

The Relationship between Hepatitis C Virus Status and Medication Adherence for Adults
with Cardiac Issues

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DEDICATION

This dissertation is dedicated to my husband Tony, my children Austin and Braden, and my parents Ray and Clarissa. Tony, thank you for always encouraging and supporting me to achieve my dreams. Austin and Braden, thank you for your love and support. Daddy and Mommy, although you are no longer with us, your love and work ethic still empowers me to reach my goals.

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ABSTRACT

The prevalence of hepatitis C virus infection and cardiovascular disease in the United States is on the rise and affects millions of people. CVD is more predominant among individuals with HCV infection and is reduced when HCV is treated and sustained virologic response is achieved. A gap in the literature exists regarding HCV infection and medication adherence among adults with cardiac issues. The purpose of this study was to: (1) to examine the characteristics of individuals infected with HCV experiencing cardiac issues and (2) to evaluate the relationship between HCV infection and medication adherence among those with cardiac issues. Guided by an adapted version of the Self-Regulation Model for Control of Chronic Disease, this retrospective, observational, longitudinal study used combined data from the National Health and Nutrition Examination Survey years 2011–2016. The weighted sample included 9,918,628 adults with cardiac issues. Descriptive statistics were obtained and a multivariate logistic regression model was used to estimate the relationship between HCV status and medication adherence, while controlling for intrapersonal and external factors. The findings revealed younger age, Hispanic ethnicity, and substance use had a positive impact on cardiac medication adherence. Participants with depressive symptoms, arthritis, health insurance, and access to care were less likely to adhere to cardiac medications. Multiple factors may impact medication adherence among adults with cardiac issues. Implications for future research, policy, and practice were identified and discussed.

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Abbreviations and Symbols

CVD	Cardiovascular Disease
CDC	Centers for Disease Control and Prevention
DAAs	Direct-Acting Antivirals
FDA	Food and Drug Administration
HBM	Health Belief Model
HCV	Hepatitis C Virus
HCV RNA	Hepatitis C Virus Ribonucleic Acid
HIV	Human Immunodeficiency virus
MEC	Mobile Examination Center
NHANES	National Health and Nutrition Examination Survey
SCT	Social Cognitive Theory
SVR	Sustained Virologic Response
TPB	Theory of Planned Behavior
UN	United Nations
U. S.	United States
WHO	World Health Organization

CHAPTER I: INTRODUCTION

Hepatitis C virus (HCV) is a blood-borne virus that can cause acute and chronic liver disease (World Health Organization, 2019a). The World Health Organization (WHO) estimates 71 million people globally have chronic HCV infection. In 2015, an estimated 1.74 million people worldwide were newly infected with HCV and only 19% of those with HCV knew their status in 2017 (WHO, 2019a; WHO, 2019b). In 2016, WHO member states endorsed strategies to guide actions toward eliminating HCV by 2030 (WHO, 2019b). In a progress report addressing the success of the measures to reduce HCV, the WHO found that testing and treatment are low and must “accelerate massively” to achieve the targets (2019b).

In the United States (U.S.), the Centers for Disease Control and Prevention (CDC) estimate 2.4 million people have chronic HCV infection (2019). From 2003–2013, mortality from HCV infection surpassed all other 60 notifiable infectious diseases combined in the U.S. (Ly et al., 2016). The risk for chronic liver disease, such as cirrhosis, for individuals infected with HCV is 10–20% over 20–30 years (Centers for Disease Control and Prevention [CDC], 2019). From 2003 to 2013, the CDC reported an increase of 75% in mortality from HCV infection (2016). In addition, the number of acute cases of HCV infection are rapidly increasing in the U.S. (Barritt et al.; CDC 2017; Hofmeister et al., 2018).

Treatment of HCV Infection

The goal of HCV treatment is to cure the infection, thus avoiding the long-term complications associated with the virus (European Association for the Study of the Liver [EASL], 2014). Few individuals clear the HCV infection spontaneously (CDC, 2019). Diagnosis of chronic HCV infection is confirmed after a four- to six-month period of measurable HCV ribonucleic acid (HCV RNA). HCV infection treatment is initiated after confirmation HCV RNA

testing and the presence of symptoms of chronic hepatitis by laboratory or histological findings (EASL, 2014).

Guidelines for treating HCV infection vary according to genotype, presence of cirrhosis (compensated or uncompensated), and previous exposure to treatment (American Association for the Study of Liver Diseases [AASLD], 2019). A sustained virological response (SVR) is an undetectable HCV RNA 12 weeks after treatment completion and is considered a cure (EASL, 2014).

Medication Adherence during HCV Treatment

Since the approval of oral direct-acting antiviral (DAA) agents for treatment of HCV infection in 2011, treatment regimens have improved in tolerability, efficacy, and availability. Less than 25% of individuals that initiated treatment with older treatment protocols, including injectable peg-interferon, completed the treatment regimen (Butt, McGinnis, Skanderson, & Justice, 2010). Medication adherence is higher with DAAs with less early discontinuation of the medication during treatment (de Avila Machado et al., 2019; Muller et al., 2019; Serper et al., 2019). Research has shown assistance from a multidisciplinary team improves medication adherence among individuals with HCV infection (Muller et al., 2019). Nurses have assisted in developing tailored treatment plans with success in reaching SVR among HCV-infected individuals (Sublette, Smith, George, McCaffery, & Douglas, 2015).

Treatment of HCV infection has evolved since the introduction of DAA drugs along with advancements in technology targeted at improving medication adherence in all diseases. With the development of phone applications and electronic medication dispensers for home use,

medication adherence has improved in the area of cardiac disease, thus similar results might be possible in the area of HCV infection (Hoffmann et al., 2018; Morawki et al., 2018).

Cardiac Disease among HCV-Infected Individuals

Cardiovascular disease (CVD) risk is elevated among individuals with HCV infection (Kakinami et al., 2013), including significantly increased risk of sick sinus syndrome, atrial fibrillation, and arrhythmia death (Wu et al., 2019). Treatment and eradication of HCV has shown improvement of cardiovascular outcomes in the clinical setting (Petta et al., 2016). HCV eradication is associated with a decreased rate of cardiovascular events, improved carotid atherosclerosis, and reduced risk of cardiovascular disease (Cacoub et al., 2018; Lapumnuaypol, Thongprayoon, Wijarnpreechac, & Cheungpasitporn, 2019; Petta et al., 2016). A gap in knowledge exists regarding medication adherence among HCV-infected individuals, especially those with cardiac issues.

Summary

This dissertation is divided into five chapters. This first chapter provides a brief introduction to HCV infection. The second chapter provides a literature review determining the state of the science regarding the impact of nursing interventions in the treatment of HCV infection. A discussion of what is known and what is not known about nursing interventions in the treatment of HCV is provided along with suggestions for future research. The third chapter discusses the identification of a nursing middle-range theory to guide research and provides examples of theory application on the impact of nursing interventions on medication adherence during HCV infection treatment. The fourth chapter is divided into two parts. Part A reports the findings of a descriptive study using publicly available data from the National Health and

Nutrition Examination Survey (NHANES) exploring the characteristics of individuals with HCV infection from years 2015–2016. Part B reports the findings of a retrospective, observational, longitudinal study using combined NHANES data years 2011–2016. A multivariate logistic regression model was used to estimate the relationship between HCV status and medication adherence among individuals with cardiac issues. Lastly, chapter five provides a brief discussion of policy, practice, and research implications for nurses and health care providers caring for HCV-infected individuals.

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CHAPTER II:
REVIEW OF THE LITERATURE. IMPACT OF NURSING INTERVENTIONS ON
MEDICATION ADHERENCE DURING HEPATITIS C TREATMENT: STATE OF THE
SCIENCE

As the dissertation was developed and a state of the science publication was completed, the knowledge gained highlighted the need for further research in the area of medication adherence using sophisticated statistical approaches with longitudinal data. A gap in the research was found to be gender-specific research and the impact of education level on medication adherence among HCV-infected individuals. By identifying factors that influence medication adherence, targeted educational plans might be developed for improved treatment adherence. An updated review of the literature and significance was completed. See Chapter IV B: The Relationship between HCV Status and Medication Adherence for Adults with Cardiac Issues.

Chapter 2, in full, is a reprint of the material as it appears in *Gastroenterology Nursing* 2018. The dissertation author was the primary investigator and author of this paper. This is a non-final version of an article published in final form in: Sheila Williams, 2018, "Impact of Nursing Interventions on Medication Adherence during Hepatitis C Treatment: State of the Science," *Gastroenterology Nursing*, 41/5. Reproduced with permission from Society of Gastroenterology Nurses and Associates, Inc.

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Abstract

This paper is a literature review to determine the state of the science regarding the impact of nursing interventions in the treatment of hepatitis C. Hepatitis C is a chronic disease impacting millions of people globally. Treatment is currently available that has the potential to cure the disease. Medication adherence is vital to the eradication of the disease. Nursing interventions could possibly assist in the improvement of medication adherence. By reviewing the literature, the identification of factors influencing patient outcomes was determined. Four themes identified in the literature are: influence of comorbidities, self-motivation, psychological factors, and provider support. The research studies are compared and contrasted within and across the themes. Identification of what is known and what is not known about nursing interventions in the treatment of hepatitis C is illustrated in the conclusion of the paper. Finally, suggestions for future research is presented. Specific areas of study are identified for focus in the future research.

Keywords: medication adherence, nursing interventions, hepatitis C

Hepatitis C is one of the leading causes of liver disease in the United States (Strinko, Bisceglie, & Hoffman, 2004). The current treatment regimen requires strict medication adherence to obtain virologic remission. Poor medication adherence among patients diagnosed with hepatitis C has been observed by providers who treat these patients. The purpose of this paper is to review the current literature on the implementation of nursing interventions during hepatitis C treatment and the impact of the interventions on treatment outcomes.

According to the Centers for Disease Control and Prevention (CDC, 2015), there are approximately 2.7 million Americans have chronic hepatitis C infection. Of those infected, 60-70% will develop chronic liver disease and 5-20% will develop cirrhosis over a period of 20-30 years (CDC, 2015). Until recently, chronic hepatitis C was treated by pegylated interferon and ribavirin. Both medications had multiple side effects which contributed to, along with other factors, in decreased medication adherence by patients. With advances in pharmaceutical research, new and more tolerable medications have been made approved by The Food and Drug Administration (FDA).

A contributing factor to patient difficulty with medication adherence was the complex treatment regimens and multiple doses of certain medications with strict timing rules. The newer antivirals approved for treatment of chronic hepatitis C have fewer side effects and less treatment length but still have strict dosing and timing guidelines (Sublette, Smith, George, McCaffery, & Douglas, 2015). As patients begin treatment it is important to recognize groups who may need extra guidance during therapy so medication adherence can be maintained and virologic response is improved. By conducting a literature review, identification of the impact of nursing

interventions on medication adherence during hepatitis C will guide and identify further research on factors influencing adherence.

Methods

A review of the literature was conducted by narrowing the research for nursing interventions in hepatitis C to the last five years. To identify the published research articles on nursing interventions in hepatitis C treatment, several databases were searched. The databases included were CINAHL, OVID, PsycINFO, PubMed, and Scopus. Keywords initially included hepatitis C, adherence, medication, and nursing intervention. After identification of another term used in research for medication adherence, compliance was added to the list of keywords.

The initial search of CINAHL was 64 finds which included 58 academic journals and five magazines. A search of PsycINFO yielded in the finding of 103 articles, and of those, 97 scholarly articles. The PubMed search found zero articles on the initial search but, after refining the search criteria to include keyword medication compliance, 37 articles were identified. OVID database search found eight related articles. After the initial search was completed, a brief scan of the article abstracts was completed. Articles included for consideration in the review were identified by relevance to the topic of medication adherence in hepatitis C. Fifteen articles were identified for review.

Upon review of the 15 selected articles, several similarities in the references of these articles were identified. A search of the Scopus database was completed for identification of related articles. This search found three additional articles thought to be the leading research in the area of nursing interventions and treatment of hepatitis C due to their appearance in several other research articles. These articles did extend further back in the timeframe that was initially

set a five years. All three research articles were dated 2008. These earlier articles were included in the review. Several articles were excluded after further review. One article was excluded due to the timeframe. It was more than 11 years old. Another article was excluded because it wasn't a research study. After the process of article selection was completed, 11 articles were identified for review.

Findings

After review and analysis of the selected articles, four themes were identified as important considerations for the impact of nursing interventions on hepatitis C treatment: (a) influence of comorbidities, (b) self-motivation, (c) psychological factors, and (d) provider support. This paper will critically analyze the research literature related to the identified themes. A conclusion with a summary of what is known and what is unknown about the impact of nursing interventions on hepatitis C treatment will be presented and the identification of areas for future research will be revealed.

Influence of Comorbidities

Two quantitative studies identified comorbidities as influencing factors in the treatment of hepatitis C. Bruce et al. (2012) completed a randomized control trial investigating hepatitis C treatment access and retention in a methadone maintenance treatment setting. Twenty-one subjects were randomized to receive hepatitis C treatment as modified by directly observed therapy or a liver specialty clinic as self-administered therapy. The researchers identified a high level of psychiatric comorbidity required increased level of vigilance by staff. Despite the weakness of a low sample size (N=21), the study design provided data comparisons between

nursing interventions during treatment, such as frequent contact with patients, and self-administered therapy.

Pizzirusso et al. (2014) investigated whether initiating hepatitis C treatment affected adherence to concomitant medications. The authors discovered that patients who were co-infected with human immunodeficiency virus (HIV) were less adherent to hepatitis C treatment during the first 12 weeks of treatment. Although not the purpose of the prospective quantitative study, these findings identify the need for future studies involving the relationship of comorbid medical illnesses and adherence to medication. The authors relied on patients self-reporting of adherence which weakened the study. Overall, adherence to concomitant medications did not decrease in patients who initiated hepatitis C treatment (Pizzirusso et al., 2014).

Although the two studies differ in their purpose and research design, both found comorbidities influence hepatitis C medication adherence. The impact of nursing interventions on hepatitis C treatment needs to account for the patient comorbidities when developing strategies for medication adherence. By identifying patient comorbidities prior to the initiation of hepatitis C treatment, barriers to medication adherence can be acknowledged and nursing interventions can be modified.

Self-Motivation

Shutt, Robathan, and Vyas's (2008) retrospective quantitative study assessed the impact on referral, assessment, and treatment of patients with chronic hepatitis C before and after the introduction of clinical nurse specialist. The authors obtained the records of patients diagnosed with hepatitis C between a designated timeframe from the Public Health Laboratory at Salisbury District Hospital. A comparison between patients who did not have clinical nurse specialist

intervention and who did have intervention was completed. The study findings showed significant improvement in patient follow-up and treatment rates. Self-motivation and frequent clinical contact improved medication adherence during hepatitis C treatment. Self-motivation was determined by the authors as compliance of the treatment regimen. Although the study size was small (N=118), the discovery of improved medication adherence when patients had improved clinic follow-up attendance was important as shown by improved treatment rates in the post-clinical nurse specialist period (7 vs 15 cases; $P=0.09$).

Sublette et al. (2015) focused on the perceptions of patients receiving treatment for hepatitis C. This existential phenomenological research study explored what factors influenced a patient's decision to commence treatment, ability to maintain adherence, and complete their treatment program. Patients undergoing hepatitis C treatment were recruited by a purposive sampling method. The authors found provider communication, identified as feedback of their clinical performance and personalized information regarding their illness, influenced the treatment experience. They also found social and emotional support facilitate treatment adherence and completion. Fear, stigma, and shame were identified as motivators for treatment initiation and completion.

Psychological Factors

Several of the articles selected for review identify psychological factors as impacting medication adherence. Sublette et al. (2014) evaluated the efforts of physicians and nurses to work around the lack of available resources such as multidisciplinary and shared-care psychosocial support. The study included 17 face-to-face interviews and three interviews via telephone from 10 physicians and eight nurses. The researchers estimated the sample to be

sufficient to achieve data saturation given the restricted purposive sample and narrow focus of the research. The study found motivators for treatment initiation to be fear and stigma. The following year, Sublette et al. (2015), also identified shame as another motivator for the initiation of treatment. Sublette et al. (2014) identified barriers to hepatitis C treatment adherence and completion including stigma, physical side effects, lack of practical support, limitations of the public medical system, unemployment, poor communication with healthcare professionals, complex treatment regimen, lack of social support, and psychological side effects. The study found physicians and nurses who treat hepatitis C experienced increased role expectations and responsibilities. No other studies have evaluated provider stress and the impact on patient medication adherence in hepatitis C treatment. A strength of the study was the identification of the need for future studies to analyze the professional cost for physicians and nurses, in regards to emotional support and burnout, who provide support to patients on treatment.

Sublette et al. (2015) also identified facilitators of hepatitis C treatment adherence and completion. They include fear of death, reducing feelings of stigma, emotional support from family and friends, planning for the future, exercise, good communication with healthcare professionals, resilience, unemployment, and effective practical support from healthcare professionals. The patients in this study were mostly male gender (90%), which is found frequently in the studies of this literature review.

Provider Support

Seven research studies indicated the importance of provider support to medication adherence during hepatitis C treatment. Cacoub et al. (2008) concluded from their prospective quantitative study that significant improvements in adherence to treatment occurred if patients

received therapeutic education. The therapeutic education was provided by a third party (healthcare professionals other than the provider). There was no protocol-specific intervention. A survey was completed to evaluate medication adherence. The researchers analyzed 674 patient relationships between adherence or virological response and a set of potential explanatory variables such as patient characteristics and treatment regimen. The sample size was large. The weaknesses of the study include comparisons that were completed on non-randomized groups and the data was self-reported. There was no instructions given on patient selection for education or how the education was provided. Along with the findings of improved adherence to treatment in the patients who received therapeutic education, the study revealed an improved sustained virological response in those patients who received therapeutic education (77% vs 70%, $P = 0.05$). The discovery of improved virologic response in relation to therapeutic education can have an impact on the long-term cost of hepatitis C such as a means to decrease these costs.

Larrey et al. (2008) evaluated the effects of systematic consultations with a nurse on patient adherence and the efficacy of hepatitis C therapy. Virologic response was better in the therapeutic education group compared to the standard clinical group. The randomized, comparative, multicentric prospective study included 244 patients allocated to two parallel groups by open-label randomization. Group A received systematic standardized consultation with a nurse while group B followed conventional clinical evaluation. Therapeutic education had a significant beneficial effect on several factors known to influence sustained virologic response such as treatment-naïve status, difficult-to-treat genotypes, and advanced fibrosis. The centralization of therapeutic education to only a specialized nurse is a weakness of the study. Although the use of a specialized nurse provided consistent delivery of the educational

interventions, other methods of education along with the specialized nurse would have been beneficial such as pharmacist education at the point of dispensing medications and provider education throughout the treatment regimen. Larrey et al. (2008) and Cacoub et al. (2008) both found an improvement in virological response with therapeutic education in the treatment of hepatitis C even though Cacoub et al. (2008) wasn't specifically investigating the virological response.

Lo Re et al. (2011) evaluated adherence to hepatitis C treatment in the real-world setting in their retrospective cohort study. The authors found, from a sample of 5706 patients obtained from the National Veterans Affairs Hepatitis C Clinical Case Registry, that adherence to medication during hepatitis C treatment resulted in higher rates of virologic response. In contrast to Larrey et al. (2008) and Cacoub et al. (2008), they found adherence to a specific medication, ribavirin, was less likely. Lo Re et al.'s (2011) findings contradict the findings of Bruce et al. (2012) and Pizzirusso (2014) in that they found comorbidities such as depression and bipolar disorder have no effect on medication adherence during treatment of hepatitis C. The large sample size of the study by Lo Re et al. (2011) is a strength along with the use of logistic regression for statistical analysis. There are several weaknesses of the study including the data source. Although the data was from a large national registry, the medication adherence was based on pharmacy fill dates, dosages, number dispensed, and dosing frequency (Lo Re et al., 2011). This method of data collection may not reflect the actual number of pills taken. Even though the sample size is a strength, the sample was mostly men (5482 out of total sample of 5706) which limits the study's generalizability.

