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CONCERN BELIEFS IN MEDICINES: DESCRIPTION, CHANGES OVER TIME AND IMPACT ON PATIENT OUTCOMES

by

Olayinka Omobolanle Oladimeji

An Abstract

Of a thesis submitted in partial fulfillment
of the requirements for the Doctor of
Philosophy degree in Pharmacy
in the Graduate College of
The University of Iowa

July 2009

Thesis Supervisor: Professor Karen B. Farris

ABSTRACT

Concern beliefs in medicines are patients' anxieties about the harmful effects of a specific prescribed medication. Three papers examined the importance of concern beliefs in medicine, specifically its relationship to patient outcomes such as self-reported adverse drug events (ADEs) and symptom attribution, and the factors that might drive a change in concern beliefs over time. For the first and second paper, a cross-sectional internet survey of Medicare enrollees who were English speakers, 65 years and older and enrolled in the Medicare Part D program was done. In the third paper, a longitudinal internet survey of the same sample was done before Medicare Part D in 2005 and after Medicare Part D in 2007, and adults 40 years and older with physical limitations were interviewed using telephone. Multiple logistic regressions showed that having stronger concern beliefs in medicine and more symptoms was related to self-reported ADE, rather than using an inappropriate medicine or the number of inappropriate medicines used. Using independent sample t-tests, concern beliefs in medicine were found to be unrelated to symptom attribution for any causal reason, irrespective of whether there was patient-clinician agreement on attribution. Multiple linear regressions showed that concern beliefs changed over time for some older adults and having an ADE in the past year was related to this change. Among adults with physical limitations, though concern beliefs changed for some individuals; only one factor included in this study, changes in number of medicines, was related to this change. Establishing the importance of concern beliefs in medicines as a socio-psychological variable to consider in medication use outcomes will enhance the understanding of clinical researchers and practitioners concerning the mechanism of ADEs and symptom reporting.

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Graduate College
The University of Iowa
Iowa City, Iowa

CERTIFICATE OF APPROVAL

PH.D. THESIS

This is to certify that the Ph.D. thesis of

Olayinka Omobolanle Oladimeji

has been approved by the Examining Committee
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To God, my helper and giver of all good things

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ABSTRACT

Concern beliefs in medicines are patients' anxieties about the harmful effects of a specific prescribed medication. Three papers examined the importance of concern beliefs in medicine, specifically its relationship to patient outcomes such as self-reported adverse drug events (ADEs) and symptom attribution, and the factors that might drive a change in concern beliefs over time. For the first and second paper, a cross-sectional internet survey of Medicare enrollees who were English speakers, 65 years and older and enrolled in the Medicare Part D program was done. In the third paper, a longitudinal internet survey of the same sample was done before Medicare Part D in 2005 and after Medicare Part D in 2007, and adults 40 years and older with physical limitations were interviewed using telephone. Multiple logistic regressions showed that having stronger concern beliefs in medicine and more symptoms was related to self-reported ADE, rather than using an inappropriate medicine or the number of inappropriate medicines used. Using independent sample t-tests, concern beliefs in medicine were found to be unrelated to symptom attribution for any causal reason, irrespective of whether there was patient-clinician agreement on attribution. Multiple linear regressions showed that concern beliefs changed over time for some older adults and having an ADE in the past year was related to this change. Among adults with physical limitations, though concern beliefs changed for some individuals; only one factor included in this study, changes in number of medicines, was related to this change. Establishing the importance of concern beliefs in medicines as a socio-psychological variable to consider in medication use outcomes will enhance the understanding of clinical researchers and practitioners concerning the mechanism of ADEs and symptom reporting.

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CHAPTER I

INTRODUCTION

Concern beliefs in medicines are patients' anxieties about the harmful effects of a specific prescribed medication. Concern beliefs in medicines are important because they impact behaviors related to medications such as adherence and the self-report of adverse drug events (Horne & Weinman, 2002; Oladimeji, Farris, Urmie, Doucette, 2008). Qualitative studies have shown that people have beliefs about medicines in general, as well as beliefs about medication prescribed for specific illnesses (Horne & Weinman, 1999). Patients' beliefs about the specific medication prescribed for them can be grouped under two themes. These are their beliefs about the necessity of the prescribed medication for maintaining health now and in the future (necessity beliefs), and concerns about the potential adverse effects of taking it e.g. becoming too dependent on the medication or that regular use would lead to long term adverse effects (concern beliefs) (Horne, Weinman & Hankins, 1999). Concern beliefs in medication reflect patient's perceptions and experiences of specific medications.

These perceptions and experiences have been shown to also explain variation in coping behaviors such as symptom-reporting and outcomes such as self-reporting an adverse drug event (ADE) (Horne & Weinman, 1999; Oladimeji, Farris, Urmie & Doucette, 2008). An adverse drug event is defined as an injury resulting from medical interventions related to the use of a drug (Bates et al., 1995). Previous literature has linked beliefs in medicines and patient behaviors via the extended self-regulatory model (Horne, Weinman & Haskins, 1999; Horne, 2003). This model includes medication beliefs as well as illness beliefs into its theoretical framework and proposes that a

combination of illness and treatment perceptions are predictive of coping behaviors such as adherence (Horne & Weinman, 2002). The beliefs patients have about their medicines influence their coping responses to health threats which may then influence their behaviors (Levanthal, Levanthal & Cameron, 1998; Horne, 2003). Based on this model, treatment perceptions such as patients' beliefs in medicines may impact other coping behaviors for dealing with symptoms.

Symptom-reporting, for example, is an important coping behavior in managing medications and is associated with self-reporting an ADE (Oladimeji, Farris, Urmie & Doucette, 2009 (forthcoming); Dewitt & Sorofman, 1999). Patients may consider their medication beliefs when determining how to interpret and manage symptoms and correctly attributing it to the right cause. Symptoms precede the identification of an ADE and if there is misattribution of symptoms by patients, it is important to understand what patient factors may be related to it. Patients who are experiencing an ADE do not always think the problem is caused by a drug that they are taking (Kelly, 2008). Instead, they may suspect foods that they have eaten recently or new products they have used, such as cosmetics or laundry agents (Kelly, 2008). Sometimes, all symptoms experienced by patients are attributed to degenerative disease or old age by either patients or physicians. Patient and clinician symptom attribution may differ and be related to certain patient characteristics. Subsequently, the attribution of a symptom to a cause may impact the strategy for dealing with it which may include reporting or not reporting the symptom or ADE.

Concern beliefs in medication have also been associated with self-reporting an ADE (Oladimeji et al., 2008; Oladimeji, Farris, Urmie & Doucette (in review)). In a

cross- sectional study that included a baseline survey of Medicare enrollees before the start of Medicare Part D, patients with strong concern beliefs in medicines were more likely to report an ADE after controlling for socio-demographic, clinical and behavioral factors. These patients may be more sensitive to symptoms and pay particular attention to unwanted reactions that occur possibly making them likely to report an adverse effect (Oladimeji et al., 2008). Similar significant results were seen in the follow-up study and also among respondents who answered both the baseline and follow-up survey (Oladimeji et al (in review)). Socio-psychological variables such as concern beliefs in medicines may be more important than number of medicines (which was not significant in any of the studies) in self-reporting an ADE because symptom interpretations and attribution to medicine which leads to reporting an event to a health provider may be based on a motivation to tolerate or not tolerate the adverse effects and past experience with using the medicine (Oladimeji et al (in review)).

Beliefs in medicines appear to be an important mechanism or variable associated with adherence, symptom reporting and ADE (Bultman & Svarstad, 2000; Jorgensen, Anderson & Mardby, 2006; Neame & Hammond, 2005; Oladimeji et al., 2008; Ownsworth, Fleming & Hardwick, 2006). Yet, little is known about which individuals hold what level of beliefs and the responsiveness of beliefs in medicines to factors such as an experiencing ADE or symptoms or an educational intervention. Little is also known about the relative importance of beliefs in medicines in relation to other clinical variables such as number of medications and use of inappropriate medications in predicting ADEs.

A better understanding of beliefs in medicines may impact ADEs. This is important because ADEs result in more than 770 000 injuries and deaths each year in the

US and cost up to $5.6 million per hospital, depending on size. National hospital expenses to treat patients who suffer ADEs during hospitalization are estimated at between $1.56 and $5.6 billion annually (Bates, 1995; Bates, 1997). Patients who have ADEs have expensive hospitalizations than patients who with no ADEs. These patients are usually hospitalized an average of 1 to 5 days longer than patients with no ADEs (Classen, Pestonik & Evans 1997). The proportion of outpatients with an ADE ranges from 5 to 35 percent, depending upon the exact definition used (Budnitz, Pollock, Wiedenbach, Mendelsohn, Schroder & Annest, 2006). In 2004 and 2005, more than 700,000 patients were treated for ADEs in US emergency departments annually, and 1 of every 6 required a hospital admission (Budnitz et al., 2006). Adverse drug events lead to patient morbidity and mortality which are subsequently associated with large economic costs. Since concern beliefs in medicines have been linked to the reporting of this outcome, and this outcome has great health and economic impact, it is important to further explore the concept, its relationship to other adverse outcomes and its processes in managing health threats and coping behaviors.

Objectives of the study

This project consists of three studies that aim to examine concern beliefs in medication in more depth. The research questions addressed in these three studies are:

1) Do concern beliefs predict self-reported ADEs, when controlling for use of an inappropriately prescribed medication?
2) How does attribution of symptoms compare across patients and clinicians and are these attributions related to concern beliefs?

3) Do concern beliefs in medication change over time or remain stable and what are the factors that may drive changes in concern beliefs?

The first study sets the stage for understanding whether concern beliefs remain consistent in their relationship to self-reported ADEs when clinically important variables such as inappropriate medication use are included in the analysis. It is expected that concern beliefs will remain a significant risk factor for predicting ADEs despite the addition of inappropriate medicine use. Even if this is not the case, it does not preclude the importance of concern beliefs and their relationship to ADEs. The second study examines how patient symptom attributions may be related to concern beliefs. It is expected that patient symptom attributions that are correctly attributed to medicines will have high scores on the concern belief in medicine scale; and patient symptom attributions that are correctly attributed to other reasons will have lower scores on the concern beliefs scale. The third study investigates how concern beliefs may behave over time and examines factors that may be related to its stability. It is expected that patients' concern belief will change over time and be related to patient behaviors and personal factors.

The tables at the end of this section (Table 1.1, Table 1.2 and Table 1.3) give a description of the studies in each chapter, the datasets to be used and the variables to be included in the analysis of each chapter.

Literature review

In this section, the literature related to beliefs in medications is discussed as it relates to the three studies. The review begins with a description of beliefs as a concept and its relationship to health and illness behavior. More specifically, beliefs in medicines as a construct, its measurement, factors that are related to it and its relationship to behaviors such as adherence is described. Socio-behavioral models in the past have used beliefs in explaining health related behaviors and in developing educational interventions and a brief summary on these theories are shown. Other coping behaviors, such as symptom reporting and reporting an adverse drug event (ADE), are also related to beliefs in medicines. Detailed description of adverse drug events, its definitions and risk factors and a summary of ADE studies that have shown the relationship of risk factors such as 'using an inappropriate medicine' and beliefs in medicines to the reporting of an event are provided. Symptom reporting as a coping behavior and its relationship to beliefs in medicines is also explained. The theoretical framework of the extended self-regulatory model that ties these health, illness and coping behaviors to beliefs in medicines concludes this section.

To conduct this literature review, search terms such as beliefs in medicines, concern beliefs in medicines and medication beliefs were used. Very few studies have examined concern beliefs in medicines specifically and this makes the description of this concept very important. Studies on symptom reporting are also rare when compared to studies on ADEs which are vast in the literature. Despite the huge availability of ADE studies, only those related to this proposal such as risk factors including use of inappropriately prescribed medicines are included.

Beliefs in medicines

A belief is a 'subjective probability that an object has a particular attribute or that an action will lead to a specific outcome' (Fishbein & Ajzen, 1975 pp 131). Knowledge is 'information leading to understanding or for taking an informed action' (Glanz, 2002), while attitudes are 'beliefs that behavioral performance is associated with certain attributes or outcomes and there is a value attached to the outcome' (Ajzen & Fishbein, 2005). Beliefs seem similar to attitudes, but actually differ from attitudes because the latter encompasses beliefs in its definition; also, attitudes may further suggest whether beliefs are good or bad. Attitudes are a 'relatively enduring organization of beliefs, feelings, and behavioral tendencies towards objects, groups or events' (Hogg & Vaughan, 2005). Though beliefs can be explained as a likely characteristic of a concept, it does not need to be based on fact or rational thinking (Ajzen & Fishbein, 2005; Albarracin, Zanna, Jonson & Kumkale, 2005). When individuals form beliefs about certain objects, they can shape attitudes towards the object and subsequently lead to behaviors.

Beliefs in health behavior models

Several socio-psychological and health behavior models have linked beliefs to health and illness behavior. Examples of these models include the Health Belief Model (HBM), the Theory of Reasoned Action (TRA), the Theory of Planned Behavior (TPB), and the Self-regulatory Model.

The Health Belief Model (HBM) examines how the threat of an illness can lead to a behavioral response to the threat. In this model, four beliefs or perceptions are used to predict a health- related behavior. These include patients' perception of susceptibility, perception of severity of condition, and the benefits of and barriers to performing a

behavior. Recently, the concept of 'cues to action' that makes the individual aware of his/her feelings has been added to the model (Mardby, 2008). Perceived susceptibility is one's belief concerning the probability of getting a condition; perceived severity is one's belief of how serious a condition is; perceived benefits is an individuals belief in the efficacy of the advised action to reduce the risk or seriousness of the threat and perceived barriers is one's belief about the costs of the advised action or behavior. These could be tangible, social or psychological costs. Finally, cues to action are strategies taken to ensure the readiness of the individual towards taking the action (Glanz, 2002). The HBM proposes that patients evaluate the possibility of performing a health related behavior by considering their perceived susceptibility to an illness or health threat, the seriousness of the illness, as well as the benefits of the action. The barriers to action and cues might prompt the performance of the behavior (Jorgensen, Anderson & Mardby, 2006). These health belief variables influence health-related behaviors and can be modified via educational or behavioral interventions.

The theory of reasoned action (TRA) focuses on the relations between beliefs (behavioral and normative), attitudes, intentions and behavior. It was developed to understand the relationship between attitudes and behavior and has been widely used in theoretical and empirical research-based studies. According to the TRA (Ajzen & Fishbein (1980), the primary determinant of behavior is a person's behavioral intention. Behavioral intentions can be divided into two parallel cognitive processes: attitudes towards the behavior which is determined by the individual's beliefs about outcomes of performing the behavior (behavioral beliefs) and an evaluation of the outcome, and subjective norms (a consideration of social norms, the beliefs of others and how they are

likely to support your behavior), or normative beliefs. This model assumes that behavioral and normative beliefs are linked to behavioral intention and behavior through attitude and subjective norms (Glanz, 2002; Ajzen & Fishbein, 1980). The theory of planned behavior (TPB) was derived from the theory of reasoned action by adding the construct of perceived behavioral control. Perceived behavioral control accounts for factors supposed to be outside of an individual's control that may influence their intention and behavior. This perceived control is determined by control beliefs concerning the presence or absence of barriers to behaviors and perceived power of a factor to inhibit the behavior. The TPB theory describes action as being secondary to intention where intention can be derived from attitude, other people's opinions (subjective norm) and perceived control over the behavior (Ross, Walker & MacLeod, 2004).

Though patients' beliefs and how they affect behaviors regarding medications are consistent with other theories that explain health behaviors such as the HBM and the TPB; Horne and his colleagues examined patients beliefs in medication using the self-regulatory model (Dolovich, Nair, Sellors, Lohfeld, Lee & Levine, 2008; Horne 2003).

The self-regulatory model focuses on illness representations and coping behaviors. This model can be used to assess specific health beliefs and how they influence medication-taking behavior. These beliefs are focused on five themes: What is the illness (identity)?; What caused the illness (cause)?; How long will the illness last (time-line)?; How will the illness affect me (consequences)?; Can it be controlled or treated (controllability)? Patients form their own commonsense beliefs or illness perceptions across these five elements. In the identity dimension, the patient associates

the symptoms with an illness; the 'cause' theme explains the patients view about the etiology of the illness; the time-line dimension explains the perceived duration of the illness; the expected outcomes of the illness is seen in the 'consequences' dimension and the control-cure dimension examines the patient's beliefs about the potential for control and cure of the illness. These perceptions guide the individual's coping responses and behaviors (Byer & Myers, 2000).

According to the self-regulatory model, when there is a health threat, two parallel responses are created: an emotional and a cognitive one. These two threat responses can be linked to the coping procedure for dealing with the threat which then leads to an appraisal. For example, a coping strategy such as adhering/or not adhering to medications has been explained using this model (Horne, 2003). Patients respond to health threats they are experiencing by taking or not taking their medication. The decision is active and the process is dynamic, hence the coping strategy may change based on an evaluation of the outcome (Jorgensen, Anderson & Mardby, 2006).

The HBM, TRA and TPB and the self-regulatory model can be used to explain health behavior but some differences exist between the first three and the latter. The self-regulatory model differs from other behavior models because it can be used to explain actual coping behaviors for dealing with health threats such as adherence, while the other models predict behaviors of individuals based on their intentions (Mardby, 2008). Though all four models focus on the cognitive representation of the health threat, the self-regulatory model differs from the other models in that its emphasis is on the processes involved in coping appraisal and the resulting feedback on cognition, emotion and

behavior. Therefore, the interaction between cognition and behavior is seen as a dynamic process rather than the result of a single decision (Pennebaker, 2000).

The self-regulatory model better links beliefs to health and illness behavior compared to the more general models. For example, the self-regulatory model explicitly considers both the cognitive and emotional dimensions in an individual's representation of his illness and links these perceptions to their beliefs and coping behaviors. Since coping behaviors are strongly influenced by patients' illness perceptions and beliefs, beliefs about medicines are important attitudinal variables that can be incorporated into the self-regulatory model and provide a mechanism by which adherence to medications and other coping strategies can be explained (Brown, Battista, Bruelman, Sereika, Thase & Dunbar-Jacob, 2005; Ross, Walker & MacLeod, 2004).

The importance of examining how beliefs affect whether patients think they need their medication or not has been examined by Horne. In a study by Dolovich (2008), (2008), patients noted that taking medications took away the control they have over their health. The patient's belief on how medications took away control of their health could influence their expectations of their medications. These expectations were also affected by their past experiences with their medicines. Despite this knowledge, no published study has examined how beliefs in medications change over time which may be related to these past experiences with medicines. Also, since a patient's coping behavior and appraisal arise from the individual's representation of the health threat and treatment, and the perceived outcome of the coping may feedback to influence the representations, his or her perceptions of treatment may change over time.

Description of beliefs in medicines

Early qualitative studies have examined patients' ideas about medicines and their relationship to adherence (Britten, 1994). It was observed that powerful negative images of medicines exist and that patients' beliefs may differ from the health providers' assumptions. During consultations, Britten noted that it should not be assumed that the medicines being prescribed are the acceptable form of treatment in every situation. The patients' general orientation towards medicines such as whether they had fears about it should be established in such consultations (Britten, 1994).

Medication beliefs can be about drugs in general or about specific medicines used to treat a particular disease. Some studies have examined people's ideas about medicines in general, whereas others have focused on the specific medication prescribed for a particular illness (Horne & Weinman, 1999). Specific beliefs in medicines are formed by patients based on their experience with prior use of similar medications or other treatments used to treat the same condition. Adverse effects and long-term risk related to medications may also shape patients medication beliefs. In addition, patients may base their beliefs on the extent to which the medications interfere with their day-to-day activities (Phatak & Thomas, 2006). Based on this knowledge, it can therefore be inferred that factors such as medication use experience which influence and shape prior beliefs about medications may change it over time.

Beliefs can be potentially modified and are accessible from patients in the clinical setting. They can also be a valuable guide when physicians are involved in decision making. When generalizing across medical conditions and treatment regimens, beliefs are defined as 'medication beliefs' or 'beliefs in medicines'. According to Horne, beliefs in

medicines are the "hidden determinant of treatment outcome" (Horne & Weinman, 1999). The expectation of patients about their medicines has been shown to be grounded in the 'reality of their experiences, beliefs, health care and social situations' (Dolovich et al., 2008).

Beliefs about medicines can be classified under certain 'central themes', such as views about the inherent nature of medicines, the capacity of medicines to do harm or to benefit, and views about the extent to which they could be overused by doctors. These themes are useful in identifying patients' orientation and perceptions towards medicines in general (Horne, 2000; Horne, Graunpner, Frost & Weinman, 2004). However, patients do not just differ in their beliefs about the nature and uses of medicines, there are also differences in the degree to which they perceive themselves as sensitive or susceptible to the potential adverse effects of the medications. For example, people who view themselves as being particularly sensitive to the medication side effects will be more likely to view medicines as being harmful and overprescribed by doctors (Horne, 1997; Horne et al., 2004). Horne and colleagues noted that these perceptions of sensitivity to medicines are likely to arise from each 'individual's general perceptions of self and hardiness, past experiences (either from the individual or others) and their beliefs about the nature of medicines' (Horne et al., 2004).

Factors related to beliefs in medicines

Socio-demographic factors and clinical characteristics of individuals have been shown to be related to beliefs in medicines. For example, Horne et al., 2004 showed that men had more negative beliefs about medicines than women. Conversely, a population-based study found women to view medicines as being harmful and possibly having

negative beliefs about the medicines. In terms of age, older people have more positive views about medicines than the younger ones and people with lower incomes view medicines as both harmful and beneficial than individuals on higher incomes (Isacson & Bingefors, 2002). Cultural backgrounds have also been related to beliefs in medicines. In the study by Horne et al., 2004, people with an Asian background were seen to have more negative beliefs about medicines than those with a European background. In that study, a strong association between cultural background and beliefs about medicines was observed after controlling for other confounding factors such as experience with taking medicines and gender (Horne et al., 2004). Similarly, among Japanese patients, a strong association between intentional non-adherence and beliefs about taking medicines has been observed (Iihara, Tsukamoto, Morita, Miyoshi, Takabatake & Kurosaki, 2004). Country of birth has also been seen as an important factor related to beliefs about medicines. Mardby, Akerlind & Jorgensen noted in their study that individuals born in the Nordic countries considered medicines to be more beneficial than those born outside the Nordic countries (Mardby, Akerlind & Jorgensen, 2007).

Other factors such as level and type of education and patients own experience using medications have been significantly related to general beliefs about medicines (Horne, Weinman & Haskins, 1999; Horne et al., 2004; Isacson & Bingefors, 2002). For example, pharmacy clients with lower education considered medicines as more harmful and less beneficial than those with higher education.

Direct to consumer advertising has a powerful influence on the perceptions of individuals about their medications, both positive or negative (Iosifescu, Halm, McGinn, Siu & Federman, 2008). Factors such as the social environment, social influences from

the media and direct to consumer advertising of drugs also influence patients' beliefs in medicines and their concerns about adverse effects.

Clinical factors, such as having a chronic illness, have shown significant relationships to beliefs in medicines. Specifically, necessity beliefs are strong in patients with these illnesses and may be more influential in acute conditions (Horne et al., 1999). The use of medicines has been associated with beliefs in medicines. For example, people presently using prescription medicines regard medicines as more beneficial and less harmful than those not using prescription medicines. Similarly, individuals with experience of taking prescribed medications have stronger beliefs in the beneficial rather than the harmful effects of medicines compared to people without such experience (Ramstrom, Afandi, Elofsson & Peterson, 2006). Pharmacy clients with experience of herbal/homeopathic medicines and those not currently using medicines are more likely to believe that doctors overprescribe (Mardby et al., 2007). Also, the use of herbal/homeopathic medicines has been related to negative beliefs about medicines (Horne et al., 2004; Isacson & Bingefors, 2002). Practitioners of complementary medicine hold more negative views about medicines than practitioners of conventional medicine and this may impact patients' beliefs about their medicines if these views are influenced by their opinions on patients seeking alternative healthcare (Cronin & Horne, 2008).

Differences in views about beliefs in medicines also occur between patients and health providers. For example, patients' in a Swedish study expressed a more negative attitude about medicines than pharmacists. Among the pharmacists, there were stronger beliefs in the beneficial rather than the negative effects of medications (Ramstrom,

Afandi, Elofsson & Petersson, 2006). A study of physicians' communication style showed a positive influence of patients' beliefs about their medications on satisfaction with treatment, which in turn was predictive of better adherence (Bultman & Svarstad, 2000). Beliefs in medicines can affect communication with clients in an advisory situation (Jorgensen, Anderson & Mardby, 2006) and can influence patients' treatment preferences, pathways to care and adherence to medications (Horne, 2000; Horne et al., 2004).

Measurement of beliefs in medicines

To measure beliefs about medicines, Horne, Weinman & Haskins developed the Beliefs about Medicines Questionnaire (BMQ) from extensive qualitative research (Horne et al., 1999; Mardby, Akerlind & Jorgensen, 2007). This questionnaire has been validated and tested for its internal consistency and psychometric properties, and it assesses the cognitive representation of medication. The BMQ has been used together with existing health belief models in improving the ability to predict treatment-related behaviors.

Based on this questionnaire, a distinction between general beliefs about medicines and specific beliefs about medicines for specific diseases has been made. These two parts of the BMQ called the BMQ-General and the BMQ- specific can be used separately or together. Specific beliefs about medicines can be used in specific patient groups and it describes their beliefs about their specific medicines. General beliefs about medicines measure beliefs in general and are broader in concept (Horne et al., 1999). The two sections of the BMQ each comprise two five-item subscales. The BMQ-Specific is comprised of the specific-necessity subscale which contains items related to patient's

perceived need for taking their medicine in order to stay healthy, and the specific-concern subscale which is comprised of items related to the concerns about the adverse effects of medicines. The BMQ-General contains the general-overuse subscale which is made up of items related to beliefs that medicines are being over-prescribed and the general-harm subscale which contains items that show beliefs about medicines as harmful, addictive and poisonous (Grunfield, Hunter, Sikka & Mittal, 2005).

In the BMQ-specific scale, the necessity sub-scale assesses necessity beliefs in medicines and consists of items such as 'My health at present depends on my medicines', 'My life would be impossible without my medicines', 'Without my medicines, I would be very ill', 'My health in the future will depend on my medicines', and 'My medicines protect me from becoming worse'. This sub-scale represents the patients' perceived role of the medication preventing the deterioration of their present and future health (Horne, Weinman & Haskins, 1999; Kumar et al., 2008).

The specific concern sub-scale assesses concern beliefs in medicines and consists of items such as 'I sometimes worry about the long term effects of my medicines', 'Having to take my medicines worries me', 'I sometimes worry about becoming too dependent on my medicines', 'My medicines disrupt my life', and 'My medicines are a mystery to me'. This construct comprises of both the emotional (e.g. having to take my medicines worries me) and cognitive representations (My medicines are a mystery to me). The response options for both sub-scales is a five point Likert scale (ranging from strongly disagree to strongly agree) where individuals indicate their level of agreement or disagreement with each of the individual statements in each scale (Horne et al., 1999; Kumar et al., 2008).

The BMQ-General scale has two sub-scales, the General Harm and the General Overuse sub-scales. The General Harm sub-scale assesses beliefs about the nature of medicines and the degree to which they are perceived to be harmful, poisonous and addictive including,'Most medicines are addictive', 'People who take medicines should stop their treatment for a while every now and again', 'Most medicines are poisons', and 'Medicines do more harm than good'(Kumar et al., 2008; Horne et al., 1999). During the development of this sub-scale, the internal consistency was shown to be disappointing and therefore the use of this scale is limited and if used, is done with caution (Horne et al., 1999).

The General Overuse sub-scale assesses beliefs about the way in which medicines are prescribed and the degree to which they are overused by clinicians' including, 'Doctors place too much trust in medicines', 'Doctors use too many medicines', 'Natural remedies are safer than medicines' and 'If doctors had more time with patients they would prescribe fewer medicines'. The Specific and General measures can be used separately or combined (Horne et al., 1999). However, in this research/study, the BMQ-specific measure that examines beliefs about the necessity and concern with regard to taking medicines was used. The BMQ-specific measure is a flexible instrument that can be adapted when measuring beliefs about specific medicines or for a particular condition (Horne et al., 1999).

To develop the scales, Horne, Weinman & Haskins used a sample of people with chronic illness: asthmatic, diabetic and psychiatric in-patients. The inclusion criteria were they had to have been prescribed one or more medicines for regular use in the treatment of their illness at least two months prior to the study, they could read and understand the

questionnaire and felt well enough to complete it. Participants answered a series of items representing commonly held beliefs about medicines. In the pool, 34 statements representing commonly held beliefs about specific (n=16) and general statements (n=18) identified in the literature among patients with a range of chronic illnesses. Also, interviews were conducted with the chronic illness sample to elicit their views about medicines prescribed for them and their thoughts in general about medicines in general. An exploratory components analysis (PCA) was done to select items from the pool into the scales and a confirmatory factor analysis was done to confirm the validity of the scales and the separation of Specific beliefs such as concern beliefs in medicines and General beliefs in medicine. An evaluation of the psychometric properties of the BMQ included testing the criterion-related validity, the discriminant validity and the internal consistency and reliability using test-retests and Cronbach's alpha. The test-retest reliabilities between initial and repeated test scores for each scale showed that the correlation coefficients (0.60-0.78, with 0.76 for the concern beliefs scale) were within accepted limits.

Concern beliefs in medication are the concept of focus in this proposal. The next section focuses more specifically on concern beliefs in medicines and an overview of its description and relation to health behaviors.

Concern beliefs in medication

In the management of chronic illnesses, the appropriate use of medication is important. Several theoretical models for understanding the use of medication and treatments such as social cognition models and self-regulatory theories have been developed and these frameworks have a common assumption that people develop beliefs

that influence their interpretation of information and experiences which guide their behaviors (Horne & Weinman, 1999).

A study involving about 1200 participants representing a range of chronic illness groups showed that patients' beliefs about their specific medication could be grouped into necessity beliefs about the prescribed medication and concern beliefs (e.g. becoming too dependent on the medication or that regular use would lead to long term adverse effects (Horne et al., 1999). These two types of beliefs have been linked to medication-taking behaviors. For example, patients are active decision makers who are motivated to use their medication as instructed if their belief in its necessity displaces their concerns about taking it. People with strong beliefs in their necessity of taking medication to maintain their health are usually more adherent to treatment, and those with greater levels of concern about medication, commonly about the dangers of dependence and long term effects are more likely to be non-adherent (Neame & Hammond, 2005). A greater perceived need for medicines prescribed therefore results in greater adherence and conversely higher concerns results in lower adherence levels (McCracken, Hoskins, & Eccleston, 2006).

Though literature has shown the relationship of beliefs in medicines to health behaviors such as adherence; the concept of concern beliefs in medication and its relationship with coping health behaviors such as symptom reporting and reporting an ADE needs to be explored.

In a study by Oladimeji et al (2008), a relationship between concern beliefs in medicines and ADEs among older adults was established. This study was based on a sample of Medicare enrollees before the start of Medicare Part D (Oladimeji et al., 2008).

It was shown that patients with stronger concern beliefs in medicine were more likely to self-report an ADE. Oladimeji et al., 2008 (in review) further revealed in a longitudinally designed study that even after the start of Medicare Part D; though number of medications and rate of ADEs increased, number of medications was not a significant predictor of ADEs. Number of medications has been shown as one of the most significant risk factors for reporting an ADE in previous studies (Chrischilles, Segar, & Wallace, 1992; Chrischilles, Rubenstein, Van Glider, Voelker, Wright, & Wallace, 2007; Field et al., 2004). Concern beliefs in medications remained a risk factor for self-reporting an ADE in the year before and after the start of Medicare Part D. Also, another recent study (Oladimeji et al., 2009 (forthcoming)) showed that concern beliefs in medication can be linked to the reporting of symptoms to health providers. Patients with stronger concern beliefs were more likely to report the symptoms they experienced to their doctor.

Concern beliefs may be a motivation for the reporting of patient adverse health outcomes such as unwanted symptoms and ADEs. The self-regulatory model has been used to explain illness-related behavior, including adherence to treatment recommendations. In this context, adherence to treatment is viewed as one of a number of behaviors that patients can adopt to cope with their illness (Horne & Weinman, 2002). If a patient experiences an unwanted symptom, reporting the symptom/unwanted reaction and/or reporting the injury (ADE) represents a way of coping with it. This next section examines how beliefs in medicines are related to adherence.

Beliefs about medicines in adherence

As stated earlier, social cognitive models such as the HBM and TPB share the assumption that beliefs developed by individuals influence the interpretation of

information available to the person and then impact the behavior. However, these models are limited by a tendency to understand adherence as a result of a patient's rational thinking (Grunfield, Hunter, Sikka & Mittal, 2005). In contrast, the self-regulatory model examines adherence as a decision based on the individual's perceptions of illness and treatment. Using this model, medication adherence may be investigated and enhanced by assessing patients' beliefs about their medication, illness and/or treatment outcomes (Horne & Weinman, 1999).

Beliefs held by patients about their medicines could be complex and for some of them, failing to take medicines as prescribed is a result of a rational but erroneous belief about their medicines (Grunfield et al., 2005; Horne & Weinman, 1999). Decisions about taking medications could also be informed by beliefs about the illness which the medication is intended to prevent or treat (Horne, 1997). Although beliefs about medicines in general influence the patient's orientation towards medicines, adherence behavior is likely to be strongly related to personal views about the specific prescribed medications. In particular, adherence decisions are influenced by a cost-benefit assessment in which patients' personal beliefs about the necessity of the medication for maintaining or improving health are balanced against concerns about the possible adverse effects of taking it (Horne & Weinman, 1999; Grunfield et al., 2005). Inherently, a patient who perceives that a medicine is unimportant and unnecessary to stay healthy (benefit appraisal) may choose not to take his medication so that the perceived harmful and adverse effects of the medicine can be mitigated (cost-appraisal) (Grunfield et al., 2005).

Specific beliefs about medicine have been related to adherence in specific patient groups. For example, these beliefs have predicted adherence in illness groups such as HIV, asthma, renal disease, cancer, coronary heart disease, depression, and rheumatoid arthritis (Brown, Battista, Bruelman, Sereika, Thase & Dunbar-Jacob, 2005; Clifford, Barber, & Horne, 2008; Horne et al., 1999; Menckenberg et al., 2008).

Patients' beliefs in medicines in general may differ from their specific beliefs especially in relation to adherence. For example, Brown et al (2005) showed no association between the general beliefs in medicines and adherence among patients with depression (Brown et al., 2005). Mardby Akerlind & Jorgensen however noted that people's general beliefs and their specific beliefs about their medicines could both be related to adherence (Mardby, Akerlind & Jorgensen, 2007). Patients' who attain higher scores on the specific concern scale than on the specific necessity scale are usually less adherent (Horne et al., 1999; Phatak & Thomas, 2006).

Variations in beliefs about medicines have also been reported among patients who report adherence and non-adherence. For example, Clifford et al (2008) showed that intentional non-adherers were more likely to doubt their need for their prescribed medication and to have stronger concerns about taking it compared to adherers. Specifically, concerns about potential adverse effects of the medication were rated high relative to their perceived need for it (Clifford et al., 2008).

Beliefs in medicines predict adherence, even more than clinical and socio-demographic factors. For a specific disease condition, the choice of using medications as an ideal coping strategy for dealing with health threats and illnesses is determined partially by patients beliefs about the specific necessity of using the medicine including

their benefits, as well as their concerns related to adverse effects (Horne, 2003; Phatak & Thomas, 2006).

Adherence is a complex behavior influenced by many factors and patients beliefs about their medicines play a key role. These beliefs have significant influences in health behaviors and in the development of educational, cognitive and behavioral interventions.

