Cough resolved, follow-up not needed	1 (1.3)	

Note. *unable to do electronic medical record review on 5 subjects included as they withdrew from the study

Completion of an Intervention Receipt Form by the Subject

Subject receipt of the interventions prescribed by the cough specialist for chronic cough was measured using the Intervention Fidelity Monitoring Questionnaire for Subject Receipt Evaluation described in Chapter 3. This form was adapted from a form previously developed for use in a pediatric intervention study (Bova & Sullivan-Bolyai). Internal consistency reliability was excellent with a Cronbach's alpha of 0.84 for the 7-item checklist. The 7-item self report checklist that was part of this questionnaire resulted in subjects rating fidelity to the application of the guidelines as high with a mean score of 10.6 (*SD*=3.45) out of a possible 0-14 with 14 being equivalent to the highest fidelity.

Data were collected 3 months post initiation of the cough specialists' prescribed treatment (see Table 18). Of those completing the 3 month data collection (*n*=65), the majority

of subjects were advised about the reason, response, side effects and length of treatment and the need for follow-up. However, fewer than half of the subjects were told about additional treatments if cough remained a problem or the possible need for further testing.

At the time of the 3 month data collection only 24 (30%) of the 65 responding subjects reported closely following their cough specialists' instructions all of the time. Of these 65 subjects 35 (43.8%) reported following their cough specialists' instructions most of the time and 6 (7.5%) reported only following instruction some of the time.

An additional question asked what treatment recommendations were not followed and why? Thirty four (52.3%) of the 65 study subjects offered a comment regarding a recommendation not followed and why it was not followed. Analysis of this open-ended question revealed that subjects who do not closely follow the cough specialists' instructions have a variety of problems associated with prescribed treatments and many have more than one issue with treatment. These problems with prescribed treatments include cost, side effects, feeling the treatment was not useful, and ability to incorporate treatment into one's lifestyle.

Table 18

Intervention Fidelity Monitoring 7 item Questionnaire for Participant Receipt Evaluation at 3 Months Post Treatment for Chronic Cough (n=65)

Variable	0 *n (%)*	1 *n (%)*	2 *n (%)*
1. Advised you of the reason for prescribing treatment to manage chronic cough		7(10.8)	58 (89.2)
2. Ask about your response to treatment	10 (15.4)	10 (15.4)	45 (69.2)
3. Ask about side effects of treatment	9 (13.8)	13 (20.0)	43 (66.2)
4. Talk about the length of time you would need to continue to use the treatment.	10 (15.4)	15 (23.1)	40 (61.5)
5. Talk about the need for additional treatment if cough is still a problem	13(20.0)	23 (35.4)	29 (44.6)
6. Talk about the need for further testing if cough is still a problem	19(29.2)	17 (26.2)	29 (44.6)
7. Was follow up arranged?	1 (1.5)	9 (13.9)	55 (84.6)

Note. 0=not covered did not give any information; 1=covered somewhat would have liked more information; 2=covered completely; given all the information needed. Range 0-14 (14=highest fidelity).

Electronic Medical Record Review and Establishing Subject and Cough Specialist Concordance

Subjects' responses on the intervention receipt questionnaire, that included checking off or writing in diagnoses made and treatments recommended, were compared to data documented in the electronic medical record and rated for concordance of understanding by the PI. The focus of the concordance rating was on the subject and cough specialist both documenting the same or similar diagnoses and treatments. Investigator rating of subject-physician concordance of understanding of the implementation of the guidelines was found to be high with 83.1% in complete or almost complete agreement (see Table 19).

Table 19

Concordance with of Participant Receipt and EMR Documented Intervention Delivery Based on Chart Review at 3 Months Post Treatment for Chronic Cough (n=65)

Variable	0	1	2	3
	n (%)	*n (%)*	*n (%)*	*n (%)*
Concordance	1 (1.5)	10 (15.4)	24 (36.9)	30(46.2)

Note. 0= No agreement; 1= somewhat agree; 2= almost complete agreement; 3 complete agreement.

CHAPTER 5

Discussion

This chapter discusses changes in psychologic factors at 3 months post treatment with the ACCP cough management guidelines; the relationships between baseline cough severity and cough-specific quality-of life and demographic factors; and the influence of physiologic, psychologic, and situational factors on cough severity and cough-specific quality-of-life at baseline and 3 months post treatment. Additionally, this chapter provides empiric support for the Theory of Unpleasant Symptoms and the measurement of intervention fidelity in the application of the ACCP guidelines. Chapter 5 concludes with study limitations, conclusions, implications for research and practice.

The need to employ the use of valid outcome measures when assessing the impact of treatments for chronic cough is noted by the ACCP guidelines (Irwin, 2006a). The Punum Ladders used in this study, were supported as both a reliable and valid outcome tools based upon strong test-retest correlations and the fact that cough severity, urge-to-cough, and ability to speak being bother by cough improved as post treatment cough severity and cough quality of life simultaneously improved. Concurrent and construct validity for the CQLQ were demonstrated as cough severity was significantly related to cough-specific quality-of-life and as cough severity improved, improvements were also found in cough-specific quality-of-life. The CQLQ was further supported as a valid measure of quality-of-life, in that concurrent validity was demonstrated with the total CQLQ score being significantly related to the SF12v2 mental and physical scales. Moreover, the post treatment scores of the CQLQ and SF12v2 physical scores simultaneously significantly improved, also supporting the validity of the CQLQ as a valid measure of quality-of-life.

Change in Psychologic Factors at 3 Months Post Treatment

In this study, whose primary purpose was to describe changes in the symptoms of depression, anxiety, and stress in adults with chronic cough after treatment using the ACCP guidelines, the population was composed of predominately white middle aged non-smoking adults presenting to a cough specialty clinic with a long standing severe cough. In this population, all psychologic symptom scores were significantly reduced and within the normal range, based upon established norms, at 3 months post treatment with the guidelines. Baseline depression and stress symptom scores in this group were found to be within the normal severity range, based upon a normative sample of 1044 males and 1870 females that were 17-69 years of age (S. H. Lovibond & P. F. Lovibond, 1995). Based on the same normative sample, the baseline anxiety symptom scores were found to be within the mild severity range (S. H. Lovibond & P. F. Lovibond, 1995). Despite being within or close to the normal range this study demonstrated that, in those with chronic cough, all of these symptoms could be further reduced with treatment of the chronic cough using the ACCP guidelines.

Relationships with Demographic Factors

While not proposed by this study as situational factors, the Theory of Unpleasant Symptoms does propose demographic factors, such as financial strain and gender, as situational factors that can influence the symptom experience (A. Gift, 2009). In this study, cough severity was found to be more severe in those who had financial strain compared to those who did not have financial strain. In contrast, the negative effects of chronic cough on cough-specific quality-of-life were found to be significantly greater in those with financial strain, of female gender, and in those who used self-prescribed remedies. The difference in the findings of female gender likely relate to the problem with urinary incontinence and while a physical problem, this

may have a negative impact on psychologic factors (C. T. French et al., 2004). In the population studied, 75% of subjects noted at baseline that they used a self prescribed remedy. It is possible that the use of self prescribed remedies is the result of poor cough-specific quality-of life. This finding would be consistent with the feedback mechanism described by the Theory of Unpleasant Symptoms, in that an alteration of a situational factor may result from the consequences of a symptom on quality-of-life (A. Gift, 2009; Lenz & Pugh, 2008; Lenz et al., 1997).