A study similar to Lo Re et al. (2011) in design and data collection was conducted by Mitra, Davis, Beam, Medjedovic, and Rustgi (2010). The authors investigated real-world treatment patterns, medication adherence, and the impact of adherence on healthcare costs. Like Lo Re et al. (2011), Mitra et al. (2010) obtained the data for the retrospective study from a large database. Data was obtained from a database of medical and pharmacy claims from a national sample of 40 managed care health plans. A sample of 5086 patients who had no evidence of hepatitis B and had been recently treated for hepatitis C were included. Similar to Lo Re et al. (2011), the study by Mitra et al. (2010) found the demographic characteristics included higher number of male patients (3371) vs female patients (1715). Mitra et al. (2010) found hepatitis C treatment is costly and adherence to treatment appears suboptimal, which negatively impacts on medical costs.

The weakness of the study by Mitra et al. (2010) was the data could be influenced by database user error and record keeping. Described as a limitation, Lo Re et al. (2011) identified similar findings regarding user error in the database collection used in their study. Mitra et al. (2010) acknowledged patients may have been misidentified as having hepatitis C, medication records may not reveal prescriber intent, and failure to refill medication may be interpreted as completion of treatment and medication adherence. Strengths of the study by Mitra et al. (2010) included the large sample size and the identification of the impact of adherence in relation to medical cost.

Mitra et al. (2010) identified comorbidities such as thyroid disorder, bipolar disorder, depression, and schizophrenia as patient characteristics in the study. Unlike Bruce et al. (2012) and Pizzirusso et al. (2014), Mitra et al. (2010) did not investigate the effects of the

comorbidities on medication adherence during hepatitis C treatment. The inquiry of the patient comorbidities by the authors would have provided relevant data for use by others in research and approach to treatment. Mitra et al. (2010) evaluated the impact of adherence on healthcare costs among chronic hepatitis C patients. Including this study in the theme of provider support contributes to the importance of the financial effect provider support could have on medication adherence. Although Lo Re et al. (2011) investigated the relationship between medication adherence during treatment and virologic outcomes, it was also included in the theme of provider support to demonstrate the importance of adherence on virologic response.

The purpose of the case-control quantitative study by Namba et al. (2014) was to investigate the associations between nursing support and drug adherence during interferon therapy. The study strength was the study design, which was a case-control study of 24 patients with chronic hepatitis C who received combination therapy with interferon and ribavirin. A control group of 24 patients, who did not receive nursing support, was matched for age, sex, platelet count, and treatment regimen. All patients receiving nursing support completed a questionnaire, depression assessment, and nursing counseling. The results of the comparison of these two groups revealed that precise assessments of a patient's physical and mental health status by a nurse may help in the maintenance of drug adherence when the patients suffer from poor mental condition. Although the authors avoided labeling the physical and mental health issues as comorbidities, similarities could be made between the issues of physical and mental health in Namba et al. (2014) and the comorbidities in the articles by Bruce et al. (2012) and Pizzirusso et al. (2014).

Namba et al. (2014) were not able to verify the impact of nursing support in comparison with other factors affecting therapeutic outcomes such as quality of life. One possible reason for the inability to complete the comparison was the small sample size ($N = 24$). The authors found a higher sustained virologic response in patients with worse mental and physical health status during treatment of hepatitis C than non-sustained virologic response patients. Identification of this factor is important because continuously worsening conditions might pose a risk of lowered drug adherence (Namba et al., 2014). Nursing interventions could improve patient understanding of the importance of medication adherence and the effect adherence has on sustained virologic response.

Rodis and Kibbe (2010) investigated the impact of a partnership of care between patient, pharmacist, and nurse practitioner. The study was a quantitative study in which patients were recruited to participate in the study from a pharmacist-run hepatitis C virus education and monitoring service in collaboration with a partnering physician and nurse practitioner. Data of only 12 patients was used for analysis due to attrition.

The design of the study was poor. Before initiating hepatitis C treatment, the patients completed a survey, which evaluated medication adherence and quality of life. A follow-up survey was completed after receiving structured training on hepatitis C treatment and a monthly monitoring phone call from a pharmacist. There was no control group for comparison. The results of the study are based on the findings of the pre and post interviews. The study had multiple weaknesses. The survey results could have been biased as patients might have responded with the awareness that the surveys were received and reviewed by providers

responsible for their care. Medication adherence was self-reported as in the studies by Pizzirusso et al. (2014) and Sublette et al. (2015).

Despite the numerous weaknesses of the study (Rodis & Kibbe, 2010), the study was included in the review because of the identification of important areas for future research. The interdisciplinary model approach to hepatitis C treatment used by the authors presented new findings including patient satisfaction and the effect of patient satisfaction on medication adherence. The authors found involvement of a healthcare team may have an impact on medication adherence.

A relationship between medication adherence and the presence of comorbidities was evaluated. Rodis and Kibbe (2010) found participants with no comorbidities were more likely to find medication administration times inconvenient. The researchers' hypothesized healthier patients undergoing hepatitis C treatment may have more problems with medication adherence than patients with comorbidities who are more comfortable with multiple medications, dosage times, and dosage forms (Rodis & Kibbe, 2010). The theory of healthier patients demonstrating less medication adherence is the opposite of the findings by Bruce et al. (2012) and Pizzirusso et al. (2014). Patient adherence to psychotropic medications may have serve a protective factor against nonadherence to concomitant medications (Pizzirusso et al., 2014). The use of psychotropic medications may improve medication adherence in patients suffering from psychological conditions. Rodis and Kibbe (2010) identify depression as a comorbidity in which they found improved medication adherence.

Discussion

Much of the research on the impact of nursing interventions during hepatitis C treatment has been conducted on small sample size. Of the 11 research studies reviewed, six studies had a sample size of 78 or less participants. Most of these studies had fewer than 50 participants with several studies having 20 or less participants (Rodis & Kibbe, 2010; Sublette et al., 2015; Sublette et al., 2014). The authors identified the sample size as limitations of the studies. More studies involving larger sample size is needed.

Lo Re et al. (2011) and Mitra et al. (2010) obtained the samples for their studies from large data bases in the United States. The sample size of these studies was in the thousands. Both study designs were retrospective. The limitations of the studies included data base user error and record keeping. The advantages of retrospective studies include reliance on existing data, which results in less expense, and the measurement of the data cannot be biased by prior knowledge of the problem (Fink, 2010).

The research studies in the review spanned across several countries and settings. Sublette et al. (2015) recruited participants from metropolitan-based hospitals in Sydney, Australia. The authors included patients in various stages of hepatitis C treatment. They attempted to recruit patients who discontinued treatment but were unable to contact any candidates. Sublette et al. (2014) advertised on a popular nursing website for study participants. The authors investigated nurses and physicians who had experience in treating hepatitis C instead to the standard patient on treatment. Nurses and physicians from Australia and New Zealand were included in the study. Shutt et al. (2008) obtained data for their retrospective case study from the computer records of the Public Health Laboratory at Salisbury District Hospital in United Kingdom. Namba et al.

(2014) investigated 24 patients diagnosed with chronic hepatitis C who were being treated with pegylated interferon and ribavirin in a hospital outpatient clinic in Japan. The failure of the authors to identify participant inclusion criteria limits the study. Larrey et al. (2008) completed a randomized, comparative, multicentric prospective study in France. Cacoub et al. (2008) evaluated adherence to chronic hepatitis C treatment in the real-life setting in France. The settings for the prospective study were teaching hospitals, non-teaching hospitals, and private practice offices. A conclusion about the significance of nursing interventions in the treatment of hepatitis C can be completed based on the wide variety of settings and the global awareness of the issue.

The global impact of hepatitis C has been reported by the World Health Organization. Current treatment available has the ability to cure the disease. The research studies have shown medication adherence to treatment improves sustained virologic responses. A tailored treatment plan, instead of a general plan in which everyone is given the same instructions, would improve medication adherence (Sublette et al., 2015). A tailored treatment plan accounts for patient characteristics.

Several studies in the review implemented interventions based on patient characteristics, location, and co-infections. Participants were excluded from studies if they had previous liver transplant (Pizzirusso et al., 2014), diagnosis of human immunodeficiency virus and hepatitis B (Larrey, et al., 2008), and acute hepatitis C (Mitra, et al., 2010).

Patient characteristics include education level. Research is lacking in regards to patient education and medication adherence to hepatitis C treatment. Sublette et al. (2015) found communication between healthcare professionals and patients was a barrier when patient's

understanding of health information is low. Two studies in the review presented data on patient education but failed to analyze the relationship of the level of education and medication adherence in hepatitis C treatment (Cacoub, et al., 2008; Sublette et al., 2015).

All of the studies in the review reported the patient characteristic of gender. The authors failed to conclude any correlation between medication adherence during hepatitis C treatment and gender. Male gender accounted for far more of the participant population. The CDC reports a higher number of males infected with the virus than females but the gap between the numbers is narrowing (CDC, 2015). The authors failed to report if their findings of increased male gender statistic was due to study design or if more males are infected with the hepatitis C virus. Bruce et al. (2012) reported 10 female and 11 male participants. Only the study by Sublette et al. (2014) reported higher number of female participants (14 vs. 6) but the participants of the study were nurses and physicians, not patients.

Cacoub et al. (2008) included information such as employment status, origin of income, and debts as patient characteristics. The characteristics are important to report so the relationship between the characteristic and medication adherence, if any, could be analyzed. Other studies included ethnicity as a patient characteristic (Bruce et al., 2012; Lo Re et al., 2011; Pizzirusso et al., 2014; Rodis & Kibbe, 2010; Sublette et al., 2015). One study included geographical and insurance information (Mitra et al., 2010).

The reviewed studies varied in the data presented as patient characteristics. The studies also varied in participants and themes. Multiple studies crossed several themes. Influence of comorbidities on medication adherence during hepatitis C treatment was identified by Bruce et al. (2012) and Pizzirusso et al. (2014). The authors found comorbidities decreased medication

adherence. Other studies discovered comorbidities improved medication adherence during hepatitis C treatment (Lo Re et al., 2011; Rodis and Kibbe, 2010). They found patients who had comorbidities had better medication adherence when compared to patients who had no comorbidities. Rodis and Kibbe (2010) linked the improved adherence to the multiple medication regimen patients with comorbidities are accustomed to being prescribed. Lo Re et al. (2011) found similar medication adherence rates among patients with and without comorbidities. The comorbid medical conditions the authors identified were bipolar disorder, depression, and schizophrenia. Over half of the study participants had one of these diagnoses. Pizzirusso et al. (2014) suggested the possibility that medication adherence to psychotropic medications served as a protective factor against nonadherence.

The theme of self-motivation was identified in the study by Sublette et al. (2015). The authors found patients were motivated to complete treatment due to the shame and embarrassment they had experienced from having the condition. Patients were also motivated to initiate and complete treatment by their fear of morbidity and mortality (Sublette et al., 2015). In the study by Shutt et al. (2008), self-motivation ensured very good compliance. The authors never discussed the evaluation of self-motivation or the measurement used to determine self-motivation in the study.

Psychological diagnoses are prominent in the hepatitis C population. Several of the review studies included psychological factors in the patient characteristics as comorbidities. Sublette et al. (2014) investigated physician and nurse experiences of the barriers and facilitators to treatment adherence. The authors found physicians and nurses identified patient willingness to comply with treatment regimen, severe psychiatric issues, patient experience of side effects, and

patient determination as psychological factors affecting treatment outcomes. Bruce et al. (2012) found “psychiatric comorbidity required an increased level of vigilance and ongoing assessment by nursing and counseling staff” (p. 210). By identifying psychological factors prior to the initiation of treatment for hepatitis C, improved medication adherence could be achieved with diligent nursing interventions.

The theme of provider support included the majority of the review articles. Provider support includes phone calls and text reminders, healthcare professional advice regarding treatment decisions, and psychological support (Sublette et al., 2014). Factors identified as barriers to provider support are culture, environment, social network, and education level (Sublette et al., 2014). For patients starting treatment for chronic hepatitis C, identification of those barriers would improve medication adherence.

Cacoub et al. (2008) findings showed a significant improvement in adherence to treatment in patients who received therapeutic education. Larrey et al. (2008) found therapeutic education was especially important during the first three months of treatment. With the newer treatments approved by the FDA, shorter courses of treatment are going to be available. The findings by Larrey et al. (2008) recognized the importance of early interventions to sustain medication adherence to achieve virologic response. Lo Re et al. (2011) reported adherence to medication resulted in higher rates of virologic response.

Mitra et al. (2010) found hepatitis C treatment is costly and adherence to treatment appears suboptimal, which negatively impacts on medical costs. They identify possible factors for the increase cost such as disease progression, development of liver cirrhosis, and the need for expensive inpatient procedures. The researchers evaluated real-world treatment patterns and

adherence rates in a selected population. They did not investigate the positive impact of provider support on medication adherence during treatment for hepatitis C. Namba et al. (2014) did address provider support in their quantitative study. The researchers found nursing support can help patients to better understand the side effects of their drugs and the necessity of good drug compliance.

Rodis and Kibbe (2010) and Shutt et al. (2008) investigated the impact of the introduction of provider support to medication adherence during treatment for hepatitis C. Rodis and Kibbe (2010) evaluated the partnership of care between patient, pharmacist, and nurse practitioner. They found the partnership can have an impact on medication adherence. Shutt et al. (2008) investigated the impact on compliance of treatment for hepatitis C before and after the introduction of a clinical nurse specialist. They found frequent clinical contact ensured good compliance with treatment.

Conclusion

After completing the review of the current literature on the implementation of nursing interventions during hepatitis C treatment and reviewing the impact they have on treatment outcomes, recommendations regarding the future focus of research regarding the topic can be identified. Four themes emerged from the review including the influence of comorbidities, self-motivation, psychological factors, and provider support. The recommendations for future research will include key factors from each of these themes.

The World Health Organization (WHO) has identified hepatitis C as a worldwide problem. It is estimated that more than 185 million people around the world have been infected with the hepatitis C virus (WHO, 2015). One third of those who become chronically infected are

predicted to develop liver cirrhosis or hepatocellular carcinoma (WHO, 2015). The financial burden of untreated hepatitis C will have an impact on world nations for many years in the future. This review of the literature identified the importance of medication adherence's impact on sustained virologic response forgoing the need for unnecessary medical costs (Mitra et al., 2010). Improved medication adherence during treatment of hepatitis C can have a direct impact on healthcare costs.

Self-motivation improves medication adherence (Shutt, Robathan, & Vyas, 2008) is what is known about the impact of medication adherence during hepatitis C treatment. Factors contributing the self-motivation are fear, stigma, and shame (Sublette et al. 2015). By assessing for the presence of these factors before the initiation of treatment for hepatitis C, some risks for treatment failure can be identified. Nursing interventions could focus on other possible motivating factors for treatment of hepatitis C such as improved overall health. Future research might investigate barriers to motivation such as medication costs, availability of provider resources, and side effects of medication. An interview-based qualitative study conducted in a gastroenterology clinic that evaluates and treats patient with the diagnosis of hepatitis C could identify these barriers.

Psychological factors influence the impact of nursing interventions on medication adherence. Whether they have a positive or negative impact on medication adherence has yet to be shown. Pizzirusso et al. (2014) found patient adherence was unaffected in patients with the diagnosis of depression who are treated with psychotropic medications. The researchers theorized that patients have improved psychological well-being thus have improved medication compliance. Bruce et al. (2012) found the need for increased vigilance by staff in patients with

psychiatric comorbidity. Further research investigating the role of psychological factors in the treatment of hepatitis C and the relationship to medication adherence is needed. A mixed method study would be an appropriate approach to investigate the relationship of psychological factors and medication adherence in the hepatitis C population.

Provider support improves medication adherence in patients undergoing treatment for hepatitis C. Significant improvements in medication adherence have been seen in patients receiving therapeutic education during treatment for hepatitis C (Cacoub et al., 2008). Larrey et al. (2008) found improvement of medication adherence in patients receiving 48-week treatment with therapeutic education but saw no improvement in those patients receiving 24-week treatment regimen with therapeutic education. The researcher found overall improvement of virologic response in the therapeutic education group. Further research in a controlled setting evaluating the impact of therapeutic education by nursing on medication adherence and thus the virologic response is needed.

Namba et al. (2014) found better adherence to medication regimens with nursing support than with those who did not receive nursing support. Although these findings were not statistically significant, the identification of larger studies investigating similar criteria is needed. There needs to be clarification of the associations between nursing support services and either drug adherence or other therapy-associated factors. Larger scale studies need to be conducted using the case-control study design.

Involvement of a healthcare team or a collaborative approach to hepatitis C treatment may improve medication adherence during hepatitis C treatment. Rodis and Kibbe (2010) evaluated the impact of a partnership on the education of patients undergoing treatment of

hepatitis C. The benefit of a clinical nurse specialist was highly significant improvement in patient follow-up and treatment rates (Shutt, Robathan, & Samir, 2008). Larger studies evaluating the impact of a healthcare team and a collaborative approach to improved medication adherence is needed.

What is not known about the impact of nursing interventions on the treatment of hepatitis C includes gender specific research. Most of the reviewed studies involved larger numbers of male vs. female participants (Mitra et al., 2010; Namba et al., 2014; Pizzirusso et al., 2014; Larrey et al., 2008). Research specifically guided toward female gender is needed to enhance the current body of knowledge. Recruiting only female participants into a study on the impact of nursing interventions during hepatitis C would be a valuable study to complete.

The impact of education on medication adherence during hepatitis C treatment needs to be investigated further. Only two studies included the identification of education as a patient characteristic (Cacoub, et al., 2008; Sublette et al., 2015). Neither of these studies analyzed any relationship between education and improved medication adherence. A potential research question would address improved medication adherence in those patients with higher education. A study designed to investigate the relationship between education and medication adherence is a possible topic for future research.

The influence on employment during hepatitis C on medication adherence needs investigated. Sublette et al. (2015) and Cacoub et al. (2008) reported employment status in their studies but no correlation was made between employment status and medication adherence during hepatitis C treatment. Further studies directly evaluating the results of employment including full-time, part-time, and unemployed status on medication adherence are needed.

A large randomized control trial investigating a tailored treatment plan would be a recommended study for evaluating the impact of nursing interventions on medication adherence during hepatitis C treatment. The tailored treatment plan would account for gender, education, and employment status. The study could analyze the impact to quality of life after nursing interventions are included in the treatment plan. The timing of medication administration, including multiple doses of different medications, could be evaluated as an important factor influencing medication adherence. The impact of comorbid conditions on medication adherence and how nursing interventions could alleviate barriers to treatment should also be included in the investigation process.

This literature review shows the impact of provider support, including nursing interventions, on the reduction of medical cost and the improved virologic response rate. The identification of focus for future research was noted. Improved eradication rates of hepatitis C would have a global impact on the healthcare systems. Current treatment available requires strict medication adherence to obtain virologic response and with the proven action of therapeutic education, further research could identify improved ways to deliver this education.

Medication adherence will likely remain an issue for some time even with the newer, shorter courses of therapy available (Sublette et al., 2015). The development of a tailored treatment plan and the identification of groups who made need this approach will improve medication adherence in the treatment of hepatitis C. Nursing interventions such as emotional support, monitoring support, and teaching of adaptive coping strategies are a few of the components to improving health outcomes of patients with hepatitis C (Sublette et al., 2015).

The global eradication of hepatitis C can be impacted by a tailored treatment plans which includes nursing interventions throughout the course of treatment.

