INFORMING THE DESIGN OF INFORMATION DISSEMINATING TOOLS FOR PATIENTS INTERESTED IN COMPLEMENTARY AND ALTERNATIVE MEDICINE

by

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ABSTRACT

The use of the various complementary and alternative medicine (CAM) modalities for the management of chronic illnesses is widespread, and still on the rise. Unfortunately, tools to support consumers in seeking information on the efficacy of these treatments are sparse and incomplete. The goals of this work were to understand CAM information needs in acquiring CAM information, assess currently available information resources, and investigate informatics methods to provide a foundation for the development of CAM information resources.

This dissertation consists of four studies. The first was a quantitative study that aimed to assess the feasibility of delivering CAM-drug interaction information through a web-based application. This study resulted in an 85% participation rate and 33% of those patients reported the use of CAMs that had potential interactions with their conventional treatments.

The next study aimed to assess online CAM information resources that provide information on drug-herb interactions to consumers. None of the sites scored high on the combination of completeness and accuracy and all sites were beyond the recommended reading level per the US Department of Health and Human Services.

The third study investigated information-seeking behaviors for CAM information using an existing cohort of cancer survivors. The study showed that patients in the cohort continued to use CAM well into survivorship. Patients felt very

much on their own in dealing with issues outside of direct treatment, which often resulted in a search for options and CAM use.

Finally, a study was conducted to investigate two methods to semi-automatically extract CAM treatment relations from the biomedical literature. The methods rely on a database (SemMedDB) of semantic relations extracted from PubMed abstracts. This study demonstrated that SemMedDB can be used to reduce manual efforts, but review of the extracted sentences is still necessary due to a low mean precision of 23.7% and 26.4%.

In summary, this dissertation provided greater insight into consumer information needs for CAM. Our findings provide an opportunity to leverage existing resources to improve the information-seeking experience for consumers through high-quality online tools, potentially moving them beyond the reliance on anecdotal evidence in the decision-making process for CAM.

To my husband Mark, my mother Roselyn, and my beautiful daughters Susan, Angelina, and Nicole, who believed in me even when I doubted myself. I love you all dearly and could not have crossed my finish line without your love and support.

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CHAPTER 1

INTRODUCTION

1.1 Objectives and Research Questions

Existing studies focused on consumer behaviors in complementary and alternative medicine (CAM) usage demonstrate that CAM use in the management of chronic illness is high and continues to rise [1-3]. Some online resources exist for CAM, but patients continue to rely primarily on anecdotal evidence when making decisions on CAM use [4, 5]. These behaviors, combined with a low rate of CAM disclosure to physicians [6, 7], pose many risks to the patients, including under-treatment when conventional treatment is delayed, herb-disease interactions, and drug-herb interactions [8]. Patients spend billions out-of-pocket each year on CAM [9] with little or no evidence of safety or efficacy. In order to move patients past the reliance on anecdotal evidence, to help them use CAMs that have some evidence of efficacy, and to help them avoid spending thousands on treatments that are ineffective, we need a greater understanding of patient motives, information-seeking behaviors, and what they view as "evidence" in making a decision to include a CAM in their treatment plan.

In the present dissertation, we aimed to investigate consumers' CAM information needs and information-seeking behaviors, consumers' attitudes towards reporting CAM use to their physicians via tablet devices, the quality of existing CAM online resources, and informatics approaches to help build the foundation of CAM information retrieval tools. In order to achieve these goals, we investigated four study aims as follows:

Aim 1: This study assessed the feasibility of gathering CAM data directly from the patient via an application presented on a tablet device. Specifically, we assessed the feasibility of gathering CAM use information at a cardiology clinic by older adult patients prior to their appointments. Our specific research questions were:

1) Are patients willing to self-report their CAM using tablet devices while waiting for their appointments with a physician?
2) How does the patient-reported CAM usage agree with usage documented in their electronic health records?
3) Are patient demographics such as age and education level a factor in their willingness to self-report CAM use via the tablet device?
4) What percentage of the study participants are at risk for drug-herb interactions due to the specific CAMs they are taking with known interactions to common cardiac medications?

Aim 2: In the second study, we assessed the completeness, accuracy, and overall quality of existing online resources for drug-herb interactions. We evaluated sites appearing in the first two pages of search results across several popular Web browsers to answer the following research questions:

1) How complete is the information for ten drug-herb pairs? Do the sites provide interaction information for these pairs with known interactions?
2) How accurate is the information presented? Do the sites provide interaction severity and does it agree with the severity found in our reference standard?
3) What is the quality of the information presented? Does the presentation follow existing guidelines on the presentation of information for consumers? Does the reading level of the information conform to the recommendations provided by the US Department of Health and Human Services?

Aim 3: We investigated the CAM information-seeking behaviors of a cohort of cancer survivors. Through this cohort, we sought to understand:

1) What are the preferred resources for CAM information for this cohort?
2) How have the preferred sources of information changed between the original 2004 study and the 2015 study? What role has the increase in online resources played in this change in preference?
3) What constitutes "evidence" in the mind of the consumer and helps them make a decision to include a CAM therapy?

Aim 4: We evaluated the performance of an algorithm to automatically extract treatment-related predications from the biomedical literature. Our specific study question was:

1) How does the algorithm perform in terms of precision and recall in comparison with a baseline method?

1.2 Rationale for Analysis

Patients most often still rely on anecdotal evidence in making CAM decisions [5, 10]. Therefore, it is important for both safety and value for consumers to properly identify and evaluate information on CAM. Even when the initial introduction to CAM is anecdotal, many patients still look for further evidence through patient testimonials and online resources [11]. Some patients would prefer to obtain CAM information from their physicians, but physicians are often not equipped to provide the necessary information [12]. For these reasons, patients must go to outside resources to find information and many of the resources are unreliable.

These issues highlight the need for online CAM information resources that satisfy all the information needs of consumers, including information such as scientific evidence

and social "evidence" through patient testimonials. There are gaps in the existing literature regarding consumers' CAM information needs, information-seeking behaviors, and information resources that can help consumers meet their information needs. One of the goals of this research was to identify and fill those gaps in order to guide the design of potential solutions.

For patients who are unable or unwilling to search for information on their own, the clinic is one possible setting for gathering CAM information with the aid of clinic staff. Older patients represent a large percentage of the consumers dealing with chronic disease such as diabetes, multiple sclerosis, heart disease, and Alzheimer's disease. Eighty percent of adults over the age of 65 have cellular phones, but only 42% use a smartphone [13]. The goal of the study in Aim 1 was to investigate whether older patient groups are willing and capable of self-reporting CAM use during a clinic visit using a tablet device. A willingness of these patients to share CAM use information in a clinic setting creates opportunities to improve CAM documentation in patient records and to discuss potential implications with the patient's provider, such as interactions with the patient's conventional treatment.

For consumers who do turn to online resources to find out about CAM options or for further evidence, prior studies have found that many of the CAM healthcare sites are of poor quality [14-16]. If consumers rely on Web searches for additional information on CAM, the quality of the information presented is important and the implications of incomplete data, particularly where drug-herb interactions are concerned, can be serious. If no interactions are listed for the drug-herb combination entered, this could imply that no interaction exists. The consumer may not be aware that many of the interactions could

simply be missing from the site. Aim 2 uses one area of concern to consumers, drug-herb interactions, as a test case to assess the completeness, quality, and accuracy of consumer health information available online for CAM.

One possible explanation for continued reliance on anecdotal evidence, in spite of the increasing availability of online resources, is that existing sites that provide information on the safety and efficacy of CAM fail to meet consumers' information needs. Important questions that are not answer in the literature include: 1) What specifically are they looking for, and what is lacking in current resources to meet their needs? 2) Are these consumers simply going with initial anecdotal evidence, or are they searching for additional evidence but simply do not know how to find it? Aim 3 investigates the information-seeking behaviors of a cohort of long-term cancer survivors. The goal of this study was to better understand how to meet their information needs and to understand their preferences in the design of Web-based resources to fill the gaps in existing resources.

Lastly, as a first step toward the design of consumer portals for CAM, Aim 4 investigates a pipeline method for extracting CAM treatment-related predications from the biomedical literature leveraging the Semantic Medline Database (SemMedDB). The resulting pipeline can be used to help build CAM treatment ontologies, which are essential building blocks for the development of CAM information resources and information retrieval tools [17].

In the absence of reliable CAM information resources, as well as physicians knowledge gaps about the efficacy of and potential interactions between CAM and allopathic treatments [18], it is often very difficult and frustrating for patients to find the

information they need to make an informed decision [19]. Tools for CAM information-seeking are needed that provide scientific evidence, information on interactions, and social "evidence" through patient testimonials. Studies have demonstrated that even for those that would like to see scientific evidence, patient testimonials are often important and many consumers will use a CAM in the absence of scientific evidence when there is sufficient social "evidence". One study showed that patients will continue to use a CAM even when scientific evidence showed it to be ineffective [11]. The ideal solution would provide a combination of evidence sources to satisfy the information needs of a larger consumer base.

1.3 Significant Contributions

This research takes an in-depth look at consumer preferences in sharing and receiving CAM information, taking into consideration demographic preferences including age, gender, and education level. First, Aim 1 showed that older adults were willing to and capable of self-reporting CAM use through tablet devices during clinic appointments, and that a large percentage of those patients are at risk for drug-herb interactions. The Aim 2 study found that a set of information resources about drug-herb interactions are not adequate to meet consumers' CAM information needs and could lead to continued risk due to missing or inaccurate information.

With the understanding from the prior studies that consumers lack a comprehensive, scientifically-based information resource for CAM information, Aim 3 provided a deeper, more detailed understanding of what consumers desire in Web-based tools to meet their CAM information needs. Finally, Aim 4 laid the groundwork for

consumer CAM information resources through a pipeline system that automatically extracts CAM treatment-related predications from the biomedical literature. The system performed well against a reference standard and can be used in developing the first treatment-related ontology for CAM information-retrieval systems. This method could be extended to support disease-herb interactions and drug-herb interactions to support both consumer information needs as well as clinical decision support tools within EHR systems, such as alerting on potential CAM interactions. The information needs and preferences, as well as a treatment-related ontology about CAM, be would valuable to several audiences, including informatics researchers, developers of information-sharing portals, and medical librarians who support CAM users in finding and evaluating CAM information.

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CHAPTER 2

BACKGROUND

2.1 Complementary and Alternative Medicine (CAM)

Complementary and Alternative Medicine (CAM) generally refers to medical interventions that are not commonly used in conventional medicine or taught in US medical schools [1]. It can include many modalities, including prayer, yoga, chiropractic, meditation, and biologically-based therapies such as herbal and dietary supplements. There is a strong interest in biologically-based CAM, as studies have shown that this is the most common form of CAM use reported by patients with chronic illness and also presents the greatest risk to the patient due to potential drug-herb interactions [2-5].

2.1.1 CAM Use

CAM use in the management of chronic disease is well documented and on the rise. The use in cardiology was shown to be as high as 65% through a systematic review of the literature [6]. Use in oncology has also been shown to be high with one study reporting a 49% usage [7], with even greater usage patterns for studies involving women with breast cancer [8]. Usage can be higher in radiation oncology, with one study showing overall use to be 59%, but as high as 91% for breast cancer patients receiving radiation therapy [9]. Multiple studies have found that women have a tendency to use CAM more often than men and make most of the healthcare decisions for the family [10, 11].

A study conducted by the National Center for Complementary and Integrative Health (NCCIH, formerly the National Center for Complementary and Alternative Medicine) found that consumers spent $33.9 billion on CAM out of pocket in 2007 [12]. The willingness to spend that much on interventions that are not covered by insurance

implies that consumers may have a strong interest in these alternative treatments. Therefore, there is a need for tools to help consumers make appropriate decisions for CAM use allowing them to understand the potential risks and benefits of the products they are considering.

2.1.2 Drug-Herb Interactions

With increased CAM use in the management of chronic disease comes the concern of drug-herb interactions where biologically-based CAMs are used and not reported to the care provider. Many of these drugs and biologically-based CAMs are metabolized through the liver. The drug metabolizing enzymes in the liver are known as cytochrome P450 microsomal enzymes. Often biologically-based CAMs can act as inducers or inhibitors of these enzymes, ultimately resulting in drug-herb interactions with the CAM interaction resulting in sub-therapeutic or supra-therapeutic doses of the allopathic treatments [13-17]. One manuscript discusses multiple case studies where the conventional treatment was not as effective as expected. After further investigation, it was discovered that the patient was taking CAMs without reporting their use, which were disrupting how conventional drugs were metabolized [18].

These interactions can often lead to ineffective treatments or adverse effects whose underlying cause the prescribing physician may not recognize. An example of the risk to patients is the combination of Warfarin and St. John's Wort. St. John's Wort has been shown to decrease prothrombin time, resulting in sub-therapeutic anticoagulation and increased risk of thromboembolism [19].

2.1.3 Patient Motivations for CAM Use

Patients state many reasons for CAM use, including treatments providing a more "gentle" effect [20], to "sustain one's own strength" [21], fewer side effects [22], and that they are not simply a "symptomatic cure" [23] . There is also an association between CAM use and a belief that certain lifestyle and psychological behaviors contributed to the development of the disease [24]. Although patients have expressed frustration with the lack of insurance reimbursement for their preferred method of treatment, they are still willing to pay out of pocket if necessary [23]. Patients seek information on CAM as a means of understanding their options, for a sense of hope and control, and for alternative options when the prognosis is poor or they experience a recurrence [2].

There has also been an association between a higher internal health locus of control (HLOC, which measures the perception of controlling one's own outcomes) and positive treatments outcomes. An internal HLOC has also been associated with increased CAM use [25]. This association between internal HLOC and positive outcomes have been shown in other studies demonstrating the potential for improved outcomes through patient empowerment [26]. Other factors in the decision to use CAM include active coping strategies that are often necessary with diseases posing an immediate threat to the patient, such as cancer and its treatments [27, 28].

Patients often use CAM because they feel it offers them more freedom in making treatment decisions than conventional medicine. Physicians should be aware that CAM usage can also be associated with negative attitudes toward conventional medicine [29] and open communication and physician support may mitigate this problem.

2.1.4 CAM Disclosure

Patients do not always report CAM usage to their physician. This failure to disclose puts the patient at risk, particularly for drug-herb interactions [30, 31]. It is estimated that as many as 72% of CAM users do not discuss CAM use with their physicians [1]. Reasons for nondisclosure include fear of a negative response [32], their physician did not ask [3], and their physician did not need to know [31]. One study suggested that a focus on patient-centered communication may encourage patients to talk about their CAM use [33]. Since patients often do not feel discussing CAM use with their physicians is important [1, 31, 32], physicians should initiate discussions with patients and emphasize the importance of this communication. A recent study of CAM use during pregnancy indicated that with heightened awareness of potential interactions between CAMs, drugs, and conditions, reporting of CAM use may be increasing [34].

2.1.5 Benefits of Use

Studies on the use of CAM in the treatment of cancer have shown favorable results, particularly improved survival, better pain control, and reduced anxiety, nausea, and vomiting [35]. Another study of inpatients in an oncology unit at Beth Israel found an enhancement to cancer care as well as cost reduction in patients participating in an integrative medicine (see section 2.5) study. This study included interventions such as yoga, holistic nursing, and attention to a healing environment. The study resulted in decreased hospitalizations and infections [36]. A Cochrane review on the effects of music therapy in patients with cancer showed a beneficial effect on anxiety, heart rate, blood pressure, and quality of life [37]. These combined studies suggest that the optimal

approach to caring for patients with life-threatening illnesses would take a patient-centered approach utilizing a combination of conventional and CAM therapies to address all patient needs, including quality of life.

2.1.6 Challenges in CAM Information Seeking

Studies have shown that 48% of cancer patients use at least one CAM and the search for CAM information starts with the initial diagnosis but continues along the treatment and survivorship trajectory [4, 5]. When patients seek CAM options, they may experience significant challenges in finding and evaluating the information they need [4, 11, 23, 38, 39]. They become frustrated and overwhelmed by conflicting messages pertaining to the efficacy of CAM and are frequently unaware of interactions and complications. Along with these challenges, the comprehension level of the information they encounter is often beyond that of the average consumer [40].

Patients often prefer to receive information on CAM from their physician, but providers are not necessarily equipped to provide CAM information [41] and patients are often uncomfortable discussing CAM use with physicians [3]. As a result, patients often seek CAM information from other channels that may not be reliable [41]. With minimal guidance on CAM use from their physician, patients run the risk of adverse reactions and misinformation on the efficacy of the CAM [41].

2.1.7 Existing CAM Resources

Many sites exist for information on the safety and efficacy of CAM in the treatment and prevention of disease. These sites include:

1. The National Center for Complementary and Integrative Health

(https://nccih.nih.gov/) . NCCIH contains CAM efficacy information, but does not support consumer input.