Influence of Physiologic, Psychologic and Situational Influencing Factors

This study lends empiric support to the Theory of Unpleasant symptoms in that these psychologic factors were significantly related to the symptom of chronic cough and cough-specific quality-of-life, and they improved as these two outcome variables improved (Lenz et al., 1997). Similar findings were noted with the physiologic factors. Both urge-to-cough and ability to speak being bothered by cough were also found to be significantly related to cough severity and cough-specific quality-of-life and again both improved as the outcome variables improved. At the same time the physiologic factor of number of diagnoses and the situational factor of social support were not found to be related to either cough severity or cough-specific quality-of-life. While social support was measured in this study, no social support interventions were offered. Higher levels of social support have been identified by others as being related to better physical and emotional health (Broadhead et al., 1983; Powers et al., 2004). During the development of the CQLQ subject interviews revealed that family and friends could often not tolerate the cough any more (C. L. French et al., 1998; C. T. French et al., 2002). This finding indicates that it is possible that social support is not offered as willingly by friends and family and the need for social support may be an issue for those with chronic cough. Additionally, with

the median duration of the chronic cough being 24 months and the post treatment timeframe for measuring follow-up social support being 3 months, this may be too short a timeframe for any change in social support related to improved chronic cough to be realized. Also, there could be a ceiling affect with the tool used to measure social support as initial scores were high. Finally, the population in this study was primarily well educated, white, employed individuals with no reported financial strain and consulting in a highly specialized cough clinic may not be representative of the general chronic cough population as it pertains to this issue.

Number of diagnoses was included as a physiologic factor in this study as it was assumed that the more diagnoses a patient had the more complex the symptom experience would be. No relationship was found with number of diagnoses and cough severity or cough-specific quality-of-life. In this study, as demonstrated in other studies (Irwin, Corrao, & Pratter, 1981; Ribeiro, De Castro Pereira, Nery, Beppu, & Silva, 2006), the use of the ACCP guidelines was associated with improvement in cough supporting the accuracy of the diagnoses. The most common diagnoses identified were gastroesophageal reflux disease, upper airway cough syndrome, and asthma, as is consistent with the findings of others (Pratter, 2006b; Ribeiro et al., 2006). Also, consistent with the findings of others, more than one condition was often simultaneously identified as causing cough (Pratter, 2006b). Others have reported anger in patients with chronic cough and distress related to frequent physician visits (Kuzniar et al., 2007), suggesting that outlining the extended plan for care necessary to address the multiple causes early on may be important. Because, it seems intuitive that the more diagnoses, the more complex the treatment and the more difficult it would be to comply with a complex treatment plan, this area is worthy of further study.

Empiric Support for the Theory of Unpleasant Symptoms

This study provides empiric support for the Theory of Unpleasant Symptoms in that, core symptoms reflective of the psychologic factors of depression, anxiety, and stress were found to be related to cough severity. Cough severity was found to be related to cough-specific quality-of-life. Both of these variables improved in association with the use of the ACCP guidelines for management of cough as did the symptoms of depression, anxiety, and stress (psychologic factors), suggesting the presence of the feedback mechanism proposed by the theory. Moreover, the consequences of cough severity, as reflected by the items of the CQLQ (the theory surrogate for performance), help us understand why symptoms of depression, anxiety, and stress may co-exist with chronic cough and why they improve as cough improves. The CQLQ individual items reveal that those with chronic cough often suffer from many chronic cough induced problematic effects on their quality of life. These problems include embarrassment, feeling self-conscious, the need to avoid social activities, feeling upset that people feel something is wrong with them, the fear of tuberculosis or cancer, the need for reassurance that nothing is seriously wrong, feeling family can't tolerate it anymore and other issues. Intuitively as chronic cough resolves, and as suggested by this study, its negative impact on cough-specific quality-of-life, the individual problems described by the CQLQ, and any associated psychologic distress would be ameliorated. These findings support the feedback mechanism suggested by the theory (Lenz & Pugh, 2008).

Findings of this study also support the theory's assumption that the presence of more than one symptom can result in the symptoms catalyzing each other resulting in a multiplicative effect on the consequences of the symptom experience expressed as quality-of-life (Lenz & Pugh, 2008; Lenz et al., 1997). This is demonstrated in that baseline cough severity was not found to differ significantly by gender, yet cough-specific quality-of-life did differ by gender with

females having worse scores. The population studied had more females than males as is common in studies of those with chronic cough (C. T. French et al., 2004; Kelsall et al., 2009) and urinary incontinence was found to be a significantly greater problem for females, as has been found in past studies (C. T. French et al., 2004). Urinary incontinence was found to have weak but significant and positive relationship with cough severity. In contrast, with regards to cough-specific quality-of-life, urinary incontinence was found to have a moderately positive and strong significant relationship. This finding would support the assumption of the theory in that urinary incontinence may be less a physiologic factor influencing the symptom experience, and more an additional symptom that adds to the impact of the symptom of chronic cough on cough-specific quality-of-life (Lenz & Pugh, 2008; Lenz et al., 1997).

Additionally, those taking antidepressants had worse total psychologic factor and depression and anxiety symptom scores. Simultaneously, cough-specific quality-of-life was worse in those taking antidepressants at baseline but not cough severity; yet, 3 months post treatment for cough, there was no difference in either variable. This suggests that psychologic factors are likely influenced by the consequences of the impact of cough on cough-specific quality-of-life and that when cough improves so do the psychologic symptoms. This finding supports the assumption that the outcome of the symptom experience, as reflected by cough-specific quality-of-life, likely feeds back to the psychologic factors. It also suggests that the psychological symptoms of our subjects when initially seen would have been worse had they not been on antidepressants and anxiolytics.

Intervention Fidelity to the Study Plan

We are not aware of any prior study addressing the issue of intervention fidelity as it relates to the diagnosis and management of chronic cough using established guidelines.

Measuring intervention fidelity is important to establish the validity of an interventions effect (Bellg et al., 2004; Santacroce et al., 2004). Fidelity to the treatment protocols is important as the diagnosis of a cause of chronic cough is dependent upon response to specific treatment and because the cough guidelines advise that the diagnosis of unexplained chronic cough only be used after failure of guideline protocols (Pratter, 2006c). While the observed physician evaluation and management visits were associated with very high fidelity, intervention fidelity could have been better. Two of the original planned 12 visits did not occur. Both of these subjects were scheduled for their first follow-up outside of the 4-6 week timeframe recommended and did not return. While there was very high fidelity in the observed visits, electronic medical record review revealed less than a quarter of the subjects had baseline cough severity rating documented as outlined in the intervention fidelity manual. Additionally, the manual noted a plan for 4-6 week follow-up visits, yet record review revealed only just over half of the subjects had a 4-6 week follow-up booked. Investigator ratings of concordance of subject-physician understanding resulted in almost 50% being in complete agreement. More than 50% of subjects noted that the physician asking about response to treatment, side effects and follow-up had been completely covered. Yet, less than 50% of subjects noted that the need for further treatment or testing if cough remains a problem had been completely addressed.

Despite the high rates of fidelity and concordance reported in this study, at the 3 month data collection only (30%) of the subjects noted that they were closely following their physicians instructions. More than half of the subjects offered a reason they were not following the physicians recommendations including: side effects, cost, feeling the treatment was not useful, and difficulty incorporating treatment into one's lifestyle 3 months post initiation of treatment. While reports of problematic side effects or other issues resulting secondary to treatment for chronic cough are sparse in the literature pertaining to the use of cough guidelines, our finding of

lack of adherence with prescribed treatment is consistent with that of Al–Mobeireek and associates (2002). These investigators found that 23% of those with chronic persistent cough (*N*=100) stopped therapy during treatment. The reasons for stopping therapy were not elaborated upon in this study, yet it was noted that cough only resolved after resuming therapy (Al-Mobeireek et al., 2002).