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CHAPTER III:
STUDY METHODS. NURSING INTERVENTIONS ON MEDICATION ADHERENCE
DURING HEPATITIS C TREATMENT: APPLICATION OF SELF-REGULATION
MODEL

Further dissertation development included identifying a theory to guide research involving HCV-infected individuals and medications adherence. A gap in the literature was found to be the lack of theory-guided research in the area. Thus, several theories were evaluated. This chapter includes the manuscript that evaluated four different theories for consideration. The Self-Regulation Model for Control of Chronic Disease theory was determined to be the best fit. As continued development of the dissertation study was completed, it became apparent that an adaption of the Self-Regulation Model was needed to guide the study. The adapted version of the model is presented in the unpublished manuscript titled “The Relationship between HCV Status and Medication Adherence for Adults with Cardiac Issues.” See Chapter IV B, Figure 4B.1 and description on pages 110–112.

Chapter 3, in full, is a reprint of the material as it appears in *Gastroenterology Nursing* 2018. The dissertation author was the primary investigator and author of this paper. This is a non-final version of an article published in final form in: Sheila A. Williams: “Nursing Interventions on Medication Adherence During Hepatitis C Treatment: Application of Self-Regulation Model.” *Gastroenterology Nursing* 41(6) (2018): 525-531. Reproduced with permission from Society of Gastroenterology Nurses and Associates, Inc.

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Purpose and Research Questions

The purpose of the research is to understand the relationship of HCV infection and medication adherence among individuals with cardiac issues. Therefore, the specific aims were:

Aim 1: Describe the characteristics of individuals infected with HCV infection with cardiac issues.

Aim II: Examine the relationship between HCV infection and medication adherence among individuals with cardiac issues.

The research design, variables, and analysis are presented in the unpublished manuscript: “The Relationship between Hepatitis C Virus Status and Medication Adherence for Adults with Cardiac Issues” See Chapter IV B, pages 112–119.

Abstract

Hepatitis C virus is a common cause of liver disease nationally and globally. Medication adherence to hepatitis C treatment is important for viral eradication and the prevention of chronic disease. The purpose of this paper is to identify a nursing middle-range theory to guide research on the impact of nursing interventions on medication adherence during hepatitis C treatment and to apply the theory to practice by providing examples of the theory application. A gap in the literature is identified as the lack of research using theories or models as a guide to investigate nursing interventions and hepatitis C treatment. The lack of theory-based research may contribute to medication non-adherence. Several theories are evaluated for application in the phenomena of medication adherence in hepatitis C treatment. Self-regulation model provides the most complete guide for nursing interventions during hepatitis C treatment. Nursing interventions and hepatitis C research, guided by theory, generates knowledge specific for nursing.

Keywords: self-regulation model, medication adherence, nursing interventions, hepatitis C treatment

Hepatitis C virus (HCV) infection is a common cause of liver disease nationally and globally. The estimated prevalence of HCV infection in the United States is 5.2 million diagnosed and another 1.1 million undiagnosed (Chak, Talal, Sherman, Schiff, & Saab, 2011). The Centers for Disease Control (CDC) estimated there were 29,718 new cases of HCV infection in 2013 (CDC, 2016). The World Health Organization estimates 130-150 million people worldwide are infected with hepatitis C virus and 500,000 people die annually from liver disease (WHO, 2016). Current treatment therapies and those expected in the next couple of years increase the probability of cure to greater than 90% for most patients (Nguyen et al., 2015).

In April 2014, an update to the 2011 comprehensive cross-agency action plan to combat hepatitis C virus was released. *Combating the Silent Epidemic of Viral Hepatitis: Action Plan for the Prevention, Care, & Treatment of Viral Hepatitis* (Department of Health and Human Services, 2014) identified a priority area as improve testing, care, and treatment to prevent liver disease and cancer. Adherence to treatment for HCV infection is associated with successful eradication of infection (Lo Re et al., 2011; Sublette, Smith, George, McCaffery, & Douglas, 2015). Nursing interventions contribute to virologic responses of patients during HCV treatment by promoting medication adherence (Cacoub et al., 2008; Larrey et al., 2011; Namba et al., 2014; Shutt, Robathan, & Vyas, 2008).

Review of the Literature

Multiple studies have explored the impact of nursing interventions on HCV treatment adherence (see Table 3.1) (all tables and figures are located in the appendix) but none were guided by nursing theory. A search of literature via PubMed, CINAHL, and PsychoINFO using a range of search terms relating to nursing, theory, adherence, and hepatitis C found no theory

guided research regarding the impact of nursing interventions on medication adherence during HCV treatment. The search resulted in the discovery of several studies investigating medication adherence using nursing theories as models (see Table 3.2).

A meta-analysis of theory use in medication adherence intervention was completed by Conn, Enriquez, Ruppap, and Chan (2016). The authors investigated what theories and models have been used to design medication adherence interventions and how researchers used theory in medication intervention research. Their search of the literature resulted in 124 eligible studies linking theory or models to medication adherence interventions. They found motivational interviewing (34) is the most common theory or model used to guide the research. Other theories or models included: (a) social cognitive theory (31), (b) health belief model (15), (c) transtheoretical model (14), (d) self-regulation model (11), (e) cognitive theory (9), (f) self-management theory (7), (g) adult learning theory (5), and (h) theory of planned behavior (3); Conn, Enriquez, Ruppap, & Chan, 2016).

A systematic review of research examining the adherence to medications using health psychology theories over the last 20 years was completed by Holmes, Hughes, and Morrison (2014). The authors sought to identify the empirical evidence for the application of models at predicting patient adherence to medications. Of the 535 articles assessed for eligibility, 67 studies were included in the review. Sociocognitive theory, self-regulation theory, and social support theory were the framework categories the authors identified. The most common theoretical models were: (a) health belief model (20), (b) self-regulation theory (16), (c) social support theory (5), (d) theory of planned behavior (3), and (e) self-determination theory (3). The most common therapeutic indication or medication of the review was human immunodeficiency

virus antiretroviral (22). The authors reported only 18% of the medication adherence interventions identified in the search reported using a theory or conceptual framework for developing interventions. Of note, no studies in the review were identified as HCV related (Holmes, Hughes, & Morrison, 2014).

Based on the meta-analysis and systemic review investigating the use of theory in relation to medication adherence (Conn et al., 2016; Holmes et al., 2014), a gap has been identified as evidenced by the lack of research using theory or models as a guide for HCV medication adherence. The lack of theory-based research may contribute to HCV treatment non-adherence. With this acknowledgment, there is a need to identify a nursing middle-range theory for use as a guide for further research regarding nursing interventions and their impact on medication adherence during HCV treatment. The purpose of this paper is an attempt to identify a nursing middle-range theory to guide the research on the impact of nursing interventions on medication adherence during HCV treatment and to apply the theory to practice by providing examples of the theory application.

Identification of a Theory

Interventions linked to evidence-based theories are more successful than interventions based on observed associations (Holmes et al., 2014). Conclusions from their meta-analysis of theory use in medication adherence intervention, Conn et al. (2016) recommends future medication adherence intervention research should include both individual determinants, social and environmental context of behavior, and include theories using both cognitive and behavioral components of interventions. Holmes et al. (2014) identified the need for theory components to

include personality traits and efficacy beliefs which have a significant role in predicting adherence to medication.

Since studies investigating nursing intervention on medication adherence during HCV treatment are atheoretical and based on the recommendations of the authors of the systematic review and meta-analysis of theory in relation of medication adherence (Conn et al., 2016; Holmes et al., 2014), a theory focusing on the constructs mediating the relationship of variables and adherence to HCV treatment is the most beneficial to guide research.

Several theories were evaluated for their utility in the realm of nursing interventions and medication adherence during HCV treatment. Based on the findings of Holmes et al. (2014), the most commonly applied theories were evaluated. Self-regulation theory provides a unifying framework for the research on nursing interventions and the impact of medication adherence during HCV treatment.

Theory Evaluation

Health belief model, social cognitive theory, theory of planned behavior, and self-regulation model were analyzed for application in research related to nursing interventions and medication adherence during HCV treatment. Each theory are examined and critically evaluated for use.

Health Belief Model

Health belief model (HBM) and theory of planned behavior (TPB) describe the reasons why problems exist (National Cancer Institute, 2005). Health belief model's focus is individual behavior and health motivation. The concepts of HBM are: (a) perceived susceptibility, (b)

perceived severity, (c) perceived benefits, (d) perceived barriers, (e) cues to action, and (f) self-efficacy (National Cancer Institute, 2005).

Perceived susceptibility and perceived severity are the beliefs of a person as to how susceptible they are to the condition and how serious the consequences are of the condition. In regards to hepatitis C virus, often patients are asymptomatic so these elements may be lacking. Perceived benefit is the action that will reduce the severity or their susceptibility to the condition. Cost, including material and psychological, is the perceived barrier. Cost is important in regards to hepatitis C treatment. The cost of treatment can be expensive (Nguyen et al., 2015). Cues to action prompt change. Self-efficacy is confidence to perform an action (National Cancer Institute, 2005).

Hepatitis C virus treatment involves complex treatment regimens and strict medication adherence to obtain virologic response. Applying HBM to research on nursing interventions and medication adherence, the focus is behavior change strategies. HBM is a belief-based theory. The theory only contains attitudes and beliefs and lacks suggestions for intervention (Noar, 2005). Understanding the need for the theory to incorporate both individual and social behavior along with cognitive and behavioral components of intervention, HBM is lacking critical aspects needed to guide the research. The goal for the research is for nursing interventions to improve adherence to the complicated HCV treatment regimen. The theory selected for guidance needs to include suggestions for interventions.

Theory of Planned Behavior

The theory of planned behavior (TPB) is an extension of the theory of reasoned action (Noar, 2005). As stated previously, the focus of TPB is the individual and behavior intentions.

The concepts of TPB are: (a) attitudes, (b) subjective norms, and (c) perceived behavioral control. Attitudes are the belief engaging in the behavior yields positive outcomes and how much value a person holds for the outcome. Subjective norms include motivation and approval or disapproval of the behavior. Perceived behavioral control is the perceived factors and resources that influence behaviors and the impact of the factors (Noar, 2005).

The TPB has been applied to predict adherence behaviors in various health contexts (Manning & Bettencourt, 2011). Even though the literature indicates the predictive power of TPB in determining behavioral intention, the inclusion of other variables as being able to improve the explanation of variability of motivation and its predictive power for behavior is warranted (Jannuzzi, Rodrigues, Cornélio, São-João, & Gallani, 2014). Such variables include depression (Manning & Bettencourt, 2011) and self-efficacy (Jannuzzi et al., 2014). Mathes, Antoine, and Pieper (2014) found depression decreased medication adherence during HCV treatment. The theory lacks the elements of perceived susceptibility and severity, cues to action, and environmental influences (Noar, 2005). The theory lacks characteristics to explain how people change, ability to help us understand how people react to fear and messages, and intervention suggestions (Noar, 2005).

The lack of the element of self-efficacy in the theory limits its use for research in the area of nursing interventions and HCV treatment. Bonner, Esserman, Golin, and Evon (2015) found self-efficacy influences medication adherence during HCV treatment. Jannuzzi, Rodrigues, Cornélio, São-João, and Gallani (2014) suggest understanding self-efficacy along with behavioral beliefs assist in the development of interventions to promote adherence to medications.

Social Cognitive Theory

Social Cognitive theory (SCT) includes the reciprocal interactions of attitudes, beliefs, and environmental influences (Noar, 2005). Self-efficacy is the confidence one has to complete an action (Resnick, 2014). Self-efficacy is the central concept of SCT (Rowbotham & Owen, 2015). The stronger the person's perceived self-efficacy, the goals are set higher and the more commitment to obtain the goals (Rowbotham & Owen, 2015).

High self-efficacy beliefs are demonstrated as playing an important role in how patients pursue goal-oriented health behaviors (Bonner, Esserman, Golin, & Evon, 2015). Self-efficacy is important during HCV treatment. Lack of self-efficacy results in a decline of treatment adherence rates (Bonner et al., 2015). Several studies used SCT to predict adherence to medications (Abraham, Clift, & Grabowski, 1999; Amico, ToroAlfonso, & Fisher, 2005; Starace, Massa, & Fisher, 2006). A characteristic of the theory is the explanation of how people change their behavior (Noar, 2005). The theory includes the elements of knowledge, attitudes, self-efficacy, rewards, reminders, and environmental influences (Noar, 2005). The theory lacks the element of behavioral intentions and perceived threat (Noar, 2005).

Self-Regulation Model

While SCT, TPB, and HBM are useful in understanding the role of patient-related factors including behavioral and individual intentions, a theory including social and environment influences along with the consideration of cognitive and behavioral components is needed to guide nursing interventions to improve medication adherence during HCV treatment. The criteria for choosing a theory is the containment of the components thought to be important to that behavior (Noar, 2005).

Self-regulation model has the theoretical underpinnings of social cognitive theory (Clark, Gong, & Kaciroti, 2001). The element of self-regulation model is the content and skills of disease management a person acquires through a process of self-regulation. Self-regulation model includes internal and external factors, management strategies, and end points (Clark et al., 2001). Each of these processes are discussed individually.

Internal and External Factors

Internal and external factors are the information and beliefs a person has concerning the specific problem. Intrapersonal factors include the person's beliefs, knowledge, feelings, and attitudes. External factors influence the response to knowledge and beliefs (intrapersonal factors). Financial factors, social support, role models, technical advice and service are external factors. There is a reciprocal and continuous relationship between internal and external factors, observations, judgments, and reactions which includes outcome expectations and self-efficacy (Clark et al., 2001).

Management Strategies

Management strategies result from the reaction of internal and external factors. It includes the elements of disease prevention and control. Management strategies evolve from a person's observations and judgments. The management strategy employed depends on the individual's goals, internal and external factors, and the degree of self-regulation. Self-regulation is specific to the problem and behavior (Clark et al., 2001).

End Points

Collaboration between the patient and clinician regarding end points help to ensure a successful therapeutic regimen. End points are modified by judgments, observations, and

reactions. They influence management strategies, internal and external factors. End points may or may not be disclosed. End points include reaching personal goals, physiological status, functioning, healthcare use, and perceptions of quality. The primary motivating factor to reach the end point is the person's personal goal (Clark et al., 2001).

Assumptions

Self-regulation model proposes being self-regulating is observant and making judgments based on those observations. Motivation to be self-regulating is driven by the endpoint or desired goal. Through self-regulatory processes individuals learn strategies to manage disease. By enabling people to improve self-regulation skills and modify external factors, one has the ability to be self-regulating (Clark et al., 2001).

Application of Self-Regulatory Model

Lack of theory guided research investigating nursing interventions to improve medication adherence during HCV treatment provides the opportunity to develop and apply the self-regulatory model to the phenomena. A three stage process consisting of planning, implementation, and evaluation is recommended to begin after choosing a theory (Noar, 2005).

Planning stage answers the “why” questions (Noar, 2005). Why do patients display non-adherence to life saving HCV treatment? Possible answers to this question based on the self-regulatory model are related to external factors such as the lack of social support, intrapersonal factors related to lack of knowledge of the importance of adherence during HCV treatment, reaction (lack of self-efficacy) to disease control, or lack of a goal (end point).

Implementation stage answers the “how” questions (Noar, 2005). How can nursing interventions improve medications adherence during HCV treatment? Nursing interventions

focusing on judgments, reactions, and observations might include weekly telephone conversations assessing the individual's ability to undertake disease management.

Lastly, the third stage is evaluation. Evaluation focuses on the success, failure, and change in theoretical factors (Noar, 2005). Did the implementation of nursing interventions during HCV treatment improve medication adherence? Was the individual's perception of quality of life changed (end point)? Did the individual reach their personal goal? Did the individual's physiological status improve (sustain virologic response)? After completion of the three stage process, application of the theory to the phenomena can be initiated.

Observation

Did the patient observe any decline in health status related to the diagnosis of hepatitis C? Has the patient observed positive outcomes of HCV treatment or negative outcomes related to the lack of HCV treatment? Using a Likert-type scale, a measurement of observation is achieved (Clark et al., 2001).

Judgment

Did the patient skip a dose of HCV treatment medication due to side effects? Did the patient decrease the dose of the HCV treatment medication? Adherence to a prescribed medication regimen is fundamental for the treatment to be effective (Berben, Dobbels, Engberg, Hill, & De Geest, 2012). Missed doses are a measurement of judgment.

Reactions

Outcome expectations (expected outcome) are the results of action (Clark et al., 2001). Often patients with positive hepatitis C viral load are asymptomatic. The absence of symptoms can hinder accomplishment of the expected outcome. Adherence is particularly difficult in the

case of complex treatment for asymptomatic illness (Konkle-Parker, 2001). Patients undergoing HCV treatment have no physiologic response to confirm viral eradication. The results of the action in relation to medication adherence to HCV treatment is the lab value evidenced by a negative hepatitis C viral load. Other outcome expectations are measurable by the patient. For example, the complex and multiple dose medication regimen is improved with the use of medication boxes with times and days of week. Patients can experience the results of the action of taking their medication as evidenced by empty pill containers at the end of the week.

Confidence to continue the action is self-efficacy (Clark et al., 2001). Bonner et al. (2015) evaluated self-efficacy and adherence to HCV treatment. The researchers found aspects of self-efficacy likely influence aspects of HCV treatment adherence. Higher self-efficacy ratings were found among participants who were in a relationship, better educated, employed, or privately insured (Bonner et al., 2015). Nursing interventions impact self-efficacy by provide the information to the patient to maintain or increase confidence. Sublette, Smith, George, McCaffery, and Douglas (2015) found communication between patients and providers impacted patient self-efficacy. Patients reported the knowledge of negative viral loads provided them with confidence to continue with treatment. Self-efficacy scales measure the confidence of the participant.

Management Strategies

Management strategies involve from observations, judgments and reactions (Clark et al., 2001). If the individual noticed a decline in health related to hepatitis C, did they seek treatment? If so, when started on treatment, were they compliant? How did the individual respond to the goal of hepatitis C clearance and were they confident in their ability to adherence to the

treatment regimen? Management strategies are measured by compiling the results of observations, judgments, and reactions.

Intrapersonal Factors

Knowledge or information that HCV treatment could cure hepatitis C was a strong motivator for medication adherence during HCV treatment in the study by Evon, Golin, Bonner, Grodensky, and Velloza (2015). The intrapersonal factor of knowledge based on this finding positively influences the concept of management strategies. Other intrapersonal factors not included in the theory need to be investigated. Holmes et al. (2014) recommend future studies investigate personality traits, generic beliefs, and generalized efficacy beliefs. The intrapersonal factors attitudes, feelings, and beliefs are assessed via questionnaire. The measurement of these factors can predict management strategies based on the patients reactions, judgment, and observations to intrapersonal factors.

External Factors

By providing examples of successful completion rates, nurses provide a role model for the participant. Nurses provide technical support related to viral load counts, nutrition, sleep patterns, and exercise during HCV treatment.

The medication cost of HCV treatment can range from \$84,000 to \$94,500 for a 12 week course of treatment (Nguyen et al., 2015). Assessment of the financial impact on the participant provides a source of intervention for nursing. If the participant is unable to purchase medication, treatment will be unsuccessful.

Social support provides strength during HCV treatment (Sublette et al., 2015). Evon et al. (2015) found social support is a strong motivator of adherence. A measurement of social support in the form of a questionnaire provides information related to the availability of support.

Endpoints

Quality of life is a measurement of endpoints. Rodis and Kibbe (2010) investigated medication adherence and quality of life. They found quality of life may be associated with adherence. Another end point measurement is hepatitis C viral load. Clearance of hepatitis C virus is the expected outcome of medication adherence during HCV treatment. With the clearance of the hepatitis C virus, improved physiological status is an expected outcome. A decline in healthcare use and improved functioning are expected outcomes of hepatitis C viral clearance and improved physiological status.

Discussion

Self-regulation model emphasizes self-regulatory processes to improve disease management. The application of the model to the phenomena of nursing interventions to improve medication adherence in HCV treatment is exploring a new frontier in HCV medication adherence research. Previous research regarding the phenomena is atheoretical. The lack of theory-based research may contribute to HCV non-adherence. Self-regulation model provides a comprehensive guide to the development of nursing interventions to impact adherence to HCV treatment. Self-regulation processes includes continuous and reciprocal relationships between observations, judgments, and reactions to internal and external factors, management strategies, and end points. Future research, guided by self-regulation model, explores nursing interventions in various elements of the model. Research exploring the impact of nursing interventions on

interpersonal factors, on improvement of knowledge related to hepatitis C, and on related social support are a few examples of future theory-based research.