Significance

Patients beliefs in medicines and illness perceptions have been linked to medication adherence and illness behaviors. These beliefs may therefore be important in understanding individual coping behaviors. If medication adherence is a form of coping based on the self-regulatory model, patients' decision to follow treatment recommendations which will be influenced both by their views about the illness and the treatment will also be important in other coping behaviors including self-reported ADE and symptom reporting to health providers (Brown et al., 2005).

Based on the relationship of beliefs in medicines to health behaviors such as adherence, it is important for healthcare professionals to discuss patient beliefs during health care consultations and office visits. The discussion of the patient's perceptions about their medicines is essential to patient-centered care and will have positive health effects on the patient, especially in the management of his medication. Discussing patients' beliefs about their medicines may influence their expectations, symptom interpretations as well as future attributions (Oladimeji et al., 2008). In addition, an assessment of specific concerns may give healthcare providers opportunities to identify and address concerns about adverse effects associated with the medications (Phatak & Thomas, 2006).

A better understanding of patients' beliefs about their medications will improve the ability to educate patients about their treatment regimen and guide the development of interventions to improve medication adherence and other coping behaviors (Brown et al., 2005; Mardby, Akerlind & Jorgensen, 2007). The creation of these types of interventions is a new and possible way to improve health and coping behaviors.

One of the objectives of this project is to examine if concern beliefs remain a significant risk factor for predicting self-reported ADEs, when controlling for use of an inappropriately prescribed medication. Beliefs in medicines appear to be an important mechanism or variable associated with ADE. In this next section, ADEs are described, clarifications on the definitions that exist in the literature are shown and a description of its measurement, detection and impacts on the health care system is illustrated.

Adverse drug events

The amount of literature describing the evaluation, identification, risk factors, and prevention of adverse drug events (ADEs) is large and diverse. To be able to understand this patient outcome, a review of what the past literature has shown is essential. However, only studies related to its risk factors especially among older adults and its prevention will be examined. Older adults are identified as individuals who are 65 years and older. The reason for this focus is that though beliefs in medicines as a variable related to ADE is investigated here, the context of its relationship is as a risk factor for ADEs especially among older adults. Beliefs in medicines show relationships to coping behaviors that can be linked to preventing ADEs.

As stated earlier, past studies have examined ADEs using different constructs and definitions. For example, while some studies focus on adverse drug events, others

encompass all adverse events, including adverse drug reactions (ADRs) and medication errors (Johnston, France, Bryne, Murff, Lee, Stiles et al., 2006). The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human use, of which the U.S. Food and Drug Administration (FDA) and the World Health Organization are members, defines an adverse event as "any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with the treatment" (Weissman et al., 2008). Adverse events in patients are expressed as symptoms, signs, or laboratory values and if a relationship between the event and a drug is suspected and possible, then an ADE can be assumed (Naranjo, Shear & Lanctot, 1992). The term 'adverse event' which may not be useful to a physician provides a context for the more clinically useful term, adverse drug reaction (White, Arakelian, & Rho, 1999).

There have been confusions about the use of the terms 'adverse drug reactions' and 'adverse drug events' in the literature. Although the terms may appear identical and may be used interchangeably in many studies, the definition of an adverse drug event is considered broader and can include injuries caused by "errors in administration or by noncompliance" (White, Arakelian, & Rho, 1999). The Joint Commission on Accreditation of Healthcare organizations defines an adverse drug event (ADE) as "any incident in which the use of a medication (i.e., drug or biologic) at any dose, a medical device, or a special nutritional product (e.g., dietary supplement, infant formulas, medical food) may have resulted in an adverse outcome in a patient" (Schade, Hannah, Ruddick, Starling & Brehm, 2006). The Institute of Medicine however defined it as 'an injury resulting from medical interventions related to the use of a drug' (Institute of Medicine,

2006). This definition has been widely used and accepted in major studies. This is because it is more comprehensive and clinically significant. An adverse drug reaction is "a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for the modification of physiologic function" (Nebeker, Barach & Samore, 2004; Hanlon, 2001). This definition excludes events associated with errors, while the term ADE includes preventable and non-preventable events including errors due to under dose and over dose (Bates, 1999; Nebeker, Barach & Samore, 2004). ADEs extend beyond adverse drug reactions in their definition.

Measurement and Detection of ADEs.

Methods relating to the identification, measurement and detection of ADEs have been described (Field et al., 2004; Gurwitz et al., 2003; Morimoto, Gandhi, Seger, Hsieh & Bates, 2004). In the study by Field et al (2004), drug-related incidents were limited to those occurring in the ambulatory setting and there were different methods for detecting if a possible drug-related incident had occurred. These included 1) reports from healthcare providers, 2) review of hospital discharge summaries as an evidence of a drug related incident that led to an hospital admission, 3) review of emergency notes, 4) computer-generated signals of elevated drug levels, abnormal laboratory results and the use of medications in certain diagnoses that reflect an ADE, 5) automated free-text review of electronic clinic notes, and 6) review of administrative incident reports concerning medication errors (Field et al., 2004). In addition to these methods, other means of collecting incidents have been used in other settings. For example, Morimoto et al (2004) 1) collected practice data; 2) solicited incidents from health professionals and 3)

surveyed patients for drug related events. Practice data included charts, laboratory, prescription data, as well as administrative data. Screenings of administrative data were based on ICD-9 codes associated with ADEs and medication errors. The use of self-reports from health providers is especially useful in the identification of incidents in the inpatient settings. These include 1) self-report from physicians, nurses, pharmacists or other health professionals who become aware of any ADE, potential ADE or medication error and 2) self-report generated by research assistants or nurses who visit the wards or clinics to examine if there is any possible incident and then record it (Morimoto et al., 2004).

In the outpatient settings, incidents may not be recorded in a patient's medical record and this makes patient surveys especially important. These surveys could include direct interviews in the office or patient's home, mail surveys, telephone surveys, or web-based surveys and in some cases, a combination of more than one type of survey.
Also, all the methods for detecting ADEs are complementary. For example, Morimoto et al (2004) showed that chart reviews, self-reports and computer based triggers are useful in the inpatient settings while patient surveys and chart review identify ADEs in the outpatient setting (Morimoto et al., 2004).

Self-reported ADEs has been used as a means of detecting and measuring ADEs. In a study by Green, Hawley & Rask, ADEs were measured using an adapted version of a previously published survey. In this survey, patients were asked five questions: 1) whether they had experienced an ADE within the last 6 months, 2) which drugs were involved in the ADE, 3) whether a physician had been notified about the ADE, 4) what changes were made to the treatment regimen because of the ADEs and 5) whether

hospitalization was required because of the ADE (Green, Hawley & Rask 2008). An original version of this method where patients are asked if they noticed any side effects, unwanted reactions, or other problems from medications being taking has been used in other studies (Chrischilles et al., 1992, Chrischilles et al., 2007; Gandhi et al., 2000; Oladimeji et al., 2008). While evaluating the value of self-reports of potential ADEs in both inpatients and outpatients older adults, Hanlon et al (2001) found that the detection rates for potential ADEs using this method were higher than those shown in previous studies. Eighty-eight percent of the events were judged to be plausible ADEs therefore confirming that older adults can accurately self-report ADEs (Hanlon et al., 2001). Self-report of ADEs by older adults are accurate and frequent and usually less time-consuming than chart reviews. Despite these advantages, getting patient report of adverse events may be difficult because of problems with recall, clinical knowledge, and social desirability bias (Hanlon et al., 2001; Weissman et al., 2008). In these studies, self-report of ADEs by patients will be used in measuring ADEs. This is especially important because these patients are seen in the out-patient setting.

Impact and costs of adverse drug events

Adverse drug events (ADEs) have unwanted effects on patients' health and are common in most clinical settings including adult inpatients with a reported incidence of 6.5%, adult outpatients with an incidence of 27.4%, and pediatric inpatients with a reported incidence of 2.3% (Morimoto et al., 2004; Al-Tajir & Kelly, 2005). Drug related injuries also occur in 6.7% of hospitalized patients (Bates, 1999; Schade, Hannah, Ruddick, Starling & Brehm, 2006).

ADEs have significant impact on health utilization and outcome. For example, they have been shown to cause significant increases in lengths of stay and costs of hospitalization (increasing length of stay by about 1.7-2.2 days), and an almost 2-fold increased risk of death. In addition, they lead to substantial consequences such as additional resource utilization, time away from work as well as lower patient satisfaction (Morimoto et al., 2004; White, Arakelian & Rho, 1999).

Adverse drug events may be the fourth to sixth leading cause of death and can also result in a number of different physical consequences including allergic reactions (Bates, 1999; Schade et al., 2006). An estimated 9.7 % of events cause permanent disability, (Thomas et al., 2000) while the increased risk of death for a patient who experiences an ADE is nearly twice that of a patient who does not experience an ADE (Classen et al., 1997). In a summary analysis of descriptive studies on significant ADEs over 21 years, 15% of all ADEs are life-threatening, 4% result in permanent disability and 8% end fatally (Kelly, 2001; Schade et al., 2006). Though ADEs in general have significant health effects on patients, preventable ADEs have major consequences that cannot be ignored and this is important because the health outcomes could have been avoided if proper measures had been taken. For example, the Institute of Medicine estimated that 44 000 deaths that occur annually in the US are attributable to preventable adverse events. Of these deaths, 5.5% were said to occur as a result of a preventable adverse event in ambulatory care settings (Institute of Medicine, 2006).

ADEs in the ambulatory setting significantly increase the healthcare costs of older adults. For example, Field et al (2005) showed that based on cost estimates and ADE incidence data across the entire population of Medicare enrollees aged 65 and older in

2000, the estimated annual cost for ADEs occurring in the ambulatory setting was more than $2 billion, of which $887 million was associated with preventable adverse drug events. These estimates are however based on a single multispecialty group practice that is aligned to an HMO and provides care to older adults living in a single geographic area. Despite this, reducing the rate of preventable ADEs can result in large cost savings which will offset the substantial amount of money required to implement effective patient safety efforts (Field et al., 2005). The result from the present studies will contribute towards identifying a means of reducing these costs associated with ADEs.

In the three present studies, one of the samples that will be used includes older adults. With an effort to understand their beliefs and the mechanism by which their perceptions of medications can help in reducing ADEs, this next section examines the literature on ADEs among older adults, prevention of these effects and the risk factors associated with ADEs including clinical variables like using an inappropriate medicine.

ADEs among older adults

Patient safety has become a major concern in recent years. Accordingly, many measures have been taken to ensure patient safety, especially in relation to medications for older adults (Lin, Liao, Cheng, Wang & Hseuh, 2008). Medication related morbidity and mortality are major health care concerns among older adults and they contribute to thousands of deaths each year, also costing the US health care system billions of dollars (Page & Ruscin, 2006). With the aging of the US population, people are taking more medications, and this is especially true for older adults. For example, although Americans aged ≥ 65 years and older account for <15% of the US population, they consume nearly one-third of all prescription drugs (Blalock l, 2005; Maio et al., 2006). A national survey

of the ambulatory US population showed that more than 90% of adults age 65 years and older use at least one medication per week, with 40% using 5 or more (Maio et al., 2006). With increases in the use and consumption of prescription medication by older adults, they are prone to experiencing adverse effects.

Adverse drug events occur in older adults (Gurwitz et al., 2003) and 10-25% experiences an event (Gurwitz et al., 2003; Gandhi et al., 2003; Weingart et al., 2005). It is estimated that community-residing older adults experience approximately 2.2 million physician visits and 146 000 hospitalizations as a result of ADEs every year (Spiker, Emptage, Giannamore & Pedersen, 2001). Also, Huang, Bachmann, He, Chen, McAllister & Wang reported that among older adults, ADEs cause 5 to 23% of hospitalizations, 1.5% of ambulatory visits, and 0.1% of deaths (Huang, Bachmann, He, Chen, McAllister, & Wang, 2002).

Ambulatory patients have a significant risk of experiencing ADEs especially among older adults. A large proportion of these ADEs are preventable, and nearly half of the preventable ADEs require hospital admission (Thomsen, Winterstein, Sondergaard, Haugbolle & Melander, 2007). Studies have shown that 15-56% of ADEs are preventable (Bates, Boyle, Vander Vliet, Schnieder, & Leape, 1995; Bates et al., 1997). Having full knowledge of patients' medical history, an understanding of drug contraindications, and a reduction in medications used could decrease the prevalence of drug-related events (Peyriere et al., 2003). According to Pham and Dickman, increasing the number of medications of a patient increases the risk of drug-drug interactions and ADEs, therefore, reviews of patients' medication should be routine as a way of preventing ADEs. In addition, they noted that if a drug is listed on the Beers criteria, (a widely-adopted list of

drugs that labels medications as "potentially inappropriate" for older persons or for older persons with specific medical conditions), physicians can avoid those drugs that are apt to cause a severe adverse drug event simply by selecting alternatives (Pham & Dickman, 2006). On the contrary, Budnitz, Shebaba, Kegler & Richards showed that strategies to prevent adverse drug events should focus on warfarin, insulin, and digoxin rather than 'Beers criteria drugs', as the former are drugs that patients often need (Budnitz, Shebaba, Kegler & Richards, 2007). One of the present studies examines the importance of the types of medications used by older adults in the prediction of adverse drug events.

Risk factors of ADEs among older adults

One possible strategy for preventing ADEs is to prospectively identify patients who are at high risk of an ADE and to target additional resources toward this group (Bates et al., 1999). According to Bates et al (1999), ADEs can be prevented by "risk stratification", in which patients are stratified based on their potential risk, using information that had been gathered prior to the occurrence of the event. An example of this approach might be that when a patient is determined to be of high risk, the pharmacy would be notified so that they can pay extra attention to all medications given (Bates et al., 1999). An understanding of the factors associated with increased risks for ADEs would enable health providers to take account of patients' risk when making decisions about the prescribing and monitoring of drug therapy (Field, Gurwitz, Harrold, Rothschild, DeBellis, Seger et al., 2004). Several patients' characteristics make having an ADE more likely to occur. Some risk factors include age, number of drugs that patient is receiving, and factors that alter drug distribution or metabolism such as renal or hepatic insufficiency, congestive heart failure, anemia, and alcoholism (Bates et al., 1999). Poly-

pharmacy, impaired renal function, female gender, and history of experiencing an ADE have also been found to be factors increasing the risk of an ADE (Field et al., 2004).

Evans, Lloyd, Stoddard, Nebeker, Samore (2005) showed in their 10-year analysis that patient age, gender, number of drugs, comorbidity, and medical service were risk factors for ADEs. Though there are inconsistencies in the evidence of risk factors such as age, gender, chronic conditions and physical function (Chrischilles, et al., 2006; Evans, Lloyd, Stoddard, Nebeker, Samore, 2005; Peyriere et al., 2003); scores on the Charlson Comobordity index were associated with all ADEs after controlling for number of medications, age, and sex (Field et al., 2004). The number and types of drugs taken and perhaps the higher prevalence of chronic diseases lead to greater risk of ADEs in older adults. Drugs significantly associated with having an ADE include anticoagulants, antidepressants, antibiotics/anti-infectives, cardiovascular drugs, diuretics, hormones and corticosteroids (Field et al., 2004).

Limited studies have highlighted the factors that could predict a self-reported ADE, although this measure is usually used in the outpatient settings. Gurwitz & Avorn showed that chronological age is not an independent risk factor for self-reported ADEs (Gurwitz & Avorn, 1991). Similarly, Chrischilles et al (2006) found that neither age, extent of mobility limitations nor comorbidity was independently associated with self-reporting an ADE. The number of medications as a risk factor for ADEs has been widely inconsistent across literature. Number of medications was seen to be an independent risk factor for self-reported ADEs (Chrischilles et al., 2006). Several other studies also found the number of regularly scheduled medications to be a risk factor for ADEs (Bates et al., 1999; Field et al., 2001; Fortescue et al., 2003; Gandhi et al., 2005). However, Hanlon et

al., 1997 and Oladimeji et al., 2008 did not find an association between ADEs and the number of medications. The former study was based on a high risk population, all of whom were taking five or more scheduled medications (Hanlon et al., 1997)

Adverse drug events are a significant medical problem for older adults and in addition to these risk factors; inappropriate drug prescribing is implicated as one of the reasons for such problems (Spiker et al., 2001). Between 14 and 23% of older adults receive a medication they should not be prescribed (Budnitz et al., 2006). The use of inappropriate medications by older adults makes them vulnerable to ADEs and this vulnerability is due to concurrent diseases, multiple prescriptions, reduced liver and kidney function, and forgetfulness (Fu, Liu, & Christensen, 2004).

The study in Chapter Two examines the importance of the use of inappropriately prescribed medicines and socio-psychological variables among older adults. This will significantly contribute towards understanding other risk factors among this population.

Use of inappropriately prescribed medications and ADEs

Inappropriate medication prescribing among older adults is a potential problem that has received a significant amount of attention in the medical literature. One reason is that inappropriately prescribed medication is a common cause of adverse drug events (ADEs) in all types of patient settings (Fu et al., 2004) including physician's offices or hospital outpatient departments (Goulding, 2004). However, the studies that have examined this relationship have not considered that patients' interpretation of their symptoms and subsequent reporting of ADEs, which may be due to their beliefs and treatment representations may play a significant role in this mechanism.

Inappropriate medication prescribing includes the use of medicines that introduce a significant risk of an adverse drug related event where there is evidence of an equally effective but lower-risk alternative therapy available for treating the same condition. It also includes the use of medicines at a higher frequency and for longer than clinically indicated; the use of multiple medicines that have known drug-drug interactions; and the use of beneficial medicines that are clinically indicated but not prescribed for age or other reasons (Gallagher, Barry & O'Mahony, 2007).

Among older adults, inappropriateness of drug therapy is a significant issue because they take many more medications than younger groups (Fu et al., 2004). The developments of specific lists of medications that are considered potentially inappropriate for older adults such as the Beers Criteria make it easy to study prescribing patterns and examine the relationship of these medications to ADEs. Medications included within the Beers Criteria are generally considered to be ineffective or to have potential risks that exceed the benefits. Therefore, the likelihood of older patients experiencing ADEs with these medications are considered high (Page et al., 2006).

The Beers Criteria are a list of medicines that have been identified as potentially inappropriate for use in older adults. The criteria were introduced in 1991 to help researchers evaluate prescription quality in the nursing homes. Based on expert consensus developed through an extensive literature review and a questionnaire evaluated by nationally recognized experts in geriatric care, clinical pharmacology, and psychopharmacology, the criteria were developed. In 1997 and 2003, the criteria were updated to apply to persons aged 65 years or older, to include new medications judged to be ineffective or pose unnecessary risk and to rate the severity of adverse outcomes

(Budnitz, Shebab, Kegler & Richards, 2007). Three categories of inappropriate medications are found within these criteria including: 1) medications that generally should be avoided in older adults because of a high risk of adverse effects, 2) drug prescriptions that should not exceed a maximum recommended daily dose, and 3) medications to be avoided with certain co-morbidity.

The Beers Criteria have been established as a standardized tool for pharmacologic research and have been used to examine the prevalence and trends of prescribing potentially inappropriate medications to older people. Associations between inappropriate drug use and patient health outcomes have been observed. For example, a study of nursing home residents showed that those who received any potentially inappropriate medication had a greater risk of being hospitalized and death than those not receiving an inappropriate medication (Gallagher et al., 2007; Lau, Kasper, Potter, Lyles, & Bennett, 2005). In addition, Perri III et al (2005) found a positive and significant association between inappropriate medication use and the occurrence of hospitalizations, emergency department visits and deaths among older adults in a Georgia nursing home (Perri III et al., 2005). Though these studies were based on local populations or health care settings which limited the generalizability of the results, Fu et al (2004) found a relationship between inappropriate prescription drug use and health outcomes in older adults among a nationally representative population sample. Also, among a Medicare Managed care population, patients receiving inappropriate medications were found to use more healthcare services including hospital in-patient and outpatient visits, emergency department and general practitioner visits (Fick et al., 2001; Fu et al., 2004). These

studies suggest that inappropriate prescription drug use can be costly in healthcare resources and outcomes.

Studies have examined the relation of inappropriate medication prescribing and the occurrence of ADEs and other health outcomes in different clinical settings. For example, an Italian study showed that potentially inappropriate medication use (defined as Beers Criteria medications) in hospitalized older patients was not significantly associated with ADEs, length of stay, or in-hospital mortality (Onder et al., 2005). Based on a review by Jano and Aparasu, 2007, combined evidence from all healthcare settings suggested that inappropriate medication use was associated with adverse events, health costs and hospitalization in the community setting. However, only one study examined the relationship of the use of a Beers Criteria drug and experiencing an adverse drug reaction (ADR) in the community setting. In this study by Chang et al (2005), inappropriate medication use as determined by the Beers Criteria increased ADRs. It was the first study to suggest a positive association between ADRs and prescribing practices that fail to comply with the Beers Criteria (Chang, Liu, Yang, Yang, Wu, & Lu, 2005).

These studies that have examined the relationship of Beers Criteria medication prescribing and ADEs among patients have identified and defined ADEs in different forms. For example, Chang et al., 2005, Onder et al., 2005, and Page et al., 2006 used the Naranjo scale with different cut off points as a means of identifying ADEs. This is the first study to examine the relationship of a Beers Criteria medication to self-reported ADEs in an outpatient setting. This is important because the Food and Drug Administration has estimated that the cost of hospitalizations due to inappropriate medication use averages $20 billion annually (Fu et al., 2004). Also, self-reported ADE is

an important measure of adverse outcomes especially in the ambulatory setting. A description of the list of Beers Criteria medicines used in the analysis is seen in Appendix A.

In addition to the Beers Criteria, there are other quality measures used in evaluating medication use and determining proper management of medications among older adults. This next sub-section describes this quality measure.

The ACOVE Criteria

Recognizing the magnitude of drug-related issues among older adults, panels of geriatric experts rated medication problems among the most important quality-of-care problems for older adults. Hence, mechanisms to evaluate and improve the quality of medication management were developed. To this end, Higashi et al (2004) provided a systematic evaluation of medication management for a sample of older adults by using a set of "explicit process of care indicators developed and implemented in the Assessing Care of Vulnerable Elders (ACOVE) project" (Higashi et al., 2004). In this project, a set of quality indicators were used to evaluate the care provided to vulnerable older patients. The processes of care included the domains of prevention, diagnosis, treatment and follow-up and this spectrum of care contained 22 conditions which are considered important in the care of older patients. The methods for selecting the conditions and developing quality indicators included using systematic literature reviews and various judgments by expert panels. From the final ACOVE set of quality indicators, 43 quality indicators that pertained to pharmacologic care were identified. These included quality indicator descriptors such as avoiding inappropriate medications and prescribing indicated medications.

The indicators were stratified into 4 domains of pharmacologic care. For example, the “prescribing indicated medications” domain contained 17 indicators. Notable among these quality indicators was calcium and vitamin D for patients with osteoporosis. The “avoiding inappropriate medication” domain contained nine indicators. Seven of the quality indicators restricted the use of specific drugs or drug classes, and the other two quality indicators specified choice of drug or drug class to treat a certain condition. In the present study, in addition to using the Beers Criteria, inappropriate medication use and prescribing was identified using the ACOVE Criteria and the relationship between failed quality indicators and ADEs was examined. This is the first study to use these set of quality indicators in identifying an inappropriately prescribed medication and examining its relationship to self-reported ADEs. A description of the ACOVE quality indicators used in the analysis and the operationalization of the Criteria are shown in Table B1 and Table B2 respectively.

The reporting of adverse drug events to a health provider is a means by which patients may cope with the symptoms, unwanted reactions or drug-related problems that they are experiencing. Similar to adherence, the patient’s illness beliefs and their perceptions of treatment may inform this coping strategy. However, symptoms occur before ADEs and the reporting of these symptoms which may/may not be due to a medicine is an example of a coping behavior that may be influenced by similar beliefs. This next section discusses symptom reporting as a coping behavior, its relation to ADEs and the relationship with beliefs in medicines.

Symptom reporting as a coping behavior

Adverse drug events (ADEs) usually occur before symptoms are reported by patients yet the process by which these symptoms may be identified are applicable to the attribution of adverse drug events. Symptom recognition, identification and cause attribution are important means of identifying and preventing ADEs (Dewitt & Sorofman, 1999). Patients can attribute the symptoms being experienced to causes such as age, disease or medication (Oladimeji, Farris, Urmie, & Doucette 2009 (forthcoming). Attribution of causality may however be wrongfully represented and may differ from person to person. If the occurrence of an adverse drug event is due to the use of a medication, it is important for patients to report these medication-related symptoms.

The reporting of symptoms is important because if predictive factors of ADEs can be identified, health providers may be able to identify early symptoms of these events and prevent the ADE and/or respond quickly to the health threat (Field et al., 2001). Also, if patients and physicians and/or health providers communicated more effectively about medication related symptoms, then the intensity and duration of the symptoms experienced may be reduced (Weingart et al., 2005).

Though the reporting of medication-attributable symptoms is an important process in identifying ADEs, patients sometimes fail to report their symptoms to physicians. In one study, patients discussed 196 (69%) of their 286 medication symptoms with a physician and 22% of these symptoms were serious enough to require a visit to a physician's office, clinic or emergency department (Weingart et al., 2005). Another study showed that of 742 patients reporting symptoms in a questionnaire, only 54.2% claimed to have reported some or all of these symptoms to their doctor (Jarensiripornkul, Krska,

Capps, 2002). In a similar study, Jarensiripornkul and colleagues showed that only 42% of patients who claimed to have symptoms they suspected to be an adverse effect reported them (Jarensiripornkul, Krska, Richards, Capps, 2003). Patients may not understand the importance of medication symptoms and therefore fail to report them. These patients may not be sure if the medication actually caused the symptom. Also, they may not want to bother the physician or tell him/her disappointing news of not being able to tolerate the therapy. The tendency to refuse to report symptoms however has implications. Patients unreported medication symptoms may lead to preventable ADEs (Weingart et al., 2005). The report of medication symptoms by patients is therefore a valuable source of information about medication safety.

Limited studies have examined factors that may be related to symptom reporting. The environment has been shown to influence the reporting of symptoms by individuals. For example, when individuals live alone, in rural environments or work in an un-demanding or un-stimulating environment, symptom reports have been shown to be elevated. Symptom reports are also influenced by individual's disposition to stress and/or trauma. People who have a history of negative moods and reports or recent traumatic experiences may be especially prone to increased symptom reporting (Pennebaker, 2000).

Few socio-demographic factors have shown relations in the identification, labeling and reporting of symptoms. For example, gender differences exist in the way individuals notice, define and react to the symptoms that are experiencing. Specifically, women have been shown to be more sensitive to cues from their external environment than men who may focus on their internal 'physiologic cues' in defining their symptoms. This may inherently influence their report of symptoms which may differ across both

groups. For example, women usually report more intense and frequent somatic symptoms; pain in more body sites and pain of longer duration than men. These differences occur regardless of the time period/time-line of the symptoms experienced and after excluding both gynecologic and reproductive symptoms. It has therefore been suggested that man and women may have varying styles of symptoms and symptom reporting (Pennebaker, 2000; Barsky, Peekna & Borus, 2001).

Socioeconomic factors such as social class status have also shown significant influences on symptom perception and reporting. Among a German population, elevated levels of symptom reporting have been significantly associated with a low social class status among both male and female groups (Ladwig, Marten-Mittag, Formanek & Dammann, 2000). In another study, Kauhanen, Kaplan, Julkunen, Wilson & Salonen showed that people in lower socio-economic groups with less education have significantly more difficulty identifying, processing and verbally expressing their inner feelings to their health providers (Kauhanen, Kaplan, Julkunen, Wilson & Salonen, 1993). On the other hand, individuals on higher social strata may have broader and numerous coping mechanisms available to them and subsequently, the use of these coping strategies will reduce the perceptions of symptoms and the report to health providers (Ladwig, Marten-Mittag, Formanek & Dammann, 2000). Hence, if attribution of cause precedes the identification and reporting of symptoms, certain socio-demographics or clinically significant factors may be related to symptom attribution.

The symptoms reported to a physician by a patient may be related to the patient's reporting style, readiness or reluctance to disclose the distress associated with the symptoms, the social context the patient uses in evaluating his symptoms and whether

symptoms being asked about are current or occurred in the past (Barsky, Peekna & Borus, 2001). An individual's perception of his symptoms may influence the healthcare he seeks. The type of information that is sought, the decision to seek care and the urgency at which this care is sought may be influenced by symptom perceptions. Understanding a patient's perception of his or her symptoms may give a health provider clues about the overall health behavior of the individual. It is important for health providers to determine the relationship of patient's symptom perception to their responses to their health problems so that proper patient education and individualized interventions can be devised in order to maximize positive patient outcomes (Posey, 2006).

However, patients and clinicians may differ in the perceptions of illnesses. Kleinman developed an 'explanatory model of illness' which emphasizes variations in patients and clinicians notion of illness (Kleinman, 1980). If there are variations in symptom attribution and illness representations between both groups, it becomes important to compare these attributions and examine if there is incongruence. This is significant in the development of individualized interventions to improve patient health outcomes because an observation of incongruence will require appropriate education of the patient about his symptom, symptom perceptions and illness before these programs can be developed.

Eliciting patients' perceptions of their symptoms during clinical assessments and consultations may provide insight into their beliefs and coping style which will inform the development of treatment interventions. Patients' beliefs and attribution of causality play a critical role in symptom reporting (Ownsworth, Fleming & Hardwick, 2006). In the extended self-regulatory model, patients' beliefs in medicine and their illness

representations influence the coping strategy the individual uses in managing his symptoms. Since adherence as a coping behavior has shown significant relationships with concern beliefs, symptom reporting should also be influenced by these beliefs theoretically. In addition, a recent study showed that concern beliefs in medicine were significantly related to the reporting of symptoms to health providers after controlling for socio-demographics, clinical and behavioral factors (Oladimeji et al., 2009 (forthcoming)).

In Chapter Three, patients' attributions of the causes of the symptoms that they experienced and how this compares to clinicians' assessments is examined. Since patients' symptom reporting is related to concern beliefs in medication and symptom identification and attribution to a cause precedes the reporting of a symptom, it is important to understand if symptom attributions might be related to concern beliefs.

In this project, concern beliefs are examined in more depth. Specifically, their description, changes over time and their relationship to patient health outcomes such as symptom reporting and reporting an ADE are examined. The theoretical framework that ties the three chapters in this project together and explains the different objectives within each of them is the extended self-regulatory model. This model also relates concern beliefs as a concept to coping behaviors other than adherence. This next section discusses the Self-regulatory model and the conceptual model for this project.

The Self-regulatory model

The Common Sense Model and the Self-regulatory model overlap each other theoretically and the extended self-regulatory model which is the theory of focus is based on these two previous models. Explanations for variations in responses to health threats

can be done using these models. However, since the 'common sense representations' of individuals about their symptoms were first identified and subsequently lead to the development of the extended self-regulatory model, a description of these representations will first be done (Lau, 1997).

Levanthal and his colleagues wanted to know what adaptations and coping efforts need to made and maintained for those experiencing chronic illnesses. This led to the development of the Common Sense Model (CSM) which examined three main constructs: 1) representating illness experience, 2) planning of coping responses and behaviors guided by the experience, and 3) monitoring the success or failure of the coping efforts (Difenbach & Levanthal, 1996; Hale, Treharne, & Kitas, 2007; Nerenz & Levanthal, 1983;). The Common Sense Model describes the dynamic parallel cognitive processing of how individuals regulate their responses both to 'illness danger' ('what is this health threat, what can I do objectively do about it?') and to the person's regulation of 'emotional control' ('How do I feel about it, what can I do to make myself feel better about it?') (Hale et al., 2007).

A response to a health threat is the result of a regulated system which can be classified into three broad processes. First, the cognitive and emotional representations of the health threat are developed. These representations reflect the individual's interpretation of the health threat and can be due to internal cues such as symptoms. Second, the individual develops an action plan also called a coping strategy. The coping strategy adopted by the individual is perceived by him/her to be appropriate to the beliefs that are presently being held. Lastly, there is the coping appraisal process. This involves

evaluating whether the coping strategy was effective in achieving (or not) the outcome or goal (Levanthal, Nerenz, & Straus, 1978; Levanthal, Levanthal, & Cameron, 1998).

In essence, the central proposition of this theory is that patients' illness beliefs and representations influence their coping responses which subsequently impact the evaluation of their outcomes. Illness beliefs are formed based on both the abstract and actual sources of information available to people. Providing patients with information gives them a map against which they can evaluate their actual illness experience which can further enhance or determine their behavior (Levanthal, Levanthal, & Cameron, 1998; Levanthal, Nerenz, & Straus, 1978; Llewellyn, McGurk, &Weinman, 2007).

Variations in patient outcomes that cannot be explained by socio-demographics, disease or treatment related factors can be explained using the Common Sense Model (Llewellyn et al., 2007). The illness beliefs and representations within this model combined with people's prior ideas about illness enable them to make sense of their symptoms and guide any coping actions (Llewellyn et al., 2007).

Five components of these illness representations have been described as:

1) Identity: This is the label or name given to the condition or illness and the symptoms that appears to go with it. People like to label or give a name to their symptoms although, once given a label, they will seek to identify the symptoms as an evidence of the label (Meyer, Levanthal, Guttmann, 1985).
2) Cause: This is the person's personal ideas about the perceived cause of the condition which may not be completely accurate. These representations are based on information that may have been gathered from personal experiences as well as

from the opinions of significant others and/or health providers (Diefenbach & Levanthal, 1996; Meyer, Levanthal, Guttmann, 1985).

3) Time-line: This is an individual's predictive perspective on how long the condition he is experiencing might last, i.e. is the illness acute or chronic? (Diefenbach & Levanthal, 1996; Meyer, Levanthal, Guttmann, 1985)
4) Consequences: These are individual's beliefs about the consequences of the condition and how it might impact them physically and socially. These representations may sometimes develop into realistic beliefs over time (Diefenbach & Levanthal, 1996; Meyer, Levanthal, Guttmann, 1985).
5) Curability/Controllability: The beliefs about whether the condition can be cured or kept under control and the degree to which the individual can contribute to achieving this control (Diefenbach & Levanthal, 1996; Meyer, Levanthal, Guttmann, 1985).

The way illness representations are related to coping and subsequently a strategy for dealing with symptoms has been described. Illness representations initially influence coping efforts and these efforts lead to outcomes; therefore, coping acts as a mediator. On the other hand, coping responses of an individual could influence illness representations which may then impact the subsequent choice of a coping strategy (Hale et al., 2007). For example, when people with chronic illnesses obtain new information about their illness or condition, they assess their attempts to moderate or cope with its effects, which then cause new representations to be formed and developed based on their experiences. It is expected that these representations will be linked to the selection of a coping procedure or an action plan. Also, the representations may guide the patients' preference for

treatment, and subsequently the behaviors they engage in, e.g. adherence to treatment (Hale et al., 2007). The extended self-regulatory model incorporates constructs from the Common Sense Model of illness such as illness representations and includes perceptions of treatment in the prediction of coping behaviors. This next section describes the model.

The extended self-regulatory model

From a review of the literature, it is understood that the self-regulatory model provides an explanatory framework for how beliefs and behavior are related based on illness perceptions. Theoretically, the beliefs underlying these illness representations suggest that the selection of a coping procedure, either to seek (or not seek) medical care, is driven by patient's beliefs about the nature, duration, causes, consequences and control of the symptoms experienced (Horne, Weinman & Haskins, 1999).