Limitations

Potential limitations of this study included the use of a non random sample drawn from one highly specialized cough clinic. Because this cough specialty clinic attracts patients who have seen multiple other providers/specialists, the subjects may have reflected a different population of those with chronic cough than those seeing a specialist for the first time. Moreover, because 16 patients were not willing to enroll, this could have biased the findings so that the results are less likely to be generalized to the population of those with chronic cough at large.

Of the initial 111 patients presenting to the Cough Clinic, 8 were excluded due to being unable to either speak or read English. Of those unable to either speak or read English first languages included Spanish (*n*=5), Portuguese (*n*=1), Chinese (*n*=1), and Albanian (*n*=1). As is consistent with other studies of those with chronic cough the population in this study was predominately female (C. T. French et al., 2004). Therefore the findings are limited in that they can only be generalized to the population studied and that is those who are English speaking, primarily white, middle aged, and predominately female.

With regards to the monitoring of intervention fidelity it was recognized that by sitting in on visits the Hawthorne effect could have been induced adding a bias to this study. While subject-physician concordance was measured by chart review, fidelity to the study plan

(guidelines) was not measured in this manner. Additionally, the measurement of subject-physician concordance was subjective and completed by a single investigator. Electronic medical record review is a potential bias in that the information was not always in the same electronic location and it is dependent upon the information being accurately documented in the record.

Implications for Research

This study has several important implications for future research. Financial strain, gender, and use of self prescribed remedies may have a role as situational factors that can influence cough-specific quality-of-life and are worthy of further study. While social support was not found to be related to cough severity or cough-specific quality of life, this study did not provide any intervention that would specifically attempt to augment social support. Moreover, the timeframe for this study may have been too short to see change, the tool used to measure social support may be subject to a ceiling effect, and/ or the population studied may not be representative of all those with chronic cough. Because social support has known positive effects on physical and psychological health further study is warranted. We also suggest that studies should include non-English speaking patients in their samples.

Our findings suggest that the Theory of Unpleasant Symptoms may be useful in the study of chronic cough as it helps us to understand the complex relationships of factors that may influence cough severity and cough-specific quality-of-life. Furthermore, these findings help us understand the complexity of the management of chronic cough. The findings noted in this manuscript stress the importance of measuring both cough severity and cough-specific quality-of-life when trying to define the impact of the problem and the response to treatment. Future research should further stratify the data based on varying levels of cough severity and or cough-

specific quality-of-life to assess for the presence of subpopulations where psychologic factors may play a greater influencing role. Additionally, longitudinal studies should be conducted to see if the findings of this study are sustained over time.

This study highlights the importance of addressing intervention fidelity in research related to the management of chronic cough. Fidelity to guideline core elements by the subject and physician is important and it should be measured because it augments the validity of the results of the diagnostic workup and the outcome of specific treatment that will be prescribed. While observed visit intervention fidelity was very high, chart review demonstrated lack of fidelity in the area of documenting initial cough severity to provide a basis for future reference when trying to determine response to treatment and in scheduling a 4-6 week follow-up visit. Lack of fidelity in these 2 areas could be reflective of an overall lack of fidelity to the study plan that was not apparent during observed visits. Future research may benefit from other methods of measuring intervention fidelity such as post visit patient or physician interviews. While this study measured use of self prescribed remedies at baseline only, the fact that 75% were using self-prescribed remedies suggests the need to ask about these proscribed interventions at more than one time point for future studies. Because, fidelity to the intervention is essential to valid conclusions about treatment outcomes, future studies of management strategies for chronic cough should include strategies to monitor and enhance intervention fidelity.

This is the first study, that we are aware of, that used the DASS 21 to quantify psychologic symptoms in adult subjects with chronic cough. When compared to an earlier pre and post intervention study that used a different scale for measuring psychological symptoms and that found different results (Dicpinigaitis et al., 2006), this study did not find the presence of more serious levels of psychologic symptoms in those with chronic cough. The results of this earlier study that sought to establish the prevalence of depressive symptoms in those with

chronic cough using the Center for Epidemiologic Studies Depression Scale (CES-D), suggested that the patients with chronic cough had significant depressive symptomatology. None of the subjects in this group were reported to be taking antidepressants or as having a history of a diagnosis of depression (Dicpinigaitis et al., 2006). However, the results of this study are difficult to interpret for the following reasons: the CES-D identifies a score of $\geq$ 16 as the cut point signifying risk for depression and in this study while the mean was 18.6 (*SD*=13.4), the median was 16 and it was noted that the data were skewed making the median more reflective of the population studied (Dicpinigaitis et al., 2006). Moreover, this study did not use a survey instrument that was designed to assess anxiety. The DASS was chosen for our study as it was designed to define separate core symptoms of depression, anxiety, and stress that would allow for differentiation between the conditions (S. H. Lovibond & P. F. Lovibond, 1995). Because, anxiety and depression share a component of general affective distress and have a potential overlap in symptomatology, it is possible that the CES-D scores reflected some component of anxiety. In this study, as cough improved the CES-D scores also improved with the mean and median falling into the normal range (Dicpinigaitis et al., 2006). Similarly, after treatment, in our study, all psychologic symptoms were lower. Because some of our patients were taking antidepressants and anxiolytics, their use in those with chronic cough should be further explored.

In a study that used the Hospital Anxiety and Depression Scale to assess the prevalence of psychomorbidity in those with chronic cough, the findings were similar to ours, in that the mean scores (*N*=57) for both anxiety and depression were found to be in the normal range (McGarvey et al., 2006). Similarly, our findings are similar to those found in chronic cough subjects unresponsive to medical management by Vertigan and Gibson (2011) where anxiety and depression symptom scores, measured using the Hospital Anxiety and Depression Scale, were also found to be within the range of normal. In our study the DASS scores for anxiety fell within

the mild category indicating to us that the DASS may indeed be strongly discriminative in its ability to assess symptoms of anxiety and depression. Because depression and anxiety commonly co-occur in patients seeking care in the primary care setting (Hirschfeld, 2001), it is important to differentiate between the two conditions.

Implications for Practice

This study has identified a number of issues related to clinical practice. Depression, anxiety, and stress symptoms should be considered when counseling patients. For example, it may be important to share the meaning of a negative chest x-ray as it relates to ruling out more serious causes of chronic cough. Because those using self prescribed remedies, females, and those with financial strain have worse cough-specific quality-of-life, and because patients may be hesitant about sharing this information, we recommended that physicians incorporate a plan for asking about these issues as part of routine care of those with chronic cough.

Qualitative review found that patients have problems following recommended treatment plans secondary to issues such as side effects, cost, not feeling the treatment is useful, and problems incorporating treatment into their lifestyle. These findings suggest that scheduling a 4-6 week follow-up visit is likely to be important, as it would allow for treatment plan adjustments in an effort to improve treatment adherence and successful management of chronic cough. Also, the need for an extended treatment plan based upon the potential for multiple causes of chronic cough should be shared with patients at the onset of care. Patients should be advised that the problem of chronic cough is complex and that we do have a systematic way of working through the issues with them but it will take time and multiple visits.