In the proposed research, guided by self-regulation model, nursing interventions focus on the disease control of management strategies. A weekly telephone call from a nurse reminding participants to take medication, assessing side effects of medications, and providing emotional support is the nursing intervention. The awareness of the researcher that management strategies are in a continuous and reciprocal process with observations, judgment, and reactions provides beneficial knowledge in tailoring responses to the participant.

From the proposed study, each element of self-regulation is explored. As discussed in the application of self-regulation model section of this paper, each process of the model is evaluated and measured. Findings from the study include: (a) the impact of social support, (b) the impact of attitudes, beliefs, and feelings, and (c) the influence of outcome expectations on medication adherence during HCV treatment.

Theory is useful to practitioners because understanding interventions and outcomes provide a basis for the application of the process to other situations (Johnson, 1999). Thinking in terms of theoretical propositions instead of specific tasks is more effective (Johnson, 1999). In relation to self-regulation model, intrapersonal factors and external factors impact use of management strategies and end points and vice versa. For example, the lack of knowledge regarding the HCV medication regimen decreases a person's confidence in their ability to adhere to the plan thus they never reach the goal of virus eradication.

Upon completion of the analysis and evaluation of the behavioral theories, self-regulation model provides the most complete guide for nursing interventions during HCV treatment. Part of

the reason self-regulation theory is appropriate for medication adherence during HCV treatment is the measurement and reporting of mediating variables. Conn et al. (2016) found less than one-third of the studies using theory in medication adherence research included mediating variables. Mediating variables in self-regulation theory are knowledge and beliefs.

The behavioral theories evaluated for potential application in research involving HCV treatment adherence lacked specific key elements needed to provide clear guidance. Several theories lack the intervention suggestion portion, environmental influences, and behavioral intentions. Jaccard and Jacoby (2010) provides criteria for a “good” theory. The requirements include: logical consistency, adequately explains a phenomenon, and being testable. The theory of self-regulation is able to fulfil these requirements.

Conclusion

Hepatitis C is a national and global health problem. The total healthcare cost related to HCV in the United States is estimated to be \$6.5 billion (Tandon et al., 2014). Adherence to the HCV treatment regimen improves clearance rates of the virus thus improving the long-term health status of those individuals completing treatment. Previous studies investigated nursing interventions and the impact of HCV adherence (see Table 1) but lack theory guidance.

In a search of the literature for research guided by nursing theory investigating nursing interventions and HCV treatment adherence, the discovery of the absence of such research prompted the investigation for the proper theory or theories to guide the research. Self-regulation theory provides and includes many of the variables influencing and predicting HCV medication adherence. A combination of theories guiding research on the phenomena may provide a better understanding of HCV treatment adherence.

Holmes et al. (2014) suggest that no one theory be used to guide research in the area of medication adherence. Conn et al. (2016) discovered in their meta-analysis of theory use in medication intervention few studies used combinations of theories for designing interventions. This combination of theories is a possibility for the future research regarding nursing interventions and HCV treatment adherence. A combination of behavioral, cognitive, and ecological theories is the most comprehensive combination to address the adherence to HCV treatment.

Many health behavior theories and models predict behavior but fail to suggest how to change behavior (Conn et al., 2016). The authors suggests considering theories for use in medication adherence research that involve resources outside of the individual. One possible model is the ecological model. Berben, Dobbels, Engberg, Hill, and Geest (2012) posits many of the behavioral theories ignore the influence of the health care system on behavior. The authors suggest focusing on interventions at the micro, meso, and macro levels to fully improve medication adherence.

Theory and model explanations in research are often inadequate (Conn et al., 2016). Clinicians completing research may not have an advanced background in behavioral sciences for the application of theories to intervention design (Conn et al., 2016). Application of the self-regulation model is presented in this paper demonstrating the use of theory in various situations such as participate behavior and intervention development.

Because adherence to a medication regimen is required for treatment to be effective, it is important to know which factors influence adherence and non-adherence behaviors (Berben et al., 2012). Research, guided by self-regulation model, help to identify these intrapersonal and

external factors. The elements of self-regulation are observation, judgment, and reaction. The reciprocal relationships between these elements, management strategies, and the end points provide the basis for exploration and modification through education and other strategies (Clark et al., 2001).

Theory based research regarding nursing interventions and the impact to medication adherence during hepatitis C treatment needs to include both individual traits, beliefs, attitudes, and explore both interventions and outside resources. Due to the lack of theory-based research investigating this phenomena, finding the most appropriate theory is of the upmost importance for future research. Self-regulation model provides guidance for exploration of the phenomena incorporating many of the elements recommended for theory-based research. Medication adherence during hepatitis C treatment improves the success rate of viral clearance. Nursing interventions and hepatitis C research, guided by theory, generates knowledge specific for nursing.

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APPENDIX

Table 3.1

Studies Regarding the Impact of Nursing Interventions during Hepatitis C Treatment

Author(s)	Nursing Intervention	Theory-Guided
Cacoub et al. (2008)	Nursing support	No
Larrey et al. (2011)	Nursing education	No
Namba et al. (2014)	Nursing support	No
Shutt, Robathan, & Vyas (2008)	Nursing support	No
Strinko, Di Bisceglie, & Hoffman (2004)	Nursing support	No
Sublette et al. (2015)	Nursing support	No

Note: Nursing support includes telephone calls, emotional support, coping strategies, and barriers to treatment. Nursing education includes therapeutic education regarding disease and treatment.

Table 3.2

Nursing Interventions and Medication Adherence

Authors	Nursing Intervention	Theory
Bruin et al. (2005)	Nursing support and nursing education	Theory of Planned Behavior and Theory of Self-Regulation
Manning and Bettencourt (2011)	Nursing support and nursing education	Theory of Planned Behavior
Starace et al.(2006)	Nursing support	Informational-Motivation-Behavioral Skills Model
Yue et al. (2015)	None	Health Belief Model

Note: Yue et al. (2015) study provided no nursing intervention. The intervention provided was by pharmacists.

CHAPTER IV
A) STUDY FINDINGS. CHARACTERISTICS OF ADULTS WITH HEPATITIS C
VIRUS: EVIDENCE FROM THE NHANES 2011-2012

As dissertation development continued, a need to understand better the characteristics of the HCV-infected population was identified. To further knowledge in the area, a descriptive study using data from the National Health and Nutrition Examination Survey was conducted. The findings of the analysis assisted in the refinement of the dissertation study.

Chapter IV A, in full, is a reprint of the material as it will appear in *Gastroenterology Nursing* 2020. The dissertation author was the primary investigator and coauthor of this paper. Sheila Williams completed the data management and analysis under the mentorship of Dr. Lisa Lindley. Sheila Williams developed the manuscript with the guidance of Dr. Lisa Lindley. This is a non-final version of an article accepted and awaiting publication in final form in:

Sheila Williams & Lisa Lindley. "Characteristics of Adults with Hepatitis C Virus: Evidence from the NHANES 2011-2012" *Gastroenterology Nursing*. Reproduced with permission from Society of Gastroenterology Nurses and Associates, Inc.

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Abstract

Introduction: Hepatitis C virus (HCV) infects over three million people in the United States.

Long-term complications of hepatitis C infection result in increased liver disease and financial burden for the nation. The purpose of the present study was to identify characteristics of adults with hepatitis C virus in the United States.

Methods: This secondary, descriptive study analyzed data from the 2011-2012 National Health and Nutrition Examination Survey. The weighted sample included 2,075,749 adults diagnosed with hepatitis C virus. Descriptive statistics were calculated.

Results: The findings revealed most adults in the U. S. with HCV were insured non-Hispanic, white males, age 45 to 64 years old. Almost half of adults with HCV denied a liver condition. Several participants were either co-infected or had previous infection (82%) with other hepatitis. Substance use (53.5%), alcohol use (96%), and cigarette use (88.6%) among adults with HCV was higher than previously reported. Majority of adults were non-compliant with hepatitis A and B vaccination series completion (67% and 65.1%, respectfully). Medication adherence was higher than other reported cases. Adults with HCV have increased mental health symptoms (67.1%) and do not routinely visit a mental health professional (90.2%).

Conclusion: HCV infected adults are likely to use alcohol, cigarettes, and/or other substances.

Adults with HCV have significant mental health issues, but rarely access care. Medication adherence was higher than expected for this cohort. The findings provide information for nurses to develop individualized plans of care and identify at-risk individuals for treatment non-compliance.

Keywords: Hepatitis C virus, NHANES, substance use, alcohol

In the United States (U.S.), an estimated 3.5 million people have chronic hepatitis C (Centers for Disease Control and Prevention [CDC], 2018b). According to the CDC (2018b), approximately 41,200 acute cases of hepatitis C occurred in 2016. The risk of cirrhosis for those infected chronically with hepatitis C virus (HCV) is 10-20% and, of those, a 15-20% risk of death if liver decompensation occurs (CDC, 2018b). Individuals infected with HCV have shown higher incidence of insulin resistance (Shaheen et al., 2007), cardiovascular disease (Kakinami et al., 2013), and alcohol use (Taylor, Denniston, Kleven, McKnight-Eily, & Jiles, 2016). With the development and evolution of newer therapies for treatment of hepatitis C, the cost of HCV infection has increased dramatically. The first of these landmark medications for treatment of HCV was available at the end of 2014. The total cost of HCV infection in the U.S. in 2013 was estimated at \$6.5 billion with an expected peak in 2024 at \$9.1 billion (Razavi et al., 2013). Thus, HCV is a chronic, costly, and pervasive problem in the U.S.

Past research that has explored characteristics of adults is limited. In France, researchers examined patients with acute hepatitis (Brouard, Pradat, DeLarocque - Astagneau, & Silvain, & the Hepatitis C Surveillance System Steering Committee, 2007). Others have investigated the characteristics of patients coinfecting with human immunodeficiency virus (Osilla et al., 2011). Recently, clinical characteristics, healthcare costs, and resource utilization by genotype were studied by Hunter and colleagues (2017). However, no studies were identified that explored the functional status, physical and mental health, and laboratory characteristics of HCV positive adults for a specific timeframe. Thus, a comprehensive profile of the adult with HCV in the U. S. is lacking.

Knowledge of HCV patients is critical to nursing practice. Identifying behavioral risk factors, contributing factors for liver decompensation, and social characteristics of individuals with HCV might assist clinicians in improving treatment outcomes, influencing policy, and tailoring prevention. Nurses, with an understanding of the characteristics of HCV positive adults, might develop individualized plans of care to improve medication adherence, identify risk factors for non-compliance, and incorporate appropriate referrals for the best outcomes when patients undergo treatment for HCV. Therefore, the purpose of the present study was to examine the characteristics of individuals positive for HCV.

Methods

Design and data sources

This retrospective, descriptive study used the 2011-2012 National Health and Nutrition Examination Survey (NHANES). NHANES is a survey conducted by the National Center for Health Statistics (NCHS), a section of the CDC, for collection of health and nutrition information from the non-institutionalized civilian U. S. population. NHANES is an ongoing, continuous survey that examines approximately 5,000 persons each year (CDC, 2018a). NHANES consists of a multiyear, complex sample design with 2-year data releases. Beginning 1959, the surveys focused on particular health topics or groups and, in 1999, NHANES became a continuous survey that evolves as population needs change. The most current data is available for years 2015-2016. NHANES data are initially released nine months after collection with intermediate releases as data are processed (CDC, 2018a). Participants are selected using a multistage, probability sampling. Participation in the survey is voluntary. Oversampling was done during 2011-2012 cycle for Asians, Hispanics, non-Hispanic blacks, older adults, and low-income white

populations to improve estimates of health status indicators (CDC, 2013). Data are collected via personal interviews, physical examinations, laboratory tests, nutritional assessment, and deoxyribonucleic acid (DNA) repository (CDC, 2018a). For our study, we used NHANES 2011-2012 because it included the most current data regarding prescription medications and hepatitis C follow-up. A total of 9,756 surveys were completed for 2011-2012 cycle (CDC, 2018a). Since NHANES is publicly available, the study is determined to be exempt by the University of Tennessee Institutional Review Board.

Sample

The sampling frame for this study was adults with HCV infection. The inclusion criteria was individuals positive to hepatitis C ribonucleic acid (RNA). Hepatitis C RNA measures the exact amount of HCV in the blood (U.S. Department of Veterans Affairs, 2018). Participants over 18 years were included in our sample. Exclusion criteria included all survey data for individuals negative for hepatitis C RNA. All outliers in our data were assessed individually. For example, the white blood count number was above the normal value, but because of the population, it was determined to include in the data analysis. Data were evaluated for missing information (i.e. *refused* and *don't know* responses). For continuous variables, the method used for treating missing data was mean imputation. After applying the inclusion and exclusion criteria, the final weighted sample was 2,075,749 adults.

Measures

Sociodemographic. Ten measures were created from the NHANES 2011-2012 data to examine sociodemographic characteristics of adults with HCV. A binary variable was created for gender (1 = male, 2 = female). Categories for age were created for 25-44 years, 45-54 years, 55-

64 years, and 65 or older. Race was categorized in NHANES 2011-2012 as Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, non-Hispanic Asian, and other race - including multi-racial. A variable was created for race/ethnicity (Hispanic = 1, non-Hispanic, white = 2, non-Hispanic, black = 3, non-Hispanic, other = 4). A binary variable was created for birth country (1 = U. S., 2 = non – U. S.). A variable was created for education (1 = less than high school, 2 = high school, 3 = more than high school, 4 = unknown). Marital status was categorized in NHANES 2011-2012 as married, widowed, divorced, separated, never married, and living with partner. A binary variable was created for marital status (1 = married, 2 = not married). Categories for income were created for less than 20,000, 20,000-54,999, greater than 55,000, and unknown. A binary variable was created for health insurance (1 = yes, 2 = no). Based on a *yes* response to health insurance, insurance type was operationalized as private only, public only (Medicare, Medicaid), coinsurance, and unknown. A binary variable was created for prescriptions covered (1 = yes, 2 = no).

Physical health, functional status, and mental health. Ten measures were created from the NHANES 2011-2012 survey to examine the physical health characteristics of adults with HCV. Individual variables were created for diabetes (1 = yes, 2 = no, 3 = borderline, 4 = unknown), arthritis (1 = yes, 2 = no), thyroid disease (1 = yes, 2 = no), liver condition (1 = yes, 2 = no), and history of cancer (1 = yes, 2 = no). Respiratory disease measure (1 = yes, 2 = no) was derived from asthma, emphysema, and chronic bronchitis variables. Cardiac disease measure (1 = cardiac symptoms/disease, 2 = no disease/symptoms) was derived from variables: hypertension (HTN), elevated cholesterol, congestive heart failure (CHF), heart disease, angina/angina pectoris, myocardial infarction (MI), and cerebral vascular accident (CVA). A variable was

created for received blood transfusion (1 = yes, 2 = not, 3 = unknown). Based on *yes* response to received blood transfusion, a variable was created for year of blood transfusion (1 = before 1992, 2 = 1992 to present, 3 = unknown). A variable was created for human immunodeficiency virus (HIV) blood test completed (1 = yes, 2 = no, 3 = unknown).

Four measures were created to examine functional status of adults with HCV: ability to complete activities of daily living (ADLs), general health condition rating, number days pain hard usual activities, and number of days health not good. Ability to complete ADLs (1 = limitations, 2 = no limitations, 3 = unknown) was derived from variables: limited amount of work can do, household chores difficult complete, meal preparation difficult, dressing difficult, attend social event difficult, and leisure activity difficult. Categories for general health condition rating were created for *excellent/very good*, *good*, *fair/poor*, and *unknown*. Number of days pain makes usual activities hard was derived from single-item question from the questionnaire dataset, “During the past 30 days, for about how many days did pain make it hard for you to do usual activities, such as self-care, work, or recreation?” (CDC, 2018a). Number days health not good per 30 days was derived from single-item question from the questionnaire dataset, “Now thinking about mental health, which includes stress, depression, and problems with emotions, for how many days during the past 30 days was mental health not good?” (CDC, 2018a).

Three measures were created to examine mental health of adults with HCV: mental health symptoms, number days not good mental health, and number of days feel anxious. Mental health symptoms measure (1 = yes, 2 = no) was derived from *yes* responses to variables: little interest in doing things, feel down/ depressed/hopeless, trouble too much sleep, tired/low energy, and feel

bad about self. Number days not good mental health and number days feel anxious per 30 days were derived from single-item questions from questionnaire dataset.

Laboratory and exam. White blood cell count (WBC), red blood cell (RBC), hemoglobin (HGB), hematocrit (HCT), platelet (PLT), albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, blood urea nitrogen (BUN), creatine phosphokinase (CPK), cholesterol, creatinine, iron, lactate dehydrogenase (LDH), bilirubin, protein, glucose, and glycohemoglobin were derived from the laboratory dataset in NHANES 2011-2012. Exam weight, exam height, exam body mass index (BMI), exam pulse were derived from the examination data file in NHANES 2011-2012. Exam systolic blood pressure and exam diastolic blood pressure were derived from first reading exam systolic and diastolic blood pressure readings. Hepatitis A antibody, hepatitis B core antibody, hepatitis B surface antigen, hepatitis B surface antibody, hepatitis D, hepatitis E immunoglobulin (IgG) antibody, and hepatitis E immunoglobulin M (IgM) were derived from laboratory exam dataset reported as either positive or negative. Hepatitis C genotype was reported as genotype 1a, genotype 1b, genotype 2, genotype 3, genotype undetermined, or genotype unknown in the laboratory exam dataset.

Health behavior. Thirteen measures were created from the NHANES 2011-2012 data to examine health behaviors – general. A binary variable was created for had 12 drinks within last year (1 = yes, 2 = no). Based on *yes* response to had 12 drinks within last year, the variable how often drink last year per 350 days was created. Substance use measure (1 = yes, 2 = no, 3 = unknown) was derived from *yes* response to variables: use marijuana/hashish, use cocaine/heroin/ methamphetamine, use any form cocaine, use any form heroin, and use any form

methamphetamine. Based on a *yes* response to substance use variable, binary variables use needle inject drug not prescribed (1 = yes, 2 = no) and ever been in rehab program (1 = yes, 2 = no) were created. Based on a *yes* response to use needle inject drug not prescribed, the variable how often inject drug was created (1 = daily, 2 = weekly, 3 = monthly, 4 = unknown). A binary variable was created for smoke 100 cigarettes in life (1 = yes, 2 = no). Based on *yes* response to smoke 100 cigarettes in life, the variable how often currently smoke cigarettes was created (1 = everyday, 2 = some days, 3 = not at all). A variable was created for if ever had vaginal, anal or oral sex (1 = yes, 2 = no, 3 = unknown). Based on *yes* response to ever had vaginal, anal, or oral sex, the variable age first had sex was created. Hepatitis A vaccination was measured categorically (1 = yes, at least 2 doses, 2 = less than 2 doses, 3 = no doses, 4 = unknown). Hepatitis B vaccination was measured categorically (1 = yes, at least 3 doses, 2 = less than 3 doses, 3 = no doses, 4 = unknown). Self-improvement measure (1 = trying to improve health, 2 = not trying to improve health) was derived from variables trying weight loss control and trying to increase exercise.

Six measure were created to examine health behaviors – medication adherence characteristics. A binary variable was created for prescription use (1 = yes, 2 = no). Based on a *yes* response to hypertension variable (1 = yes, 2 = no), taking prescription for hypertension (1 = yes, 2 = no) was created. Based on *yes* response to elevated cholesterol (1 = yes, 2 = no), told to take cholesterol prescription was created (1 = yes, 2 = no, 3 = unknown). Based on *yes* response to told to take cholesterol prescription, taking cholesterol prescription (1 = yes, 2 = no, 3 = unknown) was created.