The Self-regulatory model attempts to explain how people may adapt to and/or manage the health threats they experience such as symptoms. Based on this model, individuals are viewed as active problem-solvers who try to assign meaning to their symptoms, and this typically involves a representation of the symptom and a coping strategy for dealing with it (Difenbach & Levanthal, 1996). The coping behavior has been described as a 'common sense' response to cognitive and emotional interpretation of symptoms. A continuation of the behavior may be dependent on an evaluation of whether the coping strategy has worked in the past or not (Horne & Weinman, 2002). When an individual experiences a symptom, the illness representations such as identity, timeline, cause, control and consequences may drive coping and subsequent appraisal and may lead to self-management of symptoms (Horne & Weinman, 2002; Levanthal, Brissette & Levanthal, 2003). The mechanism of an individual's symptom representation is similar in

both the Common Sense Model and the Self-regulatory Model. However, the latter model examines how these processes are involved in the self-regulation and self-management of symptoms experienced based on a feedback mechanism. To further explain how individuals manage their symptoms in relation to their medicines, similar illness representations in addition to treatment perceptions and beliefs are described in a model called the extended self-regulatory model (shown in Figure 1 below). This model is the best approach to study concern beliefs in medicines compared to other health behavior models because it takes account of these psychosocial factors which are usually involved in treatment decisions. It has also been suggested that the ability of the self regulatory model to predict medication-taking behaviors such as adherence can be enhanced by including treatment or medication beliefs into the model (Horne, 1997).

In the extended self-regulatory model, Horne, Weinman & Haskins showed that necessity and concern beliefs about medicines are two main themes that patients use when interpreting the symptoms they are experiencing and the casual attributions related to their medicines (Horne, Weinman & Haskins, 1999). For example, people with similar medicines for the same health condition may differ in their perceptions of the need for the medicine, their concerns regarding experiences of medication adverse effects, the disruptive effect of the medicines on their daily life, as well as anxieties or worries that regular use of the medicine would lead to dependence, accumulation within the body and long term effects (Horne., 2003; Horne, Weinman & Haskins, 1999). Beliefs about the need for a treatment or medicine are directly related to illness perceptions while concern beliefs reflect the perceptions and experiences encountered as a result of using solutions to deal with the illness (Horne & Weinman, 2002).

The extended self-regulatory model has both a cognitive and emotional representation of treatment which is parallel processed when a symptom experienced requires a treatment or medicine for dealing with it. The cognitive representations are reflected in responses on the concern belief scale such as “My medicines disrupt my life”. Cognitive representations are based on how the individual rationalizes the symptoms based on his prior experiences, information and illness perceptions which then informs his/her behavior related to the treatment. Emotional representations occur concurrently as treatment perceptions are processed and these are reflected as concerns about the medication. For example, “Having to take my medicine worries me’ from the concern belief scale. Anxieties are emotional representations of concern beliefs in medicines and they can influence coping responses through a direct effect on illness representations. For example, in response to a health threat, anxieties may stimulate the planning and use of problem-focused strategies to manage the threat. Also, emotion focused strategies that are guided by illness representations may be enhanced by anxiety. Though anxiety is just one the representations of concern beliefs, these concerns can “foster sustained vigilant coping over time by enhancing accessibility to representations and coping plans”. Protective behaviors such as seeking medical care for unusual symptoms by first of all reporting them to the health provider may also be developed (Cameron, 2003).

When an individual is involved in self-regulation or self-management of illness, they do not just have their ideas about the nature of the illness; they also have views about the solution to control the illness that is being offered by the health provider. For example, in deciding whether to tell a health professional about symptoms being experienced, the patient does not only have to think about whether the symptom warrants

reporting but also about whether reporting the symptom will be helpful. In particular, a decision to report an unwanted reaction or problem from a medicine, such as an ADE, or any other symptoms will be influenced by an interaction of individual beliefs about the necessity of taking that action towards improving the illness and concerns about the potential adverse effects of doing it (Horne & Weinman, 2002).

The extended self-regulatory model as shown below is the theoretical framework underlying how concern beliefs in medicines are related to illness perceptions and coping behaviors. Based on this model, it has been proposed that illness representations and treatment perceptions are interwoven when a coping procedure for dealing with a symptom also involves making a decision about a treatment. These decisions may include adhering to the treatment, reporting a symptom related to the treatment or self-reporting an adverse event experienced due to the treatment.

Treatment perceptions are triggered by symptom experiences and information available to the individual. These perceptions may differ depending on the attribution of cause by the individual. For example, attribution of symptoms to a specific illness which may also be influenced by the individual's emotions reinforces the need for the specific medication prescribed for the condition, while attribution of symptoms to side effects reinforces their concerns about taking the treatment (pathway 1a &1b). In this model, cognitive and emotional representations of treatment are processed in a parallel manner (pathway 2a for the cognitive & 2b for the emotional).

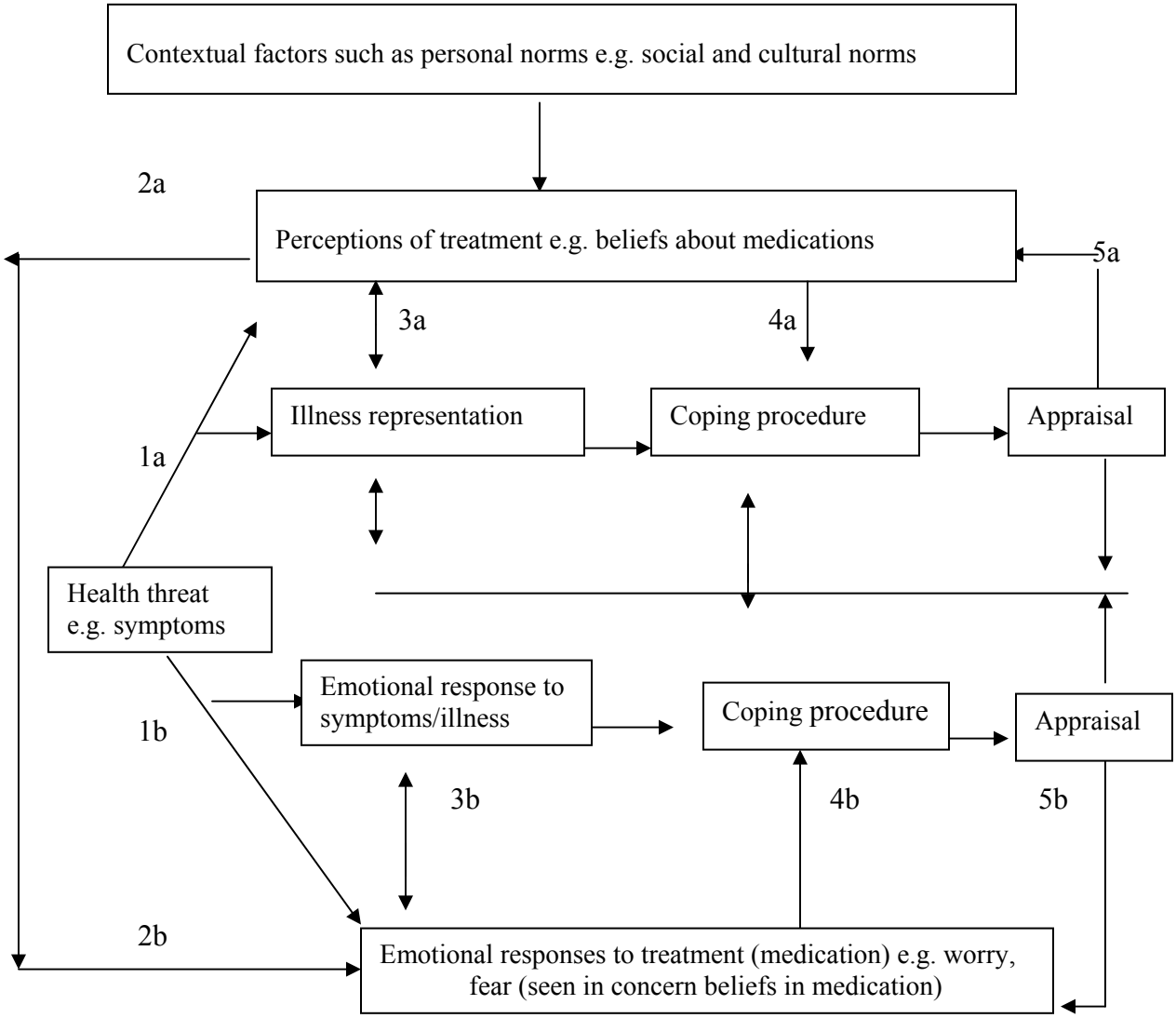

Figure 1. Conceptual model of treatment perceptions (beliefs in medication) in the extended self-regulatory model.

Using these representations, illness perceptions and treatment beliefs are internally evaluated by an individual and a 'common sense coherence' of both is attempted by a person (pathway 3a & 3b). Also, these treatment perceptions influence the coping procedure for dealing with a symptom e.g. report (or not report) a symptom or ADE (pathway 4a & 4b) and when the outcome of doing this coping behavior is appraised, treatment representations such as beliefs about medicines could change (pathway 5a & 5b). The process of self-regulation then goes on again in a feedback loop with the same mechanisms completed when performing a coping behavior.

Considering reporting of symptoms and their attribution to ADEs, it is possible that individuals think of these mechanisms in the reporting of health threats (Difenbach & Levanthal, 1996; Horne et al., 1999; Levanthal, Difenbach, & Levanthal, 1992). The representation of the symptom experienced by people may guide their coping strategy for dealing with it, which may involve adhering to treatment, reporting the symptom or self-reporting an ADE. Beliefs in medicines are important variables involved in these processes; yet, limited research has examined this concept in more depth. Their importance as a mediator in determining health behaviors and their responsiveness to health outcomes such as experiencing an ADE or symptom is not known. Beliefs in medicines, especially concern beliefs in medicines can predict behaviors related to managing medicines and provide a mechanism for reducing adverse health outcomes. For example, an individual who experiences a symptom and reports it to his/her health provider compared to another individual who experiences a similar symptom but does not report it may have different beliefs about their medicines and concerns about its effect. The former person probably has stronger concern beliefs related to the adverse effects of

the medicine and may employ such coping behavior because a past negative experience with a similar medication or negative outcome due to using the medication has impacted his/her beliefs. Both persons have different coping procedures for dealing with their health threats and the outcome of the strategy (report symptoms or not) will determine future perceptions of their treatment. Beliefs in medicines are influenced by the appraisal of an outcome which can then determine future illness representations and behaviors related to managing symptoms and medicines. The extended self-regulatory model is the theoretical framework that allows for further exploration of the concept of concern beliefs in medicines because it examines the relationship between cognitions, emotions, individual definition of health threats and the outcome behaviors related to these beliefs.

Summary

People have beliefs about medicines in general, as well as beliefs about medications prescribed for specific illnesses. Beliefs in medicines are related to health and illness behaviors via the extended self-regulatory model. This model shows that a combination of illness and treatment perceptions is predictive of a coping behavior such as adherence. Other coping behaviors such as symptom-reporting are important in managing medications and are associated with self-reporting an ADE. Though beliefs in medicines appear to be an important variable associated with ADE, little is known about which individuals hold what beliefs and the responsiveness of beliefs in medicines to factors such as an experiencing ADE or symptoms. Beliefs in medicines may be an important intervening variable in understanding health behaviors. This concept needs to be more fully explored and its potential impact on patient outcomes investigated.

This project consists of three studies that aim to examine concern beliefs in medication in more depth. The research questions to be answered include: 1) Do concern beliefs remain a significant risk factor for predicting self-reported ADEs, when controlling for use of an inappropriately prescribed medication?, 2) How does attribution of symptoms compare across patients and clinicians and are these attributions related to concern beliefs?, and 3) Do concern beliefs in medication change over time or remain stable and what are the factors that may drive changes in concern beliefs?

The first study sets the stage for understanding if concern beliefs remain consistent in their relationship to self-reported ADEs, despite the addition of clinically important variables such as inappropriate medication use and number of medications. Previous studies have shown that concern beliefs is associated with self-reporting an ADE and this result remained consistent after the start of Medicare Part D (Oladimeji et al., 2008; Oladimeji et al., 2008 (in review)). However, inappropriately prescribed medicines is an important clinical variable related to an ADE and it may be significantly associated with the adverse outcome, not concern beliefs (Onder et al., 2005; Page et al., 2006). It was hypothesized that concern beliefs will remain as the main risk factor for self-reported ADE despite the use of inappropriate medication by patients. This is because the way symptoms are attributed to a medication may be based upon an individual's toleration (or not) of the adverse effects and the individual's concerns about using the medicines which may drive his/her interpretation. Also, patients may not be aware of whether they received an inappropriate medicine or not. The interpretation of the unwanted symptoms the individual experiences may not be reflected by the inappropriateness of the medication.

The second study examines how patient symptom attributions may be related to concern beliefs. In a recent study, concern belief was associated with the reporting of symptoms that may not necessarily be related to a medicine (Oladimeji et al., 2009 (forthcoming). Since the attribution to medications was done by individuals, the symptoms experienced could be related to a medicine or be due to other reasons such as their disease conditions. In fact, it is known that patients and clinicians have different notions about symptoms, illnesses and its treatment and these could guide choices for the behavior that would be exhibited by both groups including adhering to treatment and reporting unwanted side-effects of treatment (Kleinman, 1980; Cohen, Reimer, Smith, Sorofman & Lively, 1994). In this study, patient's symptom attribution will be compared to an expert panel's assessment of symptom attribution. Also, concern beliefs which can influence illness representations may drive these attributions. Beliefs in medicines might inform a patient's expectations and 'represent a source of bias in symptom cause attribution in situations of symptom ambiguity' (e.g. whether the symptoms are medication related, illness-related or signs of ageing) (Siegel, Dean, & Schrimshaw, 1999; Horne, 2003). Therefore, the relationship of these attributions to concern beliefs will be explored.

The third study investigates how concern beliefs may behave over time and examines factors that may be related to its stability in two populations including Medicare enrollees and people with self-reported physical limitations. An examination of how concern beliefs behave over time is pertinent because its association with health behaviors will guide how it can be used theoretically and clinically in future studies. Also, an understanding of the stability of the concept in populations will allow

determinations of the factors that may drive the change (if present). Interventions may also be focused elsewhere if found to be stable.

Beliefs in medicines are important in predicting important behaviors related to managing medications, which may provide a mechanism for reducing adverse drug events. If concern beliefs in medicines are more closely linked to ADE, it is important to explore the concept, its relationship to other adverse outcomes and its processes in managing health threats and coping behaviors.

Practice implications

By examining illness representations and intertwining them into interventions, health professionals might be able to predict certain outcomes that are potentially alterable in a favorable way for an individual. Knowledge of these individual representations may therefore guide and contribute to the 'development of interventional programs such as cognitive behavioral interventions' (Hale et al., 2007). Also, with careful guidance, explanation and education, patients can be helped in constructing useful treatment representations that will enhance medication taking outcomes and assist in developing and improving individualized patient self-management education programs.

If health providers can perceive what patients are prone to having unstable concern beliefs about their medication, a program or intervention that seeks to reduce this anxiety or allows them self-monitor any unwanted symptoms or reactions may help reduce these beliefs and subsequently increase symptom reporting. An increase in symptom reporting can help reduce preventable ADEs and the costs associated with medication therapy problems and outcomes. On the other hand, patients with stable beliefs may not require such cognitive interventions, therefore, other programs aimed at

managing medicines and adverse outcomes can be developed for them. In addition, examining whether concern beliefs are related to symptom attribution may be a significant step towards improved clinical consultations between patients and clinicians. If patients "cause" attribution of symptoms is correct, attributions will not be misplaced, patients and clinicians' explanatory models on illness and treatment will not differ greatly and the communication between a patient and the health provider about their symptoms and ADEs can be enhanced.

Concern beliefs in medication is a socio-psychological concept which influences patient's representations of the symptoms they experience. Establishing the importance of this socio-psychological variable as a risk factor for self-reported ADEs, despite the use of inappropriate prescription drugs by a patient, will enhance the understanding of clinical researchers and practitioners concerning the mechanism of ADEs and symptom reporting. As well, having previous ADEs and stronger concern beliefs in medicines can lead to less adherence to medicines. Patients who have experienced previous ADEs are less likely to take their medicines as directed (Neame & Hammond, 2005; Phatak & Thomas, 2006). Also, they may develop strong concerns and anxieties about their medicines based on their negative experience with use. If patients perception of their medicine can change based on their medication use which may then impact their adherence to medicine;, further description of concern beliefs in medicines and its relationship with ADEs will enhance the understanding of the mechanism of medication adherence. Also, the link between ADEs and medication adherence may be enhanced with a better understanding of concern beliefs in medicines and its mechanism in patients' medication use.

Table 1.1: Concern beliefs in medicines and inappropriate prescriptions: risk factors for self-reported adverse drug events in older adults (for submission in Journal of American Geriatric Society)

Data	**Study objectives**	**Dependent variable**	**Predictor variables**	**Control variables**
Medicare 2007 data	1. Identify the frequencies of inappropriate medication use among older adults in the outpatient setting	Inappropriately prescribed medicines using Beers Criteria and modified ACOVE quality indicators		
	2. Examine if there is an association between the use of inappropriate medication, concern beliefs in medicines and self-reported adverse drug events (ADEs) among older adults in the outpatient setting	Self-reported ADE measured as "did you see a doctor about any side effects, unwanted reaction or other problems from medicines you were taking in the past year?".	1) Inappropriately prescribed medicines using Beers Criteria and modified ACOVE quality indicator 2) Concern beliefs in medicines	1) Socio-demographics 2) Clinical characteristics 3) Behavioral characteristics

Table 1.2: Variation in patients' and clinicians' attribution of symptoms and its relationship to concern beliefs in medicines (for submission in Research in Social and Administrative Pharmacy journal)

Data	**Study objectives**	**Dependent variable**	**Predictor variables**
1) Medicare 2007 data 2) Clinician ratings	1. Determine if attribution of symptoms to a cause is different by comparing attribution across patients and clinicians	Open ended question of why subjects did not report the symptoms they experienced to their doctor	
		Clinician confidence ratings about patient symptoms due to medicine	
	2. Quantify the association between concern beliefs and attribution of symptoms	Concern beliefs in medicines	Agreement between patients and clinicians on patients symptom attribution to medicines or another reason (agree/disagree)
	3. Examine if individuals with similar symptom attributions have certain clinical and/or socio-demographic characteristics	1) Socio-demographics 2) Clinical characteristics	Agreement between patients and clinicians on patients symptom attribution to medicines or another reason (agree/disagree)

Table 1.3: Concern beliefs in medicines: changes over time and factors related to its stability (for submission in Social Science & Medicine journal)

Study	Data	Study objectives	Dependent variable	Predictor variables	Control variables
Study 4.1	Medicare 2005 and 2007 data	1. Examine if concern beliefs remain stable or change over time	Concern beliefs in medicines.	Time (Before and After Medicare Part D)	
		2. Examine the characteristics of the groups of individuals whose beliefs change or remain stable	Concern beliefs in medicines.	1) Socio-demographics 2) Clinical characteristics 3) Behavioral characteristics	
		3. Investigate what factors might drive the change in concern beliefs.	Change in concern beliefs from time 1 to time 2.	1) Self-reported adherence 2) Self-reported ADEs 3) Symptom reporting to physicians 4) Self-rated health	Number of medicines, Number of symptoms experienced, Age, Gender, Race
Study 4.2	LWD/CMM data	1. Examine if concern beliefs remain stable or change over time	Concern beliefs in medicines	Time (Before and After six months follow-up)	
		2. Examine the characteristics of the groups of individuals whose beliefs change or remain stable	Concern beliefs in medicines	1) Socio-demographics 2) Clinical characteristics 3) Behavioral characteristics	

Table 1.3 continued

Study	Data	Study objectives	Dependent variable	Predictor variables
	3. Investigate what factors might drive the change in concern beliefs if they indeed do change	Change in concern beliefs from time 1 to time 2	1) Self-reported adherence 2) Self-reported ADEs 3) Symptom reporting to physicians 4) Self-rated health	Number of medicines, Number of symptoms experienced, Age, Gender, Race

CHAPTER II

CONCERN BELIEFS IN MEDICINES AND INAPPROPRIATE PRESCRIPTIONS: RISK FACTORS FOR SELF-REPORTED ADVERSE DRUG EVENTS IN THE ELDERLY

Medication toxicity and drug-related problems have profound health, safety, and economic consequences for older adults and have been implicated in 30 percent of their hospital admissions. Adverse drug events (ADEs), which has been defined by the Institute of Medicine (IOM), 2006 as an injury resulting from medical interventions related to a drug have unwanted health outcomes and may be related to preventable problems in older adults 65 years and older, such as depression, constipation, falls, immobility, confusion and hip fractures (Al-Tajir & Kelly, 2005; Bates, 1995; Fick et al., 2001; Hanlon, 1997). Hanlon and his colleagues found that 35% of ambulatory older adults on five or more medications experienced an ADE and 29% required health care services such as physician visits, emergency room visits, or hospitalization for the ADE (Hanlon, 1997). Drug-related problems cause 106,000 deaths annually at a cost of $85 billion. It has been estimated that the cost of medication-related problems is $76.6 billion for ambulatory care, $20 billion for hospitals and $4 billion for nursing home facilities (Bates et al., 1997; Bootman, Harrison & Cox, 1997). If medication-related problems were ranked as a disease by cause of death, they would be the fifth-leading cause of death in the United States (Bootman, Harrison & Cox, 1997; Hanlon, 1997). Though the impact of ADEs is huge, about 15-56 percent is largely preventable (Bates, Boyle, Vander Vliet, Schnieder, & Leape, 1995; Bates et al., 1997; Gandhi et al., 2003). One potential strategy

is to identify prospectively those patients who are at high risk of an ADE and to target interventions towards this group (Bates et al., 1999).

Despite the identification of risk factors, few studies have examined the relationship of these factors to self-reported ADE. Self-reports of ADEs in older patients have high detection rates and are often more accurate than other means of detecting ADEs such as chart reviews and medical records (Chrischilles et al., 1992; Hanlon et al., 2001). Patient self-reports can identify ADEs not obtained by other methods (Ernst & Grizzle, 2001; Gandhi et al., 2003;) and in one study, it resulted in a five-fold greater frequency of ADEs than clinician report and computerized searching of electronic notes (Gandhi et al., 2003; Gurwitz et al., 2003). This measure of ADE is therefore important especially in outpatient settings, as self-reported ADEs represents the patients' view of their symptomatology and is an important basis for identifying ADEs among community-dwelling older adults.

In terms of risk factors, the use of an inappropriately prescribed medication has been identified as a risk factor for an ADE in two studies (Chang, Liu, Yang, Yang, Wu, & Lu, 2005; Passarelli et al., 2005). The frequencies of inappropriate medicine use based on the Beers Criteria, a consensus based list of medications to be avoided among older adults has ranged from 11.6% to 45% (Beers, Ouslander & Fingold, 1992; Blalock et al., 2005; Chang et al., 2005; Curtis et al., 2004; Fick, Mion, Beers & Waller, 2008; Rothberg et al., 2008; Viswanathan, Bharmal & Thomas III, 2005) while using the Assessing Care of Vulnerable Elders (ACOVE) Criteria, one study showed that more than 50% of the patients received at least one inappropriate medicine (Spinewine et al., 2007) . The wide range in the prevalence across studies may be due to differences in the clinical settings,

specific criteria adopted and patient characteristics. Most studies of ADEs have focused on identifying patient risk factors such as number of medications, types of medications used, number of comorbidities and other socio-demographic factors such as age and gender, probably because these factors are available in payer databases (Bates et al., 1999; Chrischilles, et al., 2006; Evans, Lloyd, Stoddard, Nebeker, Samore, 2005; Peyriere et al., 2003; Field et al., 2004).Very few studies have examined the role of socio-psychological variables as a risk factor for ADEs.

Concern beliefs in medication is a socio-psychological variable or concept that may help in understanding why people perform the health behaviors they do. Concern beliefs are patients' anxieties about the harmful effects of their medicines (Horne, 2003) and it has been found to be important in patient self-reporting an ADE (Oladimeji et al., 2008; Oladimeji et al (in review)). This study aims to explore the importance of concern beliefs in self-reporting ADEs and the rationale for the study is driven by both evidence-based research and a theoretical framework, the extended self-regulatory model. From the empirical research of previous studies, concern beliefs have been shown to be a significant predictor of self-reported ADEs (Oladimeji et al., 2008; Oladimeji et al (in review)). Concern beliefs showed a positive significant relationship (rather than number of medicines) with self-reported ADEs among Medicare enrollees. This result was similar in both a cross-sectional and longitudinally designed study. The results of these two studies inform the evidence of this socio-psychological variable as an important variable to consider for future studies of ADEs. In addition to these evidence-based findings, the extended self-regulatory model may explain why concern beliefs in medication may impact self-reported ADEs.

The extended self-regulatory model is a framework that attempts to explain how people may adapt to and/or manage health threats such as symptoms, unwanted problems from taking medicines and ADEs. This model views people as active problem solvers who assign meaning to symptoms and involves both a representation of the symptom and a coping procedure for dealing with it (Difenbach &Levanthal, 1996). The representation of symptoms guides the coping strategy for dealing with the symptoms. Using this model, Horne showed that when a coping procedure involves decisions about treatment, treatment perceptions as well as the illness and coping representations are interwoven (Horne, 2003). There are different pathways through which this occurs. In one pathway, treatment perceptions such as patients' beliefs in medications and the concerns they have about their adverse outcomes and long term effects impact the coping procedure the patient adopts in dealing with their symptoms or health threats. For example, coping procedures could be self-reporting a symptom and/or ADE to health providers. In addition, previous studies have shown that concern beliefs in medication predict coping behaviors such as adhering to medication using the extended self-regulatory model (Horne & Weinman, 1999; Horne & Weinman, 2002); it can therefore be inferred that these beliefs could also predict a coping procedure such as self-reporting an ADE.

The objectives of this study were to 1) quantify the frequencies of inappropriate medication use among older adults in the outpatient setting and 2) examine if there is an association between the use of inappropriate medication, concern beliefs in medicines and self-reported adverse drug events (ADEs). It was hypothesized in this study that 1) the frequencies of inappropriate medication among older adults in the outpatient setting using the Beers list and Assessing Care of Vulnerable elders (ACOVE) Criteria will be

high (about 12-49%) similar to previous studies, 2) there will be no independent association between the use of inappropriate medication and self-reported ADE, and 3) concern beliefs will be a significant risk factor for predicting self-reported ADE.

It was expected that concern beliefs will remain as the primary risk factor for self-reported ADE despite the use of inappropriate medication by patients. This is because the way symptoms are attributed to a medication may be based upon an individual's toleration of the adverse effects and the individual's concerns about using the medicines may drive his/her interpretation. The use of an inappropriate medicine does not reflect the perception of the patient about his/her symptom. Patients may not know whether they are receiving an inappropriate medicine or not, therefore, the interpretation of the symptom they are experiencing will not be related to the inappropriateness of the medication, but rather their beliefs about the medicine and how it affects their health.

Research Methods

Design: The design was a cross-sectional study including a survey of Medicare beneficiaries just after the implementation of the Medicare drug benefit in October 2007. The survey was an internet-based survey administered by Harris Interactive® on behalf of the University of Iowa, College of Pharmacy. The survey was designed by the University of Iowa investigators and the project was approved by the Institutional Review Board of the University of Iowa.

Patients/Setting: For this study, Harris Interactive® invited individuals in their online panel to participate in the survey. In appreciation of their time, participants received points from Harris Interactive for completing the on-line survey. The inclusion criterion for the survey was being 65 or older, English speakers, U.S. residents and is

enrolled in the Medicare health plan. In the survey, Harris Interactive provided data to University of Iowa researchers from a convenience or non-probability sample of 1024 anonymous respondents nationwide who completed the survey.

Data collection: An internet-based survey was administered in October 2007. In the survey, respondents completed a 161-item survey that took approximately 23 minutes to complete. Numerous skip patterns for questions that did not apply to some respondents were included and respondents could answer part of the survey and return later if necessary for completion. The data collected included socio-demographics, self-rated health, number of prescription medications used, sum of symptoms experienced, concern beliefs about medicines, necessity beliefs about medicines, number of pharmacies, self-reported ADE and whether subjects skipped doses of their medications to save money or stop taking the medicines due to cost.

Measures: In this section, descriptions of the measures that were used in this study are described (Appendix C). The dependent variable was self-reported ADE defined as "did you see a doctor about any side effects, unwanted reaction or other problems from medicines you were taking in the past year?." This question had been used in previous studies for the identification of self-reported ADEs (Chrischilles et al., 1992; Weingart et al., 2005).

The independent variables included important predictor variables such as the use of an inappropriately prescribed medicine and concern beliefs in medicine. Control variables included socio-demographics, clinical factors including number of medicines and behavioral characteristics such as the number of pharmacies used by the respondent. These control variables were included because of their addition in similar previous

models that examined self-reported ADE (Oladimeji et al., 2008). Further details of these measures and how they were defined and used in the analysis are seen in Appendix C.

In terms of inappropriate medication, Beer's Criteria and a modified version of the Assessing Care of Vulnerable Elders (ACOVE) quality indicators were applied to self-reported diagnosis and self-reported medication lists to determine the appropriateness of medicines. In this study, the patients were asked to give the name and strength of the medications they had taken in the past month. Patients also indicated the directions for use, how much they used in the last 30 days and the reason for taking each prescription medication they took. These reported medications, dosage, and conditions/diagnoses for taking the drug were used in identifying whether the patient received an inappropriate medication or not (as defined by the Beers and modified ACOVE Criteria).

The Beers Criteria have been used for older patients in the ambulatory setting (Aparasu & Mort, 2004; Chang et al., 2005; Fick et al., 2001; Fu, Liu & Christensen, 2004; Goulding, 2004; Hanlon et al., 2002; Huang, Bachmann, He, Chen, McAllister & Wang, 2002). It includes 48 agents or classes of medication considered inappropriate irrespective of diagnosis as well as medications and classes considered inappropriate in 20 conditions. Both sets of criteria were used. Since subjects reported the reason why they were taking the medications, the list of reasons reported by each patient was used as a condition list for identifying a Beers Criteria medication. The data was coded using a MULTUM database which has a list of medications available in the US market. The MULTUM database assigns a code to each medication used and this makes the drug identifiable. The survey had 1024 respondents with a total of 4025 drugs used by the

respondents. The Beers Criteria list of medications that was used is shown in Appendix A.

The modified ACOVE Criteria were also used to identify which medications should be avoided and if the medications prescribed for patients with a diagnosis were appropriate for their condition. In the original ACOVE Criteria, there are 43 quality indicators that pertain to pharmacologic care. The indicators are stratified into four domains of pharmacologic care including 'prescribing indicated medications', 'avoiding inappropriate medications', 'education, monitoring and documentation' and 'medication monitoring'. In this study, the 'prescribing indicated medication' domain which contains 17 indicators and the 'avoiding inappropriate medication' domain which has nine indicators were used because not all the data needed to code the quality indicators in the ACOVE Criteria were available in the dataset. For example, 'antibiotics started within 8 hours after admission for pneumonia' was one of the quality indicators recommended. Hospital in-patient information required to examine this indicator was not available in the dataset. In the final assessment, 11 indicators in the 'prescribing indicated medication' domain and six indicators within the 'avoiding inappropriate medication' domain were used based on availability of data (Appendix B). Limited studies have examined the use of an inappropriately prescribed medication using the ACOVE Criteria (Peterson, Kuperman, Shek, Patel, Avorn & Bates, 2005; Shrank et al., 2006; Spinewine et al., 2007; Wenger & Young, 2007). This is the first study that will use this criterion in identifying failed quality indicators in the medication management of older adults and examine its association with a health outcome such as ADEs.

To identify and generate the list of medications used in the Beers and ACOVE Criteria, the American Hospital Formulary Service and www.drug.com were used to identify the medications in the drug classes. The numeric medications codes in Multum were identified that were specific to the classes of medicines identified in the Beers and ACOVE criteria. For example, if muscle relaxants were indicated as high risk drugs, the generic names of muscle relaxants available were noted and then the numeric Multum codes were identified for those generic names. The codes and list of medicines generated were then checked by a team of clinical pharmacists, epidemiologist and statistician. Specific coding for both the Beers and ACOVE Criteria are available upon request from the University of Iowa Center for Education and Research on Therapeutics (UI-CERT).

To examine respondents concerns and necessity beliefs about their medications, the 10 items from Horne et al (1999) scale were used. Five items ask about concern beliefs and include items such as 'Having to take medicines worries me' and, 'I sometimes worry about the long term effects of my medicines'. Necessity beliefs were assessed with five items, including for example, 'My life would be impossible without my medicines' and 'Without medicines, I would be very ill'. Five point Likert scales anchored with strongly disagree and strongly agree were used as response options. The scale for this measure was derived by summing up the responses of each individual across the five questions. The values on the scale range from 5-25 with a higher score on the concern belief or necessity scale meaning stronger concern beliefs about the adverse and long term effects of medicines and stronger perception of the necessity of medicines respectively. Previous studies using these scales show reliability estimates ranging from 0.65-0.86 and its construct validity has been established (Horne et al., 1999). The

Cronbach alpha for concern beliefs was 0.80 in this study. A frequency description of the concern beliefs items, the scale distribution and a descriptive analysis of the predictor variable is shown in Appendix D.

The control variables in this study were socio-demographics, clinical and behavioral characteristics. The socio-demographic data included the age of the respondent, racial background, gender, highest level of education completed, household income and geographical region/territory where they resided.

For the clinical characteristics, self-rated health status was determined using a five-item response scale anchored with poor and excellent (Idler, Benyamini, 1997; Bailis, Segall & Chipperfield, 2003). To determine the number of medications used, respondents stated the number of different prescription medicines they had used in the past month. Then, respondents were asked to indicate the number of medications that they took on a regular basis, among those they had taken in the past month. Information on health symptoms that subjects said they experienced in the past month (yes/no) was collected. To improve recall, 'past month' was used. The pre-set list of symptoms was used because it had been used in a previous study to identify ADEs (Weingart et al., 2005). Symptoms such as headaches, dizziness or problems with balance, stomach or gastrointestinal problems, muscle aches, incontinence or problems with urinating, rash or itching, problems with sleep, changes in mood, fatigue and sexual problems were reported by respondents. There was also opportunity to report other non-listed symptoms. The number of symptoms experienced by patients' were summed to generate the variable 'sum of symptoms experienced'. The number of symptoms reported may however be

lacking in reliability because patients were not asked about the severity of the symptoms which may impact its reporting.

For behavioral factors, respondents were asked for the number of pharmacies where they got their prescription medicines in a typical month. Also, on a scale of 'Never, 1-2 times, 3-4 times, to More than 4 times' they stated whether they had stopped taking their medications due to cost or skipped their doses to save money..

Analysis: Descriptive analyses of the socio-demographic, clinical and behavioral characteristics of the sample population were completed. Though 1024 respondents completed the survey, only those who reported the name of the medication(s) being taken, dose and/or medical condition were included as the sample (n=874). The frequencies of inappropriately prescribed medications and medication under-use were calculated using descriptive analyses, based upon the Beers and modified ACOVE Criteria. The Beers and ACOVE Criteria coding allowed the number of inappropriate medicines used by respondents to be determined (interval level variable); and whether they had (or did not have) an inappropriate drug (categorical variable). Also, if patients did not receive a recommended drug therapy, this was identified as medication under-use. Both the Beers Criteria list of drugs (non-condition specific) and the condition-specific list of drugs were used. Though condition-specific, condition non-specific Beers drugs and ACOVE indicator drugs were identified and coded separately; they were summed as an inappropriate medicine, and instances of under-use were not included. In addition, the ACOVE quality indicators which were duplicated in the Beers Criteria were removed from the total number of inappropriate medicines examined. These quality indicators

were ‘avoid chlorpropamide’, ‘avoid meperidine’, and avoid strongly anticholinergic medications’.