Conclusions

In conclusion, this study found that use of the ACCP guidelines for the management of chronic cough resulted in improved psychologic symptoms as cough severity and cough-specific quality-of-life. Symptoms of depression, anxiety, and stress were of normal or near normal severity at baseline; yet, all of these psychologic factors were found to improve as cough severity and cough-specific quality-of-life improved. The Theory of Unpleasant Symptoms has been useful in understanding these complex relationships of factors that influence chronic cough and these relationships should be further delineated in future studies. There are multiple areas when fidelity to guideline core element implementation may be problematic for both patients and physicians. Intervention fidelity to guideline core elements, by the subject and physician is important and it should be measured as an independent study variable, as a valid diagnosis of a cause of chronic cough is dependent upon response to specific treatment.

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Appendix A

Sociodemographic Questionnaire Baseline

Date_____ Collected in person, online, via postal mail (please circle one)
Study number
How would you prefer to be contacted for reminders and follow-up data collection (please circle and complete those that apply to you) • **Phone (please provide preferred number):** • **Email (please provide preferred email address):** • **Postal mail (please provide preferred address) :** • **Please indicate the day(s) of the week that might work best for you to be contacted by circling one or more Monday, Tuesday, Wednesday, Thursday, Friday, Saturday, Sunday** • **Please indicate the time of day that might work best for you to be contacted AM or PM (please circle one)**
How many months have you been coughing (enter number of months)?
Age (in years)
Do you use over the counter or self prescribed or home remedies to treat your cough (circle one)? **Yes / No** **If yes please list type** **Over the counter self prescribed cough medicine** **Honey** **Zinc** **Echinacea** **Mucinex** (Guaifenesin) **Robitussin** **Cough drops** **Herbal Supplements** **Neti Pot** **Other please list**
Gender (circle one) • Male / Female
Race (circle one) • White / American Indian and Alaska Native / Asian / Black or African American / Native Hawaiian / Other Pacific Islander
Ethnicity (circle one) • Hispanic or Latino / Not Hispanic or Latino
Marital status (circle one) • Single / Married / Widowed / Divorced

Currently Employed (circle one)
Yes / No
For those answering yes please check off type of employment
Clerical
Administrative
Management
Public Service
Teacher
Lawyer
Other

Highest level of education completed (circle one)

- Less than high school
- High School
- College
- Graduate School

How hard is it for you to pay for the very basics like food, housing, medical care, and heating? Would you say it is very hard, somewhat hard, or not very hard at all?

1 VERY HARD
2 SOMEWHAT HARD
3 NOT VERY HARD AT ALL
-8 DON'T KNOW
-7 REFUSED

Is there anything else you would like share with us about your chronic cough experience?

Appendix B

Cough Quality of Life Questionnaire

NAME: STUDY RECORD #: DATE:

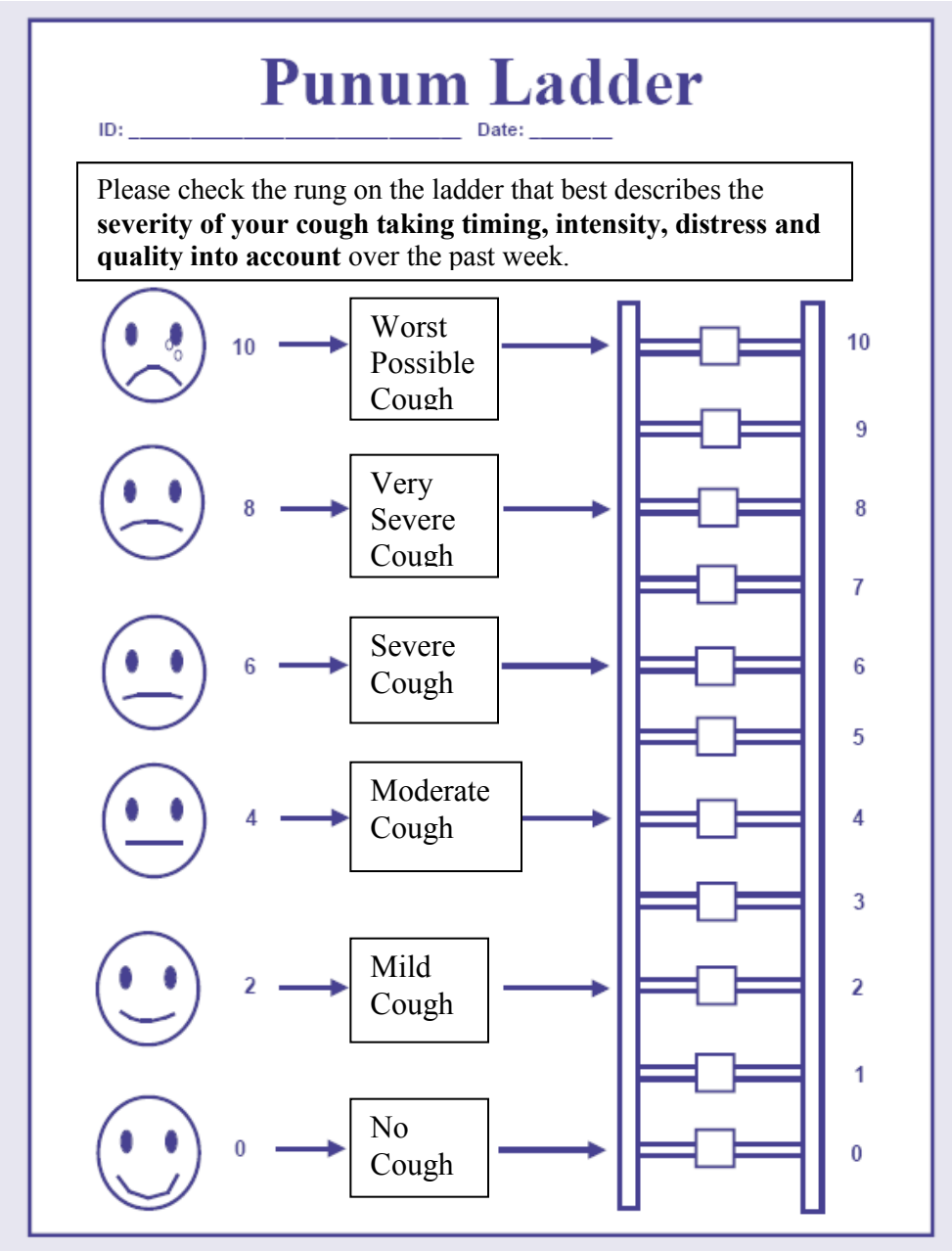
Please indicate below how your <u>cough</u> affects you. Circle the answer that best describes your agreement with each item. Please respond to every item. Thank you for your help.