Access to care. Five measures were created from the NHANES 2011-2012 data to examine access to care characteristics. Use of healthcare services was operationalized as routine place of healthcare, overnight stay in hospital within last year, and seen by mental health professional last year. A binary variable was created for each (1 = yes, 2 = no). Type of place you go for healthcare was categorized in NHANES 2011-2012 as clinic or health center, doctor's office or health maintenance organization (HMO), hospital emergency room, hospital outpatient department, and some other place. Based on a *yes* response to routine place of healthcare, a variable was created for location of healthcare place (1 = clinic, health center, and other, 2 = doctor's office or HMO, 3 = hospital). Number of times receive healthcare last year in NHANES 2011-2012 was categorized as none, one, two to three, four to nine, ten to twelve, and thirteen or more. A variable was created for number of healthcare visits per year (1 = none, 2 = 1, 3 = 2 to 3, 4 = 4 to 9, 5 = 10 or more).

Data Analysis

The primary aim of the present study was to identify characteristics of individuals with HCV. Descriptive statistics, including frequency, percentile, range, minimum, and maximum, were calculated for sociodemographic, physical health, functional status, and mental health, laboratory and exam, health behavior, and access to care characteristics. Survey weights were applied to all analyses because of the complex nature of the NHANES data, and results are reported as weighted frequencies and means. Analyses were completed using SPSS v24 (SPSS Inc, Chicago, IL, USA).

Results

Sociodemographic characteristics of adults with hepatitis C virus are presented in Table 4A.1 (all tables and figures are located in the appendix). More males (64.3%) than females (35.7%) participated in the survey. Most common age category was 45-64 years old (70.3%) and the least common category was 65 or older (10.7%). The majority of participants were non-Hispanic, white (64.1%). Most participants were born in the U. S. (93.1%). The most frequent level of education was more than high school education (42.8%). Marital status was evenly distributed. The most common annual income category was \$20,000 – \$54,999 (35.2%), while the least common was less than 20,000 (28.2%). The majority of participants had health insurance (78.5%), with the most participants having either private only (39.4%) or public only (34.4%) insurance. Among those participants who were insured, most had prescription coverage (88.5%).

Physical health, functional status, and mental health characteristics of adults with hepatitis C virus are presented in Table 4A.2. Majority of adults with HCV denied having diabetes (79.6%), respiratory disease (90.8%), arthritis (63.9%), thyroid disease (84%), and any history of cancer (94.1%). Most participants reported cardiac symptoms/disease (73.9%). Most participants had liver condition (53.0%), while a majority had not received a blood transfusion (68.8%). Among those who did report having a transfusion, they received it before 1992 (85.9%). Majority of adults with HCV had HIV blood test completed (61.8%). When asked about ability complete ADLs, majority of responses were unknown (45.8%) with limitations being reported in 41.7%. Almost half of participants surveyed rated general health condition as good (47.4%) with majority rating as good and excellent/very good (74.8%). The average number of

days pain made usual activities hard was 8.68/30 days ($SD = 11.934$). The average number of days health not good was 4.77/30 days ($SD = 8.288$). It was common for participants to have mental health symptoms (67.1%). The average number of reported days not good mental health was 6.83/30days ($SD = 7.394$) days and number days feel anxious was 9.43/30 days ($SD = 10.040$) days.

Table 4A.3 lists the laboratory and exam characteristics of adults with HCV. The average white blood count, red blood cell, and platelet count were 7.268, 4.5812, and 208.53, respectfully. The average alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase were 93.49, 81.51, and 80.40, respectfully. Creatine phosphokinase average was 130.07 ($SD = 91.630$). Cholesterol average was 184.17 ($SD = 32.953$). Lactate dehydrogenase (LDH) average was 148.29 ($SD = 35.878$). Renal function laboratory results revealed blood urea nitrogen mean was 10.77 ($SD = 4.615$) and creatinine mean was .8647 ($SD = .2000$). The average albumin, iron, and protein were 4.114, 124.40, and 7.537, respectfully. The bilirubin mean results was .863 ($SD = .5210$). The average glucose was 116.04 ($SD = 70.352$). The glycohemoglobin average was 6.0575 ($SD = 1.7677$). The average weight in kilograms, height in centimeters, and body mass index were 81.679, 169.08, and 28.558, respectfully. The average pulse, systolic blood pressure, and diastolic blood pressure were 72.301, 125.13, and 73.415, respectfully. About as many adults with HCV were positive for hepatitis A antibody (50.7%) as were not (49.3%). Majority of participants were negative for hepatitis B core antibody (75.8%), hepatitis B surface antigen (98.9%), hepatitis B surface antibody (79.7%), hepatitis E IgG antibody (94.4%), and hepatitis E IgM antibody (99.6%). All adults were negative for hepatitis D (100%). Most participants were hepatitis C genotype 1a (73.0%).

Health behavior characteristics of adults with hepatitis C virus are presented in Table 4A.4. Majority of adults with HCV had 12 drinks in the last year (96%) with the mean number of days drinking occurred was 5.63 ($SD = 15.008$). Over half of participants reported substance use (53.5%). Of those who reported substance use, half (52.9%) denied using a needle to inject a drug not prescribed. Participants who reported using a needle to inject a drug (38.5%), most injected daily (50.9%) and over half had been to a rehab program (55.3%). More individuals had smoked 100 cigarettes in lifetime (88.6%) than not (11.4%). Of the adults with HCV who had smoked 100 cigarettes in lifetime, over half smoke daily (64.2%) and about a third don't smoke at all (28.9%). Majority of participants had sex (93.1%) with the mean age of first intercourse was 14.99 ($SD = 3.077$) years. More participants had not received any doses of hepatitis A vaccination (65.1%) and hepatitis B vaccination (63.2%) than had received partial or complete vaccination of hepatitis A (24.7%) and hepatitis B (18.4%). More adults with HCV were trying to improve health (54.2%) than not trying to improve health (45.8%). Majority of participants reported prescription use (67.5%). Of those adults diagnosed with hypertension (61.6%), most were taking prescription for hypertension (88.3%). A few participants reported elevated cholesterol (18.8%) with over half (55.9%) denying be told to take medication for elevated cholesterol. The participants told to take cholesterol medication (35.3%), about one fourth (23.6%) was taking cholesterol medication.

Access to care characteristics of adults with hepatitis C virus are presented in Table 4A.5. Majority of participants had a routine place of healthcare (75.2%). More adults visited doctor's office or health maintenance organization (69.3%) than clinic, health center, and other sites (24.2%). Majority of participants reported three or less (62.8) healthcare visits per year. More

adults had not spent the night in a hospital (91.2%) and had not seen a mental health professional in the last year (90.2%).

Discussion

The goal of this study was to investigate the characteristics of adults with HCV. The study sought to describe the sociodemographic, physical health, functional status, mental health, laboratory, exam, health behavior, and access to care characteristics of adults diagnosed with HCV. Most adults with HCV were insured non-Hispanic, white males, age 45 to 64 years old. This study found sociodemographic characteristics, such as gender, age, race/ethnicity, education, marital status, and annual income, consistent with other studies (Brouard et al., 2007; Kakinami et al., 2013; Kim et al. 2018; Pyenson, Dieguez, Ferro, Mavinkurve, & Gonzalez, 2018; Osilla et al., 2011).

Among the health, functional, and mental health characteristics, this study found that adults with HCV also had co-occurring mental health problems. A majority of those with HCV had mental health symptoms and suffered more than a week each month with these problems. Kasraian and colleagues (2016) conducted a study of the prevalence depression among individuals with HCV and reported that HCV infected individuals had higher prevalence of depression than non-infected persons. Other studies have found similar results (El-Serag, Kunik, Richardson, & Rabeneck, 2002). One possible explanation for this finding in our study is the chronic nature of HCV initiates or contributes significantly to stressors already present in the lives of those with HCV (Golden, O'Dwyer, & Conroy, 2005). As an example, HCV has the potential to significantly impact a variety of systems and that potential can be anxiety producing in many adults. When a person's long-term health is unknown because of an infection, patients

can begin to worry and focus on the negative outcomes of their health, thereby fostering increased anxiety. An alternative reason is that because HCV requires constant healthcare appointments, testing, and laboratory work that mental health issues are overlooked and not managed (King, Bornschlegel, Johnson, Rude, & Laraque, 2016; Rogal et al., 2017). For example, adults with HCV may spend up to a total of 19 hours in a clinic treating their HCV, which limits the attention given to mental health problems (Kaan, Jones, & McCaughan, 2016). More information on the link between HCV and mental health is clearly warranted.

Health behavior characteristics in this analysis differed from other studies in that a much higher percentage of adults with HCV reported drinking alcohol (96%). Taylor and colleagues (2016), although using combined cycle data from earlier NHANES datasets, found alcohol use was significantly associated HCV infection yet the percentage of non-excessive current drinkers (41.7%) was lower in comparison. Alcohol use among individuals with HCV infection can have detrimental systemic effects on the body. Heavy alcohol use among HCV positive individuals results in significantly increased risk of liver decompensation (Mankal et al., 2015). This study found over half of adults with HCV acknowledges substance use. Substance use among the HCV infected population is a known risk factor for transmission. Even though new cases of HCV infection have decreased over the last 25 years, injection drug use remains the most common mode of transmission (Williams, Bell, Kuhnert, & Alter, 2011). A possible reason for increased substance use in adults with HCV is self-medication for mental health issues. As reported earlier, mental health issues are present among this population with rare access to care. Illicit substance users displayed higher levels of anxiety, stress, and emotion regulation than nonusers (Prosek, Giordano, Woehler, Price, & McCullough, 2018). Among young adults, reasons for substance

use (alcohol and marijuana) were conformity, positive effects, calm/coping, and social reasons (Patrick, Fairlie, & Lee, 2017). Important for further investigation is whether substance use is a coping behavior mechanism due to HCV infection or related to mental health issues.

Another interesting finding from this study is the high rate of cigarette smoking among adults with HCV (88.6%) compared to other studies (El Khoury, Vietri & Prajapati, 2012; Kim et al., 2018; Taylor et al. 2016). Majority of HCV adults have smoked 100 cigarettes in their life and over half continue to smoke daily. Kim and colleagues (2018) found the rate of smoking among individuals with HCV (62.4%) was triple the rate of HCV negative persons. Smoking has shown to increase the risk for developing hepatocellular carcinoma (HCC) among HCV infected individuals (Chuang, Lee, Hashibe, Dai, Zheng, & Boffetta, 2010). Yu and colleagues (1991) found increased HCC risk (44.9%) when HCV was present among cigarette smokers. Exposure to chemical compounds in cigarette smoke causes inflammation of hepatic cells that result in HCC (Wang et al., 1998). Theories as to why HCV infected individuals have higher incidences of substance use, alcohol use, and smoking are numerous. Health vulnerability and lack of social support were found to be contributing factors to destructive health behaviors among HCV population in Brazil (Machado, Silva, Torres, & Cerqueira, 2014). Zayed and associates (2018) linked vasculitis with the development of neuropsychiatric involvement among HCV patients. Further research is needed to investigate whether alcohol, substance use, and cigarette smoking is on the increase in either the general population or only the HCV infected population.

Medication adherence is a critical health behavior for adults with HCV to possess for complete eradication of the virus with treatment. Although this study did not specifically study medication adherence during HCV treatment, medication adherence for hypertension and

cholesterol conditions among adults with HCV was higher than expected at 88.3% and 23.6%, respectfully. In contrast, Mitra and associates (2010), found medication adherence during HCV treatment (60%) suboptimal which impacts medical costs. A possible explanation is Mitra and associates (2010) studied individuals on a complex hepatitis C treatment protocol with multiple, serious side effects. Adults with HCV, in the current study, may consider compliance with medications for comorbidities more important and the potential for side effects may be less. Rodis and Kibbe (2010) suggest the presence of comorbidities might enhance medication adherence due to rigorous medication regimens already follow by the patients for other conditions. Further research might investigate the relationship among medication adherence and comorbidities in HCV adults.

The present study has several limitations. First, NHANES dataset only includes the U.S. non-institutionalized population thus generalizability is limited to that population. High occurrence of HCV infection is among the homeless population, individuals in correctional institutions, and hospitalized patients (Edlin, Eckhardt, Shu, Holmberg, & Swan, 2015). Since the survey questionnaires are self-reported, recall bias and participant knowledge of their medical history may affect reliability. Another limitation is related to selection bias. Although survey data included individuals age six and older, a small number of individuals age 34 and less ($n = 122,082$) participated in the study. With a nationwide increase in acute cases of HCV infection among persons thirty years or younger (CDC, 2015; Pyenson et al., 2018), a large portion of individuals with HCV may have not been included in the survey. There is the potential for omitted variable bias since there was no measure for actual respiratory disease, cardiac

disease, ability to complete ADLs, mental health symptoms, or substance use so the measures were derived from several different variables.

Despite the limitations, the findings from this study have clinical implications for nurses suggesting adults with HCV use substances, smoke, and drink alcohol. Compliance with provider prescribed regimens including medications is acknowledged although not fully adhered. Understanding the characteristics of adults diagnosed with HCV is important for healthcare providers in determining treatment protocols, influencing policy, and development of prevention strategies. Nurses can use the study findings to develop future research focused on examining the relationship between health behaviors, mental health, and comorbidities of adults with HCV.

In summary, the goal of this study was to investigate the characteristics of adults with HCV. This study showed that adults with HCV have a high occurrence of drinking alcohol, smoking cigarettes, and substance use. Mental health symptoms were increased among adults with HCV infection. Adults with HCV were more adherent to a medication regimen than complaint with preventive measures such as vaccination. With this knowledge, providers and nurses may better understand adults with HCV so that disease outcomes are improved.

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Appendix

Table 4A.1

Sociodemographic Characteristics of Adults with Hepatitis C Virus (N = 2,075,749, weighted)

Characteristics	Number	Percentage/Mean (SD)
Gender		
Male	1,334,561	64.3%
Female	741,188	35.7%
Age		
25-44 years	394,676	19.0%
45-54 years	766,788	36.9%
55-64 years	692,447	33.4%
65 or older	221,838	10.7%
Race/Ethnicity		
Hispanic	260,740	12.6%
Non-Hispanic, white	1,330,381	64.1%
Non-Hispanic, black	450,825	21.7%
Non-Hispanic, other	33,802	1.6%
Birth Country		
U.S.	1,932,207	93.1%
Non-U.S.	143,542	6.9%
Education		
Less than high school	744,744	35.9%
High school	432,990	20.9%
More than high school	888,678	42.8%
Unknown	9,337	.4%
Marital Status		
Married	1,035,181	49.9%
Not married	1,040,568	50.1%
Annual Income		
Less than 20,000	584,417	28.2%
20,000-54,999	731,557	35.2%
Greater than 55,000	720,525	34.7%
Unknown	39,250	1.9%
Health Insurance		
Yes	1,630,491	78.5%
No	445,258	21.5%
If Insured, Insurance Type		
Private only	642,385	39.4%
Public only	561,318	34.4%
Coinsurance	183,043	11.2%
Unknown	243,745	14.9%
If insured, Prescriptions Covered		

Table 4A.1 Continued

Characteristics	Number	Percentage/Mean (SD)
Yes	1,442,524	88.5%
No	187,967	11.5%

Note: U.S. = United States

Table 4A.2

*Physical Health, Functional Status, and Mental Health Characteristics of Adults with Hepatitis**C Virus (N = 2,075,749, weighted)*

Characteristics	Number	Percentage/Mean (SD)
Physical Health		
Diabetes		
Yes	389,991	18.8%
No	1,651,278	79.6%
Borderline	11,862	.6%
Unknown	22,617	1.1%
Respiratory disease		
Yes	191,483	9.2%
No	1,884,266	90.8%
Arthritis		
Yes	749,779	36.1%
No	1,325,970	63.9%
Cardiac disease		
Cardiac symptoms/disease	1,534,409	73.9%
No disease/symptoms	541,340	26.1%
Thyroid disease		
Yes	331,895	16%
No	1,743,853	84%
Liver condition		
Yes	1,099,640	53.0%
No	976,109	47.0%
History of cancer		
Yes	123,390	5.9%
No	1,952,358	94.1%
Received blood transfusion		
Yes	594,383	28.6%
No	1,428,518	68.8%
Unknown	52,848	2.5%
Year of blood transfusion		
Before 1992	510,305	85.9%
1992 to present	75,079	12.6%
Unknown	8,999	1.5%
HIV blood test completed		
Yes	1,282,713	61.8%
No	755,750	36.4%
Unknown	37,286	1.8%

Table 4A.2 Continued

Characteristics	Number	Percentage/Mean (SD)
Functional Status		
Ability to complete ADLs		
Limitations	865,993	41.7%
No limitations	258,657	12.5%
Unknown	951,098	45.8%
General health condition rating		
Excellent/Very good	568,695	27.4%
Good	983,193	47.4%
Fair/Poor	523,861	25.2%
Unknown	37,286	1.8%
Number days pain makes usual activities hard (per 30)	2,075,749	8.68(11.934)
Number days health not good (per 30)	2,075,749	4.77(8.288)
Mental Health		
Mental health symptoms		
Yes	1,392,436	67.1%
No	611,729	29.5%
Unknown	71,583	3.4%
Number days not good mental health (per 30)	2,075,749	6.83(7.394)
Number days feel anxious (per 30)	2,075,749	9.43(10.040)

Note: HIV = human immunodeficiency virus, ADLs = activity of daily living

Table 4A.3

Laboratory and Exam Characteristics of Adults with Hepatitis C Virus (N = 2,075,749)

Characteristics	Minimum	Maximum	Number	Frequency/Mean (SD)
Laboratory Findings - General				
WBC	3.0	34.0	-	7.268 (2.7605)
RBC	3.28	5.33	-	4.5812 (.44259)
HGB	10.9	17.3	-	14.591 (1.1689)
HCT	32.4	49.6	-	42.747 (3.6820)
PLT	48	389	-	208.53 (69.609)
Albumin	2.1	4.6	-	4.114 (.2824)
ALT	10	1363	-	93.49 (170.558)
AST	19	597	-	81.51 (82.030)
Alkaline phosphatase	42	141	-	80.40 (26.267)
BUN	4	25	-	10.77 (4.615)
CPK	22	615	-	130.07 (91.630)
Cholesterol	108	244	-	184.17 (32.953)
Creatinine	.50	1.91	-	.8647 (.20000)
Iron	37	259	-	124.40 (58.723)
LDH	92	292	-	148.29 (35.878)
Bilirubin	.3	4.4	-	.863 (.5210)
Protein	6.1	9.2	-	7.537 (.5462)
Glucose	31	497	-	116.04 (70.352)
Glycohemoglobin	4.30	12.30	-	6.0575 (1.76767)
Exam Findings - General				
Exam weight (kg)	46.6	167.8	-	81.679 (19.1207)
Exam height (cm)	150.0	186.2	-	169.08 (10.4241)
Exam BMI	17.4	50.9	-	28.558 (5.9738)
Exam pulse	54.0	102.0	-	72.301 (9.2658)
Exam systolic blood pressure	80.0	192.0	-	125.13 (14.4317)
Exam diastolic blood pressure	50.0	110.0	-	73.415 (8.8548)
Laboratory Findings - Hepatitis				
Hepatitis A antibody				
Positive	-	-	1,053,095	50.7%
Negative	-	-	1,022,654	49.3%
Hepatitis B core antibody				
Positive	-	-	502,779	24.2%
Negative	-	-	1,572,970	75.8%