2. The Natural Medicines Comprehensive Database (NMCD) (http://naturaldatabase.therapeuticresearch.com/home.aspx?cs=&s=ND. NMCD is intended for pharmacists and physicians and charges an annual licensing fee for access to safety and efficacy studies.
3. PatientsLikeMe (PLM, https://www.patientslikeme.com/member_home). PLM supports patient input, but does not link CAMs to the literature.
4. Life Extension (LE, lifeextension.com). Life Extension sells supplements and provides efficacy information on those supplements with linkage to the literature free of charge, but access to online information and phone consultations on supplements that have been shown to be effective for specific diseases requires purchasing an annual license.

All the above sites except PatientsLikeMe provide CAM information that is backed by the scientific literature, but they do not support patient forums and testimonials. Studies have shown that some patients are skeptical of evidence provided solely through scientific studies. PatientsLikeMe does support forums for CAM use, but there is not linkage to the literature for scientific evidence of efficacy and safety.

2.1.8 Women as Healthcare Decision Makers

Multiple studies have demonstrated that women make up to 80% of the healthcare decisions for the family [42] and that women are also known to make greater use of healthcare portals [43, 44], with women making approximately 78% of eVisits and 63%

of access to patient portals. One study also showed that women tend to use CAM more often than men (1 in 5 vs. 1 in 8) [4, 45]. For these reasons, special attention should be paid to the information needs of women both as more frequent users of online resources and CAM and as the primary decision-makers for their families.

2.2 The Use of the Internet for Health-related Information

Studies have indicated that consumers are increasingly turning to the Internet for healthcare information, with up to 80% of Internet users looking for health-related information, making it the third most popular topic in Web searches. Information of interest includes specific disease information (66%), treatments (56%), doctors and medical facilities (44%/36%), health insurance (33%), and environmental health hazards (22%) [46]. Patients often search across several sites looking for information they deem trustworthy, and although not always available, they would feel more confident if the site were endorsed by a recognized professional body [47].

The rise in the use of the Internet for healthcare purposes raises many questions as to the quality of information available to the consumer. A study for consumer information on Inflammatory Bowel Disease showed that 57% of the 76 Web Sites available were rated fair to poor in quality of content [48].

2.3 Social Networking

The emergence of Web 2.0 and social networking has had important implications for the dissemination of medical information. Patients look for information and become involved in discussions about medications, disease, diet, and lifestyle topics. They look for information on side effects, efficacy, symptoms, and survival statistics [49]. In one

study on social networking and antibiotic use, the most common categories for information were general use, advice and information, and side effects [49].

Social networking sites not only help patients find useful information, but also provide opportunities for research organizations to uncover potential issues with side effects, compliance, use, and misuse of prescription medications [50]. Platforms such as Facebook and PatientsLikeMe provide patients with the opportunity to actively engage in their health as well as connect with other patients who have already been through the management of a medical condition such as cancer from diagnosis to survivorship and who have a wealth of information to share [51]. A study of disease-specific information sharing on Facebook showed that the majority (66%) of the posts sampled were about users sharing their personal experiences in the management of their disease [52]. One problem noted in a study on social networking sites was advertising content and commentary from the pharmaceutical industry, raising questions of misinformation, commercial influence, and even conflict of interest [53].

2.4 Integrative Medicine

Cancer patients are increasingly looking for integrative therapies to optimize well-being and improve quality of life during and after treatment. These therapies have been shown to be effective and resulted in cost savings with patients using fewer medications and experiencing reduced infections and hospitalizations [36]. Those therapies found to be effective and easily accessible include music, aromatherapy, exercise, and mindfulness practices.

The emergence and continued growth of integrative medicine is largely due to

public demand, particularly for life-threatening diseases such as cancer [54]. Another study on the use of IM in inpatient oncology showed significant decreases in anxiety, fatigue, and depression in the intervention group. This study showed that with the decreases in these scores, patients used fewer medications, resulting in substantial cost savings [55].

In making a shift from patient CAM use to IM, there is a need for open dialogue and shared decision making (SDM) between patients and their providers, with providers considering all patient needs, including personal lifestyle preferences and a focus on quality of life [56]. Beyond the patient-provider relationship, patients also view IM programs as a place to connect with other patients, share information on treatments and outcomes, and to simply receive emotional support from others experiencing similar health challenges [57].

2.5 Theoretical Frameworks for Understanding Consumer Behaviors

Multiple consumer health models are common in research pertaining to consumer behaviors and preferences. The Uses and Gratification Theory (UGT) examines why a specific media satisfies the needs of information seekers. This theory assumes that the information seeker is goal-oriented and purposive. These individuals have expectations for a specific media use and target a media to fulfill their goals [58, 59]. The Health Belief Model (HBM) looks at how perceptions of health, such as perceived threat and perceived benefit, can be used to explain health behaviors and choices [60, 61]. As an example of the HBM construct of perceived threat, the threat of specific events in the cancer trajectory, such as diagnosis, progression, recurrence, and treatment side-effects,

are possible triggering events for a CAM information-seeking process. Chapter 5 provides a more in-depth discussion of these theories and their application within this research.

2.6 References

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CHAPTER 3

FEASIBILITY AND POTENTIAL BENEFIT OF COLLECTING COMPLEMENTARY AND ALTERNATIVE MEDICINE DATA THROUGH A COMPUTERIZED PATIENT INTERVIEW

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Feasibility and Potential Benefit of Collecting Complementary and Alternative Medicine Data Through a Computerized Patient Interview

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Abstract

Objective: To determine the feasibility of gathering Complementary and Alternative Medicine (CAM) data directly from the patient via a computerized patient interview.

Design: A quantitative descriptive study was utilized to determine whether patients would be willing to self-report their CAM usage and whether the self-reported data complements clinicians perceptions and medical records.

Measurements: 40 patients were recruited to test the computerized patient interview application. Clinicians and staff (n=15) were also surveyed to determine their perceived CAM usage. In addition, a retrospective chart review (n=100) was done to estimate the documented CAM usage rate.

Results: In this study, we had a 85% participation rate, suggesting patients are willing to share their CAM use through the computer application. The self reported usage rate was 85%, as compared to the chart documented usage rate of 9.5% and the average clinician/staff estimated usage rate of 43%.

Introduction

The use of CAM amongst patients in the US is well documented. CAM has grown to an estimated 50 billion dollar industry with an estimated 30-50% of patients utilizing some form of CAM in their healthcare [1-10]. In spite of this trend, there appears to be a hesitance on the part of the patients to share this information with their healthcare provider [11, 12]. Many patients have adopted an attitude of "if they don't ask, I won't offer" toward the communication on this topic with their primary care providers [12]. On the other hand, there is a significant risk of herbal supplements interacting with prescriptions medications and causing harm to the patient [2-4, 13, 14]. Given the potential for drug-herb interactions, it becomes increasingly important to document dietary supplement use along with prescription medications. The ability to search for potential interactions and to alert the patient and clinicians is dependent on the continuous maintenance of both lists.

To improve patient safety and better monitor CAM usage, we sought to study the feasibility and potential benefit of gathering this data from the patient utilizing a computerized patient interview system. Our research questions are 1) Are patients willing to disclose their CAM usage using the computer application? 2) Can the patient self-reported data complement the information gathered by clinicians and recorded in medical records? 3) Can this data be gathered with a level of quality that enables clinical decision support and therefore makes the effort worthwhile?

Materials and Methods

We developed a simple computer interview application to collect CAM usage data directly from patients. After a brief usability study and user interface (UI) improvements, we conducted a feasibility study of the application in an outpatient cardiology clinic. To measure the potential benefit of the self-reported data collected by the application, we surveyed clinician's perceived CAM usage as well as reviewed a random sample of charts from the same clinic. The rates of CAM usage from the three sources (patients, clinicians, and chart review) were compared.

Setting

The study was completed in the Cardiovascular Clinic at the University of Utah.

Recruitment

Inclusion criteria were patients referred to the University Cardiovascular center for various reasons, excluding transplant patients. This includes consults, heart failure, congenital, and all other areas of cardiology except transplant. Transplant patients are excluded because 100% of those are taking dietary supplements and all are physician prescribed and very tightly monitored by the physician and the pharmacist. All other CV patients are included as CAM usage tends to be higher amongst the chronically ill. All patients were at least 18 years of age and English speaking.

CAM Interview Application

The interview application was implemented as a web portal displayed in a browser on an iPad, with a MySQL database backend for storage. The site was coded in Java/JSP. The first page is an introductory page, which explains why this study is important to the patient. This is followed by a description of the three categories of pills that a patient might take, to ensure that they understand the difference. These include prescription drugs, over-the-counter drugs, and dietary supplements. The dietary supplement information is what we are focusing on. Next, the application invites patients to select from a list of common dietary supplements (Figure 1). The list contains the supplements with known interactions to prescription cardiology drugs, along with a few of the most common dietary supplements taken by cardiac patients. We consulted the Natural Medicines Comprehensive Database to create the list.

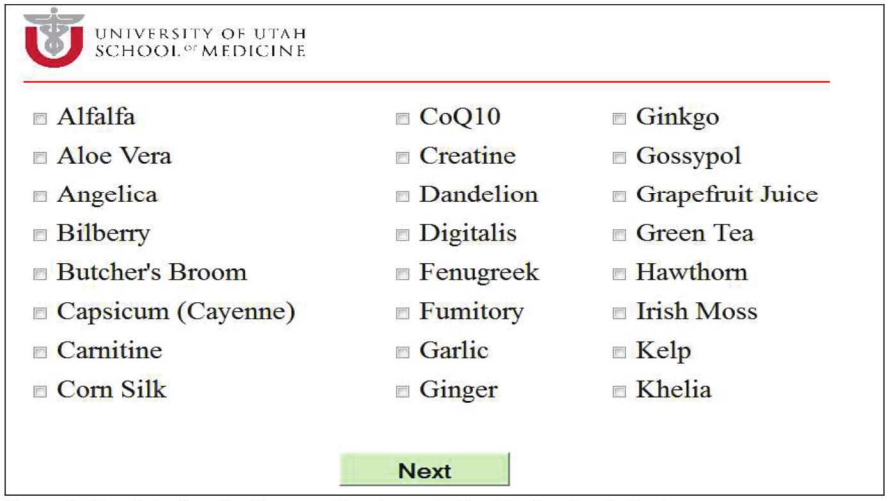

Figure 1. *User Interface for Common Supplements Used by Cardiac Patients*

To provide for future functionality such as identifying additional interactions, as well as to avoid the inevitable question of why a patient's supplements were not included in the list, a free-form data entry screen was also provided. Auto-suggest capability was built into the UI to decrease the typing required and to prevent spelling errors (Figure 2).

Usability Testing

A pre-study test phase included 4 patients, which was adequate to expose usability issues in the user interface. The patient was asked to navigate through the web site, indicating verbally any information that was not clear to them. The research assistant looked over their shoulder, noting any confusion on the part of the patient as to intended use and flow of the site. The discovered flaws were corrected.

Feasibility Testing

Each patient was interviewed in the examination room after the mid-level providers gathered the pertinent clinical data and before the physician entered the room for examination (Figure 3). The research assistant (RA) knocked on the door, entered the room, introduced herself and the study, and asked if the patient would be interested in participating in a research study as they waited for their physician.

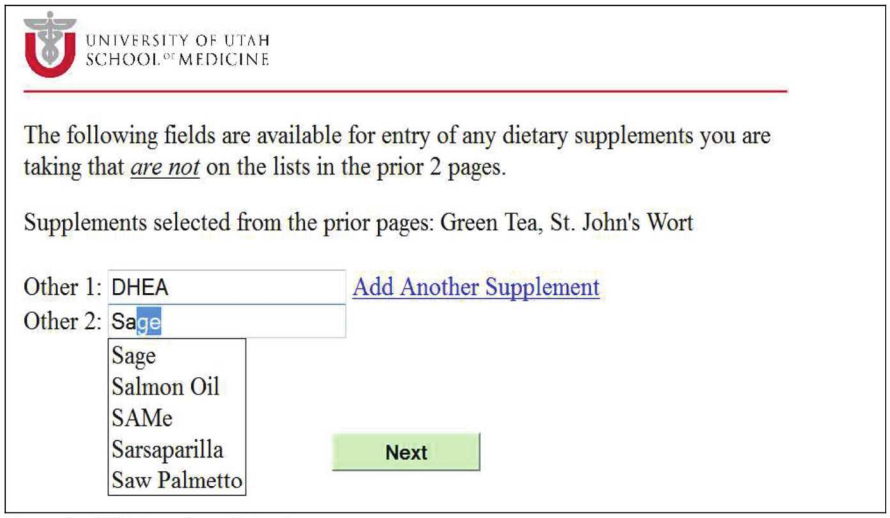

Figure 2. *CAM Free-form Entry Screen*

The patient was then presented with the study consent form that contained all the usual elements of a consent form, as well as a study ID field. This study ID was retrieved from the web site at the end of the online interview and noted in this field. This is the only link between the patient's identifying information (from the signature field on the consent form) and the study data stored in the database.

After signing the consent form, the patient was presented with an iPad with the study home page displayed in the browser. Consenting patients then proceeded to the computer interview.

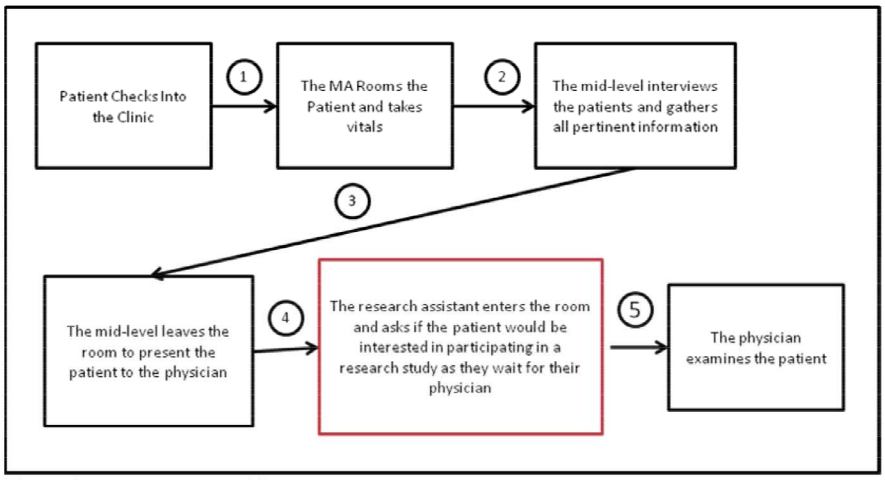

Figure 3. *Recruitment Workflow*

Survey of Clinician and Staff Perceptions of CAM Use

Physicians, mid-level providers, and MAs were surveyed in order to form some insight into their perceptions of the prevalence of CAM use in Cardiology. The goal here was to weigh these perceptions against the reality per the results of the actual prevalence as evidenced by patient self-reported use.

Chart Review to Determine CAM Use Documentation Rate

A random selection of 100 patients notes were examined from the cardiology clinic records via a retrospective chart review to determine the documentation rate of CAM usage in order to compare this percentage against the self-reported use as determined by the computerized patient interview.

Results

The recruitment rate proved to be extremely positive at 85% of the 47 patients approach, for a total of 40 participants. It is likely that this high rate is attributed to a minimally intrusive and carefully timed patient approach. Because the patient is waiting for their physician and also are ensured that their visit with the physician takes priority over the study interview process, the patients seemed to have a favorable attitude toward participation. Several patients went beyond that and expressed enthusiasm toward the study as either they or a loved one took a large number of dietary supplements along with their prescription drugs. Those patients expressed interest in a system that would allow them to maintain an up-to-date list of their dietary supplements which would ultimately be paired with their medication lists to detect potentially harmful interactions.

The preliminary findings from the usability study of the computerized patient interview system show the CAM usage rate to be approximately 85%. Unlike the results found in the chart review, 33% of the participants taking dietary supplements were taking at least 1 supplement from the known interactions list. One of those patients was taking 3 supplements from the interactions list and also reported taking 9 prescription drugs. One additional patient was taking 3 supplements from the interactions list, one taking 4, and one taking 5.

The age of the study participants ranged from 18 to 88 with a mean age of 55 years. The time spent searching for online health information seemed to be fairly evenly distributed between never, occasionally, and at least once per week. 79% of the participants had some college or were college graduates. The participants were fairly evenly distributed between male and female (**Table 1**).

Age (years)	
Min. : 18.00	
Mean : 55	
Max. : 88.00	
Education Level	
High School	7 (18%)
Some college/technical school/vocational training	12 (30%)
College graduate	15 (38%)
Time spent searching for online health related information	
Never	10 (25%)
Occasionally	12 (30%)
Once/week	10 (25%)
Gender Distribution	
Male	23 (58%)
Female	17 (42%)

Table 1: *Demographic profile of the 40 patients included in the study*

The survey of clinicians and staff showed differing perceptions of CAM usage amongst cardiac patients with the physicians falling below the mid-level providers and MAs in their estimates and with all those surveyed falling significantly below those percentages as discovered through the preliminary findings of the computerized patient interview (Table 2). The range for the perceived use was 10% to 80%.

