A STUDY OF NURSE PRACTITIONER CHARACTERISTICS AND KNOWLEDGE OF DRUG-DRUG INTERACTIONS

by

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As members of the Practice Inquiry Committee, we certify that we have read the practice inquiry project prepared by Cathrin Carithers

entitled A Study of Nurse Practitioner Characteristics and Knowledge of Drug-Drug Interactions

and recommend that it be accepted as fulfilling the practice inquiry requirement for the

Degree of Doctor of Nursing Practice

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Final approval and acceptance of this practice inquiry is contingent upon the candidate's submission of the final copies of the practice inquiry to the Graduate College.

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DEDICATION

This manuscript is dedicated to my family; my parents, Patricia and Richard Smith and my children, Kendall and Cole Carithers. Thank you for believing in me and supporting me with your love and patience throughout the journey to completion of my Doctor of Nursing Practice degree.

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ABSTRACT

Purpose: Drug-drug interactions (DDIs) place a burden on our nation and cause potential harm to patients. Awareness of potential DDIs is essential for safe prescribing. Nurse practitioners (NP) have prescriptive authority throughout the nation, however, little is known about NP prescribing habits. The purpose of this study was to identify NPs' demographic and practice characteristics, DDI knowledge and factors that influence this knowledge.

Data Sources: A survey was administered to NP prescribers recruited from a national conference. Data was collected on demographics, practice and technological characteristics, and perceptions and knowledge of DDIs.

Conclusions: Data from 305 questionnaires were analyzed. NPs correctly classified 31% of drug pairs. Nitroglycerin and Sildenafil (drug combination to avoid) was classified correctly by the most respondents (90.8%, n = 305); Warfarin and Gemfibrozil (drug combination to usually avoid) the fewest 15.7% (n = 302). A positive correlation was found between NPs in acute care hospital settings and DDI knowledge, indicating higher knowledge scores. Neither hierarchical linear regression model was significant at predicting NPs' DDI knowledge.

Implications for Practice: Continuing education needs to be targeted to enhance NPs identification and management of potential clinically significant DDIs. Increased recognition of potential DDIs among NPs will enhance patient safety.

BACKGROUND

Preventable adverse drug events (ADEs) are a national safety priority due to their very nature; they can be prevented and yet, they still occur (Institute of Medicine [IOM], 2007). One of the goals of Healthy People 2020 for our nation in the next decade is to "reduce emergency department visits for common, preventable adverse events from medicine", (United States Department of Health and Human Services, 2009, p. 1). ADEs are the most frequent errors found in health care, comprising 19% of all medical errors. Thirty-nine percent of potentially serious ADEs occur in the prescribing stage of the "medication use process" (Leape et al., 1995). First identified in the 1940's (Jankel & Speedie, 1990), drug-drug interactions (DDIs) account for a significant portion of preventable ADEs (Bates et al., 1995; IOM, 2007).

The primary mission set forth by the IOM for the next decade is to improve medication safety through research targeted toward the prevention of medical errors (2007). Referred to as "the silent epidemic" (Sandson, 2005, p. 22), DDIs have been identified by some as the leading cause of preventable ADEs (Bates, et al., 1995). Research findings indicate that as many as 11% of patients complain of symptoms resultant from DDIs. The ADE prevention study reported 3% of preventable ADEs were due to DDIs (Leape, et al., 1995). A more recent study that utilized 2000 to 2002 data from the National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Care Survey (NHACS) to determine significant DDIs in outpatient office-based settings reported there were approximately 6.80 million ambulatory visits with potential DDIs from prescribed drug combinations. This equates to 8.12 outpatient visits per 1000 persons annually or 0.63% of ambulatory visits that involved two or more medications. The majority of

the potential DDI prescribing (93%) transpired in provider offices (Aparasu, Baer, & Aparasu, 2007).

Potential outcomes as a result of DDIs vary from being unnoticeable to significant morbidity and mortality (Preskorn & Flockhart, 2009). It has been reported that up to 2.8% of hospital admissions have been attributed to DDIs (Grymonpre, Mitenko, Sitar, Aoki, & Montgomery, 1988; Jankel & Fitterman, 1993; Jankel & Speedie, 1990). A more recent study undertaken at a teaching hospital in Temple, Pennsylvania determined 25% of the 154 ADEs identified were resultant from DDIs (McDonnell & Jacobs, 2002). In another study, data from published case reports were analyzed to determine the incidence of mortality from ADEs. Findings indicated a 6% mortality rate from ADEs linked to DDIs (Kelly, 2001). Because of their potential for harm and resource utilization, DDIs are a concern for patients, prescribers, health care systems and society.

Preventable ADEs can also lead to increased cost and resource utilization (Hamilton, Briceland, & Andritz, 1998; Jankel, McMillan, & Martin, 1994). Between 2005 and 2006, ADEs made up 2.5% of all unintentional injury visits to hospital emergency departments; 16.7% of those required hospital admission (Budnitz et al., 2006). Results from a systematic review of preventable ADEs that occur in ambulatory care revealed nearly 50% of preventable ADEs required hospital admission (Thomsen, Winterstein, Sondergaard, Haugbolle, & Melander, 2007). Study findings of data from computerized based monitoring of ADEs reported costs of preventable ADEs exceeded $10,000 per event with an annual cost of $1.2 million (Jha, Kuperman, Rittenberg, Teich, & Bates, 2001). More recent estimates indicate annual costs for preventable ADEs in the hospital setting to be $3.5 billion (IOM, 2007).

Several factors have been identified to increase the potential for the occurrence of DDIs. An FDA report cited that in 1999 there were over 10,000 prescription medications on the market (IOM, 2007). Additionally, in the US, over 300 over-the-counter medicines are available on retailers' shelves (Roper Starch Worldwide, 2001). To add to the equation, new medications are being added monthly to prescribers' treatment options (Langdorf, Fox, Marwah, Montague, & Hart, 2000). Approximately 340 drugs are approved by the FDA annually. This is a considerable amount of information to incorporate safely into practice (2000). In addition, as the number of pharmacotherapeutic treatment options increase so does the risk for harm from DDIs (Chao & Maibach, 2005).

Medication use has consistently increased over the last decade. Data from the National Health and Nutrition Examination Surveys report prescription drug use in the US is up 4% from 1999 (Gu, Dillon, & Burt, 2010). In outpatient clinic settings, prescription medications increased by 40%, up from 2.7 billion in 1998 to 3.8 billion in 2005 according to FDA adverse drug event reports (Moore, Cohen, & Furberg, 2007). Currently, 48% of Americans indicate prescription drug use within the last month (Gu, et al., 2010). Greater use of over-the counter and prescription drugs are thought to play a role in the increased incidence of serious injury from ADEs (Moore, et al.).

Polypharmacy has been found to be correlated with an increased risk of DDIs (Aparasu, et al., 2007). In 2006, pharmacologic therapy occurred in seven out of ten ambulatory care encounters and totaled 1.28 billion drugs (Schappert & Rechtsteiner, 2008). Gandhi et al., (2003) found that each medication added to an individual's medication profile increased the frequency of ADEs by 10% in adult outpatient clinical settings. Research to determine the

incidence of adverse drug interactions in the emergency department, a population at high risk for such events, reported the incidence of DDIs increased as the number of drugs increased. Findings indicated that chances of experiencing an adverse drug reaction in persons taking two medications was 13% , four medications 38%, and an 82% risk with seven or more drugs (Goldberg, Mabee, Chan, & Wong, 1996). Results from analysis of 2000 to 2002 data from outpatient settings found similar results, citing the majority of potential DDIs occurred when five or more medications were involved (Aparasu, et al.).

Advancing age has also been cited as a risk factor for DDIs (Aparasu, et al., 2007). The incidence of comorbid conditions, the use of multiple medications (Buajordet, Ebbesen, Erikssen, Brors, & Hilberg, 2001) and the involvement of multiple health care providers in their plan of care are factors that contribute to this risk (Seymour & Routledge, 1998). Persons 60 years of age and older use the most drugs of any age group. Seventy-six percent of older Americans used two or more prescription drugs and 37% used at least five (Gu, et al., 2010). In addition, data from the 2001 National Ambulatory Medical Care Survey determined that outpatient clinic visits related to ADEs were more prevalent in older adults aged 65 to 74 years (Zhan et al., 2005). Furthermore, persons with Medicare insurance were also found to be at increased risk of DDIs (Aparasu, et al.).

Significance to Advanced Practice Nursing

Nurse Practitioners (NPs) are among health care providers with prescriptive authority. In the U.S. there are more than 140,000 NPs in practice. NP practice settings vary with 18% rural, 68% primary care and 31% nonprimary care such as inpatient, ED, surgical, or specialty practices. A recent survey found that NPs write an average of 19 prescriptions daily. Annually,

nurse practitioners prescribe approximately 556 million medications in the management of acute and chronic conditions (American Academy of Nurse Practitioners [AANP], 2010).