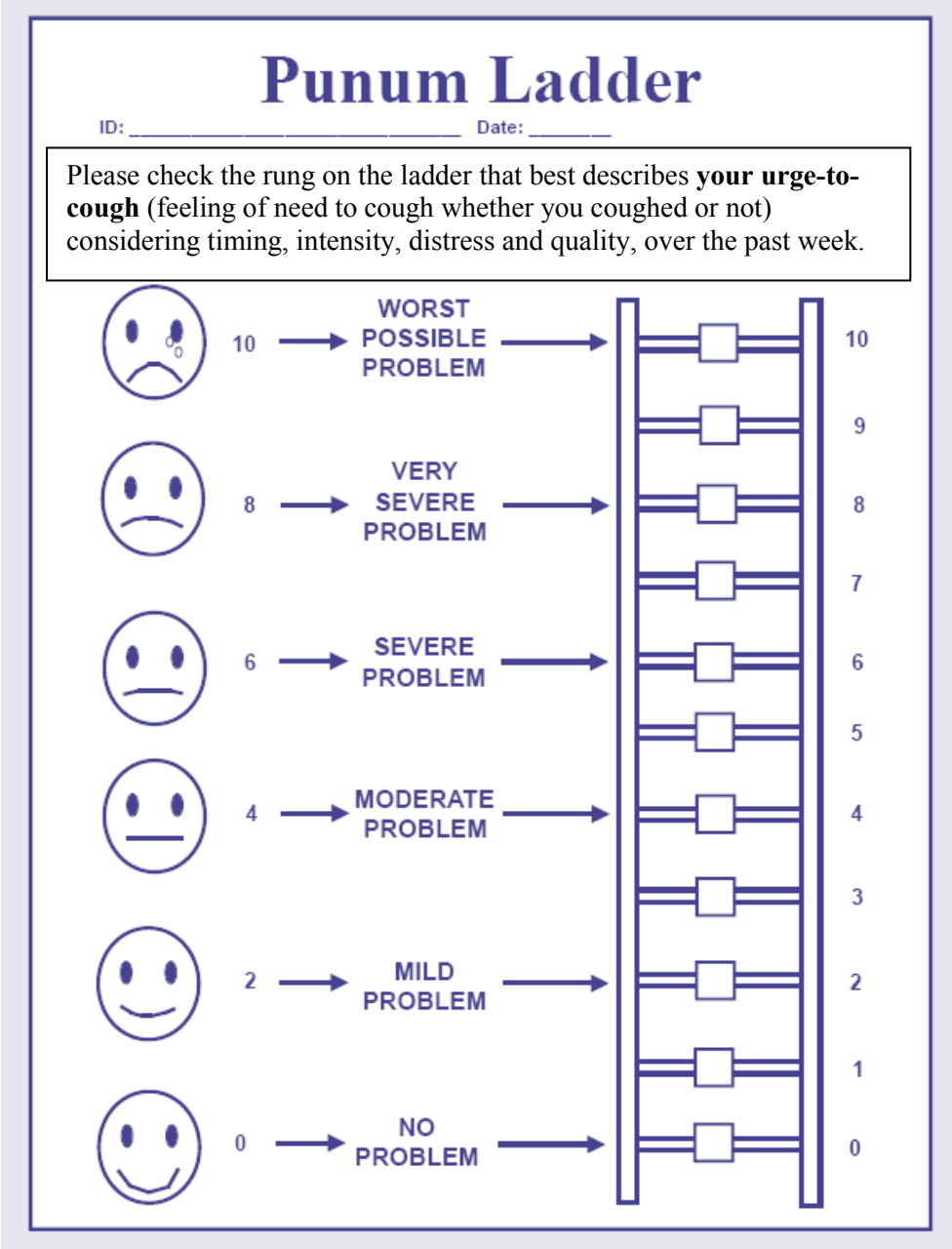
1. Family and or close friends can't tolerate it any more.	**STRONGLY DISAGREE**	**DISAGREE**	**AGREE**	**STRONGLY AGREE**
2. I have experienced prolonged absences from important activities such as work, school, or volunteer services.	STRONGLY DISAGREE	DISAGREE	AGREE	STRONGLY AGREE
3. I have been completely prevented from engaging in important activities such as work, school, or volunteer services.	**STRONGLY DISAGREE**	**DISAGREE**	**AGREE**	**STRONGLY AGREE**
4. I have lost my appetite.	STRONGLY DISAGREE	DISAGREE	AGREE	STRONGLY AGREE
5. I am sick to my stomach and vomit.	**STRONGLY DISAGREE**	**DISAGREE**	**AGREE**	**STRONGLY AGREE**
6. I cough and it makes me retch (dry heaves).	STRONGLY DISAGREE	DISAGREE	AGREE	STRONGLY AGREE
7. I have a fear that I might have AIDS or tuberculosis.	**STRONGLY DISAGREE**	**DISAGREE**	**AGREE**	**STRONGLY AGREE**
8. I have headaches.	STRONGLY DISAGREE	DISAGREE	AGREE	STRONGLY AGREE
9. I am concerned that I have cancer.	**STRONGLY DISAGREE**	**DISAGREE**	**AGREE**	**STRONGLY AGREE**
10. I am dizzy.	STRONGLY DISAGREE	DISAGREE	AGREE	STRONGLY AGREE
11. I wet my pants.	**STRONGLY DISAGREE**	**DISAGREE**	**AGREE**	**STRONGLY AGREE**
12. I soil my pants.	STRONGLY DISAGREE	DISAGREE	AGREE	STRONGLY AGREE
13. I sweat.	**STRONGLY DISAGREE**	**DISAGREE**	**AGREE**	**STRONGLY AGREE**

14. I am hoarse.	STRONGLY DISAGREE	DISAGREE	AGREE	STRONGLY AGREE
15. It hurts when I breathe.	**STRONGLY DISAGREE**	**DISAGREE**	**AGREE**	**STRONGLY AGREE**
16. I broke a rib.	STRONGLY DISAGREE	DISAGREE	AGREE	STRONGLY AGREE
17. I cannot sleep at night.	**STRONGLY DISAGREE**	**DISAGREE**	**AGREE**	**STRONGLY AGREE**
18. I have difficulty speaking on the phone.	STRONGLY DISAGREE	DISAGREE	AGREE	STRONGLY AGREE
19. I can no longer sing, for instance in church.	**STRONGLY DISAGREE**	**DISAGREE**	**AGREE**	**STRONGLY AGREE**
20. I have stopped going to social activities such as movies, plays, town meetings.	STRONGLY DISAGREE	DISAGREE	AGREE	STRONGLY AGREE
21. I have had to change my lifestyle.	**STRONGLY DISAGREE**	**DISAGREE**	**AGREE**	**STRONGLY AGREE**
22. I ache all over.	STRONGLY DISAGREE	DISAGREE	AGREE	STRONGLY AGREE
23. I am exhausted.	**STRONGLY DISAGREE**	**DISAGREE**	**AGREE**	**STRONGLY AGREE**
24. I am embarrassed.	STRONGLY DISAGREE	DISAGREE	AGREE	STRONGLY AGREE
25. I am upset by people thinking that I have something wrong with me.	**STRONGLY DISAGREE**	**DISAGREE**	**AGREE**	**STRONGLY AGREE**
26. I want to be reassured that I do not have anything seriously the matter with me.	STRONGLY DISAGREE	DISAGREE	AGREE	STRONGLY AGREE
27. I am self conscious.	**STRONGLY DISAGREE**	**DISAGREE**	**AGREE**	**STRONGLY AGREE**
28. I am concerned that I have something seriously the matter with me.	STRONGLY DISAGREE	DISAGREE	AGREE	STRONGLY AGREE