Table 4A.3 Continued

Characteristics	Minimum	Maximum	Number	Frequency/Mean (SD)
Hepatitis B surface antigen				
Positive	-	-	22,550	1.1%
Negative	-	-	2,053,199	98.9%
Hepatitis B surface antibody				
Positive	-	-	422,287	20.3%
Negative	-	-	1,653,462	79.7%
Hepatitis D				
Negative	-	-	2,075,749	100%
Hepatitis E IgG antibody				
Positive	-	-	116,591	5.6%
Negative	-	-	1,959,158	94.4%
Hepatitis E IgM antibody				
Positive	-	-	8,999	.4%
Negative	-	-	2,066,749	99.6%
Hepatitis C genotype				
Genotype 1a	-	-	1,515,717	73.0%
Genotype 1b	-	-	260,108	12.5%
Genotype 2	-	-	214,966	10.4%
Genotype 3	-	-	31,954	1.5%
Genotype undetermined	-	-	24,257	1.2%
Genotype unknown	-	-	28,746	1.4%

Note: WBC= white blood cell count, RBC = red blood cell, HGB = hemoglobin, HCT = hematocrit, PLT = platelet, ALT = alanine aminotransferase, AST = aspartate aminotransferase, BUN = blood urea nitrogen, CPK = Creatine phosphokinase, LDH =lactate dehydrogenase, kg = kilogram, BMI = body mass index, IgG =Immunoglobulin G, IgM = Immunoglobulin M, RNA (HCV-RNA) = hepatitis C virus ribonucleic acid

Table 4A.4

Health Behavior Characteristics of Adults with Hepatitis C Virus (N = 2,075,749, weighted)

Characteristics	Number	Percentage/Mean (SD)
Health behaviors - General		
Had 12 drinks/year		
Yes	1,992,798	96%
No	35,786	1.7%
How often drink last year	1,992,798	5.63 (15.008)
Substance Use		
Yes	1,109,818	53.5%
No	35,786	1.7%
Unknown	930,144	44.8%
Use needle inject drug not prescribed		
Yes	799,754	38.5%
No	1,097,639	52.9%
How often inject drug		
Daily	406,982	50.9%
Weekly	141,941	17.7%
Monthly	215,120	26.9%
Unknown	35,711	4.5%
Ever been in rehab program		
Yes	613,466	55.3%
No	496,352	44.7%
Smoke 100 cigarettes/life		
Yes	1,839,302	88.6%
No	236,446	11.4%
How often currently smoke cigarettes		
Everyday	1,181,105	64.2%
Some days	127,037	6.9%
Not at all	531,160	28.9%
Ever had vaginal, anal, or oral sex		
Yes	1,932,929	93.1%
Unknown	142,820	6.9%
Age first had sex	1,932,929	14.99 (3.077)
Hepatitis A vaccination completed		
Yes, at least 2 doses	473,746	22.8%
Less than 2 doses	39,247	1.9%
No doses	1,350,338	65.1%
Unknown	212,416	10.2%
Hepatitis B vaccination completed		
Yes, at least 3 doses	341,480	16.5%
Less than 3 doses	39,247	1.9%

Table 4A.4 Continued

Characteristics	Number	Percentage/Mean (SD)
No doses	1,311,437	63.2%
Unknown	383,585	18.5%
Self-improvement		
Trying to improve health	1,126,020	54.2%
Not trying to improve health	949,729	45.8%
Health Behaviors - Medication Adherence		
Prescription (Rx) use		
Yes	1,400,417	67.5%
No	675,331	32.5%
Hypertension (HTN)		
Yes	1,279,547	61.6%
No	796,202	38.4%
Taking Rx for HTN		
Yes	1,129,633	88.3%
No	149,914	11.7%
Elevated cholesterol		
Yes	391,054	18.8%
No	1,684,695	81.2%
Told to take cholesterol Rx		
Yes	137,999	35.3%
No	218,758	55.9%
Unknown	34,297	8.8%
Taking cholesterol Rx		
Yes	92,122	23.6%
No	12,074	3.1%
Unknown	286,858	73.4%

Note:

Table 4A.5

Access to Care Characteristics of Adults with Hepatitis C Virus (N = 2,075,749, weighted)

Characteristics	Number	Frequency/Mean (SD)
Routine place of healthcare		
Yes	1,560,098	75.2%
No	515,650	24.8%
Location of healthcare place		
Clinic, health center, and other	378,270	24.2%
Doctor's office or HMO	1,081,395	69.3%
Hospital	100,433	6.4%
Number of healthcare visits per year		
None	284,604	13.7%
1	403,773	19.5%
2 to 3	614,326	29.6%
4 to 9	386,082	18.6%
10 or more	386,964	18.6%
Overnight stay in hospital within last year		
Yes	183,643	8.8%
No	1,892,105	91.2%
Seen by mental health professional last year		
Yes	204,367	9.8%
No	1,871,382	90.2%

Note: HMO = health maintenance organization

**B) STUDY FINDINGS. THE RELATIONSHIP BETWEEN HEPATITIS C VIRUS
STATUS AND MEDICATION ADHERENCE FOR ADULTS WITH CARDIAC ISSUES**

Based on knowledge gained from the previous chapters and three manuscripts, a gap in the literature was discovered regarding the relationship between HCV infection and medication adherence among adults with cardiac issues. Therefore, a retrospective, observational, longitudinal study was conducted.

Chapter IV B, in full, is a copy of the prepared manuscript to be submitted for journal acceptance reporting the overall findings of the study. The dissertation author was the primary investigator and coauthor of this paper. Sheila Williams completed the data management and analysis under the mentorship of Drs. Joel Anderson and Lisa Lindley. Sheila Williams developed the manuscript with the guidance of Drs. Sandra Mixer, Lisa Lindley, Joel Anderson, and Elizabeth Dobbins.

Abstract

Background: Hepatitis C virus (HCV) is on the rise and infects millions of persons in the United States. Cardiovascular disease (CVD) is more prevalent among persons infected with HCV than the general population. Further, CVD incidence is reduced when HCV is treated and eradicated, which, is only possible with strict medication adherence. A gap in research exists examining the relationship between HCV infection and medication adherence among individuals with cardiac issues.

Objective: Using an adapted version of the Self-Regulation Model for Control of Chronic Disease as a framework, this study investigated the relationship between HCV status and medication adherence among adults with cardiac issues.

Methods: This retrospective, observational, longitudinal study used combined data from the National Health and Nutrition Examination Survey (NHANES) from 2011–2016. The weighted sample included 9,918,628 adults with cardiac issues. Descriptive statistics were obtained for HCV status and intrapersonal and external factors. A multivariate logistic regression model was used to estimate the relationship between HCV status and medication adherence, while controlling for intrapersonal and external factors.

Results: Adults with cardiac issues were more frequently non-Hispanic White, middle-aged males. Younger age, Hispanic ethnicity, and substance use had a positive impact on cardiac medication adherence. Participants with depressive symptoms, arthritis, health insurance, and access to care were less likely to adhere to cardiac medications.

Conclusion: Multiple factors may affect medication adherence among adults with cardiac issues. The study findings provide insight for nurses and health care providers developing and testing comprehensive interventions to improve medication adherence for persons with chronic diseases.

Keywords: hepatitis C virus, medication adherence, cardiac issues

Hepatitis C virus (HCV) infection has increased since 2013 (Centers for Disease Control and Prevention [CDC], 2019a). The Centers for Disease Control and Prevention (CDC) estimate 2.4 million individuals are infected with HCV in the United States (U.S.) (CDC, 2019a). Health care costs associated with HCV infection in 2011 were estimated at \$6.5 billion (Razavi et al., 2013) with an expected peak in 2024 of \$9.1 billion (World Health Organization [WHO], 2018).

HCV-infected individuals are at increased risk of developing cardiovascular disease (CVD) and dying from associated cardiovascular conditions (Badawi, Di Giuseppe, & Arora, 2018; Kakinami et al., 2013; Petta et al., 2016; Wu et al., 2019). CVD is a disease of the heart and blood vessels that affects half of the U. S. adults and includes numerous problems such as myocardial infarction, stroke, congestive heart failure, arrhythmia, and heart valve problems (American Heart Association [AHA], 2019a; AHA, 2019b). Hypertension and high cholesterol have been identified as the two main risk factors for development of CVD (CDC, 2011). With successful treatment of HCV, cardiovascular outcomes, are improved (Adinolfi, Rinaldi, & Nevola, 2018; Cacoub et al., 2018; Lapumnuaypol, Thongprayoon, Wijarnpreechac, & Cheungpasitpornd, 2019; Petta et al., 2016).

Although there are multiple treatments for CVD such as lifestyle adjustments, reduction of modifiable risk factors, and invasive maneuvers, one of the most widely used treatment options for CVD is cardiac medications. The most common cardiac medications prescribed in the U.S. include anticoagulants, antihypertensives, and cholesterol lowering medications (Heart Foundation, 2019). However, cardiac medication adherence is low among adults. (AHA, 2019a; Naderi, Bestwick, & Wald, 2012). Adherence, according to the World Health Organization (WHO), is “the extent to which the patient follows medical instructions” (Sabate, 2001). A

person is described as adherent to a medication when 80% of the prescribed dose is taken (Brown et al., 2016). Cardiac medication adherence has been estimated to be around 57% resulting in poor clinical outcomes and death (AHA, 2019a; Kripalani et al., 2015; Naderi et al., 2012). The health care industry cost for cardiac medication non-adherence is estimated at \$300 billion a year and attributed to increased inpatient hospital stays and emergency room visits (AHA, 2019a; Lloyd, Maresh, Powers, Shrank, & Alley, 2019).

Several factors contribute to cardiac medication non-adherence. One study reported the high-cost of medications, polypharmacy, and poor patient-provider relationships as barriers to cardiac medication adherence (Awad, Osman, & Atayib, 2017). Khera and colleagues (2019) found between 8%–10% of persons prescribed cardiac medications missed doses, took lower than prescribed doses, or delayed medication fills because of costs. Other researchers have found similar barriers to medication adherence among HCV-infected individuals undergoing HCV treatment including provider apprehension, lack of self-motivation, psychological factors, and substance use (Lynch et al., 2018; North, Pollio, Sims, Jain, & Hong, 2018; Sims et al., 2017; Williams, 2018; Zibbell et al., 2018). For example, in a phase 2a clinical trial for the newer direct acting antiviral HCV treatment, recent drug use was found to be a risk factor for medication non-adherence (Peterson et al., 2016).

Although numerous elements contribute to medication non-adherence, medication adherence was improved in persons diagnosed with multiple chronic conditions when simultaneous treatment of the diseases occurred (Gokhale et al., 2019; Rossom et al., 2017). Individuals with coexisting CVD and HCV demonstrated knowledge regarding medication regimens and the importance of adherence to benefit overall health evidenced by completion of

strict medication protocols (Gagnani et al., 2017; Simon et al., 2016). While no link between improved CVD outcomes and successful HCV treatment is known, data show that when HCV is eradicated (i.e., undetectable HCV ribonucleic acid [RNA] 12 weeks after completion of treatment) there is a reduction in atherosclerosis and inflammation that contributes to CVD (Adinolfi, Rinaldi, & Nevola, 2018; Dowdle, 1999; Petta et al., 2016). Thus, those with HCV infection might have improved cardiac medication adherence because of their experience with rigid HCV medication protocols.

Understanding the relationship of HCV infection and medication adherence among patients with cardiac issues is imperative to reach the goals set by the United Nations (UN) and the WHO to reduce deaths from CVD and eliminate HCV as a public threat (United Nations [UN], 2015; WHO, 2017). This study is timely and relevant for nurses and health care providers caring for individuals with chronic conditions as they address the challenges of medication adherence. Providers may use the findings to tailor clinical treatment plans designed to improve health outcomes and reduce overall health care costs associated with CVD and HCV infection.

Despite the association between HCV infection and CVD, a thorough review of the literature found no studies that explored the relationship between HCV infection and medication adherence among individuals with cardiac issues. Also absent from the literature were studies using sophisticated statistical approaches with longitudinal data. Therefore, the purpose of this study was: 1.) to examine the characteristics of individuals infected with HCV experiencing cardiac issues and 2.) to evaluate the relationship between HCV infection and medication adherence among those with cardiac issues.

Conceptual Model

An adapted version of the Self-Regulation Model for Control of Chronic Disease provided the framework to explore the relationship between HCV status and medication adherence among adults with cardiac issues. The Self-Regulation Model is a model of disease management, with a theoretical foundation of social cognitive theory, that incorporates intrapersonal and external factors and the use of management strategies to achieve a desired end point (Clark, 2013; Clark, Gong, & Kaciroti, 2001). Self-efficacy, mediated by internal and external factors, is an ongoing and reciprocal response that determines behavior (Clark & Dodge, 1999). Being observant, using judgment, and reacting to experiences influence learned strategies to achieve disease management (Clark, 2013; Clark et al., 2001). Models that include individual determinants, the social and environmental context of behavior, and both cognitive and behavioral components improve successful disease management outcomes (Conn, Enriquez, Ruppar, & Chan, 2016). For this study, three elements of the Self-Regulation Model provided perspective regarding the understanding of medication adherence among individuals with chronic disease: intrapersonal factors, external factors, and management strategies.

An adapted version of the Self-Regulation Model with a focus on the intrapersonal factors, external factors, and management strategies is depicted in Figure 4B.1 (all tables and figures are located in the appendix) (Clark, 2013; Clark et al., 2001). Intrapersonal factors, influenced by observations, judgments, and reactions to individual experiences, include knowledge, attitudes, feelings, and beliefs (Clark, 2013; Clark et al., 2001). For this study, HCV status (the independent variable) was considered an intrapersonal factor because the developers of the Self-Regulation Model posit that knowledge and beliefs about a specific problem are

central intrapersonal factors (Clark, 2013; Clark et al., 2001). Zucker (2006) found HCV-infected women with knowledge regarding HCV status, accurate health information, and social integration experienced enhanced individual motivation and engagement in disease treatment and management. Sociodemographic characteristics were considered intrapersonal characteristics because the knowledge and beliefs concerning the disease are influenced by age, gender, marital status, race, and education. Lastly, mental health, substance use, health behaviors, and comorbidities represent the knowledge, attitudes, feelings, and beliefs comprising intrapersonal factors.

External factors have an impact on the extent of one's knowledge and influence beliefs regarding the disease and its management. According to Clark et al. (2001), role models, technical advice, money, and material resources are included as external factors because each of these influences disease management behaviors. Role models have been described as role factors and operationalized as the ability to complete activities of daily living (Clark, Dodge, Partridge, and Martinez, 2009). Functional status was considered a role factor because the ability to complete activities of daily living affects an individual's disease management behaviors.

External factors were adapted to include annual income, health insurance, and access to health care. Annual income was operationalized for money. Material resources, as described by Clark et al. (2001), include the price of medication. Health insurance and access to health care were operationalized as material resources. Both being insured as well as the type of health insurance have an impact on disease outcomes (Duquette et al., 2015; Koenig, Tsai, Sborov, Horst, & Pollom, 2018; Roetzheim et al., 2000). Money affects access to medication, health care

resources, and transportation to health care facilities. Access to health services improves disease management and health outcomes (Campbell, Alberga, & Rosella, 2016; Parikh et al., 2013).

Use of management strategies includes a response, either effective or ineffective, based on learned strategies. Medication adherence (the dependent variable) was considered use of management strategies because management strategies are described as an individual action to control a disease and its effects in the Self-Regulation Model (Clark, 2013; Clark et al., 2001). Medication adherence involves complex factors including real or perceived disease burden, disease beliefs and knowledge, trust in the health care system, personal experience, and individual health literacy (McGinnis, Kauffman, Olson, Witt, & Raebel, 2014).

Methods

Design and Data Source

Data for this retrospective, observational, longitudinal study were sourced from the National Health and Nutrition Examination Survey (NHANES, data from 2011–2016). NHANES, focused on the U.S. civilian, noninstitutionalized population's health and nutritional status, is a cross-sectional survey that has evolved based on various health problems and risk factors among the U.S. population (CDC, 2019b). There were three distinct time periods and participants were comparable from one period to the next, therefore the study was treated as an unbalanced longitudinal design. NHANES, conducted by the National Center for Health Statistics of the CDC, is voluntary and uses a complex, multistage sampling design to obtain data using standardized interviews and physical examinations with laboratory tests. Of the approximately 5,000 persons who complete the survey each year, oversampling of Asian, Hispanic, and non-Hispanic Black individuals, as well as older adults, and low-income

individuals, was completed from 2011 to 2014 (CDC, 2015). For cycle years 2015–2018, these same groups were over-sampled and the income threshold was increased for low-income individuals. The cross-sectional study data are released in 2-year cycles nine months after data collection, with intermediate releases as data become available (CDC, 2019b).

For the current study, we used publicly available NHANES data from 2011–2012, 2013–2014, and 2015–2016, which represented the most recent, complete data. A total of 29,170 surveys, including interviews and examinations, were completed for the three cycles. Quality assurance and control of NHANES included extensive training by CDC staff and completion of nondisclosure affidavits, storage and protection of collected data in the Integrated Survey Information System, and data collection instruments tested for accuracy (CDC, 2019b). The University of Tennessee Institutional Review Board has approved NHANES public data for use with no further review needed.

Sample

The sampling frame for this study was adults with cardiac issues. A flowchart illustrating the study sample is presented in Figure 4B.2. The inclusion criteria were adults aged 18 years and older who completed both the in-home interview and mobile examination center (MEC) exam. Adult age was important for the study because NHANES participant data for drug use, mental health, and alcohol use for age 17 years and younger were not released publicly (CDC, 2019b). Additionally, medication treatment regimens for HCV were only approved for individuals age 18 years and older. Since that time, new American Association for the Study of Liver Diseases treatment guidelines were published that approve and recommend direct-acting

antivirals for pediatrics (American Association for the Study of Liver Diseases- Infectious Diseases Society of American Hepatitis C Guidance Panel, 2020).

Because individuals with HCV have higher rates of CVD (Kakinami et al., 2013) and have improved cardiac outcomes with HCV treatment (Lapumnuaypol et al., 2019), additional inclusion criteria included participants with cardiac issues: (a) hypertension, (b) high cholesterol and (c) cardiac disease (i.e., congestive heart failure, coronary heart disease, or myocardial infarction). Participants were included if they answered yes to the survey questions “have you ever been told by a doctor or other health professional that you had hypertension, also called high blood pressure” or “have you ever been told by a doctor or other health professional that your blood cholesterol was high?” Participants with cardiac disease were identified if they answered yes to any of the following questions: (a) “has a doctor or other health professional ever told you that you had congestive heart failure?”, (b) “has a doctor or other health professional ever told you that you had coronary heart disease?”, or (c) “has a doctor, or other health professional ever told you that you had a heart attack (also called myocardial infarction)?” Lastly, during the interview portion of the NHANES survey, participants were asked, “because of your (high blood pressure/hypertension), have you ever been told to take prescribed medicine” or “to lower your blood cholesterol, have you ever been told by a doctor or other health professional to take prescribed medicine?” Participants were included if they answered yes to either of these questions (CDC, 2019b). There were no specific exclusion criteria for the study.

A total of 6,713 adults with cardiac issues met eligibility criteria. Matching was explored and determined to be warranted based on the available sample. Individual matches were generated based on age, gender, and race/ethnicity because those variables have been identified

as strong confounders between the independent and dependent variables used in this study (Wacholder, Silverman, McLaughlin, & Mandel, 1992). Matching was performed at the subject level instead of the group level because individual matching uses actual case characteristics. For each HCV RNA positive case, three HCV RNA negative or HCV antibody negative control matches were selected because of the limited number of cases in the dataset. The increased number of controls improved the power to detect a difference. A total number of 94 HCV RNA positive participants were matched to yield 376 participants.

Data were evaluated for missing information (i.e., *refused*, *do not know*, and *missing responses*). Frequency tables calculated for the variables revealed less than 5% of data were missing, thus analysis was continued. Initially, missing information responses were combined for an *unknown* category. Once analysis was completed, it was determined to remove the *unknown* category related to erroneous odds ratios. Because all variables in the study were categorical, case-wise deletion was completed for missing data.