The determination of pharmacologic therapy is a complex process and requires prescribers to examine many factors. Patient considerations include current medications, dietary intake, age, disease processes or diagnoses and genetics. In addition, consideration of the pharmacokinetic and pharmacodynamic properties of each medication is essential. The potential for DDIs in medical decision making is real and the outcomes can be serious (Preskorn & Flockhart, 2009).

Errors in prescribing are not uncommon (Leape, et al., 1995; Winterstein et al., 2004). Among primary care settings, prescribing error rates have been reported to be as high as 8% (Gandhi et al., 2005). A systematic review of the literature of prescribing errors in the hospital inpatient setting found an error rate of 7% in medication orders (Lewis et al., 2009).

Studies have reported that health care providers lack knowledge of potential DDIs (Buajordet, et al., 2001; Ko, Malone, Skrepnek, et al., 2008; Leape, et al., 1995; Melmon, 1971). Leape et al. (1995) performed a systems analysis of ADEs in 11 medical surgical units in two tertiary care hospitals. Their findings indicated that the highest number of errors (35%) occurred during physician prescribing with lack of drug knowledge (including DDIs) being the most frequent cause. Glassman, Simon, Belperio & Lanto (2002) also studied knowledge of common DDIs among clinicians in a VA health system utilizing 10 drug pairs. Fifty-three percent of clinicians identified interacting drug pairs and 54% recognized drug pairs that were contraindicated. Another study to determine provider's use of cisapride in children with GERD testified that at least 50% of health care providers were unaware of potential DDIs (Shaoul,

Shahory, Tamir, & Jaffe, 2002). Researchers to determine the effects of warfarin or theophylline and potentially interacting drugs on patient outcomes reported significant impact to those who experienced DDIs and purported that physicians are unaware or unconcerned of DDIs that involve theophylline and potential interacting medications (Jankel, et al., 1994). A more recent study conducted by Ko, Malone, Skrepnek, et al. (2008) utilized a US postal survey to assess DDI knowledge from a national sample of prescribers derived from data from a large pharmacy benefit manager. Findings revealed that on average, respondents identified 42.7% of the drug pairs correctly. Researchers concluded that health care providers' knowledge of DDIs was lacking.

Physician prescribing habits and drug knowledge have been studied; however, limited research has been conducted to identify NP prescribing practices, their knowledge of DDIs or their usual source of information on this topic (Mahoney & Ladd, 2010). A review of the literature revealed one study that examined demographic and practice characteristics to determine factors related to prescribers' knowledge of potential DDIs. Health care providers from a national pharmacy claims database were surveyed. Poorer potential DDI knowledge was associated with NPs in solo office-based practice (Ko, Malone, D'Agostino, et al., 2008).

DDIs place a major burden on our nation and cause potential harm to patients. With the focus of our nation on patient safety, the prevalence and complexity of prescribing, and the knowledge that DDIs may be prevented it is important to understand NP prescribing habits. The aims of this study are three-fold. First, is to describe the organizational environment in which NPs operate. Secondly, to determine what factors are associated with NPs' knowledge of DDIs.

Finally, the study aims to evaluate nurse practitioner's perception of the rate and severity of DDIs.

This data is important in the reduction of patient risk for DDIs. The initial step in the evolution of change is to gain an understanding of the factors inherent in the problem. The IOM (2007) suggests the major focus of medication error research should be directed toward prevention. With the knowledge gained from this study, prevention efforts can be targeted to increase NPs' knowledge of DDIs and in turn improve prescribing habits. Such interventions can lead to significant health care savings and reduce morbidity and mortality attributable to DDIs and adverse drug-drug reactions. This can result in improvements in patient safety, outcomes and ultimately in health care quality.

Conceptual Framework

Cognitive continuum theory (CCT) is a middle-range theory that originated in the field of psychology (Hammond, Hamm, Grassia, & Pearson, 1987). It has been adapted for uses in both medicine (Hamm, 1988) and nursing (Standing, 2008) to attempt to identify health care providers' decision making process. Theoretical constructs include "*task conditions*", "*modes of cognition"* and "*modes of practice*" (Hamm, p. 81). CCT postulates that health care provider approaches to clinical decision making vary on a continuum from analysis to intuition. The analytical process tends to be more accurate and is described as time-intensive, methodical, and consistent. Intuition, at the opposite end of the spectrum is less precise, faster, more instinctive and inconsistent and involves processing by combining available data. These cognitive processes or *modes of cognition* applied to decision making are thought to vary depending upon the structure of the *task conditions* or elements. These range on a continuum from poorly or ill-

structured to well- structured. Tasks that induce more analytical thinking have greater structure opposed to less structured tasks that promote intuitive thinking (Hamm). Tasks can be divided into three main categories; "complexity of task structure, ambiguity of task content, and form of task presentation" (Hamm, p. 83). Task complexity relates to the number, relevance and predictability of information cues. The more numerous, straight forward and predictable the tasks the more intuition is engaged. Task complexity encourages analytical cognition. Ambiguity of task content relates to knowledge or task content expertise and availability of multifaceted organizational principles that are known to promote accuracy. Content expertise and identified multi-step formulas or algorithms that promote accuracy lead to analytical cognition, conversely, unfamiliar, less delineated single-step processes provoke intuition. Finally, form of task presentation denotes the manner in which tasks are presented, measured and the time required for task completion. Tasks that are presented in a quantitative nature requiring multiple steps and more time induce analytic cognition. Intuition is instigated with tasks that are faster, utilize more visual illustrations and require fewer steps. The more analytic and structured along the cognitive/task continuum the greater the potential of manipulation, process transparency and time and resources required. The opposite is true with more intuitive and poorly structured tasks. A basic tenet of CCT is that decision making is more effective when the cognitive and task features are congruent (Hamm).

Social and practice institutional context or environment may also impact clinicians' decision making. Social contextual influences encompass practice setting, composition and availability of members of the health care team for consultation/support. Institutional factors include availability of continuing education and training, time allowed per patient visit,

accessibility of patient information, resources, research evidence, electronic tools and outcome-based rewards for patients and providers. The decision making process is fluid and requires flexibility to match cognition with task requirements in varying environments (Hammond, 1996).

Six cognitive/task *modes of inquiry* are identified and illustrated in figure 1. Mode one is where the most analytical thought occurs in comparison with mode six which entails the most intuitive thought. Quasirationale thought provides a link between the two forms of cognition, blending them along the cognitive continuum with modes two and three more analytical based and four and five, intuition based (Hammond, 1978). Hamm (1988) adapted the modes of inquiry for use in medicine and labeled them as *modes of practice*. Modes one through three are referred to as "scientific experiment", "controlled trial" and "quasi-experiment" respectively. In these modes, relationships among variables is assessed with less variable control, randomization and manipulation required along the continuum. In these modes, experimental outcomes may be more generalizable and provide evidence to base decisions upon. At mode four, intuition begins to play a role in clinical decision making. In this mode, deemed "system-aided judgment" intuition is coupled with evidence and diagnostic reasoning based upon decision analysis frameworks. Computer-aided decision making is included in this mode. Health care providers are said to practice predominantly in modes five and six, "peer aided judgment" and "intuitive judgment" (Hamm, p. 87). Mode five decisions are mainly based upon data that is known, derived from a mixture of intuition and evidence including peer consultation and expert advice. Health care providers are able to support their decisions with evidence, policy or principles. In contrast, mode six reflects purely intuitive thought based upon inconsistent or uncertain rules.

Decisions from this mode are the most subjective and are considered to contain the most risk (Hamm).

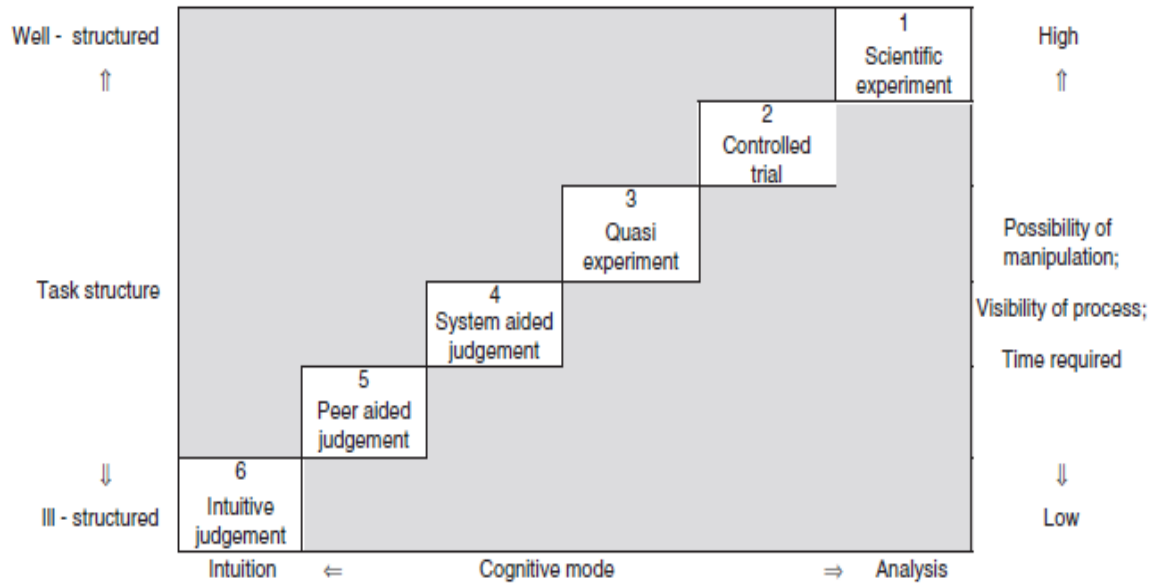

Figure 1. Six Cognitive/Task *Modes of Inquiry* of Cognitive Continuum Theory (Hamm, 1988, p. 87)