Role	Average Estimated CAM Usage
Physician	34%
Mid-level	48%
Medical Assistant	52%

Table 2: *Perceived CAM Use by Clinicians and Staff*

Of the 100 charts reviewed, 9.5% included notes about dietary supplement use, which is well below the usage being reported by the patients during the online interview. Of those 9.5%, only 2 listed a dietary supplement that has been identified as having known and potentially harmful interactions with some cardiac drugs. However, just as in the medications lists, it is not likely that these lists are complete or up to date. The most common supplements listed in the charts included calcium, fish oil, vitamin D, and glucosamine/chondroitin. Some of these particular supplements are often clinician recommended therapies and might not be considered CAM.

Discussion

Although the sample size of these preliminary findings was small, the numbers look very promising from the perspective of patient participation as well as the ability of the patient to use a computerized interview system at almost any age.

The participation rate was 85% with approximately 15% of those participants expressing enthusiasm for the CAM data gathering and interaction detection system.

The limitations of the study include a small sample size of 40 patients. However, this small sample size is only for the usability portion of the study. Subsequent studies that link to the patient's medication list for medication

reconciliation as well as CAM data gathering are planned. In both the chart reviews and patient entered CAM data, it's difficult to determine what is truly CAM and what is physician recommended. Finally, the validity portion of the study is still underway, so it still remains to be seen how accurate patient entered CAM data is.

Early indications are that it is feasible to ask patients to enter and review their CAM data in their record and it is assumed that this can be extended to include medication reconciliation. It remains to be seen how valid this data is. This will be measured through a return visit where the patient is asked to bring all of their prescription medications as well as their dietary supplements. The data entered during this return visit will be input by the RA, not by the patient.

Various interview workflows were considered and tested. These included approaching patients in the waiting area, as soon as they were roomed, before their time with their mid-level and physician, and after their office visit/before they left the clinic.

The concerns with approaching the patient in the waiting area included either jeopardizing their privacy by interviewing them publicly, or causing concern with or interrupting clinic workflow by pulling them out of the waiting area and into a more private setting. This would cause delays and frustrations to the front office staff by requiring that they come to the interview room to retrieve the patient, especially during high traffic periods.

Another workflow considered was to either have the MA or mid-level recruit for us as they either roomed or examined the patient. What we discovered was that as supportive and well-intentioned as the staff were, they rarely remembered to do this as it is not part of their normal workflow or daily responsibilities. In light of this, the recruitment rate was approximately 3 patients per week.

As far as approaching the patient at the end of their appointment, although not tested, there is little doubt that the recruitment rate would also be low with this method. By the time they waited in the reception area, in the examination room, and were visited by multiple clinicians and support staff such as MAs, mid-levels, physicians, and phlebotomists, they are unlikely to be willing to extend their visit to talk to students and participate in a study.

Careful attention was paid to ensure that the clinic workflow was not affected at any level. Each step in the clinic workflow was carefully studied to determine the optimal time to insert the patient interview with no interruption. This careful analysis and choice of timing is credited to both maximum staff support of the study and extremely high participation rates. 90% of the time, the RA had completed the interview and left the room before the physician entered. When this was not the case, the interview was completed as soon as the physician stepped out of the room.

The pre-study phase proved to be very helpful in identifying usability issues in the UI and once those were addressed, the feasibility study was much more successful. Only minor UI issues were uncovered, with the exception of unintended behaviors from the iPad such as entering cut/paste mode and magnification mode. Both of these behaviors were most often encountered on the free-form data entry screen while the user was trying to click into and begin data entry. They then became frustrated and did not know how to get out of that mode, or even what mode they were in. Because of these unintended behaviors, we will be most likely not be utilizing the iPad in the next phase of the study. We will instead look into one of the many kiosk options available today.

Future work in the this area will include the review of the medication list for the sake of medication reconciliation, a validity study to ensure not only that the patient would be willing to enter or review this data, but also that they can do so with a reasonable level of accuracy. Finally, a clinical decision support system will be built to detect the known interactions between prescription drugs and dietary supplements as well as the scientific evidence of and severity of the interaction. That severity will be used to determine whether an alert will be generated. However, a physician note can be generated in the patients record to alert both the patient and the clinician to the potential interaction at any severity.

The validity portion of the study will involve either an in-person interview or over the phone where the patient has the supplement bottles in front them. They will be asked to read each label including manufacturer and full product name. This commercial product information can then be used to retrieve the component breakdown from the NMCD. This supplement list is stored in a different database table from the original list and compared against what the patient entered from memory in the clinic. A check box could also be included here to indicate whether this is physician recommended . A text field could also be included to gather information from the patient as to why they take and feel each supplement is helpful to them. This data could be compared against NMCD and literature data on efficacy.

These preliminary findings show the prevalence of CAM usage to be significantly higher than indicated in the literature. One reason for this could be the location of the study. Utah is major producer of CAM products such as dietary supplements, essential oils, etc. Consequently, Utahns might use these products at a higher rate than in other parts of the country. The prevalence could also be higher due to the clinic from which the data was gathered. CAM usage tends to be higher amongst the chronically ill such as those interviewed in the cardiovascular clinic.

Conclusion

It is feasible to involve the patient in the maintenance of their CAM data in their medical record. The timing of the request is important to ensure that they agree to review their records and to ensure that they do not abandon the process before they have made all the necessary updates, thereby decreasing validity. Patients expect delays upon check in to the clinic and after being roomed, so these provide excellent opportunities for such requests.

A simplified UI and touch screen also proved to be critical to the usability of such a tool across all patient demographics. Some options still need to be weighed and evaluated such as a kiosk option in the waiting room as well as the use of the iPad due to some fairly consistent problems experienced by the patients.

The paper increases awareness of the importance of including this information as part of a patient's medication record. Information on CAM in the patient's record (chart) is important to contribute to overall information that considers patient safety.

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CHAPTER 4

COMPLETENESS, ACCURACY AND PRESENTATION OF DRUG-HERB INTERACTION INFORMATION: AN INTERNET REVIEW

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Completeness, Accuracy and Presentation of Information on Interactions Between Prescription Drugs and Alternative Medicines: An Internet Review

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Abstract

Background—As the use of the Internet continues to increase across all age groups and education levels, with usage in the US around 78%, consumers are increasingly turning to the Internet for health related information.

Objective—To assess the completeness, accuracy, and consumer friendliness of information on the Internet pertaining to drug-Complementary and Alternative Medicine (CAM) interactions with cardiac drugs.

Methods—A review of online information was performed across three search engines and ten drug-CAM pairs.

Results—Overall, the quality of the drug-CAM interaction information available online to consumers is fairly poor. Only one site contained an interaction checker that provided interaction information for all ten pairs, but with an accuracy rate of 50%. Reading levels ranged from 10.5–23.5, with a mean of 16.7. A value greater than 22 indicates a graduate level reading skill.

Conclusion—Web site developers should be cautious in presenting drug-CAM interaction information unless it is comprehensive and regularly maintained. Consumers should also know how to evaluate sites before trusting the content where the consequences are potentially severe.

Keywords

complementary medicine; alternative medicine; drug-herb interactions; consumer health

Introduction

Complementary and Alternative Medicine (CAM) use is on the rise in the US and patients are becoming aware of potential interactions between prescription drugs and CAM through information provided by their physicians, pharmacists, and via the Internet. [1–6] When consumers want more information on healthcare, increasingly they are turning to the Internet. One study showed that 80% of Internet users have used it for healthcare purposes. [7] Similar behavior is expected when consumers are concerned about interactions between

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their prescription drugs and CAM. Therefore, there is cause for concern as to the quality of information consumers may be receiving via the Internet to make informed decisions.

In this study, we analyzed the quality of drug-CAM interaction information for consumers on Internet sites. CAM includes herbals such as St. John's Wort, supplements such as Coenzyme Q10, and minerals such as magnesium. Although CAM is a more inclusive term to refer to these substances, other terms are more commonly used, such as "herbs" or "dietary supplements."

Our research questions were: 1) How complete and accurate is the information found on the Internet? 2) How readable is the information? 3) How is the information presented? 4) Is scientific evidence available? 5) Does the site provide a recommended action?

Background

According to Medline Plus, the first approach to evaluating online health information is to consider the source. Is the site government sponsored, a university, a hospital, or a business? Is the information peer-reviewed? Is the site trying to sell you something? How current is the information?

Another means of instantly assessing the reliability of the information provided on a consumer health site is to verify if the site is certified by Health on the Net (HON). HON is a nonprofit, non-governmental organization accredited to the Economic and Social Council of the United States. The mission of the HON Foundation is to provide multi-stakeholder consensus to protect citizens from misleading health information. [1]

Increasingly, patients are turning to the Internet for health related information. [7] Due to the large volume of information available to healthcare consumers, there is evidence that consumers are becoming more proactively involved in the management of their own health. [8] For these reasons, as well as the fact that consumer content is for the most part unregulated, [9] it is becoming increasingly important that consumers understand how to assess the quality of the information they are receiving from online sources. One study on consumer information for Inflammatory Bowel Disease indicated that 57% of the 76 Web sites evaluated were of fair to poor quality. [10]

Studies addressing the quality of healthcare information online, in particular encouraging the use of CAM, have shown the potential for harm to patients. One study showed that 25% of the sites contained misleading or false information that could lead to direct harm to the consumer if acted upon, while 97% had omitted information. [11] Studies show that 78% of the information patients are receiving comes from commercial organizations, with 69% for the purpose of commerce and 52% had no references. [12] Those sites, although intended for consumers, most often contain language at a minimum 11th grade reading level, which is considerably higher than the recommended 7th grade level per the United States Department of Health and Human Services (USDHHS). Another common problem amongst these consumer health sites is invalid and omitted information.

[1] http://www.hon.ch/

Many studies exist pertaining to Internet use and the quality of online information for health specific topics such as online pharmacies and drug information, diabetes self-care, asthma, general health information, personal health records, HIV/AIDS, nutrition and exercise, clinical trials, and chronic disease treatments and options. However, very few studies exist assessing the quality of online drug-CAM interaction information and none of these studies evaluated sites that are intended for the consumer. One prior study evaluated drug-CAM interaction sites for use by physicians in answering questions asked by their patients. [13] That study took the information at face value, making no attempt to evaluate accuracy. Another study assessing the quality of CAM information for consumers reported similar results to this study, but did not address drug-CAM interactions. [12]

Materials and Methods

Drug-CAM interaction sites

To identify sites for this study, an Internet review was conducted using popular Web search engines and various search terms. To identify relevant sites, we used three search engines and search terms such as 'drug-herb interactions' and 'drug-supplement interactions'. The search strings related to drug-CAM interactions listed at the bottom of the page in a Google search were used as a means of feeding the search term list used in the study.

According to search engine optimization (SEO) sites, which provide information on the usage of the various search engines, Google was the most popular, with Bing and Yahoo contending for second and third place. [14, 15] One of the studies showed Google at 72%, Yahoo at 14%, and Bing at 10%. Therefore, utilizing these three search engines for this study covered 96% of all Web searches. [16] The 2006 iProspect Search Engine User Behavior study showed that 62% of search engine users clicked on only sites found in the first page of results and 28% in the second and third pages. [16] Using that as a criterion for site selection, we remained within the first two pages of search results across all search engines and search terms.

All search terms were entered across the three search engines. The sites listed on the first or second page were analyzed. We only selected sites containing an interaction checker that provided the ability to enter either a drug or a supplement and view its corresponding drug-CAM interactions. Many sites were excluded because they provided a minimal hard-coded list of CAM or drugs and discussed common interactions, with little or no detail for the individual interactions. Searching for your own medication or CAM in those sites was not possible.

Reference standard

To assess the quality of the information presented on the sites identified, we selected a list of four medications commonly prescribed in the practice of cardiology. Those selected were Warfarin, Lipitor, Simvastatin, and Plavix.

As a reference standard, we searched the Natural Medicines Comprehensive Database (NMCD) to identify major and moderate interactions between the selected drugs and commonly used CAM. The major and moderate interactions were inspected and interactions

with well-known and commonly used substances were selected. They included St. John's Wort, Ginkgo Biloba, and grapefruit. Although this study did not cover interactions between drugs and foods, grapefruit was used as it has severe interactions with many cardiac medications and comes in a highly concentrated extract form for use as a dietary supplement.

A total of 10 drug-CAM pairs were entered into the NMCD and we purposefully selected 10 moderate or major interactions based on how common the interacting CAM was in the management of chronic disease. The interaction description (clinician version), consumer description, and severities were obtained.

Assessment criteria

Web sites were assessed with respect to five criteria: completeness and accuracy, readability, quality of presentation, scientific evidence, and recommended action

Completeness was measured by comparing the ten drug-CAM pairs in the reference standard with those available on each Web site. Because the drug-herb pairs were common and interactions were severe or moderate, it would be important that all 10 pairs were present.

Accuracy was measured by agreement between the sites evaluated and our reference standard regarding the severity of drug-CAM interactions. Five of seven sites evaluated provided interaction severity.

The presentation format was analyzed based on existing guidelines for presentation of information to consumers. Particular attention was paid to visual displays, because prior studies have shown that coloration and simple graphics are preferred to relay information to patients over textual descriptions. [17, 18] Coloration and icons are important to draw attention to critical information, with minimal textual descriptions to corroborate what the consumer believes the icon to be reporting.

To assess readability, the interaction descriptions, when found, were cut and pasted into read-able.com to evaluate the Flesch-Kincaid grade level. Although this tool works best with higher word counts, it is still considered the best tool for readability analysis. Its use is so common that it is bundled with the most common word processing software including Microsoft Word and WordPerfect. Our target age for consumer health sites is grade 7, which is the average reading level as identified by the USDHHS. [19] Anything beyond the 9th grade reading level would be considered difficult per the USDHHS.

Results

Overall, seven Web sites were selected that met our inclusion criteria. Those sites were evaluated for completeness, accuracy, presentation, recommended action, and readability. Scientific evidence was excluded from our results, as this information was not included on any of the sites (see Table 1).

The interaction descriptions varied significantly across sites. Some sites indicated there was an interaction, but provided very little detail. Other sites would go into great detail, including describing the effect on drug metabolism via the particular CYP450 subclass. This level of detail in most cases would provide no value to the consumer and is likely intended for professionals.

The presentation styles also varied widely, with some sites making generous use of coloration and graphics, while others provided only text (see Table 2).

Discussion

This study sought to evaluate drug-CAM interaction Web sites based on completeness, accuracy, readability from the consumer perspective, and presentation. According to our evaluation criteria, the overall quality was fairly low.

None of the sites evaluated scored high on the combined criteria of completeness and accuracy. Only one of the sites had 100% coverage, although that site had a low accuracy rate of 50%. The other sites had lower completeness and accuracy scores. Two sites provided no severity information; therefore accuracy could not be evaluated.

The result of incomplete and inaccurate information on any given drug-CAM pair could be serious. The lack of interaction information could imply to the consumer that no interaction exists. There is also a risk when the severity is inaccurate, since patients may react differently depending on the level of interaction severity.

The best score achieved from a readability perspective indicated a reading level of approximately grade 11. The scores increased substantially from there, with the highest score indicating graduate level text. Therefore, most of the sites evaluated are written in a language that is inadequate for the majority of the population.

The presentation styles of these sites varied greatly, with some sites using no icons or coloration at all. Prior studies in healthcare and other industries provide several criteria for the presentation of information to consumers, such as simplified and uncluttered user interface, the use of coloration and icons, and minimal text. [17, 18]

None of the sites evaluated would pass HON certification, failing on multiple criteria, such as authority and attribution. The sites did not provide information on who researched the interactions or what studies or trials were used to determine the interaction and severity.

Prior studies show that the predictors of content reliability include the display of the HON logo, having an organization (.org) domain, and citing references. The absence of financial interest is also associated with content accuracy. [20, 21]

Scientific evidence was not included in any of the sites other than our reference standard. This may be acceptable for a consumer site, as many consumers would not understand the evidentiary support provided by scientific studies.

Limitations

This study had four main limitations. First, only seven interaction checkers were analyzed. Yet, we comprehensively searched the Web for eligible sites using several search terms and search engines. Several sites were excluded because they did not meet the definition of an interaction checker as defined for this study. To be considered, the consumer must have the ability to enter either the drug or CAM from the 10 drug-CAM pairs used in the study. They often had hard-coded lists of drug-CAM combinations, or simply provided a link to another site.

Second, the use of SEO in considering the sites is challenging, as this is something that changes continuously and affects a sites ranking in the search order. Some sites that appeared on page one early in our research may have moved beyond page two and consequently would not have been found at a later point in time.

Third, only ten drug-CAM combinations were used in the evaluation of the sites and all but one reported a major interaction in our reference standard. It may be helpful to include common CAM with moderate and minor interactions. In addition, the drugs used were not carefully considered to ensure that a comprehensive set of drug classes was included. Nevertheless, the drugs used in the study are frequently used for a set of prevalent chronic conditions. Therefore, drug-CAM interactions sites were expected to provide complete and accurate information on these drugs.