For the calculation of the power analysis, a power calculator provided the minimum required sample size (Soper, 2018). *A priori* power analysis determined a sample size of 129 was sufficient to achieve 80% power to detect a 0.15 effect with a significance level of 0.05. Therefore, the final unweighted sample size of 247 was sufficient to show an effect if there was one. Because of the complex nature of the NHANES data, survey weights were applied to reflect a representative sample. The final weighted sample included 9,918,628 participants, permitting inferences to be made from the sample to the U.S. noninstitutionalized population.

Measures

Dependent Variables. *Medication adherence* was defined as the self-reported confirmation of taking prescribed cardiac medication. *Medication adherence* was measured as a yes/no response to the questions “are you now taking prescribed medicine” or “are you now following this advice to take prescribed medicine?” (CDC, 2019b).

Independent Variable. *HCV status* was measured as a positive/negative (i.e., negative and negative screening HCV antibody) RNA result to the COBAS AmpliPrep/COBAS TaqMan HCV Test (Roche Diagnostics) analysis. A binary measure of HCV status was created (0 = no, 1 = yes).

Intrapersonal Factors. Sociodemographic, mental health, substance use, health behaviors, and comorbidities variables were included in the model as covariates based on the conceptual model. Five measures were created from the NHANES data to examine sociodemographic characteristics: gender, age, race/ethnicity, education, and marital status. *Gender* was measured as a categorical response of male or female (1 = male, 2 = female). *Age* was measured as an ordered, categorical response to the question “what is your age in years” at the time of screening. Categories were created for 18–44 years, 45–54 years, 55–64 years, and 65 years and older based on guidelines for standard international age classifications (UN, 1982) and previous research with NHANES data revealing the majority of HCV positive participants were aged 45–64 years old (Williams & Lindley, *in press*). *Race/ethnicity* was measured as a categorical response to the question “do you consider yourself to be Hispanic Latino or of Spanish origin” and a categorical response to the question “what would you consider your race (i.e. American Indian or native Alaskan, Asian, black or African American, native Hawaiian or other Pacific islander, white, or other)” (1 = Hispanic, 2 = non-Hispanic, white, 3 = non-

Hispanic, black). *Education* was measured as a categorical response to the highest grade or level of school completed or the highest degree received (1 = less than high school education, 2 = high school graduate, 3 = some college or associate degree, 4 = college graduate). *Marital status* was measured as a categorical response to married or not married (i.e., widowed, divorced, separated, never married, and living with partner) (1 = married, 2 = not married).

Mental Health. Three measures were combined from the data to examine mental health that included lack of interest, depression or hopelessness, and suicidal thoughts. *Depressive symptoms* (0 = no, 1 = yes) were measured as yes responses to any of the following questions: (a) *have little interest in doing things*; (b) *feeling down depressed, or hopeless*; or (c) *thought better off dead*.

Substance Use. Three measures were created from the NHANES data to examine *substance use*: illicit drug use, alcohol use, and tobacco use. A binary variable was created for illicit drug use (0 = no, 1 = yes) from a yes response to any of three self-reported measures: *use marijuana/hashish*, *use cocaine/heroin/methamphetamine*, or *ever use a needle to inject illegal drug*. A variable was created for alcohol use (0 = no, 1 = yes) from the NHANES question “any one year, have you had at least 12 drinks of any type of alcoholic beverage?” The variable for tobacco use (0 = no, 1 = yes) was derived from both NHANES laboratory and questionnaire data using a yes response to any of three measures: (a) *do you now smoke cigarettes*, (b) *any tobacco/nicotine use in last five days*, or (c) serum cotinine levels greater than 10 ng/mL.

Health Behaviors. Two measures were combined to create a variable for compliance with vaccinations (0 = no, 1 = yes). First, a response of yes to the question, “at least 2 doses of hepatitis A vaccine” was operationalized as compliance with vaccinations. All other responses

were considered non-compliant (i.e., less than 2 doses or no doses). Second, a response of yes to the question, “at least 3 doses of hepatitis B vaccine” was operationalized as compliance with vaccinations. All other responses (i.e., less than 3 doses or no doses) were considered non-complaint.

Comorbidities. Four measures were created from the NHANES survey to examine the comorbidities of adults with cardiac issues: arthritis, diabetes, respiratory disease, and liver condition. Individual variables were created for arthritis and diabetes (0 = no, 1 = yes). A variable for respiratory disease (0 = no, 1 = yes) was derived from a yes response to any of the following questions: “ever been told you had asthma,” “ever been told you had emphysema,” “ever been told you had chronic bronchitis,” or “ever been told you had chronic obstructive pulmonary disease (COPD).” Liver condition (0 = no, 1 = yes) was operationalized as a yes response to the question “ever told you had liver condition.”

External Factors. Five measures were created from the NHANES data to examine external factors: (a) health insurance, (b) access to health care, (c) annual household income, and (d) functional status, which included activity limitations and general health condition rating. A binary variable was created for health insurance status (0 = no, 1 = yes). Access to health care (0 = no, 1 = yes) was operationalized as a routine place for health care using affirmative responses to the questions “there is more than one place” and “is there a place that you usually go when you are sick or you need advice about your health?” Categories for annual household income were created from the NHANES survey responses of total income for the entire family or individual in the last calendar year (1 = less than \$20,000; 2 = \$20,000–\$54,999; 3 = \$55,000–\$74,999; 4 = \$75,000–\$99,999; 5 = \$100,000 and over).

Functional Status. Two measures were created to examine functional status. A variable for activity limitations (0 = no, 1 = yes) was derived from an affirmative response to either of two questions: “limitations keeping you from working” (20 years or older) or “limited in any way with any activity because of a physical, mental or emotional condition.” Health condition rating was measured as an ordinal response to self-reported health status. Health condition ratings of excellent and very good were combined as were ratings of fair and poor.

Data Analysis

The primary question of interest was whether HCV status was associated with medication adherence among adults with cardiac issues in the U.S. Descriptive statistics, including frequencies, were obtained for HCV status and intrapersonal and external factors. Because all variables were categorical, chi-square analyses were conducted to examine the relationships between HCV status and intrapersonal and external factors, and to check for multicollinearity. Multicollinearity assesses if predictor variables are highly correlated, which can cause a misrepresentation of the relationship between the predictor variable and the dependent variable (Bannon, 2013). Also, the dataset was examined for sparse data, which can result in erroneous odds ratios (Osborne, 2015). A multivariate logistic (logit) regression was performed to identify predictors associated with medication adherence in relation to HCV status, while controlling for intrapersonal and external factors. The 95% confidence interval (CI) was calculated, and $p < 0.05$ was considered to indicate statistical significance. The results are presented as odds ratios (ORs). To assess the robustness of the multivariate regression findings, a sensitivity regression analysis was completed using age group categories (i.e., 18–44 years; 45–54 years; 55–64 years; 65 and older). Because of the complex nature of the NHANES data, survey weights were applied to all

analyses and results are reported as weighted totals. All analyses were conducted using IBM SPSS Version 25.0 (IBM Corp., Armonk, NY, USA).

Results

Descriptive Statistics

The characteristics of the sample ($N = 247$) are summarized in Table 4B.1. Most participants were HCV RNA/antibody negative (74.9%), male (69.4%), and 55–64 years old (48.6%). Roughly seventy-five percent of participants identified as non-Hispanic, White (75.8%). The majority of participants were high school graduates (29.4%), married (54.3%), and did not report any depressive symptoms (58.4%). Most participants reported alcohol use (92.1%) but did not use tobacco or nicotine (60.1%); a majority of participants used illicit drugs (61.1%). The majority of participants did not complete a vaccination series for hepatitis A or hepatitis B (70.7%) and did not report a chronic condition. The majority of participants reported having health insurance (86.9%) and access to health care (87.6%).

Bivariate Analysis

Participants adherent to cardiac medication were more often HCV positive (74.8%; $p = 0.829$) and male (71.8%; $p = 0.598$), although the difference was not significant (Table 4B.1). A higher percentage of participants age 65 and older (81.7%; $p < 0.01$) were adherent to medications. Non-Hispanic, Black participants (77.8%; $p = 0.065$) were adherent to cardiac medications at a higher percentage. Participants with higher levels of formal education ($p = 0.255$) and those who were married (77.6%; $p = 0.217$) reported greater adherence to cardiac medications. There was no significant difference in reported symptoms of depression by medication adherence status ($p = 0.612$).

Chi-square analysis indicated that participants who do not use illicit drugs (90.1%; $p < 0.001$) or do not use tobacco or nicotine (83.0%; $p = 0.002$) reported greater adherence to cardiac medications. Participants who use alcohol were more adherent to cardiac medications (73.6%; $p = 0.820$). There was no significant difference in completion of hepatitis A or B vaccinations by medication adherence (75.2%; $p = 0.513$). Participants with arthritis (84.3%; $p = 0.009$), diabetes (79.3%; $p = 0.386$), respiratory disease (77.1%; $p = 0.541$), and liver condition (77.3%; $p = 0.649$) were adherent to cardiac medications at a higher percentage. Participants with health insurance (78.4 %; $p \leq 0.001$) and access to health care (80.1%; $p \leq 0.001$) reported greater adherence to cardiac medications.

From the results of the chi-square analysis, participants with lower and middle income ($p = 0.649$) were adherent to cardiac medications. Additionally, participants with activity limitations (79.9%) and those rating their health condition as fair/poor (77.4%) were adherent to cardiac medications. However, the results of the analysis did not show a difference in reported activity limitations ($p = 0.212$) or general health condition rating ($p = 0.828$).

Multivariate Analysis

The weighted results of a fully specified logistic regression analysis examining the predictors of a study participant being adherent to cardiac medications are displayed in Table 4B.2. HCV status (OR = 0.293, $p = 0.057$) and gender (OR = 2.426, $p = 0.107$) were not significant predictors of medication adherence.

Other intrapersonal factors in the model were related to medication adherence. Age was a significant predictor of medication adherence. Those who were 45 to 54 years old (OR = 0.164, $p = 0.024$) and 55 to 64 years old (OR = 0.094, $p = 0.001$) were less likely to be adherent with

cardiac medications compared with respondents aged 18 to 44 years old. Race/ethnicity was a significant predictor of medication adherence as well. Non-Hispanic, White (OR = 0.185, $p = 0.034$) and non-Hispanic, Black (OR = 0.185, $p = 0.037$) respondents were significantly less likely to be adherent to cardiac medications compared with Hispanic respondents. Education and marital status were not significant predictors of medication adherence.

The multivariate analyses demonstrated the presence of depressive symptoms was a significant predictor of adherence to cardiac medications. Participants with depressive symptoms (OR = 0.259, $p = 0.023$) were roughly 75% less likely to adhere to cardiac medications. Participants who used illicit drugs (OR = 6.707, $p < 0.001$) were six times more likely to adhere to cardiac medications than those who did not use illicit drugs. Alcohol use (OR = 0.188, $p = 0.055$) was not a significant predictor of medication adherence. Tobacco or nicotine use (OR = 3.671, $p = 0.016$) was a significant predictor of medication adherence. The odds of cardiac medication adherence increased over three times for individuals using tobacco or nicotine when compared with those who did not use tobacco or nicotine.

Vaccinations completed were not significant predictors of medication adherence (OR = 1.369, $p = 0.571$). Arthritis was a significant predictor of cardiac medication adherence (OR = 0.294, $p = 0.017$). Those with arthritis were less likely to adhere to cardiac medications. Other chronic conditions such as diabetes (OR = 1.083, $p = 0.885$), respiratory disease (OR = 1.267, $p = 0.713$), or liver condition (OR = 0.584, $p = 0.527$) were not significant predictors of medication adherence.

External factors significantly associated with cardiac medication adherence were health insurance (OR = 0.109, $p = 0.002$) and access to health care (OR = 0.064, $p = 0.001$). Those who

had health insurance and access to care were less likely to adhere to cardiac medications compared with respondents without health insurance or access to health care. Income, activity limitations ($OR = 1.625, p = 0.441$), and health condition rating were not significant predictors of medication adherence.

Sensitivity Regression Analysis

Based on the sensitivity regression analysis for medication adherence, non-Hispanic, White race for age group 45–54 years was significant in the opposite direction. College graduate education level and income over \$100,000 were significant for age group 45–54 years in the sensitivity analysis estimating the association between medication adherence and HCV status, yet was not significant in the logistic regression. Diabetes was significant in the sensitivity analysis although it was not significant in the logistic regression analysis. Health insurance for age group 45–54 years was significant in the same direction. For age group 55–64 years, respondents of non-Hispanic, White and non-Hispanic, Black races were significant in the same direction. Illicit drug use, tobacco or nicotine use, and access to health care among those aged 55–64 years were significant in the same direction as the logistic regression. Because only a few findings were similar to the logistic regression analysis, the analysis failed to demonstrate consistent results, thus any inferences or conclusions should be interpreted with caution.

Discussion

Using an adapted version of the Self-Regulation Model as a guide, this study was one of the first to examine the relationship between HCV and medication adherence among individuals with cardiac issues. This study showed that adults with cardiac issues were predominately non-Hispanic White, middle-aged males. These findings were consistent with the most recent

national report on CVD statistics (AHA, 2019b). Given that approximately one third of study participants were HCV RNA positive, a possible explanation for male predominance is that males in comparison with females have increased high-risk behaviors (Butterfield et al., 2003; Bruneau, Roy, Arruda, Zang & Jutras-Aswald, 2012). Regarding age, Baby Boomers (individuals born between 1945–1965) are five times more likely to be infected with HCV (CDC, 2017; Hall, Rosenbury, & Sullivan, 2018)

The study findings suggest that as age advances, adherence to cardiac medications decreases, which is consistent with the literature. Previous research found older age was associated with cardiac medication non-adherence (van der Laan et al., 2019). A possible explanation may be that younger individuals prescribed cardiac medications may possess an awareness that CVD mortality is increased in younger individuals (Ford & Capewell, 2007) and, therefore, adhere to treatment protocols. Another possible explanation is medication regimens can become more complex as individuals age and as the number of medications prescribed increases, adherence becomes more difficult (Dalvi & Mekoth, 2018; Syed & McNicoll, 2009). Clinically, the findings highlight the need to initiate medication treatment at younger ages to prevent potential future complications or advancement of diseases, especially among conditions that may lack overt symptoms such as CVD. Future research might examine the relationship between age and medication adherence among HCV-infected individuals with multiple chronic conditions.

Previous studies have shown ethnicity is a barrier to medication adherence (Bazargan et al., 2017; Serper et al., 2019; Sims et al., 2017). Unexpected findings from our analysis suggest otherwise. To our knowledge, no studies have explored the HCV-infected Hispanic population's

adherence to cardiac medications. Our analysis of the NHANES data suggests race/ethnicity, specifically Hispanic ethnicity, is associated with cardiac medication adherence. A possible explanation for this finding is that over 85% of participants in this study had access to health care and health insurance. Future studies exploring the factors contributing to medication adherence among HCV-infected Hispanic individuals is warranted.

Another interesting finding from this study was not the high rate of self-reported substance use among adults with cardiac issues; it was that the sub-population demonstrated much higher adherence to cardiac medications. No previous studies found greater medication adherence among people who used substances. A possible explanation for higher adherence to cardiac medications among individuals who use substances might be individual health beliefs. Individuals who are satisfied with their treatment plans were more adherent to cardiac medications (Al-Ruthia et al., 2017). Another explanation for greater adherence might be self-acceptance of the health condition and the desire to live longer. Research found acceptance of human immunodeficiency virus (HIV) status and support from health professionals improved medication adherence among drug users treated for HIV (Ho, Holloway, & Stenhouse, 2020).

Provider apprehension in treating individuals who use substances such as illicit drugs is well established (Iverson et al., 2017; Rogal et al., 2017; Sims et al., 2017). When investigating barriers to treatment, researchers found stereotypical assumptions included that individuals who use illicit drugs were difficult to manage and non-compliant (Natan, Beyil, & Neta, 2009). Based on knowledge from our study, practice implications for nurses caring for individuals who use substances include advocating for treatment initiation despite concurrent substance use.

Similar to previous studies, depression was associated with medication non-adherence (Egmond et al., 2019; Hazaveh, Toosi, Toosi, Tavakoli, & Shahbazi, 2015; Kim et al., 2015). Nurses and health care providers equipped with this knowledge might identify and further explore depressive symptoms, and enlist the assistance of a behavioral health specialist in conjunction with medication treatment. Nurses can advocate for policy change to include both pharmacologic and non-pharmacological behavioral health treatment for those individuals with and without insurance undergoing treatment for chronic conditions.

Contrary to expectations, individuals with health insurance and access to health care were less adherent to cardiac medications. Because there was a high rate of insurance coverage among study participants and copayment costs vary among insurance types, a plausible explanation for cardiac medication non-adherence was high copayment costs. Multiple studies have shown an association between high copayment costs and cardiac medication non-adherence (Chernew et al., 2008; Cole, Norman, Weatherby, and Walker, 2006; Doshi, Zhu, Lee, Kimmel, & Volpp, 2009). The study findings suggest health care professionals should assess insurance coverage prior to treatment initiation and copayment costs. Future studies might explore the relationship between copayment costs on medication adherence among the HCV-infected population with cardiac issues.

In this study, the relationship between HCV and medication adherence among individuals with cardiac issues was examined and no significant relationship was found. This finding implies that having HCV infection did not appear to affect cardiac medication adherence, which contradicts research that has shown improved medication adherence when multiple chronic conditions coexist (Gokhale et al., 2019; Rossom et al., 2017). This finding suggests there may

be a difference between individuals with HCV infection and individuals with other chronic conditions and illustrates the need for further study.

Several study limitations should be considered. First, data were self-reported and from one point in time, which may affect reliability especially given responses involved recollecting behavior over an extended timeframe. Therefore, recall bias was a potential limitation. Second, there was a possibility for under- or over-reporting of conditions, substance use, or health behaviors resulting in the potential for response bias. Third, although NHANES survey staff members undergo extensive training and an interpreter service was available to assist in the interview process, some context may be lost in the translation process, increasing the risk of measurement error. Fourth, because several variables (e.g., illicit drug use, tobacco/nicotine use, vaccinations completed, and respiratory disease) were derived from two or more measures, omitted variable bias was a potential limitation. An attempt was made to reduce omitted variable bias by using theory to guide the study and considering all possible factors available within the dataset. Finally, a limitation was that NHANES data are not released until nine months after completion of the two-year cycle, thus a time lag occurs from data collection, analysis, and presentation of findings. However, these data are the most comprehensive available and, therefore, appropriate for use in this study.

Despite these limitations, this study contributes to the body of knowledge about a population previously unexplored, impacts the management of adults with cardiac issues, and may reduce costs associated with long-term complications of HCV infection and CVD. Because medication adherence is imperative to reduce CVD progression and eliminate HCV infection, our findings are relevant for nurses developing culturally targeted educational programs

addressing medication adherence. To achieve the UN's goal of reducing CVD by 2030, the study emphasizes the importance of early treatment and identifying and eliminating factors contributing to medication non-adherence. In collaboration with members of the health care team, such as behavioral health specialists and pharmacists, nurses could develop and test interventions to improve medication adherence among individuals identified at risk for non-adherence. Additionally, nurses could use knowledge gained from this study to advocate among policymakers for improved access to a multidisciplinary team during medication treatment. The findings from this study may have implications for those being treated for other conditions requiring strict medication adherence such as hepatitis B virus, HIV, and chemotherapeutic agents. Therefore, this study has practice and policy implications beyond adults with cardiac issues.

In conclusion, the study provides nurses and health care providers with a more complete understanding of adults with cardiac issues (those with and without HCV infection) and the multiple factors that influence medication adherence. Our study fills a gap in the literature and highlights the need for future research that develops and tests interventions to improve medication adherence in this population. Given that CVD affects half of the U.S. population, our findings have widespread implications for potentially improving disease outcomes and reducing health care costs. In addition, the adapted version of the Self-Regulation Model for Control of Chronic Disease proved useful to examine the complexity of medication adherence and contributes to further theory development.