For objective 2, two multiple logistic regression were used to relate the presence of failed quality prescribing indicators (using the Beers Criteria and modified ACOVE Criteria) and concern beliefs in medication to self-reported ADE, controlling for socio-demographics, clinical and behavioral factors. In the regressions, only the medications that should be avoided in the ACOVE Criteria were used. Since the ‘prescribed indicated medications’ domain identifies under-use of medicines by patients, this cannot lead to an ADE. The regression models are illustrated in Appendix E. A logistic regression was used because the outcome variable, self-reported ADE was a dichotomous variable (whether they reported any side effects, unwanted reactions or medication problems to their health provider). However, before this was done, it was investigated whether number of medicines and inappropriate medicine use would predict self-reported ADEs. Here, concern beliefs in medicine, the main variable of interest was not included either as a linear or a polynomial variable.

For the first logistic regression, the predictor variables included concern beliefs in medicine and use of an inappropriately prescribed medication (as defined by the Beers/ACOVE Criteria) as the primary variables of interest and age, gender, racial background, highest level of education, annual household income, geographic region (socio-demographic data); self-rated health, number of medicines used, sum of symptoms experienced, necessity beliefs in medication (clinical characteristics); and number of pharmacies, stopped medicines due to costs, skipped doses to save money and number of physicians seen regularly (behavioral characteristics) as control variables. In addition to

being characterized as a linear variable, concern belief in medicines was also included as a squared variable in the regression because the relationship between concern beliefs and self-reported ADE may not be linear. For example, patients may need to have some relative amount of concerns about their medicines in order to be involved in self-management of medicines but should not be overly concerned about their effects. Concern beliefs may only be managed to a certain extent and not necessarily reduced. Increased concerns may motivate the reporting of symptoms to health providers; however, those with stronger concerns have been shown to self-report ADEs and have low adherence to their medicines.

In the second logistic regression, similar analysis was run but inappropriate medicine was coded as a sum of inappropriate medicines by each subject based on both the Beers and ACOVE Criteria. A dose-response relationship of these criteria to ADEs was examined using this analysis.

All categorical measures were entered as dummy variables and continuous measures that are required to be categorical for logical comparisons such as age, number of medications used and number of pharmacies were recoded. For all the regressions, the odds ratio, confidence interval and p values of each variable were obtained and used in the interpretation of the results.

Results

Eight hundred and seventy four respondents self-reported the name of the medication (s) being taken and were included in the dataset. Respondents were between 65 and 94 years of age, and 56.6% were female. Most respondents were white, had some college experience, used more than one prescription medicine in the past month, obtained

their prescription drugs from one pharmacy, and had relatively good health (Table 2.1). Twenty percent (n=178) of respondents self-reported an ADE.

Overall, using the Beers Criteria and the ACOVE quality indicators, the frequency of patients' receiving either an inappropriate medicine or failing a medication use quality indicators was 45.8%. This was the total percentage after removing all duplicates occurring in both criteria.

Using the Beers Criteria only, 232 respondents had inappropriate medicines. These included the Beers Criteria independent of patient diagnoses and the Beers Criteria dependent on the diagnoses of the patient. Of these individuals, 210 older adults had at least one inappropriate medicine and the average number was 1.10 (SD= 0.31). Some respondents however had more than one inappropriate medicine (n=22).

For the Beers Criteria independent of the diagnoses of the patient, there were 204 patients with an inappropriate medicine (23.34%) while for the Beers Criteria dependent on the diagnoses of the patient; there were 45 patients with an inappropriate medicine (5.15%). Patients may be duplicated if receiving similar drugs identified in both sets of Criteria. The frequency distribution of patients' receiving each specific inappropriate medicine using the Beers Criteria independent of diagnoses and the Beers Criteria dependent on condition/diagnoses is shown in Table 2.2 and Table 2.3, respectively.

Using the modified ACOVE quality indicators, there were 303 patients with any failed quality indicators (34.67%). However, patients may have failed more than one quality indicator. After removing duplicates occurring in both the ACOVE and Beers criteria, two hundred and thirteen older adults failed one quality indicator (Table 2.4) and some failed more than one quality indicator (n=36). The average number of failed quality

medicines received was 1.17 (SD=0.42) and this included both inappropriate medicines that should be avoided, and medication under-use based on under utilization of recommended drug therapy.

Consistent with previous studies, the most frequently prescribed inappropriate medicines were estrogens, muscle relaxants and antispasmodics, short-acting nifedipine, amitriptyline and long acting-benzodiazepines (Aparasu & Mort, 2000; Chang, Liu, Yang, Yang, Wu & Lu, 2005; Fick, Mion, Beers & Waller, 2008).

In the first regression analysis, having stronger concern beliefs in medicine (OR= 1.57, 95% CI=1.02-2.39, p=0.04) and having more symptoms (OR=2.26, 95% CI=1.22-4.23, p=0.01), rather than receiving an inappropriate medicine (OR= 1.03, 95% CI= 0.65-1.64, p=0.89) were related to reporting an ADE (Table 2.5). Only concern beliefs in medicines as a linear variable was statistically significant in the model. The fit of the overall model was good (Hosmer & Lemeshow test =$\chi 2$ 12.77, p=0.12, R-square= 0.17).

Prior to this regression, it was shown that a higher number of medicines (OR=2.28, 95% CI=1.16-4.48, p=0.02), and having more symptoms (OR=2.36, 95% CI=1.28-4.35, p=0.00), rather than inappropriate medicine use (OR= 1.07, 95% CI= 0.68-1.69) were related to reporting an ADE (Hosmer & Lemeshow test =$\chi 2$ 15.27, p=0.05, R-square= 0.15) but when concern beliefs in medicine was included; only symptoms experienced and concern beliefs were significant (as shown earlier).

In the second regression analysis, it was examined if there was a dose-response relationship between the number of inappropriate medicines received and self-reported ADE. Stronger concern beliefs in medicine (OR=1.56, 95% CI=1.02-2.39, p=0.04) and having more symptoms (OR=2.27, 95% CI=1.22-4.23, p=0.01) were related to self-

reported ADE (Table 2.6). The fit of the overall model was also good (Hosmer & Lemeshow test =$\chi 2$ 11.79, p=0.16, R-square= 0.18)

Discussion

In this study, the frequency of inappropriately prescribed medicines received by older adults in the outpatient setting was high (45.8%). Having stronger concern beliefs in medicine and having more symptoms were related to self-reporting an ADE, rather than receiving an inappropriate medicine or number of inappropriate medicines received.

Though the frequencies of inappropriate medicines was high similar to previous studies, it was higher than those studies that had used the Beers Criteria only to examine the frequency of using an inappropriate medicine among older adults (Aparasu & Mort, 2004; Chang et al., 2005; Fick et al., 2001; Fu, Liu & Christensen, 2004; Goulding, 2004; Hanlon et al., 2002; Huang et al., 2002). This may have occurred because both the Beers Criteria and the ACOVE quality indicators were used in operationalizing whether an individual received an inappropriate medicine or not. Previous studies have either used the Beers Criteria independent of diagnoses only, or both the Beers Criteria independent of diagnoses and dependent on diagnoses lists. It seems that using sets of quality indicators allowed for more potential inappropriate medicines to be identified. This is important especially in the outpatient setting where older adults are likely to receive a prescription and may be at a high risk of receiving an inappropriate medicine. However, the interpretation of the frequency of receiving these medicines should be done with caution since some of the ACOVE quality indicators which were duplicated in the Beers Criteria were removed from the total number of inappropriate medicines examined. Also, some of the ACOVE indicators seemed to identify under-use among the older adults

compared to the Beers Criteria which identifies only medications of high risk. Using this criteria, older adults who did not receive prescribed indicated medications based on their condition/diagnoses were also identified and may suggest under-prescribing, an area open to more research.

As hypothesized, there was no association between the use of an inappropriate medicine and self-reported ADE, but stronger concern beliefs in medicines were related to more self-reported ADE. According to the extended self-regulatory model, patients are active problem solvers who assign meaning to their symptoms and have specific interpretations of the cause, consequences and means of controlling the symptom. Therefore, both symptom and treatment representations guide the behavior patients' perform for dealing with a symptom and this could involve reporting the unwanted reaction or side effect to a health provider (Difenbach &Levanthal, 1996; Horne, 2003). In this study, patients were asked if they had seen a doctor about any side effects, unwanted reactions or problems from taking their medicines. The performance of this behavior can be described as a coping procedure for dealing with the symptom and a means of detecting whether they experienced an ADE or not. Based on this model, patients' belief in medicines and the concerns they have about its adverse outcomes and long term effects may impact the coping procedure adopted in dealing with the side effects and unwanted reactions. This is because the way symptoms are attributed to a medicine and described as an ADE may be based upon an individual's concern about using the medicine and the ability to tolerate the adverse effects. Patients with stronger concern beliefs may be thinking about their medicines, worry about their effects and therefore more likely to attribute their symptoms to an ADE.

It is important to consider that this internet sample of older adults were highly educated; therefore, these individuals probably had more access to information on risk of medicines which could have increased their concerns about their medicines compared to the general population of older adults. Also, they were probably able to identify when their symptoms were due to medicines and readily report it to their doctor better than older adults with less education (Kauhanen, Kaplan, Julkunen, Wilson & Salonen, 1993). On the other hand, individuals with higher education may have better coping mechanisms available to them and subsequently, the use of these coping strategies may reduce the perceptions of symptoms and reporting to health providers (Ladwig, Marten-Mittag, Formanek & Dammann, 2000).

The inclusion of concern beliefs in medicine as a polynomial variable in the regression model was not significant probably because the relationship between patients concerns about the dependence and adverse effects of their medicines and self-reported ADE was only linear. The relationship of concern beliefs in medicine to health behaviors may vary. For example, studies have shown that increased concerns lead to less adherence to medicines (Horne, 1999: Phatak & Thomas, 2003) and more self-reported ADE (Oladimeji et al., 2008; Oladimeji et al (in review)). In this study, more concerns lead to more self-reported ADE.

Consistent with a previous study, inappropriate medicine use was not related to having an ADE (Onder et al., 2005). The use of an inappropriate medicine does not reflect the perception of the patient about his/her symptom. Patients do not know whether they are receiving an inappropriate medicine or not, therefore, the interpretation of the symptom they are experiencing will not be related to the inappropriateness of the

medication received , but rather their beliefs about the medicine and how is affects their health. Though many studies have related receiving an inappropriate medicine to experiencing an ADE, these studies have used objective measures of ADE such as using chart reviews or medical records (Chang et al., 2005; Onder et al., 2005; Passareli, Jacob-Filho & Figueras, 2005). Self-reported ADE is a patient's view of their symptomatology; the patients' perception of their treatment and concerns about the long term adverse effects also represents the patients' views. Both factors may therefore be associated to each other rather than inappropriate medicines because they assess and represent the patients' perception of their treatment and its effects. In addition, there was no dose response relationship between inappropriate medicines and self-reported ADEs also confirming that patients are not aware that the medicines being received are inappropriate. Patients' would not know if the number of medicines used makes them at a higher risk of having an ADE.

Patients who had more symptoms were more likely to self-report having an ADE. These patients could probably not tolerate their symptoms and therefore decided to seek the help of their doctor. Patients' interpretation of their symptom may determine the causal attribution to a medicine. Patients with fewer symptoms may believe that their symptoms can be controlled by self-care and therefore would be less likely to report the ADE to their doctor.

This study had some limitations. The use of secondary data restricted and minimized the validity of measures such as the Beers and ACOVE Criteria. For example, in the Beers Criteria, some of the information required for identifying an inappropriate medicine included the duration the patient had taken medicine and the doses being taken.

Since patients' self-reported the information about their medicines, the duration medicines were taken was not included and in some cases doses were missing. Also, due to unavailable in-patient data on respondents, the quality indicators used in the ACOVE Criteria was modified for the analysis. In addition, this was an internet sample of older adults who were highly educated; therefore, the results are not generalizable to older adults in the general US population. Finally, the use of patient self-report as a means of measuring ADE may overestimate its occurrence compared to using other objective measures such as chart reviews and medical records. It is possible that a symptom or reaction identified by a patient as an ADE may not be an ADE identified by healthcare professionals. Also, the measure included the reporting of 'other problems related to medications' which could be interpreted as cost or access problems by a patient rather than adverse events related to the use of the medicine.

Understanding the responsiveness of concern beliefs in medicines to experiencing an ADE in relation to clinical variables such as the use of an inappropriate medicine will help health providers understand that patients' perceptions of their treatment need to be elicited during clinical consultations. This is important especially because patients' are not aware that they had used an inappropriate medicine. Their symptom attribution to a medicine and an ADE is based on their own treatment beliefs, their anxieties, worries and perception of dependence on their medicines. Also, patients' concern beliefs in medicine may need to be controlled for in studies that examine risk factors predicting ADEs. Even if this variable does not show significant relationships to ADE measures, ruling out its effect may enhance studies methodologically. Future research should examine the relationship of concern beliefs to other health behaviors related to symptom and

medication management. Also, the relationship of inappropriate medicine use in older adults to other ADE measures should be examined.

Table 2.1: Descriptive characteristics of the study population (n=874) [a].

Variable	Number (%)	Mean ± SD
Socio-demographics		
Age		72.69 ± 5.71
65-74	598 (68.4)	
75-84	238 (27.2)	
≥ 85	38 (4.3)	
Gender		
Male	379 (43.4)	
Female	495 (56.6)	
Racial background		
White	817 (94.9)	
Black/ African American	18 (2.1)	
Hispanic	19 (2.2)	
Other	7 (0.8)	
Highest level of education		
≤ High school degree	167 (19.1)	
Some college	312 (35.7)	
College degree	116 (13.3)	
Graduate degree	152 (17.4)	
Other type of degree	127 (14.5)	
Annual household Income		
<$15,000	53 (7.0)	
$15,000 to $24,999	112 (14.8)	
$25,000 to $34,999	126 (16.6)	
$35,000 to $49,000	149 (19.7)	
$50,000 to $74,999	161 (21.2)	
>$75,000	157 (20.7)	
Geographic region (state of residence) †		
Mid west	253 (28.9)	
North East	183 (20.9)	
South	257 (29.4)	
West	181 (20.7)	

Table 2.1 continued

Variable	Number (%)	Mean ± SD
Clinical characteristics		
Self rated health		
Excellent	59 (6.8)	
Very good	260 (29.7)	
Good	375 (42.9)	
Fair	150 (17.2)	
Poor	30 (3.4)	
Number of medicines used		
0	99 (11.3)	
1-2	187 (21.4)	
3-4	231 (26.4)	
5-6	192 (22.0)	
7-8	80 (9.2)	
>8	85 (9.7)	
Sum of symptoms experienced		
0	273 (35.7)	
1	107 (14.0)	
2	118 (15.4)	
3	123 (16.1)	
4 or more	144 (18.8)	
Behavioral characteristics		
Concern beliefs in medicines (range 5-25), (Lower scores= less concern)		15.11 ± 3.95
Necessity beliefs in medicines (range 5-25), (Higher scores= more beliefs)		13.75 ± 3.00
Number of pharmacies		
0	86 (9.9)	
1	592 (68.0)	
2	176 (20.2)	
>3	17 (2.0)	
Stopped meds due to cost		
Never	805 (92.4)	
1 or more times	66 (7.6)	

Table 2.1 continued

Variable	Number (%)	Mean ± SD
Skipped doses to save money		
Never	784 (89.7)	
1 or more times	90 (10.3)	

SD= Standard deviation units

* Values are number (percentage) except otherwise indicated. Numbers that do not total 1024 indicate missing data.

† The North East region includes Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont. Midwest region includes Iowa, Indiana, Illinois, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin. South region includes Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia. West region includes Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming.

Table 2.2: Frequencies of potentially inappropriate medicine use among older adults using the Beers Criteria independent of diagnoses or conditions (n=874 patients)*.

Inappropriate medication	**Number of patients (n)**	**Percent of patients (%)**
Estrogens only (oral)	40	4.58
Muscle relaxants and antispasmodics	37	4.23
Short acting nifedipine	22	2.52
Amitriptyline,chlordiazepoxide-amitriptyline and perphenazine-amitriptyline	21	2.40
Daily fluoxetine	15	1.72
Doxasozin	14	1.60
Propoxyfene and combination products	14	1.60
Gastrointestinal antispasmodic drugs	11	1.26
Digoxin (Lanoxin) (should not exceed > 0.125mg/d except when treating atrial arrthymias)	10	1.14
Anticholinergics and antihistamines	10	1.14
Clonidine	10	1.14
All barbiturates (except phenobarbital except when used to control seizures)	8	0.92
Doses of short-acting benzodiazepines	7	0.80
Indomethacin	6	0.69
Dessicated thyroid	6	0.69
Long-acting benzodiazepines	4	0.46
Nitrofurantoin	4	0.46
Amidarone	3	0.34
Cimetidine	3	0.34
Short-acting dipyridamole	2	0.23
Methyldopa (aldomet) and methyldopa-hydrochlorothiazide (aldoril)	2	0.23
Ferrous sulfate >325mg/d	2	0.23
Amphetamines and anorexic agents	2	0.23
Methyltestosterone	2	0.23
Meprobomate	1	0.11
Flurazepam	1	0.11
Disopyramide	1	0.11
Doxepin	1	0.11

Table 2.2 continued

Inappropriate medication	Number of patients (n)	Percent of patients (%)
Chlorpropamide	1	0.11
Long-term use of stimulant laxatives	1	0.11
Amphetamines (excluding methylphenidate hydrochloride and anorexics)	1	0.11
Reserpine at doses 0.25mg	0	0
Diphenhydrmine	0	0
Ergot mesyloids and cyclandelate	0	0
Meperidine	0	0
Ticlopidine	0	0
Ketorolac	0	0
Long-term use of full-dosage, longer half-life, non–COX-selective NSAIDs	0	0
Orphenadrine	0	0
Guanethidine	0	0
Guanedrel	0	0
Cyclandelate	0	0
Isoxsurpine	0	0
Thioridazine	0	0
Mesoridazine	0	0
Pentazocine	0	0
Trimethobenzamide	0	0
Mineral oil	0	0
Ethacrynic acid	0	0
Total number of patients with any failed Beers Criteria	204	23.34

* There were 204 patients with inappropriate medicines identified using the Beers Criteria independent of diagnoses. Patients may be receiving more than one inappropriate medicine.

Table 2.3: Frequencies of potentially inappropriate medicine use among older adults using the Beers Criteria considering diagnoses or conditions (n=874 patients)*.

Disease condition	Inappropriate medicine	Number of patients (n)	Percent of patients (%)
Depression	Long-term benzodiazepine use. sympatholytic agents	17	1.95
Blood clotting disorders or receiving anticoagulant therapy	Aspirin, NSAIDs, dipyridamole, ticlopidine, and clopidogrel	13	1.49
COPD	Long-acting benzodiazepines, ß-blockers	7	0.80
Bladder outflow obstruction	Anticholinergics and antihistamines, gastrointestinal antispasmodics, muscle relaxants, oxybutynin, flavoxate, anticholinergics, antidepressants, decongestants, and tolterodine	6	0.69
Insomnia	Decongestants, theophylline, methylphenidate, MAOIs, and amphetamines	2	0.23
Gastric or duodenal ulcers	NSAIDs and aspirin (>325 mg) (coxibs excluded)	1	0.11
Parkinson Disease	Metoclopramide, conventional antipsychotics, and tacrine	1	0.11
Seizures or epilepsy	Clozapine, chlorpromazine, thioridazine and thiothixene	0	0
Stress incontinence	α-Blockers, anticholinergics, tricyclic antidepressants, and long-acting benzodiazepines	0	0
Arrthymias	Tricyclic antidepressants	0	0
Cognitive impairment	Barbiturates, anticholinergics, antispasmodics, and muscle relaxants. CNS stimulants	0	0
Hypertension	Phenylpropanolamine hydrochloride, pseudoephedrine; diet pills, and amphetamines	0	0
Anorexia and malnutrition	CNS stimulants	0	0

Table 2.3 continued

Disease condition	Inappropriate medicine	Number of patients (n)	Percent of patients (%)
Syncope or falls	Short- to intermediate-acting benzodiazepine and tricyclic antidepressants	0	0
SIADH/hyponatremia	SSRIs	0	0
Seizure disorder	Bupropion	0	0
Obesity	Olanzapine	0	0
Heart failure	Disopyramide and high sodium content drugs	0	0
Chronic constipation	Calcium channel blockers, anticholinergics and tricyclic antidepressant	0	0
Total number of patients with any failed condition-specific Beers Criteria		45	5.15

* There were 45 patients with inappropriate medicines identified using the Beers Criteria dependent on diagnoses/conditions. Patients may be receiving more than one inappropriate medicine.

Table 2.4: Frequencies of failed quality indicators using the ACOVE Criteria (n=874 patients)*.

Quality indicator descriptors	Number of patients (n)	Percent of patients (%)
Prescribed indicated medications		
Daily aspirin therapy for patient with diabetes	111	12.70
Calcium and vitamin D for patients taking long-term steroid therapy	26	2.97
Osteoporosis treatment medication (Hormone replacement therapy (HRT) or biphosphonate or calcitonin)	18	2.06
Warfarin or aspirin, as appropriate, for patient with atrial fibrillation	7	0.80
Proton-pump inhibitors (PPI) or misoprostol for patients with ulcer or gastrointestinal bleeding risk factors who is taking an NSAID.	1	0.11
ß-blocker for patients with heart failure	1	0.11
Calcium and vitamin D for patients with osteoporosis	1	0.11
ß-blocker for patients who had a myocardial infarction	0	0
ACE inhibitor for patients with hypertension and renal insufficiency	0	0
ACE inhibitor for patients with heart failure	0	0
Aspirin for patients with coronary heart disease	0	0
Avoiding inappropriate medications		
Avoid strongly anticholinergic medications if alternative exist	84	9.81
Avoid barbiturates unless patient has a seizure disorder	7	0.80
Avoid ß-blocker if patient has asthma	7	0.80
Avoid chlorpropamide	1	0.11
Avoid first or second generation short-acting calcium-channel blocker for patient with heart failure	1	0.11
Avoid meperidine	0	0
Total number of patients with any failed ACOVE indicators	303	34.67

* There were 302 patients with failed ACOVE quality indicators. Patients may have failed more than one quality indicator.

Table 2.5: Logistic regression (odds ratio and 95% confidence interval) analysis of risk factors for a self-reported adverse drug event considering use of an inappropriate medicine (n=638) [a]

Variable	Odd ratios (95% CI)
Socio-demographic characteristics	
Age	
65-74	1.0
75-84	1.29 (0.82-2.03)
≥ 85	2.39 (0.98-5.81)
Gender	
Male	1.0
Female	1.21 (0.78-1.86)
Racial background	
White	1.0
Black/ African American	0.86 (0.25-2.99)
Hispanic	1.44 (0.38-5.46)
Other	2.19 (0.41-11.68)
Highest level of education	
≤ High school degree	1.0
Some college	1.48 (0.80-2.75)
College degree	1.08 (0.46-2.50)
Graduate degree	1.51 (0.71-3.23)
Other type of degree	1.48 (0.68-3.24)
Annual household Income	
<$15,000	1.0
$15,000 to $24,999	0.86 (0.34-2.18)
$25,000 to $34,999	1.00 (0.39-2.59)
$35,000 to $49,000	1.30 (0.53-3.20)
$50,000 to $74,999	1.04 (0.41-2.63)
>$75,000	1.50 (0.59-3.82)
Geographic region (state of residence) †	
Mid west	1.0

Table 2.5 continued

Variable	Odd ratios (95% CI)
Geographic region (state of residence) †	
North East	1.04 (0.57-1.90)
South	1.35 (0.79-2.31)
West	1.30 (0.71-2.38)
Clinical characteristics	
Self rated health	
Excellent	1.0
Very good	1.22 (0.33-4.54)
Good	1.58 (0.43-5.82)
Fair	2.46 (0.62-9.69)
Poor	2.47 (0.46-13.31)
Number of medicines used	
1-2	1.0
3-4	1.75 (0.89-3.45)
5-6	1.66 (0.82-3.37)
7-8	0.65 (0.26-1.63)
>8	1.28 (0.52-3.13)
Using an inappropriate medicine	
No	1.0
Yes	1.03 (0.65-1.64)
Sum of symptoms experienced	
0	1.0
1	**2.06 (1.08-3.94)***
2	1.52 (0.79-2.92)
3	1.25 (0.65-2.39)
4 or more	**2.26 (1.22-4.22**)*

Table 2.5 continued

Variable	Odd ratios (95% CI)
Behavioral characteristics	
Concern beliefs in medicines (as a linear variable)	**1.57 (1.02-2.39)***
Concern beliefs in medicines (as a squared variable)	0.99 (0.98-1.00)
Necessity beliefs in medicines	0.94 (0.86-1.04)
Number of pharmacies	
0	1.0
1	1.86 (0.38-9.12)
2	1.95 (0.38-9.99)
>3	1.75 (0.23-13.17)
Stopped meds due to cost	
Never	1.0
1 or more times	0.70 (0.32-1.53)
Skipped doses to save money	
Never	1.0
1 or more times	1.53 (0.65-3.58)

a. Original survey N= 1024. Missing data were n=150 respondents who did not report the name of the medication being taken, n= 99 respondents who took no prescription drugs in the past month, n= 137 respondents who had missing data from all other variables and were excluded from analysis.

b. Pseudo-R^2 statistics = 0.176; $\chi 2$ = 13.57, df= 8, p>0.05 (Hosmer and Lemeshow test)
*. p<0.05

Table 2.6: Logistic regression (odds ratio and 95% confidence interval) analysis of risk factors for a self-reported adverse drug event considering number of inappropriate medicines used (n=638) [a]

Variable	Odd ratios (95% CI)
Socio-demographic characteristics	
Age	
65-74	1.0
75-84	1.28 (0.81-2.02)
≥ 85	2.36 (0.97-5.73)
Gender	
Male	1.0
Female	1.20 (0.78-1.85)
Racial background	
White	1.0
Black/ African American	0.84 (0.24-2.93)
Hispanic	1.45 (0.38-5.50)
Other	2.20 (0.41-11.72)
Highest level of education	
≤ High school degree	1.0
Some college	1.47 (0.79-2.72)
College degree	1.06 (0.46-2.46)
Graduate degree	1.50 (0.70-3.20)
Other type of degree	1.46 (0.67-3.19)
Annual household Income	
<$15,000	1.0
$15,000 to $24,999	0.87 (0.35-2.22)
$25,000 to $34,999	1.03 (0.40-2.65)
$35,000 to $49,000	1.32 (0.54-3.25)
$50,000 to $74,999	1.05 (0.41-2.65)
>$75,000	1.55 (0.61-3.94)
Geographic region (state of residence) †	
Mid west	1.0

Table 2.6 continued

Variable	Odd ratios (95% CI)
Geographic region (state of residence) †	
North East	1.04 (0.57-1.89)
South	1.36 (0.79-2.32)
West	1.29 (0.71-2.36)
Clinical characteristics	
Self rated health	
Excellent	1.0
Very good	1.22 (0.33-4.54)
Good	1.57 (0.43-5.80)
Fair	2.44 (0.62-9.61)
Poor	2.49 (0.46-13.43)
Number of medicines used	
1-2	1.0
3-4	1.73 (0.88-3.40)
5-6	1.65 (0.82-3.35)
7-8	0.66 (0.26-1.65)
>8	1.27 (0.52-3.11)
Number of inappropriate medicines used	1.06 (0.80-1.40)
Sum of symptoms experienced	
0	1.0
1	**2.05 (1.08-3.93)***
2	1.52 (0.79-2.93)
3	1.25 (0.65-2.38)
4 or more	**2.26 (1.22-4.22**)*
Behavioral characteristics	
Concern beliefs in medicines (as a linear variable)	**1.56 (1.02-2.39)***
Concern beliefs in medicines (as a squared variable)	0.99 (0.97-1.00)
Necessity beliefs in medicines	0.94 (0.86-1.04)

Table 2.6 continued

Variable	Odd ratios (95% CI)
Number of pharmacies	
0	1.0
1	1.86 (0.38-9.13)
2	1.95 (0.38-10.02)
>3	1.76 (0.24-13.31)
Stopped meds due to cost	
Never	1.0
1 or more times	0.70 (0.32-1.53)
Skipped doses to save money	
Never	1.0
1 or more times	1.52 (0.65-3.55)

a. N= 1024. Missing data: n=150 respondents who did not report the name of the medication being taken; n= 99 respondents who took no prescription drugs in the past month; n= 137 respondents who had missing data from all other variables and were excluded from analysis.

b. Pseudo-R^2 statistics = 0.175; $\chi 2$ = 11.02, df= 8, p>0.1 (Hosmer and Lemeshow test)
*. p<0.05

CHAPTER III

VARIATION IN PATIENTS' AND CLINICIANS' ATTRIBUTION OF SYMPTOMS AND ITS RELATIONSHIP TO CONCERN BELIEFS IN MEDICINES

Among older adults, at least one in three individuals taking five or more medications will experience an adverse drug event (ADE) each year (Pham & Dickman, 2007). An adverse drug event is an injury resulting from medical interventions related to the use of a drug (Gurwitz et al., 2003; Gandhi et al., 2003). About 95 percent of these events are predictable and about 28 percent are preventable (Pham & Dickman, 2007). ADEs are considered to be preventable if they were the result of an error and were preventable by any means available. They have also been shown to be more expensive than non-preventable ADEs in clinical settings and are more likely to be serious, life-threatening or fatal than non-preventable ADEs (Field et al., 2004). Reducing the rates of preventable ADEs could result in cost savings due to reduced healthcare costs and improved patient care.

Symptoms are usually reported by patients before the occurrence of an ADE, and the process by which symptoms are identified and characterized may be applicable to the attribution of ADEs. As well, symptom reporting is important because it may allow health providers to identify early symptoms of ADEs, prevent the ADE and/or respond more quickly (Dewitt & Sorofman, 1999; Weingart et al., 2005). If medication-related symptoms experienced by a patient are communicated to the health provider, the intensity and duration of the symptoms could be mitigated and a serious ADE can be prevented (Weingart et al., 2005).

Symptom recognition, classification and attribution of cause are important pathways to identify and prevent ADEs (Dewitt & Sorofman, 1999) and if there are misattributions of the cause of symptoms by patients, it becomes important to understand if there are certain related patient factors. Patients who experience injuries due to their drugs rarely think the problem is caused by the drug that they are taking. Instead, they suspect foods that they have eaten recently or new products that they have used (Kelly, 2008). Sometimes, symptoms experienced by the patient are attributed to degenerative disease or old age by either the patient or the physician. Patient and clinician symptom attribution may differ and be related to certain patient characteristics.

Kleinman and his colleagues developed an explanatory model of illness which emphasizes variations between patients and practitioners models of illness. These variations have been described as 'explanatory models' that both patients and clinicians have about illnesses and include their ideas about cause, etiology, symptoms onset, pathophysiology, course and treatment (Kleinman, 1980). In this model, patients and clinicians may have different notions about sickness and its treatment and these could guide choices for the behavior that would be exhibited by both groups. The explanatory model is an individual's response to a particular health threat and reflects the beliefs that are held at that particular time (Hunt & Arar, 2001; Kleinman, 1980). Incongruence between a clinician and patient explanatory model has been shown to be negatively associated with patient's health outcome such as adherence, treatment response and reporting of unwanted side-effects of treatment (Cohen, Reimer, Smith, Sorofman & Lively, 1994). Based on this variation in explanatory models, it can be inferred that differences in symptom attribution may occur between both groups and will be related to

the reporting of symptoms to health providers and subsequently identifying and/or reporting an ADE.

The explanatory model is conceptually linked to the extended self-regulatory model via beliefs, patient perceptions of treatment and coping procedures. In the extended self-regulatory model, perceptions of treatment such as concern beliefs in medicines are related to illness representations. These illness representations include the patients' views about the identity, label, cure, consequences and cause of the symptom (Horne et al., 2001; Horne, 2003). Concern beliefs in medicines are evaluative ideas of representations of threats posed by a medication and similar to illness representations, they have cognitive and emotional dimensions (Levanthal et al., 1998). If patients' concern beliefs in medicines and illness perceptions can shape the selection of a health behavior via the extended self-regulatory model; such beliefs may also influence their explanatory model and symptom attributions. For example, when patients' worry about their medicines and have concerns about the long term or adverse effects, they may be seeking to label, identify and find a causal reason and/or cure for the symptoms they are experiencing. Correctly labeling a symptom, attributing it to a reason and examining ways of controlling the symptoms through treatment may therefore be related to these worries and concerns about the treatment. In this study, the causal attribution of a symptom may be related to a patient's belief about their treatment which includes their concern beliefs in medicines. If patients' causal attribution of symptoms is attributed to the right reason, attributions will not be misplaced, patients and clinicians' explanatory models will not differ greatly and the communication between a patient and the health provider about their symptoms and ADEs may be enhanced.

The objectives of this study are to 1) compare attribution of symptoms to a cause for patients and clinicians, 2) quantify the association between patients' concern beliefs and patient-clinician agreement on patients' symptom attribution to medicines and 3) examine if individuals who attribute their symptoms to similar reasons and agreed/disagreed with the clinicians assessment have certain clinical and/or socio-demographic characteristics.

The hypothesis was that patient symptom attributions which differ from clinicians' attributions and to which the cause of symptom was attributed to medicines instead of other reasons will have higher scores on the concern beliefs in medicine scale. This is because individuals with such symptom attributions are likely to be thinking about their medicine and worry about his long term effects and adverse effects. Also, patient symptom attributions which differ from clinicians' and to which symptoms are attributed to reasons such as age or disease will have lower scores on the concern belief scale. Individuals with these symptom attributions are probably less likely to be thinking about their medicines and worry about their effects. It is expected that patients' clinical factors such as self-rated health, number of medicines used and having more symptoms will be related to their attribution of symptoms. Specifically, respondents with poor self-rated health status and those taking a high number of medicines may be likely to attribute their symptoms to other reasons besides their medicines. This is because they believe that their failing health is the major reason for the symptom they are experiencing and not their medicine.

Symptom labeling, interpretation and attribution to a cause are pathways to identifying whether an adverse drug event has occurred or not. This study is therefore

important because if there are misattributions of the cause of a symptom by patients and patients' beliefs about their treatment are related to it, health providers can provide a mechanism for addressing patients' misconceptions and inherently reframe patients' views of their symptom attributions. A correct attribution of symptoms to a cause strengthens the self-report of ADEs by patients.

Research Methods

Design: This study uses quantitative and qualitative approaches. For the quantitative component, a survey of Medicare enrollees was conducted. The design was a cross-sectional survey of Medicare beneficiaries in 2007. For the qualitative component of this study, an open-ended question in the same survey was used. This survey was an internet-based survey administered by Harris Interactive® on behalf of the University of Iowa, College of Pharmacy.

Subjects/Settings: Harris Interactive® provided data on a sample of 1024 anonymous respondents who completed the on-line survey. Harris Interactive maintains a confidential panel of individuals who have opted to be invited to participate in surveys. Individuals in the online panel were invited to participate in this study and participants received Harris Interactive points for completing the survey. The inclusion criteria for being in the study were being 65 or older, English speakers, U.S. residents and registered in the Medicare plan.

Data Collection and Measures: The details of the measures and how they were defined and used in the analysis are seen in Appendix F.

In the survey, respondents completed a 161- item survey which took approximately 23 minutes to complete. There were however numerous skip patterns for

questions that did not apply to some of the respondents. Respondents could also answer part of the survey and return to it later if necessary for completion. Included as part of the survey were open ended questions about health symptoms and their reporting.