Appendix C

Punum Ladders

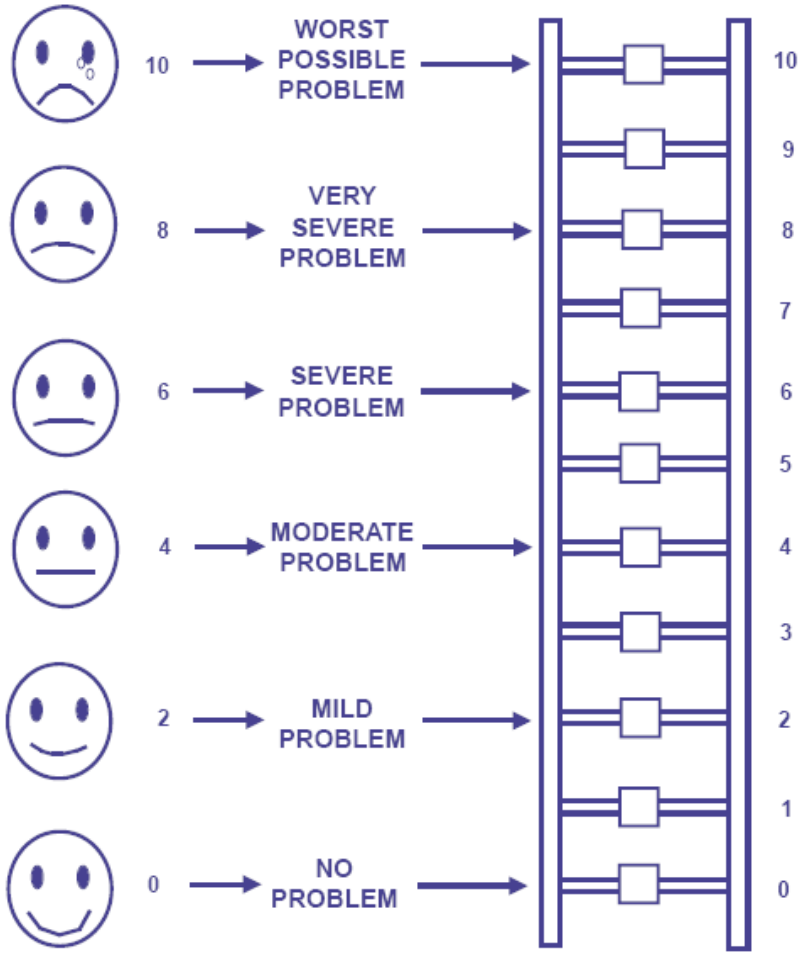



Punum Ladder
ID: _____ Date: _____
Please check the rung on the ladder that best describes **your urge-to-cough** (feeling of need to cough whether you coughed or not) considering timing, intensity, distress and quality, over the past week.
10
WORST POSSIBLE PROBLEM
8
VERY SEVERE PROBLEM
6
SEVERE PROBLEM
4
MODERATE PROBLEM
2
MILD PROBLEM
0
NO PROBLEM
10
9
8
7
6
5
4
3
2
1
0

Punum Ladder

ID: _____ Date: _____

Please check the rung on the ladder that best describes how much has your ability to speak considering timing, intensity, distress and quality, been bothered by cough over the past week?



Appendix D

Intervention Manual

Examining Change in Symptoms of Depression, Anxiety, and Stress in Adults after Treatment of Chronic Cough

Fall 2012

INTERVENTION MANUAL

Prepared by Cynthia French, RN, MS, ANP

University of Massachusetts Medical Worcester

Graduate School of Nursing

Table of Contents

Purpose of the Intervention Manual

This manual has been developed to provide a guide for monitoring intervention fidelity in the application of the 2006 American College of Chest Physicians' *Diagnosis and Management of Cough: ACCP Evidence-Based Clinical Practice Guidelines* in the study Examining Change in Depression, Anxiety, and Stress being conducted as the dissertation for the principal investigator Cynthia French.

Purpose and Specific Aims of the Study

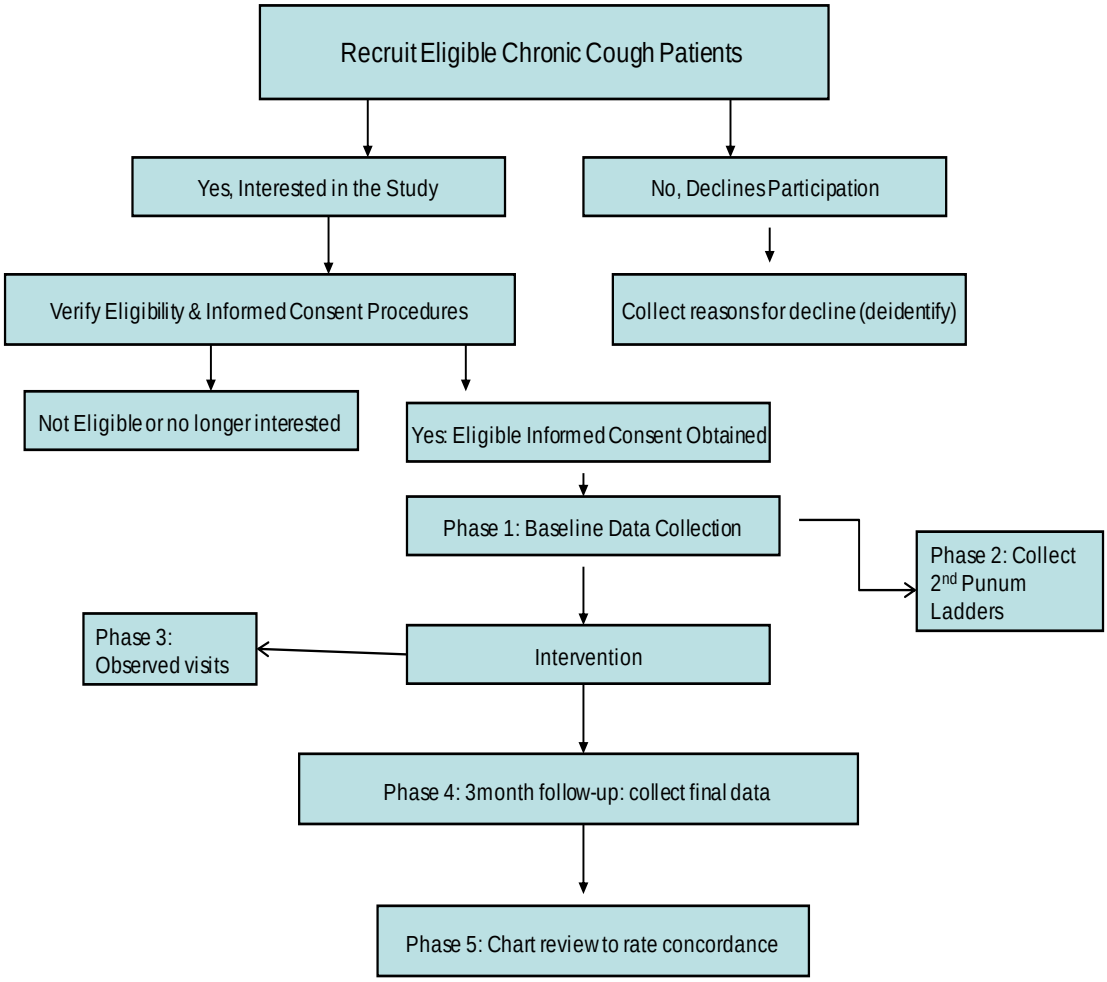
The purpose of the study for which this manual has been developed is to describe changes in the symptoms of depression, anxiety, and stress in adults with chronic cough after management using the 2006 American College of Chest Physicians' Diagnosis *and Management of Cough: American College of Chest Physicians (ACCP) Evidence Based Clinical Practice Guidelines*.

The specific aims of the study are to:

1. Describe the change in psychologic factors (symptoms of depression, anxiety, and stress) at 3 months after standardized treatment for chronic cough;
2. Describe the relationship between cough severity and urinary incontinence, financial strain, employment, number of diagnoses, ability to speak being bothered by cough, and social support score, DASS-21 subscale scores, and concordance with prescribed therapy score.
3. Describe the influence of physiologic factors (ability to speak without coughing, urge- to-cough and number of diagnoses), situational factors (social support), and psychologic factors (symptoms of depression, anxiety, and stress) on cough-specific quality-of-life and cough severity (global symptom/cough measure of timing, intensity, distress, and quality) at baseline and at 3 months post standardized treatment;
4. Describe the process of measuring intervention fidelity in the application of the ACCP guidelines for managing cough using the Technology Model.