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Appendix

Table 4B.1

Descriptive Statistics of Study Variables among Adults with Cardiac Issues (n = 9,918,628, weighted)

Variable	Full Sample <i>N</i> %	Adherent to Cardiac Medication <i>n</i> (unweighted) (%)	Non-adherent to Cardiac Medication <i>n</i> (unweighted) (%)	<i>p</i> -value
<i>HCV Status</i>				
HCV RNA positive	25.1	55 (74.8)	14 (25.2)	0.829
HCV RNA/antibody negative	74.9	133 (72.9)	45 (27.1)	
<i>Gender</i>				
Male	69.4	118 (71.8)	42 (28.2)	0.598
Female	30.6	70 (76.9)	17 (23.1)	
<i>Age</i>				
18–44 yrs	6.0	5 (18.4)	8 (81.6)	0.002**
45–54 yrs	39.4	48 (73.2)	19 (26.8)	
55–64 yrs	48.6	103 (79.3)	24 (20.7)	
65 and older	5.9	32 (81.7)	8 (18.3)	
<i>Race/ethnicity</i>				
Hispanic	5.0	11 (47.9)	9 (52.1)	0.065
Non-Hispanic, White	75.8	69 (73.9)	23 (26.1)	
Non-Hispanic, Black	19.3	108 (77.8)	27 (22.2)	
<i>Education</i>				
Less than high school	18.6	43 (72.5)	13 (27.5)	0.255
High school graduate	29.4	51 (62.0)	22 (38.0)	
Some college or AA degree	23.3	56 (83.2)	15 (16.8)	
College graduate	28.7	38 (77.5)	9 (22.5)	
<i>Marital status</i>				
Married	54.3	87 (77.6)	28 (22.4)	0.217
Not married	45.7	101 (68.3)	31 (31.7)	
<i>Depressive Symptoms</i>				
Yes	41.6	86 (75.9)	22 (24.1)	0.612
No	58.4	102 (71.6)	37 (28.4)	
<i>Illicit drug use</i>				
Yes	61.1	94 (62.8)	44 (37.2)	0.001**
No	38.9	94 (90.1)	15 (9.9)	
<i>Alcohol use</i>				
				0.820

Table 4B.1 Continued

Variable	Full Sample N %	Adherent to Cardiac Medication n (unweighted) (%)	Non-adherent to Cardiac Medication n (unweighted) (%)	p-value
Yes	92.1	151 (73.6)	54 (26.4)	0.002**
No	7.9	37 (70.1)	5 (29.9)	
<i>Tobacco/Nicotine use</i>				
Yes	39.9	70 (58.9)	29 (41.1)	0.513
No	60.1	118 (83.0)	30 (17.0)	
<i>Vaccinations completed</i>				
Yes	29.3	49 (69.0)	19 (31.0)	0.009**
No	70.7	139 (75.2)	40 (24.8)	
<i>Arthritis</i>				
Yes	38.9	91 (84.3)	23 (15.7)	0.386
No	61.1	97 (66.4)	36 (33.6)	
<i>Diabetes</i>				
Yes	20.9	52 (79.3)	14 (20.7)	0.541
No	79.1	136 (71.8)	45 (28.2)	
<i>Respiratory disease</i>				
Yes	18.2	43 (77.1)	12 (22.9)	0.649
No	81.8	145 (72.5)	47 (27.5)	
<i>Liver condition</i>				
Yes	16.4	36 (77.3)	10 (22.7)	≤ 0.001***
No	83.6	152 (72.6)	49 (27.4)	
<i>Health insurance</i>				
Yes	86.9	166 (78.4)	45 (21.6)	≤ 0.001***
No	13.1	22 (40.2)	14 (59.8)	
<i>Access to healthcare</i>				
Yes	87.6	183 (80.1)	47 (19.9)	0.652
No	12.4	5 (25.7)	12 (74.3)	
<i>Annual household income</i>				
Less than \$20,000	21.5	60 (79.9)	17 (20.1)	0.212
\$20,000–54,999	27.6	66 (72.7)	20 (27.3)	
\$55,000–74,999	12.9	21 (72.8)	7 (27.2)	
\$75,000–99,999	9.2	15 (85.6)	3 (14.4)	
\$100,000 and over	28.9	26 (65.5)	12 (34.5)	
<i>Activity limitations</i>				
Yes	27.9	73 (79.9)	20 (20.1)	0.828
No	72.1	115 (70.8)	39 (29.2)	
<i>General health condition rating</i>				

Table 4B.1 Continued

Variable	Full Sample <i>N</i> %	Adherent to Cardiac Medication <i>n</i> (unweighted) (%)	Non-adherent to Cardiac Medication <i>n</i> (unweighted) (%)	<i>p</i> -value
Excellent/Very good	33.4	41 (72.3)	12 (27.7)	
Good	36.8	80 (71.1)	29 (28.9)	
Fair/Poor	29.8	67 (77.4)	18 (22.6)	

* $p < .05$, ** $p < 0.01$, *** $p < 0.001$.

Table 4B.2

Logistic Regression Estimating Medication Adherence (n = 9,918,628, weighted)

Variable	β	OR (95% CI)
HCV Status		
HCV RNA Positive	-1.227	0.293 (0.083–1.039)
Sociodemographic		
Female	0.886	2.426 (0.823–7.147)
Unmarried	0.281	1.324 (0.486–3.605)
Age		
18–44 Years old	(ref)	(ref)
45–54 Years old	-1.808	0.164 (0.034–0.784) *
55–64 Years old	-2.369	0.094 (0.022–0.398)**
65– and older	-0.719	0.487 (0.071–3.323)
Race/Ethnicity		
Hispanic	(ref)	(ref)
Non-Hispanic, White	-1.687	0.185 (0.039–0.880)*
Non-Hispanic, Black	-1.688	0.185 (0.038–0.903)*
Education		
Less than high school	(ref)	(ref)
High school graduate	1.391	4.019 (0.958–16.867)
Some College or AA degree	0.234	1.264 (0.290–5.518)
College Graduate	0.482	1.620 (0.305–8.593)
Mental Health		
Depressive symptoms	-1.352	0.259 (0.081–0.826)*
Substance use		
Illicit drug use	1.903	6.707 (2.610–17.235)***
Alcohol use	-1.671	0.188 (0.034–1.036)
Tobacco/Nicotine use	1.301	3.671 (1.284–10.499)*
Health Behaviors		
Vaccinations Completed	0.314	1.369 (0.459–4.082)
Comorbidities		
Arthritis	-1.225	0.294 (0.108–0.800)*
Diabetes	0.079	1.083 (0.366–3.198)
Respiratory disease	0.237	1.267 (0.356–4.512)
Liver condition	-0.538	0.584 (0.109–3.120)
Health Insurance		
Health insurance	-2.212	0.109 (0.028–0.434)**
Access to health care		
Access to health care	-2.742	0.064 (0.012–0.339)**
Annual Income		
Less than \$20,000	(ref)	(ref)
\$20,000–54,998	-0.762	0.467 (0.115–1.894)

Table 4B.2 Continued

Variable	β	OR (95% CI)
\$55,000–74,999	0.248	1.282 (0.221–7.421)
\$75,000–99,999	-0.079	0.924 (0.168–5.075)
\$100,000 and Over	0.542	1.719 (0.352–8.388)
Functional Status		
Activity Limitations	0.486	1.625 (0.470–5.617)
Health Condition Rating		
Excellent/Great	(ref)	(ref)
Good	-0.637	0.529 (0.158–1.767)
Fair/Poor	-0.967	0.380 (0.114–1.264)

OR = odds ratio, CI = confidence interval, * $p < .05$, ** $p < 0.01$, *** $p < 0.001$

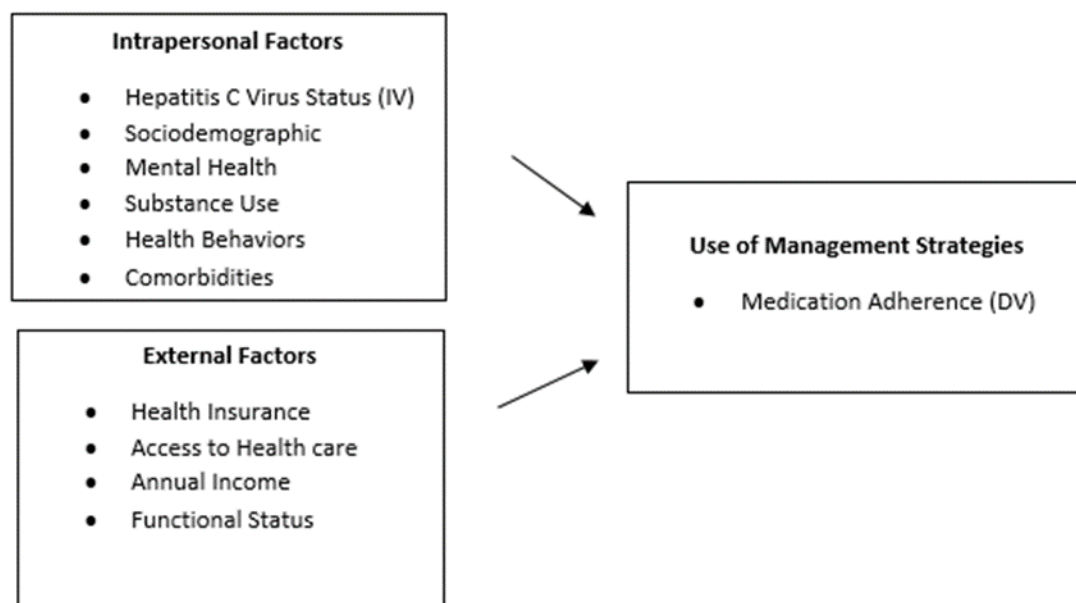


Figure 4B.1. Adapted version of the Self-Regulation Model for Control of Chronic Disease depicting the relationship of hepatitis C virus infection and medication adherence among patients with cardiac issues. DV = dependent variable. IV = independent variable. Adapted from “A Model of Self-Regulation for Control of Chronic Disease,” by N. M. Clark, M. Gong, & N. Kaciroti, 2001, *Health Education and Behavior*, 28(6) p. 771. Copyright 2001 by Society for Public Health Education.

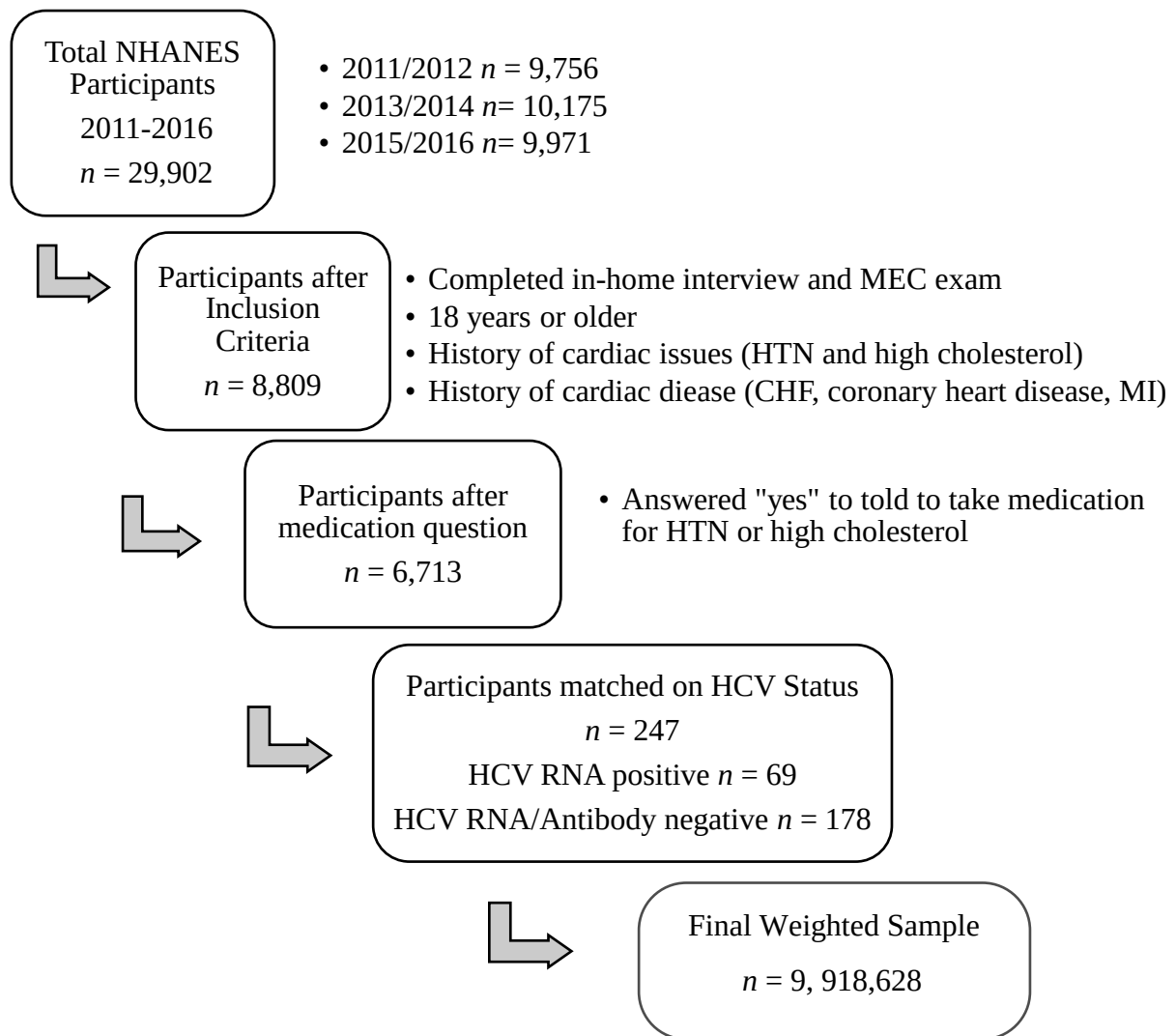


Figure 4B.2. Flow chart illustrating study sample. NHANES = National Health and Nutrition Examination Survey. MEC = Mobile Exam Center. HTN = hypertension. CHF = congestive heart failure. MI = myocardial infarction. HCV = hepatitis C virus, RNA = ribonucleic acid.

CHAPTER V: CONCLUSION

This dissertation consists of four manuscripts examining medication adherence among HCV-infected individuals. The first manuscript, a literature review, was completed to determine the state of the science regarding nursing interventions and medication adherence among the HCV-infected population. Four themes emerged from the literature influencing medication adherence among HCV-infected individuals: comorbidities, self-motivation, psychological factors, and provider support. The need for future research was identified in the area of gender-specific studies, impact of education level, and the need for a randomized control trial investigating targeted interventions to improve medication adherence among HCV-infected individuals.

The second manuscript addressed a gap in research regarding theory-guided studies in the area of HCV. The manuscript evaluated and identified a middle-range nursing theory to guide research investigating HCV-infected population and medication adherence. The Health Belief Model, Theory of Planned Behavior, Social Cognitive Theory, and the Self-Regulation Model for Control of Chronic Disease were evaluated for appropriateness and it was determined the Self-Regulation Model would provide the most complete guide for nursing in the area of HCV.

The third manuscript reports on a quantitative study designed to explore the characteristics of persons in the U.S. with HCV infection using a large national data set. The findings revealed most adults in the U.S. with HCV were non-Hispanic, white males of the Baby Boomer age group. Substance use was elevated among the population. Mental health issues were predominate among the group. The findings from the study provided nurses the knowledge to design and develop future studies exploring HCV-infected individuals and to cultivate interventions for successful medication adherence during HCV treatment.

The fourth manuscript contains the results from a quantitative study examining the relationship between HCV status and medication adherence for adults with cardiac issues. The retrospective, observational, longitudinal study using combined survey data found younger age, Hispanic ethnicity, and substance use positively impacted medication adherence among the noninstitutionalized population. The study determined multiple factors influence medication adherence and interventions designed to improve adherence need to incorporate the complexity of the individuals. Implications for practice, future research, and policy have been discussed in each manuscript. A summary of overall implications is provided below.

Implications for Practice

An important clinical practice implication for nurses and health care providers caring for HCV-infected individuals is an understanding the characteristics of those non-adherent to medications to identify individuals at risk for HCV treatment failure. With this knowledge, development of targeted, customized treatment plans for those at-risk of treatment non-adherence might improve clinical outcomes. Individuals at-risk may benefit from the pre-treatment of comorbidities identified that showed a relationship to cardiac medication adherence, such as depression and arthritis. Lastly, nurses should not assume individuals will be adherent because they have access to health care or insurance.

Implications for Research

Findings from the second manuscript identified a gap in the literature regarding theory-guided research in the area of HCV. Continued theory development is imperative to advance knowledge in the area of HCV and medication adherence. This research contributes to further

theory development as it was the first in the area of HCV studies to use the Self-Regulation Model.

In addition to theory development, the dissertation identified gaps in research needing further exploration. Future studies exploring the influence of substance use and disease severity on HCV medication adherence among certain sub-populations is warranted. Examining the effects of culturally targeted education plans among HCV-infected individuals should be a priority in the area of HCV and medication adherence research. With personal health beliefs being a factor in medication adherence, future research in the area of qualitative studies is needed to contribute to the body of knowledge.

Implications for Policy

Since this study revealed HCV-infected adults aged 18–44 years were significantly more adherent to medication regimens, nurses ought to advocate for early treatment. Findings demonstrated low rates of medication adherence despite having health insurance, therefore nurses should champion reduced copayments for direct acting antiviral medications necessary to eliminate HCV infection.

In conclusion, this work contributes to the body of knowledge regarding individuals infected with HCV with cardiac issues and medication adherence. These findings influence clinical practice, research, and policy. Results suggest incorporating a multidisciplinary team approach to the care of HCV-infected individuals may result in successful treatment outcomes and overall reduction in health care costs.

VITA

Sheila A. Williams earned her Associate of Science in Nursing from Walters State Community College in 1997 and began her career as a medical-surgical nurse. After working on the medical-surgical floor as a team leader for three years and obtaining national certification as medical-surgical nurse, Ms. Williams was promoted to clinical manager of a 40-bed medical-surgical/pediatric floor. After two years as clinical manager, Ms. Williams returned to bedside nursing on a medical-surgical floor. In 2003, Ms. Williams accepted the position of Quality and Infection Control Coordinator for Morristown Hamblen Healthcare System Home Health and Hospice. Ms. Williams returned to bedside nursing in January 2006.

While Ms. Williams gained nursing experience in a variety of settings, she also earned her Bachelor's of Science in Nursing from Lincoln Memorial University in 2004 and in December 2006 graduated from East Tennessee State University with a Master's of Science in Nursing. In 2007, after obtaining national certification for adult nurse practitioner from the American Nurses Credentialing Center, Ms. Williams began her career as a nurse practitioner for a gastroenterology office in East Tennessee.

For seven years, Ms. Williams provided care to individuals with a specific focus on treating individuals with hepatitis C virus at Morristown Gastroenterology. In 2012, Ms. Williams accepted a position as adjunct faculty at Walters State Community College. In 2014, Ms. Williams received the appointment of a full-time Assistant Professor of Nursing at Walters State Community College. As an assistant professor of nursing, Ms. Williams has participated in a variety of committees, faculty development productions, and assisted in implementing a new statewide nursing common curriculum at Walters State Community College.

In 2015, Ms. Williams enrolled in the Doctor of Philosophy program at the University of Tennessee, Knoxville with a nursing education focus. As a doctoral student, Ms. Williams authored and published two manuscripts in *Gastroenterology Nursing*. Both focused on medication adherence among the hepatitis C positive population. Ms. Williams authored a published op-ed in the Knoxville News Sentinel titled, “Hepatitis C is emerging health crisis related to opioid addiction” on December 11, 2017. In 2018, Ms. Williams co-authored a descriptive study accepted for publication in *Gastroenterology Nursing*. The study focused on the characteristics of individuals with hepatitis C virus in the United States.

Ms. Williams is a member of Sigma Theta Tau, the National League of Nursing, and the Gamma Beta Phi Society.