Finally, we utilized the Flesch-Kincaid readability assessment tool to determine the grade level for the interaction description. This tool works best with documents that have a higher number of words than is typical for an interaction description, so the reported reading age may be less accurate than expected. Nevertheless, Flesch-Kincaid is a widely used tool and has been previously applied to assess the readability of consumer health information. [19]

Future Work

A study involving more drug-CAM pairs would be valuable, including a representative sample of commonly used drugs in general.

While there is some guidance available for the presentation of consumer health information on Web sites, further studies could be conducted to determine the optimal presentation of drug-CAM interaction information to consumers to encourage communication with physicians and minimize unintended consequences.

Studies are needed to evaluate the impact of consumer health sites on the attitudes, knowledge, and behavior of healthcare consumers and whether these sites provide the intended value to the consumer.

Finally, a study focusing solely on the usability of these sites would be beneficial. There is no consistency across these sites as far as the entry of a drug name, CAM or both. Many sites use drug classes, which are often meaningless to consumers, or brand names where generics are more common these days due to insurance restrictions.

Conclusion

With the increasing use of complementary and alternative medicine by the US population, the availability of high quality online information on drug-CAM interactions is critical. However, this study shows that the overall quality of Web sites dedicated to providing drug-CAM interaction information is inadequate to the consumer.

Given the results of our study, we provide the following recommendations to Web site developers and consumers; 1) Careful consideration should be given to the ramifications of incomplete, inaccurate, and out of date information; 2) consumers should be educated on how to assess the reliability of health related content; 3) all Web sites containing drug-CAM information should warn consumers that they should consult their physician before starting or stopping any medications, including CAM.

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Table 1

Site Comparison to Reference Standard

Site	Complete ness	Accuracy	Recommended Action
CVS	80%	6/8 (75%)	Y
Dr. Oz	80%	N/A*	N
Medline Plus	50%	3/5 (60%)	Y
Drugs.com	60%	1/6 (17%)	Y
Vitamin Herb University	50%	N/A*	Y
Healthline.com	70%	5/7 (71%)	Y
Reference.medscape.com	100%	5/10 (50%)	N

* Unable to evaluate due to missing severity

Table 2

Presentation Style and Update frequency

Site	Search Style	Coloration and Graphics	Interaction Result Display	Last Update	Flesch-Kincaid Reading Level*
CVS	Type drug and supplement name	No	Bullet list with description and severity	9/4/01	N/A
Dr. Oz	Alphabetic list of supplements	No	Bullet list of drugs classes, no severity	Unknown	10.51
Medline Plus	Alphabetic list of supplements	No	List of drug classes and CYP450 substrates categorized by severity	07/14/12	23.55
Drugs.com	Type either drug or supplement, auto-suggest	Both	Detailed description, consumer or professional, severity presented in traffic sign icons	10/15/12	17.73
Vitamin Herb University	Select supplement from dropdown list	Both	"Caution" followed by interactions list by drug class, no severity	Unknown	17.46
Healthline.com	Type with auto-suggest or select from list, drug and supplement	Both	Severity, meter, coloration for specific drug-CAM pair	Unknown	14.12
Reference.medscape.com	Type with auto-suggest	Coloration	Severity colorized, short description for specific drug-CAM pair	Unknown	19.40

* Scores over 22 should generally be taken to mean graduate level text.

CHAPTER 5

UNDERSTANDING CANCER SURVIVOR'S INFORMATION NEEDS AND INFORMATION-SEEKING BEHAVIORS FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE FROM SHORT- TO LONG-TERM SURVIVAL: A MIXED-METHODS STUDY

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SURVEYS AND STUDIES

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Understanding cancer survivors' information needs and information-seeking behaviors for complementary and alternative medicine from short- to long-term survival: a mixed-methods study

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Objective: The research examined complementary and alternative medicine (CAM) information-seeking behaviors and preferences from short- to long-term cancer survival, including goals, motivations, and information sources.

Methods: A mixed-methods approach was used with cancer survivors from the "Assessment of Patients' Experience with Cancer Care" 2004 cohort. Data collection included a mail survey and phone interviews using the critical incident technique (CIT).

Results: Seventy survivors from the 2004 study responded to the survey, and eight participated in the CIT interviews. Quantitative results showed that CAM usage did not change significantly between 2004 and 2015. The following themes emerged from the CIT: families' and friends' provision of the initial introduction to a CAM, use of CAM to manage the emotional and psychological impact of cancer, utilization of trained CAM practitioners, and online resources as a prominent source for CAM information. The majority of participants expressed an interest in an online information-sharing portal for CAM.

Conclusion: Patients continue to use CAM well into long-term cancer survivorship. Finding trustworthy sources for information on CAM presents many challenges such as reliability of source, conflicting information on efficacy, and unknown interactions with conventional medications. Study participants expressed interest in an online portal to meet these needs through patient testimonials and linkage of claims to the scientific literature. Such a portal could also aid medical librarians and clinicians in locating and evaluating CAM information on behalf of patients.

See end of article for supplemental content.

INTRODUCTION

Complementary and alternative medicine (CAM) refers to health care systems and products that are not commonly used in conventional medicine [1]. CAM includes many modalities such as yoga, chiropractic, special diets, meditation, and biologically based therapies such as dietary supplements. The use of CAM therapies by cancer patients is well documented, with current usage rates as high as 50% in the United States [2–5]. Studies have suggested positive effects from the use of CAM in the management of the psychological and emotional impact of cancer [6, 7].

When faced with a cancer diagnosis, many patients seek further information on CAM as a means of understanding their options, for a sense of hope and control, and for alternative options when the prognosis is poor [8, 9]. In this process, patients often become frustrated with what they find, particularly when they receive conflicting messages

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pertaining to the efficacy of CAM treatments [8, 10, 11]. Authoritative information resources and tools are needed to help patients identify and understand CAM options.

In the absence of such resources, patients often rely on anecdotal evidence, or "social proof." Social proof is a consumer behavior where people will conform to the action of others. For example, in online shopping, social proof is often found in product reviews. Similarly, in CAM information-seeking, social proof could be found through patient testimonials [12]. Attitudes toward social proof are suggested in a recent study of CAM information seeking. One participant in that study stated, "I just kind of figured it would work well because it was a suggestion that I had heard from so many other people" [12].

To design CAM resources, it is necessary to understand the information-seeking behaviors of CAM consumers. Prior studies have focused on cross-sectional quantitative end points without considering long-term trends. One study examined the information-seeking roles of patients and caregivers [13]. The main source for CAM information was anecdotal through family and friends, with female family members playing a major role in steering male family members toward CAM use. This is not surprising, as studies have shown that women make up to 80% of the health care decisions for their families in the United States [14]. A Canadian study suggested that in many cases, patients would prefer to receive CAM information from trusted resources, such as their oncologists, but physicians were often not equipped to provide the necessary information [15].

Librarians have a professional interest in CAM information resources [16], which in part is fueled by patron requests for CAM-oriented information. In 2004, Gillaspy noted a sustained interest among consumers for information on CAM therapies [17]. In a survey of librarians, participants recorded an average comfort-level score of 3.2 (on a scale of 1–5) in responding to CAM-related information requests [18]. Professional resources supporting CAM information provision include databases [19] and website reviews [20], a study of student attitudes [21], other research published in library-focused journals, and a Medical Library Association CAM Special Interest Group. A Google search using the phrase "libguide complementary and alternative medicine" revealed that several libraries, in particular academic libraries, did provide some online guidance in locating CAM information. The outcomes of this study can further assist librarians by helping them better understand consumers' CAM information needs and information-seeking behavior and the types of resources that can serve them.

The goal of the present study was to investigate CAM information needs and information-seeking behaviors among a cohort of long-term cancer survivors. The authors employed a mixed-method approach that consisted of a survey and in-depth interviews with Flanagan's critical incident technique (CIT). The CIT is useful for addressing detailed questions around individuals' motivations and decision making by eliciting in-depth stories of events. The CIT accomplishes these goals by helping the interviewee recall significant experiences that were factors in making a health care decision [19, 20]. Specifically, we looked at whether CAM use changed over time, what patients' goals for CAM use were, where they found information, how they evaluated that information, and what their preferences were for a hypothetical CAM portal.

METHODS

Theoretical framework

Our study was guided by a theoretical framework composed of two theories: "Uses and Gratification Theory" (UGT) [21] and the "Health Belief Model" (HBM) [22]. These theories provided a template to guide research questions, questionnaire design, interview questions, and data analysis.

The UGT suggests that consumers seek specific mass media because they fulfill some utilitarian (uses) and emotional (gratifications) needs. The UGT provides a framework to assess the underlying motivations for consumers to seek information via the Internet or other mass media. This theory proposes that people utilize media that fulfill their needs, which fosters gratification derived from information seeking [23]. All categories of the UGT needs were applicable in our study: (1) cognitive: the desire to be informed and educated; (2) affective: satisfaction of emotional needs, such as by commiserating with another cancer patient; (3) personal integrative: self-esteem needs are met by gaining credibility such as supporting and

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advising other patients; (4) social integrative: the need to socialize, share experiences, and gain support from others; and (5) tension free: the use of mass media to escape from perceived reality. The UGT guided the investigation of the types of resources that would be most valuable to patients in their information-seeking processes.

The HBM examines how perceptions can be used to explain certain health behaviors [22]. Several constructs that were derived from this theory guided the investigation of the various events that triggered CAM information seeking and use. These constructs included (1) perceived threat: belief of the chances of succumbing to their disease or treatment side-effects; (2) perceived benefit: the belief in the efficacy of a treatment; and (3) perceived barriers: concerns about the impediments to successful treatment. For example, an individual's perceived threat could motivate a need to understand his or her options to respond to clinical events such as initial diagnosis, recurrence, and adverse effects of treatments. The construct of perceived benefit may play a role in the decision to use CAM, especially when anecdotal evidence suggests that other patients have experienced positive outcomes in the use of CAM.

Participants

Participants were recruited from those enrolled in the 2004 "Assessment of Patients' Experience with Cancer Care" (APECC) study. APECC was population-based study that used telephone screening and mailed questionnaires to enroll 623 cancer survivors to assess their experiences with follow-up care [24]. Therefore, this cohort provided the opportunity to examine information-seeking patterns over a long-term cancer management experience.

In November 2014, 82% (510/623) of the original APECC study participants were alive. The authors sent study surveys to all these individuals and asked if they were interested in participating in the CIT interviews. Packets were mailed to potential participants between January and May of 2015.

The study was approved by University of Utah Institutional Review Board (IRB) #00068256 and the California Committee for the Protection of Human Subjects (CPHS) IRB #13-10-1383.

Study design

Our mixed-methods approach consisted of a survey followed by CIT phone interviews of a subset of respondents. This approach combines the power of numbers and the power of stories [25, 26]. A convergent design was used where the quantitative and qualitative data collections were done sequentially, and the results were integrated after data analysis. The qualitative results provided a more detailed understanding of both significant and nonsignificant results reported by the survey.

Survey

The CAM section from the original APECC survey was utilized in the current study to compare CAM usage over time (1994 to 2015). Additional sections were added to assess Internet use, details on information sources for CAM, and interest in various functionalities possible in an online information sharing portal. Some of the new questions were formed based on the UGT and HBM (Table 1). The complete survey and phone interview script are available in online supplemental Appendixes A and B.

Phone interviews

The CIT [19] was used to elicit in-depth stories related to CAM information seeking that patients considered to be critical in their cancer management. A critical incident is any event in a cancer trajectory that motivates a need to search for alternatives. This technique is also tied to the HBM, in particular via the construct of perceived threat or perceived severity as well as all categories of the UGT (Table 2).

The CIT interviews consisted of five steps: (1) incident identification, (2) incident overview, (3) timeline, (4) deepening, and (5) what-if scenarios. Incident identification asked the participants to recall a specific CAM therapy that they believed was salient in meeting their wellness goals at the point when CAM was first considered. Next, participants provided an overview of their information-seeking experience. After the overview, a timeline was created, and major events such as diagnosis, recurrence, and cancer progression were identified as potential triggering events.

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Table 1 Theory, constructs, and sample survey questions

Theory	Construct	Sample survey question
Uses and Gratification Theory (UGT)	Cognitive Affective Social integrative Personal integrative Tension free	If we designed an online tool for cancer survivors to share CAM information such as CAMs used, good and bad outcomes, and the ability for patients with the same cancer to speak directly with one another, how useful would you find this tool? Would this satisfy your information needs?
		Please rate each portal function by interest:
	Affective	Find others with similar cancer
	Social integrative	Read testimonies of patients with similar cancer
	Personal integrative	Participate in open discussions about CAM use
	Cognitive	Generate reports for shared decision making
Health Belief Model (HBM)	Perceived benefit	What are the major reasons you used any of these [CAM] therapies?
		For which of these CAM therapies did you consult a CAM practitioner (e.g., chiropractor, naturopathic doctor)?
	Perceived barriers	Did you discuss your use of these CAM therapies with your follow-up practitioner?

Table 2 Theories, constructs, and sample phone interview questions

Theory	Construct or category	Sample phone interview question
UGT	Cognitive Affective Personal integrative Social integrative Tension free	Consider the tools available in social networking today such as communicating person-to-person, blogging, sharing links, and sending attachments, etc. What features of a site like this would you find essential for meeting your CAM information needs?
HBM	Perceived threat Perceived severity Perceived benefit	What caused you to seek out information on this particular product?
UGT	Cognitive	How did you assess the effectiveness and safety of a CAM?
UGT	Tension free	Did you have any frustrations or concerns with the information-seeking process?

The description of a cancer timeline was intended to help participants recall specific events that might have caused them to seek CAM options [27]. By defining the timeline from diagnosis to the time of the interview (i.e., into long-term survivorship), the interviewees were better able to recall specific behaviors at the various points in the trajectory. The timeline was followed by a deepening phase, in which participants were asked to provide details on each event of the timeline. Participants also were asked about details such as how they were initially introduced to a CAM, how they evaluated its effectiveness, and what, if any, frustrations or concerns they experienced with the information-seeking process. The interview ended with the discussion of "what-if" scenarios related to a hypothetical CAM information-sharing portal in order to identify which functionalities (e.g., forums, testimonials) would be useful, as well as any concerns about the use of such a tool.

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Data analysis

Quantitative analysis. Descriptive statistics were calculated for demographics and CAM use for 2015 respondents and nonrespondents. Chi-square (McNemar's test) was used to determine if there were significant differences where subjects were paired, and Pearson chi-square was used for unpaired subjects. Fisher's exact test was used for unpaired groups that did not meet the assumptions of chi-square tests. Finally, Spearman's rank correlation was used to determine if there was an association between participant demographics and interest in the functionalities available in an online CAM portal. Statistical analyses were done using Stata 14.0 and RStudio 0.99.447.

Qualitative analysis. The CIT interviews were recorded, transcribed, and independently analyzed by two coders using thematic analysis [28–30]. Each transcript was coded and analyzed using inductive coding and constant comparison. Emergent codes were independently entered into a codebook in Atlas.ti, and constant comparison was used to compare early codes with those from subsequent interviews. Throughout the process, new codes were identified and prior codes were refined and organized into higher level concepts, eventually leading to salient themes.

RESULTS

Overview

Seventy subjects (13.7%) responded to the survey. Four surveys were returned uncompleted, and 42 were returned undeliverable. Twenty-two (31.4%) of the 70 subjects returning the survey also returned a signed consent form for the phone interview. Of these, 8 (11.4%) were interviewed, 2 did not answer or return the calls, and the remaining 12 either did not seek CAM information or exclusively turned to prayer.

Demographics

Participant demographics are summarized in Table 3. The mean age of the 2015 study respondents was 70.1 years, and the mean age of nonrespondents was 73.1 years. Respondents were more educated than nonrespondents, with 90% having at least some college as opposed to 80.1% of nonrespondents. The 2015 respondents also had higher income levels than nonrespondents.

Quantitative results

Complementary and alternative medicine (CAM) use. We examined the overall use of CAM, changes in the specific CAM modalities used, and use of CAM practitioners by respondents between 2004 and 2015. Although there was no significant change in use of the various CAM modalities, there was a significant increase in use of CAM practitioners. Out of the seventy respondents to the 2015 survey, sixty-one also provided this information in the 2004 study (Table 4).

CAM information sharing portal. Figure 1 shows participants' interest in web portal functionality for helping meet CAM information needs. More than half of the study population indicated interest in each option, with the exception of participating in forums.