This manual will specifically serve as a guide for the interventions employed in the application of the ACCP guidelines for managing cough as specified by specific aim number 4.

Flow diagram of the participants' progress thorough the study



Intervention Overview and Standard of Care

The intervention that is the focus of this study is the application of the 2006 American College of Chest Physicians' *Diagnosis and Management of Cough: American College of Chest Physicians (ACCP) Evidence Based Clinical Practice Guidelines*. The chronic cough management algorithm within these guidelines will serve as a primary focus for guiding the diagnosis and management of chronic cough. See Appendix A. The entire guideline will provide the detail for recommendations for the diagnostic and management interventions to be employed in the management this symptom. The use of these guidelines is the existing standard of care for interventions employed for those ≥ 15 years of age seeking medical care for cough lasting > 8 weeks in the cough specialty clinic located within the UMass Memorial Lung and Allergy Center on the University Campus.

With regards to this study:

- Research participants' will attend a standard initial new patient evaluation and management physician visit for the primary problem of the symptom of chronic cough of > 8 weeks duration
- Initial and follow-up care will be based upon the 2006 ACCP diagnosis and management of cough guidelines as it is the existing standard for any patient visit within the cough specialty clinic.
- Follow-up care may be delivered in person or via phone call as is also the standard in the cough specialty clinic. Phone management is often employed in this clinic for any patient whose home location makes an in-person visit not feasible.
- Research participant care will be managed by a physician and augmented by nurses, nurse practitioners, and nutritionists as is standard in the cough specialty clinic.
- The data collection plan includes the principal investigator's (PI) observation of 12 randomly captured intervention sessions. **We will not be able to predict how many observations will be completed per physician due to random assignment.** The PI will unobtrusively sit in on patient visits with interventionists who volunteer to have their visits monitored and the delivery of interventions rated. The plan is to observe for consistency of application of the guidelines for the study; data will be deidentified study and complete interventionist confidentiality will be maintained. There will be no risk for the interventionist. The PI will complete the Intervention Fidelity Checklist after observing physician research participant visits. See Appendix B.
- Data collected during interventionist / research participant interaction observations will be coded using deidentifed subject identification numbers and no data will be directly associated with the interventionist. All data collected will be stored under deidentified study participant numbers; no data will be coded or stored based upon individual interventionist as this is not a study of individual interventionist intervention fidelity.
- The PI will also collect receipt of intervention data from all research participants by asking them to complete self report questions developed to measure receipt of the intervention at the conclusion of the 3 month intervention period.
- The PI will review the electronic medical record (Allscripts) and compare this to the self report of participant receipt of the intervention to assess for and rate the degree of concordance of intervention(s) prescribed and subject self report of receipt.

Roles of Interventionist and the Principal Investigator

Interventionist: The interventionist is the attending board certified pulmonology physician providing care for the research participant. He/she has at least 5 years experience and skill in using the 2006 American College of Chest Physicians' *Diagnosis and Management of Cough: American College of Chest Physicians (ACCP) Evidence Based Clinical Practice Guidelines* for managing chronic cough. The interventionist is responsible for:

- The safe and effective delivery of the interventions related to the diagnosis and management of chronic cough based upon the 2006 ACCP guidelines.
- Maintaining fidelity of the intervention according to that recommended by the intervention manual as taken directly from the 2006 ACCP guidelines for the diagnosis and management of cough and within the context of the individual research participants' medical situation.
- Participating in debriefing sessions with the investigator no more often than every 3 months or until a collective total of 12 patient sessions across all interventionists have been monitored.
- Conduct follow-up 4-6 weeks after the first visit.

Study principal investigator: Provide technical educational information related to this study and/or support the interventionist during the study. Specific study requirements to be carried out by the PI investigator include:

- Meet with each interventionist to establish willingness to volunteer to participate in this study.
- Orient interventionist to the intervention manual and its contents.
- Observe and measure intervention fidelity interactions with the interventionists and research participants.
- Offer interventionist debriefing sessions after the first 5 and then after the final 5 observed visits have been completed.
- Ask all research participants to complete a questionnaire providing their perception of receipt of the intervention at the 3 month post intervention time period. See Appendix C.
- Conduct a review of the electronic medical records (Allscripts EMR) and rate the degree of concordance between research participants self report of receipt and documented intervention prescribed. See Appendix D.
- Deidentify, code, and store data.

Intervention: Initial Visit

American College of Chest Physicians' Diagnosis and Management of Cough: American College of Chest Physicians (ACCEPT) Evidence Based Clinical Practice Guidelines Chronic Cough Algorithm

The algorithm for chronic cough (see Appendix A) systematically directs the interventionist in the assessment of the most common causes of chronic cough with the guidelines suggesting focused empiric treatment for each cause identified. After screening for and eliminating smoking and the use of angiotensin converting enzyme inhibitors, and determining that the chest x-ray is normal (or has stable and inconsequential scarring) this management algorithm proposes initial diagnostic and focused and/or empiric management interventions for the four most common causes of chronic cough. If response to focused and/or empiric intervention for the most common causes of chronic cough is inadequate, the algorithm suggests further diagnostic and treatment interventions. The 2006 ACCP guidelines also provide diagnosis and management recommendations for less common causes of chronic cough that might be suggested by the diagnostic assessment. These less common causes of chronic cough will also be considered as part of the monitoring of the interventions for this study.

A new patient visit in the cough specialty clinic most commonly includes the following as recommended by the 2006 ACCP guidelines:

1. History and Physical Examination are performed, including an assessment of cough severity using a 0-10 rating scale with 0 being none and 10 being most severe.
2. Recent chest x-ray is reviewed.
3. Smoking and ACE-I status are evaluated; if present these issues are addressed.
4. Cause(s) of cough is suggested.
5. Suggested causes of cough are identified and indicated diagnostic evaluations are performed and/ or focused and/or empiric treatment is prescribed as recommended by the guidelines and within the context of the research subjects' individual situation.
6. Rationale for treatment is explained to the research participant.
7. Actual treatment is explained to the research participant.
8. Follow-up is planned.

Initial management interventions for the 4 most common causes of chronic cough, if identified as a potential cause, include the focused or empiric use of:

1. First generation antihistamine decongestants for *upper airway cough syndrome*;
2. Inhaled corticosteroids and bronchodilators and leukotriene receptor antagonists *for asthma;*
3. Inhaled corticosteroids for *non-asthmatic eosinophic bronchitis;*
4. Acid suppression medication, diet and lifestyle changes for *gastroesophageal reflux disease* and the addition of prokinetic agents if the former do not result in adequate reduction of cough;
5. Explanation of treatment and rationale for treatment;
6. Use of query for the research participants understanding of explanations.

Intervention: Follow-up

Follow-up visits for those with chronic cough most commonly include the following as recommended by the 2006 ACCP guidelines:

1. Patient response to treatment (cough severity, side effects, tolerance of treatment) and adherences to intervention is assessed every 4-6 weeks either in person or by phone or via email.
2. For those with ongoing cough, history and/or physical exam based upon the context of the individual's situation and mode of follow-up are repeated seeking suggested cause of ongoing cough.
3. Use of query and clarification related to patient's understanding of the treatment, patient adherence to treatment, and patient response to treatment including side effects to treatment. Need to ask them about cough severity from 0 to 10 after establishing this baseline.
4. Continuation of treatment, with escalation of one or more components of treatment until the patient provides self report of resolution or evident improvement of cough has been achieved, or de-escalation if warranted by side effects that outweigh the intervention benefits as reported by the patient or as observed by the interventionist.
5. Inadequate response results in maintaining partially effective therapy, recognizing that there may be multiple concurrent causes of cough, or further optimizing therapy for each diagnosis.
6. Additional testing for newly suggested cause of cough or for those not responding to empiric treatment.
7. Provide interventions as per the ACCP guidelines for other diagnoses suggested to be causing chronic cough.