Evidence based practice (EBP) is a foundational principle for health care providers' clinical decision making. The tenets of CCT involve properties congruent with EBP, scientific evidence and clinician expertise along a cognitive/task continuum of clinical decision making. Prescribing is a complex process that requires consideration of multiple factors to arrive at a decision that is evidence-based and acceptable to the patient. CCT provided the theoretic framework in which to try to understand NPs knowledge of DDIs. Factors related to task conditions, modes of cognition and modes of practice will be evaluated to determine their impact on NPs knowledge of DDIs.

METHODS

This is a descriptive study that used quantitative methods to determine nurse practitioner characteristics and knowledge of drug-drug interactions. A cross-sectional design was employed to pursue the aims of this study to evaluate NPs organizational environment, to determine factors that are associated with NPs knowledge of DDIs and to evaluate NPs' perceptions of the rate and severity of DDIs in practice.

Sample

A convenience sample of NPs was drawn from attendees of the American Academy of Nurse Practitioners 25th annual conference in Phoenix, Arizona in June, 2010. This population was recruited because they represent the diverse primary and acute care NP specialties as well as are geographically located throughout the United States. In addition, this population was recruited because as prescribers and members of health care teams they are responsible for rational medication use.

Survey Questionnaire

A survey designed to collect data on practice characteristics, technological characteristics, and demographics was used to identify factors specific to NPs that might account for differences in identification of DDIs. The survey instrument contained four sections. The first consisted of a questionnaire to assess NPs' opinion regarding drug safety and drug interactions, their usual source of DDI information along with practice characteristics. Section two targeted NPs knowledge regarding potential DDIs of select drug pairs. This segment contained 15 common potential drug-drug pairs routinely prescribed to be given orally and in outpatient settings; eleven pairs with known potential for DDIs and four without evidence of

interaction. DDI pairs were chosen from 25 clinically relevant drug pairs identified by Malone et al. (2004) that were commonly seen in community and ambulatory pharmacies. Drugs were listed by both brand and generic names. Without the aid of references, respondents were asked to classify each drug pair in one of five categories: a) avoid combination: risk of combination outweighs benefit; b) usually avoid combination: use only under special circumstances; c) take precautions: assess risk and take one or more precautions if needed; d) no special precautions: the risk of adverse outcomes is small or evidence suggests that the drugs do not interact; and e) not sure. Variations of this tool have been used to identify prescribers' DDI knowledge in previous studies (Ko, Malone, D'Agostino, et al., 2008; Ko, Malone, Skrepnek, et al., 2008; Malone, et al., 2004; Malone et al., 2005; Murphy et al., 2009). In addition, a study to determine instrument validity found the DDI instrument to be reliable and have evidence of good validity (Warholak et al., 2010). Question set three contained four questions to identify NPs perception of DDIs. These included: a) "there are too many DDIs to keep up with"; b) "it is important for prescribers to learn about DDIs"; c) "it is the responsibility of the pharmacist to catch DDIs"; and 4) "I am likely to consider DDIs as part of prescribing decisions". Response choices consisted of a 4-point Likert scale from disagree to agree. The last section contained questions regarding participant demographics.

Data Collection

The study was conducted during three days of conference proceedings. The first and last day of the conference were omitted due to investigator convenience. Researchers recruited subjects based on conference attendance and self-selection to survey completion. A booth was staffed by researchers located in a common area of the conference venue where attendees could

participate in the study by coming to the booth to gain study information and agree and consent to participate. No compensation of any kind was offered to attendees for participation. NPs who agreed to participate were asked to complete a survey instrument to assess their knowledge and perceptions of DDIs. The survey was estimated to take about ten minutes to complete. Participants could choose not to answer some or all of the questions. A drop box was placed at the booth to provide participants with an opportunity to complete the survey during a convenient time at the conference. Study participation was strictly voluntary and no identifying information was collected.

Protection of Human Subjects

Study approval was granted from the Human Subjects Protection Program Internal Review Board at The University of Arizona. The American Academy of Nurse Practitioners Research Review Board also granted permission for data collection at the conference.

DATA ANALYSIS

Surveys were completed by 306 out of 3,500 NP conference attendees. One survey was omitted from analysis because no DDI knowledge questions were answered. Multiple responses to a single question were also excluded from analysis. In addition, responses of 75 or more patients seen per work day in a 40 hour work week in an office-based practice setting (n = 8) were omitted. It is believed that those respondents may have misread the question to ask for the average number of patients seen per work week.

Frequency distributions were obtained to depict categorical variables and means for continuous variables. DDI knowledge was analyzed first to determine the number of drug pairs that were identified correctly and second, to determine the number of responses classified appropriately. A DDI knowledge variable was created using the number of correct responses for each of the 15 drug pairs from the DDI knowledge questionnaire. Responses of "not sure" were considered to be incorrect responses.

Hierarchical linear regression analysis was performed to assess the association between nurse practitioner practice characteristics and DDI knowledge. It is generally recommended to have a minimum of ten to 15 respondents per predictor (Field, 2005). The sample size (n = 237) was large enough to perform a regression analysis with 13 predictor variables.

Independent variables were entered in two separate blocks. The sequence of variable entry for block one and block two was based upon findings from previous research. Researchers reported that prescribers who practiced in general or family practice had higher DDI scores than those who were in specialty practices (Glassman, et al., 2002; Ko, Malone, D'Agostino, et al., 2008). In addition, Ko, Malone, D'Agostino, et al., (2008) found an inverse relationship

between DDI knowledge scores and years of experience as prescribers, although statistical significance was not reached. Glassman et al., (2002) reported that the more time prescribers spent in clinic the more interacting and contraindicated drug pairs they identified. Age was also identified as a significant predictor of DDI knowledge with younger clinicians having higher DDI knowledge scores (Glassman, et al.); however, age was not included on this survey. The first block contained number of hours/week seeing patients, years as a practicing licensed prescriber and practice specialty. Responses to practice specialty were entered as a dichotomous variable of either family or specialty practice. Block two included primary practice setting, use of electronic medical records (EMR) in practice, method of prescribing medications, workload (patients seen/day, hours/week seeing patients), the extent that risk of DDI affects drug selection, usual source of DDI information, perceptions of DDIs and drug safety and whether they had witnessed a patient who had a DDI that caused harm. Two variables, method for prescribing medications and practice setting were coded to permit comparisons to a reference group in the model. EMR was the reference group for the method for prescribing and office-based clinic group practice for practice setting. Evaluations of the R^2 statistic from block one and R^2_{change} statistic from block 2 was performed to determine the amount and significance of variance that was explained in each model by the addition of the designated predictors. Tests for assumptions of independent errors, multicollinearity, influential cases, linearity and normality demonstrated that the assumptions of the regression were met.

A one-way analysis of variance (ANOVA) was utilized to compare mean DDI knowledge scores among prescriber's sources of DDI information; a pharmacist, computerized alert system, personal digital assistant (PDA) or another method. Statistical significance was determined by

an *a priori* alpha set at 0.05 for all analyses. The homogeneity of variance was violated; therefore, the Welch-F ratio was reported. Statistical analyses were conducted using SPSS 19.0 (An IBM Company, Chicago, IL).

RESULTS

Self-Reported Sample Demographic and Practice Characteristics

NP respondents' summary demographic and practice characteristics are provided in Table 1. The majority of NP survey respondents were female (94.4 %, n = 303), nationally board certified (97 %, n = 302) and averaged 9.23 ± 7.10 years (mean ± standard deviation [SD]) (n = 303) as a licensed prescriber. Responses to years as a licensed prescriber were diverse and ranged from 0 to 36 years with 38.6 % (n = 303) reporting 0 to 5 years, 24.8% (n = 303) 6 through 10 years, 21.2% (n = 303) 11 -15 years, 7.6% (n = 303) 16-20 years and 7.8% (n = 303) more than 20 years. Respondents reported seeing an average of 17.61 ± 10.12 patients per week (range 3 to 90, n = 293) and worked an average of 34.21 ± 11.84 hours per week (range 3 to 72, n = 301). Over half of respondents denied being on-call (57.1%, n = 301) and one-fourth (26.6 %, n = 301) of those who took call stated they provided care for patients outside of their usual panel of patients. There was an almost equal ratio of NPs who practice in family practice NPs (54 %, n = 278) versus those who practiced in a specialty area (46 %, n = 278). The most commonly reported practice setting (n = 299) was office-based group practice (42.6 %), while 11.5% reported being in office-based solo practice settings and hospital-based clinics respectively, 10.8% in hospital acute care and 2.6% in urgent care settings. The remaining respondents (21.6 %, n = 299) were divided among urgent care, military, correctional, long-term and home care, Indian Health Service, telemedicine, geriatric and retail practice sites. Electronic order was the most common method identified for prescribing medications (52.6%, n = 293) followed closely by hand written order (44.7 %, n = 293). Over two-thirds of respondents (68.2 %, n = 293) reported the use of electronic medical records (EMR) at their primary practice site.