Figure 1 Interest in online portal functionality

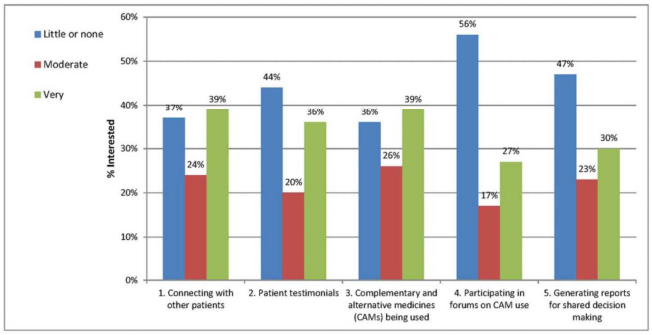

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Table 3 2015 Demographics of respondents and nonrespondents

Demographic	2015 Respondents		2015 Nonrespondents		*p*-value
Age (Years)					
Younger than 50	3	(4.3%)	27	(6.1%)	
50–64	16	(22.9%)	85	(19.3%)	
65–74	27	(38.6%)	126	(28.6%)	
75 or older	24	(34.3%)	202	(45.9%)	
Age total	70	(100.0%)	440	(100.0%)	0.209
Education level					
High school or less	7	(10.0%)	88	(20.0%)	
Some college/vocational school	15	(21.4%)	145	(33.0%)	
College graduate	20	(28.6%)	87	(19.8%)	
Some graduate school/graduate	28	(40.0%)	120	(27.3%)	
Education total	70	(100.0%)	440	(100.0%)	0.009
Gender					
Male	52	(74.3%)	236	(53.6%)	
Female	18	(25.7%)	204	(46.4%)	
Gender total	70	(100.0%)	440	(100.0%)	0.001
Race					
Hispanic	6	(8.6%)	34	(7.7%)	
White	56	(80.0%)	323	(73.4%)	
Asian	6	(8.6%)	58	(13.2%)	
Other	2	(2.9%)	25	(5.7%)	
Race total	70	(100.0%)	440	(100.0%)	0.57
Income level					
Less than $20,000	3	(4.5%)	52	(12.8%)	
$20,000–$39,999	2	(3.0%)	62	(15.2%)	
$40,000–$59,999	12	(18.2%)	60	(14.7%)	
$60,000–$74,999	5	(7.6%)	62	(15.2%)	
$75,000–$99,999	14	(21.2%)	58	(14.3%)	
$100,000–$119,999	12	(18.2%)	37	(9.1%)	
$120,00 or more	18	(27.3%)	76	(18.7%)	
Income total	66	(100.0%)	407	(100.0%)	0.001

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Table 4 CAM usage patterns for those reporting usage in both 2004 and 2015 surveys (n=61)

CAM	2004		2015		*p*-value
	n	(%)	n	(%)	
Special diets	16	(26.2%)	18	(29.5%)	0.802
Movement therapies	10	(16.4%)	14	(23.0%)	0.299
Supplementation	8	(13.1%)	6	(9.8%)	0.724
Homeopathy	2	(3.3%)	1	(1.6%)	>0.99
Mind and body	10	(16.4%)	8	(13.1%)	0.752
Oriental therapies	4	(6.6%)	5	(8.2%)	>0.99
Self help	4	(6.6%)	6	(9.8%)	0.752
Psych	4	(6.6%)	6	(9.8%)	0.724
Faith healing	7	(11.5%)	4	(6.6%)	0.505
Prayer	28	(45.9%)	22	(36.1%)	0.181
Overall CAM use	37	(60.7%)	36	(59.0%)	>0.99
CAM use excluding prayer	35	(57.4%)	29	(47.5%)	0.146
Used CAM practitioners	6	(9.8%)	16	(26.2%)	0.004

Table 5 Spearman correlations between demographics and interest in portal functionality (n=55)

	Connecting with others	Testimonials	CAMs being used	Participating in forums	Generating reports
Age	–0.419*	–0.399*	–0.439*	–0.264	–0.379*
Education	–0.034	0.022	0.109	0.002	0.068
Income	0.099	0.036	0.169	0.064	0.152
Gender	0.380*	0.341*	0.276*	0.227	0.210

55/70 completed this portion of the survey.

* $p<0.05$

There were statistically significant associations for both gender and age with the following portal functions: connecting with other patients, testimonials, and CAMs being used. Women and younger people expressed higher interest in those CAM portal functions. Income and education were not significantly correlated with interest in CAM portal functionality (Table 5).

Qualitative results: critical incident interviews

Thematic analysis. The thematic analysis resulted in the following themes.

1. *Lack of emotional and psychological support during treatment*. The study's participants were satisfied with their care for the direct treatment of their cancer but felt alone in dealing with the emotional and psychological impact.

> You go to very dark places when you get sick. I hit my breaking point many years ago, then I started feeling like I was going to give up. I got back into the program of yoga and deep breathing…I tell people you have to build yourself a little tool chest. Those tools can be group meetings, mentoring calls, yoga, it can be this, all these little things that keep you busy promoting your wellness. I really like that metaphor of my little tool kit, and I pull it out when I feel like this.

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2. *Utilization of trained CAM practitioners.* Participants used varying forms of CAM that required the use of trained practitioners.

I went to a Naturopath and got some of the candida in my body out and we started to clean me up from all the toxins I was under from eating the normal American diet, the wrong foods and that kind of stuff, over the years.

3. *Online resources as a prominent source for CAM information.* Participants discussed how their preferred information sources during their treatment had changed. Participants utilizing printed materials now used online resources. Participants who still relied on friends and family used the Internet for additional evidence of efficacy as well as possible interactions. A participant was asked if she were diagnosed with a serious illness today, where would she turn first for treatment options.

Online! Totally. I'm always looking at online things and trying to make connections. I'm just kind of curious because I'm a Chemist so I have a lot of curiosity about the science behind it.

4. *Friends and family as sources.* Participants indicated that their initial introduction to CAM was often via family or friends.

[A]t that point, I was kind of letting my Mom, you know, I kind of put my trust in her and let her make those decisions. She was the one that had access to information.

Interest in functionality for an online information-sharing portal. Study participants rated their interest in functionality that could be available through an online CAM information sharing portal. The functionality discussed includes the following.

1. *Connection with other patients.* Participants placed a strong emphasis on the need to connect with others who truly understand what they are going through.

There was a point where I told my Oncologist that I was depressed, and his answer was, "well, we'll prescribe you some Prozac",...but I didn't want a drug, I didn't want a pill, I don't want Prozac. I wanted to just be able to communicate. I'm depressed because I don't know what I'm going through, I don't understand what I'm going through, there's no one I know that can relate to what I'm going through, and it's like everything is unknown, there's no outlet, and that's what I was trying to tell him.

2. *Patient testimonials.* Study participants sought to hear about what treatment approaches others have tried and the outcomes.

That's really great. If you were diagnosed with something that gave you six months to live, and you talked to someone that said "I've tried this", they said I only had six months to live, but I'm talking to you several years later, how much better is that going to make you feel, just because it increases your chance of survival.

3. *Participation in forums.* Interviewees seemed to have a more positive picture about participation in forums compared to the survey findings.

I value my anonymity, I wouldn't want people to know who I was, but at the same time, I would like to share my story. You know, if it would be of benefit to other people, and I would like to know what other people have to say, but I don't necessarily need to know who people are.

4. *Reports for shared decision making.* Although no strong feelings were expressed about this functionality, phone interviewees expressed confidence in their physicians. One participant emphasized she would not do anything that her physician was not aware of and approved.

Yeah, and my gut tells me he wouldn't just say don't do that, he would tell me why he thinks that. I'm not going to just go out and try something without talking to my doctors first, if I think it's going to help me, or give me more energy, or boost my blood levels so they aren't just at normal or below normal all the time, I would definitely have to talk to someone first. I would definitely look at the web site, see what's going on, make some notes reminding me to talk to my doctors the next time I call them, hey, have you heard anything about this? I would definitely have to have the conversation with my doctors first.

DISCUSSION

To our knowledge, this is the first study to investigate cancer survivors' CAM information needs and information-seeking behaviors using a mixed-methods approach. This study has multiple strengths, including recruitment from an existing cohort of cancer survivors and a theory-guided, mixed-methods approach. Utilizing an existing cohort from the 2004 APECC study facilitated comparison over time with previously collected data on CAM usage and information sources.

Overall CAM usage was high (60% reported using CAM), with no significant difference between

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2004 and 2015. The primary motivation for CAM use was to manage the emotional and psychological impact of cancer and its treatments, and participants were usually left to seek options from outside sources [8]. More than 50% of the surveyed long-term survivors expressed interest in an online information sharing portal for CAM. The phone interviews indicated that use of anecdotal sources is still prevalent, and study subjects go online to find evidence from the scientific literature, seek social networks for further information on the use of a CAM, and search consumer health information sites such as WebMD®.

While assessing the reasons that survivors sought CAM options, we found that the primary motivators were the threat of treatment and posttreatment recovery. These motivations were consistent with the perceived threat construct in the HBM as well as the perceived benefit, which was consistent with a similar study of patients with Lyme disease [31]. Patients' psychological distress resulted in searches for options and increased CAM use. CAM use has been shown to provide patients with a sense of hope and control and may be motivated by multiple categories of the UGT, including cognitive, affective, and tension free.

Of the more than 50% expressing interest in an online information sharing portal for CAM, women and younger participants expressed greater interest. The role of women in information-seeking and health care decision making for family members is well documented [14, 15]. The phone interviews documented similar behaviors amongst women and men. Two of the eight interviewees indicated that their CAM usage was driven primarily by women in their lives; in one case, the mother, and in another, a wife.

Fewer than 50% of respondents expressed interest in discussion forums. The qualitative results suggested concerns over privacy. Multiple phone interviewees said they would actively participate in forums if participation was anonymous.

Similar to a previous study, we found that there was a large gap in cancer patients' needs in both dealing with the psychological and emotional aspects of the diagnosis and treatments, as well as recovering strength and overall health after treatment. In a previous study, Kent et al. found "a notable proportion of survivors of leukemia, bladder, and colorectal cancer reported symptom bother and unmet supportive care needs months or years beyond their cancer diagnosis" [32], which might have resulted in ongoing CAM needs across the cancer continuum.

Community and medical libraries might use findings from this study to guide how they provide resources and services to patrons with CAM information needs. First, libraries can help patients to evaluate evidence-based resources through criteria such as the Health on the Net (HON) Code. Second, librarians can educate patients on how to maintain privacy and anonymity while using online forums. Finally, a library's website can provide a starting point to assist with the aforementioned services as well as others related to CAM information. These efforts could be expanded to develop an online CAM portal guided by the results of the current study.

Several portals address some of the consumer needs exposed in this paper. Life Extension is a supplement company that links claims of efficacy to the scientific literature. Natural Medicines Comprehensive Database provides information on the efficacy of various CAM modalities, with links to supporting literature. A third resource, Patients Like Me, is the only portal that supports patient input. Overall, the results of this study could be used to improve these portals to meet consumer needs for CAM.

This study has several implications for future research. Participants in our study suggested health information portals would be particularly valuable if anecdotal claims were linked to the scientific literature as further support of the efficacy and safety of a CAM treatment. The lack of significant changes in CAM usage patterns many years into survivorship poses interesting questions for follow-up studies on why long-term survivors continue to use CAM at a high rate. Although one such study exists, it focuses on mind-body therapies and reports a decline in use in long-term survivorship, which is inconsistent with our findings [33]. A suggested future study could assess issues pertaining to cancer survivorship and what new CAMs patients use to address treatment-related issues such as radiation damage, nerve damage, and mood disorders.

This study has several limitations. First, the respondents to the current study were more highly educated and were from a higher income bracket. This might indicate higher health literacy as well as

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greater access to web-based resources. Second, the survey had a small response rate (13.7%), introducing selection bias. Third, the original sample was drawn from the Greater Bay Area Cancer Registry, a population-based registry that contributes to the SEER program. As documented by Arora and colleagues [24], compared with the eligible nonrespondents, respondents were more highly educated, had a higher income level, and were mostly male. Finally, the CAM information-seeking critical incidents often occurred several years ago, compromising the participants' recall of details. Given the study's limitations, the findings' generalizability to the full US cancer survivor population cannot be assessed. However, the current study's results contribute to a growing CAM literature and provide additional data to generate future research.

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SUPPLEMENTAL FILES

- **Appendix A:** Survey
- **Appendix B:** Phone interview script

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CHAPTER 6

GENERATING VOCABULARIES FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE

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6.1 Abstract

6.1.1 Objective

There is a significant consumer demand for complementary and alternative medicine (CAM) information for the treatment and prevention of chronic diseases. A controlled vocabulary for CAM could help meet those needs by facilitating information retrieval from the published literature. The purpose of this study is to design and evaluate two methods to semi-automatically extract CAM treatment-related semantic predications from the biomedical literature.

6.1.2 Methods

Predications were retrieved from SemMedDB, a database of semantic predications extracted from article abstracts available in Medline. The first method retrieved predications from any Medline citation ("all Medline"), while the second method ("sound studies") only retrieved predications from scientifically sound clinical studies. Filtering criteria were applied to identify the predications focusing on the treatment and prevention of medical disorders using various CAM modalities. The disorders were extracted for each CAM and ranked by occurrence. A reference vocabulary was developed to evaluate the performance of each method according to precision and recall of the top 100 ranked concepts as well as average precision and recall.

6.1.3 Results

The difference between *all Medline* and *sound studies* in terms of median precision for the top 100 concepts ranked by occurrence was significant (21.0% vs.

27.0%, p<.001). The *sound studies* method had significantly higher precision (7.0% vs. 11.5%, p<.001) and the *all Medline* had significantly higher recall (37.1% vs. 25.6%, p<.001).

6.1.4 Conclusion

The *sound studies* method may be useful for extracting treatment-related predications from the biomedical literature for the highest ranked concepts. Additional work is needed to improve the algorithm as well as identify and report shortcomings for future enhancements of the tools used to populate SemMedDB.

6.2 Introduction

Complementary and alternative medicine (CAM) use is ubiquitous, with an estimated 30-50% of patients utilizing some form of CAM in their healthcare [1]. Visits to CAM providers exceed those to primary care physicians, with out-of-pocket expenses exceeding $30 billion [2]. In spite of this high use, there are no reliable, easily accessible resources for consumers to obtain and evaluate CAM for specific medical conditions. Consumers most often seek CAM information on treatment options, side effects, and interactions with conventional treatments [3]. The preferred source for this information is either their physician [4] or the Internet [5]. In the absence of resources to meet their information needs, consumers are exposed to many risks in CAM use [6-8] and friends and family remain a primary source for CAM information [3, 4, 9].

Health consumers could benefit from reliable, complete, and accurate online resources on CAM that are linked to supporting evidence from the scientific literature. A controlled vocabulary is a necessary building block for any information retrieval system

in the biomedical domain. Although standard vocabularies (e.g., SNOMED CT) contain concepts for the various CAM modalities, a more specific vocabulary is necessary with relationships between medical disorders and CAM modalities, such as “massage” and “pain”, “coenzyme Q10” and “heart disease”, and “guided imagery” and “anxiety”. To date, no such targeted vocabularies exist in the CAM domain. Building these vocabularies manually is very labor-intensive and therefore cost-prohibitive. In a previous study, we proposed methods for generating disease-specific treatment vocabularies by extracting disease-treatment predications from the biomedical literature [10]. In the present study, we adapt those approaches to assist in the development of CAM treatment vocabularies by extracting predications between CAMs and diseases, symptoms, or behaviors for which a CAM has been studied.

6.3 Background

6.3.1 CAM Information Needs

Resources for information on CAM are sparse and unreliable. The quality of the information can be poor and consumers find much of the information difficult to comprehend [11]. Consumers are often presented with information that is incomplete and inaccurate, potentially leading them to incorrect conclusions on safety and efficacy [12]. In many cases, consumers would prefer to receive CAM information from their physician, but they find that physicians know little about CAM or are not supportive of its use [3]. Consumers often turn to the Internet for a variety of healthcare-related information including signs, symptoms, and treatment options. This approach to information seeking often leads to conflict and anxiety [13].

In oncology, these information needs were most pronounced immediately before and after treatments as these periods of the treatment trajectory raise the greatest concerns about treatment side effects. Patients are also warned about CAM use during treatment by their physicians [14]. Patients' motivations in seeking CAM information vary and run the gamut from recovering from treatments to curing their disease [15]. As the use of the Internet for healthcare information-seeking continues to increase and with tremendous variability in health literacy, great care must be taken to ensure that tools designed to lead consumers to information on CAM return the most pertinent results possible [16]. Results must be focused, reduce complexity, and minimize noise to avoid confusion for consumers.

Although CAM information is not as comprehensive as in allopathic medicine, there is significant and continually increasing information available. The challenge is finding the information when it is needed and in a timely manner. This presents a significant challenge for healthcare practitioners, and an even greater challenge for consumers who are not even aware of the resources available, let alone how to form the optimal search.

6.3.2 Controlled Vocabularies as the Foundation for Biomedical Applications

Controlled vocabularies have existed for centuries and allow for the standardization of terms and the formalization of the relationships between those terms [17, 18]. Many such vocabularies already exist and provide standard terms and unique identifiers for those terms in the CAM space, for example, Systematized Nomenclature of Medicine – Clinical Terms (SNOMED CT) and Consumer Health Vocabulary (CHV).