Three Month Post Intervention Follow-up

Research participants will be contacted by the PI 3 and 6 months after the initial interventionist visit for data collection. Additional reminders consisting of either email, postal letter, or a phone call will be conducted twice within the 4 weeks and then will be considered "missed data" at 4 months.

Debriefing Sessions

The purpose of the debriefing sessions is to allow the interventionists the opportunity to share any thoughts they may have related to the intervention delivery and to allow the PI the opportunity to share any issues that might arise. Debriefing with the interventionists will occur either individually or in a group after the first and second 5 observed visits.

- Providers will be given the opportunity to share their thoughts, asked how it is going, and asked to share any of their observations related to the PI being in the room during the research participant visit and asked if anything can be done better or if they have other related thoughts they would like to share.
- The PI will also share her observations with a focus on large drift in intervention delivery, if any is identified for the study (but not for individual providers).

- Field notes related to that session will be recorded, in a form where interventionists are not identified in any way, by the PIs.

Measures of Intervention Fidelity

Intervention fidelity will be measured in 3 ways:

1. Direct observation of interventionist and research participant visits by the PI for a total of 12 random observations over the course of data collection. Random numbers will be generated using SPSS to a total list of 56 numbers. The first 12 random numbers taken from this list will be used to identify the research subjects whose visits will be observed. The list will be maintained for use in the event of a research subject drops out. Baseline observation data will be collected from the out of state patients who may not plan to return for in-person follow-up care and follow-up visits will be observed for local patients who plan to return for in-person follow-up care. The observation goals are the measurement of the application of the ACCP cough management guidelines within the context of the patient visit. Adherence and dose of intervention (content and delivery process) will be measured using a 0-3 point scale. See Appendix B.
2. Patient self report of receipt of the information related to the guideline interventions prescribed using a 3 point scale. See Appendix C.
3. Concordance with patient self report and interventionist prescribed care will be established by chart review (Allscripts EMR). The PI will rate degree to which the research participant's self report of receipt of the intervention corresponds with documented prescribed interventions based upon medical record review. A data extraction sheet will be used to rate the degree to which concordance is found using a 0-3 point scale. See Appendix D.

Appendix E

Intervention Fidelity Monitoring Checklist for Observer to Use During Physician Visits

Intervention Fidelity Monitoring Checklist

Subject ID _____
Date _____
Session _____ initial visit _____ follow-up visit

a) _____Upper airway cough syndrome diagnosed and was 1st generation antihistamine prescribed. If not, was reason given?
b) _____Asthma diagnosed and was inhaled steroid, inhaled bronchodilator, or Singulair prescribed. If not, was reason given?
c) _____Non asthmatic eosinophilic bronchitis diagnosed and was inhaled steroid prescribed. If not, was reason given?
d) _____Gastroesophagel reflux diagnosed and was lifestyle change, diet, acid suppression medication, and prokinetic agent prescribed. If not, was reason given?
e) _____Other

Context of the situation will be considered in deciding if intervention fidelity has been maintained (ex. side effects may result in inability to escalate treatment)

Adherence	0= none	1=low level of IF (addressed 2 or less)	2= moderate level of IF (addressed 3)	3= high level of IF (addressed all 4)	Comments
1. Was treatment prescribed by the physician according to the guideline (this includes was the patient evaluated per the guidelines for the 4 most common causes)?					
2. Did the physician probe for patient understanding of treatment					
3. Did the physician probe for patient response (including cough severity at baseline) and compliance?					
4. Did the physician maintain treatment if indicated?					
5. Did the physician step up treatment if indicated?					
6. Did the physician ordered further testing if indicated?					
7. Was follow-up arranged?					

8. Field notes

Ratings will be prorated and indicated as such based upon context especially for follow-up visits. This will be noted in the comments area.

Appendix F

Intervention Fidelity Monitoring Questionnaire for Subject Receipt Evaluation

Intervention Fidelity Monitoring Questionnaire

Please check off the conditions that your physician advised you that are causing your cough. You may choose more than one condition.

a) _____Post nasal drip
b) _____Asthma
c) _____Gastroesophageal reflux (stomach contents flowing backwards)
d) _____Non Asthmatic Eosinophilic Bronchitis (a specific kind of asthma)
e) _____Other_____
f) _____Other_____

Please check off the treatments that your physician advised you to use to control your cough.

___ antihistamines and/or decongestants
___inhaled steroids such as budesonide, fluticasone or similar medications
___inhaled bronchodilators such as albuterol, salmeterol, fomoterol or similar medications
___Singulair
___Life style changes such as elevating the head of the bed, or avoidance of pets or similar issues
___High Protein Low Fat diet
___stomach acid suppression medications (Zantac or Ranitidine, Prilosec or Omeprazole, Prevacid or similar medications)
___Medicine to speed up stomach emptying (Reglan or Metoclopramide or similar medications)
___Other please write in

To what degree did your physician cover the following issues related to your chronic cough? (Response options: not covered, covered somewhat, covered completely).

Please enter the number that best describes your situation.	0= not covered; not given any information	1= covered somewhat, would have liked more information	2= covered completely; given all the information I needed	Comments (optional)
1. Advise you of the reason for prescribed treatment to manage chronic cough				
2. Ask about your response to the treatment				
3. Ask about side effects of treatment				
4. Talk about the length of time you would need to continue to use the treatment				
5. Talk about the need for additional treatment if cough is still a problem				

6. Talk about the need for further testing if cough is still a problem				
7. Was follow-up arranged?				
Please enter the number that best describes your situation	0= none of the time	1=some of the time	2=most of the time	3= all of the time
8. How closely have you followed the recommendations of your cough specialist?				
9. **What recommendations did you not follow and why?**				
10. Was any other treatment prescribed?				
11. Has anything changed related to your chronic cough experience since you began treatment at UMass Memorial?				

Appendix G

Measure of Concordance of Research Subject Self-Report of Intervention Delivery with Documented Prescribed Interventions based upon Principal Investigators Rating of Degree of Concordance

Measure of Concordance of Research Participant Self-Report of Intervention Delivery with Documented Prescribed Interventions based upon Principal Investigators Rating of Degree of Concordance

Subject ID _____
Date _____

a) _____Upper airway cough syndrome diagnosed and was 1st generation antihistamine prescribed
b) _____Asthma diagnosed and was inhaled steroid, inhaled bronchodilator, or Singulair prescribed
c) _____Non asthmatic eosinophilic bronchitis diagnosed and was inhaled steroid prescribed
d) _____Gastroesophageal reflux diagnosed and was lifestyle change, diet, acid suppression medication, and prokinetic agent prescribed
e) _____Other

Concordance	***No Agreement at all (0)***	***Somewhat Agreement (1)***	***Almost complete Agreement (2)***	***Complete Agreement (3)***	Comments
1. Did the subject and physician agree on diagnosis and treatment					

2. Field notes

Appendix H

EMR Data Extraction Sheet

EMR Data Extraction Sheet Subject ID			
	Medications / Management Interventions	Diagnoses	Field Notes
Baseline			
3 Months			