Table 1.
NP respondents' self-reported demographic and practice characteristics

Characteristic	**Category**	**% (n)[a]**
Gender	Male Female	5.6 (303) 94.4 (303)
National Board Certification	No Yes	3 (302) 97 (302)
Most common method used for prescribing medications	Hand-written order Telephone order Electronic order	44.7 (293) 2.7 (293) 52.6 (293)
Provides care for patients outside usual panel of patients	No Yes Not Applicable	16.3 (301) 26.6 (301) 57.1 (301)
Practice setting	Office-based solo practice Office-based group practice Hospital-based clinic Hospital acute care Urgent care Other	11.7 (299) 43.5 (299) 11.7 (299) 11.0 (299) 2.7 (299) 19.4 (299)
Electronic Medical Record [EMR] (Use of EMR at primary practice site)	No Yes	31.1 (302) 68.9 (302)
Specialty	Acute Adult Family Geriatric Neonatal Pediatric Psych/Mental Health Women's Health Student Other	3.6 (278) 5.4 (278) 54.0 (278) 1.8 (278) 0.0 (278) 2.5 (278) 1.1 (278) 3.6 (278) 0.4 (278) 27.7 (278)
Other		
	Prescriber (Number of years as a practicing licensed prescriber)	9.23 ± 7.095[b]
	Patients (Average number of patients seen per day)	17.61 ± 10.12[b]
	Work (Average hours/week seeing	34.21 ± 11.84[b]

	patients)	

a. Percentages may not total 100 because of rounding and missing data
b. Data are mean ± SD

Nurse Practitioner Perceptions of Drug Safety and Drug-Drug Interactions

NP's survey responses to questions about their perceptions of drug safety and potential DDIs are presented in table 2. The risk for drug interactions very much affected over two-thirds of respondents (69.8%, n = 302) with one-quarter (28.2%, n = 302) reporting they were affected somewhat. Three-quarters of respondents (74.8%, n = 302) indicated they had seen a patient who had a drug interaction that caused harm. Almost all respondents (92.8%, n = 296) felt an interaction caused by drugs occurred more frequently with two prescribers versus the same prescriber. One-third responded that they somewhat agreed (38.7%, n = 294) or agreed (33.1%, n = 294) there were too many DDIs to keep up with; 10.5% disagreed. The majority of respondents (92.8%, n = 298) agreed that it is important for prescribers to learn about DDIs and that they were likely to consider DDIs as part of their prescribing decisions (86.6%, n = 297). Half of NP respondents reported that they at least somewhat felt it was the responsibility of the pharmacist to catch DDIs (44.6% somewhat agree, 8.5% agree; n = 301) while close to half at least somewhat disagreed (24.9 somewhat disagree, 20.7 disagree, n = 301).

Table 2.
NP perceptions of drug safety and DDIs

NP perceptions of DDI rate and severity characteristic	Category	% (n)
Have seen a patient who had a drug interaction that caused harm?	No Yes	25.2 (305) 74.8 (305)
Which occurs more often, interaction caused by drugs prescribed by two different prescribers or same prescriber?	Same prescriber Two different prescribers	4.4 (296) 95.6 (296)
To what extent does the risk for a drug interaction affect your selection of a drug product?	Not at all A little Somewhat Very Much	0.0 (302) 1.0 (302) 28.5 (302) 70.5 (302)
There are too many DDIs to keep up with	Disagree Somewhat disagree Somewhat agree Agree	10.9 (294) 14.6 (294) 40.1 (294) 34.4 (294)
It is important for prescribers to learn about DDIs	Disagree Somewhat disagree Somewhat agree Agree	0.7 (298) 0.3 (298) 4.0 (298) 95.0 (298)
It is the responsibility of the pharmacist to catch DDIs	Disagree Somewhat disagree Somewhat agree Agree	20.9 (301) 25.2 (301) 45.2 (301) 8.6 (301)
I am likely to consider DDIs as part of prescribing decisions	Disagree Somewhat disagree Somewhat agree Agree	0.3 (297) 0.3 (297) 10.4 (297) 88.9 (297)

Nurse Practitioner Prescribers' Classification of Drug Pairs

NP respondents correctly classified from 0 to 12 out of 15 possible drug pairs on the DDI identification questions. The average number of accurately categorized drug pairs was 31.47% (n = 305) or 4.72 ± 2.29 pairs. Correct responses for drug pairs ranged from 15.7% (n = 302) for warfarin and gemfibrozil (drug combination to usually avoid) to 90.8% (n = 305) for

nitroglycerin and sildenafil (drug combination to avoid). Twenty-five percent or fewer (n = 305) of respondents correctly classified four of the five drug pairs that were considered to be usually avoided and to prescribe with precautions respectively. Warfarin and naproxen, however, were correctly classified by 27.9% (n = 305) of respondents as a combination to usually avoid and Warfarin and amiodarone (to be prescribed with precaution) were correctly identified by 37.6% (n = 298) of those surveyed. Approximately three-quarters of NPs (72.5%, n = 299) correctly classified acetaminophen with codeine and amoxicillin (no special precautions necessary). Less than one-third (n = 295) of respondents, however, correctly classified the remaining three drug pairs requiring no special precautions. Table 3 represents the percentages of NP prescriber responses for each of the 15 drug pairs on the DDI knowledge questions.

Table 3.
Responses to DDI knowledge questions (in percentages)[a,b]

Drug Pair[c]	Avoid Combination	Usually Avoid Combination	Take Precautions	No Special Precautions	Not Sure
acetaminophen/codeine (Tylenol w/ codeine®) + **amoxicillin** (Amoxil®) (n = 299)	1	2.6	9.8	**72.5**	12.1
carbamazepine (Tegretol®) + **clarithromycin** (Biaxin®) (n = 299)	27.5	22.3	**18.4**	3.6	26.2
digoxin (Lanoxin®) + **amiodarone** (eg, Cordarone®) (n = 300)	29.5	21.0	**25.6**	1.6	20.7
digoxin (Lanoxin®) + **clarithromycin** (Biaxin®) (n = 300)	19.7	18.4	**22.6**	9.2	28.5
digoxin (Lanoxin®) + **itraconazole** (Sporanox®) (n = 300)	24.3	16.1	**21.0**	3.6	33.4
digoxin (Lanoxin®) + **sildenafil** (Viagra®) (n = 301)	24.3	13.4	18.0	**23.3**	19.7

metformin (Glucophage®) + **erythromycin** (E-mycin®) (n = 295)	7.5	14.4	25.2	**26.6**	23.0
nitroglycerin (Nitro-Dur) + **sildenafil** (Viagra®) (n = 305)	**91.1**	3.0	1.3	0	4.6
simvastatin (Zocor®) + **itraconazole** (Sporanox®) (n = 300)	30.8	**20.7**	15.4	3.0	28.5
warfarin (Coumadin®) + **amiodarone** (eg. Cordarone®) (n = 298)	15.7	10.8	**37.7**	9.5	23.9
warfarin (Coumadin®) + **digoxin** (Lanoxin®) (n = 302)	5.6	7.2	36.1	**32.5**	17.7
warfarin (Coumadin®) + **fluconazole** (Diflucan®) (n = 302)	18.7	**17.4**	36.4	5.9	20.7
warfarin (Coumadin®) + **gemfibrozil** (Lopid®) (n = 302)	8.9	**15.7**	33.8	13.8	26.9
warfarin (Coumadin®) + **naproxen** (Naprosyn®) (n = 305)	41.0	**27.9**	21.0	2.6	7.5
warfarin (Coumadin®) + **sulfamethoxazole/trimethoprim** (Bactrim®) (n = 305)	17.7	**19.3**	36.1	10.8	16.1
a Correct answers in percentages are represented in bold type **b** Percentages may not total 100 due to rounding and missing data **c** US brand names were included on the survey instrument					

Factors Related to Nurse Practitioner Prescribers' Potential Drug-Drug Interaction Knowledge

Univariate correlation coefficients were obtained for DDI knowledge and demographic and practice factors entered in the hierarchical regression. A significant positive correlation was observed for NPs who reported practicing in an acute care hospital setting ($r = 0.145$, $p < .013$)

indicating a higher knowledge score. However, when added to block two of the hierarchical regression, it was not a significant predictor of DDI knowledge.