The domain-specific subset of CAM terms extracted from existing vocabularies can be structured in such a way as to optimize information retrieval in consumer facing applications and aid in interoperability and reuse of the resulting vocabulary.

Building a controlled vocabulary is a challenging and labor-intensive effort. A prior study in building a reference standard from the biomedical literature resulted in 100 man-hours from medical experts for annotation alone for only three diseases. This did not include other necessary tasks such as identifying and preparing the appropriate documents, preparing the annotation guidelines, training annotators, and mapping the concepts to the Unified Medical Language System (UMLS) [10, 19].

A controlled vocabulary could be useful in the development of information retrieval tools for CAM, particularly for consumers for whom linkage to the scientific literature is important [20]. This vocabulary must enable information retrieval algorithms to retrieve CAMs that treat a certain condition and vice-versa, for example "what CAM treats chronic fatigue?" or "what conditions are treated by acupuncture?"

6.3.3 Semantic Medline Database

The literature available in the biomedical domain is vast and finding relationships that can be used to form disease-treatment vocabularies can be daunting. One solution to this problem is to use the Semantic Medline Database (SemMedDB), a repository of semantic predications that may serve as the basis for vocabularies in any clinical domain [21]. SemMedDB contains predications regularly extracted from PubMed citations using SemRep, a natural language processing tool that extracts semantic predications using underspecified syntactic analysis and structured domain knowledge from the UMLS [22,

23]. The predications are stored as subject-predicate-object triplets with links to the sentences from which they were derived in the biomedical citations. The subject and object elements correspond to UMLS concepts, while the predicate is the semantic relation between two concepts and correspond to UMLS Semantic Network relations. For example, "coenzyme q10 TREATS heart failure " is a semantic predication where the subject is "coenzyme q10", the predicate is "TREATS", and the object is "heart failure." This predication was extracted from the sentence "nearly two thirds of a series of 40 patients in severe heart failure (classes iii and iv) treated with coq10, 100 mg daily, in an open, controlled design showed subjective and objective improvement."

SemRep is able to extract 30 predicate types relating primarily to clinical medicine [24]. In SemMedDB, the subject and object concepts are categorized according to one or more UMLS semantic types (e.g., *sign or symptom*, *disease or syndrome*, *therapeutic or preventive procedure*), which can be used to filter predications based on an area of interest.

6.3.4 PubMed Clinical Query Filters

Another resource available for identifying relevant treatment-related studies is PubMed's Clinical Query filters, which can be used to retrieve scientifically sound clinical studies [25]. Filters are available with focus on specific topics (e.g., treatment, diagnosis, etiology) and can be tuned for precision (*narrow* filter) or recall (*broad* filter). Studies on the sensitivity and specificity of each option reported the *broad treatment* filter as having a recall of 99% and precision of 10%, whereas the *narrow treatment* filter resulted in a recall of 93% and a precision of 54% [26]. PMCQ attempts to narrow search

results to stronger clinical studies.

6.3.5 Reference Standard Resources

Two resources exist that provide evidence-based, expert-curated information on the safety and efficacy of CAMs for the treatment of disease: the Natural Medicines Comprehensive Database (NMCD) and Life Extension (LE). NMCD is recognized as the gold standard for evidence-based information on CAM effectiveness, safety, and interactions with conventional treatments. LE contains over 120 evidence-based protocols to combat disease associated with aging.

6.4 Methods

This study method consisted of the following steps: 1) development of a reference standard; 2) development of two predication retrieval methods; and 3) performance of an experiment to compare the performance of the two methods against the reference standard. The method was adapted from the approach proposed by Wang et al. for the construction of disease-specific vocabularies for allopathic treatments [10]. We chose 20 biologically-based CAMs to constrain the study scope and 3 mind-body therapies to test the generalization of the methods across CAM modalities.

6.4.1 Reference Standard Development

6.4.1.1 Manual extraction of CAM treatment statements from authoritative sources

Utilizing the methods described by Wang et al. [19], we built a reference standard for development and evaluation of our methods using two existing evidence-based, expert-curated sources for CAM. Unlike the allopathic domain, evidence-based resources

for CAM are limited. Treatment-related statements were extracted from NMCD and LE for the CAMs being investigated in this study. Disorder concepts were extracted from the text during the annotation process.

The treatment-related information was independently annotated by two co-authors, LS and MJ, using a predetermined set of annotation guidelines. Multiple practice sessions were conducted utilizing a sample set of documents. The documents were annotated using eHOST [27], an open source annotation tool. eHOST provides support for calculating inter-annotator agreement (IAA). The degree of IAA was calculated according to the F-measure, using the annotations from one annotator as the gold standard and the other as the subject [28]. The two annotators worked independently on the same set of documents until the IAA reached almost perfect agreement (>.8), at which point the remaining annotations were completed by one annotator [LS]. Any discrepancies in the annotation process were resolved through consensus. The resulting annotations were extracted from the eHOST files and mapped to UMLS concepts in order to enable comparison with CAM treatment-related predications pulled from SemMedDB.

6.4.1.2 Idenitifcation of Relevant Semantic Types for Annotated Medical Disorders

In order to map the annotated disorders to the UMLS, we conducted a manual analysis to determine the appropriate semantic types for the medical disorders. We started with all semantic groups, per prior studies [10, 29]. Semantic groups categorize the semantic types, but all semantic types within a group are not always appropriate. The *procedures* semantic group is a good example, where only the semantic type *therapeutic or preventive procedure* is needed for mind-body therapies such as meditation. Examples

of other semantic types include *disease or syndrome*, *sign or symptom*, *pathologic function*, and *finding*. Because these semantic types would also be used to constrain the results of the SemMedDB queries, we used SemMedDB to analyze the semantic types of the object terms (medical disorders) returned in treatment-related predications for the CAMs in this study.

Several methods were used to determine the semantic type list for the medical disorders. First, the semantic groups were examined to exclude those that were unlikely to appear in the object term for treatment-related predications. These included *genes and molecular sequences, phenomena, occupations, concepts and ideas, devices, objects, geographic areas,* and *organizations.* Next, a random selection of disorders annotated from the reference standard were used to search the UMLS for the semantic types of those terms. SemMedDB was then used to complete the analysis by searching with the appropriate CUIs for the subject term for each CAM and the treatment-related predicates list with no semantic type constraints on the object terms. The semantic types of the object terms were noted and compared to the current version of the semantic type list to decrease the likelihood that relevant semantic types were excluded.

The final set of relevant semantic types used in the subsequent steps of the approach are listed in Table 6.1. The semantic types followed one of two potential semantic schemas; <CAM treatment> TREATS|NEG_TREATS|AFFECTS|NEG_AFFECTS|PREVENTS|NEG_PREVENTS|ADMINISTERED_TO|NEG_ADMINISTERED_TO <Disorder|Physiology|Anatomy|Living being> or <CAM treatment> COMPARED_WITH|HIGHER_THAN|LOWER_THAN <Chemicals &

Drugs|Procedures>.

6.4.1.3 Mapping of Medical Disorders to UMLS Concepts

To maximize accuracy, a multipass approach was taken in mapping the disorder concepts from the reference standard to UMLS concepts (Figure 6.1). Initially, an 'exact' match was attempted using the UMLS Terminology Services (UTS). If UMLS concepts were returned, the semantic types of those concepts were examined to determine if they matched any of the predetermined semantic types for disorders. Concepts that did not belong to a relevant semantic type were discarded ("weeding"). An example of a concept that was discarded is *depression scale*, with a semantic type of *intellectual product*. If an exact match with a relevant semantic type was found, we proceeded to the next disorder. The goal was to avoid including concepts that were clearly not represented in the reference standard to optimize algorithm precision. For example, for the annotated sentence "coenzyme q10 has been found to be effective in the treatment of breast cancer", an exact match was found for the concept *breast cancer,* with relevant semantic type *neoplastic process*. If a 'word' match was conducted, 650 additional concepts with a relevant semantic type would be returned, but representing disorders outside the scope of the annotated sentence. Examples include *bilateral breast cancer* and *carcinoma breast stage IV,* which are specific stages of breast cancer that were not specified in the reference standard.

If no concepts remained after weeding, we proceeded to a second call to UTS using a 'word' match. Once again, only the concepts with relevant semantic types were selected. After the second pass, if no concepts were identified for the disorder, we

proceeded to manual mapping. The most common reasons for terms not mapping include precoordination of diseases and body location (e.g., “osteoarthritis of the hip or knee”) and patient population groups (e.g., “postmenopausal women”). The final output of the multipass process was a list of disorder terms. Each term was associated with one or more UMLS concepts along with the concepts’ CUIs. Those terms not mapped to UMLS concepts were compiled and could be sent to pertinent vocabularies, such as SNOMED-CT and Consumer Health Vocabulary, as suggested inclusions. All UMLS queries used version 2016Ab and the UTS REST API for Perl.

6.4.2 Predication Retrieval

The process to retrieve CAM treatment-related predicates from SemMedDB consisted of the following steps (Figure 6.2): 1) identification of pertinent UMLS concepts for CAM terms; 2) retrieval of scientifically sound clinical studies using PubMed’s Clinical Query filters (PMCQ, only for the *sound studies* method); 3) retrieval of relevant treatment predications from SemMedDB; and 4) ranking of medical disorders by occurrence.

6.4.3 Identification of UMLS Concepts for CAM Terms

For the CAM terms in the reference standard, the *Chemical and Drugs* semantic group was used as a starting point [10, 30] for the biologically-based CAMs, as well as one semantic type from the *Therapeutic or Preventive Procedures* semantic group to cover mind-body therapies such as *acupuncture*. The final list of relevant CAM semantic types, along with an example of CAMs within each semantic type, can be found in Table 6.2. These semantic types were then used to map the CAM terms to UMLS concepts

using SNOMED CT as a comprehensive vocabulary and Consumer Health Vocabulary as a vocabulary to capture layman's terms. We used the UTS 'word' match to retrieve potentially relevant CAM concepts and then excluded concepts that did not belong to a relevant semantic type. An example of a nonrelevant concept for acupuncture is *Acupuncture unit, home-use*, with a semantic type of *medical device*. The output of the above process was a list of CAMs associated with one or more matching UMLS concepts.

6.4.4 Retrieval of Scientifically Sound Clinical Studies Using PubMed's Clinical Query Filters

One variation of our approach (*sound studies*) consisted of constraining predication retrieval to those that were extracted from scientifically sound clinical studies in Medline. To accomplish this, we searched PubMed for scientifically sound clinical studies on treatment using PubMed's clinical query filters (treatment narrow and systematic review filters) [26]. We further limited our search strategy to studies in humans and published in English. The PubMed IDs of the retrieved citations were then used to further constrain the predication query described in Step 3.2.3.

6.4.5 Retrieval of Relevant Treatment Predications from SemMedDB

For each CAM of interest, we queried SemMedDB matching the CAM CUIs to the predication subject. We also constrained the query to a set of relevant treatment-related predicates, to the set of disorder semantic types described in Step 3.1, and to "novel" predication objects. The novelty flag in SemMedDB identifies uninformative arguments through the hierarchical structure of the Metathesaurus [29]. For the *sound*

studies method, we further constrained the query to predications extracted from scientifically sound studies as described in Section 3.2.2. The output contained the retrieved predications as well as the source sentences from which predications were extracted using SemRep. The version of SemMedDB used for these queries included citations published through June 30, 2017. The SemMedDB SQL query can be seen in Figure 6.3.

6.4.6 Ranking of Medical Disorders by Occurrence

CAMs that have been mentioned more often in the context of a specific disease across multiple studies may be more likely to be relevant treatments for a given disease. Therefore, we used the simple frequency of citations with a given CAM-disease relation to rank disease concepts for a given CAM. Wang et al. compared this method with four other approaches (i.e., interest, occurrence, degree centrality, and weighted degree centrality), but found no significant difference among the four methods [31]. Therefore, we opted to use the simplest approach.

6.4.7 Design of the Experiment to Compare the Two Extraction Methods

Our goal was to test the null hypotheses that a) there is no difference in precision of the top 100 ranked concepts between the two methods and b) there is no difference in overall precision and recall between the *all Medline* and *sound studies* methods.

The primary outcome measure was precision at k (k=100) for all 23 CAMs. Secondary outcomes were overall precision, recall, and precision at varying levels of k. Precision at k represented the ratio of extracted disorder concepts that were included in the reference standard (true-positives) divided by k. Precision was calculated as the

number of true-positives divided by the total number of extracted concepts (true-positives + false-positives). Recall was calculated as the total number true-positives divided by the total number of concepts in the reference standard (true-positives + false-negatives). To determine if higher precision could be obtained if we only looked at the concepts with the highest occurrence, we also evaluated precision at varying levels of k. In that case, it could be argued that at a minimum, the algorithm could extract predications with the greater strength of association.

6.4.8 Statistical Analysis

In order to test the difference in overall precision and recall of the two methods, we calculated the median precision for both methods, as well as median precision at k for both methods. The Wilcoxon Signed Rank Test was then used to determine if there was a statistically significant difference in precision and recall between the two methods.

6.5 Results

6.5.1 Algorithm Results

Table 6.3 represents a sample output of the all Medline process with higher levels of occurrence for each CAM. Figure 6.4 provides a view of the top 100 treatment relations (*all Medline*) pertaining to the use of *acupuncture* for many medical disorders.

6.5.2 Performance of the Two Methods

Table 6.4 shows the overall precision and recall as well as the precision of the top 100 ranked concepts for each CAM for the *all Medline* and *sound studies* methods. We found that *sound studies* significantly outperformed the *all Medline* approach both in

terms of precision at 100 (27.0% vs. 21.0%, p<.001) and overall precision (11.5% vs. 7.0%, p<.005). However, *all Medline* outperformed the *sound studies* in terms of overall recall (37.1% vs. 25.6%, p<.001).

6.5.3 Precision at Varying Levels of k

Figure 6.5 shows the precision at k levels of 1, 5, 10, 25, 50, and 75 for both methods. We found no significant difference in median precision between the methods *all Medline* and *sound studies* for k levels of 1 and 5 (69.6 vs. 65.2, p=.665 and 48.3 vs. 54.3, p=.138). *Sound studies* resulted in a significantly higher precision than *all Medline* for k values of 10, 25, and 50 (50.0 vs. 42.2, p<.001, 40.3 vs. 33.4, p<.001, and 33.0 vs. 30.1, p<.001). We found no significant difference in median precision at k=75 (26.3 vs. 29.5, p=.118).

6.5.4 Error Analysis

We selected four CAMs with low precision or recall from the *all Medline* results in order to identify points of failure and opportunities to fine tune the algorithm. The CAMs chosen for analysis and the specific failures analyzed included:

- meditation, 99 false-negatives
- ashwagandha, 56 false-negatives
- choline, 89 false-positives from top 100 ranked concepts
- glutathione, 93 false-positives from top 100 ranked concepts

There were two primary reasons for false-negatives for meditation and ashwagandha. First, in 99/101 (98%) of false negatives for meditation, the concept

"meditation" was not assigned to a relevant semantic type in the UMLS, such as *therapeutic or preventive procedure*, resulting in a failure by SemRep to generate treatment-related predications. The concept "meditation" has a nonrelevant semantic type of *mental process* and SemRep prevents the generation of predications in the form <Mental process> TREATS <disorder>. Although other concepts exist with the appropriate semantic type (e.g., "meditation therapy" and "transcendental meditation"), the term "meditation" was used in the reference standard. As a result, treatment-related predications were not generated for many disorders, such as posttraumatic stress disorder, high blood pressure, and trauma. Second, SemRep also has specific indicator rules that are used to generate treatment-related predications. There are no indicator rules to map such terms as "reduced" or "increased" to a TREATS or AFFECTS predicate. This was a common error for ashwagandha, representing 10 out of 56 (17.6%) of the false-negatives errors.

We discovered two reasons for false-positives. First, in both CAMs analyzed, SemRep incorrectly extracted a TREATS predication in sentences that expressed a different kind of relation, such as the reduction of a choline or glutathione levels in the blood. This error represented 52 out of 89 (58.4%) of our false-positives for choline and 60 out of 93 (64.5%) for glutathione. For example, a study (PMID 21940617) discovered reduced choline levels in patients with amyotrophic lateral sclerosis (ALS), but choline was not used to treat these patients. The predication *choline TREATS ALS* was incorrectly extracted from "choline levels were reduced in ALS patients, but not in presymptomatic patients." For glutathione, most of the incorrect predications were extracted from studies that analyzed how various substances reduced glutatione levels.

Another study (PMID 3835567) assessed the toxic effect of divinyl and discovered “A significant statistic decrease of glutathione in blood”, from which SemRep incorrectly extracted the predication “Glutathione TREATS Toxic Effect.”