Qualitative component: In the qualitative study, information on health symptoms that subjects experienced was collected. These symptoms included headaches, dizziness or problems with balance, stomach or gastrointestinal problems, muscle aches, incontinence or problems with urinating, rash or itching, sleep problems, mood changes, fatigue and sexual problems. Respondents were asked to state if they experienced any of the symptoms in the past month (yes/no) and if they had experienced other non-listed symptoms. This list of ten symptoms was used because it has been used in previous studies in identifying ADEs (Gandhi et al., 2003; Weingart et al., 2005). Among respondents who indicated that they had experienced any symptom, they were asked to note who they reported the particular symptoms they experienced to, whether a physician, pharmacist, nurse or other healthcare provider. If they did not report at least one of the symptoms, the reasons for not reporting the symptoms were elicited. Also, they were asked if they had any concerns or issues about reporting the symptom(s). The patients' reason for not reporting the symptoms and the concern they had about reporting them were both open-ended questions and respondents had an opportunity to write as much as they wanted.

From the open-ended questions, 336 respondents indicated they did not report a symptom they experienced in the past month to their health provider. Respondents also gave a reason for not reporting the symptom. These reasons may be based on several rationales including a causal attribution of symptoms or perceptions of less consequence

or severity of the symptoms. Using these reasons, a content analysis was performed and the major reasons for not reporting the symptoms they experienced to their health provider were determined. The 'cause' domain within the extended self-regulatory model can help to understand why patients chose to not report their symptoms. In this analysis, 219 symptoms from the 'cause' domain were further analyzed while the other domains within the model such as the 'consequences' domain and 'control' domain were not analyzed. For example, symptom(s) that were not reported because respondents thought it was due to disease or age were examined. However, symptoms that were not reported because they were perceived to be less severe or could not be controlled by seeking a physician were not analyzed. This is because attribution of symptoms to a medicine (or not) is based on the patients perception of what might have 'caused' the symptom.

One of the characteristics of good qualitative research is credibility and this requires demonstrating that the research was designed to 'maximize the accuracy of identifying and describing whatever is being studied' (Brown, 2005). To ensure credibility, after the content analysis of the open ended questions, a colleague also coded the questions to check for clarifications and consistency of the themes. Also, consensus about the major themes was reached and disagreements across themes settled in a meeting.

Quantitative component: In order to examine if attribution may be misplaced by older adults, and to compare patients' and clinicians' attributions, a clinical panel reported two ratings about respondents' symptom attribution. These ratings included 1) the likelihood of the symptom experienced being due to a medication and 2) the probability of the symptom being due to the reason the patient stated. This clinical panel

consisted of three board-certified clinical pharmacists who have 2-10 years professional experience as clinicians and faculty members at the College of Pharmacy. They are also trained in specialty areas such as geriatrics and ambulatory care.

A symptom report form was created for each subject (Appendix G). Information on patients' socio-demographics, number of medicines used, number of pharmacies, reported medication adherence, self-reported medications taken and dose and self-reported conditions were included in the symptom report forms. Also included were the unreported symptoms and the attribution for those symptoms. To rate the forms, the clinical panel was trained by the investigator by first examining 3-4 report forms and determining how the ratings would be done. The reviewers rated their confidence about the symptom being related to a medicine using a 6 point scale. The response options on this scale were 1) little or no confidence the symptom is related to a medication, 2) slight to moderate confidence the symptom is related to a medication, 3) less than 50% confidence but a close call that the symptom is related to a medication, 4) more than 50% confidence but a close call that the symptom is related to a medication, 5) strong confidence that the symptom is related to a medication, and 6) virtually certain that the symptom is related to a medication. Symptoms were judged to be medication-related if the confidence level of the consensus judgment was 4 or greater on the 6-point scale, signifying greater than 50% certainty that an ADE had occurred. Weingart et al (2005) and Gandhi et al (2003) used similar scales in identifying the occurrence of an ADE (Weingart et al., 2005, and Gandhi et al., 2003).

Second, reviewers indicated the probability that the symptom was due to the reason the patient stated, rated on a scale of 0-1 with 0 being impossible and 1 being

certain. For example, if a patient did not report the symptom to the doctor because he/she thought the symptom was due to age, the reviewer were asked to rate the probability that the symptom was due to age. Differences of at least 0.2 points on the scale (for example, reviewers scores were 0.6, 0.8, 1.0) between the clinicians' classification were resolved by discussion to achieve consensus.

For the quantitative aspect, the dependent variable was concern beliefs in medicine. The dependent variable, concern beliefs in medicines was measured using five items from the Horne et al (1999) scale. These items include 'Having to take medicines worries me', 'I sometimes worry about the long term effects of my medicines', 'I sometimes worry about becoming too dependent on my medicines', 'My medicines disrupt my life', and 'My medicines are a mystery to me'. The response options for evaluating these items were five point Likert scales anchored with strongly disagree and strongly agree. The scale for the concern beliefs measure is derived by summing up the responses of each individual across all five questions. Hence, the values on the scale range from 5-25 with higher scores on the concern belief meaning stronger concern beliefs about the adverse and long term effects of medicines. The construct validity of this scale has been noted in previous studies and their reliability (with estimates ranging from 0.65-0.86) has been established (Horne et al., 1999). The Cronbach alpha for concern beliefs was 0.80 in this study.

The independent variables included socio-demographic characteristics such as age of the respondent, racial background, gender, highest level of education completed, household income and geographical region/territory where they resided; and clinical characteristics such as number of medicines used and self-rated health. To determine self-

rated health, respondents rated their health on a five-item response scale anchored with poor to excellent (Idler, Benyamini, 1997; Bailis, Segall & Chipperfield, 2003). For number of medicines used, respondents stated the number of different prescription medicines they had used in the past month. Then, they were asked to indicate the number of medications that they took on a regular basis, among those they had taken in the past month.

Analysis: The unit of analysis for this study was symptom because patients may have reported more than one symptom and attributed each symptom to a different causal reason. Frequencies of unreported symptoms for each reason/category were examined. Then, to examine specific attribution to medicines, an analysis of the variations between patients' and expert panel ratings of symptom attribution to medicines for each symptom was done using chi-square and fisher's exact test analysis. To do this, clinicians' confidence rating of patients' symptom(s) as due to medicines was used to classify respondents into 1) those who agreed with the clinician that symptom was due to medicine (4 or greater confidence scores) and 2) those who agreed with the clinician that symptom was not due to medicine (less than 4 confidence scores). Then, a comparison of the individuals with similar medicine attributions (both patient and clinician agreed/ both patients and clinician disagreed) and patients with different medicine attributions (patient thought symptom was due to medicines/clinician thought otherwise, patients thought symptom was not due to medicines/clinician thought otherwise) was done by their socio-demographics, clinical and behavioral characteristics.

To examine all symptom attribution, patients' attributions of all 219 symptoms were grouped into five types such as medicine, something other than medicine, age,

disease or other factors. Then, within those groups, patients were classified according to the probability ratings assigned by clinicians. To examine if patients' concern beliefs were associated with their attribution, probability scores greater than 60% were used to signify agreement with stated reason. Sensitivity analyses using 50%, 60% and 70% showed no differences in the findings. This probability score point classified subjects into 1) non-reporters who agreed with the clinicians on the cause of their symptoms (greater than 60% probability score), and 2) non-reporters who disagreed with the clinicians on the cause of their symptoms (less than 60% probability score). An examination of how attributions are related to concern beliefs was done by using an independent sample t –test across both groups within each of the attribution categories, i.e., age, medicine, disease. This test compared respondents' concern beliefs for those who agree and disagree with the expert panel assessments of their symptoms. In the final analysis, an investigation of the characteristics of the classified individuals was done by running chi-square and fisher's exact test analysis to identify associations between attribution and socio-demographic and clinical characteristics.

In summary, it was expected that patient and clinician attribution would differ and certain patient factors such as concern beliefs in medication would be related to attribution of symptoms. Specifically, it was estimated that the variation in patients' and clinicians' symptom attribution would occur, consistent with the explanatory model, and be related to patients' attribution to concern beliefs in medicines, consistent with the extended self-regulatory model.

Results

One hundred and twelve patients did not report the symptoms they experienced to their health provider based on attribution to other causes such as age. Out of these individuals, 219 symptoms were reported. Most patients thought their symptom(s) were due to their disease, something other than medicines, age and 'other reasons' (Table 3.1). Other reasons patients stated for not reporting their symptom included internal/external factors such as job stress, reactions to laundry detergent and lawn work (Table 3.2).

Regarding symptom attribution to medicines, there was no statistically significant difference between patients' and clinicians' symptom attribution ($\chi 2$= 1.376, p=0.24) (Table 3.3). These groups are not mutually exclusive as patients may have experienced more than one symptom and attributed one to medicine and one to another reason. When patients were classified as 1) those with medicine attributions similar to the clinicians (both agreed/both disagreed) and 2) those with medicine attributions different from the clinicians; those symptoms with similar attribution as the clinicians were more likely to be experienced by individuals with good-excellent health than those with different attributions ($\chi 2$= 19.41, p =0.001). Also, those individuals whose symptom attributions differed from clinicians were more likely to reside in the South geographical region ($\chi 2$= 8.23, p=0.04) and had stronger concern beliefs in medicine (t=-3.03, p=0.00) (Table 3.4).

For all symptom attribution, there was no statistically significant difference in concern beliefs with medicines when symptoms were grouped by attribution type and agreement/disagreement with clinicians, using the classification of the 60% probability that the patients stated cause was in agreement with the clinicians stated cause (Table 3.5). However, among patients who attributed their symptom to medicines, the effect of

concern beliefs was in the correct direction wherein clinicians disagreed with those who had stronger concern beliefs in their medicines (19.10 ± 2.28) while they agreed with those who had lower concern beliefs (17.40 ± 4.219), but the finding was not statistically significant.

Among the symptoms that were attributed to medicines and not caused by medicine, there was no association between clinician agreement/disagreement of symptom attribution and patient socio-demographics and clinical characteristics (Table 3.6). However, among those who attributed their symptoms to other reasons, health status was better for patients the clinicians agreed with compared to those the clinician disagreed with ($\chi 2$= 9.16, p=0.03). Also, among patients who attributed their symptoms to age, the number of medicines used was higher for patients the clinicians disagreed with than those they agreed with ($\chi 2$= 13.20, p=0.01). Among patients who attributed their symptoms to their disease/condition, there were significant differences in income ($\chi 2$= 12.98, p =0.02) and geographical region ($\chi 2$= 8.469, p =0.04) (Table 3.6)

Discussion

Older adults attributed their symptoms to age, disease, side effect of medicines, something other than medicines and other reasons such as job stress, lawn work or weather changes. There was no statistically significant difference in patient-clinician agreement on symptom attribution to medicines, although 20% did not agree. Also, patients' concern beliefs in their medicines and its adverse effects were not related to symptom attribution for any causal reason, irrespective of whether there was patient-clinician agreement on attribution.

According to the explanatory model of illness, patients and practitioners can have different ideas on illnesses and cause of symptoms (Cohen, Reimer, Smith, Sorofman & Lively, 1994; Kleinman, 1980) and in some cases, may come to agreement after dialogue and consultations. The results showed that there was no statistically significant variation between patients and clinicians ideas on symptomatology and attribution to medicines. This was not an expected finding. Based on this result, older adults seemed to be able to identify when their symptoms were due to their medicines or not probably because they take many medicines which has given them some experience with use and usual side effects. Past experience with use of medicines may have developed their ability to identify, detect and correctly attribute symptoms to medicines. This is a positive finding because it suggests that patients may be involved in the self-management of their medicines and symptoms. Also, it implies from a patient care perspective that health providers understand patients' symptomatology and could reach agreement on symptom attribution, consistent with the explanatory model of illness.

Despite the lack of statistical significance, from a clinical perspective, it is important to consider that about 20% of patients' symptom attribution to medicines disagreed with that of the clinicians. As expected, this suggests that some patients think about their symptoms differently compared to clinicians and attribute them to varying reasons based on the perception of their illness, symptom and/or treatment. These individuals may likely not take their medicines as directed, respond to treatment negatively and/or not report any unwanted side effects of treatment to their health providers (Cohen, Reimer, Smith, Sorofman & Lively, 1994).

Patients who had medicine attributions different from the expert panel seemed to have stronger concerns about their medicines and its adverse effects. This was an expected finding as these individuals who worry about their medicines could be biased in their symptom perceptions and representations. Their anxieties about their medicines could preclude their judgment about their symptom attributions. On the other hand, patients with medicine attributions similar to the expert panel seemed to have better health compared to those whose attribution to medicines differed from the clinicians. The latter patients may believe that their poor health is the reason for the symptom being experienced and not their medicines. It is important for health providers to assess patients understanding of symptom attribution especially in cases of ambiguity. In addition, those whose attributions differed from the clinician were more likely to reside in the South geographical region. It is not clear how geographical region may influence attribution to medicines but Barsky, Peekna & Borus, 2001, Kauhanen, Kaplan, Julkunen, Wilson & Salonen, 1993 and Pennebaker, 2000, showed that patients' socio-demographics and environment may influence their ability to identify, process and label symptoms.

Examining the second objective, the results showed that patients' concern beliefs were not statistically associated with their symptom attributions, irrespective of whether the expert panel agreed with patient attribution or not. It was anticipated that patients who inappropriately attributed their symptoms to age would have lower concern beliefs but this was not shown in this study. Though concern beliefs in medicines may inform patients' expectation about their medicines and represent a source of bias in symptom cause attribution (Siegel, Dean, & Schrimshaw, 1999; Horne, 2003), older patients may not consider how worried they are about the long term or adverse effects of their

medicines when asked about their symptom attribution. They may believe that their health is important and attributing their symptoms to the right reason gives them control over their health and suggests active involvement in the management of their symptoms.

As expected, patients who attributed their symptom to a medicine rather than other reasons had stronger concerns about the adverse, long term and dependence effects of their medicines. Though there was no statistical relationship, the strength of concern beliefs was in the expected direction. Patients who think about their medicines and worry about its effects would attribute any symptom being experienced to their medicine rather than other reasons (Chao, Nau, Aikens & Taylor, 2005; Gonzalez et al., 2007). However, these findings have certain implications because this was an internet sample of highly educated older adults. For example, these individuals probably have better coping mechanisms available to them and subsequently, the ability to identify, process and attribute symptoms to a reason will be different compared to the general population of older adults (Ladwig, Marten-Mittag, Formanek & Dammann, 2000). Health providers need to constantly verify patients' symptom attribution so that health problems resulting from sources other than medicines can be identified and prevented.

In the bivariate analysis that compared patients' socio-demographic and clinical characteristics by their clinician agreement/disagreement of symptom attribution, it was anticipated that among those who attributed their symptoms to other reasons, patients' self-rated health, number of medicines used and symptoms experienced would be associated with attributions. As expected, health status was better for patients the clinician agreed with compared to those they disagreed with. The latter patients would

believe that their failing health is the reason for their symptoms rather than other reasons such as diet and stress.

Among patients who attributed their symptoms to age, patients who disagreed with the clinicians were likely to be using more medicines than those they agreed with. Though this was not expected among those with symptom attributions to age, it makes logical sense that the individuals who were using more medicines thought any symptoms they experienced would be due to their medication rather than other reasons such as their age.

For patients who attributed their symptoms to their disease/condition, the income of patients with clinician agreement about their symptom attribution was lower than those with clinician disagreement. It is not clear why this may have occurred but it is possible that patients with lower income levels had more symptomatic diseases/conditions that would make symptom attributions easy to assess (Kauhanen, Kaplan, Julkunen, Wilson & Salonen, 1993; Ladwig, Marten-Mittag, Formanek & Dammann, 2000). Also, it is not clear how geographical region where patients resided could be different between patients with clinician agreement on their symptom attributions and those with disagreement.

The results of this bivariate analysis should be interpreted with caution because the cross tabulation of clinician agreement/disagreement by symptom attribution type showed few cases within each cell size and in many instances, no cases within the cell leading to no statistical significance. The sample size per symptom attribution type was also small and therefore not enough to make strong statistical inferences.

This study has limitations. The sample was older adults who responded to an online survey and the results may not be generalizable to all patients 65 years and older.

Also, after classifying patients' symptom by their cause and by their agreement with the expert panel, some of the sub-groups had small sample sizes. This may not allow statistical differences to be detected. Also, the number of symptoms reported by a patient may be lacking in reliability because patients were not asked about the severity of the symptoms which may affect its reporting. The measure of self-reported ADE had some limitations. It included reporting 'other problems from taking medications to the doctor', which could be interpreted as cost or access problems by a patient instead of side effects or adverse reactions to the medicine. The measure of ADE could therefore be overestimated. Finally, the clinical pharmacists who rated the patients' symptom attributions had expertise in geriatrics and ambulatory care and may be more knowledgeable in the symptomatology of older adults than the pharmacist in the community setting. Their ability to understand patients' symptom may not represent those of all pharmacists across the country.

Though some of our expected findings were not shown in this study, the relationship of concern beliefs in medicines with symptom attribution is still an important area for future study. Some of the results showed that concern beliefs were in the expected direction in relation to symptom attribution to medicines. With a stronger methodological design and more available data, differences in concern beliefs among patients with different symptom attributions may be detected.

Understanding patients' perception of their symptoms may give a health provider clues about the overall health behavior of the individual. It is important for health providers to determine the relationship of patient's symptom perception to their responses to health problems. If this is done, proper patient education and individualized

interventions can be devised in order to maximize positive patient outcomes (Gonzalez et al., 2007). Eliciting patients' symptom attribution during clinical assessments and consultation and appropriate education of patients about their symptoms, symptom perceptions and illness need to be done by health providers. This study further explores how important concern beliefs in medication are in the management of patient-reported adverse health outcomes such as symptoms. Further research should examine if symptom attribution is important in other patient outcomes such as adherence to medicines.

Table 3.1: Frequency of reasons patients did not report their symptoms to health providers (n=219 symptoms) [a]

Reason for not reporting symptom	**Frequencies of symptoms (N)**	**Percentage (%)**	**Number of patients**	**Percentage (%)**	**Concern beliefs (s.d.)**
Medicines	23	10.5	10	8.93	17.91 (3.66)
Age	47	21.5	25	22.32	16.68 (3.83)
Other reasons	47	21.5	27	24.11	14.70 (4.40)
Not caused by medicine	49	22.4	25	22.32	14.24 (3.46)
Disease/condition	53	24.2	26	23.21	15.42 (4.94)
Total	219	100	112	100	

a. Some patients may have causal reasons for not reporting symptom(s) in more than one category.

Table 3.2: Examples of other reasons patients gave for not reporting symptoms to health providers

Allergic reaction to laundry detergent
Surgery
Muscle aches due to much walking and farm work
Due to coffee and failing to sip water
Stress/Job Stress
Due to radiation for uterine/cervical cancer
Working out in gym
Weather changes
Son deployed to Iraq
Stomach problem due to food ate
Sleep problems due to change in time
Dizziness from getting up too fast
Drinking regular orange juice instead of low acid
Diet
Headaches due to bright sunlight and reading too much
Acid reflux due to eating late at night

Table 3.3: Association of patients' and clinicians' symptom attribution to medicines (n=219) [a, b]

	Clinician attributed symptom (s) to medicines (n=34)*	Clinician did not attribute symptom (s) to medicines (n=169)*
Variable	**Number (%)**	**Number (%)**
Patient attributed symptom to medicines	5 (14.7)	14 (8.3)
Patient did not attribute symptom to medicines	29 (85.3)	155 (91.7)

* A rating of 4 or greater on the 6 point confidence rating scale was used to classify respondents as those who agreed/disagreed with clinicians' on symptom attribution to medicines. Groups are not mutually exclusive.

a. Sixteen missing cases due to unavailable confidence ratings of symptom. Clinicians could not assess patient attribution based on missing patient characteristics such as medications used. Patient information was obtained by self-report.

b. No significant difference between patients' and clinicians' symptom attribution to medicines ($\chi 2 = 1.376$, $p=0.33$).

Table 3.4: Comparisons of patient characteristics by patient-clinician agreement on attribution to medicines (based on similar symptom attributions) (n=219)

Variable	**Agreement between patient-clinician**	**Disagreement between patient-clinician**	**P value**
	Number (%)	Number (%)	
Socio-demographics			
Age			
65-74	110 (68.8)	39 (66.1)	0.93
75-84	37 (23.1)	15 (25.4)	
85-100	13 (8.1)	5 (8.5)	
Race [a]			
White	148 (93.7)	51(91.1)	0.28
Black/African American	8 (5.1)	4 (7.1)	
Hispanic	0	1 (1.8)	
Others	2 (1.3)	0	
Gender			
Male	46 (28.8)	17 (28.8)	0.99
Female	114 (71.3)	42 (71.2)	
Education			
Less than HS/HS degree	26 (16.3)	10 (16.9)	0.77
Some college	50 (31.3)	22 (37.3)	
College degree	30 (18.8)	7 (11.9)	
Graduate degree	32 (20.0)	11 (18.6)	
Other degree	22 (13.8)	9 (15.3)	
Geographical region			**0.04***
Midwest	33 (20.6)	10 (16.9)	
East	31 (19.4)	6 (10.2)	
South	64 (40.0)	36 (61.0)	
West	32 (20.0)	7 (11.9)	

Table 3.4 continued

Variable	**Agreement between patient-clinician**	**Disagreement between patient-clinician**	**P value**
	Number (%)	Number (%)	
Income [b]			
<15, 000	12 (8.6)	10 (21.7)	0.07
$15,000-24,999	16 (11.4)	4 (8.7)	
$25,000-34,999	24 (17.1)	10 (21.7)	
$35, 000-49,000	16 (11.4)	7 (15.2)	
$50,000-74,999	34 (24.3)	10 (21.7)	
>$75,000	38 (27.1)	5 (10.9)	
Clinical/behavioral factors			
Self-rated health			
Excellent	7 (4.4)	1 (1.7)	**0.00***
Very Good	36 (22.5)	20 (33.9)	
Good	85 (53.1)	17 (28.8)	
Poor	1(0.6)	5 (8.5)	
Fair	31 (19.4)	16 (27.1)	
Number of symptoms experienced			
1	19 (11.9)	7 (11.9)	0.31
2	45 (28.1)	12 (20.3)	
3	49 (30.6)	15 (25.4)	
4-10	47 (29.4)	25 (42.4)	
Number of medicines used			0.67
1-2	41 (25.6)	11 (18.6)	
3-4	27 (16.9)	11 (18.6)	
5-6	52 (32.5)	23 (39.0)	
7-8	14(8.8)	3 (5.1)	
>8	26 (16.3)	11 (18.6)	

Table 3.4 continued

Variable	**Agreement between patient-clinician**	**Disagreement between patient-clinician**	**P value**
	Number (%)	Number (%)	
Number of pharmacies			0.50
0	4 (2.5)	2 (3.4)	
1	106 (67.5)	44 (74.6)	
>2	47 (29.9)	13 (22.0)	
	Mean ± SD	**Mean ± SD**	
Concern beliefs in medicine	15.11 ± 4.43	17.28 ± 3.14	**0.00***

*p<0.05

* Significant differences in self-rated health ($\chi 2$= 19.41, p =0.001), geographical region where they resided ($\chi 2$= 8.23, p=0.04) and concern beliefs in medicines (t=-3.03, p=0.00)

a. Five missing cases because of unavailable patient information on race.
b. Thirty three missing cases because of unavailable patient information on income.

Table 3.5: Descriptive analysis comparing patient-clinician agreement with symptom attribution and patients' concern beliefs in medicine (n=219 symptoms) * [a]

Patient symptom attribution	**Number of symptoms (n)**	**Mean (Standard deviation)**	**t statistic (p value)**
Age (n=47)			
Disagreed with clinician	28	16.79 (4.08)	-0.199 (0.84)
Agreed with clinician	17	17.00 (2.21)	
Medicine (n=23)			
Disagreed with clinician	10	19.10 (2.28)	1.030 (0.32)
Agreed with clinician	5	17.40 (4.22)	
Disease (n=53)			
Disagreed with clinician	24	15.13 (5.23)	-0.490 (0.63)
Agreed with clinician	21	15.86 (4.72)	
Not caused by medicine (n=49)			
Disagreed with clinician	13	14.08 (2.93)	-0.569 (0.53)
Agreed with clinician	33	14.70 (3.47)	
Other reasons (n= 47)			
Disagreed with clinician	9	16.67 (3.97)	1.252 (0.22)
Agreed with clinician	34	14.71 (4.23)	

* $p<0.05$

a. Twenty five missing cases because of unavailable probability score ratings from clinicians. Clinicians did not have enough patient information to be able to make judgment. Data was obtained by self-report from patients.

Table 3.6: Socio-demographic, clinical and behavioral comparisons of patients whose symptom attributions agreed/disagreed with clinicians assessment by their different causal reason (n=219) * [a]

Patient symptom attribution	**Age, Number %)**		**Medicines, Number (%)**		**Disease, Number (%)**		**Not caused my medicines, Number (%)**		**Other reasons, Number (%)**	
Variable	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed
Socio-demographics										
Age										
65-74	6 (35.3)	16(57.1)	4(80.0)	6(60.0)	19(90.5)	3(12.5)	23(69.7)	7(53.8)	23(67.6)	5(55.6)
75-84	10(58.8	9(32.1)	1(20.0)	4(40.0)	2(9.5)	21(87.5)	6(18.2)	4(30.8)	4(11.8)	3(33.3)
85-100	1(5.9)	3(10.7)	0	0	0	0	4(12.1)	2(15.4)	7(20.6)	1(11.1)
Race										
White	17(100)	23(82.1)	3(75.0)	7(70.0)	21(100)	24(100)	30(93.8)	11(84.6)	33(97.1)	9(100)
Black/African American	0	3(10.7)	1(25.0)	3(30.0)	0	0	2(6.3)	1(7.7)	1(2.9)	0
Hispanic	0	0	0	0	0	0	0	1(7.7)	0	0
Others	0	2(7.1)	0	0	0	0	0	0	0	0

Table 3.6 continued

Patient symptom attribution	**Age, Number %)**		**Medicines, Number (%)**		**Disease, Number (%)**		**Not caused my medicines, Number (%)**		**Other reasons, Number (%)**	
Variable	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed
Gender										
Male	7(41.2)	10(58.8)	0	0	9(42.9)	5(20.8)	6(18.2)	5(38.5)	10(29.4)	2(22.2)
Female	11(39.3)	17(60.7)	5(100)	10(100)	12(57.1)	19(79.2)	27(81.8)	8(61.5)	24(70.6)	7(77.8)
Education										
Less than HS/HS degree	0	4(14.3)	0	1(10.0)	2(9.5)	4(16.7)	7(21.2)	5(38.5)	6(17.6)	4(44.4)
Some college	6(35.3)	8(28.6)	1(20.0)	4(40.0)	8(38.1)	12(50.0)	10(30.3)	3(23.1)	8(23.5)	2(22.2)
College degree	5(29.4)	5(17.9)	0	0	5(23.8)	2(8.3)	3(9.1)	1(7.7)	9(26.5)	1(11.1)
Graduate degree	0	5(17.9)	4(80.0)	5(50.0)	2(9.5)	3(12.5)	8(24.2)	3(23.1)	10(29.4)	2(22.2)
Other degree	6(35.3)	6(21.4)	0	0	4(19.0)	3(12.5)	5(15.2)	1(7.7)	1(2.9)	0

Table 3.6 continued

Patient symptom attribution	**Age, Number %)**		**Medicines, Number (%)**		**Disease, Number (%)**		**Not caused my medicines, Number (%)**		**Other reasons, Number (%)**	
Variable	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed
Geographical region										
Midwest	6(35.3)	5(17.9)	1(20.0)	5(50.0)	3(14.3)	2(8.3)	4(12.1)	1(7.7)	8(23.5)	4(44.4)
East	5(29.4)	5(17.9)	1(20.0)	1(10.0)	1(4.8)	7(29.2)	7(21.2)	3(23.1)	5(14.7)	1(11.1)
South	2(11.8)	13(46.4)	3(60.0)	4(40.0)	11(52.4)	14(58.3)	12(36.4)	6(46.2)	12(35.3)	3(33.3)
West	4(23.5)	5(17.9)	0	0	6(28.6)	1(4.2)	10(30.3)	3(23.1)	9(26.5)	1(11.1)
Income										
<15, 000	0	4(16.0)	1(20.0)	4(40.0)	0	1(4.5)	8(30.8)	3(25.0)	1(4.0)	0
$15,000-24,999	0	0	0	1(10.0)	3(17.6)	1(4.5)	3(11.5)	3(35.0)	1(4.0)	0
$25,000-34,999	0	5(20.0)	0	1(10.0)	1(5.9)	11(50.0)	4(15.4)	1(8.3)	4(16.0)	0
$35, 000-49,000	7(43.8)	4(16.0)	1(20.0)	2(20.0)	0	1(4.5)	1(3.8)	0	3(12.0)	2(25.0)

Table 3.6 continued

Patient symptom attribution	**Age, Number %)**		**Medicines, Number (%)**		**Disease, Number (%)**		**Not caused my medicines, Number (%)**		**Other reasons, Number (%)**	
Variable	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed
Income										
$50,000-74,999	2(12.5)	4(16.0)	2(40.0)	2(20.0)	7(41.2)	6(27.3)	2(7.7)	0	11(44.0)	5(62.5)
>$75,000	7(43.8)	6(24.0)	1(20.0)	0	6(35.3	2(9.1	8(30.8	5(41.7	5(20.0	1(12.5)
Clinical/Behavioral characteristics										
Self-rated health										
Excellent	0	2(7.1)	0	0	1(4.8)	0	0	0	4(11.8)	0
Very Good	3(17.6)	9(32.1)	4(80.0)	6(60.0)	4(19.0)	2(8.3)	10(30.3)	2(15.4)	10(29.4)	2(22.2)
Good	8(47.1)	9(32.1)	0	2(20.0)	9(42.9)	14(58.3)	22(66.7)	9(69.2)	14(41.2)	1(11.1)
Poor	0	0	0	0	0	0	1(3.0)	2(15.4)	0	0
Fair	6(35.3)	5(17.9)	1(20.0)	2(20.0)	7(33.3)	8(33.3)	0	0	6(17.6)	6(66.7)

Table 3.6 continued

Patient symptom attribution	**Age, Number %)**		**Medicines, Number (%)**		**Disease, Number (%)**		**Not caused my medicines, Number (%)**		**Other reasons, Number (%)**	
Variable	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed
Number of symptoms experienced										
1	0	2(7.1)	1(20.0)	2(20.0)	2(9.5)	1(4.2)	5(15.2)	1(7.7)	10(29.4)	0
2	4(23.5)	12(42.9)	0	1(10.0)	8(38.1)	6(25.0)	6(18.2)	4(30.8)	9(26.5)	2(22.2)
3	7(41.2)	10(35.7)	0	2(20.0)	5(23.8)	6(25.0)	12(36.4)	3(23.1)	5(14.7)	5(55.6)
4-10	6(35.3)	4(14.3)	4(80.0)	5(50.0)	6(28.6)	11(45.8)	10(30.3)	5(38.5)	10(29.4)	2(22.2)
Number of medicines used										
1-2	1(5.9)	3(10.7)	1(20.0)	1(10.0)	4(19.0)	5(20.8)	12(36.4)	4(30.8)	13(38.2)	0
3-4	1(5.9)	9(32.1)	0	0	7(33.3)	6(25.0)	4(12.1)	1(7.7)	4(11.8)	1(11.1)
5-6	11(64.7)	9(32.1)	3(60.0)	7(70.0)	3(14.3)	5(20.8)	11(33.3)	7(53.8)	5(14.7)	5(55.6)
7-8	3(17.6)	0	0	1(10.0)	2(9.5)	4(16.7)	5(15.2)	0	2(5.9)	0

Table 3.6 continued

Patient symptom attribution	**Age, Number %)**		**Medicines, Number (%)**		**Disease, Number (%)**		**Not caused my medicines, Number (%)**		**Other reasons, Number (%)**	
Variable	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed	Agreed	Disagreed
Number of medicines used										
>8	1(5.9)	7(25.0)	1(20.0)	1(10.0)	5(23.8)	4(16.7)	1(3.0)	1(7.7)	10(29.4)	3(33.3)
Number of pharmacies										
0	0	0	0	0	2(10.0	3(13.6)	0	0	1(2.9)	0
1	12(70.6)	14(50.0)	4(80.0)	6(60.0)	17(85.0)	18(81.8)	25(75.8)	11(84.6)	19(55.9)	5(55.6)
>2	5(29.4)	14(50.0	1(20.0)	4(40.0)	1(5.0)	1(4.5)	8(24.2)	2(15.4)	14(41.2)	4(44.4)

a. Missing cases within each casual reason group due to unavailable probability score ratings from clinicians. Clinicians did not have enough patient information to be able to make judgment. Also, information on patient characteristics such as race and income were not available and accounted for some of the missing cases.

* Significant differences in self-rated health ($\chi 2$= 9.162, p =0.03) among patients who attributed symptoms to ‘other reasons’, differences in number of medicines used ($\chi 2$= 13.20, p =0.01) among those who attributed their symptoms to age and differences in income ($\chi 2$= 12.98, p =0.02) and geographical region ($\chi 2$= 8.469, p =0.04) among those who attributed their symptoms to disease.

CHAPTER IV

CONCERN BELIEFS IN MEDICINES: CHANGES OVER TIME AND FACTORS RELATED TO ITS STABILITY

Adverse drug events (ADEs) are a common and costly public health problem to the society. ADEs have been shown to occur in at least 6.5% adult in-patients, 27.4% adult out-patients and 2.3% pediatric in-patients (Morimoto, Gandhi, Seger, Hsieh & Bates, 2004) and are described as injuries due to drug related interventions (Bates, 1995). In 2004 and 2005, it was estimated that more than 700,000 patients were treated for ADEs in US emergency departments annually, and 1 of every 6 patients required a hospital admission (Budnitz, Pollock, Wiedenbach, Mendelsohn, Schroeder & Annest, 2006). Despite the incidence of ADEs across clinical settings, it has been suggested that an identification of its risk factors can help in reducing the prevalence of preventable ADEs (Bates, 1995).

Beliefs in medicines have been identified as a socio-psychological risk factor that are associated with ADEs. Specifically, Oladimeji et al., 2008 (in review) showed that concern beliefs in medicine were significantly related to self-reported ADE after controlling for clinical factors such as number of medicines and behavioral factors such as the number of physicians seen regularly. In addition, studies have shown relationships of these beliefs to health behaviors such as adherence and symptom reporting (Clifford, Barber & Horne, 2008; Oladimeji et al., 2009 (forthcoming); Phatak & Thomas III, 2006). A greater perceived need for a medication means more adherence while stronger concerns and belief about the dangers of the medicine means less adherence (Horne & Weinman, 1999; McCracken, Hoskins & Eccleston, 2006; Neame & Hammond, 2005).

Symptom reporting as a coping behavior for dealing with symptoms experienced has also been related to beliefs in medicines. Specifically, stronger concern beliefs in medicines were associated with greater reporting of symptoms to health providers. People with stronger concern beliefs may be more cognitively aware of their symptoms, be more sensitive to them and be more watchful for unwanted reactions thus making them more likely to report symptoms (Oladimeji et al., 2009 (forthcoming)).

Since concern beliefs in medication are related to health behaviors such as adherence and symptom reporting, further knowledge and exploration of these beliefs will contribute to what is known about other health behaviors. Concern beliefs in medication may be understood as an interpersonal socio-psychological variable or concept that characterizes a person and his attitudes towards taking and managing his medicines and this could change with time (Horne, 2000). Interventions that attempt to influence changes in these cognitive factors can occur through the environment and maybe based on 'reciprocal determinism' (Glanz, 2002). An understanding of the factors that would impact a change in concern beliefs over time would be helpful in interventions that could reframe patients' ideas and perceptions about their medicines. This could lead to better understanding of patients' response to illness, treatment and behavior changes in relation to managing their medications and any adverse outcomes.