Hierarchical linear regression analysis was performed to predict the impact of perceptions of DDIs and demographic and practice characteristics on knowledge of DDIs. Table 4 provides a list of model predictors. Block one predictors accounted for only 1.1% of the variation in DDI knowledge scores ($R^2 = 0.01$, $p > .479$). With the addition of the second block of variables the value increased to 5.9% of the variance in knowledge of DDIs ($R^2 = .06$, $P > .726$). The addition of the second block of variables only accounted for 4.8 % more of respondents' knowledge of DDIs ($R^2_{change} = 0.05$, $p > .726$). Neither model was significant at improving our ability to predict NPs' DDI knowledge. Table 5 reports the unstandardized (B) and standardized (β) regression coefficients for each of the blocks.

Table 4
Hierarchical linear regression model predictors

Block (Entered)	**Predictor Variable with Definition**
Block 1	
	Specialty (Area of practice) Family Practice Specialty Practice
	Prescriber (Number of years as a practicing licensed prescriber)
	Work (Average hours/week seeing patients)
Block 2 (Additional Variables)	
	Risk (The extent the risk for a drug interaction affects your selection of a drug product)
	Experience (Have seen a patient who had a drug interaction that caused harm)

	Patients (Average number of patients seen per day)
	EMR (Most common method used for prescribing medications) Reference: Electronic order Rx Tele (Telephone order) Rx Hand (Hand-written order)
	Setting (Primary office/clinic practice site) Reference: Office-based group practice Setting Office Solo (Office-based solo practice) Setting Hosp Clinic (Hospital-based clinic) Setting Hosp Acute (Hospital acute care) Setting Urgent (Urgent care) Setting Other (Practice setting not included in above choices)
	EMR (Do you use electronic medical records at your primary practice site?)
	Too Many DDI (There are too many DDIs to keep up with)
	Important DDI (It is important for prescribers to learn about DDIs)
	Pharmacist DDI (It is the responsibility of the pharmacist to catch DDIs)
	Self DDI (I am likely to consider DDIs as part of prescribing decisions)

Table 5
Hierarchical regression results: NP practice characteristics, DDI perceptions and DDI knowledge

	B	***SE B***	***p-Value***
Block 1			
Constant	4.62	0.56	*.00*
Specialty	0.08	0.29	.79
Prescribe	-0.03	0.02	.23
Work	0.01	0.01	.48
Block 2			
Constant	3.20	2.39	.18
Specialty	-0.02	0.32	.96
Prescribe	-0.03	0.02	.20
Work	0.01	0.01	.73
Risk	-0.20	0.32	.53
Experience	-0.01	0.34	.99
Patients	0.00	0.02	.93
Rx Hand	0.01	0.40	.99
Rx Tele	-0.84	0.89	.34
Setting Office Solo	-0.45	0.51	.37
Setting Hosp Clinic	-0.38	0.51	.45
Setting Hosp Acute	0.88	0.52	.09
Setting Urgent	0.58	0.84	.49

Setting Other	-0.09	0.42	.83
EMR	-0.07	0.44	.88
Too Many DDI	-0.14	0.16	.39
Important DDI	-0.06	0.48	.91
Pharmacist DDI	0.16	0.16	.31
\ Self DDI	0.69	0.43	.11
NOTE: R^2= .011 for block 1, ΔR^2= .049 for block 2 (total R^2 = 0.06)			

Prescribers' Source of Drug-Drug Interaction Information and Drug-Drug Interaction Knowledge Scores

When asked about their usual method of being informed that a patient is about to be exposed to a potential drug interaction, computerized alert systems was reported by 40.3% (n = 253) of respondents, 31.6% (n = 253) by pharmacists and 22.1% (n = 253) by their personal digital assistant (PDA). Almost 6% (n = 253) reported using other references which included drug reference books and on-line sources. A one-way ANOVA was performed on NP prescribers' usual source of DDI information and DDI knowledge scores. Results of the one-way ANOVA revealed there were no significant effects of sources of DDI information on DDI Knowledge scores, $F(3, 71.45) = 1.003$, $p = .397$.

DISCUSSION

The purpose of this study was to identify NPs' knowledge of DDIs and whether there was an association with DDI knowledge and demographic and practice characteristics. The study aimed to describe the organizational environment in which NPs operate and to determine if these factors are associated with NPs knowledge of DDIs. In addition, the study sought to identify NPs' perception of the rate and severity of DDIs. A discussion of study findings is presented below.

Demographic and Practice Characteristics

Nurse practitioner demographic and practice characteristics were identified. Overall, NP study respondents were representative of the national sample of NPs. Similarities between practice characteristics were found between NP respondents from this study and those from a national NP practice site survey (AANP, 2010). Both samples were primarily female, maintained national board certification and prescriptive authority. Over half of NPs nationally see three to four patients per hour (60%) which is comparable to NP conference attendees who saw an average of 18 patients per day. NP respondents in this study were nearly equally divided among general (family practice) and specialty practice areas (54% versus 46% respectively, n = 278) which is congruent with national statistics (49.2% versus 50.7% respectively) (AANP). Just over nine years was the average number of years cited as a practicing licensed prescriber. While national statistics did not report specifically on number of years as a prescriber, it did report the average number of years in practice which approximated 10.5 years. National survey responses included only NPs who were in clinical practice (AANP), however, it is unknown whether all NP respondents to the national survey were licensed practicing prescribers. Office-

based practice setting was identified by over half of NP respondents (55.2%, n = 299) as their primary practice setting; 43.5% (n = 299) in group practice and 11.7% (n = 299) in solo practice. These statistics are slightly lower than national NP statistics that revealed 66% of NPs practice in primary care (AANP). NP respondents in hospital-based acute care and hospital-based clinic settings each comprised approximately 11% (n = 299) of NP respondents.

Knowledge of Potential Drug-Drug Interactions

Overall, NPs had low scores on the potential DDI knowledge questions, averaging 31. 5% (n = 305) correct responses to the management of drug-drug pairs. Fifteen drug pairs were chosen for inclusion in the DDI knowledge survey based on their clinical significance in the outpatient setting. NP respondents were asked to categorize each of the drug pairs according to the recommended management of the interaction as this is the expectation in clinical practice. Responses of "not sure" ranged from 4.6% (n = 305) for nitroglycerin and sildenafil to 33.4% (n = 300) for digoxin and itraconazole, with an average of 20.4% (n = 301). While different management strategies (Avoid Combination, Usually Avoid Combination and Take Precaution) for drug pairs could be argued depending upon the drug reference used (Abarca et al., 2004), responses of "not sure" were considered incorrect and reflect a lack of knowledge of potential DDIs.

NP DDI knowledge scores parallel overall findings from previous studies that found prescribers' knowledge of DDIs to be lacking (Glassman, et al., 2002; Ko, Malone, Skrepnek, et al., 2008). Glassman et al., (2002) reported VA prescribers correctly categorized 44% of the 10 drug-drug pairs included in the survey, although NPs comprised only 13% (n = 168) of their sample. Nearly 43% (n = 950) of correct responses for potential clinically significant DDIs were

reported in the study by Ko, Malone, Skrepnek, et al., (2008) to identify prescribers' knowledge of potential DDIs from prescribers identified from a national pharmacy benefit manager. However, NPs made up only 3.5% (n = 950) of their sample. It is also important to note that drug pairs contained in each of the studies, including the present study differed. Previous studies utilized data from the NAMCS to describe prescribing habits of NPs and physician assistants (PAs) in primary care settings and compared findings with physician prescribers. No differences were found in the type of drugs NP, PAs and physicians used in the pharmacotherapeutic management of their patients (Cipher, Hooker, & Guerra, 2006; Hooker & Cipher, 2005). Although DDI knowledge in this study is comparable to DDI knowledge of other providers, the level of knowledge of DDIs among NP respondents in this study is of concern.

In this study, NPs were asked to answer the DDI questions without the use of any type of drug reference. This was to determine their overall knowledge of potential DDIs. This is not the expectation in clinical practice and may partially explain low potential DDI knowledge scores. Drug references are readily available to prescribers in many forms. All NP respondents reported the use of a drug reference to assist in the identification of potential DDIs. Methods that NP respondents identified included computerized alert system, pharmacist, PDA or web based references (Epocrates, PEPID, Lexi-Comp), drug reference books, and physician colleagues. Although it was implied that respondents were to provide their usual (single) resource for potential DDIs, multiple methods were reported by 17% (n = 305) of respondents. It is unknown if these respondents could not decide upon one primary resource or whether they read the question to ask for all methodologies utilized. In future use of the survey, the amendment of the question to specify either one or all responses that apply would be helpful in data analysis.