Second, 27 out of 182 errors (14.3%) were due to potential gaps in the reference standard. Some examples of predications and supporting sentences include: PMID 6348967, *Choline Magnesium Trisalicyclate* TREATS *rheumatoid arthritis* “There was a statistically significant improvement in the indices of inflammation” and PMID 2511054, *Choline* TREATS *fibrosis*, “choline may be an essential nutrient in malnourished cirrhotic patients and its deficiency may be associated with adverse hepatic effects." A similar type of error was identified in the study by Wang et al., where 40% of the false-positives were caused by gaps in the reference standard [10].

6.6 Discussion

This work investigated a methodology for assisting the development of a controlled treatment-related vocabulary for CAM. Such a vocabulary would contain not only CAM treatment relations, but also PubMed links to the source studies that investigated the use of the CAM to treat a particular condition. This kind of information could be provided to consumers to help them better assess the potential utility of a CAM in the prevention or treatment of a disease of interest. The proposed approach can help fill an important gap in the coverage of biomedical terminologies in the domain of CAMs.

We analyzed the precision of both methods at k values of 1, 5, 10, 25, 50, and 100. At k=100, the highest precision achieved was 54%, using the *sound studies* method. The *all MedLine* method achieved a maximum precision of 51% at k=100. Although the

sound studies method outperformed the *all Medline* method in precision, the *all Medline* method had a significantly higher recall. The two predication extraction methods resulted in a median recall of 37.1% for *all Medline* and 25.6% for *sound studies*. Therefore, there was a trade-off between precision and recall between the two methods. Although *sound studies* outperformed *all Medline* in median precision at k=100, it did not consistently do so for all CAMs. The *all Medline* method had a precision at 100 that was greater than or equal to that of the *sound studies* method for 10/23 (44%) of the CAMs. We conclude that these methods may be useful in identifying studies for specific CAM/disease combinations for the purpose of building a CAM treatment-related ontology. Although for some CAMs the precision and recall was quite low, programmatically identifying studies and extracting supporting sentences is still more efficient than searching PubMed manually and reading entire abstracts for all studies, which is essentially performing the functions of SemRep manually. However, certain considerations must be factored in before using these methods. First, it must be decided whether precision or recall is more important for the task. Secondly, in deciding which method to use, it would be necessary to determine if the exclusion of animal studies would be appropriate and desired. Unlike allopathic treatments, many CAM studies do not progress past animal studies due to a lack of funding, and some argue that CAM research should not be funded at all [32]. Consequently, these studies may be the only level of evidence available in the CAM domain. Finally, given the low precision, manual inspection of the sentences would be imperative before including the CAM/disease pair into an ontology.

We were not able to reach the precision found in a prior study [10], even at lesser values of k. Wang et al. found that these methods performed better in diseases that were

studied more frequently and had more biomedical publications. We may experience better performance for other CAMs that have been studied extensively, although further studies would be required to test this hypothesis. There were clearly factors other than how often a CAM was studied, as even CAMs that are quite common and well studied, such as Ginkgo Biloba and Glucosamine (146 and 227 disorder concepts retrieved, respectively), had very low recall and precision at 100. For the CAMs evaluated in this study, other factors such as incorrect predication generation by SemRep, missing semantic types for CAM concepts in the UMLS, and gaps in the reference standard seemed to play a large role in reduced precision and recall.

Given the limitations of the tools identified in the error analysis, an important next step to this study would be to conduct a more complete error analysis of all CAMs to determine the cause of errors with the highest occurrence. These error reports could be used to identify gaps in the UMLS as well as failures in SemRep resulting in inappropriate semantic predications. It may be possible to address these failures, making these methods more reliable for the generation of a CAM treatment-related vocabulary in the future, as well as vocabularies for other domains.

This study does have multiple notable limitations. First, the error analysis exposed potential gaps in the reference standard, exposing imperfections in its use for evaluating these methods. Second, only 23 CAMs were evaluated, and we found extreme variability in both precision and recall across those CAMs. Third, the relations extracted from SemMedDB do not imply efficacy of the CAM as a treatment for a disorder, since SemRep extracts treatment relations not only from study conclusion sentences, but also from statements regarding the study aims and methods.

6.7 Conclusion

This study investigated approaches to extract CAM treatment-related knowledge from the biomedical literature. For the 23 CAMs evaluated, the median precision at 100 was 23.7% and 26.4% for the *all Medline* and *sound studies* methods, respectively, and median recall was 33.5 and 25.0%. The *all Medline* method resulted in a significantly higher recall, while *sound studies* had higher precision. Therefore, the approach selection needs to be driven by the requirements of specific vocabulary development efforts. Despite low precision and recall, our approach could be used to help fill a critical gap in biomedical terminologies, assisting manual vocabulary development processes by identifying potential CAM-treatment relations along with supporting evidence. Future efforts should focus on improving the underlying tools and resources (e.g., SemRep, UMLS semantic types) that are used to extract CAM treatment relations.

6.8 References

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Table 6.1 – Semantic types for medical disorders and patient groups treated or affected by a CAM

Semantic Type	**Semantic Group**	**Example concept**
Congenital Abnormality	Disorders	Congenital megacolon
Acquired Abnormality	Disorders	Muscle damage
Finding	Disorders	Cardiac output
Injury or poisoning	Disorders	Soft tissue injuries
Pathologic function	Disorders	Bladder dysfunction, cardiac arrhythmia
Disease or syndrome	Disorders	Asthma
Mental or behavioral dysfunction	Disorders	Drug dependence
Cell or Molecular Dysfunction	Disorders	Nerve degeneration
Sign or symptom	Disorders	Shoulder pain
Neoplastic process	Disorders	Malignant neoplasm of breast
Organism attribute	Physiology	Heart rate
Physiologic function	Physiology	Excretory function, brain activity
Organism function	Physiology	Blood flow
Organ or tissue function	Physiology	Gastric function
Cell function	Physiology	Cell death
Molecular function	Physiology	Lipid peroxidation
Clinical attribute	Physiology	Bladder emptying
Organic chemical	Chemicals & drugs	Activated charcoal, Metformin
Biologically Active Substance	Chemicals & drugs	Chromium, Selenium
Pharmacologic function	Chemicals & drugs	Topical form corticosteroids
Hormone	Chemicals & drugs	Epinephrine
Amino Acid, Peptide, or Protein	Chemicals & drugs	Immunoglobulin
Immunologic Factor	Chemicals & drugs	Platelet activating factor
Antibiotic	Chemicals & drugs	Penicillin g
Element, Ion, or Isotope	Chemicals & drugs	Lithium, oxygen
Body system	Anatomy	Peripheral nervous system
Body Part, Organ, or Organ Component	Anatomy	Neural pathways
Cell component	Anatomy	Muscle fibers
Tissue	Anatomy	Smooth muscle (tissue)
Therapeutic or Preventive Procedure	Procedures	Operative surgical procedures
Patient or Disabled Group	Living beings	Hospice patient

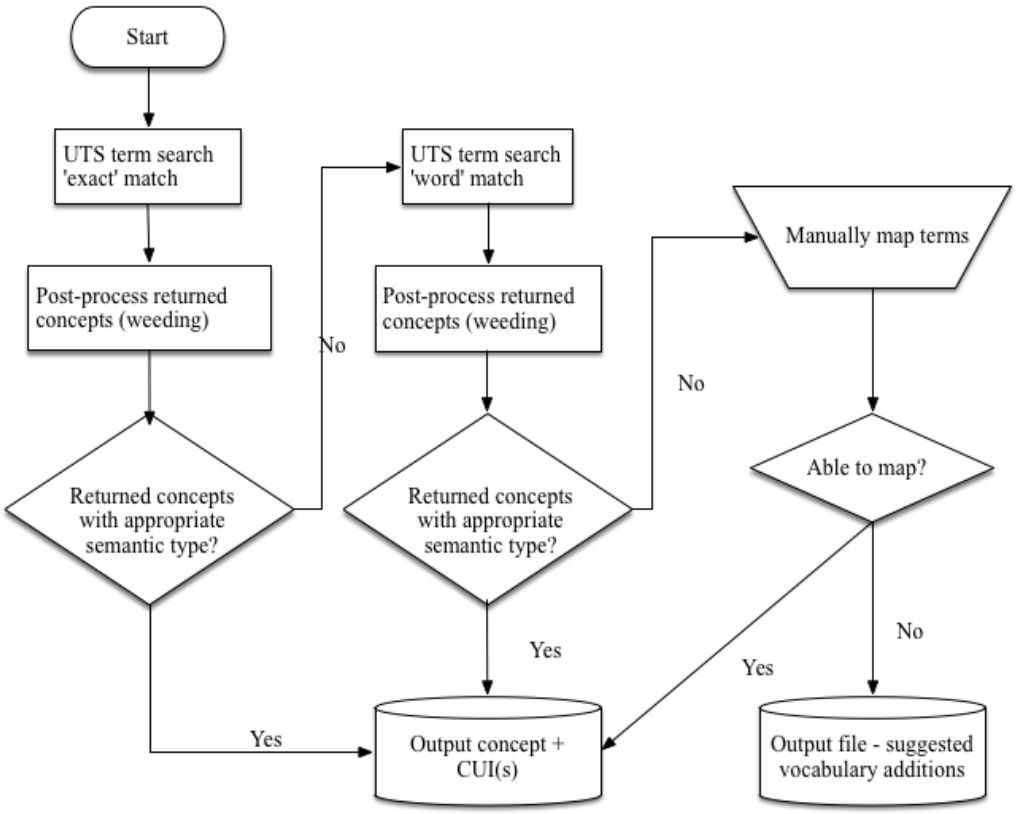

Figure 6.1 - Multipass mapping of disease terms to UMLS concepts.

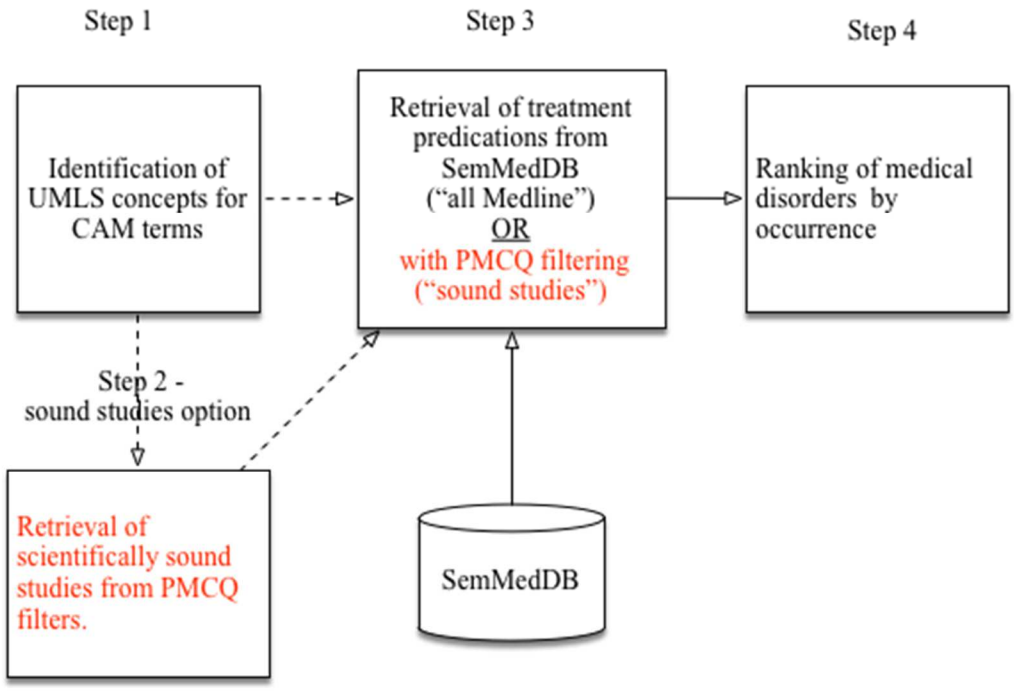

Figure 6.2 - Predication retrieval process. Items in red are specific to the "sound studies" approach.

Table 6.2 - Examples of semantic types for CAM terms in the reference standard

Semantic Type	**Semantic Group**	**Example of a concept within the type**
Therapeutic or Preventive Procedure	Procedures	Acupuncture
Organic Chemical	Chemicals & Drugs	Coenzyme Q10
Amino Acid, Peptide, or Protein	Chemicals & Drugs	Glutathione
Pharmacologic Substance	Chemicals & Drugs	Ashwagandha
Biologically Active Substance	Chemicals & Drugs	Zinc
Hazardous or Poisonous Substance	Chemicals & Drugs	Selenium
Element, Ion, or Isotope	Chemicals & Drugs	Zinc
Inorganic Chemical	Chemicals & Drugs	Magnesium sulfate
Clinical Drug	Chemicals & Drugs	Zinc lozenge
Lipid	Chemicals & Drugs	Capsaicin

```
SELECT DISTINCT predication.pmid, subject_cui, subject_semtype, subject_name,
predicate, object_name, object_semtype, object_cui, sentence
FROM predication p, sentence s
WHERE subject_cui IN (<cuis from the control file for current CAM of interest>) AND
PMID IN (PMIDs of scientifically sound studies) AND
object_semtype IN (disorders semantic group, Table 6.1) AND
predicate IN
('TREATS','NEG_TREATS','PREVENTS','NEG_PREVENTS','AFFECTS','NEG_AFFECT
S','COMPARED_WITH','ADMINISTERED_TO','NEG_ADMINISTERED_TO','HIGHER_
THAN','LOWER_THAN') AND
p.sentence_id = s_sentence_id AND
object_novelty = 1
```

Figure 6.3 - SQL query used to retrieve CAM treatment predications from SemMedDB. The term in red was included only in the "sound studies" method.

Table 6.3 - Sample treatment-disorder relations retrieved from SemMedDB along with the number of citations (occurrence) in which those relations were found.

CUI	CAM	Unique Disorders*	Semantic Type	Sample Disorders	Occurrence (citations)
C0394664	Acupuncture Procedure	1882	topp	Pain	580
				Migraine disorders	131
C0613707	Ashwagandha	19	phsu	Endurance	2
				Parkinson's disease	1
C0006931	Capsaicin	376	lipd	Pain	71
				Coughing	40
C0024875	Massage	630	topp	Pain	137
				Stress	20
C0008405	Choline	1180	phsu	Alzheimer's disease	188
				Malignant neoplasm of prostate	32
C0008574	Coenzyme Q10	340	phsu	Heart failure	26
				Parkinson's disease	17
C0008574	Chromium	162	bacs	Insulin resistance	27
				Diabetes, non-insulin dependent	21
C0009968	Copper	736	bacs	Hepatolenticular degeneration	84
				Alzheimer's disease	49
C0556110	Folic acid supplementation		phsu	Neural tube defects	544
C0016410	Folic acid	617	phsu	Hyper-homocysteinemia	99
C0885057	Garlic preparation	120	orch	Risk factor, cardiovascular	7
C0772125	Ginkgo biloba extract	146	orch	Dementia	18
C0017720	Glucosamine sulfate		phsu	Osteoarthritis, knee	47
C0017817	Glutathione	612	aapp	Toxic effect	94
C0017837	Glutathione s-transferase		aapp	Injury	58
C0024480	Magnesium sulfate		phsu	Eclampsia	168

Table 6.3, continued

C0024467	Magnesium	852	bacs	Cardiac arrhythmia	43
C0814263	Meditation therapy	2	topp	Anxiety disorders	1
				ADHD	1
C0025219	Melatonin	983	horm	Sleep	175
				Neoplasm	38
C0033979	Psyllium	54	phsu	Hypercholesterolemia	10
				Irritable bowel syndrome	7
C0034392	Quercetin	560	phsu	Oxidative stress	94
				Irritable bowel syndrome	7
C0302583	Iron	1295	phsu	Kidney failure, chronic	109
				Restless legs syndrome	50
C0242606	Resveratrol	612	comd	Oxidative stress	133
				Inflammation	80
C0036581	Selenium	470	hops	Malignant neoplasm of prostate	88
			bacs	Apoptosis	32
C0042866	Vitamin D	1615	phsu	Osteoporosis	336
				Malignant neoplasm of prostate	123
C0043481	Zinc	1206	phsu	Diarrhea	123
				Wound healing	32

* Include disorders from all concepts associated with a CAM (e.g., magnesium, magnesium sulfate)

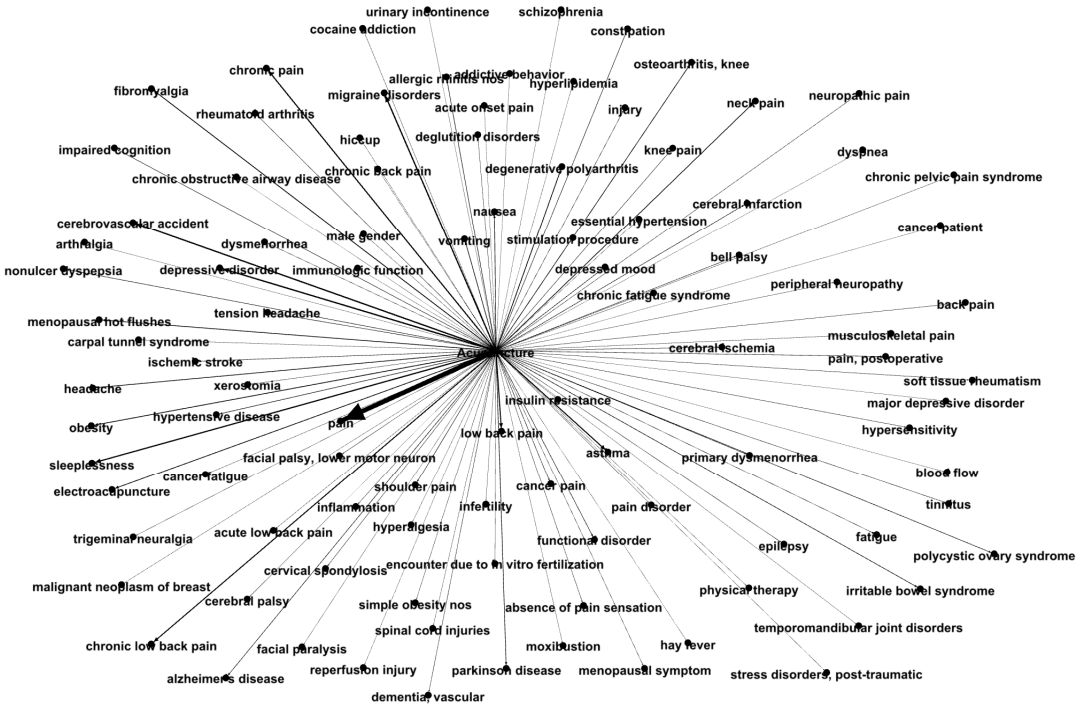

Figure 6.4 – Weighted graph of top 100 treatment relations of acupuncture from the all Medline method

Table 6.4 - Precision at top 100, precision, and recall of the all Medline and sound studies approaches for each CAM in the reference standard.