The extended self-regulatory model and social cognitive theory can be used to examine the stability of concern beliefs over time. In the social cognitive theory, health behavior is understood as dynamic and reciprocal in which behaviors, personal factors including cognitions and past experiences, and the environment interact together (Bandura, 1991). Therefore, a person's experience with medicines, the environment and

past behaviors can work together to influence a change in beliefs in medicines. Also, factors such as the adverse effects and long term risk due from using medications, social network and media, and the extent to which the medicines interfere with day-to-day activities and social events may shape concern beliefs in medicines (Phatak & Thomas III, 2006) and therefore impact it over time. In the extended self-regulatory model, both illness and treatment beliefs can affect a behavior such as reporting symptoms to health providers. When the health behavior for coping with a symptom has been performed, the individual appraises the outcome of the behavior which may affect the patients' perceptions or beliefs in treatment via feedback (Horne & Weinman 1999, Horne, 2003). In this study, concern beliefs in medicine which represent an individual's worries and anxieties about taking his medicine may influence the individual's adherence to the medicine or the reporting of an adverse drug event. The appraisal of the outcome of these behaviors may then feedback to influence the individual's concern beliefs in medicines. To test the variables that may change concern beliefs in medicines, factors related to medication use are therefore important.

Several behaviors or perceptions of medicines influenced by information from the media may impact concern beliefs in medicines and change it over time (Iosifescu, Halm, McGinn, Siu & Federman, 2008). These behaviors include adherence to medicines, self-reporting an ADE or reporting symptoms to health providers. When a patient experiences a symptom such as pain, the patient performs a behavior for coping with the threat. This could include adhering to the medicine prescribed for dealing with the symptom, reporting the symptom as an ADE if it is suspected to be due to a medicine and/or reporting the symptom to a health provider. If the medications used and behaviors

performed produce a favorable outcome, the beliefs of the individual about his or her medicines, his or her concerns about its adverse and long term effects may be changed. Specifically, respondents may have less concern about their medicines because they perceive that taking such health actions will improve their health. Conversely, if an individual experiences an adverse outcome from using a prescribed medication, perceptions of the treatment may change and lead to more concerns about the medication. As well, the health status of the individual may influence a change in patient's beliefs about their medicines. For example, if the health of the individual worsens over time, the medicines may no longer control the condition or the number of medicines used may be increased by the health provider. These outcomes could influence the patient's beliefs about the prescribed treatment, particularly, increase their concerns. The outcome of past behaviors and encounters related to medication use and an individual's health status may therefore be linked to his/her perception of treatment.

This study investigates how concern beliefs may behave over time and examines four factors that may be related to its stability. The objectives of this study were to 1) examine if concern beliefs remain stable or change over time, 2) examine the characteristics of the groups of individuals whose beliefs change or remain stable and 3) investigate what factors might impact a change in concern beliefs. It was expected that concern beliefs will change for some patients over time. Variables that may lead to a change over time and were tested include self-reported ADE, self-reported adherence, symptom reporting to health providers and illness-related factors such as patients' health status. It was expected that among individuals whose health status worsened over time, their number of medicines may increase and they would have stronger concern beliefs

about their medicines and its adverse effects. Also, patients who reported the symptoms they experienced to their health provider and/or were adherent to their medicines may have less concerns about their medicines and its adverse effects over time while those who experienced an ADE due to their medicines may have more concerns about its effects.

Research Methods

To examine these objectives, two similar analyses were completed in two different populations.

Study 1

Design: An internet-based survey of Medicare enrollees was conducted prior to the implementation of the Medicare prescription drug benefit in 2005 and after the start of the program in 2007. The design was a longitudinal study of baseline and follow-up studies across two years. Both internet-based studies were administered by Harris Interactive® on behalf of the University of Iowa College of Pharmacy. The survey was designed by the University of Iowa investigators and the project was approved by the University of Iowa Institutional Review Board.

Patients/Setting: Confidential panels of individuals who have asked to be invited to participate in telephone and/or online surveys are maintained by Harris Interactive®. The individuals in the online panel were asked to participate in this study and respondents were given Harris Interactive credit points for completing the survey. The inclusion criteria for being in both the baseline and follow-up surveys were being 65 or older, English speakers, U.S. residents and signed up in the Medicare health plan. In the baseline survey, Harris Interactive used their online panel of potential subjects and

provided data to University of Iowa researchers from a convenience or non-probability sample of 1220 anonymous respondents. In the follow-up survey, Harris Interactive provided data on a sample of 1024 anonymous respondents who completed the survey. Only the respondents who answered both the baseline and follow-up survey were included in this study and this sample contains 41% of baseline survey respondents who responded to the follow-up survey resulting in 436 respondents.

Data collection: A baseline internet survey was administered in October 2005 and a follow-up was done in October 2007. The baseline survey was a 166 item-survey and it took respondents about 18 minutes to complete. The follow-up survey included 161 items and approximately 23 minutes was used by respondents to complete it. Because of the survey length, numerous skip patterns that did not apply to some of the respondents were included. Also, respondents could answer part of the survey and return later to complete it at their own time and if necessary.

Measures: The dependent variable was a change in concern beliefs in medicines, defined as time 2 – time 1, a difference across two years. Five items were used to assess concern beliefs in medicines at each time (Horne et al., 1999). Items included 'I sometimes worry about the long term effects of my medicines', 'I sometimes worry about becoming too dependent on my medicines', 'Having to take my medicine worries me', 'My medicines disrupt my life', and 'My medicines are a mystery to me'. Five point Likert scales anchored with strongly disagree to strongly agree were used as the response options. The scale was derived by summing the responses of each individual across the five items. The scale ranged from 5-25 with a higher score meaning stronger concern beliefs about the dependence/worry/adverse effects of medicines. Previous studies show

reliability estimates ranging from 0.65-0.86 for using this scale. Horne, Weinman & Hankins, 1999 evaluated the test-retest reliabilities between initial and repeated scores for the scale among a sample of asthmatic patients and showed reliabilities within accepted limits with no significant difference in internal consistencies. Among 31 patients, correlation coefficients were 0.77 for necessity belief scales and 0.76 for concern belief scales ($p<0.001$). The construct validity of the scale has also been established (Horne et al., 1999). The Cronbach alpha for concern beliefs was 0.79 at time 1 and 0.80 at time 2 in this study.

Four independent variables were selected to test their effect on concern beliefs over time. These variables include self-rated health status, self-reported ADE, self-reported medication adherence and reporting of symptoms to health providers. Respondents' health status was self-rated and measured as a five item response scale ranging from poor to excellent (Idler, Benyamini, 1997; Bailis, Segall & Chipperfield, 2003). Self-reported ADE was measured as yes/no to "seeing a doctor about any side effects, unwanted reaction or other problems from medicines you were taking in the past year". A study by Chrischilles et al (1992) had used this question in the identification of self-reported ADE. Self-reported adherence was assessed using the Morisky scale (Morisky, Green, & Levine, 1996). This scale asks respondents to specify 1) if they had forgotten to take any of their medications in the past four weeks, 2) if they had been careless about taking any of their medication, 3) if they had stopped taking any of their medication when they felt better, and 4) if they had taken any of their medications less than the doctor prescribed because they felt better. The response options were yes, no and don't know. These four items were summed in the analyses. For symptom reporting,

respondents indicated if they had reported the symptom they experienced in the past month to a physician, pharmacist or other healthcare provider.

The surveys also contained data related to socio-demographics including age, geographical region, racial background, gender, highest level of education completed and household income and these were used as independent variables in the study. Clinical and behavioral characteristics such as number of medicines and using more pharmacies were also assessed. Specifically, respondents were asked for the number of pharmacies where they got their prescription medicines in a typical month and the number of different prescription medicines used in the past month. Then, they indicated the number of medications that they took on a regular basis, among those they had taken in the past month. To examine the number of symptoms experienced by respondents, information on health symptoms that subjects said they experienced in the past month (yes/no) were collected and 'past month' was used to improve recall. This preset list of symptoms was used because other studies of adverse drug events (ADEs) had used similar measures in identifying ADEs (Weingart et al., 2005). Symptoms such as headaches, dizziness, stomach problems, muscle aches, incontinence or problems with urinating, rash or itching, problems with sleep, changes in mood, fatigue and sexual problems were reported by respondents and there was no opportunity to report other non-listed items in the symptom list of the baseline survey. Further details of these measures and how they were defined and used in the analysis are seen in Appendix H.

Analysis: Descriptive analyses of change in concern beliefs in medicines were done. A clinically significant change was defined as a 2.0 minimum change in patients concern beliefs score. The criterion for choosing this level of change is based on at least a

10% change for significance (Hajiro & Nishimura, 2002; Zisapel & Nir, 2003). Similar to the concern beliefs scale, other scales that have five-point response scales ranging from 0-5 suggest at least a 10% change for significance. Since the range of scores for the concern beliefs scale is 20 (25-5), a 10% minimum change is equivalent to a 2.0 score change. After describing at least a 2.0 score change as clinically significant, respondents were classified into three groups based on their scores. These were 1) those whose scores remained the same, 2) individuals whose scores increased over time and 3) those whose scores decreased over time. Significant differences across the groups based on socio-demographic and clinical characteristics were examined using chi-square analysis.

To understand what factors may drive a change in concern beliefs, a multiple linear regression was run. A multiple linear regression was used here because the difference scores on the concern beliefs scale was continuous and on an interval level of measurement. The dependent variable was a change in concern beliefs. In study 2, due to space in the survey, a four-item concern belief scale was used. To determine if using this modified version of the scale would lead to variation in results across both studies, change in concern beliefs was determined using both the five-item original scale and a four-item scale in study 1.

The predictor variables included self-rated health, symptom reporting to physicians, self-reported ADE and self-reported adherence while age, gender, racial background, clinical characteristics such as the number of symptoms experienced and the number of medicines used were the control variables. The predictor variables in the follow-up survey in 2007 were used in the regression. This is because these variables were expected to influence the change in concern beliefs over the past year before its

measurement in 2007. Self-rated health and self-reported adherence were included in the regression as a change variable. Specifically, it was expected that respondents whose health status worsened over time will show more concern about their medicines compared to those whose health status remained the same. This is because the former group may believe that the medicines being used did not improve their health, may pose dangers with more use and inherently more dependence to further improve their health. Similarly, for self-reported medication adherence as a change variable, it was expected that those who had better adherence compared to those with no change in their adherence would have less concern beliefs in medicines over time because they believe that their health will improve as a result of taking their medicines. It is perceived that such a behavior is a positive behavior which may produce favorable outcomes. When these outcomes are appraised by the individual, it may lead to positive perceptions of treatment over time. All categorical measures were entered as a dummy variable. The regression coefficients, F, t statistic and p value were obtained and used in the interpretation of the results of the linear regression. The regression models are illustrated in Appendix I.

Results

For all respondents to both surveys, 379 respondents had concern beliefs scores in both years available in the dataset. Fifty seven respondents had missing concern belief scores either in 2005 and/or 2007. Among the 379 respondents, the mean change in concern beliefs in medicines was 3.37 (SD= 4.33), showing an increase over two years, from 11.62 ± 3.81 in 2005 to 15.11 ± 3.77 in 2007 (p=0.00). Using 2.0 as a cut-off point for a clinically significant change, 27 respondents had stable concern beliefs, 67 respondents had decreased concern beliefs and 285 respondents had increased concern

beliefs. Among the three groups, there were significant differences in self-rated health status ($\chi 2$= 17.27, p=0.027), geographical region ($\chi 2$= 16.93, p=0.01) and number of medicines ($\chi 2$= 48.73, p= 0.00) (Table 4.1). Specifically, individuals with decreased concerns in their medicines over time had better health status and were using lower numbers of medicines. Having stable concerns in medicines was associated with residing in the Mid-West region. In the regression analysis, being female, having an increase in number of medicines over time and reporting a self-reported ADE to a physician in 2007 were positively associated with an increase in concern beliefs in medicine over time. Having better adherence was associated with a decrease in concern beliefs over time (Table 4.2). There was no difference in the findings using the four-item concern belief scale.

Study 2

This second study investigates similar objectives among a different population of adults with self-reported physical limitations. It is possible that individuals with stronger concern beliefs may have self-selected to complete the previously used data (the Medicare survey) because of its topic. Also, it is possible that medication use factors impacting the concern beliefs of older adults may be different from adults in general, especially those with physical limitations. The objectives of this study were to examine if concern beliefs change over time or remain stable, what factors may drive the change and what characteristics are associated with individuals whose beliefs change. The individuals in this study were interviewed by telephone at baseline and also followed up after 6 months. Similar to study 1, only respondents who had concern belief scores available in both the baseline and follow-up interview were used as the sample.

Design: Secondary data analysis using data from the randomized controlled trial evaluating Living Well with a Disability & Collaborative Medication Management were conducted. This trial uses a population-based sample of 308 adults with activity limitations.

Subjects: Potential subjects were mailed a screening survey in Dubuque, Cedar Rapids, and Des Moines, Iowa. The sample was chosen among age groups, 40-65 and >65 years old from the list of registered voters. Responses to the screening survey were used to determine inclusion criteria for the randomized study, which included using more than three or more medicines, experiencing at least one problem or symptom fairly often or very often in the past four weeks, not planning to move out of the area in the next year and having at least one activity limitation. One activity limitation was defined as giving qualifying responses to either of two disability screening questions. These questions were: "Are you limited in any way in any activities because of an impairment or health problem and if so, how much?" or "If you use special equipment or help from others to get around, what type do you use?. Qualifying responses included "yes, limited a lot" to limitations and type of assistance included wheel chair, walker, cane, or another person. Those who self-reported the inclusion criteria in the recruitment survey were then contacted by telephone to ask for participation in the study.

Data collection: The data collected for the randomized controlled trial were obtained by telephone interviews at baseline, 6 months follow-up and 12 months follow-up. For the whole study, three and hundred and eight people were recruited over three waves with about 100 subjects in each wave. Only data from one wave were used for the

analysis in this study, the baseline and 6 month follow-up data. Similar interview items were collected in both the baseline and 6 month follow-up study.

Measures: The dependent variable was a change in concern beliefs in medicines defined as time 2- time 1, a difference across six months. Four items from Horne et al (1999) scale were used at each time. In the original scale, five items ask about concern beliefs (Horne et al., 1999). However, in this study due to space limitations and to allow for shorter interviews, only four items from the concern beliefs scale were used. These items included 'Having to take my medicine worries me', 'I sometimes worry about becoming too dependent on my medicines', 'I sometimes worry about the long-term effects of my medicines', and 'My medicines disrupt my life'. In order to use this short version of the scale, a reliability and correlation analysis was run by the investigators of the randomized control trial to determine the validity of using such a version. Based on this analysis, the item, 'My medicines are a mystery to me' was deleted and the Cronbach alpha lowered from 0.797 to 0.795. This item also had the lowest item-total correlation. Five point Likert scales anchored with strongly disagree and strongly agree were used as response options. The scale was derived by summing the responses of each individual across the four items with a range from 4-20 and a higher score on the concern belief scale meaning stronger concern beliefs about becoming dependent on medicines. The Cronbach alpha at time 1 was 0.67 and 0.68 at time 2.

The four independent variables that were selected to test their effect on concern beliefs over time included self-rated health status, self-reported ADE, self-reported medication adherence and reporting of medication-related symptoms to health providers, as in the previous studies. Self-rated health was assessed by asking respondents how they

would describe their health. Response options were anchored from poor to excellent. Self-reported ADE was defined as 'In the past six months, have you had any side effects, unwanted reactions, or other health problems from medications you were taking?. Response scales were either Yes, No, or don't know. The reporting of medication-related symptoms to physicians was assessed by asking respondents if they talked to a doctor about the problem they had with their medications. The measurement of symptom reporting in this study was different compared to study 1 because patients' symptoms were already attributed to their medicines. Self-reported adherence was assessed using the Morisky scale (Morisky, Green & Levine, 1986). This scale asked respondents to specify 1) if they had forgotten to take any of their medications in the past four weeks, 2) if they had been careless about taking any of their medication, 3) if they had stopped taking any of their medication when they felt better, and 4) if they had taken any of their medications less than the doctor prescribed because they felt better in the past four weeks. Response scales were yes, no and don't know. These four items were then summed in the analyses.

Other independent variables included socio-demographics such as age of respondent, gender, racial background, and highest grade of school completed. Clinical factors such as symptoms experienced and number of medications used were also assessed. Respondents were asked about the symptoms they had experienced in the past four weeks. The symptom checklist contained 21 symptoms and was based on three instruments: the Prevention of Secondary Conditions (PSC) Secondary Impairments Rating Scale, the Washington State Behavioral Risk Factor Surveillance System (BRFSS) survey and a symptom checklist developed by Gandhi et al (2003) to appraise

adverse drug events (Gandhi et al., 2003). The symptoms experienced by each respondent were summed up across these 21 symptoms to create a variable, 'sum of symptoms experienced' which describes the total number of symptoms experienced by each respondent. Respondents were also asked if they had any medications that were prescribed to them by their doctor and they were supposed to take regularly in the past two weeks. For those who answered positively, they were then asked to complete a prescription medication table with the number of medications taken, the purpose of the medication and the name of the medicine. Since the design of this study was a randomized control trial, the sample population were either in a control group, a living well with a disability intervention group or a living with a disability and collaborative medication management intervention group. The study group each individual was randomized into was controlled for in the analysis.

Analysis: Similar descriptive analyses conducted among older adults in study 1 were done. In this study, a clinically significant change was defined as a 1.6 minimum change in patients concern beliefs score. The criterion was based on at least a 10% change for significance (Hajiro & Nashimura, 2002; Zisapel & Nir, 2003). Since the range of scores for the concern beliefs scale is 16 (20-4), a 10% minimum change is equivalent to a 1.6 score change. Using chi-square analysis, possible significant comparisons between the three groups based on their socio-demographics and clinical and factors were examined.

To understand what factors may have an effect on concern beliefs over time, a multiple linear regression was run. The dependent variable was change in concern beliefs over six months. The predictor variables included self-rated health, reporting of

medication related symptoms, self-reported ADE and self-reported adherence while age, gender, race and clinical characteristics such as number of medicines and number of symptoms experienced were the control variables. The predictor variables in the follow-up survey after six months were used in the regression while self-rated health and self-reported adherence were measured as a change variable. The fully specified regression model is shown in Appendix I.

Results

For all respondents to both surveys, 101 respondents had concern belief scores available at both baseline and follow-up times. Five respondents had missing concern beliefs either at baseline and/or after six months follow-up. Among the 101 respondents, the mean change in concern beliefs in medicines was -0.267 (SD=3.63) showing little change in concern beliefs across six months from 10.23 ± 3.25 at baseline to 9.93 ± 3.80 at six months follow-up (p=0.46) . Using 1.6 as the cut-off point for a clinically significant change, 43 individuals had stable concern beliefs over time, 29 had decreased beliefs and 29 had increased beliefs. There was no significant difference across the groups in terms of their socio-demographics, clinical and/or behavioral characteristics (Table 4.3). In the regression analysis, having a change in number of medicines over time influenced a change in concern beliefs over time though the regression model was not statistically significant (Table 4.4).

Discussion

In these set of studies, concern beliefs changed for some older adults and adults with self-reported physical limitations while it remained the same for others. In study 1, being female, having an increase in number of medicines and having a self-reported ADE

were related to an increase in concern beliefs over time. Better adherence to medicines over time lead to a decrease in concern beliefs over time. In study 2, a change in number of medicines over time was associated with an increase in concern beliefs over time.

Concern beliefs did change over time, as expected for some individuals. There was however no statistically significant change in beliefs among adults with physical limitations. A difference of six months between the baseline and follow-up time period may not have been enough time for such change to be evident. Among older adults, the change in concern beliefs was both statistically and clinically significant. A two-year period between the baseline and follow-up times may have been long enough for a change in beliefs to be evident. This finding is positive because it shows that possible interventions to reframe patients' perception of their treatment can be developed and may lead to positive outcomes such as improved adherence to medicines. Since patients' beliefs about the dependence and long term effects of medicines only change for some individuals, health providers should be informed that patients' medication management education programs need to be tailored to a specific individual.

As hypothesized, having an adverse drug event was related to a change in concern beliefs over time compared to having no ADE among older adults only. Beliefs about medicines are formed and shaped by an individual's experience with using medicines which could include an adverse effect or a long term risk (Phatak & Thomas, 2006). An individual who has had a side effect or problem from taking his medicine is likely to be more concerned about taking them because such a negative experience has changed his perception or representation of his treatment. According to the extended self-regulatory model, treatment perceptions are triggered by symptom experiences available to an

individual. An individual's representation of his treatment such as their concern about their medicines and whether it is harmful or not can be shaped and changed based on the experience of a symptom using medicines. Therefore, if attribution of a symptom to side effects reinforces concerns about taking treatment (Horne et al., 1999), an appraisal of that outcome may then feedback to influence a change in beliefs in medicines over time.

Being female was related to an increase in concern beliefs in medicines over time compared to being male. This finding was consistent with literature as a population based study found women to view medicines as more harmful and possibly have negative beliefs about medicines compared to men (Isacson & Bingefors, 2002). Concerns about medicines which may suggest a negative view of prescribed medicines may therefore be higher among this group and increase with age.

Having an increase in number of medicines used over time lead to an increase in concern beliefs among older adults. This finding makes logical sense because if medicines prescribed for older adults cannot control their health, more medicines may be added by the physician. Older adults may therefore worry about their medicines and have anxieties about its dependence effect because they have seen their health worsen over time and the number of medicines being used to control their health problems increase with time. A change in number of medicines also lead to an increase in concern beliefs over time among adults with physical limitations but the regression model was non-significant. This may have occurred because the overall model had no predictive capability or we chose our predictors poorly (Dallal, 2000). However, similar predictors were chosen in study 1 and the regression model was statistically significant. The sample size for study 2 was not enough to conduct a multiple linear regression as there were 13

variables for a sample size of 100 cases. This may have allowed the model to have no predictive capability. In addition, the results were not consistent between study 1 and study 2 and may have occurred because there were varying measures of the predictor variables such as self-reported ADE and the reporting of symptoms to health providers.

It was hypothesized that being adherent to medicines over time would lead to better health outcomes and an appraisal of the positive effect would lead to lower concerns about medicines. Consistent with the hypothesis, having better medication adherence over time was related to a change in concern beliefs among older adults. Patients who changed their behaviors and took their medicines as prescribed by their doctors may have observed better health or a reduction in symptoms which would therefore reduce the concerns they had about their medicines. They may have related the positive effect to the medicines being used.

Reporting symptoms to health providers was not related to a change in concern beliefs over time for either population. It was hypothesized that those who reported their symptoms to their health providers may believe that taking such action would improve their health and reduce their concerns about their medicines over time. Patients who reported their symptoms may have reported the most severe ones which seemed intolerable and not all the symptoms they experienced. In this case, a patient would not believe that his/her health was improving because of symptom reporting; rather, he/she would be trying to alleviate the discomfort he/she was experiencing due to the symptoms. Hence, any anxiety about medicines and its adverse of long term effects for such patient would stay the same.

The worsening of health status of patients over time was not related to a change in concern beliefs over time for either population. Older patients who know their health status have probably accepted their position and therefore feel no need to worry about their medicines or its adverse effects. They may believe that a decline in their health is due to their age and not related to their medicines. Adults with physical limitations were taking at least three or more medicines and had reported having symptoms fairly often to be included in the study; therefore, they may not attribute their worse health to their medicines but to their prior health problems.

Across both studies 1 and 2, it was observed that concern beliefs in medicines seems to be an important variable affecting the reporting of adverse drug events among older adults than other populations. This is probably because older adults tend to use more medicines and are prone to having more adverse events (Bates, 1995; Chrischilles, Segar & Wallace, 1992); they may therefore worry about their medicines more than other populations. Also, older adults have more chronic illnesses and diseases that require long term use of medicines; this may therefore contribute to their perceptions of dependence on their medicines compared to other populations. Since the sample population in study 1 was an internet sample of highly educated older adults, it is important to consider that the ability to identify and recognize symptoms may be better compared to the general population of older adults because of the medical resources and information available to an internet sample. This internet group may therefore worry about their medicines more than other older adults. Adults with physical limitations may believe that their physical limitation is already a major issue to be concerned about and may be less concerned about their medicines.

Though study 2 had a small sample size which was a limitation in this study, there were weak non-significant correlations between concern beliefs and other predictor variables therefore minimizing the potential of observing statistical relationships. Also, the time frame between the baseline and follow-up was only six months. This may not be enough time for a significant difference or change in concern beliefs to be evident among the population.

Other limitations in both set of studies included the use of secondary data for the analysis. Factors such as the use of media and the influence of social network such as family and friends could have been related to a change in beliefs over time (Difenbach & Levanthal, 1996). This is because in the extended self-regulatory model, it is conceptualized that contextual factors such as these environmental and social influences could impact beliefs in medicines (Horne, 2003). Social and cultural relationships can influence illness representations, beliefs and the selection and performance of coping strategies to manage health threats (Brissette, Scheier & Carver, 2002; Cameron, Levanthal E, & Levanthal H, 1993; Levanthal H, Levanthal E, & Contrada, 1998). These measures were not available in the datasets and therefore, not testable. The measure of self-reported ADE had some limitations. It included reporting 'other problems from taking medications to the doctor', which could be interpreted by a patient as cost or access problems instead of side effects or adverse reactions to medicines. The measure of ADE could therefore be overestimated.

Patients' concern beliefs may change when there is a negative experience associated with using medicines such as having an ADE. In the extended self-regulatory model, emotions such as worry, fear and anxieties are evoked when an individual has a

symptom. Similarly, when an individual has an adverse drug event, such emotions may arise. Negative emotions and experiences of a symptom or ADE may therefore change an individual's representation of treatment rather than a positive medication use experience because patients are quick to adapt to experiences that may negatively affect their health. Also, having better adherence to medicines and reporting symptoms to health providers may have produced a positive health outcome but it may not have been sufficient enough to change patients' beliefs in their medicines. Patients may not associate their improved health to their past positive behaviors but to other factors in their present environment.

Understanding whether concern beliefs in medicines change or remain stable over time and examining the factors that may lead to a change in these beliefs may contribute to the development of individualized cognitive-behavioral and educational interventions for patients using medicines. This will subsequently become important in the self-management of medicines and its adverse outcomes. Future studies should further examine changes in concern beliefs over time among different populations or individuals with specific medical conditions. Also, external factors such as influences of the social environment and an individual's social and cultural norms should be assessed when examining such changes in patients' concern beliefs (Horne, 2003).

Table 4.1: Characteristics of older adults whose concern beliefs stayed the same, increased or decreased over time (n=379) [a]

	Concern beliefs stayed the same (n=27)	**Concern beliefs decreased over time (n=67)**	**Concern beliefs increased over time (n=285)**	**P value**
Variable	**Number (%)**	**Number (%)**	**Number (%)**	
Socio-demographics				
Age				0.43
65-74	20 (74.1)	38 (56.7)	158 (55.4)	
75-84	6 (22.2)	25 (37.3)	114 (40.0)	
85-100	1 (3.7)	4 (6)	13 (4.6)	
Race				0.37
White	25 (92.6)	63 (95.5)	263 (92.9)	
Black/African American	2 (7.4)	0	6 (2.1)	
Hispanic	0	2 (3.0)	11 (3.9)	
Others	0	1 (1.5)	3 (1.1)	
Gender				0.50
Male	15 (55.6)	31 (46.3)	125 (43.9)	
Female	12 (44.4)	36 (53.7)	160 (56.1)	
Education				0.44
Less than HS school/HS degree	4 (14.8)	11 (16.4)	51 (17.9)	
Some college	7 (25.9)	27 (40.3)	112 (39.3)	
College degree	6 (22.2)	9 (13.4)	37 (13.0)	
Graduate degree	4 (14.8)	10 (14.9)	57 (20.0)	
Other type of degree	6 (22.2)	10 (14.9)	28 (9.8)	
Geographical region				**0.01**
Midwest	14 (51.9)	18 (26.9)	97 (34.0)	
East	4 (14.8)	8 (11.9)	62 (21.8)	
South	9 (33.3)	25 (37.3)	67 (23.5)	
West	0	16 (23.9)	59 (20.7)	

Table 4.1 continued

	Concern beliefs stayed the same (n=27)	**Concern beliefs decreased over time (n=67)**	**Concern beliefs increased over time (n=285)**	**P value**
Variable	**Number (%)**	**Number (%)**	**Number (%)**	
Income				0.71
<15, 000	2 (8.3)	3 (4.6)	12 (4.6)	
$15,000-24,999	6 (25.0)	12 (18.5)	34 (13.1)	
$25,000-34,999	2 (8.3)	13 (20.0)	51 (19.6)	
$35, 000-49,000	4 (16.7)	8 (12.3)	54 (20.8)	
$50,000-74,999	6 (25.0)	16 (24.6)	60 (23.1)	
>$75,000	4 (16.7)	13 (20.0)	49 (18.8)	
Clinical/Behavioral characteristics				
Self-rated health				**0.03**
Excellent	2 (7.4)	6 (9.0)	12 (4.2)	
Very Good	7 (25.9)	23 (34.3)	71 (24.9)	
Good	14 (51.9)	34 (50.7)	124 (43.5)	
Poor	3 (11.1)	3 (4.5)	66 (23.2)	
Fair	1 (3.7)	1 (1.5)	12 (4.2)	
Number of symptoms experienced				0.21
0	9 (33.3)	32 (47.8)	98 (34.4)	
1	4 (14.8)	8 (11.9)	44 (15.4)	
2	4 (14.8)	14 (20.9)	37 (13.0)	
3	5 (18.5)	5 (7.5)	47 (16.5)	
4-10	5 (18.5)	8 (11.9)	59 (20.7)	
Number of medicines used				**0.00**
1-2	8 (29.6)	34 (50.7)	45 (15.8)	
3-4	11 (40.7)	16 (23.9)	83 (29.1)	
5-6	5 (18.5)	14 (20.9)	79 (27.7)	
7-8	0	2 (3.0)	36 (12.6)	
>8	3 (11.1)	1 (1.5)	42 (14.7)	

Table 4.1 continued

	Concern beliefs stayed the same (n=27)	**Concern beliefs decreased over time (n=67)**	**Concern beliefs increased over time (n=285)**	**P value**
Variable	**Number (%)**	**Number (%)**	**Number (%)**	
Number of pharmacies				0.07
0	0	6(9.0)	8 (2.8)	
1	24 (88.9)	49 (73.1)	205 (72.2)	
2	2 (7.4)	11 (16.4)	65 (22.9)	
>3	1 (3.7)	1 (1.5)	6 (2.1)	

a. Significant differences in self-rated health ($\chi 2$= 17.27, p=0.027), geographical region where they resided ($\chi 2$= 16.93, p=0.01) and number of medicines used ($\chi 2$= 48.73, p= 0.00).

Table 4.2: Multiple linear regression of factors predicting a change in concern beliefs in medicines over time among older adults (n=379) [a]

	Unstandardized coefficients (standard errors)
Variable	**B (Standard Error)**
Socio-demographics	
Age	
65-74	Reference group
75-84	-0.296 (0.478)
85-100	0.303 (1.105)
Gender	
Male	Reference group
Female	1.197 (0.462)*
Race/ethnicity	
White	Reference group
Black/African American	1.323 (1.632)
Hispanic	0.812 (1.198)
Other race	0.805 (2.124)
Clinical characteristics	
Change in self-reported medication adherence	
No change in adherence over time	Reference group
Worse adherence over time	-0.698 (1.044)
Better adherence over time	-2.792 (1.169)*
Self-reported adverse drug event (ADE)	
Had no adverse drug event	Reference group
Had an ADE in past year	1.846 (0.504)**
Change in self rated health status	
Had same health status over time	Reference group
Health status became better	0.274 (0.557)
Health status became worse over time	-0.193 (0.752)
Symptom reporting to health provider	
Did not report symptom	Reference group
Reported symptom to health provider	-0.257 (0.468)
Change in number of symptoms experienced	0.117 (0.146)

Table 4.2 continued

Variable	B (Standard Error)
Change in number of medicines used	
Same number of medicines	Reference group
Decrease in number of medicines	0.005 (0.619)
Increase in number of medicines used	1.130 (0.530)*

a. F= 2.344, p= 0.03; R^2 = 0.09; Adjusted R square= 0.05 *p<0.05 **p<0.001

Table 4.3: Characteristics of adults, 40 years and above with physical limitations, whose concern beliefs stayed the same, decreased and increased over time (n=101)

	Concern beliefs stayed the same (n=43)	**Concern beliefs decreased over time (n=29)**	**Concern beliefs increased over time (n=29)**	**P value**
Variable	**Number (%)**	**Number (%)**	**Number (%)**	
Socio-demographics				
Age				0.68
40-55	12 (28.6)	5 (17.2)	8 (27.6)	
56-75	16 (38.1)	15 (51.7)	14 (48.3)	
>75	14 (33.3)	9 (31.0)	7 (24.1)	
Race				0.35
White	39 (90.6)	29 (100)	27 (93.1)	
Black/African American	3 (6.9)	0	2 (6.9)	
Others	2 (4.7)	0	0	
Gender				0.35
Male	12 (27.9)	12 (41.4)	12 (41.4)	
Female	31 (72.1)	17 (58.6)	17 (58.6)	
Education				0.86
Less than high school/HS degree	14 (32.5)	13 (44.8)	14 (48.2)	
Some college	12 (27.9)	7 (24.1)	6 (20.7)	
College degree	12 (27.9)	7 (24.1)	8 (27.6)	
Other type of degree	5 (11.6)	2 (6.9)	1 (3.4)	
Clinical/Behavioral characteristics				
Self-rated health				0.64
Excellent	1 (2.3)	0	0	
Very Good	3 (7.0)	2 (6.9)	3 (10.3)	
Good	23 (53.5)	10 (34.5)	10 (34.5)	
Poor	13 (30.2)	14 (48.3)	12 (41.4)	
Fair	3 (7.0)	3 (10.3)	4 (13.8)	

Table 4.3 continued

	Concern beliefs stayed the same (n=43)	**Concern beliefs decreased over time (n=29)**	**Concern beliefs increased over time (n=29)**	**P value**
Variable	**Number (%)**	**Number (%)**	**Number (%)**	
Number of symptoms experienced				
0	0	0	0	0.42
1	2 (4.7)	2 (6.9)	0	
2	5 (11.6)	3 (10.3)	2 (7.4)	
3	7 (16.3)	4 (13.8)	2 (7.4)	
4-10	29 (67.5)	20 (68.9)	23 (85.1)	
Number of medicines used				
1-2	24 (55.8)	22 (75.9)	19 (65.5)	0.85
3-4	1 (2.3)	0	0	
5-6	4 (9.3)	2 (6.9)	1 (3.5)	
7-8	4 (9.3)	1 (3.5)	2 (6.9)	
>8	11 (25.6)	4 (13.8)	6 (20.7)	

Table 4.4: Multiple linear regression of factors predicting a change in concern beliefs in medicines over time among adults aged 40 years and above with physical limitations (n=100) [a]

	Unstandardized coefficients (standard errors)
Variable	**B (Standard Error)**
Socio-demographics	
Age	
40-55	Reference group
56-75	-0.232 (1.019)
>75	0.165 (1.133)
Gender	
Male	Reference group
Female	0.040 (0.809)
Racial background	
White	Reference group
Black/African American	2.866 (1.963)
Others	1.074 (1.583)
Clinical characteristics	
Change in self-reported medication adherence	
No change in adherence over time	Reference group
Worse adherence over time	0.692 (1.510)
Better adherence over time	5.692 (4.144)
Self-reported adverse drug event (ADE)	
Had no adverse drug event	Reference group
Had an ADE in past year	-1.441 (1.404)
Change in self rated health status	
Had same health status over time	Reference group
Health status became better	-0.763 (1.111)
Health status became worse over time	-0.618 (0.968)
Symptom reporting to health provider	
Did not report symptom	Reference group
Reported symptom to health provider	-0.552 (1.598)
Intervention received	
Control group	Reference group
Disability only intervention	0.939 (1.027)

Table 4.4 continued

Variable	**B (Standard Error)**
Intervention received	
Pharmacist and Disability intervention	-1.303 (1.428)
Change in number of symptoms experienced	0.246 (0.233)
Change in number of medicines used	0.286 (0.142)*

a. The overall model was non-significant (F= 1.107, p= 0.363; R^2 = 0.168; Adjusted R square= 0.02) *** p<0.05**

a.