Another possible mitigating factor for the low DDI knowledge scores is that there were a large number of cardiovascular agents due to their prevalence and risk for serious adverse drug events (Warholak, et al., 2010). If NP respondents do not routinely care for persons with cardiovascular disease, they may be unfamiliar with potential DDIs of many of the drug pairs in this questionnaire. Almost 50% (n = 278) of respondents reported practicing in a specialty area. These included pediatrics (2.3%, n = 278), women's health (3.3%, n = 278), and psych/mental health (1%, n = 278). In addition, "other areas" were reported by 27% (n = 278) of respondents. Areas of practice most commonly added in the comments section included pain management, dermatology, hematology/oncology, gastroenterology, neurology, ENT and hospice/palliative care. It is not known what percentage each of the "other" listed specialties comprises; however, NPs in non-cardiology related specialty practices may not routinely provide care for patients on these drugs and this could impact NPs' potential DDI knowledge scores.

Demographic and Practice Characteristics Related to Nurse Practitioners' Potential Drug-Drug Interaction Knowledge

While statistical significance was not reached with any of the predictor variables in the hierarchical regression analysis, examination of the data for possible implications and areas for further study is important. The study described above by Glassman et al. (2002) found that generalist prescribers' had higher potential DDI knowledge scores compared to those in specialty practices. Similar findings were echoed in previous research by Ko, Malone, D'Agostino, et al., (2008) that utilized a pharmacy claims database of national prescribers to identify demographic and practice factors that impact prescribers' knowledge of potential DDIs. These findings were not upheld among NP prescribers in the current study. The lack of a significant difference of

DDI knowledge between family and specialty NPs may be explained by their education. NPs receive a generalist education. Although there are a few exceptions, most NPs obtain specialty training on the job; therefore, they have the same basic drug knowledge.

Number of years as a licensed practicing prescriber was entered in the first block of the regression model based upon previous research (Ko, Malone, D'Agostino, et al., 2008). NPs' years of prescribing were inversely related to DDI knowledge, although it was not statistically significant. These findings mirrored previous results (Ko, Malone, D'Agostino, et al.). A possible reason this relationship may exist is the increased national focus on patient safety and ADEs (IOM, 2007). With the increased emphasis on the prevention of DDIs, it is possible that NP curricula have included more content related to potential DDIs. NPs with more experience have been out of school longer and may not have had the depth of education regarding potential DDIs as those with fewer years of experience. Those who have been out of school longer may not remember potential DDIs that were learned throughout NP education, especially if they do not routinely prescribe the drug pairs included in the DDI knowledge survey.

Number of hours worked per week was not found to be a significant predictor of DDI knowledge. The number of drugs that are on the market may partially explain this. With the vast quantity of pharmacologic options, not to mention the new drugs that are being introduced, it is impossible for prescribers to remain current on all potential DDIs. The majority of NPs felt that there were too many DDIs to keep up with. Nearly all NP respondents considered DDIs as a part of their decision making process when prescribing which testifies to the awareness NPs have regarding potential DDIs. With the enormity of both the pharmaceutical choices as well as the

incidence of DDIs and potential for harm, it is possible that NPs do not commit DDI knowledge to memory but rely on different drug resources to assist in their identification.

According to cognitive continuum theory, social and practice environments impact clinical decision making (Hamm, 1988) including safe prescribing. This was demonstrated in findings from a study discussed above of national prescribers. Researchers reported that NPs in office-based solo practice had lower scores on DDI knowledge questions (Ko, Malone, D'Agostino, et al., 2008). In this study, a positive correlation between NP prescribers in hospital acute care settings and potential DDI knowledge scores ($p < .02$) was found, indicating higher knowledge scores. When entered as a variable in block two of the hierarchical regression model, however, no practice setting, including hospital acute care or office-based solo practice settings were a significant predictor of DDI knowledge. The explanation for this discrepancy is not clear. Perhaps a larger sample is needed to evaluate factors with multiple response options such as practice settings and specialties. With further exploration, these factors could be examined more fully.

Perceptions of Rate and Severity of Drug-Drug Interactions

NPs' perception of the rate and severity of DDIs was identified and evaluated to determine their association with NPs' DDI knowledge. The majority of NP respondents reported having seen a patient that had experienced a drug interaction that caused harm (74.8%, n = 305), felt that DDIs were more often caused by drugs that were prescribed by two different prescribers (95.6%, n = 296), and that the risk for a drug interaction very much affected their drug selection (70.5%, n = 302). These factors, however, were not found to be significant predictors of DDI knowledge. This is contradictory to prior research that demonstrated an increased number of

correct drug pair responses in respondents who reported that their drug selection was very much affected by the risk for a drug interaction (Ko, Malone, D'Agostino, et al., 2008; Ko, Malone, Skrepnek, et al., 2008). It is possible, that while the risk of DDIs greatly impacts their drug selection, the drug pairs selected for inclusion in the study are not ones that are commonly prescribed by NPs and therefore, the DDI scores were not representative of NP knowledge.

Almost all NPs surveyed (95%, n = 298) agreed that it is important for prescribers to learn about DDIs. In light of the poor DDI knowledge scores, and the importance placed on DDI education by NPs, the development of continuing education (CE) offerings and resources that address potential DDI information should be a priority. Concepts from the cognitive continuum theory to promote analytical thinking should be used to guide CE development. A study of NPs in Nevada found that attendance of educational conferences, print and read self-study materials and interactive video conferencing were the top three preferred methods of obtaining CE (Charles & Mamary, 2002). Information regarding NPs' preferred CE delivery methods could be beneficial in the development and dissemination of potential DDI CE for NPs.

Sources of Potential Drug-Drug Interaction Information

A computerized alert system (40.3%, n = 253) was the most cited by NP respondents as their main source of potential drug interaction information. It is surprising this number is not higher due to the number of NPs that reported the use of an EMR (68.9%, n = 302) at their primary practice site. However, a study of nationwide prescribers reported that DDI information provided by 'other' sources was of significantly more benefit to prescribers than computerized DDI alerts. Prescribers in the same study identified PDAs and printed materials as the most common sources of DDI information (Ko, Malone, Skrepnek, et al., 2008). Approximately 22%

(n = 253) of NPs in the current study reported the use of PDAs. Prescribers selected from a pharmacy claims database reported that 68.4% (n = 316) of respondents identified the pharmacist as their usual source of DDI information (Ko, Malone, D'Agostino, et al., 2008) compared to 31.6% (n = 253) of NP prescribers in this study.

Results of the one-way ANOVA to examine the effects of the different sources of DDI information on NP DDI knowledge scores found no significant effects. The resources used by the NP respondents may not have any true relationship to DDI knowledge. Perhaps the reference type is not as important as the use of safe drug prescribing habits which would include the use of DDI drug references. Future studies to compare the use of different drug references to determine DDI knowledge scores would contribute to the understanding of factors that influence DDI knowledge.

Limitations of This Study

A limitation of this study was the small sample size. To further explore differences in DDI knowledge among factors that may predict this knowledge such as practice specialties and practice settings, a larger sample is needed.

The second limitation was the sampling method. The study used a cross sectional sample of convenience from a nurse practitioner national convention that convenes annually. The overall response rate for study participation approximated 10% (n = 306 out of 3,500 conference attendees). Characteristics of nonparticipants are unknown. These factors may restrict the representativeness of the sample (Trochim & Donnelly, 2007). However, demographic and practice characteristics from this sample were representative of a larger group of NPs with membership in the American Association of Nurse Practitioners, a national NP professional

organization. In addition, the convention was held in Phoenix, Arizona. It was hoped that conference attendees and survey respondents would be representative of all regions of the United States. This might not be the case, however. For future studies, it may be prudent to add a question regarding practice region to assist in the determination of the representativeness of the sample.

To encourage participation, the survey was designed as a self-report questionnaire. Conference participants who completed the survey may have responded inconsistent with how they would have actually responded in clinical practice. This may be because a) the circumstances for responding to the questionnaire could have been less than ideal due to distractions, b) they had difficulty with accurate recall, or c) they wanted to represent themselves in a more favorable manner which adds a potential for response bias (Donaldson & Grant-Vallone, 2002). Study participation was by self-selection as there were no inclusion or exclusion criteria. It is possible that conference attendees who knew the most or least about DDIs were more or less likely to participate respectively. Questionnaire instructions asked respondents not to use references during categorization of the drug pairs. To encourage survey completion and because of time constraints respondents were allowed to complete the questionnaire and return it to the drop box located at the conference booth. Since survey completion was not monitored, attendees could have used a drug reference to complete the DDI questionnaire, thus artificially inflating the DDI knowledge scores.

Limitations with the DDI knowledge assessment tool were also recognized. Several factors that have been identified to have potential influence on drug prescribing habits were not addressed. Further refinement of the tool is needed to include such practice locations as

region/state and rural versus urban areas. The DDI knowledge assessment questionnaire demonstrated good reliability and validity among health professional students (Warholak, et al., 2010). It is important for further validation of the questionnaire to be performed in the NP population to ensure it is reflecting true NP knowledge of DDIs.