CAM	Precision at top 100		Overall Precision		Overall Recall	
	All Medline	Sound Studies	All Medline	Sound Studies	All Medline	Sound Studies
Acupuncture	50.0	53.0	7.6	11.3	54.8	49.4
Ashwagandha	10.5	16.7	7.1	16.7	3.5	1.2
Capsaicin	14.0	19.0	3.4	11.2	64.3	61.9
Choline	11.0	9.0	1.4	3.9	52.7	36.4
Chromium	15.0	20.0	6.7	18.9	21.6	17.2
CoenzymeQ10	36.0	42.0	17.0	27.7	21.1	16.5
Copper	4.0	4.0	1.0	3.7	39.4	27.3
Folic Acid	31.0	31.0	7.0	11.2	48.0	41.6
Garlic	15.0	28.6	13.5	28.6	16.7	9.0
Ginkgo Biloba	21.0	30.1	14.6	30.1	18.8	13.4
Glucosamine	7.0	6.0	2.1	4.8	17.7	13.4
Glutathione	5.0	4.0	1.2	2.2	44.4	16.7
Iron	8.0	8.0	0.9	2.1	39.1	30.4
Magnesium	33.0	39.0	7.6	14.0	38.3	32.9
Massage	29.0	27.0	6.7	11.0	32.4	29.0
Meditation	50.0	50.0	50.0	50.0	1.0	1.0
Melatonin	45.0	52.0	8.6	20.1	37.6	27.0
Psyllium	5.6	9.3	5.3	9.3	33.3	33.3
Quercetin	13.0	14.0	4.6	9.6	36.6	17.9
Resveratrol	27.0	27.0	7.1	12.8	40.8	20.4
Selenium	22.0	21.0	8.9	17.4	29.8	17.6
Vitamin D	51.0	54.0	6.4	11.5	41.9	35.1
Zinc	42.0	42.0	8.6	17.5	37.1	25.6
Mean	23.7	26.4	8.6	15.0	33.5	25.0
Median	21.0	27.0	7.0	11.5	37.1	25.6
Range	4.0 - 51.0	4.0 - 54.0	9.0 - 50.0	2.1 - 50.0	1.0 - 64.3	1.0 - 61.9
p-value	<.001		<.001		<.001	

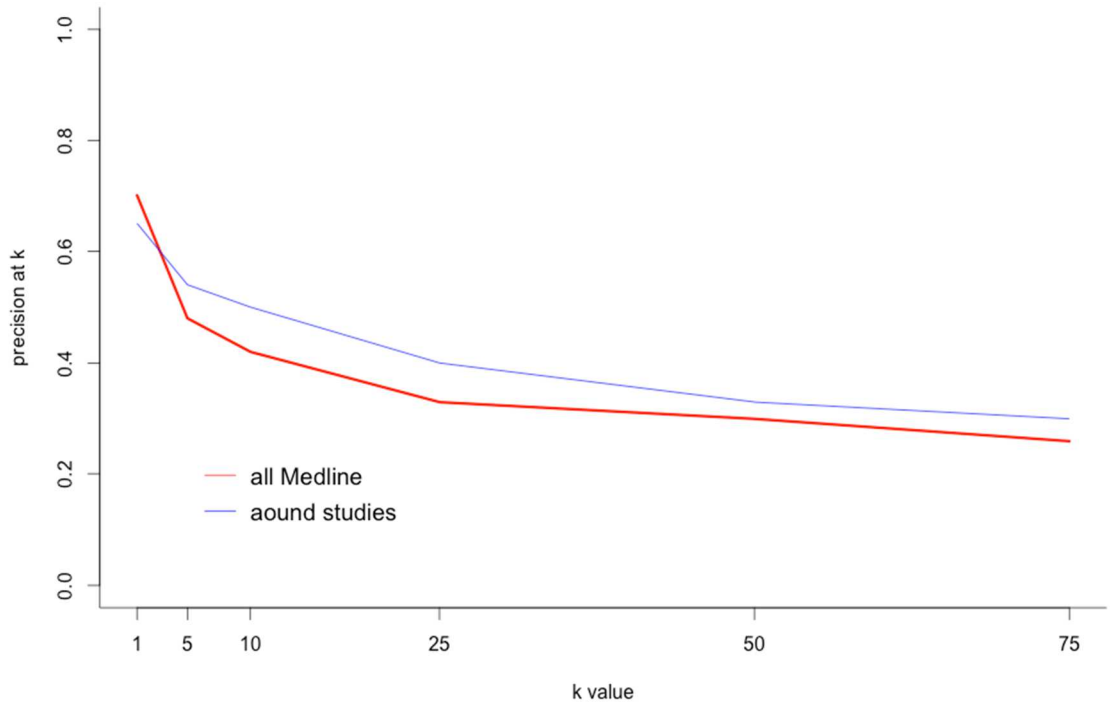

Figure 6.5 - Median precision at varying levels of k

CHAPTER 7

DISCUSSION

7.1 Summary of Important Findings

One of the goals of informatics is to deliver to clinicians and consumers the most essential information with minimal effort and in a timely manner. Previous studies and our study conducted in Aim 3 showed that consumers still rely primarily on anecdotal evidence in making decisions on CAM use [1, 2]. Overall, this dissertation fills several gaps in the understanding of CAM information needs and information-seeking behavior among consumers and provides a technical approach that can help with the foundation of CAM online resources for consumers. Three studies were conducted to better understand what information is desired by CAM users, what delivery method is preferred, and what problems exist with some Web-based resources currently available to consumers. It is important to understand consumer information-seeking behaviors and preferences in order to design solutions that provide high-quality information for CAM and help consumers move beyond the reliance on anecdotal evidence. Finally, various methods are explored for extracting treatment-related knowledge for CAM from the biomedical literature. Treatment-related knowledge extracted in Aim 4 can be used to construct ontologies that can provide the foundation for Web-based resources to help consumers find and evaluate information on the safety and efficacy of CAM treatments.

The goal of the first study was to determine if it is feasible for patients, particularly elderly patients, to self-report CAM use on table devices prior to clinic appointments. This is an important question before considering Web-based applications that gather and utilize CAM use data. The study showed that 85% of those patients approached were able to enter information about their CAM use into an iPad application [3]. The CAMs being used suggested that as many as 33% of the patients participating

were at risk for drug-herb interactions, as the biologically-based CAMs in use were on the list of those with potential interactions with common cardiac medications. It was also discovered that the patient-reported CAM usage rate of 85% far exceeded the 9% rate documented in patient charts. This has important implications for patient safety and presents opportunities for expansion of existing patient portals, which can be used to gather CAM use information and notify patients and their providers about the presence of potential interactions between a patient's CAM and allopathic therapy. This study also exposed opportunities within the clinic workflow for requesting information on patient-reported CAM use for addition to their medical record. Patient self-reported CAM use could potentially lead to increased CAM reporting, better patient documentation, and an opportunity to expand electronic health record systems to include the detection of drug-herb interactions.

In the second study, we evaluated online resources that provide drug-herb interaction information to consumers. We found that the coverage of the available resources was incomplete, potentially suggesting to the consumer that no interactions exist between the entered CAM/drug pair. The information was also not presented in a consumer-friendly manner; i.e. the reading level was determined to be many years beyond that recommended for consumer-facing information portals per the guidelines provided by the US Department of Health and Human Services [4]. Finally, the study showed a very low 50% accuracy rate, in many cases indicating to the consumer that the severity of the interaction was less than that reported in the literature. This may cause safety issues, such as the consumer misinterpreting a CAM-drug interaction as mild severity, when the severity reported in the literature is actually moderate or severe.

The third study used a mixed-methods approach to investigate the information-seeking behaviors of cancer survivors. Two theories, the Health Belief Model (HBM) and the Uses and Gratifications Theory (UGT) were used in the design of the survey tool and the script for phone interviews using the critical incident technique (CIT). The HBM is a psychological model used to explain and predict health behaviors, whereas the UGT is an approach to understand why specific media satisfy the needs of the user. Utilizing an existing cohort of cancer survivors, this study showed a high rate of CAM use throughout the cancer trajectory, including into long-term survivorship. This study and others have shown that patients would prefer to get CAM information from their physician, but physicians are most often not equipped to provide that type of information [5]. As a result, patients often need to search for CAM information from other sources. Although the initial introduction to CAM is still often anecdotal [6, 7], consumers often looked online for additional evidence. In searching for CAM information, patients indicated a desire for both linkage to the scientific literature as well as input on efficacy from other patients. Scientific evidence alone is often met with skepticism by consumers [8]. Regardless of what the literature states, consumers want to know how other patients feel about the use of a CAM in the management of their disorder. A primary motivator for CAM information-seeking and use expressed by the participants was to fill a void in cancer treatment where the psychological and emotional challenges are concerned, as well as recovering from the treatments. Patients indicated satisfaction in the direct treatment of their cancer, but felt very much on their own in finding options for handling health issues beyond the treatment prescribed by their healthcare providers.

In the fourth study, we investigated two methods to assist in the development of

CAM vocabularies, which are a necessary foundation for the development of information retrieval systems. These vocabularies could form the basis for the development of CAM resources containing information on topics such as efficacy, safety, and prevention. Manual extraction of CAM treatment-related knowledge from two scientifically-based, expert-curated CAM resources, Natural Medicines Comprehensive Database (NMCD) and Life Extension (LE), were used to construct a reference standard for twenty biologically-based CAMs and three mind-body therapies. Two methods were then developed to semi-automatically extract treatment-related knowledge from the biomedical literature using predications from SemMedDB. The extracted concepts were compared against the reference standard for precision and recall. Although performance was not adequate to avoid extensive manual analysis of the retrieved results, the results can still be used reduce manual efforts as well as to provide further insight into the failures and gaps in SemRep and the UMLS for improved performance of these methods in the future.

7.2 Significance to Biomedical Informatics

Biomedical Informatics is defined as "the interdisciplinary field that studies and pursues the effective uses of biomedical data, information, and knowledge for scientific inquiry, problem solving and decision making, motivated by efforts to improve human health." These goals affect many application areas, including bioinformatics, clinical informatics, public health informatics, and consumer health informatics [9]. These applications must have the ability to provide the information to the right people at the right time. Tremendous effort has been applied to studying and satisfying these needs

across all the above disciplines, but tools for providing CAM information to consumers are lacking, in spite of the continually increasing use of CAM for the management of chronic disease [8].

The goal of this dissertation was to extend the literature in the area of Consumer Health Informatics by assessing patient information needs and preferred avenues for receiving that information. This research provides a fairly clear picture of what those information needs are and direction for meeting those needs, such as patient-specified preferences toward Web-based information-retrieval systems, linkage to the scientific literature, and disease-specific forums. By utilizing Informatics techniques to enhance the information-seeking process for the consumer, future research may enable tools that empower consumers through the combination of patient testimonials and linkage to the scientific literature.

Ontologies are valuable and necessary tools in the field of Biomedical Informatics. The methods investigated in this dissertation could be used to support the development of CAM information retrieval and clinical decision support systems for consumers, physicians, and medical librarians. The methods described in this dissertation were investigated to assist in building vocabularies for CAM-disorder relations, but could be extended to handle other areas of concern to consumers, such as drug-herb interactions. Tools for the management of CAM data and detection of CAM interactions also have important implications in clinical decision support systems.

7.3 Limitations

This research has several limitations in addition to those described in the discussion sections of each study. First, we only investigated CAM information needs for consumers. It is unknown how these compare to the CAM information needs of healthcare providers and researchers. Understanding the CAM information needs of professionals could help inform the design of information retrieval systems that meet the needs of those audiences. Second, one study showed that patients would prefer to receive information on alternative therapies from their practitioners [5]. Integrative medicine is an approach to bring evidence-based alternative therapies into the treatment plan in a safe, coordinated way. However, this dissertation focused primarily on the consumer and did not investigate information needs and approaches to assist with information seeking in the context of integrative medicine settings.

7.4 Challenges in this Research

The greatest challenge in this research was the reliance on patient-provided data for aims 1 and 3. As is most often the case, we had to rely on patient recall in the cardiology clinic while requesting that patients self-report the CAMs they were taking. In only one of the fifty patients participating did the patient bring their bag of medications and CAMs. Fortunately, this was not a significant problem as the patients were only taking a few supplements, so recall was not as big a problem as with those taking many. In the study of cancer survivors, we were also relying on recall in requesting that the patients talk about their cancer trajectory and events leading to a CAM information-seeking process. This presented a much greater challenge when we focused on a single

CAM, how they were introduced to it, and where they went for further information on efficacy, side effects, and interactions with their conventional treatments.

7.5 Future Direction for Research

Through this body of work, we demonstrated the need and desire for more readily available information for consumers interested in complementary and alternative medicine. Ideally, this information would be structured in a Web-based consumer portal. Such a portal could provide the ability to search for options by health condition or goal, to search by CAM/health condition combinations, and to generally search for conditions for which a particular CAM has been found to be effective. Finally, for the available retrieved information on any area of interest (efficacy, interactions, etc.), a consumer portal should provide the ability to link to pertinent studies in support of the claims suggested by the relationships (i.e., treats, prevents).

The methods for extracting predications for use in a baseline vocabulary covered only treatment-related studies of CAMs. This is a good start for CAM information-retrieval systems, although another important extension to this would be the addition of data for drug-CAM interactions as well as CAM-condition interactions. A CAM interactions knowledge base would be a necessary next step for our first study (aim 1). This would provide the data necessary to detect and alert on potential drug-herb interactions as CAM and medication data are entered into the patient record. Similarly, such a knowledge base would provide more complete and current interaction data for other online information resources that were lacking in completeness and accuracy per our second study (aim 2).

The final study that compared methods for extracting knowledge for the construction of ontologies exposed gaps in the UMLS vocabularies. Continued work in this area utilizing the methods studied would also provide the opportunity to contribute to those vocabularies, thereby increasing their usefulness in similar applications.

The next step toward generating a treatment-related ontology for CAM would be to validate the predications returned from SemMedDB, removing those that were not supported by the source sentences stored in SemMedDB. From the remaining predications, a process must be designed to move the validated predications into the CAM ontology.

This study focused on consumer needs. A CAM ontology is a useful tool in any area of medicine requiring structured data, including physician support, community and medical libraries, inclusion in other treatment-related ontologies, and for research by various industries, including the pharmaceutical industry. Further studies would be necessary to determine the information needs for CAM in these other areas.

Finally, the findings in these studies have important implications for integrative medicine (IM). The National Center for Complementary and Integrative Health (NCCIH, formerly the National Center for Complementary and Alternative Medicine) defines IM as the integration of both CAM and mainstream therapies for which some evidence of efficacy exists [10]. Information retrieval resources can help realize the vision of IM helping both patient and providers identify evidence to guide the integration of nonconventional therapies as alternatives or adjuncts to a patient's treatment plan. Brooks et al. propose a conceptual framework for shared decision making in IM that considers patient values including their particular beliefs and preferences [11]. Information retrieval

systems could provide the patient with the information necessary to come to appointments prepared for shared decision making (SDM), with the patient and provider acting as partners in creating a treatment plan that is consistent with the patient's values and needs; mind, body, and spirit.

7.6 References

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