CHAPTER V

DISCUSSION

Concern beliefs in medicine have been associated with patient health outcomes such as medication adherence, self-reported adverse drug event and symptom reporting to health providers (Horne, 2003; Oladimeji et al., 2008; Oladimeji et al., 2009 (forthcoming)). Three studies focused on concern beliefs in medicine were conducted to further examine the important role of this concept in medication use behaviors. It was observed that concern beliefs in medicine changed over time for older adults, were not related to symptom attribution but were related to patient outcomes such as self-reported adverse drug events (ADEs). This chapter summarizes what was learned about concern beliefs in medicine in general, the theoretical models and methodology used in the studies, practice implications, and what the next steps should be in this program of research.

Three main things were found in these studies about concern beliefs in medicines. First, concern beliefs in medicine remained important in predicting self-reported ADE and is an important socio-psychological concept to consider in the management of symptoms, unwanted reactions and prescription medicine use. Previous studies that had showed the relationship of receiving an inappropriate medicine to ADEs had inconsistent results. While Chang, Liu, Yang, Yang, Wu & Lu, 2005 and Passarelli, Jacob-Filho & Figueras, 2005 found an association between inappropriate medication use and an adverse event, Onder, Landi, Liperoti, Fialova, Gambassi, & Bernabei, 2005 and Page II & Ruscin, 2006 showed no association. Consistent with these latter studies, the use of an inappropriate medicine was not related to self-reported ADE, rather concern beliefs in

medicine was a risk factor for the outcome. This suggests that when patients attribute symptoms being experienced to side effects of medicines and an ADE, the perceptions of their treatment play an important role in attributions. Older adults who worry about their medicines and their long term and adverse effects are likely to report having an ADE probably because they are thinking about medicines more often or in some serious manner. These patients are not likely to be aware of the inappropriateness of the medication being used; therefore, the experience of an ADE in their own perspective may not be related to its use. In a situation where the inappropriate medicine use may have actually caused the ADE, patients may be unsure of the source of the adverse effect and therefore could attribute it to something else.

Concern beliefs in medicine may, however, need to be studied by disease states/chronic illnesses, as some evidence suggests that patients' concern beliefs may vary by chronic condition or diagnoses or by the type of medications taken. Horne, Weinman & Hankins (1999) initially examined the concept among those with four different chronic illnesses. Subsequently, studies have examined concern beliefs in medicine as a concept without considering patients' diagnoses (Horne, 2003; Jorgensen, Andersson & Mardby, 2006; Mardby, Akerlind & Jorgensen, 2007) while some have examined it among patients with certain illnesses (Bryne, Walsh & Murphy, 2005; Kumar et al., 2008; Brown, Battista, Bruehlman, Sereika, Thase, Dunbar-Jacob, 2005). It is possible that individuals who have chronic illnesses such as diabetes or hypertension may worry about the long term and dependence effects of their medicines more than others with acute illnesses. Patients with symptomatic conditions such as asthma may have stronger concerns about their medicines compared to those with asymptomatic

conditions. In addition, concerns and anxieties about medicines may differ when patients take prescription medicines compared to when they take over-the-counter medicines. Patients who take the latter drugs may be less likely to believe their medicine is going to have a long term or dependence effect, while patients who take prescription medicines may worry about such effects. Also, patients on high risk medications such as warfarin and digoxin may worry about their medicines differently compared to patients on low risk drugs. The former group may have stronger anxieties about their medicines compared to the latter group. The relationship of concern beliefs to patient outcomes such as self-reported ADEs may also be different by these disease or medication type variations. Studies that examine if patients vary by these clinical factors and how this variation is related to ADEs could lead to further description of concern beliefs and its importance in other patient outcomes.

Second, concern beliefs in medicine do not appear to be related to attribution of symptoms to medicines. The analyses for this conclusion, however, had an important limitation, i.e., sample size, therefore strong inferences about what was learned about concern beliefs cannot be made. It is perceived that concern beliefs may still be important in symptom attribution (Gonzalez et al., 2007), though stronger relationships to health behaviors such as medication adherence and symptom reporting to health providers, rather than patients' representations have been observed. This might occur because patients think about their symptoms differently than the way they think about their medicines. In symptom attribution, patients may label and process their symptom based on the level of severity of the symptom, the emotional reactions from having them and how strong they impact their health. In this case, they may consider their strong

emotional feelings rather than cognitively thinking through the symptom in making attributions. Concern beliefs in medicine have a cognitive and emotional dimension and reflect patients' beliefs irrespective of the severity of their illness/symptom. Despite the fact that concern beliefs and symptom attribution represent patients' views and ideas regarding medicine and symptom respectively, they may not be closely linked, though this notion needs to be fully explored.

On the other hand, it was observed that the expected direction of the relationship of concern beliefs to symptom attribution was shown among some older adults, suggesting that future research examining the association of concern beliefs in medicine to symptom attribution should still be considered. Based on the extended self-regulatory model, patients' interpretations and attribution of symptoms is an active and dynamic process that may be influenced by several factors, including their beliefs in medicine. In a future study, a stronger design where patients are recruited by their symptom attribution type may create sufficient data to detect this relationship, if it exists.

Third, concern beliefs in medicines changed over time and having a previous ADE was predictive of this change. Studies have shown that health beliefs in general change over time for individuals (Lau, Jacobs, Quadrel, & Hartman, 1990; Morin, Blais, & Savard, 2002; Troein, Rastam, & Selander, 2002). It was therefore not surprising that concern beliefs changed over time for some older adults. Since concern beliefs in medicine change, this finding indicates that a modification or reframing of these beliefs as a means of changing health behavior is possible. The relationship between concern beliefs in medicine and ADE may however be mediated psychologically through negative affect (Gonzalez et al., 2007). Having a negative experience from medicines may

provoke negative emotions and affect which could then influence patients concerns about their medicine. This variable and its relation to concern beliefs in medicines require research.

Concern beliefs in medicine changed based on the outcome or evaluation of past coping behaviors and not necessarily to the performance of the coping behavior, consistent with extended self-regulation. For example, the reporting of symptoms to health providers did not lead to a change in concern beliefs over time. It seems that the causal relationship between beliefs and symptom reporting is predictive when concern beliefs in medicine precede symptom reporting behaviors. The outcome of symptom reporting (whether positive or negative) is theorized and is likely to be the intervening variable between the performance of the behavior and a change in concern beliefs, which is consistent with self-regulation model. To further illustrate this, when taking medicines (a behavior) leads to side effects/unwanted reactions; the negative outcome may mediate the relationship between the behavior and a change in concern beliefs. This would explain why having a previous ADE can lead to a change in beliefs. Beliefs may influence behaviors but it is the outcome of the behaviors that are most likely to influence beliefs and lead to its change. Future research could examine how the outcome of behaviors leads to changes in beliefs. For example, patients who have reported symptoms in a clinic to their health provider may be followed up after their initial office visit. Using the extended self-regulatory model, patients may then be asked to state the coping procedure they performed for dealing with the symptom they experienced. The outcome of the behavior at a later time may then be elicited using telephone interviews or a mail survey. Patients who had a positive outcome from their behavior could then be compared

to those with negative experience based on their clinical characteristics and socio-demographics. Also, relationships of the outcome to a change in concern beliefs could be investigated.

In summary, concern beliefs in medicine may change based on the outcome of patients' past behavior and were an important predictor of ADE compared to presence of an inappropriate medications and number of medications. However, it is important to note that the use of an internet sample affects the generalizability of these findings. For example, these patients experience with using the internet makes them susceptible to seeking information about their health on the web. Such exposure to medical information and resources may allow anxieties and concerns about their medicines to be higher compared to a population not exposed to the web. Information on potential ADEs associated with their medicines may also be available on the web, hence, sensitizing them to notice such effects. Simply, using an internet sample of older adults may over-estimate the relationship of concern beliefs to ADE because of their access to information on medicines and its side effects. On the other hand, exposure to health information on the web may allow patients learn how to manage and cope with their symptoms and medication effects therefore, allowing their anxieties about medicines to be lower compared to a less internet-experienced population.

The sample population was also highly educated and had high income. These individuals probably had more access to information on risk of medicines which could have increased their concerns about their medicines compared to the general population of older adults. Also, they were probably able to identify when their symptoms were due to medicines and readily report it to their doctor better than older adults with less

education and income (Kauhanen, Kaplan, Julkunen, Wilson & Salonen, 1993). On the other hand, individuals with higher education and income may have better coping mechanisms available to them and subsequently, the use of these coping strategies may reduce the perceptions of symptoms, the use of health services and the reporting of medication effects to health providers (Ladwig, Marten- Marten-Mittag, Formanek & Dammann, 2000). For future studies, an understanding of the methodology and theoretical approach that may be used is pertinent.

Methodology/Theoretical Model

In this section, what was learned about the theoretical model used for examining concern beliefs in medicine is examined, its usefulness in similar future studies examining these beliefs is discussed, and other methodology issues related to the measures used in this study are stated.

The extended self-regulatory model was the theoretical approach used in this set of studies. Compared to more general health behavior models such as the TRA, TPB and the HBM, this model attempts to explain processes that lead to actual coping behaviors for dealing with health threats (Mardby, 2008; Pennebaker, 2000). Since this model emphasizes the resulting feedback on behaviors based on cognition and emotion and perceives this process as dynamic, it seemed useful in the investigation of concern beliefs and its impact on patient outcomes. The model may be useful in understanding the relationship between concern beliefs in medicine and behaviors directly related to treatment choice and coping strategies such as self-reporting an ADE, but it may not be appropriate in examining the relationship of beliefs in medicine to cognitive processes such as patients' symptom representations. Self-regulation involves making a decision

about the outcome of the health behavior performed and does not end at symptom representation. Simply, for the process of self-regulation to be considered as active and dynamic, the outcome of the coping strategy, not just the behavior, e.g. taking your medicine as directed, symptom reporting to health provider, or self-reporting an ADE needs to be explored.

The extended self-regulatory model incorporates beliefs in medicine in the process of self-regulation when a decision about treatment is to be made and should continue to be used in understanding why patients make treatment choices and how they make symptom coping decisions. The full model has not yet been tested in any study and this area may be explored in future research. The use of this model in examining concern beliefs is important, but measures and concepts may need to be operationalized differently. For example, in the future, qualitative studies may need to be done prior to quantitative analysis in order to examine patients' symptom representations and illness attributions. In such qualitative studies, patients' illness representations such as identity, label, cure, cause, control and consequences may be examined using an illness perception questionnaire or assessed using focus groups or patient interviews. Richer themes about the way patients think about their symptoms and medicines may be elicited during such exploratory studies. Also, patients can be asked direct questions about illness and symptom representations instead of trying to identify them in their open-ended but somewhat brief responses similar to what was done in this study.

In terms of the implementation of aspects of these studies, two issues should be considered regarding the definitions of ADE and inappropriate medication. Though concern beliefs have been related to self-reported ADE, the extrapolation of the

relationship of this variable to objective measures of ADE should be done with caution. As stated earlier, it is possible that the relationship of concern beliefs to this outcome is because of a general psychological concept such as negative affect. Patients who are self-reporting ADEs may already have negative anxieties and concerns about their medicines in general and therefore would have strong negative beliefs about the long term effects of their medicine (Gonzalez et al., 2007). Self-reported ADE is a patient-reported outcome, which similar to concern beliefs reflects the patient's perspective of their symptom and medicine. Therefore, the link between concern beliefs in medicine and self-reported ADE may be observed because both factors represent the patients' negative overall view. Objective measures of ADEs using chart reviews or medical records based on clinician's assessment may represent a more definitive measure of ADEs, particularly from the providers' perspective. Patients' negative affect related to self-reported ADEs may therefore not be reflected using such measures. Future studies should therefore examine the possibility of this notion by examining concern beliefs as a risk factor for objective measures of ADEs. It is expected that the relationship of concern beliefs in medicines to this measure of ADEs will be significant and important; however, this will need to be confirmed in such studies. Studies that examine risk factors for ADEs should include concern beliefs in medicine as an important control variable in their analysis.

The operationalization of self-reported ADE was different across the set of studies and this has certain implications. For example, paper 1 and 2 defined an ADE as seeing a doctor about any side effects, unwanted reactions or other problems from taking medicines while study 2 in paper 3 defined it as having any side effects, unwanted reactions, or other health problems from medications being taken. The former definition

suggests that the patient had an ADE only if they told the doctor about it while the latter does not. It is possible that the patient had an ADE and did not see their doctor about it because it was not severe enough or he did not have an opportunity to report. The identification of ADE using this measure may therefore be underestimated. Compared to the definition of self-reported ADE in past literature (Chrischilles, Segar, & Wallace, 1992; Chrischilles, Rubenstein, Van Glider, Voelker, Wright, & Wallace, 2007), which assumes that the side effect should be mentioned to the doctor, this measure seemed better because it assesses potential ADEs without assuming that the patient has reported it. Also, asking about general health problems from taking medicines seems more specific than asking about 'other problems' from taking medicines which may be cost or access related.

The use of a four-item concern belief scale and a five-item concern belief scale across the set of studies did produce varying results based on the regression analyses.

Despite the fact that inappropriate medicine use showed no association with self-reported ADEs, it is important to understand that the operationalization of the measure may have been done differently. Both the modified ACOVE and Beers criteria measures were summed and used in defining an inappropriate medicine. Each specific measure could also have been used separately in defining an inappropriate medicine. However, this was not done. In the Beers criteria, the medications that are of high risk to patients, drugs that should not be used with certain conditions, and prescriptions that should not exceed a recommended daily dose are stated. The Beers criteria condition-specific and non-condition specific lists specifically examine potential misuse/inappropriate prescribing of medications. In contrast, the ACOVE indicators within the 'prescribing

indicated medications' domain state the medicines that should have been prescribed for older adults with those conditions. It therefore identifies an under-use of appropriate medication for patients not receiving this medicine. In future, a study that would examine under-use of medicines using all the quality indicators within the ACOVE criteria and its relationship to health outcomes such as rates of hospitalization, emergency room visits or report of ADEs could be done. In this study, the modified ACOVE criteria seemed to identify more under-use of medications compared to identifying inappropriate medicines like the Beers' criteria. Therefore, a study that compares the relationship of inappropriate medicines to ADEs using the Beers criteria only; to the relationship of inappropriate medicines to ADEs using the ACOVE criteria only can be done. In this case, an investigation of the quality of both different measures in examining this relationship could be completed.

As these future studies are performed, standardization of drug codes that can be used to identify inappropriate medicines using the Beer's and ACOVE criteria should be done so that once medication and diagnoses lists are available to an investigator, identification of these medicines can be done consistently. Several investigators who study medication use outcomes have large medication databases and in some cases use prescription drug claims in their analyses. Making standard drug codes available to other investigators could help ensure comparability across studies.

The development of theories and improvement of methodology are important to the process of research; therefore, future research may propose the testing of a conceptual model that empirically links symptoms, concern beliefs, adherence and ADE. Also, it is

pertinent to translate the findings to clinical practice and understand its implications for health providers.

Practice implications

Based on an understanding of patients' concern beliefs in medicine, it is known that these beliefs are important and may vary by treatment decisions being made or by health/coping behavior being performed. For example, patients may think strongly about the perceptions of their treatment when it involves a direct decision about their treatment. Previous studies have shown that in health behaviors such as medication adherence, strong beliefs about the dependence and long term effects of their medicines lead to less adherence (Horne, Weinman & Hankins, 1999; Neame & Hammond, 2005; Phatak & Thomas III, 2006). In this case, educational interventions directed towards patients who do not take their medicine as directed may focus on reducing the concerns they have about their medicines because when they worry and have anxieties about them, it leads to negative health outcomes. However, when patients have strong concerns about effects of their medicine, they may be self-motivated to report their symptoms to their health providers and likely to self-report an ADE. This may explain why stronger concern beliefs in medicine by older adults lead to reporting of symptoms to health provider and self-reporting an ADE (Oladimeji et al., 2009 (forthcoming)); Oladimeji et al., 2008). This has some practice implications. For example, health providers in practice settings should not assume that all patients who worry about their medicines and their adverse effects will have negative outcomes and health behaviors such as medication non-adherence. Based on an understanding of concern beliefs in medicine in these set of studies, its relation to medication adherence (Horne, 2003), self-reported ADEs

(Oladimeji et al., 2008) and symptom reporting (Oladimeji et al., 2009 (forthcoming), it is perceived that patients who have manageable concern beliefs may likely be involved in self-care and managements of their illness, symptoms and medications because they are cautious of any possible adverse effect their medicines might have. Therefore, individualized patient care and management of patient behavior is important. In summary, patients' anxieties about the long term effects of their medicines and possible dependence should not be ignored because it is patients who take their medicines and they may be right about their effects.

The use of inappropriate medicines by older adults is still prevalent in the outpatient setting. Patients who receive these medicines from their clinicians may not know whether the medication is appropriate or not. Strategies to reduce the prescribing and use of these medicines should therefore be targeted at clinicians. Clinicians need to be educated about the different quality measures used in prescribing medicines for older adults such as the Beers criteria so that these findings can be translated from research to clinical practice (Fick et al., 2004; Kaufman, Brodin & Sarafian, 2005; Raebel et al., 2007; Wessel, Nietert, Jenkins, Nemeth & Ornstein, 2008). Similarly, pharmacists can help identify these inappropriate medicines during the filling of prescriptions by patients' and make drug therapy recommendations to physicians (Starner, Norman, Reynolds & Gleason, 2009).

To improve patient health outcomes, it is important for health providers to assess patients' perception of symptom and attributions during clinical consultations, especially in the outpatient setting. Appropriate education of patients about their symptoms may reduce incongruence between patients' and clinicians' perception of treatment and

improve patient-clinician communications (Cohen, Reimer, Smith, Sorofman & Lively, 1994). Subsequently, improved interactions can build rapport and satisfaction (Hunt & Arar, 2001).

Though concerns about medicines should be manageable, appropriate educational messages that increase patients' motivation for self-monitoring of their health, symptoms and adverse events and allows them to pay particular attention to the effects of their medicines should be developed. On the other hand, health professionals can help patients with strong anxieties and concerns about their medications reframe negative perceptions of treatment they might have using cognitive-behavioral interventions (Levanthal, H., Weinman, Levanthal, E.A., & Phillips, 2008). The results from these studies will contribute to the development of such programs or interventions; however, more data and research will need to be conducted for actual implementation of these interventions.

Future research

Concern beliefs in medicines which characterize a person and his/her belief towards taking and managing medicines is an important factor related to patient outcomes and should be considered in future medication use studies. As an understanding of how concern beliefs work becomes clearer, it seems that there are other factors that may be linked to these beliefs which were not included in the analysis of these studies.

In this study, the relationship of concern beliefs to self-reported ADEs may have been observed because the sample population were highly educated. These individuals probably had greater access to information and resources on their prescription medicines, monitored their health more closely, were more exposed to direct to consumer advertising

on medicines and/or studied the effects of their medicines at greater length. They may therefore worry about their medicines because so much information on side effects and unwanted reactions are available to them. Also, since the participants in the study were from an internet sample, it is possible that these individuals browsed the web for information on their health and medicines and used medical websites to seek information. Their concerns about their medicines may therefore result from information overload available to them from different internet and media outlets. Simply, the relationship of concern beliefs to self-reported ADE has implications because of this exposure to information. Future research might seek to estimate the effect of direct to consumer advertising and internet seeking on patients' concern beliefs in medicine. Patients may then be classified into groups based on how high or low they scored in their exposure to these media information. A sub-sample of individuals within these two groups could then examine if concern beliefs in medicine is associated with self-reported ADE. It is expected that individuals who had low exposure to internet/media information on their medicines would be less concerned and their medicines and an association of concern beliefs in medicine to self-reported ADE may not be observed. On the other hand, patients who had high exposure to information on their medicines through the internet/media outlets may have more concern about them and show significant relationships of concern beliefs in medicine to self-reported ADEs.

The concern beliefs in medicines measure may also be used differently in the future. For example, further examination of how medication-specific they are for patients can be determined. This investigation will expand on what is known about the nature of concern beliefs in medicines.

Attribution of symptoms to medicines was not entirely different among patients and clinicians. It was interesting to see that some patients actually agreed with clinicians on their symptom attributions. Symptom attribution to medicine precedes the identification of an ADE and if patients can report potential ADEs due to medicines to their health providers, preventable ADEs can be detected (Dewitt & Sorofman, 1999). Health providers need to understand that patients may not always be wrong about their symptom and its cause. Some patients disagreed with clinicians on the cause of their symptom showing that communication between the health provider and patient should be enhanced. A two-way conversation between patients and clinicians that examines the patients' ideas about their symptoms and the health providers' perspective about the cause can bring concordance in treatment choice and medication management (Hunt & Arar, 2001; Jackson, 2005; McColl, Jungahrd, Wiklund, & Revicki, 2005). This is an area of symptom research that may be explored. Physician-patient communication in the assessment of self-reported symptoms may not only lead to better health outcomes but also to patient satisfaction and trust (Bultman & Svarstad, 2000; Jorgensen, Anderson & Mardby, 2006; McColl, Jungahrd, Wiklund, & Revicki, 2005). Since patients and clinicians sometimes disagree on symptom/s and attribution, it is not known if this leads to a change in drug therapy of the patient (Weingart et al., 2005). For example, if a clinician encounters a patient who insists that the symptom experienced is due to his/her medicine and not another reason, the clinician may change the medication previously prescribed in order to satisfy the patient, or decide not to change the therapy. Also, it is not known if there are communication or influence strategies that can be utilized by the

patient and/or the clinician to create agreement and if patients trust in health providers is improved (Quill & Brody, 1996).

In addition, there are other areas of symptom research that need to be further explored. For example, some older adults do not report their symptoms to their health providers and make varying symptom attribution; it would be interesting to see how these patients deal with their symptoms/control them. It is not known if a response to control symptoms is based on the severity or frequency of their illness, what action or self-care strategies are implemented in dealing with them and how their symptom perceptions and attribution, general and/or specific beliefs in medicines may influence their treatment decisions or self-care practices. Using symptom diaries, older adults' symptom experience, interpretations and causal attributions can be followed over time. At the baseline point, both their general orientation about medicines and specific beliefs in medicines may be examined. At the end of the follow-up period, patients may then be asked to state what strategies they undertook to deal with their symptoms such as seeking a health care provider, waiting or using other self-care methods. Their beliefs in medicines in general and their specific beliefs in medicine would also be examined again at this point. It would be interesting to see if variations in patients' actions and self-care behaviors differed by their beliefs in medicine, severity of illness or attribution types.

Concern beliefs in medicines are important in health behaviors and patient health outcomes, but they can also change over time. By focusing on the factors that can lead to a change in these beliefs in medicines, medication management interventions can be developed. It was observed that older adults with previous ADEs were likely to have more concerns about their medicines; and, stronger concerns about medicines lead to

self-reporting ADEs. It seems that patients' concern beliefs influence their definitions of ADE and that having an ADE influences concerns about medicines. Future studies that incorporate both expected directions in their methodology should be done in order to confirm such relationships.

The factors that were tested in explaining a change in concern beliefs over time had low explanatory power in predicting a change. This suggests that patients' behaviors may not strongly lead to a change in beliefs; rather factors in the environment may influence changes in patients' beliefs. Several external factors in the environment could impact the process of self-regulation, and the general model recognizes this issue. (Levanthal, H., Brissette, Levanthal, E., 2003; Horne, 2003). Studies that examine medication use and outcomes based on self-regulation should consider the influence of these factors. For example, the influence of the media, the rise in the frequency of direct to consumer advertising, and the impact of social networks such as friends, peers, colleagues, pharmacists or health care providers are major influences on patients and possibly their beliefs (Levanthal, H, Levanthal, E, & Cameron, 1998; Horne, 2003; Bell, Kravitz & Wilkes, 1999). During clinical consultations, poor communication between the patient and the health provider can influence whether a patient leaves the hospital concerned or not about his medicine. A lack of communication between the clinician and the patient about the long term and dependence effect of the drug can lead to concern by the patient (Jackson, 2005). Also, if a patient constantly listens to television advertisements about his medicine which states all the contraindications and side effects of his drug, the patient may become concerned about his medicine over time.

Future studies should examine the importance of these external factors in the environment and patients' social network in changing patients concern and anxieties about their medicine over time. First, qualitative interviews or focus groups that ask patients to state what factors can change their concerns about their medicines and the beliefs they have about their adverse effects can be done. Using the results from these interviews, a longitudinally designed mail survey can be done where patients' concern beliefs are measured over time and the influence of these factors on their beliefs can be examined. It would be interesting to see what significant environmental factors lead to changes in concern beliefs and how health providers can target these sources in their interventions to reframe patients' ideas and beliefs about their treatment or medicines.

Health literacy is an important variable that could be related to patients' concern beliefs in medicine. Health literacy describes the ability of patients to process, understand and use health information in order to make appropriate health decisions (Healthy People, 2010). Gatti, Jacobson, Gazmararian, Schmotzer & Kripilani, 2009 noted that inadequate health literacy may be a factor associated with provider-patient communication and negative beliefs regarding disease management such as long term medication use. Based on this understanding, individuals with low health literacy who cannot adequately use the information available to them may not understand their prescription medication and the adverse and long term effects, and likely worry about them. A future study that can examine the relationship of this factor to patients' concerns about their medicines would be significant in medication use research. Here, patients' health literacy may be assessed using measures such as the Newest vital sign (NVS) or Test of functional health literacy in adults (TOFHLA) (Chisolm & Buchanan, 2007; Baker, 2006). Subsequently, using

their scores, patients may be categorized into those with low health literacy and those with high health literacy. The concern beliefs of such individuals could then be assessed at a point in time and as a follow-up. Factors in the external environment, past health behaviors, report of previous ADEs and their socio-demographics would be controlled for in the analysis of this study. It would be interesting to know if health literacy may be associated with patients concerns in medicine as this would contribute to information required in the development of medication management interventions.

Summary

In this set of studies, the relationship of concern beliefs in medicine to self-reported ADE, when considering important clinical variables such as number of medicines and use of an inappropriate medicine was established. Concern beliefs in medicine were not related to patient symptom attribution to medicine, but these beliefs were shown to change over time for some individuals and having a previous ADE was linked to this change.

APPENDIX A: THE BEERS CRITERIA LIST OF POTENTIALLY INAPPROPRIATE MEDICATIONS

Table A1: 2002 Beers criteria for potentially inappropriate medication use in older adults: independent of diagnoses or conditions.*

Drug
Propoxyfene (Darvon) and combination products (Darvon with ASA, Darvon-N, and Darvocet-N)
Indomethacin
Pentazocine (Talwin)
Trimethobenazmide(Tigan)
Muscle relaxants and antispasmodics: methacarbamol (robaxin), carisoprodol (Soma), chlorzoxazone (paraflex), metaxalone (skelaxin), cyclobenzaprine (flexeril), oxybutinin (Ditropan). Do not consider the extended release Ditropan XL.
Flurazepam (Dalamane)
Amitriptyline (Elavil), chlordiazepoxide-amitriptyline (limbitrol), and perphenazine-amitriptyline(Triavil)
Doxepin (Sinequan)
Meprobomate (Miltown and Equanil)
Doses of short-acting benzodiazepines: doses greater than lorazepam (Ativan), 3 mg; oxazepam (Serax), 60 mg; alprazolam (Xanax), 2 mg; temazepam (Restoril), 15 mg; and triazolam (Halcion), 0.25 mg
Long-acting benzodiazepines: chlordiazepoxide (Librium), chlordiazepoxide-amitriptyline (Limbitrol) clidinium-chlordiazepoxide (Librax), diazepam (Valium), quazepam (Doral), halazepam (Paxipam), and chlorazepate (Tranxene)
Disopyramide (Norpace and Norpace CR)
Digoxin (Lanoxin) (should not exceed > 0.125mg/d except when treating atrial arrthymias)
Short-acting dipyridamole (Persantine). Do not consider the long-acting dipyridamole (which has better properties than the short-acting in older adults) except with patients with artificial heart valves.
Methyldopa (aldomet) and methyldopa-hydrochlorothiazide (aldoril)
Reserpine at doses 0.25mg

Table A1 continued

Drug
Chlorpropamide (Diabenese)
Gastrointestinal antispasmodic drugs: dicyclomine (Bentyl), hyoscyamine (Levsin and Levsinex), propantheline (Pro-Banthine), belladonna alkaloids (Donnatal and others), and clidinium- chlordiazepoxide (Librax)
Anticholinergics and antihistamines: chlorpheniramine (Chlor-Trimeton), diphenhydramine (Benadryl), hydroxyzine (Vistaril and Atarax), cyproheptadine (Periactin), promethazine (Phenergan), tripelennamine, dexchlorpheniramine (Polarmine)
Diphenhydrmine (Benadryl)
Ergot mesyloids (Hydergine) and cyclandelate (Cyclospasmol)
Ferrous sulfate >325mg/d
All barbiturates (except phenobarbital except when used to control seizures)
Meperidine (Demerol)
Ticlopidine (Ticlid)
Ketorolac (Toradol)
Amphetamines and anorexic agents
Long-term use of full-dosage, longer half-life, non–COX-selective NSAIDs: naproxen (Naprosyn, Avaprox, and Aleve), oxaprozin (Daypro), and piroxicam (Feldene)
Daily fluoxetine (Prozac)
Long-term use of stimulant laxatives: bisacodyl (Dulcolax), cascara sagrada, and Neoloid except in the presence of opiate analgesic use
Amidarone (Cordarone)
Orphenadrine (Norflex)
Guanethidine (Isemelin)
Guanedrel (Hylorel)
Cyclandelate (cyclospasmol)
Isoxsurpine (Vasodilan)
Nitrofurantoin (Macrodantin)
Doxasozin (Cardura)
Methyltestosterone (serentil)
Thioridazine (mellaril)

Table A1 continued

Drug
Mesoridazine (Serentil)
Short acting nifedipine (Procardia and Adalat)
Clonidine (catapres)
Mineral oil
Cimetidine (Tagamet)
Ehacrynic acid (Edecrin)
Dessicated thyroid
Amphetamines (excluding methylphenidate hydrochloride and anorexics)
Estrogens only (oral)

* Contains 48 individual medications or classes of medications to avoid in older adults and their adverse outcomes, whether low or high in severity. Fick et al. (2003). Updating the Beers criteria for potentially inappropriate medication use in older adults. *Arch Intern Med*, 163, 2716-2724.

Table A2: 2002 Beers criteria for potentially inappropriate medication use in older adults: considering diagnoses or conditions.*

Disease or conditions	**Drug**
Heart failure	Disopyramide (Norpace), and high sodium content drugs (sodium and sodium salts [alginate bicarbonate, biphosphate, citrate, phosphate, salicylate, and sulfate])
Hypertension	Phenylpropanolamine hydrochloride (removed from the market in 2001), pseudoephedrine; diet pills, and amphetamines
Gastric or duodenal ulcers	NSAIDs and aspirin (325 mg) (coxibs excluded)
Seizures or epilepsy	Clozapine (Clozaril), chlorpromazine Thorazine), thioridazine (Mellaril), and thiothixene (Navane)
Blood clotting disorders or receiving anticoagulant therapy	Aspirin, NSAIDs, dipyridamole (Persantin), ticlopidine (Ticlid), and clopidogrel (Plavix)
Bladder outflow obstruction	Anticholinergics and antihistamines, gastrointestinal antispasmodics, muscle relaxants, oxybutynin (Ditropan), flavoxate (Urispas), anticholinergics, antidepressants, decongestants, and tolterodine (Detrol)
Stress incontinence	α -Blockers (Doxazosin, Prazosin, and Terazosin), anticholinergics, tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride, and amitriptyline hydrochloride), and long-acting benzodiazepines
Arrthymias	Tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride, and amitriptyline hydrochloride)
Insomnia	Decongestants, theophylline (Theodur), methylphenidate (Ritalin), MAOIs, and amphetamines
Parkinson Disease	Metoclopramide (Reglan), conventional antipsychotics, and tacrine (Cognex)
Cognitive impairment	Barbiturates, anticholinergics, antispasmodics, and muscle relaxants. CNS stimulants: dextroAmphetamine (Adderall), methylphenidate (Ritalin), methamphetamine (Desoxyn), and pemolin
Depression	Long-term benzodiazepine use. sympatholytic agents: methyldopa (Aldomet), reserpine, and guanethidine (Ismelin)

Table A2 continued

Disease or conditions	Drug
Anorexia and malnutrition	CNS stimulants: DextroAmphetamine (Adderall), methylphenidate (Ritalin), methamphetamine (Desoxyn), pemolin, and fluoxetine (Prozac)
Syncope or falls	Short- to intermediate-acting benzodiazepine and tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride, and amitriptyline hydrochloride)
SIADH/hyponatremia	SSRIs: fluoxetine (Prozac), citalopram (Celexa), fluvoxamine (Luvox), paroxetine (Paxil), and sertraline (Zoloft)
Seizure disorder	Bupropion (Wellbutrin)
Obesity	Olanzapine (Zyprexa)
COPD	Long-acting benzodiazepines: chlordiazepoxide (Librium), chlordiazepoxide-amitriptyline (Limbitrol), Clidinium-chlordiazepoxide (Librax), diazepam (Valium), quazepam (Doral), halazepam (Paxipam), and chlorazepate (Tranxene). ß-blockers: propranolol
Chronic constipation	Calcium channel blockers, anticholinergics, and tricyclic antidepressant (imipramine hydrochloride, doxepin hydrochloride, and amitriptyline hydrochloride)

* Fick et al. (2003). Updating the Beers criteria for potentially inappropriate medication use in older adults. *Arch Intern Med*, 163, 2716-2724.

APPENDIX B: MEDICATION QUALITY INDICATORS (THE MODIFIED ACOVE CRITERIA).*

Table B1: Quality Indicator descriptors

Prescribing indicated medications
Proton-pump inhibitors (PPI) or misoprostol for patients with ulcer or gastrointestinal bleeding risk factors who is taking an NSAID.
Calcium and vitamin D for patients with osteoporosis
Daily aspirin therapy for patient with diabetes
ß-blocker for patients with heart failure
ß-blocker for patients who had a myocardial infarction
Osteoporosis treatment medication (Hormone replacement therapy (HRT) or biphosphonate or calcitonin)
ACE inhibitor for patients with hypertension and renal insufficiency
ACE inhibitor for patients with heart failure
Aspirin for patients with coronary heart disease
Calcium and vitamin D for patients taking long-term steroid therapy
Warfarin or aspirin, as appropriate, for patient with atrial fibrillation

Avoiding inappropriate medications
Avoid strongly anticholinergic medications if alternative exist
Avoid barbiturates unless patient has a seizure disorder
Avoid meperidine
Avoid chlorpropamide
Avoid first or second generation short-acting calcium-channel blocker for patient with heart failure
Avoid ß-blocker if patient has asthma

* Higashi et al, 2004. The Quality of pharmacologic care for vulnerable older patients, *Ann Intern Med*, 140, 714-720.

Table B2: Operationalization of the modified ACOVE criteria*

ACOVE criteria: Notes of analysis and selection criterion for drugs included in the list.