Areas for Further Study

This and other studies have documented low DDI knowledge among prescribers. The ultimate goal was to identify factors that influence knowledge of potential DDIs and safe prescribing habits, thus preventing the prescription of drugs with potentially dangerous DDIs. This study does not provide sufficient data to identify factors associated with NPs limited DDI knowledge. Further research is warranted to explore possible factors that influence knowledge of potential DDIs. Such factors include differences among geographic regions, practice locales and practice areas. In addition, practices used in prescribing such as the use of drug reference materials should be evaluated. Finally, further studies should target interventions to improve NP knowledge of potential DDIs.

In light of the positive correlation between NPs in hospital acute care settings and DDI knowledge, further exploration of practice settings is warranted. While practice settings were described in the current study, specific states or regions of the US were not. This is important because regulations for NP prescriptive authority differ from state to state (Phillips, 2010) and this may impact NPs drug choices and their knowledge of potential drug pair interactions.

Differentiation of practice locale between rural and urban sites also may be meaningful. The role of the NP grew out of the need for primary care services in underserved areas (Brush & Capezuti, 1996). Current statistics indicate that approximately 20% of NPs practice in rural

areas (AANP, 2010). Many NPs in rural areas may not have access to physician or NP colleagues in which to informally consult regarding treatment options that include the potential for DDIs (Hooker & Berlin, 2002). Findings from a recent study revealed that NPs in rural practices wrote a significantly greater number of prescriptions compared to their PA and physician colleagues (Hooker & Cipher, 2005). In consideration of these factors, it would be prudent to add practice locale to the DDI survey. This data could be used to determine whether practice locale is a meaningful factor in NPs knowledge of potential DDIs.

Further studies need to be undertaken that consider NPs' different areas of practice specialties and their relationship to knowledge of potential DDIs. Ko, Malone, D'Agostino (2008) reported prescribers in psychiatry/neurology, obstetrics/gynecology, pediatrics, cardiology and "other" specialty practices had lower potential DDI knowledge scores than those in family/general practice. Cardiovascular drugs are among the most common drug classes prescribed (Schappert & Rechtsteiner, 2008) and have been identified as common offenders of potential DDIs (Warholak, et al., 2010). Persons on psychotropic agents have also been identified as being at high risk for DDIs because of the incidence of polypharmacy (Preskorn & Flockhart, 2009). Specialty providers may have little experience with medications outside their field of expertise. In this study, the numbers in each specialty area were too small to examine potential DDI knowledge among NPs in different specialty areas. Further studies should be designed with adequate sample sizes to examine the association between NPs who practice among different specialty areas and their knowledge of potential drug interaction pairs consistent with their practice specialty.

The use of drug references is consistent with NP prescribing practice. The current study asked respondents to categorize drug pairs without the aid of references. Further studies to determine NPs knowledge of potential DDI with the use of drug reference material need to be performed. The study of VA providers to identify clinicians' recognition of DDI knowledge allowed prescribers to use drug references (Glassman, et al., 2002). Clinicians' correctly classified 54% of contraindicated drug pairs, 53% of interacting pairs and 44% (n = 168) of all drug-drug pairs. The incidence or method of drug reference use in DDI classification was not reported, however. Perhaps those who used drug references had higher correct response rates. The option to use typical drug references to categorize management of drug-drug pairs would allow for critical thinking versus memorization. Additionally, it would assist in the identification of NP prescribers' prescribing habits in regard to drug references, their preferred methods and usefulness in clinical practice.

An important area for further study is the identification of interventions that promote safe NP prescribing habits. Strategies that aim to enhance NP knowledge of potential DDIs are essential to reduce the incidence of preventable ADEs. Warholak et al. (2010) reported a lack of knowledge of DDIs among health professional college students which included nurse practitioner students. Efforts to improve knowledge of potential DDIs must begin in NP education and continue post graduation. Remaining current on drug information is challenging for prescribers with the number of new drugs available, additional indications for use of drugs already on the market and the discovery of factors that lead to new drug prescribing guidelines. Research is needed to identify effective methods that foster the identification and correct management of possible drug interactions in clinical practice. Interventions that are found to

improve safe drug prescribing practices should be disseminated to nurse practitioner prescribers and translated into practice. Educational efforts that target increased recognition and management of DDIs among nurse practitioners is crucial to reduce the incidence of potential DDIs and improve patient safety.

Conclusion

Study findings lend support to the body of knowledge that purports prescribers' have limited knowledge of potential DDIs in the absence of drug references. Data is provided to describe NP prescribers' demographic and practice characteristics, however, these factors did not significantly predict NPs' knowledge of potential DDIs. All NP prescribers reported the use of either a pharmacist, computerized drug alert or drug reference material to alert them of a potential DDI. Nearly all NPs considered DDIs as part of their prescribing decisions and most agreed that there were too many DDIs to keep up with. NPs also identified learning about potential DDIs as important. In light of these findings, it is imperative to identify methods to assist NP prescribers in the identification and management of potential DDIs. Improved identification of potential DDIs will lead to a reduction in preventable adverse drug events.

REFERENCES

Abarca, J., Malone, D. C., Armstrong, E. P., Grizzle, A. J., Hansten, P. D., Van Bergen, R. C., & Lipton, R. B. (2004). Concordance of severity ratings provided in four drug interaction compendia. *Journal of the American Pharmacists Association 44*(2), 136-141.

American Academy of Nurse Practitioners [AANP]. (2010). Nurse practitioner facts, from http://aanp.org/NR/rdonlyres/18B3CED3-2586-42F4-8855-607E21733FA5/4307/NPWeekNPFacts1.pdf

Aparasu, R., Baer, R., & Aparasu, A. (2007). Clinically important potential drug-drug interactions in outpatient settings. *Research In Social & Administrative Pharmacy, 3*(4), 426-437.

Bates, D. W., Cullen, D. J., Laird, N., Petersen, L. A., Small, S. D., Servi, D., . . . Leape, L. L. (1995). Incidence of adverse drug events and potential adverse drug events: Implications for prevention. *Journal of the American Medical Association, 274*(1), 29-34.

Brush, B. L., & Capezuti, E. A. (1996). Revisiting "a nurse for all settings": The nurse practitioner movement, 1965-1995. *Journal of the American Academy of Nurse Practitioners, 8*(1), 5-11.

Buajordet, I., Ebbesen, J., Erikssen, J., Brors, O., & Hilberg, T. (2001). Fatal adverse drug events: the paradox of drug treatment. *Journal of Internal Medicine, 250*(4), 327-341.

Budnitz, D. S., Pollock, D. A., Weidenbach, K. N., Mendelsohn, A. B., Schroeder, T. J., & Annest, J. L. (2006). National surveillance of emergency department visits for outpatient adverse drug events. *Journal of the American Medical Association, 296*(15), 1858-1866.

Chao, S. D., & Maibach, H. I. (2005). Lack of drug interaction conformity in commonly used drug compendia for selected at-risk dermatologic drugs. *American Journal of Clinical Dermatology, 6*(2), 105-111.

Charles, P. A., & Mamary, E. M. (2002). New choices for continuing education: A statewide survey of the practices and preferences of nurse practitioners. *Journal of Continuing Education in Nursing, 33*(2), 88-91.

Cipher, D. J., Hooker, R. S., & Guerra, P. (2006). Prescribing trends by nurse practitioners and physician assistants in the United States. *Journal of the American Academy of Nurse Practitioners, 18*(6), 291-296.

Donaldson, S. I., & Grant-Vallone, E. J. (2002). Understanding self-report bias in organizational behavioral research. *Journal of Business and Psychology, 17*(2), 245 - 260.

Field, A. (2005). *Discovering statistics using SPSS* (2nd ed.). Thousand Oaks, CA: Sage Publications.

Gandhi, T. K., Weingart, S. N., Borus, J., Seger, A. C., Peterson, J., Burdick, E., . . . Bates, D. W. (2003). Adverse drug events in ambulatory care. *New England Journal of Medicine, 348*(16), 1556-1564.

Gandhi, T. K., Weingart, S. N., Seger, A. C., Borus, J., Burdick, E., Poon, E. G., . . . Bates, D. W. (2005). Outpatient prescribing errors and the impact of computerized prescribing. *Journal of General Internal Medicine, 20*(9), 837-841.

Glassman, P. A., Simon, B., Belperio, P., & Lanto, A. (2002). Improving recognition of drug interactions: Benefits and barriers to using automated drug alerts. *Medical Care, 40*(12), 1161-1171.

Goldberg, R. M., Mabee, J., Chan, L., & Wong, S. (1996). Drug-drug and drug-disease interactions in the ED: Analysis of a high-risk population. *American Journal of Emergency Medicine, 14*(5), 447-450.

Grymonpre, R. E., Mitenko, P. A., Sitar, D. S., Aoki, F. Y., & Montgomery, P. R. (1988). Drug-associated hospital admissions in older medical patients. *Journal of the American Geriatrics Society, 36*(12), 1092-1098.