ACOVE quality indicator descriptors	**Operationalization of selection criteria**	**Therapeutic drug class codes**	**Notes**
Prescribing indicated medications			
Proton-pump inhibitors (PPI) or misoprostol for patients with ulcer or gastrointestinal bleeding risk factors who is taking an NSAID.	PPI as a therapeutic class is classified as it is in MULTUM. Misoprostol is classified as a miscellaneous GI agent (96) and an NSAID (61)	PPI- 272 Misoprostol- 96, 61	
Calcium and vitamin D for patients with osteoporosis	Calcium is classified as a mineral and electrolyte (117). Vitamin D is classified as a Vitamin (119).	Calcium- 117 Vitamin D - 119	Calcium is identified both as a mono-ingredient in some drug products and in combination with other active ingredients including vitamin D. Vitamin D is identified as a mono-ingredient and as a combination drug.

Table B2 continued

ACOVE quality indicator descriptors	Operationalization of selection criteria	Therapeutic drug class codes	Notes
Prescribing indicated medications			
Daily aspirin therapy for patient with diabetes	Aspirin is classified as an analgesic combination (63), a narcotic analgesic (191) and a salicylate (62).	Aspirin- 62, 63, 191.	Only aspirin as a mono-ingredient, buffered aspirin, aspirin-pravastatin and aspirin-dipyridamole were used here. This criterion was based on a consensus meeting between three pharmacists involved in the project.
ß-blocker for patients with heart failure	Beta blockers are classified as cardioselective (274) and non-cardioselective (275) in MULTUM.	Cardioselective ß-blocker- 274 Non-cardioselective ß-blocker -275	
ß-blocker for patients who had a myocardial infarction	Same as above	Same as above	
Osteoporosis treatment medication (Hormone replacement therapy (HRT) or bisphosphonate or calcitonin)	HRT is classified as estrogens (183) and progestins (185) in MULTUM. Bisphosphonate is classified as it is in MULTUM. Calcitonin is classified as a miscellaneous hormone (100) in MULTUM.	HRT- 183, 185 Bisphosphonate -217 Calcitonin- 100	Hormone replacement therapy was operationalized as estrogens and progestins. This classification was based on the Nelson, Humprey, Nygren, Teutsch & Allan review article. All hormonal therapies used

Table B2 continued

ACOVE quality indicator descriptors	Operationalization of selection criteria	Therapeutic drug class codes	Notes
Prescribing indicated medications			
			for fertility, cancer, anorexia and contraception were removed from the list.
			Calcitonin is identified as 'calcitonin, salmon' in MULTUM.
ACE inhibitor for patients with hypertension and renal insufficiency	Angiotensin converting enzyme inhibitors (42) is classified as it is in MULTUM.	ACE inhibitors- 42	Angiotension II receptor blockers were also added to the list.
ACE inhibitor for patients with heart failure	Same as above	Same as above.	Same as above.
Aspirin for patients with coronary heart disease	Aspirin is classified as an analgesic combination (63), a narcotic analgesic (191) and a salicylate (62).	Aspirin- 62, 63, 191.	Only aspirin as a mono-ingredient, buffered aspirin, aspirin-pravastatin and aspirin-dipyridamole were used here. This criterion was based on a consensus between three pharmacists involved in the project.

Table B2 continued

ACOVE quality indicator descriptors	Operationalization of selection criteria	Therapeutic drug class codes	Notes
Prescribing indicated medications			
Calcium and vitamin D for patients taking long-term steroid therapy	Calcium is classified as a mineral and electrolyte (117). Vitamin D is classified as a Vitamin (119). Long term steroid therapy is classified as glucocorticoids (301)	Calcium- 117 Vitamin D – 119 Long term steroid therapy- 171, 245, 296, 165, 166, 138, 141.	Calcium is identified both as a mono-ingredient in some drug products and in combination with other active ingredients including vitamin D. Vitamin D is identified as a mono-ingredient and as a combination drug. Steroid therapy is operationalized as glucocorticoids.
Warfarin or aspirin, as appropriate, for patient with atrial fibrillation	Aspirin (see previous entries) Warfarin is identified as warfarin sodium and classified as coumarins and indandiones.	Aspirin (see previous entries) Warfarin- 262	Aspirin as a mono-ingredient, buffered aspirin, aspirin-pravastatin and aspirin-dipyridamole were used, based on consensus.

Table B2 continued

Avoiding inappropriate medications			
Avoid strongly anticholinergic medications if alternative exist	These medications were obtained from a streamlined list of all anti-cholinergics. Some of the drugs on this list are not identified as anti-cholinergic in MULTUM but something else. For example, amitriptyline is classified as a tricyclic anti-depressant and psychotherapeutic combination.	See table below for the full medication list and therapeutic codes.	Some drugs with strong anti-cholinergic properties were not seen in MULTUM. This includes dothiepin and pericyazine.
Avoid barbiturates unless patient has a seizure disorder	Barbiturates are classified as it is.	Barbiturates-68	
Avoid meperidine	Meperidine is classified as a narcotic analgesic (60) and a narcotic analgesic combination (191)	Meperidine- 60, 191	
Avoid chlorpropamide	Chlorpropamide is classified as a sulfonyl urea (213)	Chlorpropamid e-213	
Avoid first or second generation short-acting calcium-channel blocker for patient with heart failure	Calcium channel blockers are classified as first or second generation short-acting channel blockers including nifedipine, nicardipine, diltiazem, verapamil, isradipine, nimodipine, nisoldipine, amoldipine, nitrendipine & felodipine.	Calcium channel blockers-48	Not all calcium channel blockers are entered in MULTUM. Only those classified into first or second generation according were used.

Table B2 continued

ACOVE quality indicator descriptor---- Avoid strongly anti-cholinergic medications if alternative exist*

Drug	MULTUM therapeutic drug class
amitriptyline	Psychotherapeutic combinations- 79; Tricyclic anti-depressants- 209
amitriptyline-perphenazine	Psychotherapeutic combinations- 79
atropine	Antidiarrheals- 90; Anti-cholinergic-antispasmodics- 89; Urinary antispasmodics- 264; Upper respiratory combinations-132; cholinergic muscle stimulants- 108; Mydriatics- 286
atropine-diphenoxylate	Antidiarrheals- 90
belladonna-opium	Narcotic analgesic combinations-191
benztropine	Anti-cholinergic anti-Parkinson agents- 205
brompheniramine	Antihistamines- 123; Upper respiratory combinations-132
carbinoxamine	Antihistamines- 123; Upper respiratory combinations-132
chlorpheniramine	Antidotes- 106; Antihistamines- 123; Upper respiratory combinations- 132
chlorpromazine	Phenothiazine antiemetics- 196; Phenothiazine antipsychotics- 210
clemastine	Antihistamines- 123; Upper respiratory combinations-132
clomipramine	Tricyclic anti-depressants- 209
clozapine	Atypical antipsychotics- 341
codeine-promethazine	Upper respiratory combinations- 132
darifenacin	Urinary antispasmodics- 264
desipramine	Tricyclic antidepressants- 209
dicyclomine	Anti-cholinergic anti-spasmodic- 89
dimenhydrinate	Anti-cholinergic antiemetic- 197
diphenhydramine	Analgesic combinations- 63; Anti-cholinergic anti emetics- 197; Anti-cholinergic anti-Parkinson agent- 205; Antihistamines- 123; Miscellaneous anxiolytics, sedatives, and hypnotics- 70; Miscellaneous topical agents- 140; Upper respiratory combinations- 132
dothiepin	Not in MULTUM

Table B2 continued

Drug	MULTUM therapeutic drug class
doxepin	Miscellaneous anxiolytics, sedatives, and hypnotics- 70; Miscellaneous topical agents- 140; Tricyclic anti-depressants- 209
flavoxate	Urinary antispasmodics- 264
glycopyrrolate	Anti-cholinergic antispasmodics- 89
hydroxyzine	Anti-asthmatic combinations- 131; Antihistamines- 123
hyoscyamine	Anti-cholinergic antispasmodics- 89; Digestive enzymes- 91; Urinary antispasmodics- 264
imipramine	Tricyclic antidepressants- 209
ketamine	General anesthetics- 72
meclizine	Anti-cholinergic antiemetics- 197
meclizine-niacin	Anti-cholinergic antiemetics- 197
nortriptyline	Tricyclic antidepressants- 209
orphenadrine	Skeletal muscle relaxant combinations- 179; Skeletal muscle relaxants- 178
oxybutynin	Urinary antispasmodics- 264
pericyazine	Not in MULTUM
procyclidine	Anti-cholinergic anti-Parkinson agent- 205
promethazine	Antihistamines- 123; Narcotic analgesic combinations-191; Phenothiazine antiemetics- 196; Upper respiratory combinations- 132
propantheline	Anti-cholinergic antispasmodics- 89
protriptyline	Tricyclic antidepressants- 209
pyrilamine	Analgesic combinations- 63; Antihistamines- 123; Miscellaneous anxiolytics, sedatives, and hypnotics- 70; Nasal antihistamines and decongestants- 246; Upper respiratory combinations- 132
scopolamine	Anti-cholinergic antiemetics- 197; Anti-cholinergic antispasmodics- 89; Mydriatics- 286; Upper respiratory combinations- 132
scopolamine topical	Anti-cholinergic antispasmodics- 89
thioridazine	Phenothiazine antipsychotics- 210
tolterodine	Urinary antispasmodics- 264
trihexyphenidyl	Anti-cholinergic anti-Parkinson agent- 205
trimipramine	Tricyclic antidepressants- 209

* The MULTUM therapeutic drug classification was done for both the modified ACOVE criteria and the Beers criteria but only the ACOVE criteria is reported here because of the large number of drugs in the Beers list. Codes are available on request from the University of Iowa CERT.

APPENDIX C: VARIABLE DEFINITION IN CONCERN BELIEFS IN MEDICINES AND INAPPROPRIATE PRESCRIPTIONS: RISK FACTORS FOR SELF-REPORTED ADES IN THE ELDERLY STUDY

Dependent variable= Self-reported ADE (In the past year, did you see a doctor about any side effects, unwanted reactions or other problems from medicines you were taking)

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
Main predictor variables			
Use of an inappropriate medication (Based on Beers criteria in Appendix A and the modified ACOVE criteria in Appendix B)	Information used in coding an inappropriate medication: Please list the drug name, strength, and directions for use, how much you took and your reason for taking each prescription medication in the past month.	Open ended responses	Using any inappropriate medicine measured as either a Beers drug and/or failing one of the 17 ACOVE quality indicators, Not using an inappropriate medicine (comparison group). Number of inappropriate medicines used on an interval level scale (0 and above).
Concern beliefs in medicines	Please indicate the extent to which you agree or disagree with the following statements: Having to take medicine worries me, I sometimes worry about becoming too dependent on my medicines, I sometimes worry about the long-term effects of my medicines, My medicines disrupt my life,	Strongly disagree, disagree, neither agree or disagree, agree, strongly agree	Sum of the five items ranging from 5-25 (higher scores is stronger concern beliefs) Concern beliefs as a linear and squared variable

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
	My medicines are a mystery to me.		
Control variables			
Socio-demographics			
Age	What is your age?	Respondent enters age as open ended response	65-74 (comparison group), 75-84, ≥ 85
Gender	What is your gender?	1- Male, 2- Female	Male (comparison group), Female
Race	What is your race?	White, Black, Asian, Native American, Mixed racial background, Hispanic, African American, Other race	White (comparison group) , Black/African American, Hispanic , Other
Education	What is the highest level of education you have completed?	Less than high school (HS), Some HS, HS or equivalent, Some college but no degree, College, Some grad school but no degree, Graduate school, Associate degree, Other	Less than HS/Has high school degree (comparison group); Some college/Associate degree/ Some grad school but no degree; Has college degree; Has a graduate degree; Other type of degree
Geographical region	What geographical region do you reside in?	East, MidWest, South, West, Non-US state, Unknown	Midwest (comparison group), Northeast, South, West
Income	Which of the following income categories best describes your total household income?	Less than $15,000; $15,000-24, 999; 25,000-34,999; 35,000-49,999; 50,000-74,999; 75,000-99,000; 100,000-124,999; 125,000-149,000;150,000-	< $15,000 (comparison group), $ 15,000-24,999, $25,000-34,999, $35,000-49,999; 50,000-74,999, $ 75,000 or more

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
		199,000; 200,000-249,000; 250,000 or more	
Clinical characteristics			
Self-rated health	Which of the following best describes your current overall health?	Poor, Fair, Good, Very good, Excellent	Poor, Fair, Good, Very Good, Excellent (comparison group)
Necessity beliefs in medicines	Please indicate the extent to which you agree or disagree with the following statements: My life would be impossible without my medicines, My health at present depends on medicines, Without medicines, I would be very ill, My health in the future will depend on medicines, My medicines protect me from my conditions becoming worse	Strongly disagree, disagree, neither agree or disagree, agree, strongly agree	Sum of the five items ranging from 5-25 (higher scores is stronger necessity beliefs)
Sum of symptoms experienced	Have you experienced any of these symptoms in the past month? Headache, Dizziness, Stomach/GI problems, Muscle aches, Incontinence, Rash/itching, Sleep problems, Mood changes, Fatigue, Sexual problems	Yes, No for each symptom	Number of symptoms experienced are summed and categorized as 0 (comparison group), 1, 2, 3, 4 or more
Number of medications	How many different prescriptions have you used	Respondent enters the number of medicines as	1-2 (comparison group), 3-4, 5-6, 7-8 , >8

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
	in the past month?	an open ended response	
Behavioral characteristics			
Stop medicine due to cost	In the past year, how often did you stop taking a prescription because of cost?	Never, 1 or 2 times, 3 or 4 times, More than 4 times	Never (comparison group), 1 or more
Skip doses due to cost	In the past year, how often did you skip doses of a prescription medication in order to save money?	Never, 1 or 2 times, 3 or 4 times, More than 4 times	Never (comparison group), 1 or more
Number of pharmacies	In a typical month, from how many pharmacies do your get prescription medicines?	Respondents enter number of pharmacies as an open ended response	0 (comparison group), 1 , 2 , >3

APPENDIX D: DESCRIPTION OF CONCERN BELIEF ITEMS IN CONCERN BELIEFS AND INAPPROPRIATE PRESCRIPTIONS: RISK FACTORS FOR SELF-REPORTED ADEs AMONG OLDER ADULTS STUDY

Table D1: Frequency distribution of concern belief items

Concern belief items	**Mean ± Standard deviation**	**Strongly agree Number (%)**	**Disagree Number (%)**	**Neither agree nor disagree Number (%)**	**Agree Number (%)**	**Strongly agree Number (%)**
Having to take medicines worries me	2.55 ± 1.09	154 (19.9)	232 (30.1)	209 (27.1)	159 (20.6)	18 (2.3)
I sometimes worry about the long term effects of my medicines	2.90 ± 1.17	118 (15.2)	167 (21.6)	213 (27.5)	224 (28.9)	52 (6.7)

My medicines are a mystery to me	2.15 ± 0.98	225 (29.3)	280 (36.4)	194 (25.2)	58 (7.5)	12 (1.6)
My medicines disrupt my life	1.91 ± 0.88	284 (32.5)	309 (40.2)	139 (18.1)	28 (3.6)	8 (1.0)
I sometimes worry about the becoming too dependent on my medicines	2.30 ± 1.09	219 (28.3)	242 (31.3)	189 (24.5)	104 (13.5)	19 (2.5)

Table D2: Concern belief scale: Cronbach alpha and distribution

	Cronbach alpha
Concern belief scale	0.80

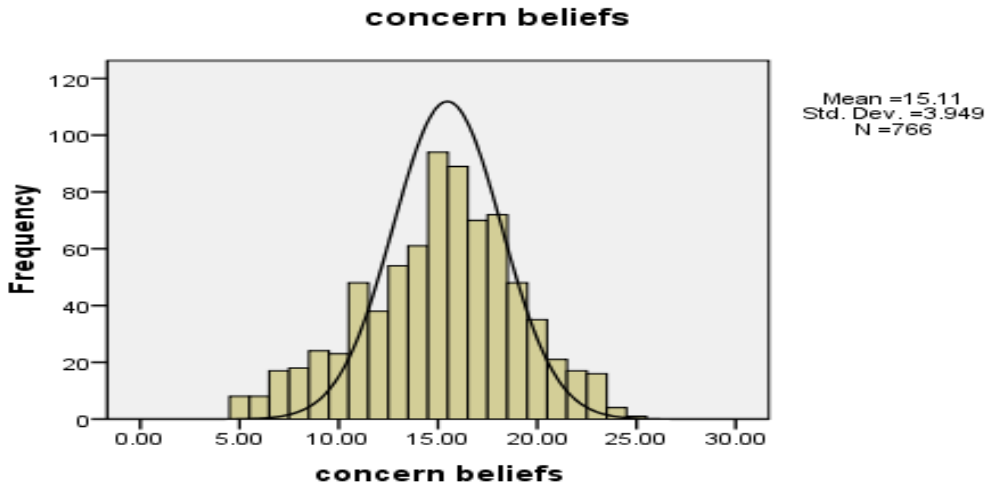

Table D3: Descriptive analyses of concern beliefs in medicines with demographics

One-way ANOVA	**Mean square**	**F Statistic**	**P value**
Concern beliefs by age		1.55	0.21
Between groups	24.20		
Within groups	15.58		
Concern beliefs by race		1.45	0.23
Between groups	22.45		
Within groups	15.51		
Concern beliefs by income		0.99	0.42
Between groups	15.36		
Within groups	15.43		
Concern beliefs by education		3.13	0.02*
Between groups	48.21		
Within groups	15.43		

* $p<0.05$

APPENDIX E: DESCRIPTION OF THE REGRESSION MODELS THAT WERE USED IN THE CONCERN BELIEFS AND INAPPROPRIATE PRESCRIPTIONS: RISK FACTORS FOR SELF-REPORTED ADEs IN OLDER ADULTS STUDY.

For this study, three regression analyses were done to examine research objective 2. The research objective was: Examine if there is an association between the use of inappropriate medicines, concern beliefs in medicines and self-reported ADEs among older adults in the outpatient setting.

Analysis 1: Multiple logistic regression using socio-demographic, clinical and behavioral characteristics as control variables and the use of a Beers drug (categorical) and concern beliefs in medicines as predictor variables. The regression model was as follows:

Self-reported ADE (Yes/No) = $ß_0$ + $ß_1$ concern beliefs in medicines + $ß_2$ use of an inappropriate medication (either Beers drug or failed modified ACOVE criteria coded as Yes, No) + $ß_3$ age + $ß_4$ race + $ß_5$ gender + $ß_6$ income + $ß_7$ education + $ß_8$ geographical region + $ß_9$ self-rated health + $ß_{10}$ sum of symptoms experienced + $ß_{11}$ necessity beliefs in medicines + $ß_{12}$ number of medications + $ß_{13}$ stop medicines due to cost + $ß_{14}$ skip doses due to cost + $ß_{15}$ number of pharmacies.

Analysis 2: Multiple logistic regression using socio-demographic, clinical and behavioral characteristics as control variables and the use of Beers drug (interval level)

and concern beliefs in medicines as predictor variables. This examines whether there is a dose-response relationship between use of a Beers drug and an ADE. The regression model was as follows:

Self-reported ADE (Yes/No) = $ß_0$ + $ß_1$ concern beliefs in medicines + $ß_2$ number of inappropriate medications (either Beers drug or failed ACOVE criteria coded on an interval level) + $ß_3$ age + $ß_4$ gender + $ß_5$ race + $ß_6$ education + $ß_7$ geographical region + $ß_8$ income + $ß_9$ self-rated health + $ß_{10}$ sum of symptoms experienced + $ß_{11}$ necessity beliefs in medicines + $ß_{12}$ number of medications + $ß_{13}$ stop medicines due to cost + $ß_{14}$ skip doses due to cost + $ß_{15}$ number of pharmacies.

APPENDIX F: VARIABLE DEFINITION IN VARIATION IN PATIENTS' AND CLINICIANS' ATTRIBUTION OF SYMPTOMS AND ITS RELATIONSHIP TO CONCERN BELIEFS IN MEDICINES STUDY

Dependent variable= Concern beliefs (Sum of the five items on the concern beliefs scale with scores ranging from 5-25).

DEPENDENT VARIABLE	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
STUDY (Medicare data)			
Concern beliefs in medicines	Please indicate the extent to which you agree or disagree with the following statements: Having to take medicine worries me, I sometimes worry about becoming too dependent on my medicines, I sometimes worry about the long-term effects of my medicines, My medicines disrupt my life, My medicines are a mystery to me.	Strongly disagree, disagree, neither agree nor disagree, agree, strongly agree.	Sum of 5 items ranging from 5-25 (higher scores is stronger concern beliefs)

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
STUDY			
Open ended questions			
Reasons for not reporting symptoms experienced to health provider	Why did you not report your symptoms to your health provider? What concerns or issues did you have about reporting your symptoms?	Open ended responses	Open-ended responses
Control variables			
Socio-demographic data			
Age	What is your age?	Respondent enters age as open ended questions	65-74 (comparison group), 75-84, ≥ 85
Gender	What is your gender?	1- Male, 2- Female	Male (comparison group), Female
Race	What is your race?	White, Black, Asian, Native American, Mixed racial background, Hispanic, African American, Other race	White (comparison group), Black/African American, Hispanic , Other
Education	What is the highest level of education you have completed?	Less than high school (HS), Some HS, HS or equivalent, Some college but no degree, College, Some grad school but no degree, Graduate school,	Less than HS/Has high school degree (comparison group); Some college/Associate degree/ Some grad school; Has college degree; Has a graduate degree; Other type of degree

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
		Associate degree, Other	
Geographical region	What geographical region do you reside in?	East, MidWest, South, West, Non-US state, Unknown	Midwest (comparison group), Northeast, South, West
Income	Which of the following income categories best describes your total household income?	Less than $15,000; $15,000-24, 999; 25,000-34,999; 35,000-49,999; 50,000-74,999; 75,000-99,000; 100,000-124,999; 125,000-149,000;150,000-199,000; 200,000-249,000; 250,000 or more	< $15,000 (comparison group), $ 15,000- 24,999, $25,000-34,999, $35,000-49,999; 50,000-74,999, $ 75,000 or more
Clinical characteristics			
Self-rated health	Which of the following best describes your current overall health?	Poor, Fair, Good, Very Good, Excellent	Poor, Fair, Good, Very Good, Excellent (comparison group)
Sum of symptoms experienced	Have you experienced any of these symptoms in the past month? Headache, Dizziness, Stomach/GI problems, Muscle aches, Incontinence,	Yes, No for each symptom	Number of symptoms experienced are summed and categorized as 0 (comparison group), 1, 2, 3, 4 or more

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
	Rash/itching, Sleep problems, Mood changes, Fatigue, Sexual problems		
Number of medications	How many different prescriptions have you used in the past month?	Respondent enters the number of medicines as an open ended question	0 (comparison group), 1-2, 3-4, 5-6, 7-8 , >8

APPENDIX G: CLINICIAN ADVERSE DRUG EVENT DATA COLLECTION FORM

Listed in the first table for this patient are the medications taken by the patient and the socio-demographic and clinical characteristics. Listed in the 2nd table are the symptoms reported by the patient, what they think caused the symptom and the reason they gave for not reporting that symptom to his/her physician or other provider. Based on these data, we are interested in opinions on the possibility of the symptom being due to a medicine.

Patient profile 1-- ID number =

Variable	Patient information
Socio-demographics	Age- Race- Education- Gender-
Clinical characteristics	Self-reported adherence- Self-reported health status- Number of medicines used- Uses _ pharmacy
Medications taken	

Symptom/s Reported	Cause of symptom according to the patient	Patient's reason for not reporting symptom to physician

RATINGS

A. CONFIDENCE. In column A, rate your confidence that the symptom experienced by the patient is due to one of his/her medicines, using the following scale

1. Little or no confidence the symptom is related to a medication
2. Slight to moderate confidence the symptom is related to a medication
3. Less than 50% confidence but a close call that the symptom is related to a medication
4. More than 50% confidence but a close call that the symptom is related to a medication
5. Strong confidence that the symptom is related to a medication
6. Virtually certain that the symptom is related to a medication

B. PROBABILITY. In column B, indicate the probability (on a scale of 0-1 with 0 being impossible and 1 being certain) that the symptom experienced by the patient is due to the cause he/she reported.

Symptom	Confidence rating	Probability rating

APPENDIX H: VARIABLE DEFINITION IN CONCERN BELIEFS IN MEDICINES: CHANGES OVER TIME AND FACTORS RELATED TO ITS STABILITY STUDY

Dependent variable= Change in concern beliefs measured as a difference in the scores on concern beliefs across year.

DEPENDENT VARIABLE	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
STUDY 1			
Concern beliefs in medicines	Please indicate the extent to which you agree or disagree with the following statements: Having to take medicine worries me, I sometimes worry about becoming too dependent on my medicines, I sometimes worry about the long-term effects of my medicines, My medicines disrupt my life, My medicines are a mystery to me.	Strongly disagree, disagree, neither agree nor disagree, agree, strongly agree.	Sum of 5 items ranging from 5-25 (higher scores is stronger concern beliefs)

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
Socio-demographics			
Age	What is your age?	Respondent enters age as open ended questions	65-74 (comparison group), 75-84, ≥ 85
Gender	What is your gender?	1- Male, 2- Female	Male (comparison group), Female

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
Race	What is your race?	White, Black, Asian, Native American, Mixed racial background, Hispanic, African American, Other race	White (comparison group) , Black/African American, Hispanic , Other
Education	What is the highest level of education you have completed?	Less than high school (HS), Some HS, HS or equivalent, Some college but no degree, College, Some grad school but no degree, Graduate school, Associate degree, Other	Less than HS/Has high school degree (comparison group); Some college/Associate degree/ Some grad school; Has college degree; Has a graduate degree; Other type of degree
Geographical region	What geographical region do you reside in?	East, MidWest, South, West, Non-US state, Unknown	Midwest (comparison group), Northeast, South, West
Income	Which of the following income categories best describes your total household income?	Less than $15,000; $15,000-24, 999; 25,000-34,999; 35,000-49,999; 50,000-74,999; 75,000-99,000; 100,000-124,999; 125,000-149,000;150,000-199,000; 200,000-249,000; 250,000 or more	< $15,000 (comparison group), $ 15,000-24,999, $25,000-34,999, $35,000-49,999; 50,000-74,999, $ 75,000 or more
Clinical/behavioral characteristics			
Self-rated health	Which of the following best describes your current overall health?	Poor, Fair, Good, Very Good, Excellent	Poor, Fair, Good, Very Good, Excellent (comparison group)

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
Sum of symptoms experienced	Have you experienced any of these symptoms in the past month? Headache, Dizziness, Stomach/GI problems, Muscle aches, Incontinence, Rash/itching, Sleep problems, Mood changes, Fatigue, Sexual problems	Yes, No for each symptom	Number of symptoms experienced are summed and categorized as 0 (comparison group), 1, 2, 3, 4 or more
Number of medications	How many different prescriptions have you used in the past month?	Respondent enters the number of medicines as an open ended question	0 (comparison group), 1-2, 3-4, 5-6, 7-8 , >8
Number of pharmacies	In a typical month, from how many pharmacies do your get prescription medicines?	Respondents enter number of pharmacies as an open ended question	0 (comparison group), 1 , 2 , >3
Predictor variables for research objective 3			
Symptom reporting to physicians	You mentioned that you had experienced at least one symptom in the past month while on prescription medication. Did you report this symptom to your physician, pharmacist or other healthcare provider?	Yes, No	Yes, No (comparison group)
Self-reported ADE	In the past year, did you have to see a doctor about any side effects,	Yes , No	Yes, No (comparison group)

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
	unwanted reactions, or other problems from medicines you were taking?		
Change in self-reported adherence	Morisky scale containing the following questions: During the past month, have you ever forgotten to take your medication?; During the past month, have you been careless at times about taking your medications?; When you feel better, do you sometimes stop taking any of your medications?; If you feel worse after you take your medication, do you sometimes stop taking them?.	Yes, No	No change in adherence (comparison group), Better adherence over time, Worse adherence over time
Change in self-rated health	Which of the following best describes your current overall health?	Poor, Fair, Good, Very Good, Excellent	Had same health status over time (comparison group), health became worse over time, health became better
Control variables for research objective 3			
Age	What is your age?	Respondent enters age as open ended questions	65-74(comparison group), 75-84, ≥ 85
Gender	What is your gender?	1- Male, 2- Female	Male (comparison group), Female
Race	What is your race?	White, Black, Asian, Native American, Mixed racial background,	White (comparison group) , Black/African American, Hispanic , Other

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
		Hispanic, African American, Other race	
Sum of symptoms experienced	Have you experienced any of these symptoms in the past month? Headache, Dizziness, Stomach/GI problems, Muscle aches, Incontinence, Rash/itching, Sleep problems, Mood changes, Fatigue, Sexual problems	Yes, No for each symptom	Number of symptoms experienced are summed and categorized as 0 (comparison group), 1, 2, 3, 4 or more
Number of medications	How many different prescriptions have you used in the past month?	Respondent enters the number of medicines as an open ended question	0 (comparison group), 1-2, 3-4, 5-6, 7-8 , >8

Study 2

Dependent variable= Change in concern beliefs measured as a difference in the scores on concern beliefs across months.

DEPENDENT VARIABLE	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
STUDY 2			
Concern beliefs in medicines	Please indicate the extent to which you agree or disagree with the following statements: Having to take medicine worries me, I sometimes worry about becoming too dependent on my medicines, I sometimes worry about the long-term effects of my medicines, My medicines disrupt my life	Strongly disagree, disagree, neither agree nor disagree, agree, strongly agree.	Sum of 4 items ranging from 4-20 (higher scores is stronger concern beliefs)

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
Socio-demographic data			
Age	What is your date of birth?	Respondent enters month, day and year	18-30 (comparison group), 31-50, 51-70, >70
Gender	What is your gender?	Male, Female	Male (comparison group), Female
Race	What is your race?	White, Black, African American, Hispanic, Other	White (comparison group) , Black/African American, Hispanic , Other

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
Education	What is the highest grade of school you have completed?	Grade school, some high school, high school diploma, some vocational, business or trade school, some college, 4 year college degree or more	Less than high school (comparison group); Has high school degree; Some college or some type of trade school; Has college degree or more
Clinical/behavioral characteristics			
Self-rated health	In general, would you say your health is:	Poor, Fair, Good, Very Good, Excellent	Poor, Fair, Good, Very Good, Excellent (comparison group)
Sum of symptoms experienced	During the past four weeks, have you had any dizziness, lightheadedness, or problems with balance?; Did you have pain?; Did you have any leaking of urine or problems with urinating?; During the past four weeks, did you have any problems with sleep?; Did you have a depressed or low mood?; Did you have extreme fatigue or persistent tiredness?; During the past four weeks did you have any skin problems, such as rashes, itching, burning, unusual bruising, pressure sores , or skin ulcers?; Did you have stomach or bowel difficulties such as nausea, vomiting, abdominal pain, constipation, or diarrhea?; Did you have any breathing difficulties?; During the past four weeks did you have any problems feeling confused or trouble concentrating?; Did you have dry mouth or blurry vision?	Yes, No for each symptom	Number of symptoms experienced are summed and categorized as 0 (comparison group), 1, 2, 3, 4 or more

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
Number of medications	Do you have any medications prescribed by a doctor that you have taken or were supposed to take regularly in the past 2 weeks? This includes medications you take by mouth, creams or ointments, eye or oral medications, injections. Please complete the prescription medication table.	Yes, No, Don't know; Enter the name and number of medication in prescription medication table	0 (comparison group), 1-2, 3-4, 5-6, 7-8 , >8
Number of pharmacies used	Here are the pharmacies you told me about when we spoke…List name of pharmacies used…Did you use any other pharmacies in the past six months?	Name of pharmacies are entered and counted for number of pharmacies used	1 (comparison group) , 2 , >3; Yes, No
Predictor variables for research objective 3			
Symptom reporting to physicians	Did you talk to a doctor about the problem you had with your medications?	Yes, No, Don't know	Yes, No (comparison group)
Self-reported ADE	In the past six months, have you had any side effects, unwanted reactions, or other health problems from medications you were taking?	Yes, No, Don't know	Yes, No (comparison group)
Change in self-reported adherence	In the past four weeks, have you forgotten to take any of you medications?; In the past four weeks, have you been careless about taking any of your medications?; In the past four weeks, have you stopped taking any of your medications when you felt better?; In the past four weeks, have	Yes, No, Don't know	No change in adherence (comparison group), Better adherence over time, Worse adherence over time

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
	you taken any of your medications less than your doctor prescribed because you felt better?		
Change in self-rated health	In general, would you say your health is:	Poor, Fair, Good, Very Good, Excellent	Had same health status over time (comparison group), health became worse over time, health became better
Control variables for research objective 3			
Age	What is your date of birth?	Respondent enters month, day and year	18-30 (comparison group), 31-50, 51-70, >70
Gender	What is your gender?	Male, Female	Male (comparison group), Female
Race	What is your race?	White, Black, African American, Hispanic, Other	White (comparison group) , Black/African American, Hispanic , Other
Sum of symptoms experienced	During the past four weeks, have you had any dizziness, lightheadedness, or problems with balance?; Did you have pain?; Did you have any leaking of urine or problems with urinating?; During the past four weeks, did you have any problems with sleep?; Did you have a depressed or low mood?; Did you have extreme fatigue or persistent tiredness?; During the past four weeks did you have any skin problems, such as rashes, itching, burning, unusual bruising, pressure sores , or skin ulcers?; Did you have stomach or bowel difficulties such as	Yes, No for each symptom	Number of symptoms experienced are summed and categorized as 0 (comparison group), 1, 2, 3, 4 or more

INDEPENDENT VARIABLES	MEASUREMENT IN SURVEY	RESPONSE SCALES	TREATMENT IN ANALYSIS
	nausea, vomiting, abdominal pain, constipation, or diarrhea?; Did you have any breathing difficulties?; During the past four weeks did you have any problems feeling confused or trouble concentrating?; Did you have dry mouth or blurry vision?		
Number of medications	Do you have any medications prescribed by a doctor that you have taken or were supposed to take regularly in the past 2 weeks? This includes medications you take by mouth, creams or ointments, eye or oral medications, injections. Please complete the prescription medication table.	Yes, No, Don't know; Enter the name and number of medication in prescription medication table	0 (comparison group), 1-2, 3-4, 5-6, 7-8 , >8

APPENDIX I: DESCRIPTION OF THE REGRESSION MODELS THAT WERE USED IN THE CONCERN BELIEFS IN MEDICINES: CHANGES OVER TIME AND FACTORS RELATED TO ITS STABILITY STUDY.

For this study, regression analyses were done to examine research objective 3. Two data sources (Medicare/CERT data and LWD/CMM data) were used to investigate this objective among Medicare enrollees and adults with self-reported physical limitations.

The research objective was to investigate what factors might drive the change in concern beliefs if they indeed do change across years. The analysis used were multiple linear regressions that examined if coping behaviors such as adherence, self-reported ADE and symptoms reporting have a direct effect on changes in concern beliefs over time. The regression model using the Medicare data were as follows:

Analysis: Change in concern beliefs (difference in the scores on the concern beliefs scale across years) = $ß_0 + ß_1$ change in self-rated health $+ß_2$ symptom reporting to physicians $+ ß_3$ self-reported ADE $+ ß_4$ change in self-reported adherence $+ ß_5$ age $+ ß_6$ gender $+ ß_7$ race

Using the LWD data, the research objective was to investigate what factors might drive the change in concern beliefs if they indeed do change across months. The regression model was as follows:

Analysis 1: Change in concern beliefs (difference in the scores on the concern beliefs scale across months) = $ß_0 + ß_1$ change in self-rated

$+ß_2$ medication –related symptom reporting to physicians + $ß_3$ self-reported ADE + $ß_4$ change in self-reported adherence + $ß_5$ age + $ß_6$ gender + $ß_7$ race

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