Gu, Q., Dillon, C. F., & Burt, V. L. (2010). Prescription drug use continues to increase: U.S. prescription drug data for 2007-2008 *NCHS Data Brief No. 42*. Hyattsville, MD: National Center for Health Statistics.

Hamilton, R. A., Briceland, L. L., & Andritz, M. H. (1998). Frequency of hospitalization after exposure to known drug-drug interactions in a Medicaid population. *Pharmacotherapy, 18*(5), 1112-1120.

Hamm, R. M. (1988). Clinical intuition and clinical analysis: Expertise and the cognitive continuum. In J. A. Dowie & A. S. Elstein (Eds.), *Professional judgement: A reader in clinical decision making* (pp. 78 - 105). Cambridge: Cambridge University Press.

Hammond, K. R. (1978). Towards increasing competence of thought and public policy formation. In K. R. Hammond (Ed.), *Judgement and decision in public policy formation* (pp. 11-32). Boulder, CO.

Hammond, K. R. (1996). *Human judgement and social policy: Irreducible uncertainty, inevitable error*. New York: Oxford University Press.

Hammond, K. R., Hamm, R. M., Grassia, J., & Pearson, T. (1987). Direct comparison of the efficacy of intuitive and analytical cognition in expert judgement. *IEEE Transactions on Systems, Man, and Cybernetics, 17*(5), 753-770.

Hooker, R. S., & Cipher, D. J. (2005). Physician assistant and nurse practitioner prescribing: 1997-2002. *Journal of Rural Health, 21*(4), 355-360.

Institute of Medicine [IOM]. (2007). *Preventing Medication Errors*. Washington, D. C.: The National Academies Press.

Jankel, C. A., & Fitterman, L. K. (1993). Epidemiology of drug-drug interactions as a cause of hospital admissions. *Drug Safety, 9*(1), 51-59.

Jankel, C. A., McMillan, J. A., & Martin, B. C. (1994). Effect of drug interactions on outcomes of patients receiving warfarin or theophylline. *American Journal of Hospital Pharmacy, 51*(5), 661-666.

Jankel, C. A., & Speedie, S. M. (1990). Detecting drug interactions: A review of the literature. *Drug Interaction and Clinical Pharmacy, 24*(10), 982-989.

Jha, A. K., Kuperman, G. J., Rittenberg, E., Teich, J. M., & Bates, D. W. (2001). Identifying hospital admissions due to adverse drug events using a computer-based monitor. *Pharmacoepidemiology & Drug Safety, 10*(2), 113-119.

Kelly, W. N. (2001). Potential risks and prevention, Part 1: Fatal adverse drug events. *American Journal of Health-System Pharmacy, 58*(14), 1317-1324.

Ko, Y., Malone, D. C., D'Agostino, J. V., Skrepnek, G. H., Armstrong, E. P., Brown, M., & Woosley, R. L. (2008). Potential determinants of prescribers' drug-drug interaction knowledge. *Research in Social and Administrative Pharmacy, 4*(4), 355-366. doi: 10.1016/j.sapharm.2007.10.004

Ko, Y., Malone, D. C., Skrepnek, G. H., Armstrong, E. P., Murphy, J. E., Abarca, J., . . . Woosley, R. L. (2008). Prescribers' knowledge of and sources of information for potential drug-drug interactions: A postal survey of US prescribers. *Drug Safety, 31*(6), 525-536.

Langdorf, M. I., Fox, J. C., Marwah, R. S., Montague, B. J., & Hart, M. M. (2000). Physician versus computer knowledge of potential drug interactions in the emergency department. *Academic Emergency Medicine, 7*(11), 1321-1329.

Leape, L. L., Bates, D. W., Cullen, D. J., Cooper, J., Demonaco, H. J., Gallivan, T., . . . Vander Vliet, M. (1995). Systems analysis of adverse drug events. *Journal of the American Medical Association, 274*(1), 35-43.

Lewis, P. J., Dornan, T., Taylor, D., Tully, M. P., Wass, V., & Ashcroft, D. M. (2009). Prevalence, incidence and nature of prescribing errors in hospital inpatients: A systematic review. *Drug Safety, 32*(5), 379-389. doi: http://dx.doi.org/10.2165/00002018-200932050-00002

Mahoney, D. F., & Ladd, E. (2010). More than a prescriber: Gerontological nurse practitioners' perspectives on prescribing and pharmaceutical marketing. *Geriatric Nursing, 31*(1), 17-27.

Malone, D. C., Abarca, J., Hansten, P. D., Grizzle, A. J., Armstrong, E. P., Van Bergen, R. C., . . . Lipton, R. B. (2004). Identification of serious drug-drug interactions: Results of the partnership to prevent drug-drug interactions. *Journal of the American Pharmacists Association: JAPhA, 44*(2), 142-151.

Malone, D. C., Hutchins, D. S., Haupert, H., Hansten, P., Duncan, B., Van Bergen, R. C., . . . Lipton, R. B. (2005). Assessment of potential drug-drug interactions with a prescription claims database. *American Journal of Health-System Pharmacy, 62*(19), 1983-1991.

McDonnell, P. J., & Jacobs, M. R. (2002). Hospital admissions resulting from preventable adverse drug reactions. *Annals of Pharmacotherapy, 36*(9), 1331-1336.

Melmon, K. L. (1971). Preventable drug reactions--causes and cures. *New England Journal of Medicine, 284*(24), 1361-1368.

Moore, T. J., Cohen, M. R., & Furberg, C. D. (2007). Serious adverse drug events reported to the Food and Drug Administration, 1998-2005. *Archives of Internal Medicine, 167*(16), 1752-1759.

Murphy, J. E., Malone, D. C., Olson, B. M., Grizzle, A. J., Armstrong, E. P., & Skrepnek, G. H. (2009). Development of computerized alerts with management strategies for 25 serious drug-drug interactions. *American Journal of Health-System Pharmacy, 66*(1), 38-44.

Phillips, S. J. (2010). Legislative update: Regulatory and legislative successes for APNs. *The Nurse Practitioner 35*(1), 24-47.

Preskorn, S. H., & Flockhart, D. (2009). 2010 Guide to psychiatric drug interactions. *Primary Psychiatry, 16*(12), 45-74.

Roper Starch Worldwide. (2001). Self-care in the new millennium. Washington, D. C.: Consumer Healthcare Products Association.

Sandson, N. (2005). Economic grand rounds: Drug-drug interactions: The silent epidemic. *Psychiatric Services, 56*(1), 22-24.

Schappert, S. M., & Rechtsteiner, E. E. (2008). Ambulatory medical care utilization efforts for 2006 *National Health Statistics Reports No. 8*. Hyattsville, MD.: National Center for Health Statistics.

Seymour, R. M., & Routledge, P. A. (1998). Important drug-drug interactions in the elderly. *Drugs & Aging, 12*(6), 485-494.

Shaoul, R., Shahory, R., Tamir, A., & Jaffe, M. (2002). Comparison between pediatricians and family practitioners in the use of the prokinetic cisapride for gastroesophageal reflux disease in children. *Pediatrics, 109*(6), 1118-1123.

Standing, M. (2008). Clinical judgement and decision-making in nursing - nine modes of practice in a revised cognitive continuum. *Journal of Advanced Nursing, 62*(1), 124-134.

Thomsen, L. A., Winterstein, A. G., Sondergaard, B., Haugbolle, L. S., & Melander, A. (2007). Systematic review of the incidence and characteristics of preventable adverse drug events in ambulatory care. *Annals of Pharmacotherapy, 41*(9), 1411-1426.

Trochim, W. M. K., & Donnelly, J. P. (2007). *The research methods knowledge base* (3rd ed.). Cincinnati, OH: Atomic Dog Publishing.

United States Department of Health and Human Services. (2009). Proposed healthy people 2020 objectives: Medical product safety, from http://www.healthypeople.gov/hp2020/objectives/TopicArea.aspx?id=33&TopicArea=Medical+Product+Safety

Warholak, T. L., Menke, J. M., Hines, L. E., Murphy, J. E., Reel, S., & Malone, D. C. (2010). A drug-drug interaction knowledge assessment instrument for health professional students: A Rasch analysis of validity evidence. *Research in Social and Administrative Pharmacy*. doi: 10.1016/j.sapharm.2010.01.001

Winterstein, A. G., Johns, T. E., Rosenberg, E. I., Hatton, R. C., Gonzalez-Rothi, R., & Kanjanarat, P. (2004). Nature and causes of clinically significant medication errors in a tertiary care hospital. *American Journal of Health-System Pharmacy, 61*(18), 1908-1916.

Zhan, C., Arispe, I., Kelley, E., Ding, T., Burt, C. W., Shinogle, J., & Stryer, D. (2005). Ambulatory care visits for treating adverse drug effects in the United States, 1995-2001. *Joint Commission Journal on Quality & Patient Safety*, *31*(7), 372-378.